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ORIGINAL RESEARCH

Association Between Nutritional Risk Screening Score and Prognosis of Patients with Sepsis

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Background: Malnutrition is one of the most critical factors affecting patients' risk of infection and length of stay, and it may affect the prognosis of patients with sepsis. There have been no studies that have applied nutritional risk screening tools to stratify patients with sepsis according to prognosis.

Methods: We retrospectively analyzed the clinical data of 425 adult sepsis inpatients who were grouped based on nutritional risk screening (NRS) score, including a nutrition score, disease severity score, and age score. Prognostic factors were analyzed using univariate and multivariate regression analyses.

Results: Of the enrolled patients, 174 had an NRS score of ≥3; these patients were older and had a longer hospitalization time but lower body mass index (BMI), albumin (ALB) than others. Univariate Cox regression analysis showed that age, ALB, C-reactive protein (CRP), and NRS score were significantly (P<0.05) associated with in-hospital mortality. Multivariate analysis showed that age (hazard ratio [HR]=1.020, 95% confidence interval [CI]: 1.005–1.036; P=0.008) and ALB (HR=0.924, 95% CI: 0.885–0.966; P<0.001) were independent risk factors for sepsis-related mortality. The Kaplan–Meier analysis revealed that the cumulative in-hospital mortality of sepsis patients with an NRS score of ≥3 was significantly higher than that of patients with an NRS score of <3 (P=0.022).

Conclusion: NRS scores can effectively risk stratify sepsis patients. Patients with high NRS scores should be monitored more closely to halt further disease progression.

Keywords: sepsis, malnutrition, NRS, risk stratification, prognostic assessment

Introduction

Sepsis is a disease with a high mortality,[1,2] as it can easily progress to septic shock and death. It is estimated that there are 30 million cases of sepsis worldwide each year resulting in more than 8 million deaths.[3] Although early diagnosis and treatment of sepsis have improved, the mortality rate remains above 15% and is as high as 50% when septic shock occurs.[4,5] Early identification and management of high-risk sepsis patients can decrease the burden on health services and long-term mortality rates, but is clinically challenging.[6–8] Delayed treatment may result in septic shock and/or refractory multi-organ failure, the leading cause of death in sepsis. The 2016 Surviving Sepsis Campaign (SSC) international guidelines for managing sepsis and septic shock recommend immediate initiation of treatment and resuscitation.[9] This spectrum of care bundle includes measurement of lactate levels, microbiology cultures, early antimicrobial therapy, and efficient fluid resuscitation. Malnutrition is an important contributor to mortality in patients with sepsis,[10,11] who are in a prolonged state of high stress and severe catabolism and are thus more

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prone to malnutrition, reduced immunity, and organ dysfunction, all of which worsen their prognosis.[12] On the other hand, the so-called obesity paradox is that sepsis patients who are obese have lower mortality than those who are not obese[13–16] for reasons that are unclear.

Nutritional Risk Screening (NRS) is an instrument for assessing nutritional risk for hospital inpatients recommended by the European Society of Parenteral and Enteral Nutrition (ESPEN) in 2002.[17] The Society of Critical Care Medicine (SCCM) and the American Society for Parenteral and Enteral Nutrition (ASPEN) also recommended the use of NRS-2002 for the screening of nutritional risk and disease severity in critically ill patients.[18] NRS-2002 evaluates nutritional impairment based on recent changes in BMI, weight, and food intake; disease severity is determined by evaluating nutritional status in the context of recent medical history (eg, fracture, surgery, tumor, hemodialysis, and intensive care treatment) and chronic diseases (eg, metabolic disorder). NRS-2002 is a nutritional screening tool widely used in adult inpatients that has high sensitivity and specificity and is easier to use.[19] Some studies have shown that NRS-2002 is a valuable independent risk score for malnutrition-associated mortality and poor clinical outcome in inpatients.[20–22]

Patients with sepsis are at higher risk of acute disease- or injury-related malnutrition. Applying appropriate nutritional screening tools to patients with sepsis could improve clinical outcomes through the early implementation of appropriate management strategies.[23,24] However, to date, there have been no studies in which patients with sepsis were stratified according to nutritional risk. To this end, we evaluated the utility of the NRS score for predicting the prognosis of in-hospital patients with sepsis in a large cohort in this study.

Subjects and Methods

Subjects

In this retrospective study, we obtained data of patients diagnosed with sepsis through electronic medical records, from January 2018 to December 2019 at Nanfang Hospital of Southern Medical University (Guangzhou, China). Inclusion criteria were as follows: 1) age ≥18 years; and 2) diagnosed with sepsis following the 3rd International Consensus Definitions for Sepsis and Septic Shock.[25] Exclusion criteria were as follows: 1) diagnosed with congenital malnutrition or related diseases; 2) HIV infection; and 3) incomplete/missing clinical data. The flow chart of the study protocol is shown in Figure 1. This retrospective study was approved by the Institutional Review Board/Independent Ethics Committee of Nanfang Hospital of Southern Medical University, and the need for informed consent was waived since all data were anonymized. Patient privacy and confidentiality of data were maintained in accordance with the Declaration of Helsinki.

Data Collection and NRS Assessment

Demographic and clinical data included sex, age, height, body weight, medical history, hospitalization time, white blood cell count (WBC), lymphocyte count (LYM), hemoglobin (HB), C-reactive protein (CRP), procalcitonin (PCT), albumin (ALB), total protein (TP), major comorbidities, source of infection, antimicrobial treatment condition, and sequential organ failure assessment (SOFA) score. Body mass index (BMI) was calculated based on the patient's height and weight measured on admission. NRS score was calculated based on NRS-2002,[17] which includes age, undernutrition, and disease severity with a total score of 0–7, where the "nutrition score" ranges from 0 to 3 and the "disease severity score" ranges from 0 to 3. The disease severity assessment criteria included hip fracture, chronic diseases (diabetes, cirrhosis, chronic obstructive pulmonary disease, and hemodialysis), abdominal surgery, stroke, craniocerebral trauma, severe pneumonia, bone marrow transplantation, and admission to the intensive care unit. Parameters for assessing impaired nutritional status were changes in BMI, percentage of recent weight loss, and food intake. Additionally, 1 point was given for age ≥70 years. Patients with an NRS score of ≥3 are considered at high nutritional risk on hospital admission.

Statistical Analysis

Continuous variables are expressed as mean ± standard error and were compared with the Student's *t*-test. One-way ANOVA was used for multiple group comparisons. Categorical variables are expressed as a number (percentage) and were compared with the Chi-squared test. Univariate and multivariate Cox regression analyses were carried out and the results are presented as hazard ratios (HRs) with 95% confidence intervals (CIs). The Kaplan–Meier survival method was used to analyze the cumulative survival rate of patients with sepsis and the Log rank test was used for intergroup

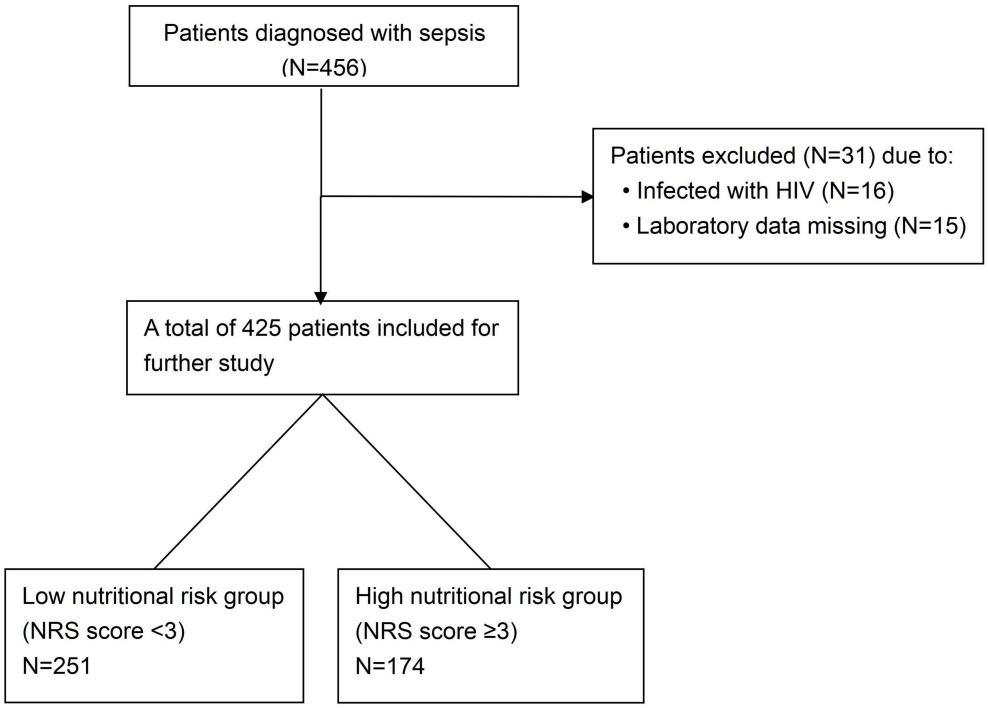

Figure 1 Flow chart of the two phases in the study.

comparisons. All analyses were performed using SPSS v21.0 and GraphPad Prism 6.0 with an alpha level of 0.05.

Results

Clinical Characteristics of Patients with Sepsis Grouped by NRS Score

A total of 425 patients with sepsis were included in our study. The average age of the patients was 43.7±17.3 years and 281 (66.1%) were male. The patients were divided into 2 groups according to NRS score as followed: NRS score <3 (N=251, low nutritional risk group) and score ≥3 (N=174, high nutritional risk group). The high nutritional risk group was older (P=0.005), had lower BMI (P<0.001), lower ALB (P<0.001), lower HB (P<0.001), higher serum CRP (P=0.048), longer hospitalization time (P<0.001), and higher SOFA score (P<0.001) compared to the low nutritional risk group (Table 1).

Relationship Between BMI, ALB Levels, and NRS Score

To evaluate the relationship between nutritional risk and clinical parameters, we compared BMI and serum ALB levels in patients with different NRS scores (points 0 to 5). Lower BMI and ALB levels were associated with a higher NRS score (both P<0.001; Figure 2).

Relationship Between NRS Score and Clinical Outcome

Further prognostic analysis was performed in 372 patients with sepsis who had complete survival data. Of the 372 patients, 308 survived and 64 died. There were significant differences in the proportions of surviving or non-surviving patients in the subgroups with different NRS scores (P=0.020; Figure 3). We therefore performed a Kaplan–Meier analysis and found that the cumulative in-hospital survival rate of sepsis patients with an NRS score of ≥3 (high nutritional risk group) was significantly lower than that of patients with an NRS score of <3 (low nutritional risk group) (P=0.022; Figure 4).

Univariate and Multivariate Analysis of Factors Associated with Prognosis of Sepsis Patients

Univariate Cox regression analysis showed that age, ALB, CRP, and NRS scores were significantly (P<0.05) associated with in-hospital mortality. Multivariate analysis showed that age (HR=1.020, 95% CI: 1.005–1.036;

Table 1 Basic Clinical Data of Sepsis Patients in Different NRS Score Groups

Variable	Total	Nutritional Risk Screening Score		*P* value
		<3	≥3	
Sample size, N	425	251	174	
Gender, male, N(%)	281(66.1)	174(69.3)	107(61.5)	0.094
Age, years	43.7±17.3	42.5±17.1	47.8±17.9	0.005
BMI, kg/m^2	21.8±3.9	23.0±3.7	20.8±3.8	<0.001
Hospitalization time, days	13.2±9.7	11.1±7.6	16.4±11.4	<0.001
Major comorbidities, N(%)				
Hypertension	14(3.3)	6(2.4)	8(4.6)	0.210
Diabetes	21(4.9)	14(5.6)	7(4.0)	0.467
Kidney failure	42(9.9)	17(6.8)	25(14.4)	0.010
Source of infection, N(%)				0.126
Respiratory infections	128(30.1)	65(25.9)	63(36.2)	
Urinary infections	38(8.9)	24(9.6)	14(8.0)	
Biliary infections	18(4.2)	9(3.6)	9(5.2)	
Bloodstream infections	124(29.2)	82(32.7)	42(24.1)	
Others or unexplained sources	117(27.5)	71(28.3)	46(26.4)	
ALB, g/L	36.6±6.3	39.3±5.1	32.5±5.4	<0.001
TP, g/L	67.8±8.6	69.2±7.1	64.5±9.2	<0.001
HB, g/L	113.7±25.2	122.2±22.6	99.2±23.5	<0.001
WBC, $\times 10^9/L$	11.1±51.6	13.2±69.7	9.7±6.6	0.549
LYM, $\times 10^9/L$	1.6±1.5	1.7±1.8	1.4±1.0	0.030
CRP, mg/L	64.8±67.1	61.5±66.9	76.1±70.6	0.048
PCT, ng/mL	2.6±16.5	1.5±5.7	5.0±27.0	0.135
SOFA score	3.1±1.8	2.9±1.6	3.7±2.1	<0.001
Nutrition support, N(%)	144(33.9)	86(34.3)	58(33.3)	0.842

Abbreviations: NRS, nutritional risk screening; BMI, body mass index; ALB, albumin; TP, total protein; HB, hemoglobin; WBC, white blood cell count; LYM, lymphocyte count; CRP, C-reactive protein; PCT, procalcitonin; SOFA, sequential organ failure assessment.

P=0.008) and ALB (HR=0.924, 95% CI: 0.885–0.966; P<0.001) were independent risk factors for mortality in patients with sepsis (Table 2).

Discussion

The results of this study demonstrate that older age and lower ALB levels are independent risk factors for adverse prognosis in sepsis patients. Additionally, patients at high nutritional risk (NRS score ≥3) had a significantly higher cumulative in-hospital mortality rate. These results can help stratify patients with sepsis according to prognosis. Based on our findings, timely interventions, such as nutritional assessment and support, are needed for sepsis patients with a higher NRS score.

NRS-2002 is a nutritional screening tool widely used in adult inpatients with high sensitivity and specificity. The NRS-2002 covers age, recent nutritional status, and disease severity and can effectively identify individuals at high nutritional risk or poor nutritional status. Patients with a total NRS score of ≥3 are considered to be at high nutritional risk and require nutritional support, while weekly nutritional risk screening is recommended for those with a score of <3.[17,26] Sepsis is a complex condition that can rapidly progress to death. Sepsis patients are in

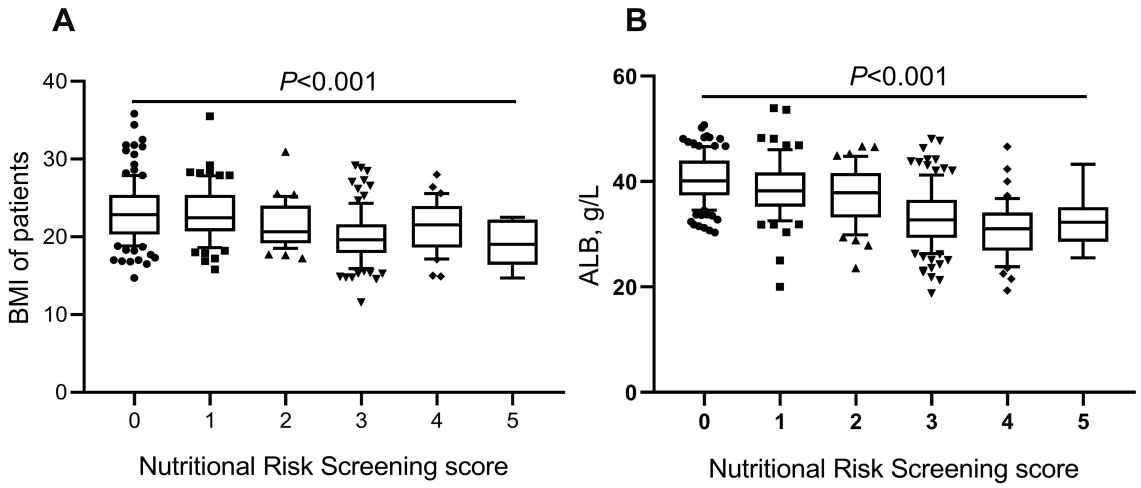

Figure 2 BMI and ALB in different nutritional risk screening score subgroups. (**A**) There were statistically significant differences in BMI among the six subgroups with different NRS scores (23.2±3.9 vs 22.9±3.6 vs 21.5±2.9 vs 19.9±3.8 vs 21.2±3.4 vs 19.1±3.1, P<0.001). (**B**) There were statistically significant differences in ALB among the six subgroups with different NRS scores (40.3±4.5 vs 38.6±5.6 vs 37.6±5.4 vs 33.4±5.8 vs 31.1±5.5 vs 32.6±5.2, P<0.001).

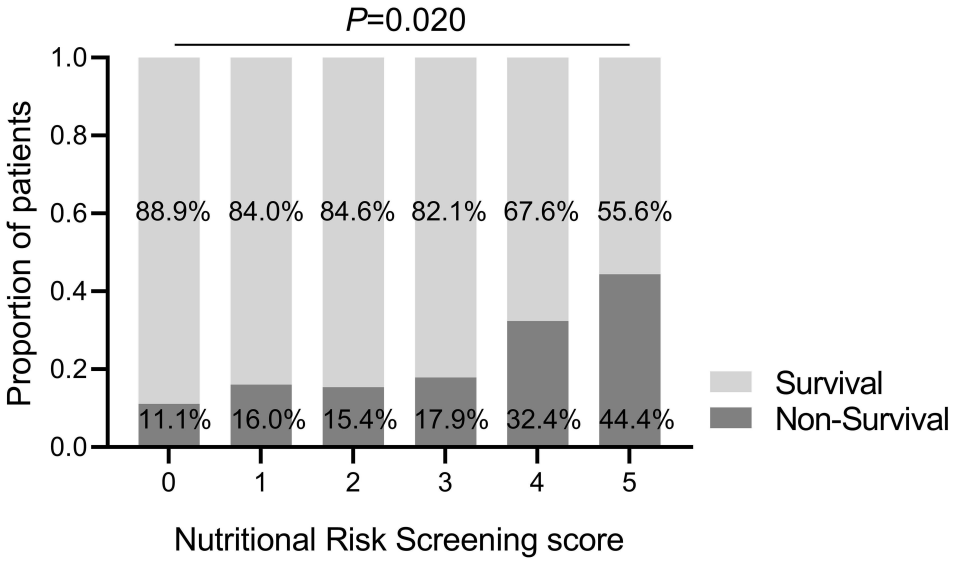

Figure 3 Clinical outcomes in different nutritional risk screening score subgroups. The composition of survivors in hospitalized patients with sepsis was statistically different across the six subgroups with various NRS scores (88.9% vs 84.0% vs 84.6% vs 82.1% vs 67.6% vs 55.6%, P=0.020).

a state of sustained immune activation or inhibition and often exhibit an excessive inflammatory response accompanied by disordered metabolism of macronutrients such as carbohydrates, proteins, and lipids,[27] which increases the risk of malnutrition.[28] Dysregulation of metabolic pathways and severe energy deficiency caused by infections can lead to poor clinical outcomes.[29–31] Nutritional support is considered indispensable for the treatment of sepsis to improve metabolic balance and alleviate adverse outcomes related to diseases.[32,33] The 2016 SSC international guidelines stated that the management of patients with sepsis is multisystemic and multifaceted, including nutritional support, and that inadequate nutritional intake may lead to immune hyporesponsiveness and an increase in infectious complications.[9] Therefore, it is critical that clinicians assess the nutritional risk of patients with sepsis.

We found that survival rates differed significantly between sepsis patients with an NRS score of <3 (low nutritional risk group) and those with a score of ≥3 (high nutritional risk group). In our study, as in others, malnutrition was associated with an increased risk of adverse clinical outcome.[34] Adejumo et al. indicated that protein-energy

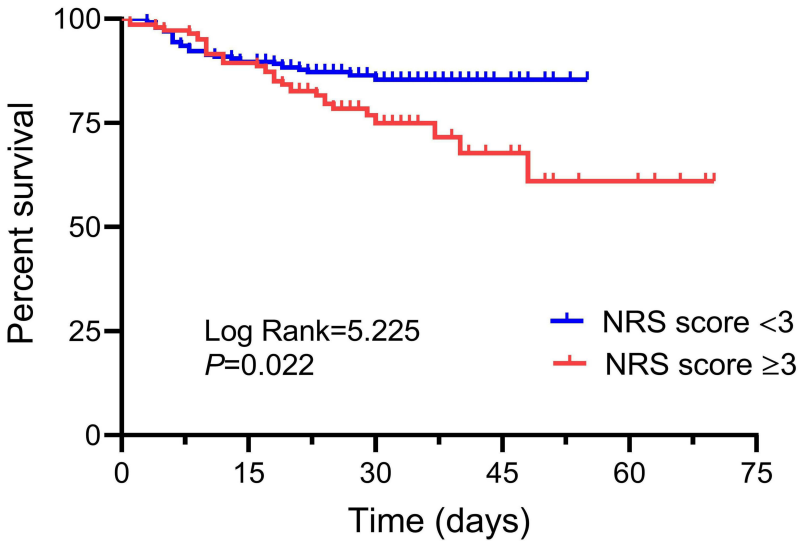

Figure 4 Kaplan–Meier survival estimates of sepsis mortality by nutritional risk screening score groups. Cumulative in-hospital survival was significantly lower in sepsis patients with an NRS score of ≥3 (high nutritional risk group) than in those with an NRS score of <3 (low nutritional risk group) (76.6% vs 86.6%, Log Rank=5.225, P=0.022).

malnutrition is a risk factor for sepsis and associated with poorer outcomes among patients with sepsis.[35] However, there is a paucity of data relating to NRS-2002 for the septic population. A prospective observational study of patients from the ICU in Thailand indicated that being at risk based on NRS-2002 and enteral feeding or combination with parenteral nutrition were the nutrition factors affecting mortality.[36] Another prospective cohort study suggested that timely nutritional support was beneficial to the patients at nutritional risk according to NRS-2002 by a lower complication rate or malnutrition-associated mortality.[37] This was also demonstrated by Hersberger et al.[20] Considering the easy operability of NRS-2002, clinicians can readily assess the nutritional risk of this population of patients on a dynamic basis. That would help to adjust the nutritional support programs for patients with sepsis.

In the present study, patients with a higher NRS score were older and had lower BMI, ALB, TP, and HB levels. Age is incorporated into the NRS score while weight loss is a feature of malnutrition. ALB, TP, and HB are commonly used indices of nutritional status but can be influenced by inflammation, cancer, trauma, or chronic diseases.[38–40] We found that advanced age and lower ALB levels were independent risk factors for poor prognosis in patients with sepsis. Old age is an independent risk factor for many diseases including sepsis;[41,42] and older patients with immunosenescence, organ dysfunction, or other conditions tend to have worse prognosis.[41,43] Similarly, recent studies have revealed that low ALB levels are an independent predictor of outcome in patients with sepsis.[44,45] Low ALB levels disrupt physiologic homeostasis and suppress immunity and anti-inflammatory responses, leading to poor prognosis.[46,47] Moreover, reduced ALB levels were found to be associated with an increased risk of malnutrition.[48] Patients with sepsis, especially those with a high risk of malnutrition, should be paid more attention to ALB levels, and individualized timely nutritional intervention should be given when necessary. Increasing protein and energy intake can reduce mortality risk in critically ill patients with low body weight or nutritional status.[49] Thus, nutritional assessment of patients with sepsis can guide treatment decisions and potentially improve clinical outcomes.

This study had several limitations. Firstly, as this was a single-center retrospective study, the results may not be generalizable and are susceptible to selection bias. Secondly, there was variability in the NRS scores in our cohort, which may have affected the accuracy of the analyses. Multicenter prospective studies are needed to validate our findings.

Conclusion

In conclusion, we found that older age and low ALB levels were independent risk factors for poor prognosis in sepsis patients; moreover, malnutrition (NRS score ≥3) was significantly associated with increased in-hospital mortality. These results indicate that nutritional status as defined by NRS-2002 can effectively identify high-risk sepsis patients who may benefit from timely interventions such as nutritional support that can improve their clinical outcome.

Table 2 Univariate and Multivariate Analysis of Poor Prognosis of Patients with Sepsis

Variables	Univariate Analysis			Multivariate Analysis		
	HR	95% CI	*P* value	HR	95% CI	*P* value
Gender(male)	1.277	0.757–2.154	0.358			
Age	1.028	1.013–1.042	<0.001	1.020	1.005–1.036	0.008
BMI	1.024	0.951–1.102	0.531			
ALB	0.911	0.874–0.949	<0.001	0.924	0.885–0.966	<0.001
TP	0.987	0.959–1.017	0.403			
HB	0.992	0.983–1.002	0.099			
WBC	0.998	0.985–1.011	0.762			
LYM	0.784	0.587–1.049	0.101			
CRP	1.004	1.001–1.007	0.014			
PCT	1.004	0.995–1.013	0.410			
NRS score	1.284	1.094–1.506	0.002			
SOFA score	0.927	0.800–1.074	0.312			
Nutrition support (yes)	1.104	0.665–1.832	0.701			
Early antibiotic treatment (yes)	0.839	0.468–1.504	0.555			
Major comorbidities						
Hypertension (yes)	1.867	0.585–5.954	0.292			
Diabetes (yes)	0.949	0.297–3.029	0.930			
Kidney failure(yes)	1.753	0.866–3.548	0.119			
Source of infection			0.639			
Others or unexplained sources			Reference			
Respiratory infections	0.883	0.446–1.750	0.721			
Urinary infections	1.236	0.508–3.009	0.640			
Biliary infections	1.405	0.750–2.635	0.289			
Bloodstream infections	1.054	0.306–3.630	0.933			

Abbreviations: BMI, body mass index; ALB, albumin; TP, total protein; HB, hemoglobin; WBC: white blood cell count; LYM, lymphocyte count; CRP, C-reactive protein; PCT, procalcitonin; NRS, nutritional risk screening; SOFA, sequential organ failure assessment.

Availability of Supporting Data

Authors can confirm all relevant data are included in the article and materials are available on request from the authors.

Ethics Approval and Consent to Participate

This retrospective study was approved by the Institutional Review Board/Independent Ethics Committee of Nanfang Hospital of Southern Medical University, and the need for informed consent was waived since all data were anonymized before analysis. Patient privacy and confidentiality of data were maintained in accordance with the Declaration of Helsinki.

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Disclosure

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