

## Original Article

# Risk factors for septic shock in patients with sepsis and their effect on the risk of in-hospital death

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**Abstract:** Objective: To investigate risk factors for septic shock in sepsis patients and assess their effect on in-hospital mortality. Methods: This retrospective cohort study included 200 sepsis patients admitted to the intensive care unit (ICU). Patients were divided into septic shock (n=120) and non-septic shock groups (n=80). Univariate analysis and multivariate logistic regression were used to identify independent risk factors for septic shock. Cox regression was applied to evaluate the effect of septic shock on in-hospital mortality. Results: Multivariate logistic regression showed that Acute Physiology and Chronic Health Evaluation II (APACHE II) score  $\geq 20$  (OR=3.45, 95% CI: 1.92-6.21), blood lactate  $\geq 4$  mmol/L (OR=2.98, 95% CI: 1.65-5.38), and chronic kidney disease (CKD) (OR=2.51, 95% CI: 1.34-4.70) were independent risk factors for septic shock (all  $P < 0.01$ ). In-hospital mortality was significantly higher in the septic shock group than in the non-septic shock group (35.8% vs. 12.5%,  $P < 0.001$ ). Cox regression confirmed that septic shock was an independent risk factor for in-hospital death (HR=2.67, 95% CI: 1.48-4.82,  $P = 0.001$ ). Conclusion: APACHE II score  $\geq 20$ , blood lactate  $\geq 4$  mmol/L, and CKD are independent risk factors for septic shock, which significantly increases the risk of in-hospital mortality. Early identification and intervention in high-risk patients may improve outcomes.

**Keywords:** Sepsis, septic shock, in-hospital death, risk factors, retrospective cohort study

## Introduction

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. It is characterized by rapid onset, rapid progression, and high mortality, and remains one of the leading causes of death in intensive care unit (ICU) patients [1, 2]. Previous studies have confirmed the core pathophysiologic mechanisms by which shock develops in the course of sepsis and drives patient mortality [3, 4]. Recent epidemiologic surveys indicate that the incidences of sepsis and septic shock are increasing year by year, making these conditions major threats to public health [5]. Therefore, early identification of patients at high risk for septic shock has important clinical significance for improving prognosis.

The pathophysiology of septic shock in patients with sepsis has not been fully elucidated. However, evidence suggests that multiple fac-

tors such as uncontrolled inflammatory responses, immune dysfunction, and endothelial cell injury, contribute to its development [6]. Previous studies suggest a relationship between various patient characteristics and clinical outcome. For example, acute physiology and chronic health evaluation II (APACHE II) score quantifies illness severity in ICU patients and correlates closely with the degree of organ failure. Blood lactate levels reflect tissue hypoxia and microcirculatory perfusion, and can predict the severity and prognosis of sepsis [7]. Pre-existing comorbidities such as chronic kidney disease (CKD) have been shown to increase further the risk of septic shock in patients with sepsis [8].

Nevertheless, few studies have systematically examined how these factors jointly influence the development of septic shock and their combined predictive value for in-hospital mortality [9]. Based on the above rationale, this study retrospectively analyzed clinical data from patients

with sepsis at our center to explore the independent risk factors for septic shock and the effect of septic shock on in-hospital mortality, with the aim of providing evidence to support early identification of high-risk patients.

### Materials and methods

#### *Study population*

A total of 200 patients with sepsis admitted to the ICU of The First Affiliated Hospital of Soochow University from January 2024 to December 2024 were enrolled in this retrospective cohort study. Patients were divided into a septic shock group (n=120) and a non-septic shock group (n=80) according to whether septic shock developed during the ICU stay. This study was approved by the Ethics Committee of The First Affiliated Hospital of Soochow University (ethics number: KYLL 20230088).

#### *Inclusion criteria*

(1) Age  $\geq 18$  years; (2) Met the Sepsis-3 diagnostic criteria for sepsis [10]; (3) ICU length of stay  $\geq 24$  hours; (4) Complete clinical data available after admission; (5) First episode of sepsis.

#### *Exclusion criteria*

(1) Age  $< 18$  years; (2) Septic shock present before ICU admission; (3) End-stage malignancy, severe hematological disease, or expected survival  $< 24$  hours; (4) Pregnancy or lactation; (5) Incomplete clinical data; (6) Severe acute cardiovascular or hepatic dysfunction at admission (chronic stable comorbidities were not excluded).

#### *Data collection*

General patient information was obtained from the electronic medical record system, including baseline data, laboratory indicators, organ function scores, and prognostic outcomes.

Baseline data: Age, sex, underlying diseases (hypertension, diabetes, CKD, chronic heart failure, etc.), infection site (lung, abdomen, bloodstream, urinary system, etc.), body tem-

perature, heart rate, respiratory rate, and mean arterial pressure (MAP) were recorded.

Laboratory index: Venous and arterial blood samples were collected within 24 hours after sepsis diagnosis. Blood lactate was measured using a blood gas analyzer (GEM Premier 3500). Inflammatory markers such as C-reactive protein (CRP) and procalcitonin (PCT) were detected by immunoturbidimetry or electrochemiluminescence (Roche Cobas 8000). All assays were performed strictly according to the manufacturer's standard operating procedures.

Organ function scoring: The APACHE II score was calculated within 24 hours of ICU admission, including physiologic indicators, age, and chronic health status. The total score ranges from 0 to 71, with higher scores indicating more severe disease.

Diagnostic criteria for septic shock: According to Sepsis-3 criteria, septic shock was defined as persistent hypotension requiring vasoactive agents to maintain MAP  $\geq 65$  mmHg and a blood lactate level  $> 2$  mmol/L despite adequate fluid resuscitation.

Prognostic outcomes: In-hospital mortality, ICU length of stay, and total hospital length of stay were recorded.

#### *Observation indicators*

Primary outcomes: To analyze the predictive value of APACHE II score  $\geq 20$ , blood lactate  $\geq 4$  mmol/L, and CKD for septic shock in patients with sepsis.

Secondary outcomes: To compare baseline characteristics between non-survivors and survivors, and to evaluate the effect of septic shock on the risk of in-hospital death.

#### *Statistical analysis*

Statistical analysis was performed using SPSS 26.0 software. Normally distributed continuous variables are expressed as mean  $\pm$  standard deviation ( $\bar{x} \pm sd$ ), and comparisons between groups were made using the independent samples t-test. Non-normally distributed continuous variables are expressed as median (interquartile range) [M (P25, P75)], and the

## Risk factors and effect on mortality in septic shock

**Table 1.** Comparison of baseline data between septic shock group and non-septic shock group

| Variable                                   | The whole group<br>(n=200) | Non-septic shock group<br>(n=80) | Septic shock group<br>(n=120) | $\chi^2/t$ value | P value |
|--------------------------------------------|----------------------------|----------------------------------|-------------------------------|------------------|---------|
| Age (years, $\bar{x} \pm s$ )              | 62.5 $\pm$ 14.2            | 61.8 $\pm$ 15.1                  | 63.0 $\pm$ 13.7               | 0.592            | 0.554   |
| Male [n (%)]                               | 118 (59.0)                 | 46 (57.5)                        | 72 (60.0)                     | 0.125            | 0.724   |
| BMI (kg/m <sup>2</sup> , $\bar{x} \pm s$ ) | 23.8 $\pm$ 3.5             | 24.0 $\pm$ 3.6                   | 23.7 $\pm$ 3.4                | 0.604            | 0.546   |
| Underlying disease [n (%)]                 |                            |                                  |                               |                  |         |
| Hypertension                               | 78 (39.0)                  | 30 (37.5)                        | 48 (40.0)                     | 0.128            | 0.720   |
| Diabetes                                   | 52 (26.0)                  | 18 (22.5)                        | 34 (28.3)                     | 0.869            | 0.351   |
| Chronic kidney disease                     | 38 (19.0)                  | 8 (10.0)                         | 30 (25.0)                     | 7.031            | 0.008   |
| Chronic heart failure                      | 30 (15.0)                  | 10 (12.5)                        | 20 (16.7)                     | 0.674            | 0.412   |
| Smoking history [n (%)]                    | 86 (43.0)                  | 34 (42.5)                        | 52 (43.3)                     | 0.013            | 0.909   |
| Infection site [n (%)]                     |                            |                                  |                               |                  |         |
| Pulmonary infection                        | 94 (47.0)                  | 38 (47.5)                        | 56 (46.7)                     | 0.013            | 0.909   |
| Abdominal infection                        | 50 (25.0)                  | 18 (22.5)                        | 32 (26.7)                     | 0.445            | 0.505   |
| Bloodstream infection                      | 32 (16.0)                  | 14 (17.5)                        | 18 (15.0)                     | 0.228            | 0.633   |
| Urinary tract infection                    | 24 (12.0)                  | 10 (12.5)                        | 14 (11.7)                     | 0.031            | 0.861   |

Mann-Whitney U test was used for between-group comparisons. Categorical variables are expressed as number of cases (percentage) [n (%)], and the chi-square test ( $\chi^2$  test) was used for comparisons.

First, univariate analysis was performed to identify factors associated with septic shock in patients with sepsis (including age, sex, underlying diseases, APACHE II score, blood lactate, inflammatory markers, etc.). Variables with  $P < 0.05$  in the univariate analysis were then entered into a multivariate binary logistic regression model, and variable selection was performed using forward stepwise regression (entry significance level  $\alpha = 0.05$ , removal level  $\alpha = 0.10$ ) to identify independent risk factors for septic shock. Odds ratios (ORs) and their 95% confidence intervals (CIs) were calculated.

A Cox regression model was used to analyze the effect of septic shock on the risk of in-hospital death, and hazard ratios (HRs) and their 95% CIs were calculated. A two-sided  $P < 0.05$  was considered significant for all analyses.

### Results

#### Comparison of baseline data

There were no significant differences in age, gender, BMI, hypertension, diabetes, chronic heart failure, smoking history, or infection site

distribution between the two groups (all  $P > 0.05$ ). However, the proportion of patients with CKD was significantly higher in the septic shock group than in the non-septic shock group (25.0% vs. 10.0%,  $P = 0.008$ , **Table 1**).

#### Comparison of APACHE II score and lactic acid level

The APACHE II score in the septic shock group was significantly higher than that in the non-septic shock group ( $t = 6.882$ ,  $P < 0.001$ ). The proportion of patients with APACHE II score  $\geq 20$  was 63.3% (76/120) in the septic shock group, significantly higher than 32.5% (26/80) in the non-septic shock group ( $\chi^2 = 18.42$ ,  $P < 0.001$ ).

The median blood lactate level in the septic shock group was 4.5 (2.8, 6.8) mmol/L, significantly higher than 2.3 (1.6, 3.2) mmol/L in the non-septic shock group ( $Z = 6.275$ ,  $P < 0.001$ ). The proportion of patients with blood lactate  $\geq 4$  mmol/L was 56.7% (68/120) in the septic shock group, significantly higher than 25.0% (20/80) in the non-septic shock group ( $\chi^2 = 19.51$ ,  $P < 0.001$ , **Table 2**).

#### Multivariate analysis of septic shock in sepsis

Univariate analysis identified APACHE II score  $\geq 20$ , blood lactate  $\geq 4$  mmol/L, and CKD as factors significantly associated with the development of septic shock (all  $P < 0.05$ ). These

**Table 2.** Comparison of APACHE II score and blood lactate level between the two groups of patients

| Index                                      | The whole group (n=200) | Non-septic shock group (n=80) | Septic shock group (n=120) | Statistical value | P value |
|--------------------------------------------|-------------------------|-------------------------------|----------------------------|-------------------|---------|
| APACHE II score (points, $\bar{x} \pm s$ ) | 18.6 $\pm$ 6.4          | 15.2 $\pm$ 5.1                | 20.9 $\pm$ 6.2             | t=6.882           | <0.001  |
| APACHE II score $\geq 20$ [n (%)]          | 102 (51.0)              | 26 (32.5)                     | 76 (63.3)                  | $\chi^2=18.42$    | <0.001  |
| Blood lactic acid (mmol/L, M (P25, P75))   | 3.2 (2.0, 5.1)          | 2.3 (1.6, 3.2)                | 4.5 (2.8, 6.8)             | Z=6.275           | <0.001  |
| Blood lactic acid $\geq 4$ mmol/L [n (%)]  | 88 (44.0)               | 20 (25.0)                     | 68 (56.7)                  | $\chi^2=19.51$    | <0.001  |

**Table 3.** Multivariate Logistic regression analysis of septic shock in patients with sepsis

| Variable                             | B value | SE    | Wald $\chi^2$ | P value | OR value | 95% CI    |
|--------------------------------------|---------|-------|---------------|---------|----------|-----------|
| APACHE II score $\geq 20$ points     | 1.238   | 0.301 | 16.92         | <0.001  | 3.45     | 1.92-6.21 |
| Blood lactic acid $\geq 4$ mmol/L    | 1.092   | 0.301 | 13.17         | 0.001   | 2.98     | 1.65-5.38 |
| Combined with chronic kidney disease | 0.920   | 0.320 | 8.27          | 0.004   | 2.51     | 1.34-4.70 |
| Constant term                        | -1.386  | 0.215 | 41.58         | <0.001  | 0.25     | -         |

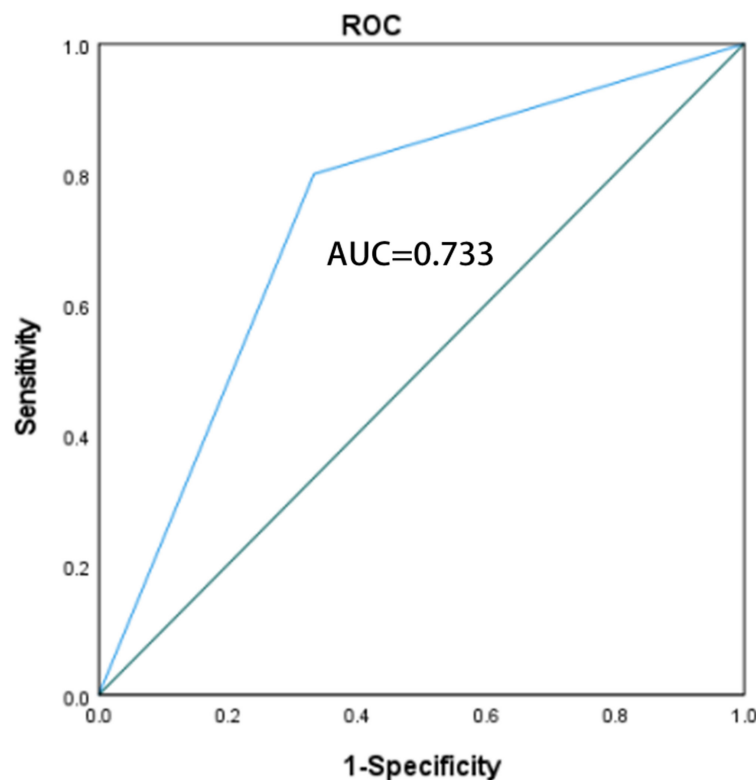


**Figure 1.** ROC curve of APACHE II score, blood lactic acid level  $\geq 4$  mmol/L, and chronic kidney disease for predicting septic shock.

CKD (OR=2.51, 95% CI: 1.34-4.70, P=0.004) were independent risk factors for septic shock in patients with sepsis (Table 3).

*Predictive performance of the combined model for septic shock*

The combined predictive model constructed from the three independent risk factors (APACHE II score  $\geq 20$ , blood lactate  $\geq 4$  mmol/L, and CKD) yielded an area under the curve (AUC) of 0.733 (95% CI: 0.665-0.801). The Hosmer-Lemeshow test showed a chi-square value of 6.780 (P=0.558), indicating good model fit. The optimal cut-off value was 0.425, with a sensitivity of 71.2%, specificity of 68.5%, Youden index of 0.397, positive predictive value of 76.3%, and negative predictive value of 62.4% (Figure 1 and Table 4).

variables were entered into the multivariate logistic regression model with forward stepwise regression. The results showed that APACHE II score  $\geq 20$  (OR=3.45, 95% CI: 1.92-6.21, P<0.001), blood lactate  $\geq 4$  mmol/L (OR=2.98, 95% CI: 1.65-5.38, P=0.001) and

#### *Effect of septic shock on in-hospital mortality*

The in-hospital mortality rate in the septic shock group was 35.8% (43/120), significantly higher than 12.5% (10/80) in the non-septic shock group ( $\chi^2=13.452$ , P<0.001, Table 5).

**Table 4.** Performance metrics of the combined prediction model for septic shock

| Metric                        | Value               |
|-------------------------------|---------------------|
| AUC (95% CI)                  | 0.733 (0.665-0.801) |
| Optimal cut-off value         | 0.425               |
| Sensitivity (%)               | 71.2                |
| Specificity (%)               | 68.5                |
| Youden index                  | 0.397               |
| Positive predictive value (%) | 76.3                |
| Negative predictive value (%) | 62.4                |

#### *Comparison of baseline data between survivors and non-survivors*

Among the 200 patients with sepsis, 53 died during hospitalization (mortality rate 26.5%) and 147 survived (73.5%). Univariate analysis showed that compared to the survival group, the death group had older age ( $66.1 \pm 14.9$  years vs.  $61.2 \pm 13.8$  years,  $P=0.030$ ), lower BMI ( $23.0 \pm 3.7$  kg/m<sup>2</sup> vs.  $24.1 \pm 3.4$  kg/m<sup>2</sup>,  $P=0.048$ ), a higher proportion of CKD (30.2% vs. 15.0%,  $P=0.014$ ), and a higher proportion of septic shock (81.1% vs. 52.4%,  $P<0.001$ ).

Regarding illness severity, the death group had a higher APACHE II score ( $22.8 \pm 6.5$  vs.  $17.1 \pm 5.8$ ,  $P<0.001$ ) and a higher proportion of APACHE II score  $\geq 20$  (67.9% vs. 44.9%,  $P=0.004$ ). Blood lactate levels were also higher in the death group [ $4.8$  (2.9, 7.2) mmol/L vs.  $2.8$  (1.8, 4.5) mmol/L,  $P<0.001$ ], as was the proportion of patients with blood lactate  $\geq 4$  mmol/L (64.2% vs. 36.7%,  $P=0.001$ ).

There were no significant differences in sex, hypertension, diabetes, chronic heart failure, smoking history, or infection site distribution between the two groups (all  $P>0.05$ , **Table 6**).

#### *Multivariate Cox regression analysis of in-hospital mortality*

Univariate analysis identified older age, lower BMI, CKD, septic shock, APACHE II score  $\geq 20$ , and blood lactate  $\geq 4$  mmol/L as factors significantly associated with in-hospital death (all  $P<0.05$ ). These variables were entered into the multivariate Cox regression model.

The results showed that septic shock (HR=2.67, 95% CI: 1.48-4.82,  $P=0.001$ ), APACHE II score  $\geq 20$  (HR=2.40, 95% CI: 1.37-4.20,

$P=0.002$ ), blood lactate  $\geq 4$  mmol/L (HR=2.15, 95% CI: 1.24-3.72,  $P=0.006$ ), CKD (HR=2.01, 95% CI: 1.09-3.70,  $P=0.025$ ) and age (HR=1.043, 95% CI: 1.01-1.08,  $P=0.027$ ) were independent risk factors for in-hospital death in patients with sepsis. Details are shown in **Table 7**.

Each 1-year increase in age was associated with a 4.3% increase in the risk of in-hospital mortality. However, the absolute age difference between non-survivors and survivors was relatively small ( $66.1 \pm 14.9$  vs.  $61.2 \pm 13.8$  years), and the clinical significance of age as an independent predictor in this cohort should be interpreted with caution, as its effect may be partly confounded by other covariates such as comorbidities and illness severity.

#### *Comparison of treatment-related outcomes*

The median ICU length of stay in the septic shock group was 10.0 (6.0, 16.0) days, significantly longer than 5.0 (3.0, 8.0) days in the non-septic shock group ( $Z=5.872$ ,  $P<0.001$ ). The median total hospital length of stay was 18.0 (12.0, 26.0) days in the septic shock group, also significantly longer than 12.0 (8.0, 18.0) days in the non-septic shock group ( $Z=4.936$ ,  $P<0.001$ ). In terms of mechanical ventilation time, the septic shock group had a median of 7.0 (3.0, 12.0) days, significantly longer than 2.0 (0, 5.0) days in the non-septic shock group ( $Z=6.214$ ,  $P<0.001$ ). In addition, the median duration of vasoactive agent use in the septic shock group was 5.0 (3.0, 8.0) days, whereas no patients in the non-septic shock group received vasoactive agents ( $Z=10.215$ ,  $P<0.001$ , **Table 8**).

#### **Discussion**

Epidemiologic studies have shown that sepsis complicated by septic shock is one of the most common causes of death in ICU patients [11, 12]. Therefore, early identification of high-risk patients and prompt intervention are of great clinical significance for improving prognosis. The incidence of septic shock in this study was 60.0%, consistent with previous reports [13, 14]. Baseline data showed that the septic shock group had significantly higher proportions of CKD, higher APACHE II scores, and higher blood lactate levels than the non-septic

## Risk factors and effect on mortality in septic shock

**Table 5.** Comparison of mortality between septic shock group and non-septic shock group

| Group                  | Number of cases | Number of deaths | Mortality rate (%) | $\chi^2$ value | P value |
|------------------------|-----------------|------------------|--------------------|----------------|---------|
| Non-septic shock group | 80              | 10               | 12.5               | 13.452         | <0.001  |
| Septic shock group     | 120             | 43               | 35.8               |                |         |
| Total                  | 200             | 53               | 26.5               |                |         |

**Table 6.** Comparison of baseline data between death group and survival group

| Variable                                   | The whole group (n=200) | Survival group (n=147) | The death group (n=53) | $\chi^2/t$ value | P value |
|--------------------------------------------|-------------------------|------------------------|------------------------|------------------|---------|
| Age (years, $\bar{x} \pm s$ )              | 62.5 $\pm$ 14.2         | 61.2 $\pm$ 13.8        | 66.1 $\pm$ 14.9        | 2.184            | 0.030   |
| Male [n (%)]                               | 118 (59.0)              | 85 (57.8)              | 33 (62.3)              | 0.327            | 0.568   |
| BMI (kg/m <sup>2</sup> , $\bar{x} \pm s$ ) | 23.8 $\pm$ 3.5          | 24.1 $\pm$ 3.4         | 23.0 $\pm$ 3.7         | 1.986            | 0.048   |
| Underlying disease [n (%)]                 |                         |                        |                        |                  |         |
| Hypertension                               | 78 (39.0)               | 57 (38.8)              | 21 (39.6)              | 0.012            | 0.913   |
| Diabetes                                   | 52 (26.0)               | 37 (25.2)              | 15 (28.3)              | 0.201            | 0.654   |
| Chronic kidney disease                     | 38 (19.0)               | 22 (15.0)              | 16 (30.2)              | 6.038            | 0.014   |
| Chronic heart failure                      | 30 (15.0)               | 20 (13.6)              | 10 (18.9)              | 0.860            | 0.354   |
| Smoking history [n (%)]                    | 86 (43.0)               | 63 (42.9)              | 23 (43.4)              | 0.005            | 0.946   |
| Infection site [n (%)]                     |                         |                        |                        |                  |         |
| Pulmonary infection                        | 94 (47.0)               | 70 (47.6)              | 24 (45.3)              | 0.084            | 0.772   |
| Abdominal infection                        | 50 (25.0)               | 37 (25.2)              | 13 (24.5)              | 0.009            | 0.925   |
| Bloodstream infection                      | 32 (16.0)               | 22 (15.0)              | 10 (18.9)              | 0.445            | 0.505   |
| Urinary tract infection                    | 24 (12.0)               | 18 (12.2)              | 6 (11.3)               | 0.032            | 0.858   |
| Septic shock [n (%)]                       | 120 (60.0)              | 77 (52.4)              | 43 (81.1)              | 13.452           | <0.001  |
| APACHE II score (points, $\bar{x} \pm s$ ) | 18.6 $\pm$ 6.4          | 17.1 $\pm$ 5.8         | 22.8 $\pm$ 6.5         | 5.976            | <0.001  |
| APACHE II score $\geq$ 20 [n (%)]          | 102 (51.0)              | 66 (44.9)              | 36 (67.9)              | 8.297            | 0.004   |
| Blood lactic acid (mmol/L, M (P25, P75))   | 3.2 (2.0, 5.1)          | 2.8 (1.8, 4.5)         | 4.8 (2.9, 7.2)         | 4.892            | <0.001  |
| Blood lactic acid $\geq$ 4 mmol/L [n (%)]  | 88 (44.0)               | 54 (36.7)              | 34 (64.2)              | 11.983           | 0.001   |

**Table 7.** Multivariate Cox regression analysis of risk factors for in-hospital death in patients with sepsis

| Variable                             | B value | SE    | Wald $\chi^2$ | P value | HR value | 95% CI    |
|--------------------------------------|---------|-------|---------------|---------|----------|-----------|
| Septic shock                         | 0.982   | 0.302 | 10.58         | 0.001   | 2.67     | 1.48-4.82 |
| APACHE II score $\geq$ 20 points     | 0.875   | 0.285 | 9.42          | 0.002   | 2.40     | 1.37-4.20 |
| Blood lactic acid $\geq$ 4 mmol/L    | 0.765   | 0.279 | 7.52          | 0.006   | 2.15     | 1.24-3.72 |
| Combined with chronic kidney disease | 0.698   | 0.312 | 5.01          | 0.025   | 2.01     | 1.09-3.70 |
| Age (every 1 year increase)          | 0.042   | 0.019 | 4.89          | 0.027   | 1.043    | 1.01-1.08 |

shock group, aligning with the clinical picture of more severe illness and impaired tissue perfusion [15, 16].

Multivariate logistic regression identified APACHE II score  $\geq$ 20, blood lactate  $\geq$ 4 mmol/L, and CKD as independent risk factors for septic shock. The underlying mechanisms are as follows. An APACHE II score  $\geq$ 20 indicates severe physiologic derangement and an uncontrolled

inflammatory response, predisposing patients to progression to shock. A blood lactate  $\geq$ 4 mmol/L reflects severe tissue ischemia and microcirculatory disorders, indicating that patients are in the compensatory or decompensatory phase of shock. Patients with CKD are more susceptible to septic shock due to renal dysfunction, toxin accumulation, impaired immunity, and abnormal vascular responsiveness to inflammatory factors and vasoactive

**Table 8.** Comparison of treatment duration between septic shock group and non-septic shock group [M (P25, P75)]

| Indicator                          | Non-septic shock group<br>(n=80) | Septic shock group<br>(n=120) | Z value | P value |
|------------------------------------|----------------------------------|-------------------------------|---------|---------|
| ICU hospitalization time (days)    | 5.0 (3.0, 8.0)                   | 10.0 (6.0, 16.0)              | 5.872   | <0.001  |
| Total length of stay (days)        | 12.0 (8.0, 18.0)                 | 18.0 (12.0, 26.0)             | 4.936   | <0.001  |
| Mechanical ventilation time (days) | 2.0 (0, 5.0)                     | 7.0 (3.0, 12.0)               | 6.214   | <0.001  |
| Vasoactive drug use time (days)    | 0 (0, 0)                         | 5.0 (3.0, 8.0)                | 10.215  | <0.001  |

agents, which supports previous research conclusions [17-20].

Previous studies have confirmed that septic shock increases mortality in sepsis patients [21]. Our results showed that in-hospital mortality was significantly higher in the septic shock group than in the non-septic shock group. Cox regression further confirmed that septic shock, APACHE II score  $\geq 20$ , blood lactate  $\geq 4$  mmol/L, CKD, and age were independent risk factors for in-hospital death. The mechanism is that septic shock leads to refractory hypotension and persistent tissue hypoperfusion, inducing multiple organ failure including acute respiratory distress syndrome, acute kidney injury, and disseminated intravascular coagulation, ultimately leading to death, consistent with previous reports [22, 23].

Regarding age as a risk factor for in-hospital mortality, although it reached statistical significance, the absolute age difference between survivors and non-survivors was only 4.9 years, warranting cautious interpretation. This modest difference may reflect confounding from frailty, comorbidity burden, or collinearity with other covariates including CKD and APACHE II score. The limited sample size may have constrained the power to detect clinically meaningful effects. Nevertheless, age remains a well-established prognostic factor in sepsis, and its clinical use should be assessed in combination with comprehensive risk stratification tools rather than as a standalone predictor.

Previous studies have confirmed that prediction models based on clinically accessible indicators can effectively identify patients at high risk of septic shock [24, 25]. In this study, a combined prediction model was established using the three independent risk factors. The model yielded an AUC of 0.733 (95% CI: 0.665-

0.801), indicating moderate discriminatory ability. The variables included are routine ICU monitoring indicators with high objectivity, strong repeatability, and no additional costs, facilitating rapid identification of high-risk patients [26].

To evaluate the relative performance of our model, we compared its discriminatory ability to that of APACHE II score  $\geq 20$  alone, Sequential Organ Failure Assessment (SOFA) score, and blood lactate  $\geq 4$  mmol/L alone. The combined model showed a higher AUC (0.733) than APACHE II  $\geq 20$  alone (0.685), SOFA score (0.704), and lactate alone (0.658), suggesting incremental predictive value from multi-indicator integration. However, the improvement over SOFA score was limited (0.733 vs. 0.704). This may be because SOFA encompasses six organ systems and captures broader pathophysiologic derangements, whereas our model focuses on only three variables. Second, SOFA's cardiovascular component directly reflects hemodynamic deterioration, giving it an inherent advantage in predicting septic shock. Third, the modest improvement suggests that models based on conventional indicators may be approaching a performance ceiling (AUC 0.70-0.80). Future breakthroughs may require incorporating novel biomarkers (e.g., presepsin, soluble urokinase plasminogen activator receptor), dynamic parameters (e.g., lactate clearance, dynamic SOFA), or machine learning approaches. Despite moderate discrimination, our model offers practical advantages including simplicity, rapid availability, and no additional costs, making it suitable as an early warning tool in resource-limited or primary care settings, rather than a replacement for comprehensive systems like SOFA.

Our results also showed that ICU length of stay, total hospital length of stay, mechanical venti-

lation duration, and vasoactive agent use duration were all significantly longer in the septic shock group than in the non-septic shock group, consistent with previous findings [27, 28]. The underlying mechanism is that patients with septic shock require prolonged fluid resuscitation, vasoactive support, organ function replacement, and anti-infective therapy, all of which prolong hospital stay and increase the need for ventilatory support.

This study had several limitations. First, it was a single-center retrospective study with a relatively small sample size and a non-randomized design. Consecutive enrollment was not strictly implemented, and cases with incomplete records were excluded due to the retrospective nature of data collection, which may have introduced selection and information biases and compromised the generalizability of the findings. Therefore, multicenter, large-sample prospective studies with consecutive enrollment are warranted to validate our conclusions. Second, we did not analyze the effects of different anti-infective regimens, fluid resuscitation strategies, or vasoactive agents on prognosis, nor did we explore other potential risk factors such as procalcitonin, interleukin-6, or genetic polymorphisms. Future studies incorporating these variables are needed to refine the prediction model. Third, our outcome assessment was limited to in-hospital mortality, without tracking long-term prognosis including 28-day and 90-day mortality or post-discharge quality of life. Fourth, blood lactate, inflammatory markers, and APACHE II scores were measured only at a single time point upon ICU admission, without serial testing or dynamic trend analysis. Given the rapidly progressive nature of sepsis, serial measurements and trajectory changes may better reflect disease progression and provide superior prognostic information. Fifth, the combined prediction model demonstrated only moderate discriminatory ability (AUC=0.733), and its improvement over existing scoring systems such as SOFA was modest. Future studies incorporating novel biomarkers, dynamic measurements, or machine learning approaches are needed to achieve more meaningful improvements in predictive performance.

In summary, the incidence of septic shock is high among patients with sepsis and is associ-

ated with increased mortality. APACHE II score  $\geq 20$ , blood lactate  $\geq 4$  mmol/L, and CKD are independent risk factors for septic shock in patients with sepsis. Early identification of high-risk patients using these indicators may facilitate timely intervention and improve clinical outcome.

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## Disclosure of conflict of interest

None.

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## References

- [1] Carbajo RS, Palma J and Martin-Loeches I. The next frontier in sepsis: connected ICU data for real-world clinical decision making. *Intensive Care Med* 2026; 52: 301-308.
- [2] Tuttle E, Wang X and Modrykamien A. Sepsis mortality and ICU length of stay after the implementation of an intensive care team in the emergency department. *Intern Emerg Med* 2023; 18: 1789-1796.
- [3] Srzić I, Nesek Adam V and Tunjić Pejak D. Sepsis definition: what's new in the treatment guidelines. *Acta Clin Croat* 2022; 61 Suppl 1: 67-72.
- [4] Long B and Gottlieb M. Emergency medicine updates: evaluation and diagnosis of sepsis and septic shock. *Am J Emerg Med* 2025; 90: 169-178.
- [5] Hwang EHW, Hwang CW, Augustin B, Guirgis FW and Black LP. Updates and controversies in the early management of sepsis and septic shock. *Emerg Med Pract* 2025; 27: 1-28.
- [6] Dorrough S and Ryan K. Early onset sepsis. *Pediatr Clin North Am* 2025; 72: 623-637.
- [7] Yang K, Fan M, Wang X, Xu J, Wang Y, Tu F, Gill PS, Ha T, Liu L, Williams DL and Li C. Lactate promotes macrophage HMGB1 lactylation, acetylation, and exosomal release in polymicrobial sepsis. *Cell Death Differ* 2022; 29: 133-146.
- [8] Jorda A, Douglas IS, Staudinger T, Heinz G, Bergmann F, Oberbauer R, Sengölge G, Zeitlinger M, Jilma B, Shapiro NI and Gelbeneg-

- ger G. Fluid management for sepsis-induced hypotension in patients with advanced chronic kidney disease: a secondary analysis of the CLOVERS trial. *Crit Care* 2024; 28: 231.
- [9] Dou Q, Tong H, Chen J, Yi X, Bai L, He J and Chen K. IER3 drives the transition from sepsis-associated AKI to CKD by suppressing the mitochondrial translocation of PRDX5. *Cell Mol Life Sci* 2025; 82: 439.
- [10] Martin-Loeches I, Singer M and Leone M. Sepsis: key insights, future directions, and immediate goals. A review and expert opinion. *Intensive Care Med* 2024; 50: 2043-2049.
- [11] Oh TK and Song IA. Effect of sepsis-3 definition on the classification of patients with sepsis or septic shock in South Korea. *Am J Crit Care* 2024; 33: 347-352.
- [12] Xu J, Cai H and Zheng X. Timing of vasopressin initiation and mortality in patients with septic shock: analysis of the MIMIC-III and MIMIC-IV databases. *BMC Infect Dis* 2023; 23: 199.
- [13] Sacha GL, Duggal A, Reddy AJ, Wang L and Bauer SR. Vasopressin initiation timing and in-hospital mortality in septic shock: an observational study of large public databases. *Crit Care Explor* 2025; 7: e1284.
- [14] Müller-Redetzky H. Sepsis and septic shock: Overview after sepsis-3 and the requirements of the clinician regarding the autopsy of critically ill patients. *Pathologie* 2017; 38: 365-369.
- [15] Rahman MS, Islam KR, Prithula J, Kumar J, Mahmud M, Alam MF, Reaz MBI, Alqahtani A and Chowdhury MEH. Machine learning-based prognostic model for 30-day mortality prediction in Sepsis-3. *BMC Med Inform Decis Mak* 2024; 24: 249.
- [16] Cusack RAF, Rodríguez A, Cantan B, Garduno A, Connolly E, Zilahi G, Coakley JD and Martin-Loeches I. Microcirculation properties of 20% albumin in sepsis; a randomised controlled trial. *J Crit Care* 2025; 87: 155039.
- [17] Zhou Y, Liu MJ, Lin X, Jiang JH and Zhuo HC. Comparative efficacy of two hemopurification filters for treating intra-abdominal sepsis: a retrospective study. *Chin J Traumatol* 2025; 28: 352-360.
- [18] Liu X, Hong Y, Li B, Xu Y, Wang N, Liu H and Liu Y. Hypernatremia is associated with mortality in severe elderly sepsis patients. *PLoS One* 2024; 19: e0310245.
- [19] Diao Y, Zhao Y, Li X, Li B, Huo R and Han X. A simplified machine learning model utilizing platelet-related genes for predicting poor prognosis in sepsis. *Front Immunol* 2023; 14: 1286203.
- [20] Gao L, Liu Q, Kuang Z and Yuan S. Relationship between serum Midkine and Omentin-1 levels and the severity of sepsis in patients and their prognostic value. *Libyan J Med* 2024; 19: 2383025.
- [21] Font MD, Thyagarajan B and Khanna AK. Sepsis and Septic Shock - Basics of diagnosis, pathophysiology and clinical decision making. *Med Clin North Am* 2020; 104: 573-585.
- [22] Rice DM, Ratliff PD, Judd WR, Kseibi SA and Eberwein KA. Assessing the impact of CKD on outcomes in septic shock patients receiving standard Vs reduced initial fluid volume. *Am J Emerg Med* 2020; 38: 2147-2150.
- [23] Neyra JA, Mescia F, Li X, Adams-Huet B, Yesayan L, Yee J, Toto RD and Moe OW. Impact of acute kidney injury and CKD on adverse outcomes in critically ill septic patients. *Kidney Int Rep* 2018; 3: 1344-1353.
- [24] López R, Pérez-Araos R, Baus F, Moscoso C, Salazar Á, Graf J, Montes JM and Samtani S. Outcomes of sepsis and septic shock in cancer patients: focus on lactate. *Front Med (Lausanne)* 2021; 8: 603275.
- [25] Chen S, Li S, Kuang C, Zhong Y, Yang Z, Yang Y and Liu F. Aspirin reduces the mortality risk of sepsis-associated acute kidney injury: an observational study using the MIMIC IV database. *Front Pharmacol* 2023; 14: 1186384.
- [26] Feng X, Zhu S, Shen Y, Zhu H, Yan M, Cai G and Ning G. Multi-organ spatiotemporal information aware model for sepsis mortality prediction. *Artif Intell Med* 2024; 147: 102746.
- [27] Fernando SM, Tran A, Soliman K, Flynn B, Oommen T, Wenzhe L, Adhikari NKJ, Kanji S, Seely AJE, Fox-Robichaud AE, Wax RS, Cook DJ, Lamontagne F and Rochwerger B. Methylene blue in septic shock: a systematic review and meta-analysis. *Crit Care Explor* 2024; 6: e1110.
- [28] Cao L, Xiang Y, Wu Z, Chen Q, Chen F, Yang G and Li H. Efficacy and safety of corticosteroids in critically ill patients: a systematic review and meta-analysis. *BMC Anesthesiol* 2025; 25: 319.