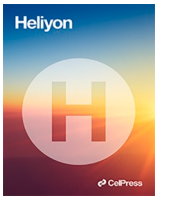
Heliyon 10 (2024) e27209

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Research article

# Prediction model of death risk in patients with sepsis and screening of biomarkers for prognosis of patients with myocardial injury

Weiwei Qian [a,b,1], Cunqiao Han [a,b,1], Shenglong Xie [c], Shuyun Xu [a,*]

[a] Laboratory of Emergency Medicine, West China Hospital, and Disaster Medical Center, Sichuan University, Chengdou, 610041, PR China
[b] Shangjinnanfu Hospital, West China Hospital, Sichuan University, PR China
[c] Department of Thoracic Surgery, Sichuan Provincial People's Hospital, Sichuan Academy of Medical Sciences, Chengdou, 610041, PR China

ARTICLE INFO

*Keywords:*
Biomarker
Myocardial injury
Predictive model
Sepsis

ABSTRACT

This study aimed to create a robust prediction model for sepsis patient mortality and identify key biomarkers in those with myocardial injury. A retrospective analysis of 261 sepsis inpatients was conducted, with 44 deaths and 217 recoveries. Key factors were assessed via univariate and multivariate analyses, revealing myocardial injury, shock, and pulmonary infection as independent mortality risk factors. Using LASSO regression, a reliable prediction model was developed and internally validated. Additionally, procalcitonin (PCT) emerged as a sensitive biomarker for myocardial injury prediction in sepsis patients. In summary, this study highlights myocardial injury, shock, and pulmonary infection as independent risk factors for sepsis-related deaths. The LASSO-based prediction model effectively forecasts the prognosis of septic patients with myocardial injury, with PCT showing promise as a predictive biomarker.

## 1. Introduction

Sepsis, a condition characterized by life-threatening organ dysfunction resulting from the body's dysfunctional response to infection, poses a growing global health challenge. Recent data indicate an annual increase of 19 million sepsis cases worldwide, with a mortality rate exceeding that of stroke [1,2]. Sepsis-related mortality in hospitals and intensive care units (ICUs) ranges from 33.5% to 48.7%, particularly among patients experiencing sepsis accompanied by multiple organ dysfunction [3]. Thus, the accurate prediction of mortality risk and identification of associated risk factors in sepsis patients are crucial for informed clinical decision-making [4].

Clinical observations reveal that approximately 50% of individuals with severe sepsis also exhibit left ventricular systolic dysfunction [5]. A critical aspect of myocardial injury in sepsis is the apoptosis of cardiomyocytes [6,7]. Numerous endotoxins produced during sepsis trigger a cascade of apoptotic processes, leading to cardiomyocyte apoptosis and necrosis [8]. Earlier studies have additionally underscored that myocardial injury serves as a significant prognostic factor in sepsis patients [9,10]. One pressing clinical challenge is the prediction of outcomes in sepsis patients with myocardial injury, enabling timely interventions.

This retrospective analysis seeks to develop a predictive model for assessing the risk of death in sepsis patients, particularly focusing on those with myocardial injury. Through an in-depth examination of biomarker trends, we aim to identify markers that can help

* Corresponding author.
*E-mail address:* 120xsy@163.com (S. Xu).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.heliyon.2024.e27209
Received 19 March 2023; Received in revised form 24 February 2024; Accepted 26 February 2024
Available online 29 February 2024

predict sepsis in combination with myocardial injury.

## 2. Methods

### 2.1. Patients collection

This study is a retrospective cohort analysis. Patients with sepsis who underwent standardized diagnosis and treatment in the hospital from January 1, 2018, to January 1, 2020, were collected retrospectively. All experiments involving human beings were conducted by conforming to the ethical standards of the national research committee and the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. This study was approved by the Ethics Committee of the West China Hospital of Sichuan University (2021YFS0189). All specimens were collected with the written consent of patients and ethical approval.

Inclusion criteria:

1) Patients with sepsis who met the Sepsis3.0 diagnostic criteria [11].
2) The patient was $\geq$18 years old.

Exclusion criteria:

1) Incomplete clinical data during hospitalization.
2) Automatic discharge affects the judgment of the outcome.

The criteria for diagnosing myocardial injury.

Clinical Symptoms and Signs: Chest pain or discomfort (angina) that may radiate to the arms, jaw, or back. Shortness of breath. Profound fatigue. Cold sweats. Nausea or vomiting.

Electrocardiogram (ECG or EKG):

Cardiac Biomarkers: Cardiac-specific biomarkers released into the bloodstream due to myocardial injury include: Troponin: Elevated troponin levels are a key indicator of myocardial injury. Creatine Kinase-MB (CK-MB): An increase in CK-MB levels can also suggest myocardial injury. Myoglobin: Elevated myoglobin levels may be an early sign of myocardial injury.

Imaging Studies:Echocardiogram (Echo): This ultrasound imaging technique can reveal abnormalities in the structure and function of the heart, such as reduced ejection fraction or wall motion abnormalities.

Cardiac MRI: Magnetic resonance imaging can provide detailed images of the heart and identify areas of damage.

### 2.2. Patient grouping

1) Patients with sepsis were divided into dead and alive groups according to the clinical outcome after treatment.
2) Patients with sepsis complicated with myocardial injury were divided into the dead group and alive group according to whether they survived after treatment.

### 2.3. Clinical information collection

1) Basic clinical data of patients: age, sex, and complications (myocardial injury and shock).
2) Patients' personal history: chronic obstructive pulmonary disease, hypertension, diabetes, renal insufficiency, cardiac insufficiency, tumor history, trauma history, and immunodeficiency. The study was conducted in accordance with the Declaration of the Helsinki and approved by the Institutional Review Board of the Sichuan Academy of Medical Science·Sichuan Provincial People's Hospital (Chengdu, China). Written informed consents were signed by all the enrolled individuals.
3) Infection sites: pulmonary infection, abdominal infection, and urinary system infection.
4) Pathogens: MRSA, fungi, *Escherichia coli*, Streptococcus pneumoniae, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, Acinetobacter baumannii, Pneumocystis carinii, and *Staphylococcus aureus*.
5) Laboratory test indexes (BNP, high sensitivity troponin I, CK-MB, myoglobin, creatinine, and PCT) before treatment, 5, 10, and 15 days after treatment in sepsis patients complicated with myocardial injury.

### 2.4. Statistical analysis

Statistical analysis was conducted using SPSS version 26.0, R version 4.0.1, and GraphPad version 8.0.1 software. To assess the normality of continuous variables, the Shapiro-Wilk (SmurW) test was employed. For normally distributed data, descriptive statistics are presented as mean $\pm$ standard deviation, and group comparisons were conducted using independent sample t-tests. Non-normally distributed data were represented as median with interquartile range (25% and 75% quartile), and group comparisons were performed using the Mann-Whitney *U* test. In R version 4.0.3, we performed the establishment and validation of multivariate analysis and the development of a clinical prediction model. Logistic proportional hazard regression analysis was applied for both univariate and multivariate analyses, leading to the creation of the corresponding clinical prediction model. To visually illustrate the impact of each risk factor, a line chart was generated to display the scores. The robustness of the model was assessed through internal validation,

including the calculation of the C-index and the construction of a calibration curve. It's worth noting that our study yielded statistically significant test results, including the multivariate Cox proportional hazard regression outcomes.

## 3. Results

### 3.1. Comparative analysis of clinical characteristics of survival/death sepsis patients

Through inclusion, exclusion criteria, and follow-up integrity, 261 sepsis patients were included in this study, of which 44 died and 217 improved after treatment. The basic clinical information of the two groups is illustrated in Table 1. The patients in the survival group were 65.41 ± 17.44 years old, and that in the death group were 66.52 ± 20.06 years old. There were 130 male patients in the survival group and 28 in the death group. There was no significant difference in age and sex between the two groups ($P > 0.05$). The proportion of myocardial injury (41 *vs*. 118) and shock (32 *vs*. 37) in the death group was significantly higher than that in the survival group ($P < 0.05$). The results of the personal history comparison demonstrated that there was no significant difference in the proportion of patients with chronic obstructive pulmonary disease (3 *vs*. 15), hypertension (8 *vs*. 54), diabetes mellitus (9 *vs*. 76), renal insufficiency (4 *vs*. 46), history of trauma (1 *vs*. 4), and immunodeficiency (3 *vs*. 7) between the death group and the survival group. However, the proportion of cardiac insufficiency (0 *vs*. 22) in the death group was significantly lower than in the survival group. The proportion of patients with personal tumor history in the death group was significantly higher than that in the survival group (9 *vs*. 16 min, $P < 0.05$). The results indicated that the proportion of pulmonary infection in the death group was significantly higher than that in the survival group (33 *vs*. 113, $P < 0.05$), and the proportion of urinary infection was significantly lower than that in the survival group (1 *vs*. 36, $P < 0.05$). Comparative analysis of pathogens demonstrated no significant difference in the proportion of patients infected with MRSA, fungi, *Escherichia coli*, Streptococcus pneumoniae, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, Acinetobacter baumannii, Pneumocystis carinii, and *Staphylococcus aureus* between the two groups.

### 3.2. Univariate and multivariate logistic analysis of survival/death in patients with sepsis

Univariate Logistic regression analysis revealed that age, myocardial injury, shock, pulmonary infection, Acinetobacter baumannii infection, and *Staphylococcus aureus* infection were the different factors between the survival group and the death group (Table 2, $P < 0.05$). The results of multivariate Logistic regression analysis revealed that myocardial injury, shock, and pulmonary infection were independent risk factors for death in sepsis patients (Table 2, $P < 0.05$).

**Table 1**
Baseline characteristics of sepsis patients.

| | | Alive(n = 217) | Dead(n = 44) | $t/x^2$ value | P value |
|---|---|---|---|---|---|
| age | | 65.41 ± 17.44 | 66.52 ± 20.06 | −0.37 | 0.45 |
| Sex | Male | 130 | 28 | | |
| | Female | 87 | 16 | 0.21 | 0.65 |
| Myocardial Injury | | 118 | 41 | 23.14 | <0.01 |
| Shock | | 37 | 32 | 58.31 | <0.01 |
| COPD | | 15 | 3 | 0.01 | 0.98 |
| Hypertension | | 54 | 8 | 0.91 | 0.34 |
| Diabetic | | 76 | 9 | 3.54 | 0.05 |
| Renal Insufficiency | | 46 | 4 | 3.47 | 0.05 |
| Cardiac Insufficiency | | 22 | 0 | 4.87 | 0.02 |
| Tumor | | 16 | 9 | 7.23 | <0.01 |
| Trauma | | 4 | 1 | 0.03 | 0.85 |
| Immune Insufficiency | | 7 | 3 | 1.28 | 0.26 |
| Infection | | | | | |
| | Pulmonary Infection | 113 | 33 | 7.64 | <0.01 |
| | Abdominal Infection | 43 | 4 | 2.85 | 0.07 |
| | Urinary Infection | 36 | 1 | 6.16 | 0.01 |
| Pathogene | | | | | |
| | MRSA | 7 | 2 | 0.19 | 0.66 |
| | Escherichia Coli | 53 | 7 | 1.53 | 0.21 |
| | Fungus | 12 | 4 | 0.81 | 0.37 |
| | streptococcus | 2 | 0 | 0.41 | 0.52 |
| | Pseudomonas Aeruginosa | 12 | 2 | 0.07 | 0.79 |
| | Acinetobacter Baumannii | 15 | 5 | 1.02 | 0.31 |
| | Staphylococcus Aureus | 12 | 2 | 0.07 | 0.79 |
| | Klebsiella Pneumoniae | 26 | 6 | 0.09 | 0.76 |
| | Pneumocystis Carinii | 1 | 0 | 0.20 | 0.65 |

**Table 2**
Univariate and multivariate Logistic analysis of survival/death in patients with sepsis.

| Coef | S.E. | Wald | Z | Pr(>\|Z\|) | S.E. | Wald | Z | Pr(>\|Z\|) |
|---|---|---|---|---|---|---|---|---|
| | Univariate | | | | multivariate | | | |
| sex | 1.7641 | 1.1171 | 1.58 | 0.1143 | | | | |
| age | 0.1562 | 0.0757 | 2.06 | 0.039 | | | | |
| Myocardial Injury | 4.8993 | 1.2329 | 2.54 | 0.0034 | 4.34 | 1.23 | 2.32 | 0.02 |
| Shock | 5.9697 | 1.8845 | 3.17 | 0.0015 | 4.54 | 1.56 | 3.12 | 0.01 |
| COPD | 1.2911 | 1.6315 | 0.79 | 0.4287 | | | | |
| hypertension | −0.9656 | 1.2602 | −0.77 | 0.4435 | | | | |
| diabetic | −1.7732 | 1.5933 | −1.11 | 0.2657 | | | | |
| Renal Insufficiency | 2.0621 | 1.3802 | 1.49 | 0.1352 | | | | |
| Cardiac Insufficiency | −7.9225 | 30.7767 | −0.26 | 0.7969 | | | | |
| tumor | 1.6077 | 1.372 | 1.17 | 0.2413 | | | | |
| Trauma | −5.0811 | 67.0713 | −0.08 | 0.9396 | | | | |
| ImmuneInsufficiency | 3.6657 | 2.1855 | 1.68 | 0.0935 | | | | |
| PulmonaryInfection | 3.0486 | 1.5099 | 2.02 | 0.0435 | 2.12 | 1.67 | 1.42 | 0.04 |
| AbdominalInfection | −0.3744 | 1.7862 | −0.21 | 0.834 | | | | |
| UrinaryInfection | 1.2183 | 1.8403 | 0.66 | 0.508 | | | | |
| MRSA | 5.6588 | 4.1478 | 1.36 | 0.1725 | | | | |
| EscherichiaColi | 1.1982 | 1.3013 | 0.92 | 0.3572 | | | | |
| Fungus | 4.2326 | 2.6802 | 1.58 | 0.1143 | | | | |
| streptococcus | −0.8773 | 108.7187 | −0.01 | 0.9936 | | | | |
| PseudomonasAeruginosa | 2.5048 | 2.1904 | 1.14 | 0.2528 | | | | |
| AcinetobacterBaumannii | 5.8981 | 2.3207 | 2.54 | 0.011 | 1.23 | 0.67 | 1.12 | 0.23 |
| StaphylococcusAureus | 6.1793 | 2.7553 | 2.24 | 0.0249 | 1.36 | 0.88 | 1.94 | 0.45 |
| KlebsiellaPneumoniae | 2.3774 | 29.7421 | −0.08 | 0.9363 | | | | |

### *3.3. Establishment and verification of survival/death prediction model for sepsis patients*

Because many factors are included in this study's initial stage, the prediction model is further established, and the dimension reduction screening variables are selected using LASSO elastic regression. The LASSO regression results are displayed in Fig. 1a, and the appropriate variables (Table S1, Fig. 1b) were chosen when they landed. The results demonstrated that nine factors, including myocardial injury, shock, hypertension, MRSA, cardiac insufficiency, personal history of tumor, pulmonary infection, abdominal infection, and urinary system infection, were screened by LASSO regression. Furthermore, multivariate regression analysis demonstrated that myocardial injury, shock and pulmonary inefction were relatively independent risk factors (Table 2, $P < 0.05$). Therefore, the nomogram is drawn based on the above nine factors, and the results can be seen in Fig. 1c. Furthermore, to evaluate the reliability of the line chart, internal verification draws calibration curve results to depict that the predicted results are in good agreement with the actual results (Fig. 1d). Internal verification draws ROC curve and calculates the curve area as 0.87 (95% CI: 0.84–0.89) (Fig. 1e–f).

### *3.4. Screening of biomarkers in patients with sepsis complicated with myocardial injury*

Previous studies showed that the prognosis of sepsis patients with myocardial injury worsened significantly. On this basis, this study retrospectively collected the expression of patients with sepsis at different stages during treatment to clarify the value of biomarkers in judging the prognosis of patients with sepsis complicated with myocardial injury. The changing trend of each biomarker is shown in Fig. 2 a-f. The results showed that the expression levels of BNP, Troponin, CK-MB, and myoglobin in the death group were significantly higher than those in the survival group during treatment. In addition, the creatinine and PCT ex After treatment, there was no significant difference in the expression of creatinine and PCT between the two groups. Based on the biomarkers before treatment, the clinical outcome events of sepsis complicated with myocardial injury were predicted, the ROC curve was drawn, and the area under the curve was calculated. Fig. 3 a-f depicts the ROC curve for each biomarker, and Table 3 depicts the area under the curve. Table 4 results showed that the AUC of PCT was significantly higher than that of the other five biomarkers, suggesting that PCT may be an effective biomarker for predicting the prognosis of sepsis patients with myocardial injury.

## 4. Discussion

In this study, sepsis patients were selected retrospectively. The results showed that sepsis patients with myocardial injury, shock, and pulmonary infection were independent risk factors for death. Furthermore, based on myocardial injury, shock, hypertension, MRSA, cardiac insufficiency, personal tumor history, pulmonary infection, abdominal infection, and urinary system infection, a predictive model and internal verification results show that the model is highly reliable.

The changing trend of biomarker expression in sepsis patients with myocardial injury was observed. ROC curve showed that PCT was a sensitive biomarker for predicting sepsis with myocardial injury [12,13]. Sepsis is a life-threatening organ dysfunction caused by the imbalance of infection response, and its morbidity and mortality are very high [14]. According to the latest report in the Lancet, 48.9 million sepsis cases were recorded worldwide in 2017, and 11 million sepsis-related deaths accounted for about 20% of global

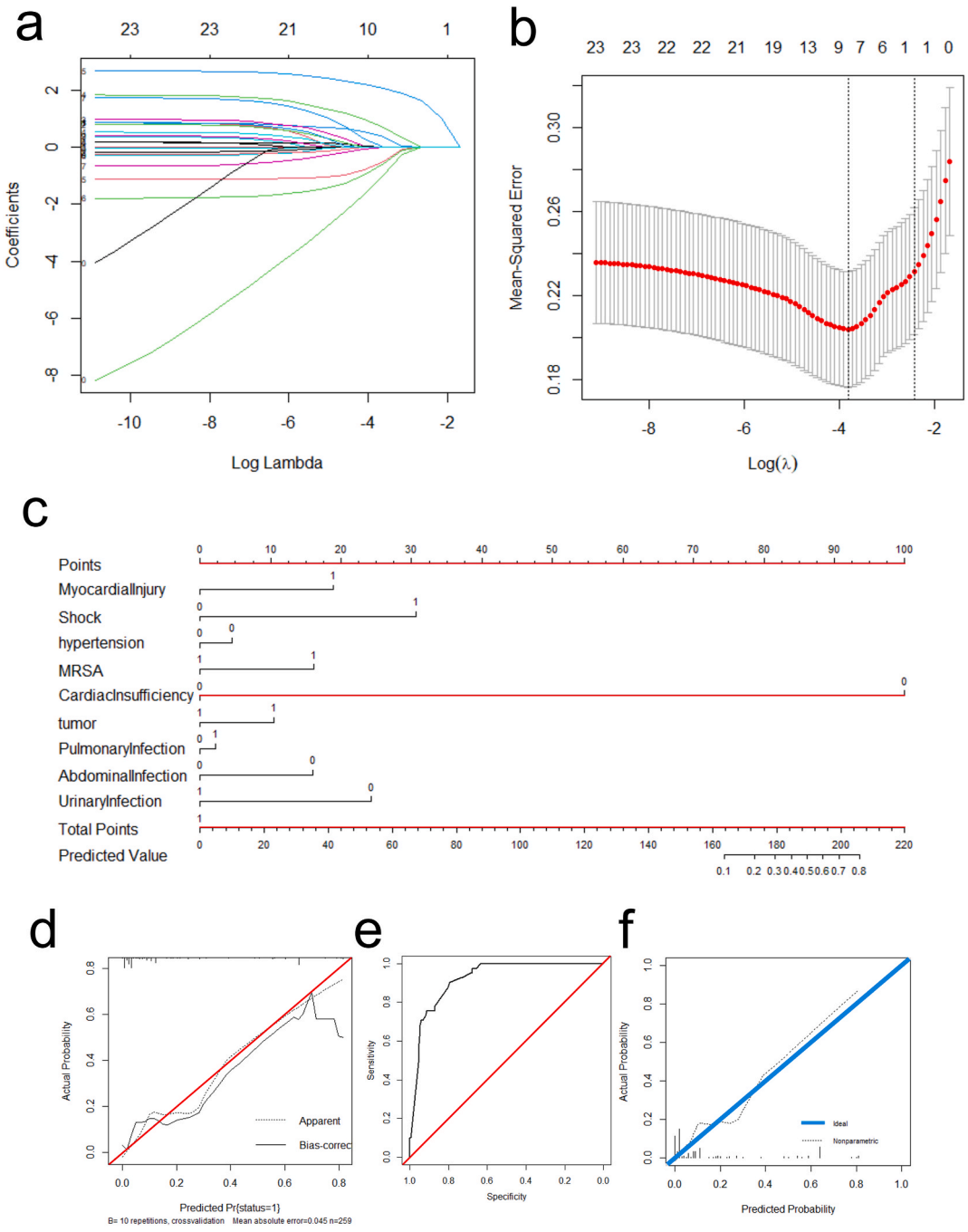



**Fig. 1.** Establishment and verification of survival/death prediction model for sepsis patients. (A–B) LASSO regression analysis based on each variable. (C) Nomogram of the prediction model for sepsis patients. (D) Calibration curve by internal validation. (E) ROC curve by internal validation. (F) DCA curve by internal validation.

deaths [15]. In developed countries, such as the United States, there are about 1.7 million cases of sepsis each year and about 270000 sepsis-related deaths [16]. Furthermore, sepsis is the leading cause of death among patients in intensive care units (ICU) in low-and middle-income countries, with a mortality rate of 80% [17]. The World Health Organization has recognized the significant threat of sepsis to global health and has strengthened the prevention, diagnosis, and treatment of sepsis [18]. This study included 261 patients, 44 of whom died, yielding a death rate of 16.8%. Therefore, identifying the risk factors that increase the risk of death in sepsis patients helps promote targeted clinical decision-making. Through retrospective analysis, it was finally shown that sepsis patients with myocardial injury, shock, and pulmonary infection were independent risk factors for poor prognosis.

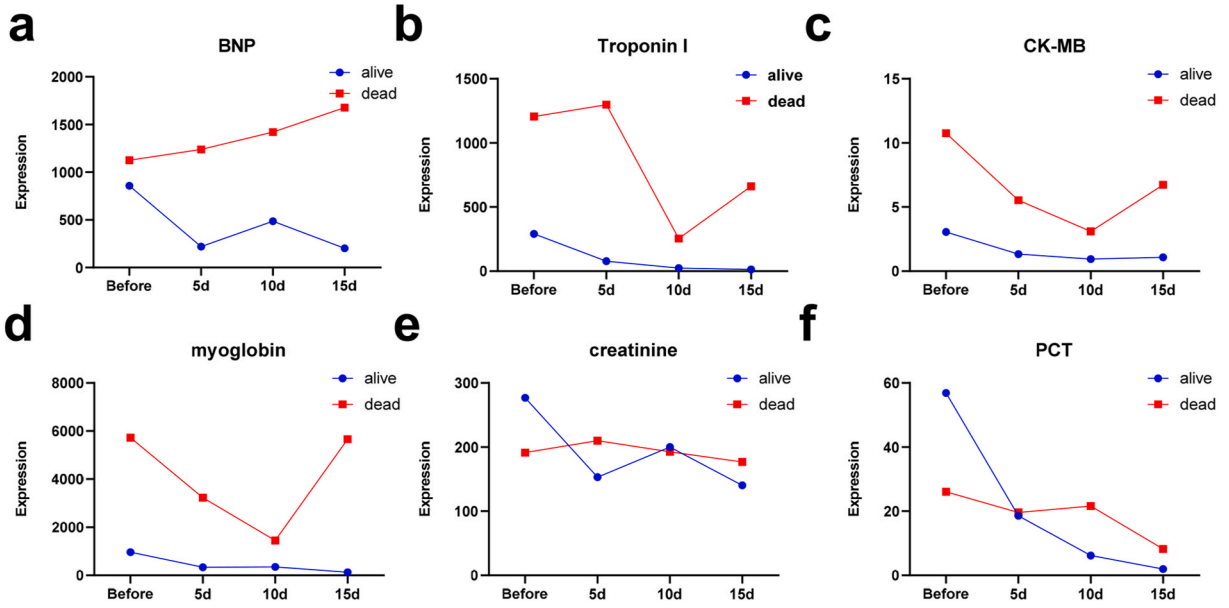



**Fig. 2.** Biomarkers expressions during treatment in septic patients with myocardial injury. Note: (A–F) The expression of biomarkers. BNP, Troponin I, CK-MB, myoglobin, creatinine, and PCT in different groups of septic patients with myocardial injury before treatment and 5, 10, and 15 days after treatment.

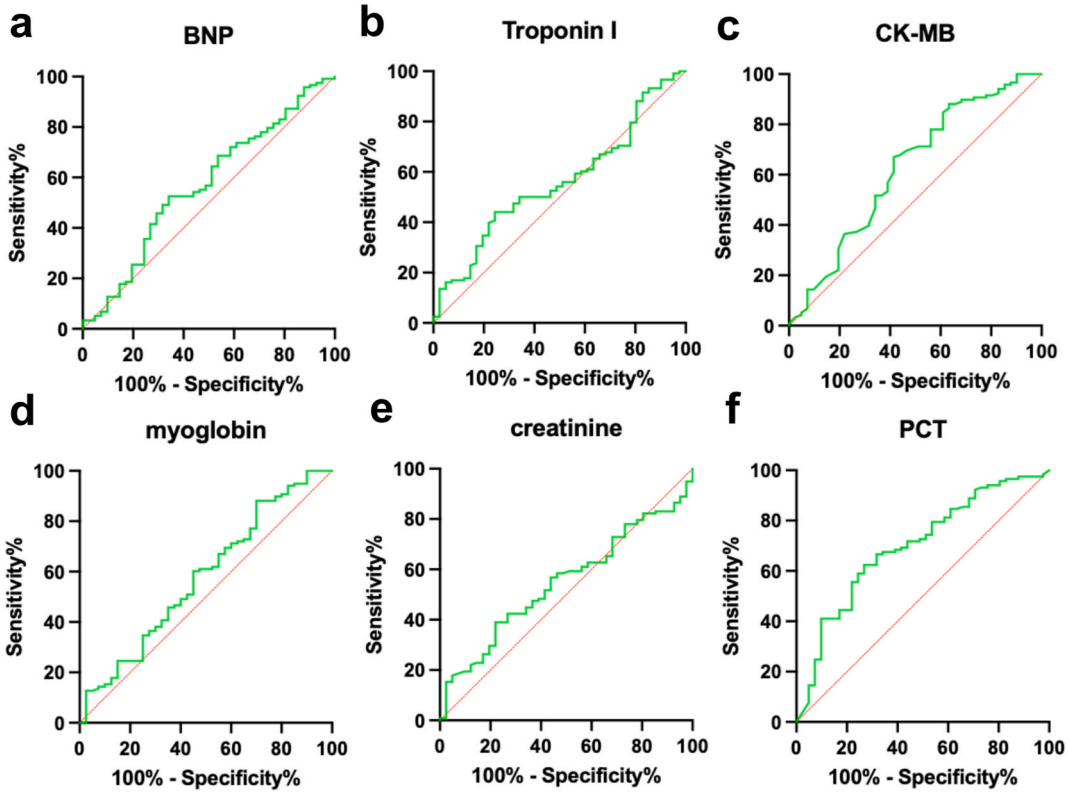



**Fig. 3.** ROC curves of each biomarker in septic patients with myocardial injury. (A–F) ROC curves of each biomarker (BNP, Troponin I, CK-MB, myoglobin, creatinine, and PCT) in septic patients with myocardial injury predict the survival of each patient.

**Table 3**
Multivariate Logistic analysis in patients with sepsis based on LASSO and univariate analysis.

| Coef | S.E. | Wald | Z | Pr(>\|Z\|) |
|---|---|---|---|---|
| Intercept | −3.8123 | 0.7784 | −4.9 | <0.0001 |
| MyocardialInjury | 1.607 | 0.6752 | 2.38 | 0.0173 |
| Shock | 2.61 | 0.4867 | 5.36 | <0.0001 |
| hypertension | −0.3895 | 0.5263 | −0.74 | 0.4592 |
| MRSA | 1.3773 | 1.1166 | 1.23 | 0.2174 |
| CardiacInsufficiency | −8.514 | 22.4798 | −0.38 | 0.7049 |
| tumor | 0.8856 | 0.6125 | 1.45 | 0.1482 |
| PulmonaryInfection | 0.1852 | 0.5661 | 0.33 | 0.7436 |
| AbdominalInfection | −1.3566 | 0.7779 | −1.74 | 0.0812 |
| UrinaryInfection | −2.0634 | 1.1174 | −1.85 | 0.0648 |

**Table 4**
The AUC of each factor under the regression analysis.

| Biomarkers | AUC | 95%CI |
|---|---|---|
| BNP | 0.5682 | 0.46–0.67 |
| Troponin I | 0.55 | 0.46–0.65 |
| CK-MB | 0.62 | 0.51–0.73 |
| myoglobin | 0.57 | 0.47–0.68 |
| creatinine | 0.54 | 0.45–0.64 |
| PCT | 0.69 | 0.61–0.79 |

The pathophysiological changes of sepsis are based on systemic inflammatory responses induced by severe infection [19]. Inflammatory mediators, cytokines, reactive oxygen free radicals, mitochondrial dysfunction, and gene expression can directly damage cardiomyocytes or lead to the abnormal energy metabolism of cardiomyocytes, resulting in myocardial injury [20]. Sepsis3.0 defines septic shock as a subtype of sepsis. If circulation cannot be maintained after initial positive goal-directed fluid resuscitation, vasoactive drugs should be used to ensure tissue perfusion pressure [21]. However, up to now, there remains a relative lack of effective indicators that can help identify sepsis-related cardiac diastolic dysfunction in the early stage [22]. The secretion and release of natriuretic peptides increase rapidly after myocardial injury, left ventricular filling pressure, and wall tension, which has a specific diagnostic value for diastolic cardiac insufficiency and myocardial injury [23]. However, many factors such as age, renal insufficiency, and pulmonary hypertension may affect the secretion of natriuretic peptides, especially in sepsis patients, which may be related to the pathophysiological changes and volume resuscitation of sepsis [24,25]. Therefore, finding more reliable and accurate biomarkers in clinical work is necessary to promote the implementation of clinical decision-making.

By drawing ROC curves based on various biomarkers, this study showed that PCT has a high predictive value for the prognosis of sepsis patients complicated with myocardial injury. Therefore, this study suggests that PCT may be a sensitive biomarker. PCT, composed of 116AA, is a kind of procalcitonin peptide with no hormone activity, which is transcribed and synthesized by the Calc-1 gene of thyroid medulla cells, which is no more than 0.05 μg/L in healthy people. PCT can rapidly increase when there is a severe bacterial infection. When it exceeds 0.05 μg/L, we should pay attention to the possibility of sepsis. Therefore, PCT is considered an important sign of bacterial infection and a reliable index to judge the severity and prognosis of the disease. Concurrently, PCT can guide the use of early antibiotics and provide a basis for selecting antibiotics, thus reducing the mortality of infected patients. The results of the univariate analysis showed that PCT in the death group was significantly higher than that in the survival group, and unconditional Logistic regression analysis also showed that PCT was a risk factor for the prognosis of sepsis. According to some studies, the level of PCT is positively correlated with the degree of inflammation and can be reduced to normal by improving the condition. Through this study, we also confirmed the importance of dynamic monitoring of PCT levels in judging the disease and guiding the treatment of sepsis.

This study still has some limitations. As it is a retrospective study, the level of evidence is not high. Therefore, this work intends to conduct a prospective cohort study to verify the conclusions further.

Sepsis patients with myocardial injury, shock, and pulmonary infection are independent risk factors for death. Based on myocardial injury, shock, hypertension, MRSA, cardiac insufficiency, personal tumor history, pulmonary infection, abdominal infection, and urinary system infection, a predictive model and internal verification results show that the model is highly reliable. Therefore, PCT is a sensitive biomarker for predicting sepsis with myocardial injury.

## Funding statement

This work was funded by Sichuan Provincial Science and Technology Department Project (2021YFS0189).

## Additional information

Supplementary content related to this article has been published online at XXXX.

## Data availability statement

All data generated or analyzed during this study are included in this published article.

## CRediT authorship contribution statement

**Weiwei Qian:** Writing – review & editing, Writing – original draft, Software, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Cunqiao Han:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Shenglong Xie:** Writing – original draft, Visualization, Project administration, Formal analysis, Conceptualization. **Shuyun Xu:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Shuyun Xu reports financial support was provided by Sichuan Provincial Science and Technology Department Project. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e27209.

## References

[1] T. Li, et al., Clinical value of prognostic nutritional index in prediction of the presence and severity of neonatal sepsis, J. Inflamm. Res. 14 (2021) 7181–7190.
[2] R. Garg, et al., Mukhopadhyay, Epidemiology of sepsis and risk factors for mortality in intensive care unit: a hospital based prospective study in South India, Infect Dis (Lond). 54 (5) (2022) 325–334.
[3] H. Huang, et al., Correlation of B-type natriuretic peptide level with hemodynamic parameters and inflammatory cytokines in patients with gram-negative sepsis], Zhongguo Yi Xue Ke Xue Yuan Xue Bao 43 (6) (2021) 879–885.
[4] Y.H. Tang, et al., Risk factors and predictive markers for early and late-onset neonatal bacteremic sepsis in preterm and term infants, J. Chin. Med. Assoc. 85 (4) (2022) 507–513.
[5] E. O.R, et al., Umbilical cord procalcitonin to detect early-onset sepsis in newborns: a promising biomarker, Front Pediatr 9 (2021) 779663.
[6] Q. Ou, G. Cai, Y. Zhou, M. Wen, [Analysis of clinical features and risk factors for mortality in patients with culture-negative sepsis: a single-center retrospective cohort study based on MIMIC-IV], Zhonghua Wei Zhong Bing Ji Jiu Yi Xue 33 (10) (2021) 1181–1186.
[7] M. Letouzey, et al., EPIPAGE-2 infectious diseases working group. early antibiotic exposure and adverse outcomes in very preterm infants at low risk of early-onset sepsis: the EPIPAGE-2 cohort study, J. Pediatr. 243 (2022) 91–98.e4.
[8] S. Guan, et al., UPLC-Q-TOF/MS-Based Plasma and urine metabolomics contribute to the diagnosis of sepsis, J. Proteome Res. 21 (1) (2022 Jan 7) 209–219.
[9] U.M. Wallgren, et al., Keywords reflecting sepsis presentation based on mode of emergency department arrival: a retrospective cross-sectional study, Int. J. Emerg. Med. 14 (1) (2021 Dec 20) 78.
[10] I.T. Albabtain, et al., Risk factors for the systemic inflammatory response syndrome and sepsis following surgical management of acute intestinal obstruction, Int. J. Health Sci. 15 (6) (2021 Nov-Dec) 28–33.
[11] J. Shibata, et al., Risk factors of sepsis among patients with qSOFA<2 in the emergency department, Am. J. Emerg. Med. 50 (2021) 699–706.
[12] Y.W. Liang, et al., Incidence, prognosis, and risk factors of sepsis-induced cardiomyopathy, World J Clin Cases 9 (31) (2021) 9452–9468.
[13] A.L. Johnson, et al., Bacteraemia, sepsis and antibiotic resistance in Australian patients with cirrhosis: a population-based study, BMJ Open Gastroenterol 8 (1) (2021) e000695.
[14] J. Hu, X. Qin, Bacteria profiles and risk factors for proven early-onset sepsis in preterm neonates, Saudi Med. J. 42 (12) (2021) 1281–1288.
[15] Y. Wu, S. Huang, X. Chang, Understanding the complexity of sepsis mortality prediction via rule discovery and analysis: a pilot study, BMC Med Inform Decis Mak 21 (1) (2021) 334.
[16] M. Wu, et al., Severe COVID-19-associated sepsis is different from classical sepsis induced by pulmonary infection with carbapenem-resistant klebsiella pneumonia (CrKP), Chin. J. Traumatol. 25 (1) (2022) 17–24.
[17] H. Zhang, D. Chen, L. Wang, et al., Influencing factors and prevention of sepsis or acute kidney injury in 85 patients with severe trauma, Evid Based Complement Alternat Med 2021 (2021) 5754114.
[18] D.C. de Souza, et al., SPREAD PED investigators and the instituto latino americano de sepsis network. the epidemiology of sepsis in paediatric intensive care units in Brazil (the sepsis PREvalence assessment database in pediatric population, SPREAD PED): an observational study, Lancet Child Adolesc Health 5 (12) (2021) 873–881.
[19] Y. Zhang, et al., Predictive value of immune cell subsets for mortality risk in patients with sepsis, Clin. Appl. Thromb. Hemost. 27 (2021) 10760296211059498.
[20] G.D. Sun, , et al.Zhao, Multiple organ dysfunction syndrome caused by sepsis: risk factor analysis, Int. J. Gen. Med. 14 (2021) 7159–7164.
[21] J.Y. Li, et al., Efficiency of monocyte/high-density lipoprotein cholesterol ratio combined with neutrophil/Lymphocyte ratio in predicting 28-day mortality in patients with sepsis, Front. Med. 8 (2021) 741015.
[22] X. Chen, et al., Clinical value of the lactate/albumin ratio and lactate/albumin ratio × age score in the assessment of prognosis in patients with sepsis, Front. Med. 8 (2021) 732410.

[23] C. Duazo, et al., In-hospital cardiac arrest in patients with sepsis: a national cohort study, Front. Med. 8 (2021) 731266.
[24] M Huang, et al., Stress ulcer prophylaxis in critically ill adult patients with sepsis at risk of gastrointestinal bleeding: a retrospective cohort study, Intern. Med. J. 53 (3) (2023) 389, 369.
[25] C. Lin, et al., Complicated streptococcus a*galactiae* sepsis with/without meningitis in young infants and newborns: the clinical and molecular characteristics and Outcomes, Microorganisms 9 (10) (2021) 2094.