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Cardiac troponin-T combined with Hemoglobin and some clinical characteristics to predict mortality of sepsis patients in adult: A retrospective cohort study

Kai-Zhi Xu
Zhejiang Provincial People's Hospital
Ping Xu
Zhejiang Provincial People's Hospital
Juan-Juan Li
Zhejiang Provincial People's Hospital
A-Fang Zuo
Zhejiang Provincial People's Hospital
Shu-Bao Wang
Zhejiang Provincial People's Hospital
Fan Han (hf200212@163.com)
Zhejiang Provincial People's Hospital

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Abstract

Objective: This study was conducted to evaluate the prognostic value of serum cardiac troponinT(cTnT) combined with hemoglobin level and some clinical characteristics in patients with sepsis in ICU.

Methods: Data were extracted from an online database called Multiparameter Intelligent Monitoring in Intensive Care III. 2886 patients were included. All patients were divided into survival group and death group according to whether they died during hospitalization. Demographic characteristics of patients and laboratory data of peripheral blood cTnT, hemoglobin, lactic acid, creatinine, sodium, potassium, glucose, white blood cell count, Sequential Organ Failure Assessment (SOFA) score , respiratory rate and heart rate of patients admitted to ICU were collected to analyze the differences of each variable between the two groups. Multivariate Logistic regression was used to analyze the influence of factors on hospital mortality We use Receiver operating characteristic (ROC) curve to analyze the value of each index to evaluate the clinical prognosis of patients admitted to ICU.

Results: Age, respiration rate, heart rate, SOFA score, troponin T, serum potassium, creatinine, urea and lactic acid levels in death group were significantly higher than those in survival group (all $P < 0.05$), while platelet, serum sodium and hemoglobin levels were significantly lower than those in survival group (all $P<0.05$).Multivariate Logistic regression analysis showed that mortality was significantly higher in older patients (OR: 1.022, 95%CI 1.015 to 1.029, $P<0.001$). At the same time, respiratory rate and heart rate at admission to ICU also significantly affected the prognosis of patients (OR: 1.019, 1.008, $P =0.001$, $P<0.001$, respectively), SOFA score was positively correlated with mortality (OR: 1.141, 95%CI 1.114 to 1.148, $P< 0.001$). Increased cTnT and lactic acid levels were associated with increased mortality (OR: 1.088, 1.292, $P =0.02$, $P<0.001$, respectively). However, hemoglobin as a protective factor was significantly negatively correlated with mortality (OR: 0.948, 95%CI 0.907 to 0.991, $P =0.018$), and serum potassium, creatinine and urea were positively correlated with mortality (ALL $P<0.05$), increased serum sodium level was associated with reduced mortality as a protective factor (OR: 0.979, 95%CI 0.965 to 0.994, $P =0.005$).ROC curve showed that for cTnT and hemoglobin alone, The area under the receiver operating characteristic curve(AUROC) were 0.548 (95% CI.: 0.53-0.567) and 0.528 (95% CI.: 0.509-0.546); After combining other variables, AUROC reached 0.732 (95% CI.:0.715-0.748). The sensitivity and specificity were 64.2% and 70.62%, respectively, which were higher than those of single index.

Conclusions: The levels of hemoglobin and cTnT in ICU patients with sepsis may affect the prognosis of patients, and the effect of multifactor combined test on the prognosis of sepsis is better than that of a single indicator. Treatment strategies that improve the factors identified in this study may improve the inpatient survival rate of these ICU patients.

Introduction

Sepsis is a systemic inflammatory response syndrome caused by bacteria and other pathogenic microorganisms. In addition to systemic inflammatory response syndrome and primary infection lesions,

severe patients often have manifestations of organ hypoperfusion. Sepsis is the main cause of death in ICU patients without heart disease [1]. In 2016, ESICM(European Society of Intensive Care Medicine) and SCCM(Society of Critical Care Medicine) proposed the definition of Sepsis 3.0[1]. Until now, sepsis was considered "a life-threatening organ dysfunction caused by the body's malfunctioning response to infection." However, myocardial injury is the most common complication of organ dysfunction in patients with sepsis. According to research, about 40%-50% of patients with sepsis are accompanied by myocardial injury of varying degrees, and the fatality rate of patients with sepsis combined with myocardial injury can be as high as 70%[2]. As for the diagnostic criteria of sepsis myocardial injury, there is still no conclusion. With the rapid development of cellular and molecular biology, it has become a research hotspot for scholars to find the latest biomarkers of sepsis myocardial injury. Unfortunately, the pathogenesis of sepsis myocardial injury has not been clarified, and the correlation between many novel biomarkers and sepsis myocardial injury is controversial. Therefore, the diagnosis of myocardial injury in sepsis still relies on troponin, echocardiography and other traditional indicators. However, echocardiography, as an imaging diagnosis method of myocardial injury in sepsis, has some shortcomings, that is, different technical levels of sonographers lead to great differences in measurement results. Troponin is a recognized indicator of myocardial injury in acute coronary syndrome[3]. troponin in plasma of patients with sepsis is elevated, which is related to myocardial injury in sepsis[4]. Some basic studies suggest that [5] the increase of troponin in sepsis myocardial injury is not caused by myocardial cell death which caused by myocardial ischemia, but is related to increased permeability of myocardial cell membrane and troponin leakage caused by myocardial inhibitory factors, oxidative stress and inflammatory response. A retrospective study[6]found that increased cTnT was closely related to the severity and mortality of sepsis, and increased the risk of death of patients with sepsis. However, another study [7] suggested that there was no significant difference between the assessment of cTnT at 24 hours upon admission and the 28-day mortality. The different results may be due to the critical threshold of cTnT elevation or the difference in the timing of troponin measurement. Masson et al. [8]suggested that early changes in troponin may be a better predictor of poor prognosis than static troponin levels.

Reduced hemoglobin (Hb) levels are often observed in patients with septic shock, and the possible causes include decreased erythropoiesis due to systemic inflammatory response, hemolysis, and increased erythrocyte destruction caused by hemorrhage[9]. Septic shock patients with low Hb levels may exacerbate tissue oxygenation damage by reducing arterial oxygen concentration. Therefore, maintaining appropriate Hb level has been proposed as one of the strategies to reduce tissue damage caused by shock [10]. Hb level < 70g/L is one of the indications for immediate transfusion, but the critical value of transfusion for critically ill patients such as septic shock has not been determined. A recent study showed that when Hb levels of patients with septic shock were determined as 70g/L and 90g/L as transfusion thresholds, the 90d mortality rates of the two patients were similar[11]. International guidelines for severe sepsis and septic shock indicate that red blood cell infusion should be performed in adults only when Hb level is < 70g/L in the absence of myocardial ischemia, severe hypoxemia or acute bleeding[12]. When hemoglobin decreases, the body needs to increase effective circulating blood volume and heart rate to meet the oxygen supply of the whole body tissues, which further increases the oxygen consumption of

the heart. In addition, decreased hemoglobin leads to decreased blood oxygen carrying and reduced myocardial oxygen supply, aggravating the imbalance between cardiac oxygen supply and oxygen demand and increasing the incidence of adverse cardiac events [13].

We focused on the effect of elevated cTnT levels in sepsis on in-hospital mortality from the first 24 hours of cTnT levels. evaluated the prognostic value of serum cTnT combined with hemoglobin level and some clinical characteristics in patients with sepsis in ICU.To analyze the evaluation value of the combined prediction of each indicator on the prognosis of patients, the clinical data of patients with sepsis were compared and analyzed in this study.

Materials And Methods

Database introduction

MIMIC is a critical Care medicine database, Medical Information Mart for Intensive Care. In 2003, with the support of NIH, the database was jointly established by emergency doctors, critical care doctors and computer science experts from Beth Israel Deaconess Medical Center, MIT, Oxford University and Massachusetts General Hospital (MGH)[14] [1]. The initial name of the database was Multiparameter Intelligent Monitoring in Intensive Care II, or MIMIC II. In September 2016, MIMIC II database was upgraded to MIMIC III and renamed as Medical Information Mart for Intensive Care[15]. The content introduced in this paper is mainly based on MIMIC III.MIMIC III is currently (June 2018) version 1.4 (V1.4), A total of more than 58,000 hospitalizations were included for 38,645 adults and 7,875 newborns admitted to Beth Israel Deaconess Medical Center between June 2001 and October 2012. These data were sorted into 26 CSV format tables for the researchers to query.Data presented in this study were extracted by author Xu, who completed the online training course of the National Institutes of Health (certification number: 43883429).Data extraction was performed using PostgreSQL tools V.5.2.

Study population and stratification method

We extracted the data using PostgreSQL 10.0 software. Structured Query Language (SQL) was used to extract the following data: Gender, age, underlying disease, sequential organ failure Assessment (SOFA), vital signs, and laboratory results on the first day of admission to ICU included peripheral blood cTnT, hemoglobin, lactic acid, creatinine, blood sodium, blood potassium, blood glucose, white blood cell count, use of vasoactive drugs, and the need for mechanical ventilation. The study included all adult sepsis patients hospitalized in ICU, excluding those younger than 18 years of age and those with incomplete clinical data. Patients admitted to ICU for multiple times due to sepsis were regarded as independent samples. The patients were divided into death group and survival group according to whether they died during hospitalization, and the primary endpoint was mortality during hospitalization.

Statistical analysis

STATA 15.1SE software was used for statistical analysis of this study. Kolmogorov-smirnov method was used to test the normality of continuous variables. The normal data were expressed as mean ± standard

deviation (X ± S), and the non-normal data were expressed as median (quartile) [M (QL, QU)]. T test (normal data) or Mann-Whitney U test (non-normal data) was used according to the distribution. The categorical variables were expressed in frequency and percentage and were compared using $\chi 2$ test. Spearman correlation coefficient is used to analyze the correlation between continuous variables. Multinomial Logistics regression is used for multivariate analysis. An index with significant regression was selected, the joint predictor L was calculated according to the regression coefficient B, and the ROC curve was drawn based on L and the dependent variable to study its diagnostic value AUC, Sensitivity and Specificity. The statistical software used in this study was SPSS 26.0 while GraphPad 7.0 for drawing, and the significance level was 0.05.

Results

Population and baseline characteristics

Baseline characteristics: A total of 2886 adult sepsis patients were included in this study, including 1704 males (59%) and 1182 females (41%). Average age is 68.23 ± 12.97, and BMI of 28.48 ± 8.03. There were 1123 (39%) in the death group and 1763 (61%) in the survival group. As shown in Table 1, there were no significant differences in gender and BMI between the two groups ($P > 0.05$). The age of death group was significantly higher than that of survival group (305.8 ± 14.8 and 321.5 ± 16.8) ($P < 0.001$), there were no significant differences in diabetes, hypertension, chronic obstructive pulmonary disease and cardiovascular disease between the two groups ($P > 0.05$). Patients in the death group were sicker when admitted to ICU than those in the control group, showing initial cTnT (0.07(0.03–0.25) and 0.1(0.04–0.31)) ($p < 0.001$), lactic acid (Lac) (1.7(1.2–2.5) and 2.3(1.4–3.7)) ($p < 0.001$), SOFA scores (6(4–8) and 8(5–11)) ($p < 0.001$), creatinine (1.4(0.9–2.2) and 1.5(0.9–2.6)) ($p < 0.001$), urea (28(18–46) and 34(21–53)) ($p < 0.001$), potassium (4.1(3.6–4.5) and 4.2(3.7–4.7)) ($p < 0.001$) were higher, while hemoglobin levels (10.1(9-11.4) and 9.9(8.8–11.2)) ($p < 0.001$) and platelet count (203(139–280) and 190(109–263)) ($p < 0.001$) were lower than those in the death group ,breathing rate(20(16–25) and 21(17–26)) ($p < 0.001$) and heart rate (91(77–105) and 94(80–111)) ($p < 0.001$) were significantly higher than those in the survival group, The need for vasoactive drugs and invasive mechanical ventilation was significantly higher(718,40.7% and 412,23.4%, respectively) in the death group than in the survival group(688,61.3% and 385,34.3%), Fig. 1 shows that the cTnT level in death group was significantly higher than that in survival group, while the hemoglobin level was significantly lower than in survival group, $p<0.001$.

Table 1 Patient characteristics

	Total	Survivors	Non-survivors	p Value
N	2886	1763 (61)	1123 (39)	
Demographics				
Age, median (IQR)	68(61–79)	68(60–78)	69(61–80)	< 0.001
Gender (male, %)	1074(59%)	1028(58.3%)	676(60.2%)	0.315
BMI, median (IQR)	27.34(23.18–31.94)	27.53(23.41–32.15)	27.18(22.99–31.59)	0.151
Comorbidities, n (%)				
COPD	84(2.9%)	45(2.6%)	39(3.5%)	0.152
coronary	681(23.6%)	445(25.2%)	236(21%)	0.059
diabetes	1112(38.5%)	701(39.8%)	411(36.6%)	0.089
hypertension	1020(35.3%)	658(37.3%)	362(32.2%)	0.065
Vital signs on admission				
Heart rate, median (IQR)	93(78-107.25)	91(77–105)	94(80–111)	< 0.001
Respiratory rate, median (IQR)	21(17–25)	20(16–25)	21(17–26)	< 0.001
Laboratory analysis on admission				
White cells (k/uL), median (IQR)	11.9(8-17.13)	12(8.3–17.1)	11.8(7.4–17.2)	0.064
Serum creatinine (mg/dL), median (IQR)	1.4(0.9–2.4)	1.4(0.9–2.2)	1.5(0.9–2.6)	0.018
Urea (mg/dL), median (IQR)	31(19-49.25)	28(18–46)	34(21–53)	< 0.001
Lactate (mmol/L), median (IQR)	1.9(1.2–2.5)	1.7(1.2–2.5)	2.3(1.4–3.7)	< 0.001
Hemoglobin (g/dL), median (IQR)	10(8.9–11.4)	10.1(9-11.4)	9.9(8.8–11.2)	0.012
potass (mEq/L), median (IQR)	4.1(3.7–4.6)	4.1(3.6–4.5)	4.2(3.7–4.7)	< 0.001
platelet (k/uL), median (IQR)	197(129–271)	203(139–280)	190(109–263)	< 0.001
Cardiac Troponin-T (ng/mL), median (IQR)	0.08(0.03–0.27)	0.07(0.03–0.25)	0.1(0.04–0.31)	< 0.001
glucose (mg/dL), median (IQR)	134(105–173)	133(104–175)	134(106–172)	0.881

Type of ICU on admission, n (%)				
CCU	304(10.5%)	172(9.8%)	132(11.8%)	0.274
CSRU	133(4.6%)	75(4.3%)	58(5.2%)	
MICU	1833(63.5%)	1142(64.8%)	691(61.5%)	
SICU	415(14.4%)	254(14.4%)	161(14.3%)	
TSICU	201(7.0%)	120(6.8%)	81(7.2%)	
Illness severity				
SOFA, median (IQR)	7(4–10)	6(4–8)	8(5–11)	< 0.001
Treatment				
Vasopressin use (n (%))	1406(48.7%)	718(40.7%)	688(61.3%)	< 0.001
Invasive ventilation (n (%))	797(27.6%)	412(23.4%)	385(34.3%)	< 0.001

Multivariate Logistic regression analysis showed that mortality was significantly higher in older patients (OR: 1.022, 95%CI 1.015 to 1.029, P < 0.001). while,the respiratory rate and heart rate at admission to ICU also significantly affected the prognosis of patients (OR: 1.019, 1.008, P = 0.001, P < 0.001 respectively), Sequential Organ Failure Assessment (SOFA) score reflects the degree of Organ dysfunction, SOFA score is positively correlated with mortality (OR: 1.141, 95% CI 1.114 to 1.148, p < 0.001). We saw that cTnT levels also significantly affected mortality (OR: 1.088, 95%CI 1.013 to 1.168, P = 0.02). There was a significant positive correlation between lactic acid level and mortality (OR: 1.292, 95%CI 1.231 to 1.356, P < 0.001), however, hemoglobin as a protective factor was significantly negatively correlated with mortality (OR: 0.948, 95%CI 0.907 to 0.991, P = 0.018), in addition, serum potassium, creatinine and urea were positively correlated with mortality (P < 0.05), increased serum sodium level was associated with reduced mortality as a protective factor (OR: 0.979, 95%CI 0.965 to 0.994, P = 0.005), as shown in Table 2

Table 2
Association between Initial characteristics of admission to ICU and mortality in patients with sepsis

	B	S.E.	Wald	P	OR	95% C.I.for OR	
						Lower	Upper
age	0.022	0.004	38.804	< 0.001	1.022	1.015	1.029
respiratory	0.019	0.006	10.155	0.001	1.019	1.007	1.032
heart	0.008	0.002	15.418	< 0.001	1.008	1.004	1.012
sofa	0.132	0.012	118.377	< 0.001	1.141	1.114	1.168
Troponin_T	0.084	0.036	5.431	0.02	1.088	1.013	1.168
platelet	-0.001	< 0.001	3.092	0.079	0.999	0.999	1
potass	0.135	0.057	5.595	0.018	1.145	1.023	1.281
scr	0.094	0.03	17.281	< 0.001	1.021	1.002	1.036
sodium	-0.021	0.008	7.755	0.005	0.979	0.965	0.994
urea	0.006	0.002	9.004	0.003	1.006	1.002	1.01
lactic_acid	0.256	0.025	107.178	< 0.001	1.292	1.231	1.356
hemoglobin	-0.053	0.023	5.593	0.018	0.948	0.907	0.991

According to receiver operator characteristic curve (ROC), cTnT and hemoglobin levels can significantly predict mortality, with AUC of 54.8 and 52.8, respectively. ($p < 0.05$). The sensitivity was 62.42 and 53.78, the specificity was 45.39 and 51.22, and the cut-off values were > 0.06ng/mL and ≤ 10g/dL,respectively.as we can see in Table 3. When troponin T > 0.06ng/mL or hemoglobin ≤ 10g/dL, the mortality was significantly increased, ($P < 0.05$), as shown in Fig. 2. Figure 3 shows an increase in mortality with increased troponin levels.

Table 3
Predictive value of troponinT and hemoglobin in mortality in patients with sepsis

	AUC	SE	95%CI	P	Cutoff	Sensitivity	Specificity	+PV	-PV
TNT	0.548	0.0109	0.53 ~ 0.567	< 0.0001	> 0.06	62.42	45.39	42.1	65.5
HB	0.528	0.011	0.509 ~ 0.546	0.0117	≤ 10	53.78	51.22	41.3	63.5

Combined with the regression coefficient B of the significant index in the regression analysis, the calculation formula of the combined predictor L is as follows:

$$L = \frac{0.022}{0.006}\,age + \frac{0.019}{0.006}\,respiratory + \frac{0.008}{0.006}\,heart + \frac{0.132}{0.006}\,sofa + \frac{0.084}{0.006}\,Troponin\_T + \frac{0.135}{0.006}\,potass - \frac{0.094}{0.006}\,scr - \frac{0.021}{0.006}\,sodium + urea + \frac{0.256}{0.006}\,lactic\_acid - \frac{0.053}{0.006}\,hemoglobin$$

thus:

L = 3.67age + 3.17respiratory + 1.33heart + 22sofa + 14Troponin_T + 22.5potass-15.6scr-3.5sodium + urea + 42.67lactic_acid-8.83hemoglobin

Combined Predictor L can significantly predicted mortality,the Receiver Operator characteristic Curve (ROC) shows an AUC of 73.2,($P < 0.05$). The sensitivity and specificity were 64.2 and 70.62, respectively, as shown in Table 4 and Fig. 4.

Table 4
Predictive value of combined predictor L in mortality in patients with sepsis

	AUC	SE	95%CI	P	Cutoff	Sensitivity	Specificity	+PV	-PV
L	0.732	0.00957	0.715 ~ 0.748	< 0.0001	> 201.106	64.2	70.62	58.2	75.6

Discussion

Our study shows that the levels of hemoglobin and cardiac troponinT,(cTnT) in ICU patients with sepsis may affect the prognosis of patients, and the efficacy of multifactor combined test for sepsis assessment is better than that of a single indicator. Treatment strategies to improve the factors identified in this study may improve the inpatient survival rate of these ICU patients. cTnT was elevated in 2866 ICU sepsis patients (< 0.1ng/ml) in 47% (1356 patients), which is similar to about 40%-50% of patients with sepsis in epidemiological studies with varying degrees of troponin elevation[16]. Troponin is an important regulatory protein of striated muscle contraction. cTnT in troponin is released into the blood when myocardial cells are damaged, which is an important marker for the diagnosis of myocardial injury. cTnT can be released into the blood for 3–4 hours at the earliest and 48 hours at the latest after the occurrence of myocardial injury in sepsis[17]. Since this study only included cTnT levels for the first time after admission to ICU, the significance of the study results may be reduced. cTnT, as a sensitive marker of myocardial injury, is not specific enough to recognize septic myocardial injury in the early stage because of its elevation in patients with various etiologies. However, when the damage range of cardiomyocytes in patients with sepsis tends to be further expanded, the dynamic increase of cTnT is proportional to the degree of dynamic damage of cardiomyocytes[18]. A study shows sepsis myocardial injury and myocardial tissue energy depletion was positively related to [19], and lactic acid as the anaerobic metabolism of the body tissues and organs of microcirculation index can well response organization

energy depletion, so when accompanied by lactic acid value increases, the myocardial tissue often cannot get enough energy supply, prompting development of myocardial injury and When myocardial injury occurs to a certain extent, it may lead to cardiac insufficiency, thus worsening the microcirculation of systemic tissues and further aggravating multi-organ dysfunction. Vasile et al.[20] showed that with the increase of cTnT level, the left diastolic function of patients with sepsis cardiomyopathy significantly decreased, and the incidence of cardiac dysfunction was positively correlated with the level of cTnT[21]. Such reversible cardiac function inhibition is called sepsis induced cardiomyopathy. (SICM)[22]. In septic cardiomyopathy, the increase of troponin is not due to the ischemic necrosis of large area of cardiomyocytes, but to the reversible inhibition of cardiac function caused by the energy metabolism disorders of cardiomyocytes. If the inhibition of cardiac function occurs, the risk of death of patients with sepsis will be increased [23].Different from the "high output low resistance" of normal sepsis patients, the hemodynamic characteristics of patients with sepsis cardiomyopathy are left heart dysfunction, with reduced cardiac output and thus unable to meet the needs of organ blood perfusion, which aggravating the occurrence and development of organ dysfunction. At present, the pathogenesis of myocardial injury in sepsis is not clear, some animal experiments have shown that inflammatory factors in inflammatory response [24] may be involved in the process of myocardial injury in sepsis. Hawkins et al.[25]found that an increase in neutrophils is accompanied by a decrease in lymphocytes in sepsis, and that an increase in neutrophils/lymphocytes ratio reflects the degree of sepsis inflammation. As early as 2001, Zahorec[26] suggested that neutrophils/lymphocytes ratio should be used as a predictor of infection in ICU patients. Some basic studies[27] have found that neutrophils can migrate into the myocardial interstitium after activation, thus inducing myocardial inflammation and affecting the blood flow distribution of cardiac microcirculation. In recent years, neutrophils/lymphocytes ratio has often been used as an important indicator to predict myocardial injury and heart failure[28–30]. This study has not found a relationship between WBC count and mortality in patients with sepsis, which needs further study possibly due to selection bias. The results of this study also showed that AUCROC and cut-off of troponin T for predicting nosocomial death of sepsis patients were 0.548 and 60ng/L. Bergenzaun et al.[31]found that the AUCROC and cut-off of troponin T in predicting 1-year death of severe patients was 0.76 and 117.5ng/L. The cutoff and AUCROC in this study are lower than those in the above study. The reason for this difference may be the difference in the study time endpoints. The hospital-based mortality was predicted in this study, while the 1-year mortality was predicted in the above study. Despite these differences, both indicate that troponin T levels in early ICU admission predict patient outcome.

2886 patients with septic shock were included in this study, and 759 patients had hemoglobin ≤ 90g/L, with the incidence of 26.2%. 3534 ICU patients were included in a large scale of observational study in Europe with an average hemoglobin level of 113g/L at admission, and 29% of them had hemoglobin level < 100g /L[32]. A prospective cohort study showed that 55% of patients with septic shock had hemoglobin levels < 90g /L[33]. The common causes of anemia are trauma, surgery, or occult gastrointestinal hemorrhage, which are rare in patients with septic shock. Septic shock is a complex pathophysiological process and Potential mechanisms include changes in microcirculation, decreased erythropoiesis, chronic anemia, hemodilution, and increased erythrocyte destruction due to changes in

erythrocyte membrane. Current guidelines suggest that hemoglobin level < 70 g /L is one of the indications for blood transfusion to maintain hemoglobin level at 70–90 g /L in patients without myocardial ischemia, severe hypoxemia, acute hemorrhage[34]. Sepsis treatment guidelines suggest that hemoglobin < 70 g/L is the indication for transfusion, but for patients with bleeding tendency or invasive procedures, prophylactic infusion of fresh frozen plasma is feasible. However, a research showed that there was no statistically significant difference in mortality between patients with septic shock whose blood transfusion threshold was 70 g/L and 90 g/L of hemoglobin [35]. It should be noted that hemoglobin level is correlated with the amount of intravenous fluids during resuscitation[36]. In this study, mortality in patients with septic shock increased as hemoglobin levels decreased at admission and the results of multivariate regression analysis showed that hemoglobin level at admission was an independent factor influencing the death of patients with septic shock, similar to the results of Muady et al[9], suggesting that hemoglobin level at admission may be a prognostic indicator for patients with septic shock. Hemoglobin < 100 g/L was independently associated with 90-day death in patients with community-acquired pneumonia[37]. The majority of septic shock patients who received red blood cell transfusion had more severe disease and lower hemoglobin levels than those who did not receive red blood cell transfusion during shock, although there was no significant difference in mortality between the two groups [38, 39]. Other studies have shown that red blood cell infusion is associated with low mortality in patients with severe septic shock [40]. In this study, ROC curve indicated that the cut-off value of hemoglobin level was ≤ 10g/ m2, so active transfusion of red blood cells or preventive transfusion of red blood cells for other special reasons may be clinically adopted for patients with low hemoglobin sepsis. Although this study adopted multiple regression analysis to explore the influencing factors of death in patients with septic shock, there are still some confounding factors that cannot be measured, such as the empirical use of antibiotics. Studies have suggested that hemoglobin < 100 g/L in patients with acute coronary syndrome(ACS), the incidence of angina pectoris, heart failure and cardiogenic death after myocardial infarction was increased..This study found that sepsis patients with decreased hemoglobin levels had significantly higher in-hospital all-cause mortality than the other group. At present, there is no relevant study on the effect of hemoglobin level on the mortality of SICM patients, and the reasons for the effect of decreased hemoglobin on the prognosis of sepsis patients are complicated. First of all, when hemoglobin decreases, effective circulating blood volume and heart rate were increased to meet the oxygen supply of the whole body tissues, which further increases the oxygen consumption of the heart. Secondly, decreased hemoglobin leads to decreased blood oxygen carrying and reduced myocardial oxygen supply, aggravating the imbalance between cardiac oxygen supply and oxygen demand and increasing the incidence of adverse cardiac events in patients with sepsis [13]. We found that heart rate and respiration rate may also increase the mortality rate for patients with sepsis, because in addition to the serious condition of such patients, the increase in respiration rate and heart rate also brings about greater oxygen consumption, which increases the burden on the heart.

This study had the following limitations :(1) the time interval between the onset of sepsis and blood collection for troponin T determination was not significant; (2) There may be information bias in evaluating the prognosis of patients with troponin T level at one point in time, and the change of troponin

level is not dynamically assessed; (3) Ultrasound parameters reflecting left ventricular diastolic function were not included in this study, which could not explain the relationship between cardiac function and troponin T level. (4) There are too few included variables.

In conclusion, hemoglobin and troponin levels in ICU patients with sepsis may affect the prognosis of patients, and the efficacy of multifactor combined test for the prognosis of sepsis is better than that of a single indicator. Treatment strategies to improve the factors identified in this study may improve the inpatient survival rate of these ICU patients.

Declarations

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Data Availability Statement

The raw datasets of this study may be available from the corresponding

author upon reasonable request.

Authors'contributions

FH, and KZX conceived the study idea and designed the study. KZX, SBW,

and PX collected the data. KZX ,AFZ performed the statistical analyses, KZX

wrote the first draft of the manuscript.All authors participated in data interpretation and critical review of the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

MIMIC III database used in the present study was approved by the Institutional Review Boards (IRB) of the Massachusetts Institute of Technology and does not contain protected health information.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

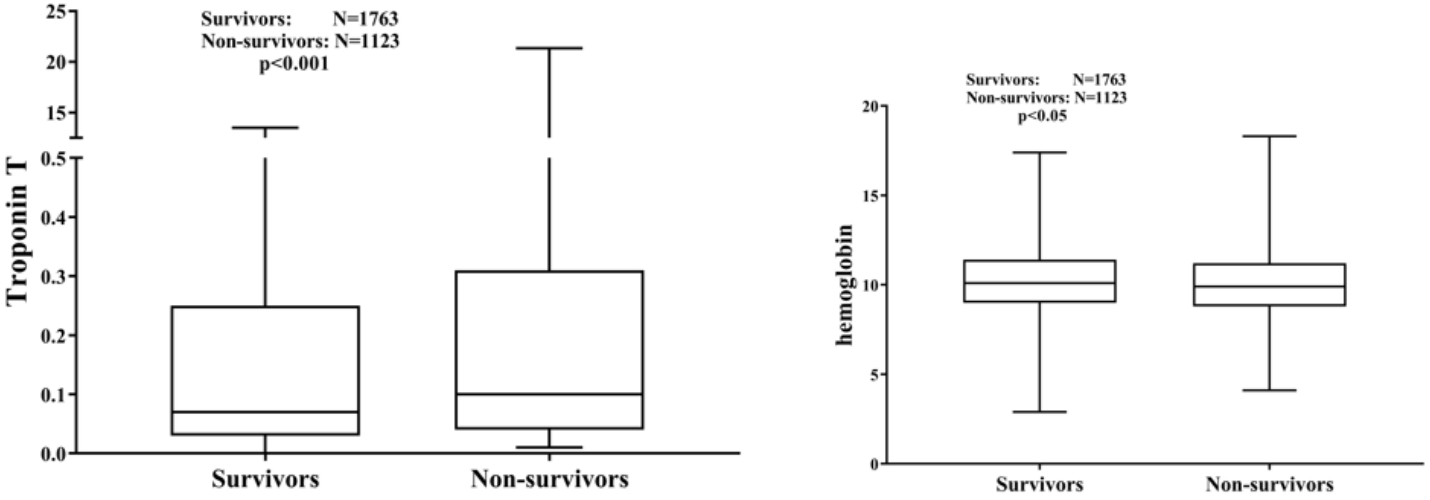

Figure 1

The cTnT level in death group was significantly higher than that in survival group, while the hemoglobin level was significantly lower than in survival group, p□0.001.

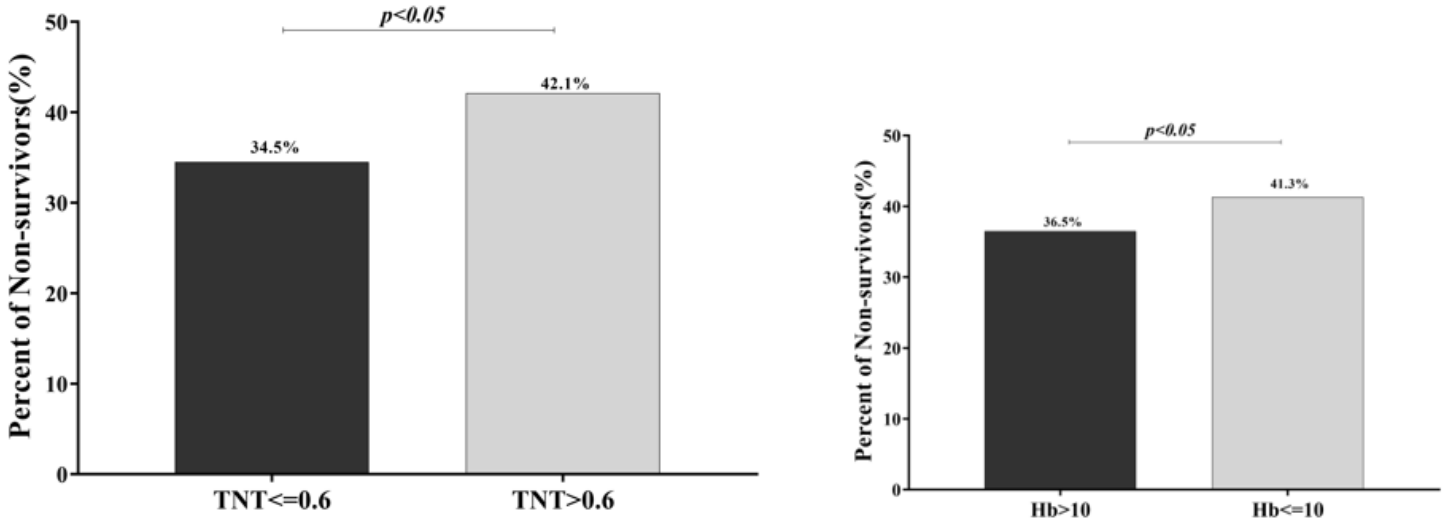

Figure 2

When troponin T>0.06ng/mL or hemoglobin≤10g/dL, the mortality was significantly increased, p < 0.05

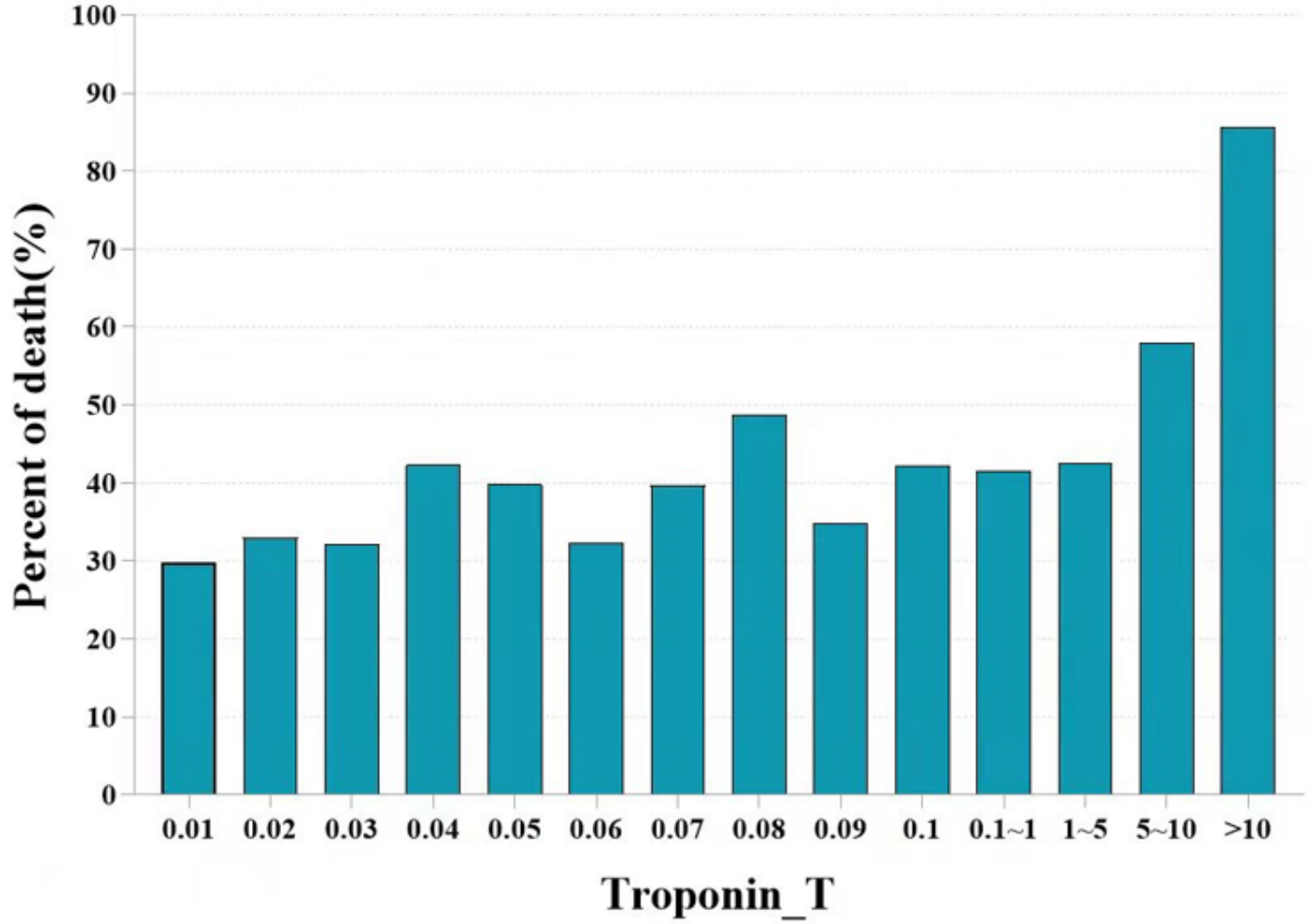

Figure 3

mortality distribution in different levels of cTnT

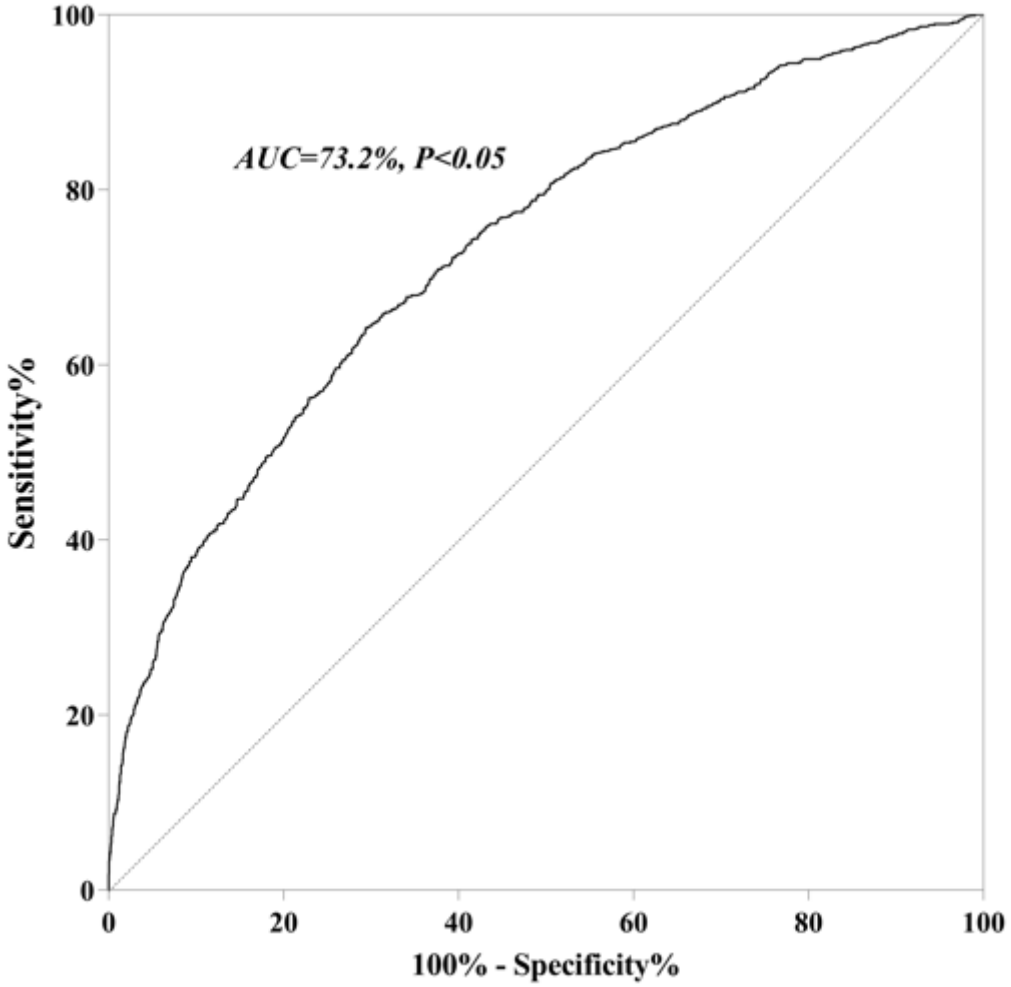

Figure 4

Predictive value of combined predictor L in mortality in patients with sepsis