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Original Article

An evaluation of the prognostic values of hs-TnI and the hemodynamic parameters in patients with sepsis

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Abstract: Background: Studies have shown that myocardial injury and hemodynamic instability are common signs of sepsis and can influence patients' prognosis. We aim to evaluate the prognostic role of the myocardial injury marker hs-TnI and the hemodynamic parameters in patients with sepsis during their hospitalization. Methods: In this study, patients with sepsis were allocated into a survival group and a death group based on their hospitalization outcomes. Laboratory parameters including infection, inflammation and myocardial injury markers were collected on admission. The hemodynamic parameters were measured by pulse indicator continuous cardiac output (PICCO). The SOFA and qSOFA scores were calculated based on the standard forms. Results: The Hs-TnI, NT-proBNP, and PCT levels were significantly higher in the death group than they were in the survival group (all $P < 0.05$). As to the hemodynamic parameters, there was a significant difference in multiple parameters between the two groups ($P < 0.05$). In addition, hs-CRP was positively correlated with the SOFA ($r = 0.523$) and qSOFA (0.547) scores (both $P < 0.01$). A further multivariate logistic regression analysis demonstrated that hs-TnI (OR = 3.455, 95% CI: 3.207-3.918, $P < 0.01$), PCT (OR = 1.736, 95% CI: 1.096-2.073, $P = 0.044$), the cardiac index (OR = 2.840, 95% CI: 2.336-4.096, $P = 0.018$), and the qSOFA scores (OR = 2.331, 95% CI: 2.175-2.627, $P = 0.021$) but not the SOFA scores were independent predictors of sepsis mortality. Conclusion: Increased hs-TnI and hemodynamic instability could be very useful predictors of the mortality of sepsis patients. More large, prospective studies with a long-term follow-up are warranted to confirm the long-term prognostic roles of hs-TnI and the hemodynamic parameters in sepsis.

Keywords: Sepsis, hs-TnI, hemodynamic parameters

Introduction

Sepsis is one of the most common acute and severe diseases that can cause multiple organ failure [1]. Heart damage is one of the most common acute and critical complications of sepsis [2]. It is often accompanied by severe arrhythmia and heart failure, especially in severe sepsis [3]. Among deaths from sepsis, 30%-80% are attributed to an impaired cardiovascular system. Hypersensitive Troponin I (hs-TnI) is a specific early stage marker of myocardial injury that increases within 4 to 6 hours of a myocardial ischemic event [4]. It is very meaningful for the early diagnosis and treatment of heart complications from sepsis.

Hemodynamic instability is a typical sign of sepsis [5]. Many hemodynamic parameters are influenced and can indicate the severity of sepsis, which have prognostic values. In the past, hemodynamic parameters were difficult to measure. However, due to the development of pulse indicator continuous cardiac output (PICCO), hemodynamic monitoring has become a common practice with severely ill patients admitted to intensive care units (ICU). PICCO technology can effectively monitor hemodynamic instability in shock, sepsis, lung injury, organ failure, and high-risk surgical patients and is used to guide the treatment of critically ill patients and improve the success rate of their treatment [6, 7]. It has been widely deployed in ICU settings and has proved to be of high value for sepsis treatment [8].

However, there is still not enough evidence to determine the prognostic value of myocardial injury markers or hemodynamic parameters in patients with sepsis. In view of this, we aim to study the role of hs-TnI and hemodynamic parameters in the outcome of sepsis treatment.

Materials and methods

Study participants

228 patients with sepsis and myocardial injury were selected from the ICU of a tertiary hospital in China from November 2016 to November 2018. All of the patients included met the diagnostic criteria of sepsis and myocardial injury. The exclusion criteria included: hospitalization time less than 3 days; patients with a history of heart-related diseases, liver and kidney dysfunction, advanced tumors, hematological diseases, or immunodeficiency diseases.

The definition of sepsis used in our study followed the clinical criteria of Sepsis 3.0 [9] for sepsis with sequential organ failure assessment (SOFA) scores [10]. This scoring system includes clinical and laboratory parameters for the respiratory system, coagulation, liver, cardiovascular system, central nervous system, and the kidneys [11].

The quick SOFA (qSOFA) score [12] ranges from 0 to 3 with one point given for each of the following critical signs: SBP ≤ 100 mmHg, RR ≥ 22/min, and an altered mental status from the baseline. When a score is more than 2, it indicates a greater risk of prolonged ICU stay or increased mortality.

Myocardial injury is diagnosed when hypersensitive cardiac troponin I (hs-TnI) is elevated beyond the normal level [13]. According to the results of color Doppler echocardiography, the left ventricular end-diastolic diameter (LVEDD) > 54 mm and left ventricular ejection fraction (LVEF) < 50% suggest myocardial dysfunction.

PICCO monitoring was conducted by femoral artery puncture [14]. The following hemodynamic parameters were collected or calculated: cardiac index (CI), global end-diastolic volume index (GEDVI), systemic vascular resistance index (SVRI), extravascular pulmonary water index (EVLWI), central venous oxygen saturation ($ScvO_2$), mean arterial pressure (MAP), heartrate (HR), central venous pressure (CVP), and left ventricular ejection fraction (LVEF) [15, 16].

In addition, the following data were extracted from the electronic health records: demographic information, ICU and hospital length of stay, physiological and laboratory parameters including hs-TnI, hs-CRP, and procalcitonin (PCT) and others for the APACHE score calculations.

Statistical analysis

Two-sample *t*-tests were conducted for the group comparisons of the continuous variables. When the variables were not normally distributed, the *t*-tests were replaced by Wilcoxon's Rank Sum test. The categorical data comparisons were calculated using Chi-square or Fisher's exact test on the condition that any cell counts were below 5. The linear dependence between related variables was assessed using Pearson's correlation coefficient. A multivariate logistic regression analysis was used to determine the association between the clinical variables and mortality using an odds ratio (OR) and a 95% confidence interval (CI). IBM SPSS 23.0 software (IBM, Inc., Armonk, NY, USA) was deployed to complete the statistical analysis with two-sided tests, and $P < 0.05$ was considered statistically significant.

Ethical consideration

This study was conducted in accordance with the ethical principles expressed in the Declaration of Helsinki and was reviewed and approved by Hospital's Medical Ethics Committee.

Results

Clinical characteristics of study participants

In the end, 228 patients with sepsis were included. According to the outcome during hospitalization, they were divided into a survival group (n = 165) and a death group (n = 63). The overall mortality from sepsis was 27.63%. As shown in **Table 1**, there was no significant difference between the survival group and death group regarding age, gender, or infection site (all $P > 0.05$). However, the SOFA, qSOFA, SAPSII, and APACHEII scores of the death group were significantly higher than those of the survival group ($P < 0.01$).

Laboratory and hemodynamic parameters of study participants

The laboratory parameters of the two groups on admission are illustrated in **Table 2**. The Hs-TnI,

Table 1. Baseline characteristics of study participants

Variables	Survival group (n = 165)	Death group (n = 63)	*P* value
Age	52.15 ± 9.34	54.24 ± 9.81	0.1376
Gender (M/F)	105/60	36/27	0.367
Infection site			
Lung	123 (74.4)	44 (69.2)	0.055
Urinary	14 (8.5)	13 (20.5)	
Abdominal	12 (7.3)	3 (5.1)	
Others	16 (9.8%)	3 (5.1)	
SOFA scores	6.41 ± 3.25	18.65 ± 5.43	< 0.01*
qSOFA scores	1.12 ± 0.16	1.94 ± 0.12	< 0.01*
SAPSII scores	35.42 ± 1.29	56.43 ± 3.24	< 0.01*
APACHEII scores	21.57 ± 0.92	29.03 ± 1.24	< 0.01*
ICU days	13.70 ± 7.34	15.85 ± 7.44	0.0500

*P < 0.05.

Table 2. Laboratory and hemodynamic parameters of the study participants

Variables	Survival group (n = 165)	Death group (n = 63)	*P* value
Laboratory parameters			
WBC	12.30 ± 5.13	13.45 ± 4.75	0.1239
Neutrophil	0.852 ± 0.283	0.832 ± 0.294	0.6373
Hs-TnI	0.004 ± 0.003	1.53 ± 0.49	< 0.01*
D-dimer	2.02 ± 1.03	3.03 ± 0.42	< 0.01*
Lactate	2.55 ± 0.48	4.35 ± 0.66	< 0.01*
CRP	87.3 ± 13.3	91.6 ± 16.7	0.0437*
PCT	2.4 ± 0.6	5.4 ± 1.5	< 0.01*
NT-ProBNP	319.16 ± 64.49	2078.91 ± 535.42	< 0.01*
Hemodynamic parameters			
CI	2.84 ± 0.69	2.11 ± 0.67	< 0.01*
GEDVI	822.57 ± 247.19	562.37 ± 185.42	< 0.01*
SVRI	1551.68 ± 506.83	1010.32 ± 336.51	< 0.01*
EVLWI	10.08 ± 3.22	12.15 ± 4.01	< 0.01*
$ScvO_2$	69.61 ± 3.52	55.96 ± 7.34	< 0.01*
HR	113.48 ± 35.01	125.18 ± 33.74	0.0214*
MAP	70.89 ± 13.35	60.14 ± 11.83	< 0.01*
CVP	7.88 ± 2.57	14.54 ± 4.69	< 0.01*
LVEF (%)	57.45 ± 6.25	42.37 ± 6.34	< 0.01*

c-TnI: troponin I; CRP: C-reactive protein; PCT: procalcitonin; CI: cardiac index; GEDVI: global end-diastolic volume index; SVRI: systemic vascular resistance index; EVLWI: Extravascular pulmonary water index; $ScvO_2$: central venous oxygen saturation; HR: heartrate; MAP: mean arterial pressure; CVP: central venous pressure; LVEF: left ventricular ejection fraction. *P < 0.05.

D-dimer, PCT, hs-CRP, NT-proBNP, and lactate levels were significantly higher in the death group than they were in the survival group (all P < 0.05). No statistical differences were observed between the two groups in terms of white blood cell count (WBC) or neutrophil count (all P > 0.05). During the hemodynamic monitoring, the CI, GEDVI, SVRI, $ScvO_2$, MAP, and LVEF were all significantly higher in the survival group than they were in the death group (all P > 0.05). However, the heart rate, EVLWI, and CVP of the survival group were significantly lower than those of death group (all P < 0.05).

Correlation analysis of hs-TnI, qSOFA, and SOFA

A two-variables correlation analysis showed hs-TnI was positively correlated with the SOFA scores (r = 0.523; P < 0.01; **Figure 1**) and the qSOFA scores (r = 0.547; P < 0.01; **Figure 2**).

Risk factors for mortality during hospitalization

A multivariate logistic regression analysis also demonstrated that the qSOFA scores, hs-TnI, CI, and PCT levels, but not the SOFA scores, are independent predictors for mortality during hospitalization (**Table 3**).

Discussion

To our knowledge, our study is the first to investigate the myocardial injury marker hs-TnI and the hemodynamic parameters derived from PICCO in the prognosis of sepsis during hospitalization. We found that, in additional to the traditional inflammation and infection markers of hs-CRP and PCT, hs-TnI was also significantly increased in the death group. Moreover, the hs-TnI level was positively correlated with the SOFA and qSOFA scores. In the multivariable logistic

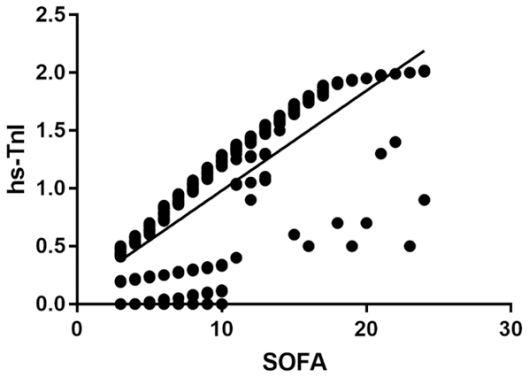

Figure 1. The correlation between hs-TnI and the SOFA scores.

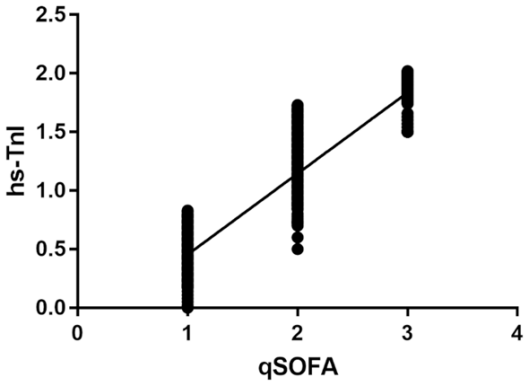

Figure 2. The correlation between hs-TnI and the qSOFA scores.

Table 3. Multiple variables analysis results

Variables	OR	OR with 95% CI	*P* value
SOFA scores	1.315	0.876-1.528	0.211
qSOFA scores	2.331	2.175-2.627	0.021*
Hs-TnI	3.435	3.207-3.918	0.004*
PCT	1.736	1.096-2.073	0.044*
CI	2.840	2.336-4.096	0.018*

*P < 0.05.

analysis, hs-TnI and CI were independent predictors of death in the patients with sepsis.

Sepsis is a critical disease in the clinic and the leading cause of death in the ICU. It is characterized by high morbidity, high mortality, and high treatment costs [17]. In recent years, although great progress has been made in the treatment of sepsis, the mortality rate remains high [18]. Exploring the risk factors related to the prognosis of sepsis and improving the risk assessment of sepsis in the early stages will help to prevent the deterioration of the patients' conditions and improve their prognoses.

We found that PCT was significantly increased in the death group, which was more sensitive than hs-CRP, white blood cells, or neutrophils counts. PCT is a glycoprotein containing 116 amino acids. It is a procalcitonin produced by thyroid C cells with a short half-life and good stability in vivo. In 1993, Assicot et al. found that the higher the level of PCT, the worse the infection and the worse the prognosis of severe infection. It was the first time that the association between PCT level and the critical course of sepsis was demonstrated. Since then, many studies have found that PCT is sensitive in the early diagnosis of sepsis. The specificity of PCT is better than that of CRP, WBC, N, IL-6 and other traditional inflammation indicators [19]. It is closely related to the severity of sepsis. Studies have found that PCT levels begin to rise within 2-4 hours after bacterial infection, peaking at 8-24 hours and lasting for several days or weeks. PCT can be used as a good marker for the early diagnosis of sepsis due to its unique dynamic characteristics [19, 20].

The SOFA and qSOFA scores are very useful tools to evaluate sepsis patients' conditions. Higher scores indicate more severe organ failure and a higher risk of mortality [21-23]. In our study, we also demonstrated that the death group had higher SOFA and qSOFA scores than the survival group. In line with this, hs-TnI was significantly increased in the death group in comparison with the survival group. Therefore, it is very meaningful to test hs-TnI among sepsis patients, which can reflect disease severity and mortality risk.

Sepsis is a life-threatening multi-organ dysfunction caused by the patient's imbalance in response to infection [24]. The heart is one of the most vulnerable organs [25]. 40% to 50% of sepsis patients suffer from cardiac insufficiency, and 7% of them suffer from heart failure. Myocardial injury is an important cause of increasing sepsis mortality. Therefore, early identification and prevention have become the focus of current research in the field of critical medicine. Hs-TnI has a high sensitivity and specificity [26]. It was found that the detection of hs-TnI in sepsis patients is helpful for the early identification of myocardial dysfunction, and an increase of hs-TnI is closely related to the severity of the cardiac injury [26].

The early detection of hemodynamic parameters can predict the severity of sepsis in order to strengthen the treatment and prevent complications such as heart failure, arrhythmia, and cardiogenic shock, so as to reduce patient mortality [27, 28]. The main manifestations of cardiac dysfunction in sepsis are impaired systolic function, decreased LVEF, and decreased left ventricular peak systolic pressure/left ventricular end-diastolic pressure. This study suggests that the cardiac index [29] and other hemodynamic parameters could reflect the severity of septic myocardial injury and have a predictive value in prognosis and survival.

Our study still has some limitations. First, in this study, a cross-sectional design was used, and it would be better to investigate the relationship between the parameters and adverse events if we had followed the surviving patients. Second, other reported inflammatory markers (IL-1, IL-6, PAF and so on) were not measured. Lastly, our sample size was relatively small, so we could not establish the diagnostic role of these parameters.

In conclusion, hs-TnI and hemodynamic parameters have a predictive value in patients with sepsis complicated by myocardial injury. They can predict the severity of the patient's condition and guide clinicians in adjusting their treatment plan in order to reduce the complications in early treatment. At the same time, they might predict patients' survival rate and reduce the mortality rate of patients with sepsis. However due to the limitations listed above, more large prospective studies with long-term follow-up are warranted to confirm the long-term prognostic roles of hs-TnI and the hemodynamic parameters in sepsis.

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Disclosure of conflict of interest

None.

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