

Original Article

The value of procalcitonin and brain natriuretic peptide in predicting the prognosis of sepsis

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Abstract: Objective: To explore the value of procalcitonin (PCT) and brain natriuretic peptide (BNP) in predicting the prognosis of sepsis. Methods: A total of 65 patients with sepsis received treatment in Deqing County People's Hospital from 2019 January and 2021 January and their data were collected retrospectively. Based on the survival and death of patients, 40 living patients were regarded as survival group, and 25 dead patients were regarded as the death group. PCT, BNP and, Acute Physiology and Chronic Health Evaluation II (APACHE II) scores of sepsis patients in both groups on the first, third, and seventh days of admission were collected and compared respectively. ROC curve was utilized to calculate the relationship between the three indicators and prognosis. Results: Compared with the death group, the PCT, BNP, and APACHE II scores in the survival group were lower on the first, third, and seventh days ($P < 0.05$). On the first, third, and seventh day, the AUC of PCT were 0.768, 0.829, and 0.831; the AUC of BNP were 0.771, 0.805, and 0.848; the AUC of APACHE II were 0.891, 0.809, and 0.974 ($P < 0.05$). Conclusion: The level of plasma PCT and BNP in sepsis patients was increased, and they are positively correlated with the severity of the disease, which can be used as an indicator of bad prognosis of sepsis patients.

Keywords: Procalcitonin, brain natriuretic peptide, sepsis, prognosis

Introduction

Sepsis is an important clinical problem faced in medicine [1]. With the aging of the population, the increase of tumor incidence rate and the increase of invasive medical means, the incidence rate of sepsis continues to rise, and millions of sepsis patients are treated every year, worldwide, and more than 1/4 of them will die [2, 3]. Studies indicate that 700,000 new cases of sepsis are diagnosed every year, and sepsis causes 200,000 deaths every year [4]. How to quickly diagnose and determine the severity of sepsis is one of the current focuses of research. Although the mortality of sepsis patients decreased significantly, the long-term prognosis of an increasing number of survivors is still poor and the survival status is not optimistic [5]. All studies have shown that sepsis patients have a high long-term mortality, a decline in long-term physiological, psychological and cognitive functions, and an increase in the economic and mental burden of families

and society [6]. The increasing number of discharged patients has been considered as a potential public health crisis. In recent years, more and more researchers have begun to pay attention to the long-term prognosis of sepsis patients. However, compared with other acute and severe diseases such as stroke and cancer requiring hospitalization, the long-term prognosis of sepsis has not attracted enough attention.

The detection of serological indicators is often used in the diagnosis and prognosis evaluation of infectious diseases and it plays an important role [7]. Serum procalcitonin (PCT) is a biomarker of systemic bacterial infection. Its level will rise rapidly and sharply in persistent inflammation or autoimmune diseases, and is used to diagnose a variety of bacterial infections [8]. The inflammatory indicators such as PCT in sepsis patients increased significantly, which can predict the severity of the patient to some extent, but there is still some controversy [9].

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BNP is one of the members of the diuretic peptide family secreted by the heart. It can promote urination and sodium excretion, effectively relax blood vessels, fight against the renin angiotensin aldosterone system, and is an important indicator for evaluating heart damage [10]. The excessive inflammatory stress reaction of sepsis will produce more cardiotoxins, and the infection of pathogenic microorganisms will also produce more endotoxins, which will induce the increase of BNP in the body [11]. APACHE-II score is an important indicator to estimate the severity of critical illness patients, which can accurately evaluate the patient's condition [12].

In this study, we collected the clinical data of emergency sepsis patients, and we compared the PCT and BNP to explore the application value of serum PCT and BNP detection in the evaluation of the condition and prognosis of emergency sepsis patients, aiming to provide a reference for the evaluation of the condition and prognosis of acute sepsis patients.

Materials and methods

The general data

A total of 65 patients with sepsis who received treatment in Deqing County People's Hospital from 2019 January and 2021 January were collected retrospectively. The end point of this study is the death and survival of patients at 28 days. Based on the survival and death of patients, 40 living patients were regarded as the survival group, and 25 dead patients were regarded as the death group. All patients signed an informed consent form. This study was approved by the Ethics Committee of Deqing County People's Hospital.

Inclusion criteria: (1) Sepsis was diagnosed on admission. Diagnostic criteria for sepsis: Refer to the diagnostic criteria formulated at the joint meeting of American Thoracic Physicians Association and Critical Care Physicians Association in 2001; (2) PCT, BNP level and APACHE II score were detected on the 1st, 3rd and 7th day after admission; (3) Age \geq 18; (4) Data was complete.

Exclusion criteria: (1) Patients with increasing PCT and BNP within the most recent month; (2) Patients with serious heart, liver, kidney diseases

and malignant tumors in the past; (3) Patients with severe surgery; (4) Patients with large area injuries; (5) Patients with long term respiratory and circulatory failure.

Indicator detection

PCT and BNP were performed in all patients on the 1st, 2nd, and 7th days after the diagnosis of the disease. In the morning in a fasting state, 2 ml of the patient's peripheral venous blood was collected, added with an appropriate amount of anticoagulant for routine anticoagulation, and centrifuged for 5 min at 3000 r/min. PCT was detected by upturn luminescence immunoassay (UPT) of Beijing Thermal View, and by UPT. Plasma BNP (NT proBNP) level was measured by time-resolved immunofluorescence method and AQT-90 detector of Radu Company in Denmark. APACHE-II score was used to evaluate patients' disease on the same day of blood drawing. Specifically, the APACHE II scoring system is composed of three parts: Acute physiology score (APS), age score, and the final score is the sum of the three. The highest theoretical score is 71, and the higher the score, the worse the disease [13].

Observation indexes

We measured PCT, BNP, level and APACHE II score of the two groups. ROC curve was used to evaluate the relationship between the three indicators and prognosis.

Statistical analysis

SPSS 26.0 statistical software was applied. The counting data were expressed by the number of cases/percentage (n/%) and analyzed using χ^2 test. The measurement data were expressed by mean \pm SEM and analyzed using T-test respectively. ROC curve was utilized to calculate the performance. $P < 0.05$ represents a significant difference.

Results

Baseline characteristics of the two groups

The baseline data of both groups were compared, and there were no differences in gender, body mass index (BMI), days in ICU, and infection site ($P > 0.05$). This indicates comparability between the two groups. The average age of

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Table 1. Baseline characteristics of the survival and death groups

| Index | Survival group (n=40) | Death group (n=25) | t/X ² | P |
|--------------------------|-----------------------|--------------------|------------------|---------|
| Age (years old) | 67.3±4.3 | 74.6±2.3 | -7.853 | < 0.001 |
| Gender (male, %) | 24 (60%) | 14 (56%) | 0.101 | 0.750 |
| BMI (kg/m ²) | 21.54±0.73 | 21.57±0.64 | -0.208 | 0.836 |
| Days in ICU | 17.08±2.06 | 17.6±1.80 | -1.049 | 0.298 |
| Biliary tract infection | 6 (15%) | 4 (16%) | 0.012 | 0.913 |
| Pulmonary infection | 22 (55%) | 15 (60%) | 0.157 | 0.692 |
| Urinary system infection | 9 (22.5%) | 5 (20%) | 0.057 | 0.811 |
| Surgical site infection | 3 (7.5%) | 1 (4%) | 0.326 | 0.568 |

Note: body mass index (BMI).

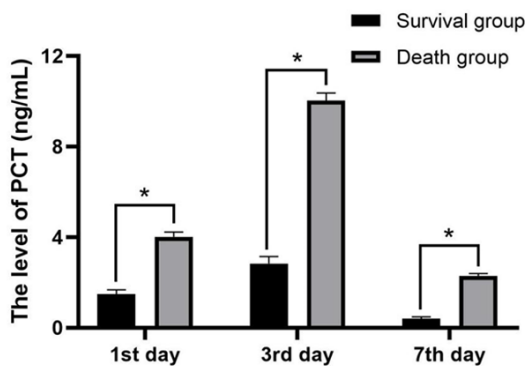


Figure 1. PCT level between the survival and death groups. *, P < 0.05. Note: procalcitonin (PCT).

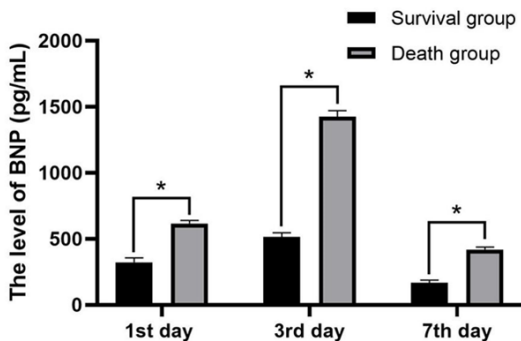


Figure 2. Comparison of the BNP level between the survival and death groups. *, P < 0.05. Note: brain natriuretic peptide (BNP).

survival group (67.28±4.27) was obviously lower in that of death group (74.56±2.26) (P < 0.05, **Table 1**).

Comparison of the PCT level between the survival and death groups

As shown in **Figure 1**, compared with the first day, the level of PCT increased in the third day,

then decreased in the seventh day in both groups. The level of PCT in the survival group was lower than that in the death group in the 1st, 2nd, and 7th day (P < 0.05).

Comparison of the BNP level between the survival and death groups

As shown in **Figure 2**, compared with the first day, the level of BNP increased in the third day, then decreased in the seventh day in both groups. The level of BNP in the survival group was lower than that in the death group in the 1st, 2nd, and 7th day (P < 0.05).

Comparison of the APACHE II score

As shown in **Figure 3**, compared with the first day, the score of APACHE II decreased in the third and seventh day in the survival group, while it increased in the death group. The score of APACHE II in the survival group was lower than that in the death group in the 1st, 2nd, and 7th day (P < 0.05).

AUC analysis of prognosis by PCT, BNP, and APACHE II

The AUC of PCT, BNP, and APACHE II were 0.768, 0.771, 0.891 on the 1st day; 0.829, 0.805, 0.809 on the 3rd day; 0.831, 0.848, 0.974 on the 7th day, respectively (**Figure 4** and **Tables 2-4**).

Discussion

Sepsis and septic shock are characterized by systemic inflammatory reactions and organ function damage caused by infection. Their high incidence rate and mortality have increasingly become a serious problem of global concern [14]. Sepsis is caused by infection, which can further develop into septic shock. Although the diagnosis and treatment methods are progressing, sepsis still has a high mortality rate. A study found that the mortality rate of sepsis in the pediatric intensive care unit (PICU) was 5%-25% [15]. Sepsis also has a very high rate of disability, which has a serious impact on the health-related quality of life of survivors and brings a great economic burden to individuals

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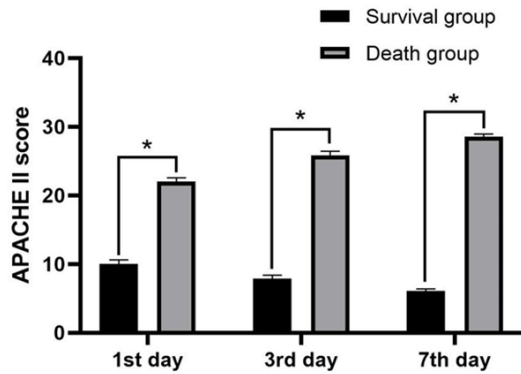


Figure 3. Comparison of the APACHE II score between the survival and death groups. *, $P < 0.05$. Note: Acute Physiology and Chronic Health Evaluation II (APACHE II).

and families, as well as a great public health economic burden to society. Therefore, early assessment of the severity and prognosis of sepsis is of great significance [16]. However, there is still a lack of specific indicators to judge the severity and prognosis of sepsis in clinical work. Therefore, it is necessary to find a sensitive and specific index to judge the severity and prognosis of sepsis patients [17]. This study showed that PCT, BNP, APACHE II scores reflected the severity of sepsis patients to a certain extent, and those with significantly higher PCT, BNP, APACHE II scores had poorer prognosis. Therefore, PCT, BNP, APACHE II scores can be used as prognostic indicators for sepsis patients.

APACHE-II score can accurately evaluate the condition of sepsis patients [18]. PCT is a 116 amino acid polypeptide, which is the precursor of a hormone regulating the calcium concentration in the body [19]. This polypeptide was originally used as a serum marker for cancer, but in recent years, researchers' interest in procalcitonin has focused on its value as a marker of bacterial infection [20]. A team of French oncologists led by Dr. Bohuon found that the presence of PCT, when using radioimmunoassay to detect the level of calcitonin (CT) was relevant in patients with thyroid tumors [21]. PCT is an inflammatory indicator. The level of PCT will increase in bacterial and fungal infections etc [22]. BNP is secreted by ventricular muscles and belongs to a type of polypeptide hormone, which can regulate the tension of the ventricular wall and cardiac load. It can also promote

the excretion of sodium and water, expand the blood vessels, and then reduce the peripheral load [23]. Research shows that [24], BNP is positively correlated with cardiac injury. However, some studies have shown that the BNP level in the blood of septic patients will also increase significantly [25]. The body will produce a lot of toxins in sepsis, which will damage the heart to a certain extent. Therefore, the level of BNP secreted by the heart will increase. In addition, endotoxins produced by sepsis in patients can induce BNP gene expression and increase BNP level in blood circulation [26].

Our study shows that there is a positive correlation between APACHE II score and mortality. The correct rate of predicting mortality is 97%. This study also confirms that APACHE II score can estimate the severity and prognosis of patients. PCT is a calcitonin prepeptide without hormone activity, which is normally synthesized by thyroid C cells [19]. The serum level of healthy adults is extremely low (less than 0.1 ng/ml). PCT not only has predictive significance for evaluating the prognosis of patients, but also is a good indicator to estimate the severity of infection in patients, and the prognosis of sepsis with continuous PCT increase is poor [27]. Studies [28] showed that the increase of PCT on the 7th day of sepsis can cause death, and the results of this study were consistent with this. BNP is the product of atrial and ventricular secretion, which is secreted by precursor proteins. BNP secretion can produce natriuretic, diuretic, vasodilator and smooth muscle relaxation use. The study shows that BNP can be used as a biochemical marker to predict myocardial injury and prognosis in severe sepsis and septic shock [24]. Some experts analyzed the BNP levels of 252 patients with severe sepsis at different time points during hospitalization, and found that if the level increased, the mortality rate increased [29]. They believed that the increase of BNP had application value in early diagnosis, clinical treatment and prognosis judgment of severe sepsis patients. To understand the relationship between inflammatory reaction and BNP release in sepsis patients, we screened 65 sepsis patients. After excluding the influence of abnormal cardiac function on BNP level, we analyzed the relationship between plasma BNP level and 28-day mortality of sepsis patients. The results suggest that monitoring the BNP

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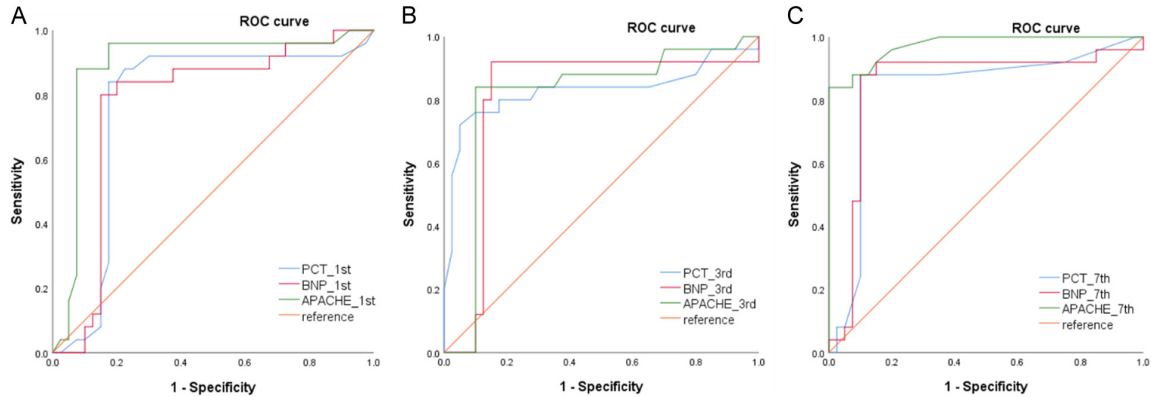


Figure 4. AUC analysis of prognosis based on the three indexes detected in 1st day (A), 3rd day (B), and 7th day (C).

Table 2. AUC analysis of prognosis in the first day

| Index | AUC | 95% CI | Sensitivity | Specificity | P |
|-------------|-------|-------------|-------------|-------------|---------|
| PCT (ng/mL) | 0.768 | 0.635-0.900 | 0.840 | 0.825 | < 0.001 |
| BNP (pg/mL) | 0.771 | 0.644-0.898 | 0.800 | 0.850 | < 0.001 |
| APACHE II | 0.891 | 0.794-0.987 | 0.880 | 0.925 | < 0.001 |

Note: procalcitonin (PCT), brain natriuretic peptide (BNP).

Table 3. AUC analysis of prognosis in the third day

| Index | AUC | 95% CI | Sensitivity | Specificity | P |
|-------------|-------|-------------|-------------|-------------|---------|
| PCT (ng/mL) | 0.829 | 0.704-0.954 | 0.800 | 0.825 | < 0.001 |
| BNP (pg/mL) | 0.805 | 0.674-0.936 | 0.920 | 0.850 | < 0.001 |
| APACHE II | 0.809 | 0.686-0.932 | 0.840 | 0.900 | < 0.001 |

Note: procalcitonin (PCT), brain natriuretic peptide (BNP), Acute Physiology and Chronic Health Evaluation II (APACHE II).

Table 4. AUC analysis of prognosis in the seventh day

| Index | AUC | 95% CI | Sensitivity | Specificity | P |
|-------------|-------|-------------|-------------|-------------|---------|
| PCT (ng/mL) | 0.831 | 0.713-0.949 | 0.880 | 0.900 | < 0.001 |
| BNP (pg/mL) | 0.848 | 0.731-0.965 | 0.880 | 0.900 | < 0.001 |
| APACHE II | 0.974 | 0.942-1.000 | 0.880 | 0.925 | < 0.001 |

Note: procalcitonin (PCT), brain natriuretic peptide (BNP), Acute Physiology and Chronic Health Evaluation II (APACHE II).

level in sepsis can reflect the severity of patients' condition and predict clinical prognosis.

In a word, PCT, BNP, APACHE II scores reflect the severity of sepsis patients, and the prognosis of sepsis patients is poor if they are significantly increased, which can be used as a prognostic indicator of sepsis patients. In view of the small sample size, the results need to be further validated by prospective, randomized

and controlled clinical studies with larger number of samples.

Conclusion

In summary, we explored the value of PCT and BNP in predicting the prognosis of sepsis. The results indicated that the level of plasma PCT and BNP in sepsis patients will increase, and it is positively correlated with the severity of the disease, which can be used as an indicator of bad prognosis of sepsis patients.

Disclosure of conflict of interest

None.

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