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Original Article

Dynamic monitoring the level of NT-proBNP in assessing the value of cardiac function and prognosis in patients with systemic infection

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Abstract: Objective: To investigate the N-terminal B-type natriuretic peptide (NT-proBNP) detection and chest wall echocardiography in joint assessing cardiac function and prognosis in patients with systemic infection. Methods: A total of 108 patients in systemic infection admitted to The Affiliated Hospital of Inner Mongolia Medical University from March 2015 to February 2017 were selected. According to the results of hospitalized echocardiography, the selected patients were divided into 87 cases of observation group (left ventricular ejection fraction (LVEF) <50%) and 21 cases of control group (LVEF value ≥50%). NT-proBNP of two groups at different time points were compared. In addition, patients were divided into death group (25 cases) and survival group (62 cases) based on 30-day prognosis. NT-proBNP and Acute Physiology and Chronic Health Evaluation-II (APACHE-II) scales were compared between two groups within one day, as well as the correlation between NT-proBNP and APECHE-II scales. The area under receiver operating characteristic (ROC) curve was calculated. Results: NT-proBNP of observation group had an increasing trend from day 1 to day 3 and decreasing trend from day 3 to day 7, whereas no significant change was detected from day 1 to day 7 in control group. NT-proBNP of observation group was significantly higher than control group at each time point (all $P<0.05$). APACHE-II score of survival group was 14.07±5.61 and NT-proBNP value was 653.15±345.26 ng/L on the first day after admission (within 24 h), which was significantly lower than those in death group (both $P<0.05$). There was a positive correlation between NT-proBNP and APACHE II ($r=0.59$, $P<0.05$). The critical point of ROC curve was blood NT-proBNP level at 1,509 ng/L, and the sensitivity and specificity were 91.37% and 79.61% respectively. Conclusion: Dynamic monitoring of NT-proBNP has a higher clinical value for the assessment of cardiac function and prognosis in patients with systemic infection.

Keywords: N-terminal-pro-brain natriuretic peptide, echocardiography, systemic infection, cardiac function

Introduction

Systemic infection is often complicated by cardiac disorder, which is difficult to treat and has high morbidity [1]. Sixty-five percent of patients with systemic infection are accompanied by heart failure and myocardial injury at early stage, the exact mechanism is still not fully understood. Researches in recent years established that excessive inflammatory factors (TNF-α, IL-6, ET-1) generated when the patients suffer from myocardial mitochondrial energy metabolism disorder and sepsis played an important part in these complications [2]. In addition, nitrate oxide regulation, damage from free radicals, toll-like receptors and apoptosis might have contributed to cardiac dysfunction [3]. N-terminal-pro-brain natriuretic peptide (NT-proBNP) is a metabolite secreted by cardiomyocytes in ventricles in response to rapid stretching. In recent years, as the relation between Renin-angiotensin-aldosterone System (RAAS) activation and systemic infection is being further explored, more and more studies confirmed the correlation between the two. NT-proBNP compensatory level increases as heart failure occurs. Compared to doppler echocardiography, it is a more sensitive heart failure indicator in clinical application and closely related to sepsis [4, 5]. Therefore, it is crucial to determine cardiac function of patients suffering from systemic infection. Ech-

Table 1. Comparison of NT-proBNP between obseration group and control group at different time points (ng/L, $\overline{x}$±sd)

Time	Cardiac function reduction group (n=87)	Normal cardiac function group (n=21)	t	P
1 d	2,212.65±368.78	1,030.11±379.78	4.941	0.000
2 d	3,002.43±600.04	1,131.12±317.33	7.389	0.000
3 d	3,125.75±624.63	978.24±332.12	8.027	0.000
5 d	1,952.13±566.77	927.89±216.37	7.462	0.000
7 d	1,471.26±410.40	968.28±257.63	4.944	0.000

Note: N-terminal B-type natriuretic peptide.

ocardiography is one of the essential diagnostic approaches for cardiovascular diseases, but less used for the dynamic monitoring of cardiac function changes in patients with severe infection in the intensive care unit. In this study, NT-proBNP levels in patients with systemic infection were dynamically monitored to investigate the correlation between NT-proBNP levels, cardiac function and APACHE-II score, so as to evaluate the predictive value of NT-proBNP in the prognosis of patients with systemic infection.

Materials and methods

Clinical materials

A total of 108 patients with systemic infection admitted to The Affiliated Hospital of Inner Mongolia Medical University from March 2015 to February 2017 were selected (78 males, 30 females; at the age of 53-77, average age of 60.9±17.6). All the enrolled patients met the criteria listed in *Guidelines for Severe Infection and Septic Shock* issued by American College of Clinical Pharmacy and Society of Critical Care Medicine in March 2004 [6]. Patients with diabetes, tumor, history of cardiac diseases, insulin allergy and in pregnancy or lactation were excluded.

According to the results of echocardiography within 5 days of admission, the selected patients were divided into 87 cases of observation group (left ventricular ejection fraction (LVEF) <50%) and 21 cases of control group (LVEF ≥50%). The clinical significance of LVEF is to reflect the percentage of stroke volume in the ventricular end diastolic volume; generally, more than 50% considered normal range. LVEF is an important index of myocardial pump function. The observation group had 62 male subjects and 25 female subjects; at the age of 55-73 with the average age of 61.9±14.3. The control group had 16 male subjects and 5 female subjects; at the age of 53-77 with the average age of 59.7±19.6. In addition, patients were divided into death group 25 cases and survival group 62 cases based on 30-day prognosis. The NT-proBNP and APECHE-II scales were compared between the two groups within one day [7].

Study methods

Cardiac function indicators were measured by transthoracic echocardiography (TTE) using Philips iE33 Ultrasound Machine, LVEF and and E/A value were recorded. The measurement was taken from 10 am to 12 pm at 1, 2, 3, 5 and 7 days after patients with systemic infection were admitted, and all measurement procedures were performed by the same TTE trained doctor.

NT-proBNP level was measured from 10 am to 12 pm under fasting conditions, at 1, 2, 3, 5 and 7 days after patients were admitted. A total of 2.5 mL of blood was drawn from elbow veins and preserved in sodium citrate (EDTA-Na) vacuum anticoagulation tube. The sample was centrifuged at 2,000 r/min for 15min at room temperature. The serum was separated and stored at -70°C environment. NT-proBNP concentration was measured by enzyme linked immunosorbent assay (ELISA). The testing kits were from USCN KIT INC., Wuhan, and the equipment was using xMark Microplate Absorbance Spectrophotometer from Bio-Rad, USA [8].

Statistics methods

SPSS13.0 statistics software was used. Count data was expressed as percentage and compared by χ^2 tests; measurement data were expressed as mean ± standard deviation ($\overline{x}$±sd) and compared by t test. A difference of $P<0.05$ was considered to have statistical significance.

Table 2. Comparison of APACHE-II scales and NT-proBNP within one day between death group and survival group (n, $\overline{x}$±sd)

Group	APACHE-II	NT-proBNP (ng/L)
Survival group (n=62)	14.07±5.61	653.15±345.26
Death group (n=25)	24.07±10.02	2,075.23±1,023.74
t	5.914	9.718
P	0.000	0.000

Note: NT-proBNP, N-terminal-pro-brain natriuretic peptide; APACHE-II, Acute Physiology and Chronic Health Evaluation-II.

Results

Comparison of NT-proBNP values between observation group and control group at different time points

NT-proBNP of observation group had an increasing trend from day 1 to day 3 and decreasing trend from day 3 to day 7, whereas no significant change was detected from day 1 to day 7 in control group. The daily NT-proBNP of observation group was significantly higher than that in control group (all P<0.05). See **Table 1**.

Comparison of NT-proBNP and APACHEII scores within one day between death group and survival group

The APACHEII scales of survival group was 14.07±5.61, and the NT-proBNP of the first day (24 h) after admission was 653.15±345.26 ng/L, which were all significantly lower than that of death group (both P=0.000). See **Table 2**.

Correlation analysis

There was a positive correlation between NT-proBNP and APACHE-II (r=0.59, P<0.05).

The value of blood NT-proBNP level of death group in the diagnosis of prognosis

The level of blood NT-proBNP at 1,509 ng/L is the corresponding critical point while the sensitivity (91.37%) and specificity (79.61%) of ROC curve are maximum.

Discussion

Systemic infection also known as sepsis or bacteremia, and its general manifestation is multiple organ failures. It is a kind of severe infection or poisoning symptom caused by pathogens entering the bloodstream and multiplying or secreting toxins in the body [9]. Systemic infection is very easily secondary to multiple organ dysfunction and lead to high mortality, which has always been a hot topic in the research of critical medicine [10]. In recent years the literature has reported that sepsis can lead to significant changes in cardiac structure, especially in the case of septic shock persists for longer period of time. Gayda et al. reported that septic rabbits have visible punctate bleeding on the myocardial surface, while there are widespread myocardial bleeding, inflammatory cell infiltration, capillary congestion, fibrous necrosis and degeneration under the light microscope [11]. An autopsy study found that there were structural changes in the myocardium of septic shock patients, manifested as a large number of interstitial cells infiltration and lipid aggregates in the myocardium [12]. Some scholars have proposed the concept of septic myocardial dysfunction [13, 14]. However, the pathogenesis of myocardial inhibition in patients with severe infection/septic shock is not well understood. At present, the possible mechanisms include gene regulation, cell apoptosis, myocardial cell energy metabolism disorders, neuroendocrine regulation, immune regulation, bacterial toxin invasion and so forth. All of these factors could cause the abnormalities in the structure and function of the myocardium, which might lead to inhibition of myocardial [15].

Myocardial inhibition persists throughout the whole pathophysiology process of severe infection/septic shock. Myocardial inhibition is often characterized by reversible left and right ventricular dilatation and LVEF reduction. Severe infection/septic shock in patients with left ventricular end-diastolic volume increase, which compensate for the decrease of ejection fraction to some extent, so that cardiac output can still be maintained in the normal range. The increase of left ventricular diastolic volume may cause ventricular wall tension increased and stimulate ventricular myocytes secreting more NT-proBNP, thus increasing the level of plasma NT-proBNP. Therefore, there is a correlation between the increase of NT-proBNP and myocardial inhibition in patients with systemic infection. However, whether NT-proBNP could determine the cardiac function changes on systemic infection has not been verified [16].

At the early stage of systemic infection, multinuclear cells entered cardiac muscle fibers, which led to a decrease in the compliance of myocardium, which in turn, caused ventricular diastolic function disorder. In addition, sediments of glycation products that existed in large quantity within ventricles during systemic infection caused damage to myocardial compliance, and damaged ventricular diastolic function [17]. In our study, daily NT-proBNP of observation group was significantly higher than control group and the former showed an increasing trend from day 1 to day 3 and decreasing trend from day 3 to day 7, which indicates a certain correlation between the degree of cardiac function damage and NT-proBNP.

The APACHE-II score is widely used in the assessment of condition and prognosis of severe patients. The higher the APACHE-II scale, the heavier the patient's condition and the worse the prognosis. In our study, the APACHEII score of the survival group was 14.07±5.61, and the value of NT-proBNP was 653.15±345.26 ng/L, which were significantly lower than those in the death group. The results of correlation analysis showed that there was a significant positive correlation between NT-proBNP and APACHEII score in patients with systemic infection. The critical point on the ROC curve was 1,509 ng/L of blood NT-proBNP, with a sensitivity and specificity of 91.37% and 79.61%, respectively.

It is important to note that there are other mechanisms of systemic infection caused by elevated NT-proBNP, such as inflammatory cytokines, renal insufficiency, fluid resuscitation and diuretic treatment [18-20]. Therefore, biomarkers such as NT-proBNP should be organically combined with the patient's clinical manifestations and echocardiography. And it is necessary to emphasize that the continuous monitoring of its dynamic changes during treatment is critical, in order to give full play to its value.

In conclusion, the dynamic monitoring of NT-proBNP has a high clinical value for the assessment of cardiac function and prognosis in patients with systemic infection.

Disclosure of conflict of interest

None.

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