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Original Article

Clinical value of serum N-terminal B-type natriuretic peptide level in the diagnosis of patients with inflammatory joint disease combined with cardiac insufficiency

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Abstract: Objective: This study aimed to explore the clinical value of serum N-terminal B-type natriuretic peptide (NT-proBNP) level in the diagnosis of elderly patients with inflammatory joint disease combined with cardiac insufficiency (I&CI). Methods: 41 patients with I&CI were enrolled in the study group (SG), and 41 healthy subjects with physical examination at the same period were enrolled in control group (CG). The expressions of NT-proBNP, BNP and TNF-α in the serum of SG and CG were detected by enzyme-linked immunosorbent assay (ELISA). The diagnostic value of each outcome was studied by ROC curve. The correlation of NT-proBNP, BNP and TNF-α in patients with I&CI was analyzed. Results: The expression levels of NT-proBNP, BNP or TNF-α in SG were higher than those in CG (P<0.001). There were positive correlations between NT-proBNP and BNP (r=0.823, P<0.001), TNF-α and BNP (r=0.554, P<0.001), and NT-proBNP and TNF-α (r=0.649, P<0.001) in peripheral blood of patient with I&CI, respectively. According to the ROC curve analysis, the sensitivity, specificity and AUC of single diagnosis were 85.48%, 53.66% and 0.8080 for NT-proBNP, 75.61%, 60.98% and 0.7864 for TNF-α, and 70.73%, 63.41% and 0.6568 for BNP, respectively. The sensitivity and AUC value of NT-proBNP diagnosis were higher than that of TNF-α or BNP alone. Conclusion: The detection of NT-proBNP is of high diagnostic value for I&CI in clinical practice, and its diagnostic efficacy is slightly higher than that of BNP and TNF-α. It is speculated that the expression levels of BNP, NT-proBNP and TNF-α can timely reflect the disease development of patients with I&CI.

Keywords: Serum N-terminal B-type natriuretic peptide, inflammatory joint disease combined with cardiac insufficiency, cardiac insufficiency, diagnosis

Introduction

Inflammatory joint disease is a broad-spectrum disease that affects the surrounding area [1, 2]. As an immune systemic disease, it can affect multiple systems of the whole body, and the disability rate is extremely high, which can cause death when it seriously affects vital organs [3, 4]. Both cardiac insufficiency and inflammatory joint disease are common diseases in middle-aged and elderly people, and the incidence rate is proportional to age. Inflammatory joint disease combined with cardiac insufficiency (I&CI) is one of the inflammatory joint diseases, and belongs to chronic systemic inflammatory diseases [1, 5]. I&CI is a common concurrent cardiac disease in patients with senile inflammatory joint disease. The onset of the disease is complicated. Patients are often accompanied by different degrees of cardiac failure. The disease itself or drugs can cause inflammatory joint disease and cardiac insufficiency [6, 7].

Related reports indicated that N-terminal B-brain natriuretic peptide (NT-proBNP) and brain natriuretic peptide (BNP) had important diagnostic value in the monitoring of patients

Table 1. General data of the two groups

Group	Observation group (n=41)	Control group (n=41)	t/X^2	P
Age (years)	57.26 ± 10.18	57.19 ± 10.72	0.030	0.976
Female (n/%)	22 (53.66)	22 (53.66)	0.000	1.000
BMI (kg/m^2)	19.21 ± 2.75	19.82 ± 1.92	1.165	0.248
History of diabetes (n/%)			0.943	0.332
No	10 (24.39)	14 (34.15)		
Have	31 (75.61)	27 (65.85)		
Fasting blood glucose (mmol/L)	4.11 ± 1.05	5.03 ± 0.18	5.530	<0.001
Blood phosphorus (mmol/L)	2.05 ± 0.14	2.12 ± 0.17	2.035	0.045
Renal function				
BUN (mmol/L)	9.58 ± 5.66	6.34 ± 1.27	3.576	<0.001
Cr (mmol/d)	15.70 ± 3.97	6.24 ± 1.63	14.110	<0.001

with cardiac failure, among which NT-proBNP and BNP had good sensitivity in the diagnosis of cardiac insufficiency [8, 9]. In recent years, with the in-depth study of inflammatory joint disease, the latest studies of inflammatory mediator have shown that tumor necrosis factor-α (TNF-α) was considered to play an important role in the pathogenesis of inflammatory joint disease [10]. I&CI has a high incidence of morbidity and mortality, and finding relevant factors that accurately reflect or predict I&CI has become the focus of research [11]. However, there are few studies on NT-proBNP, BNP and TNF-α in I&CI, and the specific relationship between them and patient with I&CI is still unclear. This study aimed to explore the expression and clinical significance of NT-proBNP and TNF-α in peripheral blood of patients with I&CI.

Materials and methods

General data

Study subjects and grouping: 41 patients who were diagnosed as I&CI and treated in our hospital were enrolled in SG, including 19 males and 22 females, aged from 41 to 81 years, with an average age of 57.26 ± 10.18 years. 41 healthy subjects with no inflammatory joint disease at the same period were enrolled in CG, including 19 males and 22 females, aged from 41 to 79 years old, with an average age of 57.19 ± 10.72 years old. Inclusion and exclusion criteria: (1) All patients in SG were diagnosed as I&CI by our hospital according to WHO's I&CI criteria [12]; (2) Patients with infectious diseases were excluded; patients with other hematological diseases such as hemolytic anemia and idiopathic thrombocytopenic purpura were excluded; patients with other primary malignant diseases were excluded; patients with other complications affecting NT-proBNP, BNP, or TNF-α levels were excluded; the drugs used in the treatment of the relevant patients did not affect NT-proBNP, BNP, or TNF-α levels. Patients and their families were informed in advance before the study was carried out, and they were asked to sign informed consent. The study was approved by the ethics committee of the Lushan Sanatorium of PLA. There were no statistical differences in the general data between the two groups including age, gender, and body mass index (P>0.05), which were comparable (**Table 1**).

Main reagents and detection methods

Fasting venous blood was extracted from all patients before 9:00 am and sent for examination in time.

(1) NT-proBNP ELISA test kit (Shanghai Guyan Biotechnology Co., Ltd.), TNF-α ELISA test kit (Shanghai Guyan Biotechnology Co., Ltd.), BNP ELISA test kit (Shanghai Guyan Biotechnology Co., Ltd.), centrifuge (Hunan Pingfan Technology Co., Ltd.), automatic washing machine (Nanjing Detie Experimental Equipment Co., Ltd.), enzyme standard analyzer (Shanghai Xinzhuang Instrument Co., Ltd.).

(2) The levels of NT-proBNP, BNP and TNF-α were measured by ELISA. The collected venous blood to be tested was placed in a centrifuge,

Table 2. Expression levels of NT-proBNP, TNF-α and BNP in peripheral blood of two groups of patients

Group	SG	CG	t	P
NT-proBNP (pg/ml)	1837.20 ± 462.37	1002.95 ± 362.42	9.093	<0.001
TNF-α (pg/ml)	38.16 ± 6.27	30.22 ± 6.15	5.789	<0.001
BNP (pg/mL)	663.81 ± 116.06	530.51 ± 107.29	5.400	<0.001

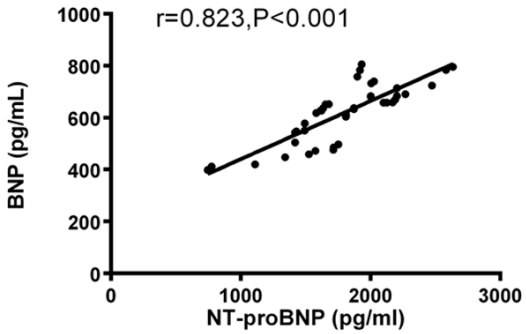

Figure 1. The results of partial correlation analysis showed that the expression levels of NT-proBNP and BNP were positively correlated in the peripheral blood of patients with I&CI (r=0.823, P<0.001).

and serum was separated at 3500 r/min. Serum levels of NT-proBNP, BNP and TNF-α were measured by ELISA. Instructions of the human NT-proBNP ELISA kit, the BNP ELISA kit, and the human TNF-α ELISA kit were referred to as follows: Fasted elbow venous blood was collected by vacuum extraction with sodium citrate. All samples were centrifuged at low temperature within 3 h (3500 r/min for 15 min at 4), and then placed at -20 in a cryogenic refrigerator for later use. The test was carried out in strict accordance with the ELISA instructions. 100 μl of the standard solution, the sample to be tested, and the negative and positive control solutions were aspirated into the reaction well. 100 μl of bioreactive antibody solution was quickly added, covered with film, mixed and let stand for 40 min. Then, 100 μl of streptavidin was added to each well, covered with a film, and allowed to stand for 40 min after mixing. The liquid in the reaction well was poured, and the washing liquid was added to each reaction well. The mixture was shaken slowly for 1 min, and the liquid in the reaction well was poured out and repeated 5 times. 100 μl of each of reaction solution A and reaction solution B was added to each reaction well, covered with a film, and let stand in the dark for 5 min. 100 μl of the stop solution was added to the reaction well. Finally, the OD value of each well was measured using a microplate analyzer at a wavelength of 450 nm, and the concentrations of NT-proBNP, BNP and TNF-α were calculated.

Statistical methods

Statistical analysis was performed using SPSS 17.0 software (Beijing Boyi Zhixun Information Technology Co., Ltd.). The count data between the two groups was tested by X^2. The count data was expressed as mean ± standard deviation (x ± sd). The measurement data between the two groups were compared using an independent t test, and the ROC results were analyzed using STATA software. When P<0.05, the difference was considered statistically significant.

Results

General data

There were no statistical differences in the general data between the two groups including age, gender, and body mass index (P>0.05) (**Table 1**).

Comparison of NT-proBNP, BNP and TNF-α in two groups

The expression levels of NT-proBNP, TNF-α and BNP in peripheral blood of patients in SG were higher than those in CG (P<0.05) (**Table 2**).

Correlation of NT-proBNP, TNF-α and BNP expression in I&CI

(1) Partial correlation analysis showed that the expression levels of NT-proBNP and BNP were positively correlated in peripheral blood of patients with I&CI (r=0.823, P<0.001) (**Figure 1**).

(2) Partial correlation analysis showed that the expression levels of TNF-α and BNP were positively correlated in peripheral blood of patients with I&CI (r=0.554, P<0.001) (**Figure 2**).

(3) Partial correlation analysis showed that the expression of NT-proBNP and TNF-α was positively correlated in peripheral blood of patients with I&CI (r=0.649, P<0.001) (**Figure 3**).

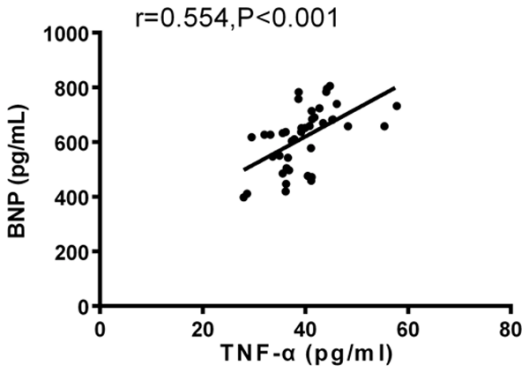

Figure 2. The results of partial correlation analysis showed that the expression levels of TNF-α and BNP were positively correlated in the peripheral blood of patients with I&CI (r=0.554, P<0.001).

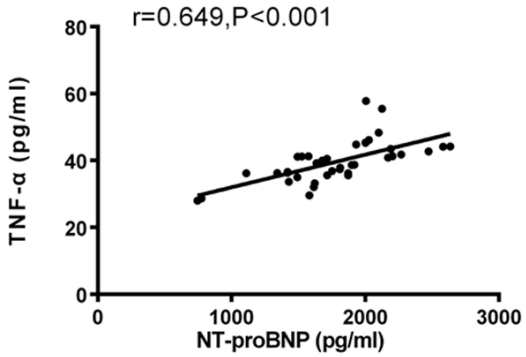

Figure 3. The results of partial correlation analysis showed that the expression levels of NT-proBNP and TNF-α were positively correlated in the peripheral blood of patients with I&CI (r=0.649, P<0.001).

Table 3. Single diagnostic value of NT-proBNP, BNP and TNF-α in I&CI

Diagnosis method	Sensitivity	Specificity	AUC
NT-proBNP	85.48%	53.66%	0.8080
TNF-α	75.61%	60.98%	0.7864
BNP	70.73%	63.41%	0.6568
X^2	0.068	9.012	5.332
P	0.867	<0.001	0.002

Single diagnostic value of NT-proBNP, BNP and TNF-α in I&CI

In the diagnosis of patient with I&CI, the sensitivity, specificity and AUC of single diagnosis were 85.48%, 53.66% and 0.8080 for NT-proBNP, 75.61%, 60.98% and 0.7864 for TNF-α, and 70.73%, 63.41% and 0.6568 for BNP, respectively. The sensitivity and AUC value of NT-proBNP diagnosis were significantly higher than those of TNF-α and BNP alone (**Table 3** and **Figure 4A-C**).

Discussion

This study compared the general data of the two groups and confirmed that there were no statistical differences in the possible influencing factors such as age, gender, and BMI, etc. The expression of NT-proBNP, BNP and TNF-α in peripheral blood of patients with I&CI and healthy subjects was analyzed. The results of ELISA showed that the expression level of BNP in peripheral blood of patients with I&CI was higher than those of subjects with no I&CI. As a common detection factor for predicting cardiac failure-related diseases, BNP is widely used in clinical testing, which is important for early diagnosis, intervention and prognosis of patients with cardiac failure [13-15]. Related reports have confirmed that BNP and NT-proBNP are overexpressed in the serum of patients with rheumatoid arthritis-related diseases [16, 17]. The level of TNF-α in the peripheral blood of SG was significantly higher than that of CG by ELISA.

In recent years, many clinical studies have shown that cardiac color Doppler ultrasound was used in routine diagnosis of cardiac insufficiency in patients with cardiac failure in clinical practice. However, there were great limitations in reflecting progression changes of disease, because it is impossible to timely and meticulously monitor the changes of cardiac function of related patients [18]. Related studies have confirmed that ventricular structural changes are closely related to changes in NT-proBNP levels [19-22]. As a neurohormone synthesized in the ventricle, NT-proBNP enters the circulation when the ventricular pressure is elevated [23, 24]. Studies have shown that serum BNP and NT-proBNP levels of patients with cardiac insufficiency are significantly higher than those of patients with early cardiac failure or healthy subjects [25-27]. Moreover, TNF-α has also been confirmed to be abnormally expressed in acute inflammatory joint disease and chronic inflammatory joint disease, and its expression in inflammatory joint disease is abnormally up-regulated [28-30]. Therefore, it was considered that the expression of TNF-α

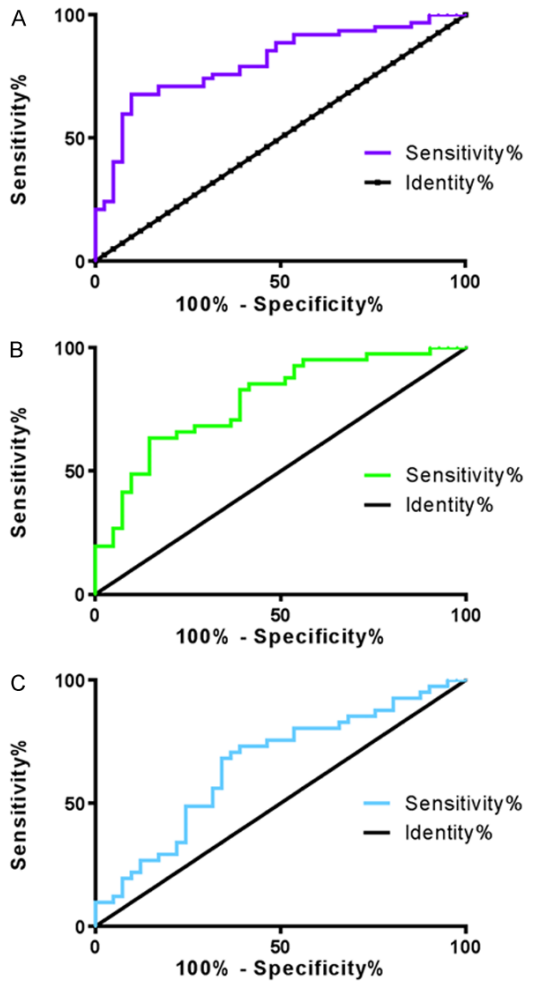

Figure 4. Single diagnostic efficacy of NT-proBNP, TNF-α and BNP in patients with I&CI. A. The sensitivity, specificity, and AUC value of single NT-proBNP diagnosis were 85.48%, 53.66% and 0.8080, respectively. B. The sensitivity, specificity and AUC value of single TNF-α diagnosis were 75.61%, 60.98% and 0.7864, respectively. C. The sensitivity, specificity, and AUC value of single BNP diagnosis were 70.73%, 63.41%, and 0.6568, respectively.

in I&CI was significantly different in the peripheral blood of healthy subjects and patients with I&CI, and BNP, NT-proBNP and TNF-α were over-expressed in peripheral blood of patients with I&CI. Then, the correlation of BNP, NT-proBNP and TNF-α expression in I&CI was analyzed. Partial correlation analysis showed that the expression levels of BNP and NT-proBNP, BNP and TNF-α, and NT-proBNP and TNF-α were positively correlated in patient with I&CI peripheral blood. Clinical studies have confirmed that the extent of NT-proBNP and BNP that increased is positively correlated with the severity of cardiac failure [31]. And many similar studies also showed that the expression levels of BNP and NT-proBNP were correlated with TNF-α, which greatly supported the results of this study [32]. Finally, the single diagnostic value of BNP, NT-proBNP, and TNF-α in I&CI was analyzed. It was found that the sensitivity and AUC value of NT-proBNP diagnosis were significantly higher than those of BNP and TNF-α alone in the diagnosis of patients with I&CI. At present, no study on the diagnostic value of combined detection of BNP, NT-proBNP and TNF-α in I&CI has been reported. However, the traditional diagnosis of patient with I&CI is limited by medical institutions. The detection factor is small, and it is easy to cause weak specificity, which is unfavorable for monitoring the development of patient's condition. In this study, the detection of NT-proBNP was found to have a high diagnostic value for clinical I&CI, and the diagnostic efficacy was slightly higher than those of BNP and TNF-α. It is speculated that the expression levels of BNP, NT-proBNP and TNF-α can timely reflect the development of patient with I&CI.

In this study, there were still insufficiencies. For example, the relationship between the expression difference of patient with I&CI and healthy subjects and the renal lesions of patients was not specifically analyzed. Changes of NT-proBNP expression were not measured at different time. Only clinically relevant factors and BNP and TNF-α were analyzed. Other tests were not considered such as uric acid of patients. All the above had a certain impact on the research design. Therefore, in future, the latest research will be referenced in time, and corresponding research plans will be added to make up for the design defects to continuously improve the research.

In summary, the expression levels of NT-proBNP, BNP and TNF-α in peripheral blood of patient with I&CI were higher than those of healthy subjects; the expression levels of NT-proBNP, BNP and TNF-α were positively correlated in peripheral blood of patients with I&CI. The detection of NT-proBNP is of high diagnostic value for I&CI in clinical practice, and its diagnostic efficacy is slightly higher than that of BNP and TNF-α. It is speculated that the expression levels of BNP, NT-proBNP and TNF-α can timely reflect the disease development of patients with I&CI.

Disclosure of conflict of interest

None.

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