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Original Article

The correlation of b-type natriuretic peptide, c-reactive protein and troponin I with cardiac function and ventricular remodeling in elderly patients with chronic heart failure

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Abstract: Objective: To study the correlation of b-type natriuretic peptide, c-reactive protein and troponin I with cardiac function and ventricular remodeling in elderly patients with chronic heart failure (CHF). Methods: Patients n=328 with CHF were selected as the observation group for this prospective study and 60 healthy subjects were selected as the control group. Patients with chronic heart failure (CHF) were grouped based on the heart function classification. Among them, 102 cases were classified as grade II heart function. Cardiac function of 137 cases belonged to grade III, while the cardiac function of 89 cases was classified as grade IV. The serum levels of b-type natriuretic peptide (BNP), c-reactive protein (CRP), troponin I (cTnI) and the related indexes of cardiac ventricular remodeling were measured. Results: The BNP, CRP and cTnI levels, left ventricular end-diastolic diameter (LVEDD) and left ventricular mass index (LVMI) of the observation group were higher than those of the control group, and the Left Ventricular Ejection Fractions (LVEF) was lower than that of the control group (all P<0.001). BNP, CRP, cTnI, LVEDD, and LVMI indexes in the grade IV group were higher than those in grade III and grade II groups, while LVEF was lower than those in grade III and grade II groups (all P<0.05). BNP, CRP, cTnI, LVEDD, and LVMI indexes in patients with grade III cardiac function were higher than those of patients with class II cardiac function, and LVEF index was lower than that of patients with class II cardiac function (P<0.01 or P<0.001). BNP, CRP and cTnI levels were positively correlated with LVEDD and LVMI levels and negatively correlated with LVEF level (all P<0.001). Conclusion: BNP, CRP and cTnI were highly expressed in CHF patients and worse cardiac function was accompanied by higher expression of these indicators. BNP, CRP and cTnI levels were positively correlated with LVEDD and LVMI and negatively correlated with LVEF.

Keywords: BNP, CRP, cTnI, chronic heart failure, ventricular remodeling, correlation

Introduction

Heart failure is a cardiac circulatory disorder characterized by the blockage of the venous blood system and low-perfusion of the arterial blood system due to systolic or diastolic dysfunction of the heart itself. According to the severity of the disease, it can be divided into acute heart failure and chronic heart failure [1, 2]. The incidence of chronic heart failure (CHF) is 0.9% and more than 60% of patients were elderly. There is an increased risk of cardiac arrhythmia with multiple organ failure in CHF patients [3, 4]. In addition, studies have shown that the 5-year mortality rate of the elderly with CHF is over 50% [5, 6]. Therefore, early diagnosis of CHF is of great significance for the improvement of the prognosis [7]. Previous studies have shown that ventricular remodeling is the basis for the occurrence and development of CHF and color Doppler ultrasound can effectively monitor ventricular remodeling and cardiac function [8, 9]. Although the assessment of cardiac function and ventricular remodeling in patients with CHF by color Doppler echocardiography is relatively accurate, the results were affected by human factors, cardiac hemodynamics and the neuroendocrine system. So, the color Doppler echocardiography cannot accurately judge all the conditions of the body [10, 11].

In clinical practice, blood-related markers are used to assist the determination of disease severity [12, 13]. Type B natriuretic peptide (BNP) can be secreted into the blood when cardiac dysfunction occurs. Its elevated level in the blood is an effective marker of CHF [14]. Studies have shown that inflammatory factors such as c-reactive protein (CRP) are highly expressed in CHF, but whether they are correlated with ventricular remodeling and cardiac function has not been determined [15]. Troponin I (cTnI) is an effective serum marker that reflects myocardial injury. Some studies have found that myocardial cell necrosis occurs due to ischemia and hypoxia in the occurrence of CHF, leading to the release of cTnI into the blood. cTnI expression is significantly increased in patients with end-stage chronic heart failure, but whether cTnI is related to ventricular remodeling and cardiac function is currently inconclusive [16]. Based on this study, we studied the correlation of BNP, CRP, cTnI with ventricular remodeling and cardiac function in patients with CHF.

Materials and methods

Clinical data

This study was approved by the Ethics Committee of The First Affiliated Hospital of Anhui Medical University. A total of 328 CHF patients admitted to the department of cardiology of The First Affiliated Hospital of Anhui Medical University from March 2018 to December 2019 were selected as the observation group for this prospective study and 60 healthy patients during the same period were selected as the controls. All the subjects were aged 60-86 years old, with an average age of 71.2±9.2 years old. All of the patients enrolled in this study have signed the informed consent.

Inclusion and exclusion criteria for patients in the observation group

Inclusion criteria: (1) Patients with CHF diagnosed in line with the 2016 European society of cardiology guidelines for acute and chronic heart failure criteria [17]; (2) patients over the age of 18; (3) patients with the diagnosis of chronic heart failure for the first time without drug intervention. Exclusion criteria: (1) Patients with congenital heart disease; (2) patients with malignant tumors; (3) patients with cardiogenic shock, hypertrophic cardiomyopathy and aortic dissection; (4) patients with myocardial infarction or undergoing vascular reconstruction surgery in the past 6 months; (5) patients with diseases of the blood system.

Methods

After admission, two 5 mL samples of cubital venous blood were collected from each participant and stored in sterile tubes with ethylenediaminetetraacetic acid (Leval Technology (Shenzhen) Co., Ltd., article number: 1186d). After storing in the refrigerator at 4C for 15 minutes, serum and plasma were centrifuged at 1106.8×g. The serum and plasma were preserved in the freezer at -80C. BNP levels (the kit comes from China, Shanghai Tongwei, article number: TWp025109) in the plasma were detected by radioimmunoassay using Triage R diagnostic equipment (USA, BIOSITE company, model: Triage MeterPro). Serum cTnI (reagent kit comes Originated from China, Shanghai Tongwei, article number: tw037076) and CRP (the kit comes from China, Shanghai Tongwei, Item No.: tw035331) levels were detected using enzyme-linked immunosorbent assay and automatic immunoassay Instrument (Germany, Siemens, model: IMMULITE 2000 XPi).

Cardiac ultrasonography: Left Ventricular Ejection Fractions (LVEF), Left ventricular end-diastolic diameter (LVEDD), Interventricular septal thickness (IVST), Left ventricular posterior wall thickness (LVPWT) and Left ventricular mass index (LVMI) were detected by using a cardiac color Doppler (Philips, USA, model: PHILPS IU22).

Cardiac function classification: According to the New York heart association (NYHA) classification standard [18], 102 cases were classified as grade II heart function, 137 cases belonged to grade III heart function, while 89 people were classified with grade IV heart function.

Statistical methods

The continuous variables were expressed as mean ± standard deviation ($\bar{x}$ ± sd) by SPSS 22.0 statistical software. Independent sample t-test was used to analyze data that conforms to normal distribution with homogeneity of variance assumed while rank sum test was used to analyze data that does not conform to normal distribution with homogeneity of variance. One-way ANOVA was used to detect whether there were differences among groups and if differ-

ences exist. Bonferroni method was further used for pairwise comparison. Pearson product-moment correlation analysis was used to analyze the linear correlation between the two variables. P<0.05 was considered statistically significant.

Results

Comparison of general data, BNP, CRP, cTnI and ventricular remodeling indexes between the two groups

There were no significant differences in age, sex and BMI between the two groups. The levels of BNP, CRP and cTnI, LVEDD and LVMI in the observation group were higher than those in the control group, while LVEF was lower than that in the control group (all P<0.001). There were no differences in IVST and LVPWT between groups (all P>0.05). See **Table 1**.

Comparison of general data of patients with different cardiac functions

There were no significant differences in sex, age, hypertension, type 2 diabetes, hyperlipidemia and cerebral infarction among the three groups. The incidence of coronary heart disease in grade IV group was higher than that in grade II and grade III groups (all P<0.05). See **Table 2**.

Comparison of BNP, CRP, cTnI and ventricular remodeling indexes in patients with chronic heart failure among different cardiac function groups

The indexes of BNP, CRP, cTnI, LVEDD and LVMI in group IV were higher than those in group III and II, while indexes of LVEF was lower than that in group III and II. The indexes of BNP, CRP, cTnI, LVEDD and LVMI in group III were higher than those in group II, while indexes of LVEF was lower than that in group II (P<0.001), but there was no significant difference in IVST and LVPWT. See **Table 3.**

Correlation between BNP and ventricular remodeling indexes in patients with chronic heart failure

BNP level was positively correlated with LVEDD and LVMI (r=0.569, P<0.001 and r=0.916, P<0.001) respectively, but negatively correlated with LVEF (r=0.349, P<0.001). See **Figure 1**.

Correlation between CRP and ventricular remodeling indexes in patients with chronic heart failure

CRP level was positively correlated with LVEDD and LVMI (r=0.458, P<0.001 and r=0.749, P<0.001) respectively and negatively correlated with LVEF (r=0.375, P<0.001). See **Figure 2**.

Correlation between cTnI and ventricular remodeling indexes in patients with chronic heart failure

cTnI level was positively correlated with LVEDD and LVMI (r=0.332, P<0.001 and r=0.559, P<0.001) respectively and negatively correlated with LVEF (r=0.221, P<0.001). See **Figure 3**.

Discussion

B-type natriuretic peptide (BNP) is an important indicator of heart failure. Some studies found that BNP can be used as a risk assessment index for patients with CHF [19]. BNP can be released into the blood when cardiac load, ventricular volume or pressure increases, resulting in a large increase of BNP levels in serum. BNP plays a role in regulating the stability of the cardiovascular system. Thus, BNP is considered to be an important index reflecting cardiac function [20]. It was found that BNP can be a good evaluator of ventricular systolic and diastolic function [21, 22]. Further study suggested that there is a correlation between the level of BNP and the degree of left ventricular injury [23]. In this study, the level of serum BNP in patients with CHF was significantly higher than that in healthy controls. Further comparison of CHF groups with different cardiac functions found that worse cardiac function was accompanied with higher BNP index. We further study the level of BNP and related indexes of ventricular remodeling, which showed that BNP level was positively correlated with LVEDD and LVMI, but negatively correlated with LVEF. Previous study confirmed that there was a correlation between BNP level and cardiac function classification [24]. Another study confirmed that the level of BNP was negatively correlated with LVEF and positively correlated with LVMI [25], which are consistent with the results in this study, suggesting a correlation between BNP and ventricular remodeling.

Table 1. Comparison of general data, BNP, CRP and cTnI levels and ventricular remodeling indexes between the two groups (n, $\bar{x}$ ± sd)

Items	Observation group (n=328)	Control group (n=60)	χ^2/t	P
Sex (Male:Female)	190:138	35:25	0.003	0.953
Age	71.9±10.7	70.7±11.9	0.661	0.501
BMI (kg/m^2)	25.21±3.62	24.82±3.54	0.645	0.520
BNP (ug/L)	597.81±192.00 (BNP)	44.92±10.87	22.282 (BNP)	<0.001
CRP (mg/L)	21.90±9.34 (CRP)	6.23±2.85	12.871 (CRP)	<0.001
CTnI (ug/L)	0.55±0.29 (CTnI)	0.05±0.01	13.342 (CTnI)	<0.001
LVEF (%)	44.66±6.46 (LVEF)	55.82±7.82	11.892 (LVEF)	<0.001
LVEDD (mm)	50.92±6.36 (LVEDD)	43.91±5.12	8.071 (LVEDD)	<0.001
LVMI (g/m^2)	158.13±18.63 (LVMI)	85.89±13.18	28.731 (LVMI)	<0.001
IVST (mm)	8.87±0.71	8.93±0.63	0.510	0.610
LVPWT (mm)	8.83±0.69	8.94±0.75	0.943	0.346

Note: BMI: body mass index; BNP: B-type natriuretic peptide; CRP: C reactive protein; cTnI: troponin I; LVEF: left ventricular ejection fraction; LVEDD: left ventricular end-diastolic diameter; IVST: interventricular septum thickness; LVPWT: left ventricular posterior wall thickness; LVMI: left ventricular mass index.

Table 2. Comparison of general data of patients with different cardiac functions (n, %, $\bar{x}$ ± sd)

Project	Grade II (n=102)	Grade III (n=137)	Grade IV (n=89)	χ^2/F	P
Sex (male/female)	62/40	82/55	46/43	1.973	0.373
Age	71.3±7.6	71.1±8.5	72.4±7.6	0.768	0.465
Hypertension (n, %)	78 (76.47)	102 (74.45)	65 (73.03)	0.140	0.932
Coronary disease (n, %)	68 (66.67)	98 (71.53)	80 (89.89)$^{*,\#}$	15.177	0.001
Type II diabetes (n, %)	47 (46.08)	56 (40.88)	48 (53.93)	3.702	0.157
Hyperlipidemia (n, %)	42 (41.18)	58 (42.34)	49 (55.06)	4.600	0.100
Cerebral infarction (n, %)	39 (38.24)	51 (37.23)	42 (47.19)	2.476	0.290

Note: Compare with grade II, *P<0.05; compare with grade III, $^{\#}$P<0.05.

Table 3. Comparison of BNP, CRP, cTnI and ventricular remodeling indexes in patients with chronic heart failure among different cardiac function groups ($\bar{x}$ ± sd)

Item	Grade II (n=102)	Grade III (n=137)	Grade IV (n=89)	F	P
BNP (ug/L)	422.82±56.98	547.82±57.34***	878.47±89.89$^{***,\#\#\#}$	1161.216	<0.001
CRP (mg/L)	11.23±4.27	24.22±5.23***	30.79±6.56$^{***,\#\#\#}$	13.892	<0.001
CTnI (ng/mL)	0.39±0.16	0.51±0.23**	0.78±0.34$^{***,\#}$	61.352	<0.001
LVEF (%)	48.78±6.15	44.12±5.82**	40.76±4.89$^{***,\#\#}$	7.287	<0.001
LVEDD (mm)	46.91±5.76	50.74±5.62***	55.78±4.59$^{***,\#\#\#}$	11.231	<0.001
LVMI (g/m^2)	138.92±7.89	156.82±8.59***	182.16±9.52$^{***,\#\#\#}$	37.923	<0.001
IVST (mm)	8.83±0.63	8.79±0.72	8.73±0.61	0.890	0.432
LVPWT (mm)	8.88±0.75	8.84±0.73	8.81±0.70	0.763	0.387

Note: Compare with grade II, **P<0.01, ***P<0.001; compare with grade III, $^{\#}$P<0.05, $^{\#\#}$P<0.01, $^{\#\#\#}$P<0.001. BNP: B-type natriuretic peptide; CRP: C-reactive protein; cTnI: troponin I; LVEF: left ventricular ejection fraction; LVEDD: left ventricular end-diastolic diameter; IVST: interventricular septum thickness; LVPWT: left ventricular posterior wall thickness; LVMI: left ventricular mass index.

Inflammatory cytokines play an important role in the occurrence and development of CHF. Previous study has shown that the injury and necrosis of cardiomyocytes in patients with CHF were aggravated with the increase of the level of inflammatory cytokines [26]. It was found that CRP had certain predictive value for myocardial infarction and heart failure [27]. Another study showed that high levels of CRP can bind to cardiomyocyte membrane-related receptors, thereby damaging cardiomyocytes [28]. In this study, the content of CRP in the

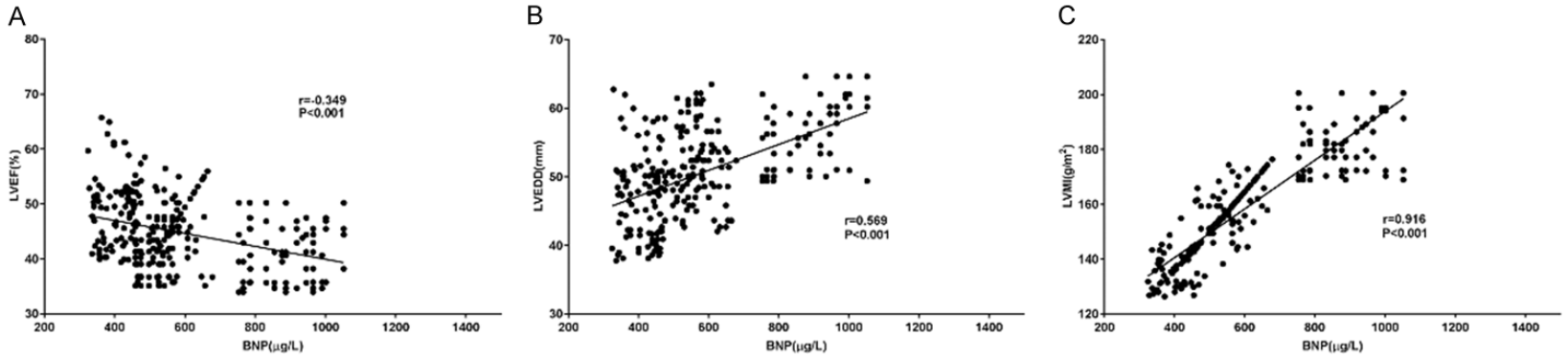

Figure 1. Correlation between BNP and ventricular remodeling indexes in patients with chronic heart failure. A: The correlation between BNP and LVEF; B: The correlation between BNP and LVEDD; C: The correlation between BNP and LVMI. BNP: B-type natriuretic peptide; LVEF: left ventricular ejection fraction; LVEDD: left ventricular end-diastolic diameter; LVMI: left ventricular mass index.

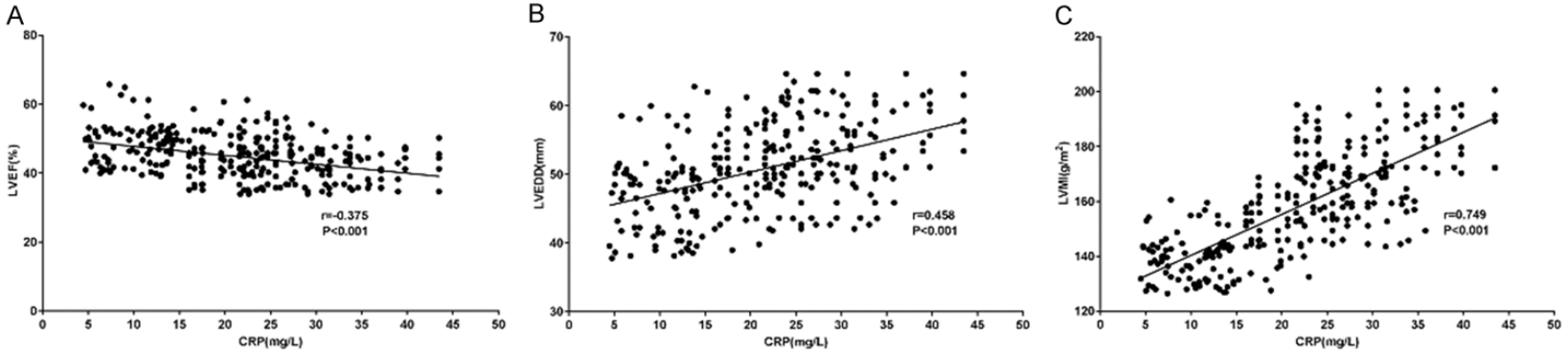

Figure 2. Correlation between CRP and ventricular remodeling indexes in patients with chronic heart failure. A: The correlation between CRP and LVEF; B: The correlation between CRP and LVEDD; C: The correlation between CRP and LVMI. CRP: C reactive protein; LVEF: left ventricular ejection fraction; LVEDD: left ventricular end-diastolic diameter; LVMI: left ventricular mass index.

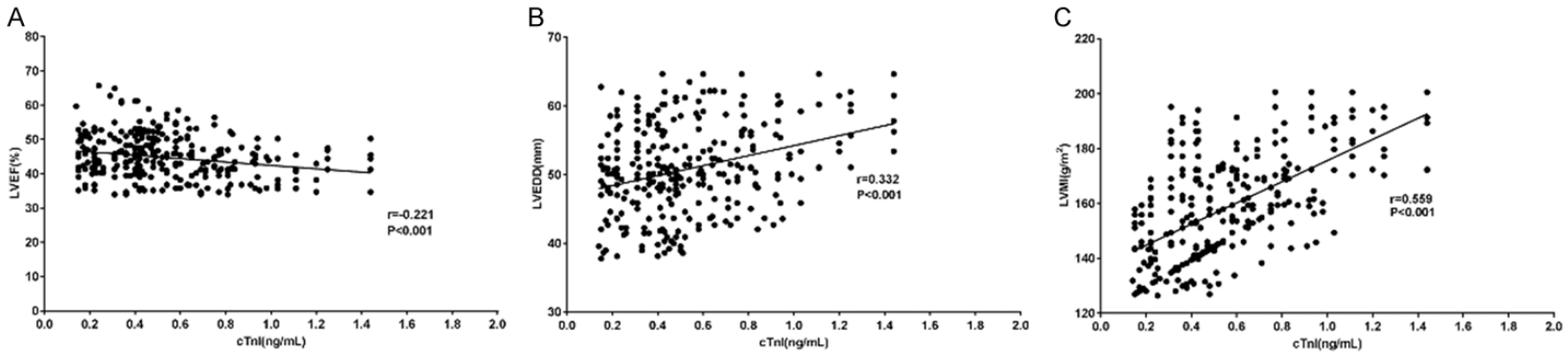

Figure 3. Correlation between cTnI and ventricular remodeling indexes in patients with chronic heart failure. A: The correlation between cTnI and LVEF; B: The correlation between cTnI and LVEDD; C: The correlation between cTnI and LVMI. cTnI: troponin I; LVEF: left ventricular ejection fraction; LVEDD: left ventricular end-diastolic diameter; LVMI: left ventricular mass index.

blood of patients with CHF was significantly higher than that of healthy controls. Further comparison of CHF groups with different cardiac function found that the worse the cardiac function was, the higher the CRP index was. Further study on CRP and related indexes of ventricular remodeling showed that CRP level was positively correlated with LVEDD and LVMI, but negatively correlated with LVEF, suggesting that higher level of CRP as accompanied by more severe myocardial injury.

A large number of proteins and molecular substances in cardiomyocytes are released into the blood after the injury of cardiomyocytes. Based on that, many previous studies found some well-known clinical indicators such as cardiac troponin I, creatine kinase, creatine kinase isoenzyme and myoglobin [29]. Among them, increased serum cardiac troponin I level is the gold standard for the diagnosis of myocardial infarction [30]. In this study, the level of blood cTnI in patients with CHF was significantly higher than that in healthy controls. Further comparison of CHF groups with different cardiac function found that the worse the cardiac function was, the higher the cTnI index was. We further studied the level of cTnI and related indexes of ventricular remodeling, which showed that cTnI level was positively correlated with LVEDD and LVMI, but negatively correlated with LVEF, suggesting that the higher the cTnI was, the more serious the myocardial injury was and the worse the cardiac function was.

The limitation of this study is that the sample size of this study is relatively small. Further studies will be conducted with larger sample size, multicenter studies and increasing the follow-up time to observe the correlation between the serum levels of B-type natriuretic peptide, C-reactive protein, troponin I and prognosis.

To sum up, BNP, CRP and cTnI are highly expressed in patients with CHF and the worse the cardiac function is, the higher the level of BNP, CRP and cTnI. The level of BNP, CRP and cTnI are positively correlated with LVEDD and LVMI and negatively correlated with the level of LVEF.

Disclosure of conflict of interest

None.

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