



Correlation between troponin T and N-Terminal brain natriuretic peptide levels and cardiac structure and function and cardiovascular disease in elderly maintenance hemodialysis patients

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ARTICLE INFO

Original paper

Article history:

Received: March 09, 2022

Accepted: June 27, 2022

Published: July 31, 2022

Keywords:

troponin T, n-terminal brain natriuretic peptide, cardiac structure, cardiovascular disease, maintenance hemodialysis patients.

ABSTRACT

With the development of chronic kidney disease (CKD), the patients showed a gradual decline in renal function, which eventually progressed to end-stage renal disease (ESRD), accompanied by various cardiovascular and cerebrovascular events. Maintenance hemodialysis (MHD) is one of the effective methods to treat ESRD, but some patients still die from cardiovascular and cerebrovascular complications. The purpose of this study was to investigate the relationship between troponin T (TnT), n-terminal brain natriuretic peptide (NT-proBNP), cardiac structure and function and cardiovascular disease in maintenance hemodialysis patients. In this experimental study, 100 patients with MHD were randomly selected as research objects. According to the level of NT-proBNP before dialysis, they were divided into two groups, namely the low NT-proBNP group and the high NT-proBNP group. The clinical and biological indicators and the average value of echocardiography were detected in the two groups. The degree of CKD disease was divided into six stages according to GFR, and the influence of different stages on the cardiac function of CKD patients was detected. The experimental results showed that the levels of TnT and NT-proBNP in MHD patients were significantly increased, and the levels of TnT and NT-proBNP and cardiac function were correlated with the patients with cardiovascular diseases. Cardiac ultrasound confirmed that the NT-proBNP level of patients with left ventricular hypertrophy was significantly higher than that of patients without left ventricular hypertrophy, and the difference between the two was statistically significant ($P < 0.005$).

Doi: <http://dx.doi.org/10.14715/cmb/2022.68.7.19>

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Introduction

Chronic kidney disease is the damage to renal function caused by various primary or secondary kidney diseases, resulting in a series of clinical syndromes caused by the disorder of the internal environment (1). The main clinical manifestations are blood creatinine (SCr), elevated blood urea nitrogen (BUN) and other toxins, disorders of calcium and phosphorus metabolism, dyslipidemia and other symptoms (2). With the progression of the primary disease, the patient first manifested renal dysfunction and then progressed to renal failure, a process that presented irreversibility (3). In the case of renal failure, the kidney cannot effectively remove metabolic toxoids and SCr, causing them to accumulate in the body, leading to substance metabolism disorders, causing patients to develop various gastrointestinal symptoms, aggravating acute and chronic kidney diseases, and more likely to induce cardiovascular diseases (4). For elderly patients, cardiovascular disease is an important cause of death, seriously affecting patients' life and quality of life (5).

TnT, one of the three subunits of troponin, increases rapidly in blood concentration after the onset of the disease. Kuroda T et al believed that human pluripotent stem cells

(HPSCs) were the main candidate raw materials for cell therapy products (CTPs) (6). To be safe, it is important to ensure that hPSCs do not form tumors after transplantation (7). TNNT1mRNA was generally upregulated in indestructible RPE cells and human induced pluripotent stem cells (HIPSCs), with self-renewal ability (8). The expression of *attnt1mrna* in some cancer tissues was higher than that in normal tissues (9). The stable expression of *tnt1* in arpe-19 cells affected the tissue of actin filaments and enhanced the migration capacity of actin filaments (10). They can consider more material candidates. Advani P et al suggested that doxorubicin (DOX) and trastuzumab (TRA) were associated with cardiac dysfunction (11). Hs-tnt showed a significant peak from the premenstrual baseline, increased 1 to 2 weeks before menstruation, and reached a peak (12). Hs-tnt increased from the early stage to the peak of the second cycle ($p < 0.002$). The transience of NT-proBNP increased after both treatments (13). DOX was associated with preconditioning baseline, peak and AUC hs-tnt levels (14). Hs-tnt can be used as a method to quantify the cumulative myocardial injury during chemotherapy before and after treatment (15). Further research is needed to quantify the cumulative damage to the heart muscle.

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NT-proBNP is the most important biomarker of cardiac function. Psołka M A et al described the relationship between long-term changes in NT-proBNP and changes in left ventricular structure and function in patients with stable coronary heart disease (16). The incidence of LVH and LVSD increased significantly over 5 years (17). The logistic regression model adjusted for baseline LV structure and function, drug use, renal function, and baseline median level above (18). Incomplete Δ NT - proBNP is independent and events LVSD patients with stable coronary artery disease (19). A long-term rise in the level of NT-proBNP may require an evaluation of the event LVEF of less than 50% (20). Their study also requires a detailed study of the relationship between NT-proBNP and coronary heart disease. Liu Y H et al. evaluated the prognostic value of NT-proBNP and Mehran risk score (MRS) in contrastive nephropathy (CIN) during the first percutaneous coronary intervention (PPCI) in patients with ST-segment elevation myocardial infarction (STEMI) (21). Both NT-proBNP and MRS in patients with CIN were higher than in those without CIN (22). For CIN, the value of NT-proBNP is similar to that of MRS (23). Compared with the original MRS model, increasing NT-proBNP to MRS did not significantly improve the C statistic (24). NT-proBNP can determine the subjects who need to take preventive measures to treat CIN (25). They need to further determine the accuracy of the assessment.

In order to reduce the risk of cardiovascular complications in MHD patients, the experimental method was used in this paper. In this paper, 100 patients with MHD were randomly selected as research objects. According to the level of NT-proBNP before dialysis, they were divided into two groups, namely the low NT-proBNP group and the high NT-proBNP group. The clinical and biological indicators and the average value of echocardiography were detected in the two groups. The degree of CKD disease was divided into six stages according to GFR, and the influence of different stages on the cardiac function of CKD patients was detected. Cardiac ultrasound confirmed that the NT-proBNP level of patients with left ventricular hypertrophy was significantly higher than that of patients without left ventricular hypertrophy, and the difference between the two was statistically significant ($P < 0.005$).

Materials and Methods

Clinical data

Clinical data of 100 patients with CKD who were treated as outpatient or inpatient in a branch hospital from January 2019 to March 2019 were collected. According to to improve the global 2012 kidney disease prognosis group (KDIGO) recommended by the kidney disease outcomes quality initiative (K/DOQI) - diagnostic criteria of chronic kidney disease (CKD) meet the following conditions can be diagnosed with CKD: one of the kidney abnormal structure or function, pathology and abnormal renal imaging examination, urine protein positive), serum creatinine, duration > 3 months, and have an impact on health; GFR (eGFR) $< 60 \text{ mL}/(\text{min} \cdot 1.73 \text{ m}^2)$ was calculated according to the Chinese dietary improvement for kidney disease (MDI) formula, $\text{eGFR} = 175 \times \text{creatinine level}^{-1.234} \times \text{age}^{-0.179} \times \text{gender}$ (male = 1, female = 0.79), and the duration was ≥ 3 months.

Staging criteria : eGFR $\sim 90 \text{ mL}/(\text{min} \cdot 1.73 \text{ m}^2)$ is

stage CKD1, eGFR $60 \sim 90 \text{ mL}/(\text{min} \cdot 1.73 \text{ m}^2)$ is stage CKD2, eGFR $\geq 30 \sim 60 \text{ mL}/(\text{min} \cdot 1.73 \text{ m}^2)$ is stage CKD3, eGFR $\geq 15 \sim 30 \text{ mL}/(\text{min} \cdot 1.73 \text{ m}^2)$ is stage CKD4, eGFR $< 15 \text{ mL}/(\text{min} \cdot 1.73 \text{ m}^2)$ is stage CKD5.

Inclusion criteria: adult (> 18 years old) patients meeting the criteria for diagnosis and staging of CKD. Exclusion criteria: patients with acute renal insufficiency and tumor.

Experimental methods

Experiment grouping. According to the level of NT-proBNP before dialysis, the patients were divided into two groups, namely the low NT-proBNP group (NT-proBNP $< 7000 \text{ pg/ml}$) and the high NT-proBNP group (NT-proBNP $> 7000 \text{ pg/ml}$). Among them, are the low NT-proBNP group (55 people), and the high NT-proBNP group (45 people).

Specimen collection. Blood samples of all patients were collected on an empty stomach in the morning before and after treatment, and the plasma concentration of NT-proBNP was determined by the ECLIA method using an automatic detector and the corresponding NT-proBNP immunoassay kit within 2 hours.

Echocardiography. Multifunctional color doppler ultrasound diagnostic instrument was used, with probe model M3X and frequency range of 1.7~3.4MHZ. Take sternum beside the left ventricular long axis section, according to the American society of echocardiography recommendations on the leading edge to leading edge measurement, measurement of the end-diastolic ventricular septal thickness (IVST), left ventricular posterior wall thickness (PwT), left ventricular end-diastolic diameter (LVEDd), left ventricular end of fiber monsieur Beaucaire diameter (LVESd), left ventricular end-systolic volume (LVESV), stroke volume (SV), ejection fraction (LVEF), short axial shortening rate (FS), the left atrioventricular valve peak early diastolic ventricular rapid filling velocity (E), late diastolic atrial systolic peak velocity (A) and E/A ratio and left atrium diameter, before and after taking the ejection. The score (LVEF) was used as the observation index.

Laboratory inspection. Conventional methods hemoglobin (Hb), white blood cell count (WBC), serum creatinine (SCr), urea nitrogen (BUN), uric acid, calcium, phosphorus, segment parathyroid hormone (iPTH), albumin, prealbumin, three acyl glycerin (TG), total cholesterol (CH), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), transferrin, ferritin and high-sensitivity c-reactive protein (hsCRP). Troponin T (TnT) was detected by electrochemical luminescence.

Determination of serum NT-proBNP. 2ml of the patient's blood was collected from the fasting vein before dialysis in the middle of the week, and was determined by the electrochemical luminescence method on the Roche Elecsys 2010 analyzer. The determination range was 5~35000pg/ml, and the reference range was: NT-proBNP $< 125 \text{ pg/ml}$ for patients < 75 years old. > 75 -year-old NT-proBNP $< 450 \text{ pg/ml}$.

Observation indicators

The age, gender composition, cardiac function indexes (BNP level, LVEF, LVEDD), and risk factors for CVD (Hb, β_2 -m, PTH, and serum potassium, serum calcium, and serum phosphorus levels) of CKD patients with dif-

ferent CKD stages were compared.

Statistical methods

SPSS17.0 software was used for data statistical analysis. The measurement data conform to the t-test of independent samples of normal distribution, but do not conform to the rank-sum test of normal distribution. The Chi-square test was used for the enumeration of data, and $P < 0.05$ was considered as statistically significant. Univariate correlation analysis was conducted between NT-proBNP and left ventricular anteroposterior diameter, left ventricular diastolic diameter, left ventricular systolic diameter, left ventricular posterior wall thickness, left ventricular septum thickness, left ventricular weight index, ejection fraction, E/A peak, pulse pressure difference, mean systolic blood pressure and mean diastolic blood pressure. $P < 0.05$ was considered as statistically significant.

Results

General conditions and indicators of MHD patients

There was no significant difference in age, dialysis age, dry body mass, dehydration, kt/v, hemoglobin, serum creatinine, albumin, serum calcium, serum phosphorus, and parathyroid hormone between the two groups ($P > 0.05$). As shown in Figure 1, it was found in this study that the average value of NT-proBNP in 94% of MHD patients was higher than normal.

As shown in Table 1, the plasma NT-proBNP level of patients with left ventricular hypertrophy confirmed by cardiac ultrasound was significantly higher than that of patients without left ventricular hypertrophy, and the difference between the two was statistically significant ($Z = 3.944, P = 0.001$).

Relationship between n-terminal brain natriuretic peptide levels and cardiovascular disease

Figure 2 shows the correlation between NT-proBNP,

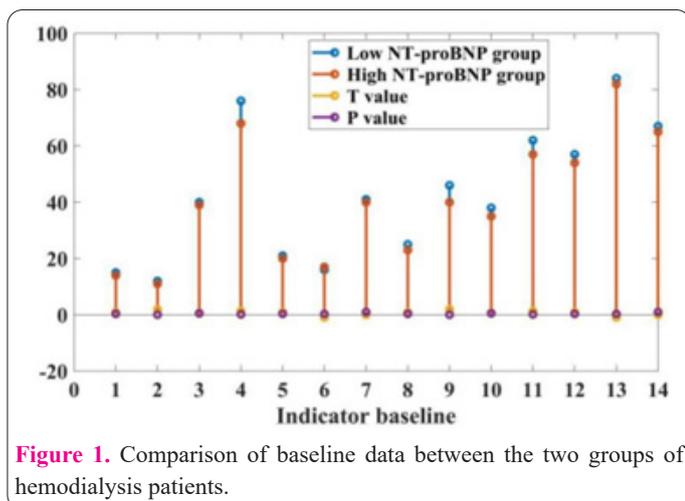


Figure 1. Comparison of baseline data between the two groups of hemodialysis patients.

cTnT and LVH. Serum level of NT - proBNP related factors of linear regression analysis and multiple linear regression analysis showed that TnT, LVMI and systolic blood pressure and serum level of NT - proBNP independence related (to univariate analysis related to the NT-proBNP level variables and history of cardiovascular disease, diabetes, smoking history, as the independent variable regression equation, skewness distribution data are natural logarithm transformation).

In this study, serum NT-proBNP level was positively correlated with systolic blood pressure, TnT, IMT and LVMI, and negatively correlated with LVEF. Moreover, multiple linear regression analysis showed that cTnT, LVMI and systolic blood pressure were independently correlated with serum NT-proBNP level, which was consistent with previous research results. It indicates that long-term capacity overload in MHD patients leads to increased cardiac preload, hypertension increases cardiac afterload, and increased ventricular wall tension stimulates the synthesis of BNP by ventricular myocytes, so the level of NT-proBNP in the blood increases. The serum NT-proBNP level can reflect the changes in the patient's heart weight and shape. Elevated serum NT-proBNP level was associated with chronic cardiac dysfunction in MHD patients. TnT is currently recognized as one of the most sensitive and specific markers of myocardial injury. Elevated TnT in MHD patients is a sign of subclinical myocardial injury, such as asymptomatic myocardial ischemia or myocardial micronecrosis and myocardial fibrosis. In addition, heart failure and LVH also increased TnT. In this study, ROC curve analysis showed that the correlation between NT-proBNP and LVH was higher than that between TnT. As a recognized indicator of subclinical atherosclerosis, IMT is an independent risk factor for cardiovascular events. In this study, the level of NT-proBNP was positively correlated with IMT. The above results suggest that NT-proBNP is not only significantly correlated with clinical cardiovascular disease but also closely correlated with the important alternative endpoint of CVD.

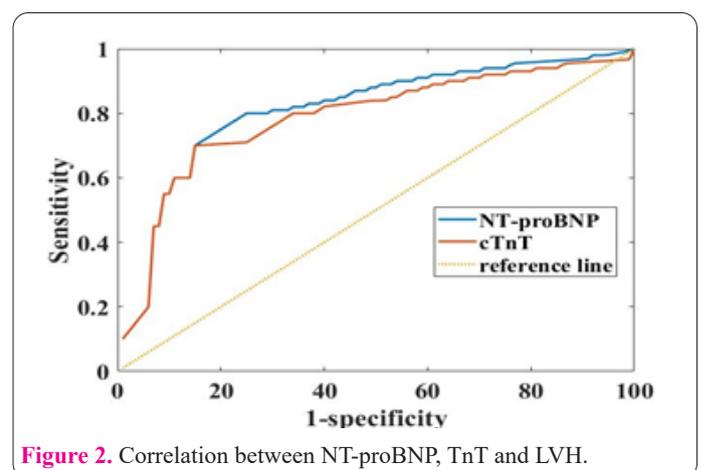


Figure 2. Correlation between NT-proBNP, TnT and LVH.

Table 1. Comparison of NT-proBNP between patients with left ventricular hypertrophy and patients without left ventricular hypertrophy.

Project	NT-pro BNP
Combined left ventricular hypertrophy (n = 23)	24717±9829
Not combined with left ventricular hypertrophy (n = 18)	2363±1790
Z value	3.94
P value	0.001

Comparison of cardiac structure, function and blood pressure between the two groups

Hypertension is the most common cause of cardiovascular disease in MHD patients. Assessment of patients' blood pressure status and timely intervention are very important to reduce the morbidity and mortality of cardiovascular disease, especially in patients without obvious cardiovascular events. Controlling blood pressure is conducive to reducing the occurrence of cardiovascular events. The results of this study showed that the serum NT-proBNP level of MHD patients was positively correlated with systolic blood pressure. Moreover, the systolic blood pressure level of patients in the high NT-proBNP group was significantly higher than that of patients in the low NT-proBNP group. Therefore, the increase of NT-proBNP in the serum of dialysis patients is closely related to the severity of hypertension, and NT-proBNP can be used as a biological indicator to reflect the degree of blood pressure control.

As shown in Figure 3, there were significant differences in the left ventricular anteroposterior diameter, left ventricular posterior wall thickness, left ventricular septum thickness, left ventricular weight index, ejection fraction, pulse pressure difference and systolic blood pressure between the low NT-proBNP group and the high NT-proBNP group (all $P < 0.05$).

Analysis of the influence of different stages on cardiac function in CKD patients

This study analyzed the effects of different stages on cardiac function in CKD patients. The results showed that the serum phosphorus, BNP, β 2-M and PTH levels of CKD stage 4 and 5 patients were significantly higher than those of CKD stage 3 patients, IVEDD was significantly higher than that of CKD stage 3 patients, and the level of Hb was significantly lower than that of CKD stage 3 patients. The differences in serum potassium, serum calcium and LVEF between the two groups were not statistically significant. The results showed that the cardiac function of CKD stage 4-5 patients was worse than that of CKD1-3 patients. At the same time, the levels of serum phosphorus, blood β 2-m and PTH in CKD4-5 patients were significantly higher than those in CKD1-3 patients, and the levels of Hb were significantly lower than those in CKD1-3 patients. This result indicated that the risk factors of CVD (high phosphorus, high β 2-m, high PTH and anemia) in

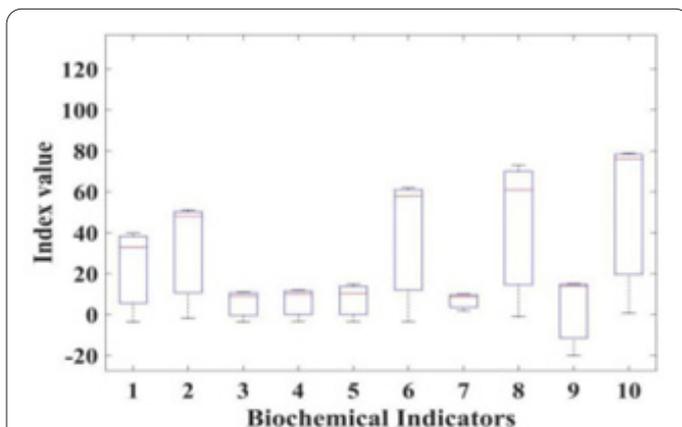


Figure 3. Comparison of cardiac structure, function and blood pressure between the two groups.

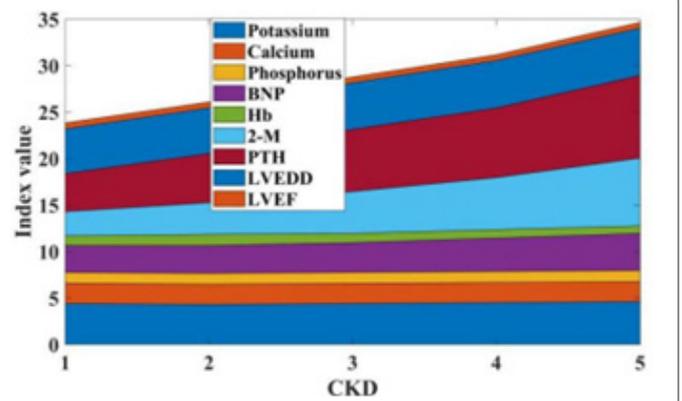


Figure 4. Comparison of biochemical indexes and cardiac function indexes in patients with different CKD stages.

CKD 4-5 patients were significantly higher than those in CKD1 - 3 patients.

As shown in Figure 4, there was no statistically significant difference in gender composition and age between patients with different CKD stages in terms of gender composition, age, blood electrolytes, Hb, β 2-M, PTH and cardiac function (all P values were >0.05). The levels of serum phosphorus, BNP, blood β 2-M and PTH in CKD4-5 stage patients were significantly higher than those in CKD1 to stage 3 patients ($P < 0.05$), LVEDD was significantly higher than that in CKD1 to stage 3 patients ($P < 0.05$), and the level of Hb was significantly lower than that in CKD1 to stage 3 patients ($P < 0.05$). The differences in serum potassium, serum calcium and LVEF between the two groups were not statistically significant (all P values were >0.05).

Discussion

Chronic kidney disease is caused by a variety of primary or secondary kidney diseases of renal function damage, resulting in the body blood urea nitrogen, creatinine and other toxins, electrolyte, calcium and phosphorus metabolism, lipid disorders such as clinical syndrome. With the progression of the disease, the patients presented with limb paresthesia, palpitations, numbness and other symptoms (26). In severe cases, the cardiovascular system was involved, and the symptoms of heart failure were manifested (27). The involvement of the blood system leads to severe anemia; The central nervous system is involved in disorders such as attention deficit, epilepsy, and even coma. Maintenance hemodialysis (MHD) is an effective life-sustaining treatment for patients with end-stage renal disease (ESRD), which can protect the residual renal function and delay. The progression of renal failure, in turn, prolongs the patient's survival. Cardiovascular and cerebrovascular complications are the main complications of MHD patients. Studies show that a considerable number of patients die of cardiovascular and cerebrovascular complications, especially elderly patients (28). Before dialysis, most patients already have cardiovascular and cerebrovascular diseases, and the cardiovascular and cerebrovascular complications will continue to worsen in the treatment process (29). Among them, hyperlipidemia, hypertension, anemia, abnormal calcium and phosphorus metabolism, diabetes and infection are the main risk factors for cardiovascular and cerebrovascular events in MHD patients.

Cardiovascular and cerebrovascular events are common complications of MHD patients, and there are many influencing factors leading to their occurrence. Each factor does not affect the patients alone, but affects each other, and the relationship between them is relatively complex. In recent years, people have repeatedly verified and explored to find out the connection and influence among various factors, so as to provide a more comprehensive pathophysiological mechanism for clinical practice. Prevention and treatment of various risk factors can effectively reduce the incidence of cardiovascular and cerebrovascular events, not only can prolong the survival of patients, but also can improve the quality of life of patients. This article has devoted a lot to the description of troponin and cardiovascular diseases in patients, but the disadvantage is that the correlation between them is not well studied. In addition, the experimental part of the article is not very well designed for dialysis. Hope it can be improved with more advanced equipment.

Acknowledgments

Not applicable.

Interest conflict

The authors declare that they have no conflict of interest.

Funding

The research is supported by: This study was supported by the Key Research and Development Program of Shaanxi Province (No. 2021SF-343).

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