

SIGNIFICANCE OF THE EVALUATION OF SERUM BNP, CTNI AND GAL-3 LEVELS TO HEART FUNCTION OF RVD-INDUCED CHF PATIENTS

MIN YANG, YINGJING GUI, HONGBO QIAN

Cardiothoracic surgery, Yijishan Hospital, the First Affiliated Hospital of Wannan Medical College, Wuhu City, Anhui Province, China-241000

ABSTRACT

Objective: To investigate the significance of serum B-Type natriuretic peptide (BNP), Cardiac troponin I (cTnI) and Galectin-3 (Gal-3) in rheumatic valvular heart disease (RVD)-induced chronic heart failure (CHF) patients.

Study design: Case-control study.

Place and duration of study: Yijishan Hospital, the First Affiliated Hospital of Wannan Medical College, China, from January 2017 to August 2021.

Methodology: Eighty-one RVD-induced CHF patients were included in the case group, and 81 healthy subjects with normal liver and kidney function and no other infection and immune diseases were selected as normal control group. Serum markers BNP, cTnI and Gal-3 were compared.

Results: Levels of serum BNP, cTnI and Gal-3 in case group before treatment were higher than those in the normal control group (all $p < 0.001$). Before treatment, the above-mentioned markers levels between patients with NYHA grade II and grade III cardiac function were significant differences (all $p < 0.001$), and the above-mentioned markers levels in case group after treatment were lower than those before treatment (all $p < 0.001$).

Conclusion: Serum BNP, cTnI and Gal-3 increased with the aggravation of cardiac function in RVD-induced CHF patients. The indexes above can be used to classify the cardiac function and evaluate the therapeutic effect in these patients.

Keywords: Rheumatic valvular heart disease (RVD), Chronic heart failure (CHF), Serum markers, Galectin-3 (Gal-3).

DOI: 10.19193/0393-6384_2022_3_274

Received March 15, 2021; Accepted January 20, 2022

Introduction

Rheumatic valvular heart disease (RVD) is a cardiac disease caused by rheumatic fever. Chronic heart failure (CHF) is a serious complication of RVD⁽¹⁾. The mortality rate of patients with CHF caused by rheumatic valvular heart disease is high. Drug therapy can alleviate the rapid development of CHF, thus prolonging the life span of patients with CHF caused by rheumatic valvular heart disease, and providing favorable conditions for surgical treatment. Therefore, early and accurate diagnosis and timely and effective treatment is the key to such sufferers.

B-Type natriuretic peptide (BNP) is a circulating hormone secreted by the heart⁽²⁾. BNP is closely related to cardiac function, and its level can reflect cardiac function⁽³⁾.

Cardiac troponin I (cTnI) is a specific marker that can reflect minimal myocardial injury⁽⁴⁾. Serum cTnI level is closely related to long-term cardiac events⁽⁵⁾. Serum cTnI is an important biochemical index reflecting the severity and prognosis of heart failure.

Galectin-3 (Gal-3) is an important inflammatory cytokine⁽⁶⁾. It has been found that serum Gal-3 is closely related to cardiac remodeling and can be used in the diagnosis of heart failure^(7,8).

It is not clear whether serum BNP, cTnI and Gal-3 can be used in the diagnosis of cardiac function damage and evaluation of the therapeutic effect in patients with CHF caused by rheumatic valvular heart disease.

The objective of this study was to investigate the significance of serum BNP, cTnI and Gal-3 in RVD-induced CHF patients.

Methodology

This study was approved by the Research Ethics Committee of Yijishan Hospital, the First Affiliated Hospital of Wannan Medical College, China. Eighty-one RVD-induced CHF patients admitted in our hospital from January 2017 to August 2021 were included in the case group. The inclusion criteria of case group were that CHF patients with RVD diagnosed by clinical symptoms, signs and cardiac color echocardiography; patients classified with grade II and grade III cardiac function by the American New York Heart Association (NYHA); patients without other complications such as hypertension, blood lipid and diabetes; conscious and without mental illness; and all patients were not treated with drugs for CHF at admission.

The exclusion criteria of case group were that patients under 18 years old or over 80 years old; patients with recurrent heart failure; NYHA grade I and IV cardiac function patients; patients with systolic blood pressure < 90 mmHg or heart rate < 55 beats/min; patients with congenital heart disease-endocrine system diseases such as Cushing syndrome, or malignant tumors; patients during pregnancy and lactation; patients with CHF induced by coronary heart disease, hypertensive heart disease, chronic pulmonary heart disease and other factors; and patients who quit midway or were unable to cooperate.

A total of 81 healthy subjects with normal liver and kidney function and no other infection and immune diseases were selected as a normal control group. All subjects signed informed consent to join in this study.

After admission, patients in the case group were given oxygen inhalation, anti-infection, correcting electrolyte disorder and controlling arrhythmia treatment. They were treated with digitalis, diuretics (which can be stopped after the control of edema symptoms), enalapril and spironolactone, and the treatment lasted for 12 weeks. Before (at admission) and after treatment in the case group and during

medical examination of the control group, 5 mL elbow vein blood was taken, and the serum was separated by centrifugation. The levels of BNP, cTnI and Gal-3 in serum were detected by enzyme-linked immunosorbent assay.

Data analysis was used by SPSS 25. Measurement data such as age, serum BNP, cTnI, Gal-3 conforming to the normal distribution were represented by Mean±SD, and independent-sample t-test or paired t-test was used. Count data such as gender were expressed as n (%), and chi-square test was used. P<0.05 was considered to be statistically significant.

Results

In the case group, there were 43 (53.09%) males and 38 (46.91%) females, aged 61-77 (66.62 ±3.85) years old. According to the cardiac function grade of NYHA, 46 (56.79%) cases were grade II and 35(43.21%) cases were grade III before treatment. In the normal control group, 41 cases (50.62%) were male and 40 cases (49.38%) were female, aged 60-76 (66.51 ±3.93) years old. Sex and age between case group and normal control group was no significant difference (p=0.753, 0.856, respectively)

Levels of serum BNP, cTnI and Gal-3 in case group were higher before treatment, comparing with normal control group (all p < 0.001, Table I).

Index	Normal control group (n=81)	Case group before treatment (n=81)	P-value
Serum BNP(μg/L)	42.16±2.44	474.03±86.96	<0.001
Serum cTnI(μg/L)	0.37±0.11	4.29±1.32	<0.001
Serum Gal-3(ng/mL)	2.34±0.70	19.01±3.52	<0.001

Table 1: Comparison of serum markers between case group before treatment and normal control group.

Index	NYHA grade II (n=46)	NYHA grade III (n=35)	P-value
Serum BNP(μg/L)	413.68±50.40	553.35±55.03	<0.001
Serum cTnI(μg/L)	3.32±0.63	5.55±0.83	<0.001
Serum Gal-3(ng/mL)	17.65±3.29	20.80±3.01	<0.001

Table 2: Comparison of serum markers in NYHA grade II and III patients before treatment.

Index	Case group before treatment (n=81)	Case group after treatment (n=81)	P-value
Serum BNP(μg/L)	474.03±86.96	386.48±70.85	<0.001
Serum cTnI(μg/L)	4.29±1.32	2.84±0.86	<0.001
Serum Gal-3(ng/mL)	19.01±3.52	16.13±2.75	<0.001

Table 3: Comparison of serum markers before and after treatment in case group.

Before treatment, above-mentioned markers levels between patients with NYHA grade II and grade III cardiac function were significant differences (all p<0.001, Table II), levels of serum BNP, cTnI and Gal-3 increased significantly with

the increase of NYHA cardiac function grade; and above-mentioned markers levels in case group after treatment were lower than those before treatment (all $p < 0.001$, Table III).

Discussion

CHF is the manifestation of the terminal stage of a variety of heart diseases, and it is also an important cause of death in patients with heart disease⁽⁹⁾. At present, there is no gold standard for the diagnosis of CHF. The diagnosis of heart failure depends to a large extent on the personal clinical judgment of doctors, mainly on the basis of clinical symptoms and signs. As clinical symptoms and signs of CHF lack specificity, imaging techniques combined with serum markers are commonly used to diagnose early CHF. At present, electrocardiogram, chest X-ray radiography, color Doppler ultrasound and other imaging techniques are often used as accessory examination of CHF,^(10,11) of which color Doppler ultrasound is the most widely used examination. However, there are few serum markers for the diagnosis and prognosis evaluation of CHF.

Vasodilation and imbalance of water and sodium excretion can lead to the increase of cardiac pressure or volume load, resulting in the increase of ventricular wall tension, which in turn promotes the secretion of BNP by ventricular cardiomyocytes in patients with CHF⁽¹²⁾. The level of serum BNP in patients with CHF was relatively high⁽¹³⁾.

When the myocardial cell membrane is degenerated and necrosis due to ischemia and hypoxia, the free cTnI in the cytoplasm can be released into the blood circulation⁽¹⁴⁾. Some studies have shown that serum cTnI can reflect myocardial damage sensitively⁽¹⁵⁾.

Our results showed that levels of serum BNP and cTnI in the case group before treatment were higher, compared with the normal control group, suggesting that levels of serum BNP and cTnI are increased in RVD-induced CHF patients. This results are consistent with the conclusion reported in previous studies that the levels of BNP and cTnI are increased in CHF patients and are closely related to heart failure⁽¹⁶⁾.

Gal-3 participates in many pathophysiological mechanisms of heart failure, such as myocardial fibrosis and inflammatory response^(17,18). Our results showed that serum Gal-3 levels in the case group before treatment were higher, compared with the normal control group, suggesting that level of serum

Gal-3 increased in patients with CHF induced by RVD. This is basically consistent with the conclusion reported in previous studies that there is abnormal expression of serum Gal-3 in patients with CHF⁽¹⁹⁾.

The higher the NYHA grade is, the more serious the impairment of cardiac function will be⁽²⁰⁾. Our results showed that levels of serum BNP, cTnI and Gal-3 increased significantly with the increase of NYHA cardiac function grade, suggesting that above 3 markers can measure the cardiac function in patients with CHF induced by RVD, and the worse the cardiac function is, the higher the levels of above 3 markers will be.

Further analysis showed that the above 3 markers levels in case group were lower than those before treatment in case group, suggesting that above 3 markers may be used to evaluate the therapeutic effect of cardiac function in RVD-induced CHF patients.

Conclusion

Serum BNP, cTnI and Gal-3 increased with the aggravation of cardiac function in RVD-induced CHF patients. The indexes above can be used to classify the cardiac function and evaluate the therapeutic effect in these patients.

References

- 1) Osteresch R, Diehl K, Kühl M, Fiehn E, Schmucker J, Backhaus T, Fach A, Wienbergen H, Hambrecht R. Impact of right heart function on outcome in patients with functional mitral regurgitation and chronic heart failure undergoing percutaneous edge-to-edge-repair. *J Interv Cardiol* 2018; 31(6): 916-24. DOI: 10.1111/joic.12566.
- 2) Hayashi Y, Yokokawa H, Fukuda H, Saito M, Miyagami T, Takahashi Y, Hisaoka T, Naito T. Association between Visceral or Subcutaneous Fat Accumulation and B-Type Natriuretic Peptide among Japanese Subjects: A Cross-Sectional Study. *J Clin Med* 2021, 10, 1315-23. doi:10.3390/jcm10061315
- 3) Nnodim J, Bako H. The Relevance of Natriuretic Peptide in Medical Laboratory Diagnosis. *Asclepius Med Case Rep* 2020; 3(2): 1-3.
- 4) Gao C, Liang C, Zhang J, Ma Y, Mu X, Xie M. The correlation between myocardial resilience after high-intensity exercise and markers of myocardial injury in swimmers. *Medicine* 2021, 100, (36), e27046-51. DOI: 10.1097/MD.00000000000027046
- 5) Lyngbakken MN, Vigen T, Ihle-Hansen H, Brynildsen J, Berge T, Rønning O M, Tveit A, Røsjø H, Omland T. Cardiac troponin I measured with a very high sensitivity assay predicts subclinical carotid atherosclerosis: The Akershus Cardiac Examination

- 1950 Study. *Clinical Biochemistry* 2021; 93: 59-65. doi:10.1016/j.clinbiochem.2021.04.005.
- 6) Espinosa-Oliva AM, García-Miranda P, Alonso-Bellido IM, Carvajal AE, González-Rodríguez M, Carrillo-Jiménez A, Temblador AJ, Felices-Navarro M, García-Domínguez I, Roca-Ceballos MA, Vázquez-Carretero MD, García-Revilla J, Santiago M, Peral MJ, Venero JL, de Pablos RM. Galectin-3 Deletion Reduces LPS and Acute Colitis-Induced Pro-Inflammatory Microglial Activation in the Ventral Mesencephalon. *Front Pharmacol* 2021; 12: 706439-58. doi: 10.3389/fphar.2021.706439
 - 7) Wettersten N. Biomarkers in Acute Heart Failure: Diagnosis, Prognosis, and Treatment. *Int J Heart Fail* 2021; 3(2):81-105. doi:10.36628/ijhf.2020.0036
 - 8) Sun Z, Zhang L, Li L, Shao C, Liu J, Zhou M, Wang Z. Galectin-3 mediates cardiac remodeling caused by impaired glucose and lipid metabolism through inhibiting two pathways of activating Akt. *Am J Physiol Heart Circ Physiol* 2021; 320(1): H364-80. DOI: 10.1152/ajpheart.00523.2020.
 - 9) Kulchitskaya D B, Shovkun T V, Yarnykh E V, Konchugova T V, Knyazeva T A, Gushchina N V, et al. Impact of external counterpulsation on microcirculation in patients with coronary heart disease complicated by chronic heart failure after surgical and endovascular myocardial revascularization. *Voprosy kurortologii, fizioterapii, i lechebnoi fizicheskoi kultury*, 2019; 96(5): 5-10. doi:10.17116/kurort2019960515
 - 10) Yao Z, Li G, Li G. Correlation between serum urea nitrogen, cystatin C, homocysteine, and chronic heart failure. *Am J Transl Res*. 2021; 13(4): 3254-61.
 - 11) Sperlongano S, D'Andrea A, Mele D, Russo V, Pergola V, Carbone A, Ilardi F, et al. Left Ventricular Deformation and Vortex Analysis in Heart Failure: From Ultrasound Technique to Current Clinical Application. *Diagnostics* 2021, 11, 892-903. doi:10.3390/diagnostics11050892
 - 12) Castiglione V, Aimo A, Vergara G, Saccaro L, Passino C, Emdin M. Biomarkers for the diagnosis and management of heart failure. *Heart Fail Rev* 2021; 1-19. doi:10.1007/s10741-021-10105-w
 - 13) Pandey KN. Molecular Signaling Mechanisms and Function of Natriuretic Peptide Receptor-A in the Pathophysiology of Cardiovascular Homeostasis. *Front. Physiol* 2021, 12: 693099-117. DOI: 10.3389/fphys.2021.693099
 - 14) Amgalan D, Pekson R, Kitsis RN. Troponin release following brief myocardial ischemia: apoptosis versus necrosis. *JACC Basic Transl Sci* 2017; 2(2): 118-21. DOI: 10.1016/j.jacbts.2017.03.008.
 - 15) Katrukha IA, Katrukha A G. Myocardial Injury and the Release of Troponins I and T in the Blood of Patients. *Clinical Chemistry* 2021; 67(1): 124-30. doi:10.1093/clinchem/hvaa281
 - 16) Li H, Wang H, Yin H, Zhao J. The value of combined detection of BNP and cTnI in the judgment of cardiac condition and function in patients with chronic heart failure. *Hebei Medical Journal* 2010;32(10):1240-1.
 - 17) Mueller T, Leitner I, Egger M, Haltmayer M, Dieplinger B. Association of the biomarkers soluble ST2, galectin-3 and growth-differentiation factor-15 with heart failure and other non-cardiac diseases. *Clin Chim Acta* 2015; 445: 155-60. DOI: 10.1016/j.cca.2015.03.033.
 - 18) Zhong X, Qian X, Chen G, Song X. The role of galectin-3 in heart failure and cardiovascular disease. *Clin Exp Pharmacol Physiol* 2019; 46(3): 197-203. DOI: 10.1111/1440-1681.13048.
 - 19) Zhang Y, Li Y, Shi L, Shen Y, Jiang J, Peng Y, Ni Y. Changes of serum galectin-3 and pentraxin-3 levels in CHF patients and their correlation with prognosis. *Chin J Cardiovasc Rehabil Med* 2019; 28(3): 289-92.
 - 20) Siegersma K R, Groepenhoff F , Onland-Moret N C , Tulevski I I, Hofstra L, Somsen G A, et al. New York Heart Association class is strongly associated with mortality beyond heart failure in symptomatic women. *Eur Heart J* 2021; 7(2): 214-5. doi:10.1093/ehjqcco/qcaa091

Authors' contribution:

MY and YG: Conception / design, drafting, data analyses, interpretation, drafting.

HQ: Critical revision of the article, design, approved the manuscript for the publication.

MY and YG contributed equally at all stages of the article.

Corresponding Author:

HONGBO QIAN

Cardiothoracic surgery, Yijishan Hospital, the First Affiliated Hospital of Wannan Medical College, Wuhu City, Anhui Province, China-241000.

Email: qianhongbo214@163.com

(China)