

RELATIONSHIP BETWEEN THE PLASMA NT-proBNP CONCENTRATION AND CHARACTERISTICS OF HEART FAILURE AND PREMATURE VENTRICULAR COMPLEXES IN STABLE ISCHEMIC HEART DISEASE

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SUMMARY

Objectives: To investigate the relationship between plasma NT-proBNP levels and characteristics of heart failure and premature ventricular complexes (PVCs) in patients with chronic ischemic heart disease.

Subjects and methods: A cross-sectional descriptive study on 136 patients with chronic heart failure who were diagnosed as stable ischemic heart disease at Military Hospital 103 and Hanoi Heart Hospital from October 2016 to January 2021. Participants were eligible for inclusion and exclusion criteria. NT-proBNP was taken at the admission and after treatment. Medical statistical algorithm was used to determine the correlation between symptoms of heart failure, PVCs and plasma NT-proBNP.

Results: Patients' median age was 70.0 ± 10.483 . NT-proBNP concentrations pre- and post-treatment were 2540.846 ± 470.484 and 1162.268 ± 178.840 pg/mL. Patient's age, heart rate, and creatinine levels were positively correlated with NT-proBNP concentration whereas left ventricular systolic function (EF%) was inversely correlated with NT-proBNP levels ($r = -0.315$, $p < 0.001$). There was a positive correlation between NT-proBNP concentrations and heart failure degree according to New York Heart Association (NYHA) ($r = 0.406$, $p < 0.001$). The severity of the post-treatment PVCs significantly decreased, with significant difference ($p = 0.027$). But there was no correlation between PVCs and the plasma NT-proBNP concentrations.

Conclusion: Plasma NT-proBNP concentrations are correlated with several features of heart failure. But there is no correlation between PVCs and plasma NT-proBNP concentrations in patients with heart failure due to ischemic heart disease.

* Keywords: NT-proBNP; Heart failure; Premature ventricular complexes; Stable ischemic heart disease.

INTRODUCTION

Chronic ischemic heart disease or chronic coronary syndrome is a condition that relates to the stability of atherosclerotic plaques, when there is not sudden rupture or after the acute phase or post -

surgery/intervention. When the atheroma progresses, the coronary is narrowed significantly [2]. According to the statistics, cardiovascular diseases cause 4 million deaths annually in Europe and 1.9 million deaths in the European Union,

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mainly due to coronary artery disease (CHD) [3]. Myocardial ischemia in chronic coronary syndrome leads to functional impairment of an area of the left ventricular heart muscle, disorders of left ventricular relaxation, and then increased passive stiffness promotes diastolic filling, hypertrophy and myocardial fibrosis. Cardiac ischemia in cardiovascular disease can trigger electrophysiological changes and arrhythmias.

When myocardial ischemia and hypoxia occur, the release of NT-proBNP is stimulated. Other factors in myocardial ischemia include increased heart rate, proinflammatory cytokines and neurotransmitters such as vasoconstriction, antidiuretic, rapidly increasing left ventricular pressure and cell proliferation. Birth also stimulates NT-proBNP synthesis [4]. Studies show that NT-proBNP test plays a pivotal role in screening, diagnosing, and predicting cardiovascular events such as heart failure, arrhythmia, etc. in patients with chronic coronary syndrome [5].

Therefore, we conducted this project with the following objectives: *To investigate the relationship between NT-proBNP levels and characteristics of heart failure and PVCs in patients with chronic ischemic heart disease.*

SUBJECTS AND METHODS

1. Subjects

136 patients with chronic heart failure were diagnosed as ischemic heart disease at Military Hospital 103 and

Hanoi Heart Hospital from October 2016 to January 2021

** Selection criteria:*

Patients with a diagnosis or a history of acute myocardial infarction; Patients with significant coronary lesions (one coronary artery stenosis of at least 50% by coronary angiography at the time of the study or before; Patients undergoing coronary revascularization or without intervention; Patients undergoing coronary bypass surgery; Patients with stable angina or unstable angina.

- Patient was diagnosed with heart failure by ESC 2016 [6].

** Exclusion criteria:*

Patients had chronic kidney disease, severe arrhythmia, pericardial disease, myocarditis, infectious endocarditis, or other severe chronic disease, or those who did not agree to participate in the study.

2. Method

A cross-sectional descriptive study.

** Sampling method:*

Convenient sample, including all patients who met the inclusion criteria.

** Research target:*

Age, sex, clinical symptoms (blood pressure, pulse, breathing rate, edema, heart failure degree according to NYHA, degree of chest pain according to CCS, ...), subclinical features (plasma NT-ProBNP, EF, Dd, ...).

** Data processing:* By SPSS statistical software version 21.0. The statistical significance level is 95% with $p < 0.05$.

RESULTS

Through a study on 136 heart failure patients with chronic ischemic heart disease, we obtained the following results:

Table 1: General characteristics of study subjects.

Characteristics	Parameters
Females (n, %)	34 (25.0)
Age ($\bar{X} \pm SD$)	70.0 \pm 10.483
Hypertension (n, %)	105 (77.2)
Smoke (n, %)	25 (18.4)
Chest pain (n, %)	118 (86.8)
Edema (n, %)	19 (3.7)
Rale in the lungs (n, %)	25 (18.4)
Enlarged liver, jugular vein (n, %)	5 (3.7)
Diastolic blood pressure (mmHg) ($\bar{X} \pm SD$)	88.49 \pm 25.212
Systolic blood pressure (mmHg) ($\bar{X} \pm SD$)	135.10 \pm 25.568
Ejection fraction (%)	54.689 \pm 17.839
NT-proBNP before treatment (pg/mL) ($\bar{X} \pm SD$)	2540.846 \pm 5486.735
NT-proBNP after treatment (pg/mL) ($\bar{X} \pm SD$)	1162.268 \pm 2085.617

Male/female ratio: 3/1. Hypertension accounted for the highest percentage (77.2%). The mean age was 70.0 \pm 10.483. Mean values of NT-proBNP pre- and post-treatment were different.

Table 2: Relationship between plasma NT-proBNP concentrations and heart failure characteristics.

Correlation index	Before treatment	
	r	p
Age	0.195	0.023
Gender	-0.065	0.454
Body mass index (BMI)	0.108	0.209
Edema	0.141	0.102
Chest pain	-0.083	0.335
Heart rate	0.302	< 0.001
Creatinine	0.322	< 0.001
Ejection fraction (%)	-0.315	< 0.001

Patient's age, heart rate, creatinine level were positively correlated with NT-proBNP concentration, left ventricular systolic function (EF%) was inversely correlated with NT-proBNP concentration. In this study, we found no correlation between gender, BMI, chest pain level, edema and NT-proBNP levels.

Table 3: Correlation between NT-proBNP and heart failure by NYHA classification

NYHA classification	NT-proBNP pre-treatment ($\bar{X} \pm SD$)
NYHA I	1235.36 ± 4118.46
NYHA II	4552.371 ± 8280.329
NYHA III	4167.684 ± 5811.875
NYHA IV	2453.262 ± 2820.500
p (medium)	0.02
r	0.406
p (correlation)	< 0.001

Plasma NT-proBNP concentration differs based on the severity of heart failure according to NYHA. The higher the NYHA level, the higher NT-proBNP concentration, the difference was significant with $p = 0.02$. There was a moderately positive correlation between plasma NT-proBNP concentrations and NYHA-based heart failure levels with $r = 0.406$ ($p < 0.001$).

Table 4: Characteristics of ventricular premature complex on the 24-hour Holter monitoring by Lown grading system.

24-hour Holter	Before treatment n (%)	After treatment n (%)	p
Lown 0	68 (50.0)	69 (50.7)	0.027
Lown 1	34 (25.0)	50 (36.8)	
Lown 2	9 (6.6)	6 (4.4)	
Lown 3	7 (5.1)	2 (1.5)	
Lown 4	18 (13.2)	9 (6.6)	
Lown 5	0 (0.0)	0 (0.0)	

There was a dramatical change between the ratio of PVCs pre- and post-treatment, the number of Lown 3-4 PVCs decreased significantly after treatment, the difference was statistically significant, $p < 0.05$.

Table 5: Correlation between NT-proBNP and premature ventricular complex.

Lown	Pre-treatment NT-proBNP	Post-treatment NT-proBNP	p
	$\bar{X} \pm SD$	$\bar{X} \pm SD$	
Lown 0	2132.715 ± 4244.692	988.613 ± 1738.441	0.008
Lown 1	4370.759 ± 8862.632	1670.962 ± 3129.067	0.013
Lown 2	1652.645 ± 2234.545	890.963 ± 1042.746	0.256
Lown 3	1675.567 ± 1194.475	756.012 ± 820.785	0.084

Lown 4-5	1647.107 ± 1787.532	1151.074 ± 1459.703	0.048
p (medium)	0.251	0.578	
r	0.046	0.048	
p (correlation)	0.595	0.583	

The plasma NT-proBNP concentration according to Lown grading system for PVCs did not differ between groups ($p > 0.05$). There was also no correlation for plasma NT-proBNP concentrations between the groups of PVCs as classified by Lown.

DISCUSSION

1. General characteristics of the patient

Patients' median age was 70.0 ± 10.483 . Previous studies showed that men had a higher risk of ischemic heart disease, stroke and other cardiovascular diseases than women. In our study, male accounted for 75.0%, female only 25.0%. The pathogenesis of later development of atherosclerosis in women is due to the protective role hormone estrogen [7].

The mean values of plasma NT-proBNP concentrations pre- and post- treatment were 2540.846 ± 470.484 and 1162.268 ± 178.840 . The study by Nuria Farre et al. on 3,580 chronic heart failure patients, of whom ischemic heart disease was the leading cause with the rate of 44.7% and mean NT-proBNP concentration was 1.638 pg/mL [8]. It is suggested that the group of heart failure patients with chronic ischemic heart disease had higher plasma NT-proBNP concentrations than those with chronic heart failure due to other causes, and myocardial ischemia contributes to increase the levels of NT-proBNP.

2. Relationship between NT-proBNP and characteristics of heart failure and premature ventricular complex

Clinical manifestations of heart failure include chest pain, edema and enlarged liver with the corresponding rates of 86.8%, 3.7% and 3.7%. The incidence of edema in our study was lower because these patients were followed up regularly at an outpatient clinic.

In this study, we found no correlation between sex, BMI, chest pain level, edema and NT-proBNP levels. According to Nguyen Thi Thu Dung et al, when studying 202 heart failure patients by stages, there was no correlation between NT-proBNP and BMI, glomerular filtration rate, hemoglobin, and left ventricular systolic [1].

Patient's age, heart rate, and creatinine level were positively correlated with NT-proBNP levels (mean $r > 0.3$). It means that the older the patients are, the faster the heart rate is, leading to an increased NT-proBNP levels. When tachycardia causes myocardial ischemia resulting in an increased myocardial contractility, which, in turn, stimulates release of NT-proBNP. Left ventricular

systolic function (EF%) had a moderately negative correlation with the NT-proBNP concentration with $r = -0.315$ ($p < 0.001$). It means that when left ventricular systolic function decreases, the concentration of NT-proBNP increases, when left ventricular function decreases, ventricular relaxation, myocardial atony loss increases, leading to the release of NT-proBNP. In this study, we found no correlation between sex, BMI, chest pain level, and edema with NT-proBNP concentration (*table 3*). According to Richards M's study on 1,049 patients with heart failure undergoing coronary intervention in Australia - New Zealand (ANZ), the author revealed that there was a moderately positive correlation between NT-proBNP concentration and age $r = 0.44$ ($p < 0.001$), and moderately negative correlation with left ventricular systolic function $r = -0.46$ ($p < 0.001$) [9].

The plasma NT-proBNP concentration differs according to NYHA classification of heart failure, the higher the NYHA level, the higher the NT-proBNP concentrations, the difference was significant ($p = 0.02$). There was a moderately positive correlation between plasma NT-proBNP concentrations and NYHA-based heart failure levels with $r = 0.406$ ($p < 0.001$). Nguyen Thi Thu Dung et al studied on 202 heart failure patients in different stages, the study results showed that there was a fairly strong correlation between the concentration of NT-proBNP and the degree of heart failure according to NYHA with $r = 0.67$ ($p < 0.0001$) [1].

The degree of PVCs according to Lown's classification on 24-hour Holter pre- and post-treatment was significantly different ($p = 0.027$). It means that after treatment, the number and the degree of severe PVCs decreased significantly compared to pre-treatment. However, there was no significant correlation between plasma NT-proBNP concentrations in the Lown-classified PVCs, indicating that NT-proBNP levels did not vary significantly between PVCs according to Lown classification with p (correlation) > 0.05 and p (general) > 0.05 . Lucian M. studied 40 neuropathic patients undergoing 24-hour electrocardiographic Holter to detect PVCs, the results revealed an NT-proBNP < 125 pg/mL in 16 patients and NT-proBNP > 125 pg/mL in 24 patients. The results showed that there was a great number of patients with PVCs in the NT-proBNP group, the presence of PVC was positively correlated with NT-proBNP with $r = 0.445$ ($p = 0.006$) [10].

Our study found no association between NT-proBNP levels and the presence of PVCs, which may be due to high degree of heart failure among our patients. Because NT-proBNP is elevated, we do not define NT-proBNP's cut-off for ventricular arrhythmias.

CONCLUSION

Plasma NT-proBNP concentrations in patients with chronic ischemic heart was correlated with several clinical and subclinical features of heart failure. But there was no correlation between plasma NT-proBNP levels and the presence of PVCs.

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