ASSESSMENT OF NT-PROBNP LEVELS IN PATIENTS WITH CARDIAC ARRHYTHMIAS

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ABSTRACT

Background: NT-proBNP is a valuable biomarker for the diagnosis and treatment of cardiovascular diseases, including arrhythmias. ***Objective:*** To evaluate NT-proBNP levels in patients with arrhythmias and analyze the correlation between NT-proBNP levels and several variables. ***Subjects and Methods:*** A cross-sectional descriptive study was conducted on 158 patients with arrhythmias from December 2023 to March 2024 at the Arrhythmias Treatment Department of Cho Ray Hospital. Clinical and paraclinical characteristics were analyzed; NT-proBNP levels were compared between patients with arrhythmias with and without heart failure (HF); and the correlation between NT-proBNP levels and several factors was analyzed using R software version 4.3.1. Statistical significance was considered at $P < 0.05$. ***Results:*** The NT-proBNP level (Median [IQR]) in patients with arrhythmias (n = 158) was 367 (61.9-1297) pg/ml. NT-proBNP levels were higher in patients with arrhythmias with HF (n = 41) than in those without HF (n = 117), at 1273 (498-4173) vs. 210 (51-875) pg/ml ($P < 0.001$). Univariate analysis showed that age, weight, HGB, EF, creatinine, and eGFR were statistically significantly correlated with NT-proBNP. ***Conclusions:*** The NT-proBNP level in patients with arrhythmias was 367.3 (61.9-1297) pg/ml; it was higher in patients with arrhythmias with HF than in those without HF. NT-proBNP level was statistically significantly correlated with age, weight, HGB, EF, creatinine, and eGFR.

Keywords: *NT-proBNP, heart failure, arrhythmia*

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I. BACKGROUND:

Cardiac arrhythmias are a major cause of cardiovascular mortality. Cardiac myocytes have special electrical properties that allow impulses to be generated and conducted through the heart, resulting in coordinated contractions. Disturbances in impulse formation or impulse conduction, or both, can lead to arrhythmias and conduction disorders of the heart.

Any abnormality in the heart, including congenital structural abnormalities or functional abnormalities, can cause arrhythmias. Systemic factors that can cause or contribute to arrhythmias include electrolyte abnormalities (especially low potassium or low magnesium), hypoxemia, hormonal imbalances, medications, and toxins.

N-terminal pro-B-type natriuretic peptide (NT-proBNP) is a precursor of BNP, a hormone secreted by the heart when the heart is failing. NT-proBNP levels are elevated in patients with heart failure and can be used to diagnose heart failure, assess the severity of the disease, and predict the prognosis of patients with heart failure.

Arrhythmias and heart failure are conditions that can occur in the same patient. This study aims to evaluate NT-proBNP levels in patients with arrhythmias and to analyze the correlation between NT-proBNP levels and several related factors. The primary objective of this study is to determine the NT-proBNP levels of patients with arrhythmias and to compare NT-proBNP levels in patients with and without arrhythmias and heart failure. The secondary objective is to assess the correlation between NT-proBNP levels and related factors.

II. SUBJECTS AND METHODS:

2.1 Subjects: Inpatients with arrhythmias treated in the Arrhythmia Treatment Department from December 2023 to March 2024. Exclusion criteria: patients with an estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m².

2.2. Study design: cross-sectional study

2.3. Content Research and variable definition:

Clinical and paraclinical characteristics of patients: History, gender, age, height, weight, BMI, complete blood count, blood chemistry, echocardiogram.

NT-proBNP quantification was performed on patient serum samples using a sandwich immunoassay method on the Siemens ADVIA Centaur system.

Heart failure was defined according to the 2022 AHA/ACC/HFSA Guideline [1].

2.4. Data processing and analysis:

Data were analyzed using the statistical software R version 4.3.1. For quantitative variables, if the data had a normal distribution, it was expressed as mean ± standard deviation (M ± SD); if the data did not have a normal distribution, it was expressed as median (interquartile range) (Median [IQR]). Qualitative variables were expressed as percentages (%). The t-test or Mann–Whitney U test was used to compare two groups of quantitative variables. The chi-squared test or Fisher's Exact Test was used to compare proportions between two groups. Spearman's correlation coefficient was used to assess the univariate relationship between two continuous or ordinal variables. Multivariate analysis was performed using multiple linear regression. Differences were considered statistically significant at $P < 0.05$.

2.5. Medical ethics: This study had been approved by the Ethics Council for Biomedical Research at the University of Medicine and Pharmacy at Ho Chi Minh City according to Decision No. 806/HDĐĐ-ĐHYD dated September 22, 2023. All patients selected for the study provided written informed consent.

III. RESULTS:

3.1. General characteristics:

Table 1: ***Anthropometric, clinical, laboratory test, and echocardiographic characteristics of 89 male and 69 female patients with arrhythmias***

	M ± SD	Median (IQR)
Anthropometric, clinical characteristics		
Age (year)	64.1 ± 16.2	69 (53-76)
Height (m)	1.60 ± 0.06	1.60 (1.55-1.65)
Weight (kg)	58.8 ± 11.5	60 (52-65)

	M ± SD	Median (IQR)
BMI (kg/m²)	22.8 ± 3.53	22.9 (20.8-24.2)
Systolic blood pressure (mmHg)	130 ± 19.7	130 (120-140)
Diastolic blood pressure (mmHg)	76 ± 10.3	77 (70-80)
Laboratory test		
HGB (g/L)	127.9 ± 19.3	130.5 (117-139)
HCT (%)	38.6 ± 5.82	38.7 (35.1-41.5)
WBC (G/L)	8.31 ± 2.55	8.02 (6.52-9.78)
PLT (G/L)	192.3 ± 65.3	175.5 (158.2-225.7)
INR	1.11 ± 0.29	1.04 (1.00-1.11)
Creatinine (mg/dL)	0.94 ± 0.25	0.90 (0.78-1.06)
eGFR (mL/min/1.73m²)	78.3 ± 21.9	78.8 (63.0-94.0)
Free T4 (pg/mL)	12.9 ± 6.21	12.3 (11.1-13.6)
TSH (mIU/L)	1.74 ± 1.56	1.42 (0.80-2.24)
Echocardiography		
EF (%)	61.1 ± 14.9	65 (56-71)
EDV (mL)	113.5 ± 52.0	101 (81.7-129.7)
ESV (mL)	51.5 ± 45.2	35 (27-58.6)
LVEDD (mm)	48.2 ± 9.08	46.6 (42.7-52.0)
LVESD (mm)	32.2 ± 10.3	30 (26-35)

BMI: Body Mass Index; **HGB:** Hemoglobin; **HCT:** Hematocrit; **WBC:** White Blood Cell; **PLT:** Platelet; **INR:** International Normalized Ratio; **eGFR:** estimated Glomerular Filtration Rate; **EF:** Ejection Fraction; **EDV:** End Diastolic Volume; **ESV:** End Systolic Volume; **LVEDD:** Left ventricular end diastolic diameter; **LVESD:** Left ventricular end systolic diameter

Among the patients with arrhythmias but not heart failure (n = 117), there were 54 females (46.1%); among the patients with arrhythmias and heart failure (n = 41), there were 15 females (36.6%). The difference in the proportion of females between the two groups was not statistically significant (chi-squared test, P = 0.378).

Table 2: ***Anthropometric, clinical, laboratory test, and echocardiographic characteristics of patients with arrhythmias without heart failure (n=117) and patients with arrhythmias and heart failure (n=41)***

	Patients with arrhythmias but not heart failure (n=117)		Patients with arrhythmias and heart failure (n=41)		P
	M ± SD	Median (IQR)	M ± SD	Median (IQR)	
Anthropometric, clinical characteristics					
Age (year)	65 ± 15.7	69 (55-76)	61.5 ± 17.3	67 (52-74)	0.24*
Height (m)	1.60 ± 0.06	1.60 (1.55-1.65)	1.59 ± 0.06	1.60 (1.55-1.65)	0.55*
Weight (kg)	58.9 ± 11.2	60 (52-65)	58.4 ± 12.4	55 (50-65)	0.80*
BMI (kg/m²)	22.8 ± 3.50	23.0 (20.8-24.2)	22.7 ± 3.67	22.2 (20.5-24.4)	0.92*
Systolic blood pressure (mmHg)	130.2 ± 18.2	130 (120-140)	129.4 ± 23.3	125 (120-140)	0.83*
Diastolic blood pressure (mmHg)	76.1 ± 10.4	77 (70-80)	75.7 ± 10.1	75 (70-80)	0.86*
Laboratory test					

	Patients with arrhythmias but not heart failure (n=117)		Patients with arrhythmias and heart failure (n=41)		P
	M ± SD	Median (IQR)	M ± SD	Median (IQR)	
HGB (g/L)	127.1 ± 16.1	130 (116-138)	130.3 ± 26.4	132 (119-143)	0.36*
HCT (%)	38.3 ± 6.00	38.8 (34.6-41.4)	39.3 ± 5.26	38.7 (36.0-42.8)	0.32*
WBC (G/L)	8.25 ± 2.54	7.80 (6.40-9.43)	8.48 ± 2.61	8.2 (6.8-10)	0.62*
PLT (G/L)	192.3 ± 64.5	165 (150-225)	192.4 ± 68.2	171 (143-235)	0.99*
INR	1.08 ± 0.28	1.04 (1.00-1.09)	1.17 ± 0.28	1.09 (1.01-1.22)	0.12*
Creatinine (mg/dL)	0.92 ± 0.24	0.88 (0.77-1.08)	0.99 ± 0.26	0.96 (0.83-1.03)	0.18*
eGFR (mL/min/1.73m²)	78.8 ± 22.1	80.2 (62.8-94.1)	77.1 ± 21.7	78.1 (64.2-93.3)	0.66*
Free T4 (pg/mL)	12.5 ± 2.25	12.3 (11.1-13.7)	14.1 ± 11.5	12.2 (11.3-13.5)	0.14**
TSH (mIU/L)	1.52 ± 1.01	1.27 (0.80-2.01)	2.37 ± 2.45	1.57 (1.13-2.71)	0.002**
Siêu âm tim					
EF (%)	67.1 ± 8.51	68 (62-72)	43.9 ± 15.9	44 (29-55)	<0.001*
EDV (mL)	96.4 ± 23.7	96 (78-112)	157.2 ± 74.8	150 (102-211)	<0.001**
ESV (mL)	34.9 ± 16.6	29.9 (24.9-41)	93.0 ± 64.1	83 (36.7-120)	<0.001**
LVEDD (mm)	45.4 ± 5.26	46 (42-49)	56.2 ± 12.4	56 (46-65)	<0.001*
LVESD (mm)	28.4 ± 4.87	28 (25-31)	43.2 ± 13.6	41.6 (31.0-50.4)	<0.001*

*: t-test

**: Mann–Whitney U test

There were no significant differences in anthropometric characteristics, systolic blood pressure, or diastolic blood pressure between the arrhythmia patients without heart failure and the arrhythmia patients with heart failure.

The TSH level was significantly higher in the arrhythmia patients with heart failure than in the arrhythmia patients without heart failure ($P < 0.001$). There were no significant differences in other hematological and biochemical laboratory parameters between the two groups.

Echocardiographic comparison revealed that the EF was lower in the arrhythmia patients with heart failure than in the arrhythmia patients without heart failure; the EDV, ESV, LVEDD, and LVESD were higher in the arrhythmia patients with heart failure than in the arrhythmia patients without heart failure; all of these differences were statistically significant ($P < 0.001$).

2. NT-proBNP levels

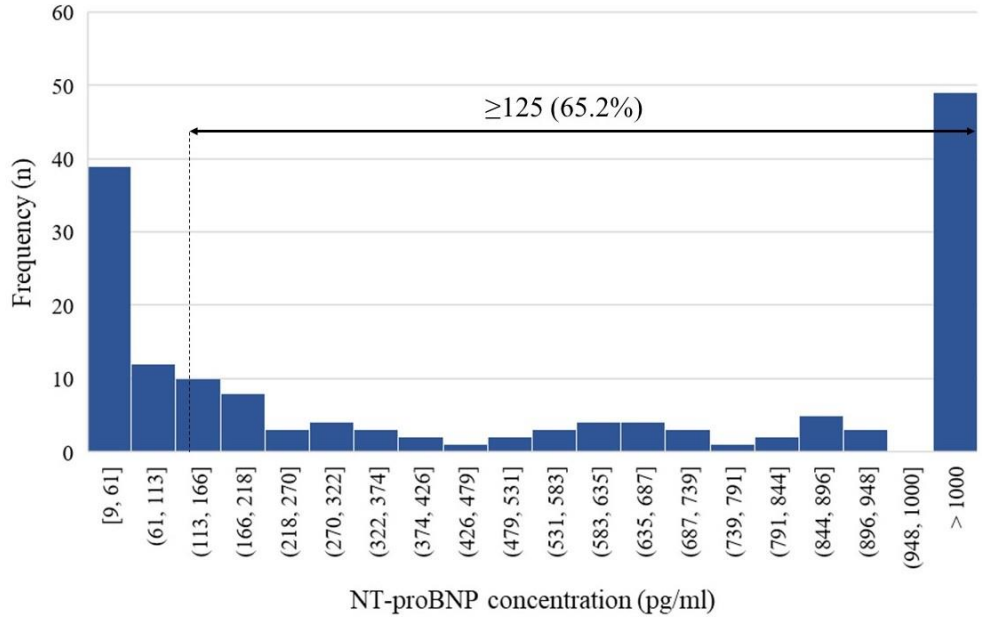

Figure 1: ***Distribution of NT-proBNP levels in patients with arrhythmias (n = 158)***

The NT-proBNP level in the arrhythmia patients (n = 158) was 367.3 (61.9-1297) pg/ml (median [IQR]). Among the arrhythmia patients, 103 patients had an NT-proBNP level ≥ 125 pg/ml, representing 65.2% of the total number of patients in this group.

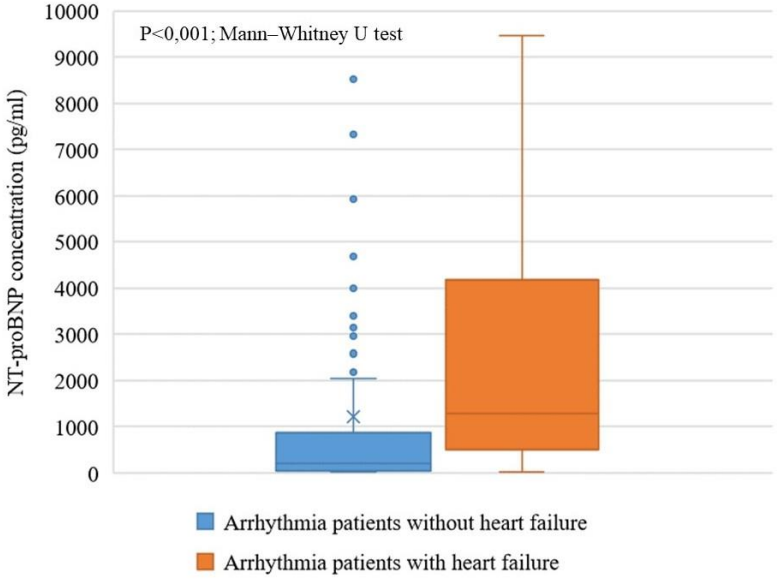

Figure 2: ***Comparison of NT-proBNP levels in arrhythmia patients without heart failure (n=117) and arrhythmia patients with heart failure (n=41)***

The median NT-proBNP level (IQR) in the arrhythmia patients with heart failure (n = 41) was 1273.7 (498.1-4173.9) pg/ml, which was significantly higher than the median NT-proBNP level in the arrhythmia patients without heart failure (n = 117) of 210.1 (51.4-875.4) pg/ml (P < 0.001).

3. Association between NT-proBNP level and some variables in the study

Table 3: ***Association between NT-proBNP level and some variables in the study***

Variable	Spearman's rank correlation coefficient	P
Age (year)	0,367	<0,001
Weight (kg)	-0,214	0,007
BMI (kg/m²)	-0,120	0,131
Systolic blood pressure (mmHg)	0,074	0,351
Diastolic blood pressure (mmHg)	-0,001	0,988
HGB (g/L)	-0,287	<0,001
EF (%)	-0,286	<0,001
Creatinine (mg/dL)	0,243	0,002
eGFR (ml/min/1.73m²)	-0,434	<0,001

The following variables were significantly correlated with NT-proBNP level: age, weight, HGB, EF, creatinine, and eGFR.

Table 4: ***Regression analysis of the association between NT-proBNP level and some variables adjusted for heart failure status***

Variable	Regression coefficient	Standard error	P
Age (year)	8,46	59,0	0,886
Weight (kg)	-37,0	103,4	0,720
BMI (kg/m²)	47,9	306,0	0,875
HGB (g/L)	-39,5	22,0	0,075
EF (%)	-60,0	35,7	0,095
Creatinine (mg/dL)	2904,1	6094,1	0,634
eGFR (ml/min/m²)	-7,83	88,0	0,929
Sex (male)	674,0	1744,5	0,699

When a patient's heart failure status is taken into account, none of the considered factors have an effect on the patient's NT-proBNP level.

IV. DISCUSSION:

Elevated NT-proBNP levels in cardiovascular diseases, especially heart failure. NT-proBNP testing is simple, easy to perform, and minimally invasive. NT-proBNP is a valuable biomarker for the diagnosis, assessment of severity, monitoring of treatment effectiveness, and risk prediction in cardiovascular diseases, including arrhythmias, a condition that can lead to many dangerous complications such as heart failure and sudden death.

Our study analyzed NT-proBNP levels in 158 patients with arrhythmias, including 41 patients with arrhythmias and heart failure. In addition to echocardiographic parameters, there were no significant differences in most anthropometric and paraclinical parameters between the two groups of patients with arrhythmias: those without heart failure and those with heart failure.

Our study found that the median NT-proBNP level in patients with arrhythmias was 367.3 (61.9-1297) pg/ml. In the arrhythmia group, 65.2% of patients had an NT-proBNP level ≥125 pg/ml. Some studies in non-cardiac adults in the US have found this proportion to be around 20-30%.[2, 3] A study by Hayley Birrell et al. (2024) in the UK on the diagnostic value of NT-proBNP in

patients with heart failure with preserved ejection fraction found that with a cut-off of 125 pg/ml, the sensitivity, specificity, positive predictive value and negative predictive value were 83.4, 25.0, 52 and 61%, respectively.[4] Therefore, with a cut-off of 125 pg/ml, the rate of NT-proBNP elevation in our study was higher in the group without cardiovascular disease and lower in the heart failure patients compared to previous studies.

In our study, the NT-proBNP levels were significantly higher in patients with arrhythmia and heart failure than in those with arrhythmia alone. While we were unable to find a study with an identical patient population for direct comparison, our results are in line with the majority of previous studies.[5, 6] Elevated NT-proBNP levels in patients with arrhythmia and heart failure may be due to several factors. Reduced pumping ability of the heart leads to increased pressure in the heart chambers and blood vessels. This high pressure stimulates the production and release of NT-proBNP from the heart. Atrial fibrillation and other arrhythmias can increase left ventricular (LV) workload, causing the heart to work harder to maintain blood flow. This increased LV workload triggers NT-proBNP production. Some arrhythmias can lead to myocardial necrosis, which damages heart muscle and releases NT-proBNP into the blood. Both heart failure and arrhythmias can activate the RAAS system, leading to increased aldosterone production. Aldosterone, in turn, can further elevate NT-proBNP levels. Age, gender, renal function, and comorbidities can also influence NT-proBNP levels. The extent of NT-proBNP elevation may vary depending on the underlying etiology and severity of arrhythmia and heart failure. In conclusion, NT-proBNP concentrations are higher in patients with arrhythmias and heart failure due to many factors, including impaired cardiac function, increased left ventricular load, myocardial necrosis, activation of the RAAS system, and other factors.

Univariate analysis revealed statistically significant correlations between NT-proBNP levels and age, weight, hemoglobin, EF, creatinine, and eGFR. However, when heart failure status was considered in a multivariate analysis, none of these factors were found to independently influence patients' NT-proBNP levels.[7]

Our study has certain limitations. First, we did not subdivide the heart failure patients based on their ejection fraction (preserved or reduced). Second, we did not differentiate between supraventricular and ventricular arrhythmias. These limitations are due to the relatively small sample size of our study. Subgroup analyses with smaller sample sizes may not have sufficient power to yield generalizable results.

Future research could focus on determining the precise relationship between arrhythmias, heart failure, and NT-proBNP levels and evaluating the utility of NT-proBNP in the diagnosis, monitoring, and treatment of arrhythmias and heart failure.

V. CONCLUSION:

The median (IQR) NT-proBNP level in the arrhythmia group was 367.3 (61.9-1297) pg/ml. NT-proBNP levels were significantly higher in arrhythmia patients with heart failure compared to those without heart failure. Univariate analysis revealed statistically significant correlations between NT-proBNP levels and age, weight, hemoglobin, EF, creatinine, and eGFR.

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