CORRELATION BETWEEN NT-PROBNP AND ECHOCARDIOGRAPHIC PARAMETERS IN PATIENTS WITH ARRHYTHMIAS

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ABSTRACT

Background: Arrhythmias are a significant public health burden, associated with increased morbidity and mortality. NT-proBNP, a biomarker of cardiac stress, has been shown to be elevated in various cardiovascular conditions. **Objective:** This study aimed to determine NT-proBNP concentrations in a cohort of patients with arrhythmias and evaluate the correlation between echocardiographic indices such as EF, EDV, ESV, and left ventricular dimensions (LVEDD, LVESD) and NT-proBNP concentrations in this patient population. **Subjects and Methods:** This study included 272 patients with various types of arrhythmias. Echocardiographic parameters, including EF, EDV, ESV, LVEDD, and LVESD were obtained. NT-proBNP levels were measured in all patients. Spearman's rank correlation coefficient was used to assess the relationship between NT-proBNP and echocardiographic parameters. Multivariate regression analysis was performed to adjust for potential confounders. **Results:** The median NT-proBNP level was 44.1 pmol/L. 69.5% of patients had levels above 15 pmol/L. Patients with ventricular arrhythmias had higher median NT-proBNP levels compared to those with non-ventricular arrhythmias (94.6 vs. 42.3 pmol/L), although not statistically significant. Spearman's rank correlation analysis revealed a significant inverse correlation between NT-proBNP and EF. Furthermore, positive correlations were observed between NT-proBNP and LVESD and LVEDD. Multivariate regression analysis, adjusting for age, eGFR, and heart failure status, confirmed independent associations between NT-proBNP and EF, ESV, LVEDD and LVESD. **Conclusions:** Higher NT-proBNP levels were associated with reduced EF and increased left ventricular dimensions, even after adjusting for potential confounders. These findings suggest that NT-proBNP may be a useful biomarker for assessing cardiac function and identifying patients at higher risk for adverse outcomes in this population.

Keywords: *NT-proBNP, echocardiography, arrhythmias*

I. INTRODUCTION

Arrhythmias, characterized by abnormal heart rhythms, are a significant public health concern with a wide spectrum of clinical presentations and associated morbidity and mortality. Conditions such as atrial fibrillation, ventricular tachycardia, and bradyarrhythmias can lead to serious complications including heart failure, stroke, and sudden cardiac death.

Echocardiography is a non-invasive imaging technique that provides valuable insights into cardiac structure and function. However, assessing the severity and prognosis of arrhythmias often requires a multi-faceted approach.

N-terminal pro-brain natriuretic peptide (NT-proBNP), a neurohormone released primarily by the ventricles in response to increased cardiac wall stress, has emerged as a valuable biomarker of cardiac dysfunction. Elevated NT-proBNP levels have been associated with various cardiovascular conditions, including heart failure [1].

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Previous studies have established a strong association between NT-proBNP levels and cardiac dysfunction. Specifically, research has shown a significant correlation between NT-proBNP and echocardiographic parameters in various patient populations, including those with heart failure and hypertension [2, 3]. However, the specific relationship between NT-proBNP and echocardiographic parameters in patients with arrhythmias remains relatively less explored. While studies have investigated NT-proBNP in patients with specific arrhythmias like atrial fibrillation [4], the comprehensive correlation between NT-proBNP and a range of echocardiographic parameters in this diverse population remains to be fully elucidated.

This study aims to:

1.Determine NT-proBNP concentrations in a cohort of patients with arrhythmias.

2.Evaluate the correlation between echocardiographic indices such as left ventricular ejection fraction (LVEF), end-diastolic volume (EDV), end-systolic volume (ESV), and left ventricular dimensions (LVEDD, LVESD) and NT-proBNP concentrations in this patient population.

By investigating the relationship between NT-proBNP and echocardiographic parameters, this study aims to enhance our understanding of the pathophysiological mechanisms underlying arrhythmias and potentially identify novel biomarkers for risk stratification and prognostication in this patient population.

II. SUBJECTS AND METHODS

Study Design: This investigation employed a cross-sectional design. Participants were recruited at a single point in time during the study period, which spanned from December 2023 to May 2024. The study site was the Arrhythmia Treatment Department of Cho Ray Hospital in Ho Chi Minh City, Vietnam.

Study Population: Participants were recruited consecutively from inpatients admitted to the Arrhythmia Treatment Department of Cho Ray Hospital throughout the study period. To minimize potential confounding factors, patients with estimated glomerular filtration rate (eGFR) less than 15 ml/min/m^2 were excluded. To further explore potential differences in NT-proBNP levels, the study group was divided into subgroups based on arrhythmia type (ventricular vs. non-ventricular).

Data Collection: Demographic and anthropometric data, along with clinical and subclinical indicators, were retrieved from patients' medical records. Acute exacerbations of arrhythmias and ventricular arrhythmias were independently confirmed by at least two electrophysiologists through analysis of 12-lead ECG, Holter ECG, and/or electrophysiological study data. The diagnosis of HF adhered to the established criteria outlined in the 2021 ESC guidelines [5].

NT-proBNP Measurement: Blood samples were collected from all participants as soon as possible after enrollment to quantify NT-proBNP levels alongside other biochemical markers. A sandwich immunoassay technology on the ADVIA Centaur (Siemens) platform was employed for NT-proBNP measurement. This assay boasts a reportable range of 4.13–4130 pmol/L (35–35,000 pg/mL) and demonstrates excellent repeatability and within-laboratory imprecision reliability with coefficients of variation less than 7% and 10%, respectively.

Statistical Analysis: Quantitative data were presented as median and interquartile range (IQR). Categorical variables were expressed as percentages. Comparisons

between two independent groups for continuous variables were performed using the Wilcoxon rank-sum test. Spearman's rank correlation coefficient was employed to assess the association between two continuous variables. Multivariate regression analysis was utilized to evaluate the relationship between a dependent variable and multiple independent variables while controlling for potential confounders. Statistical significance was defined as a p-value less than 0.05. All statistical analyses were performed using R statistical software version 4.3.1.

Ethical Considerations: This study was approved by the Ethics Council in Biomedical Research of the University of Medicine and Pharmacy at Ho Chi Minh City. All participants provided written informed consent after receiving a comprehensive explanation of the study objectives, procedures, and potential risks and benefits.

III. RESULTS

A total of 285 patients with arrhythmias were initially recruited for this study. However, 13 participants were excluded due to eGFR less than 30 ml/min/m^2. Therefore, data from 272 patients were ultimately included in the analysis.

3.1. General characteristics:

Table 1: **Anthropometric, clinical, laboratory test, and echocardiographic characteristics of 149 male and 123 female patients with arrhythmias**

N = 272	M ± SD	Median (IQR)
Anthropometric, clinical characteristics		
Age (year)	64.6 ± 15.8	68 (55 – 76)
Height (m)	1.68 ± 1.32	1.60 (1.55 – 1.65)
Weight (kg)	58.0 ± 10.07	58 (50 – 65)
BMI (kg/m²)	22.6 ± 3.33	22.4 (20.6 – 24.1)
Systolic blood pressure (mmHg)	129.2 ± 19.6	130 (120 –140)
Diastolic blood pressure (mmHg)	75.2 ± 10.3	74.5 (70 – 80)
Laboratory test		
HGB (g/L)	126.6 ± 19.4	128.5 (116 – 138)
HCT (%)	38.3 ± 5.40	38.5 (35.1 – 41.3)
WBC (G/L)	8.53 ± 3.01	8.00 (6.67 – 10.0)
PLT (G/L)	197.5 ± 80.4	189.0 (136.7 – 231.5)
INR	1.15 ± 0.39	1.05 (1.01 – 1.13)
Creatinine (mg/dL)	0.93 ± 0.26	0.88 (0.76 – 1.07)
eGFR (mL/min/1.73m²)	78.9 ± 21.9	81.4 (63.3 – 94.0)
Free T4 (pg/mL)	12.9 ± 5.39	12.3 (11.2 – 13.8)
TSH (mIU/L)	1.86 ± 1.85	1.41 (0.79 – 2.23)
Echocardiography		
EF (%)	61.4 ± 13.8	65.0 (56.3 – 71.0)
EDV (mL)	114.3 ± 49.0	102.5 (84.5 – 129.2)
ESV (mL)	49.8 ± 41.8	36.0 (27.5 – 53.2)
LVEDD (mm)	48.4 ± 8.48	47.0 (43.0 – 52.0)
LVESD (mm)	32.1 ± 9.62	30.0 (27.0 – 34.6)

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

Table 1 presents the baseline characteristics of 272 patients with arrhythmias, including both anthropometric, clinical, laboratory, and echocardiographic parameters. The study population was predominantly elderly, with a mean age of 64.6 years. There was a slight male predominance in the study population (54.7%). Hematological parameters (HGB, HCT, WBC, PLT) appeared within normal ranges. Renal function (creatinine, eGFR) was generally preserved. Thyroid function tests (free T4, TSH) were within normal limits.

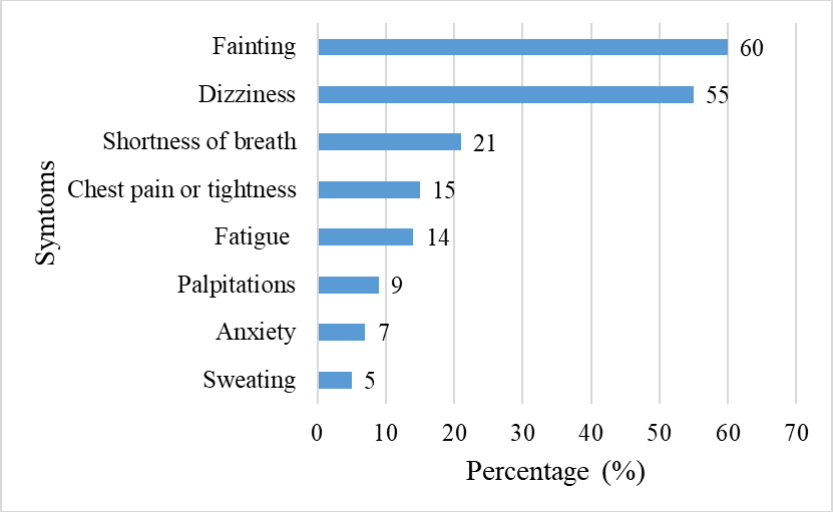

Figure 1: **Clinical Presentation of Arrhythmia Patients**

Figure 1 illustrates the frequency of various symptoms experienced by 272 patients with arrhythmias. Fainting and dizziness were the most common symptoms, reported by 60% and 55% of patients, respectively. Shortness of breath was the third most common symptom, reported by 21% of patients. Chest pain or tightness was experienced by 15% of patients, indicating that cardiac symptoms were not uncommon in individuals with arrhythmias. Fatigue, palpitations, anxiety, and sweating were reported with lower frequencies, ranging from 5% to 14%.

3.2. NT-proBNP levels in patients with arrhythmias

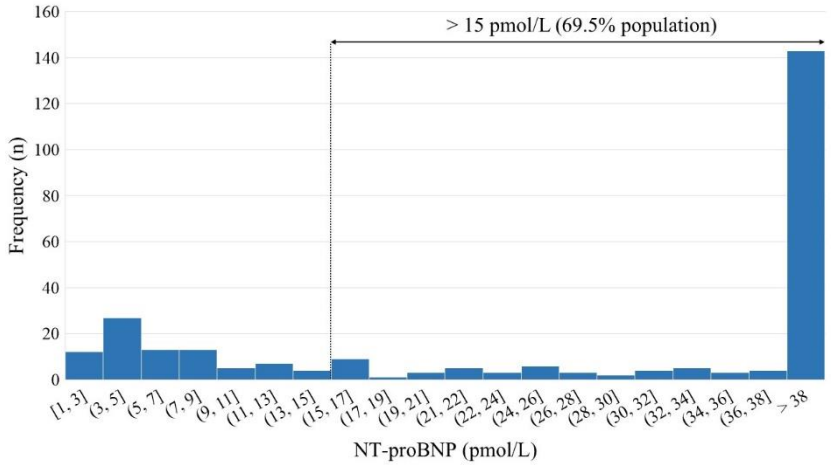

Figure 2: **Distribution of NT-proBNP levels in patients with arrhythmias (n = 272)**

The NT-proBNP level in the arrhythmia patients (n = 272) was 44.1 (10.2-163.1) pmol/L (median [IQR]). The skewed distribution of NT-proBNP levels highlighted the heterogeneity of this patient population in terms of cardiac function and disease severity. 69.5% of the population having NT-proBNP levels above 15 pmol/L indicated a substantial proportion of the study population might have elevated NT-proBNP levels, which could have clinical implications.

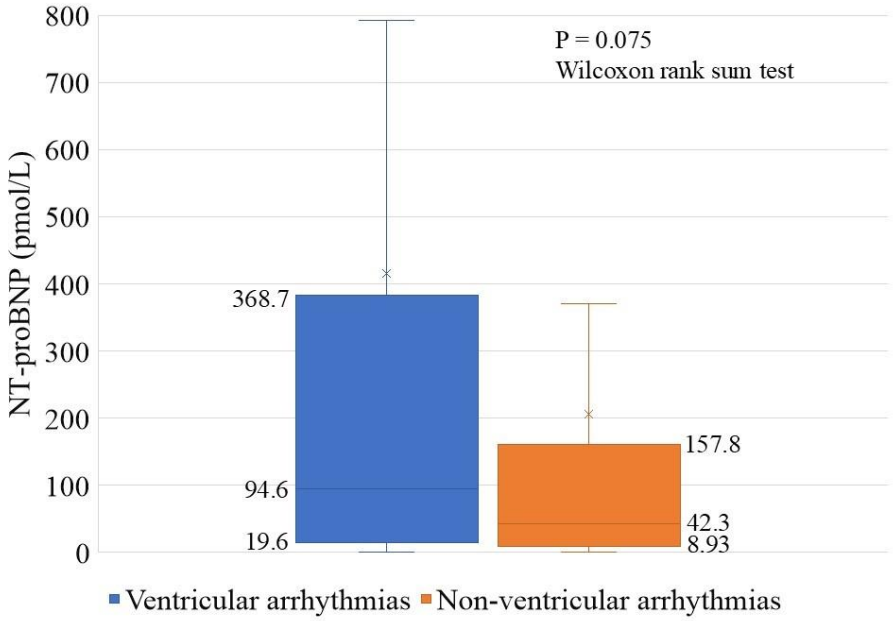

Figure 3: **Comparison of NT-proBNP Levels Across Patient Subgroups**

Patients diagnosed with ventricular arrhythmias exhibited higher median NT-proBNP concentrations compared to those with non-ventricular arrhythmias (median: 94.6 pmol/L vs. 42.3 pmol/L). However, the statistical test did not show a significant difference (p = 0.075, Wilcoxon rank sum test).

3.3. Correlation between NT-proBNP levels and echocardiographic measurements

Table 2: **Association between NT-proBNP level and echocardiographic measurements in the study**

Variable	Spearman's rank correlation coefficient	P
EF (%)	-0.289	<0.001
EDV (mL)	0.117	0.066
ESV (mL)	0.175	0.006
LVEDD (mm)	0.115	0.060
LVESD (mm)	0.177	0.003

There was a significant negative correlation between NT-proBNP levels and EF (r = -0.289, p < 0.001). There were positive correlations between NT-proBNP and other echocardiographic measurements in the table but only the correlations with ESV and LVESD were statistically significant.

Table 3: **Regression analysis of the association between NT-proBNP level and echocardiographic measurements adjusted for age, eGFR and heart failure status**

Variable	Regression coefficient	Standard error	P
EF (%)	-0.003	0.001	0.035
EDV (mL)	0.007	0.004	0.127
ESV (mL)	0.008	0.003	0.025
LVEDD (mm)	0.003	0.001	<0.001
LVESD (mm)	0.004	0.001	<0.001

After adjusting for age, eGFR, and heart failure status, higher NT-proBNP levels were independently associated with EF, ESV, LVEDD and LVESD.

IV. DISCUSSION

This study investigated the relationship between NT-proBNP levels and echocardiographic parameters in a cohort of 272 patients with arrhythmias. Our findings revealed several key observations.

Firstly, the distribution of NT-proBNP levels in our study population was skewed to the right, indicating a significant proportion of patients with elevated levels. This observation highlights the potential clinical significance of NT-proBNP in this patient population. NT-proBNP is a neurohormone primarily released by the cardiac ventricles in response to increased myocardial wall stress, a phenomenon commonly observed in conditions of volume and pressure overload. Various arrhythmias, particularly ventricular arrhythmias, can lead to impaired cardiac function, characterized by reduced EF [6, 7]. This systolic dysfunction, coupled with increased afterload, results in elevated intracardiac pressures, stimulating the release of NT-proBNP. Furthermore, some arrhythmias, such as atrial fibrillation, can contribute to the development of heart failure, both systolic and diastolic [8]. Diastolic dysfunction, characterized by impaired ventricular relaxation and filling, also elevates intracardiac pressures, thereby augmenting NT-proBNP secretion. Beyond hemodynamic factors, arrhythmias can induce structural and functional remodeling of the myocardium. For instance, atrial fibrillation can lead to atrial enlargement, fibrosis, and electrical remodeling, all of which contribute to increased myocardial stress and NT-proBNP release. Moreover, certain arrhythmias, especially those associated with underlying heart disease, can trigger inflammatory responses, further stimulating NT-proBNP production. The relationship between NT-proBNP and arrhythmias is multifaceted and complex, influenced by the specific type of arrhythmia, its duration, and the presence of co-existing cardiovascular conditions. While elevated NT-proBNP levels in patients with arrhythmias often reflect underlying cardiac dysfunction and remodeling, it is crucial to consider the interplay of various factors in interpreting NT-proBNP levels in this context.

Secondly, we found that patients with ventricular arrhythmias exhibited higher median NT-proBNP levels compared to those with non-ventricular arrhythmias, although this difference did not reach statistical significance ($p = 0.075$). Ventricular arrhythmias often arise from underlying cardiac dysfunction, such as ischemic heart disease, cardiomyopathy, or heart failure. These conditions can lead to significant myocardial damage, impaired ventricular function, and increased cardiac workload.

For example, frequent ventricular ectopic beats can disrupt cardiac rhythm and increase myocardial oxygen demand. This increased stress, along with potential structural remodeling (e.g., ventricular dilation and fibrosis) associated with ventricular arrhythmias, can contribute to elevated NT-proBNP levels. However, the observed difference in NT-proBNP levels between patients with ventricular and non-ventricular arrhythmias in this study did not reach statistical significance. This could be attributed to several factors, including limited sample size, significant variability in NT-proBNP levels within each group, and the potential influence of confounding factors such as comorbidities (hypertension, diabetes, chronic kidney disease) and the heterogeneity of the "non-ventricular arrhythmias" group. This group likely encompasses a diverse range of arrhythmias with varying degrees of impact on cardiac hemodynamics and NT-proBNP levels, such as atrial fibrillation, atrial flutter, and supraventricular tachycardia. Despite the lack of statistical significance, the observed trend towards higher NT-proBNP levels in patients with ventricular arrhythmias warrants further investigation. Ventricular arrhythmias, due to their potential impact on ventricular function and cardiac remodeling, may indeed contribute to elevated NT-proBNP levels compared to other types of arrhythmias. Further studies with larger sample sizes, detailed characterization of arrhythmia subtypes, and rigorous control for confounding factors are necessary to confirm these findings and elucidate the specific mechanisms underlying the relationship between arrhythmia type and NT-proBNP levels.

Thirdly, Spearman's rank correlation analysis revealed a significant inverse correlation between NT-proBNP levels and EF. This finding is consistent with previous studies demonstrating the association between elevated NT-proBNP and impaired cardiac function. Furthermore, we observed significant positive correlations between NT-proBNP and LVESD and LVEDD. These findings suggest that higher NT-proBNP levels are associated with increased left ventricular dimensions and may reflect underlying cardiac remodeling.

Finally, multivariate regression analysis, adjusting for age, eGFR, and heart failure status, further confirmed the independent association between NT-proBNP and LVEDD and LVESD. These findings suggest that NT-proBNP may provide valuable prognostic information beyond traditional risk factors.

This study has several limitations. Firstly, the sample size was relatively small, which may limit the generalizability of the findings. Secondly, the study did not include all possible types of arrhythmias, which may have influenced the results. Thirdly, the study did not assess the long-term clinical outcomes associated with elevated NT-proBNP levels.

In conclusion, this study demonstrates an association between NT-proBNP levels and echocardiographic parameters in patients with arrhythmias. Higher NT-proBNP levels were associated with reduced EF and increased left ventricular dimensions, even after adjusting for potential confounders. These findings suggest that NT-proBNP may be a useful biomarker for assessing cardiac function and identifying patients at higher risk for adverse outcomes in this population. Further studies with larger sample sizes and longer follow-up periods are warranted to confirm these findings and explore the clinical implications of NT-proBNP in the management of patients with arrhythmias.

V. CONCLUSION

The median NT-proBNP level in the 272 arrhythmia patients was 44.1 (10.2-163.1) pmol/L. Patients with ventricular arrhythmias exhibited higher median NT-proBNP concentrations (94.6 pmol/L) compared to those with non-ventricular arrhythmias (42.3 pmol/L) (p = 0.075, Wilcoxon rank sum test). Multivariate analysis revealed a significant association between elevated NT-proBNP levels and impaired left ventricular systolic function, as evidenced by reduced EF and increased left ventricular dimensions, including LVESD and LVEDD. These findings suggest that NT-proBNP may serve as a valuable biomarker for assessing cardiac dysfunction and identifying patients with arrhythmias at higher risk for adverse cardiovascular events. However, further investigation with larger sample sizes and longer follow-up periods is warranted to validate these findings and fully elucidate the clinical implications of NT-proBNP in this patient population.

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