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Original Article

Variability and Discordance between NT-proBNP and Left Ventricular Ejection Fraction in Patients with Heart Failure: A Cross-Sectional Study

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ABSTRACT

Background: Heart failure assessment commonly relies on left ventricular ejection fraction (LVEF) and NT-proBNP, yet discordance between these parameters may affect clinical interpretation. Aim of the study: To evaluate variability and agreement between NT-proBNP levels and LVEF in patients with heart failure. **Methods & Materials**: This cross-sectional study included 60 clinically diagnosed heart failure patients. NT-proBNP was measured and echocardiographic LVEF was assessed. Associations were analyzed using Pearson correlation and logistic regression. **Result**: Mean age was 57.88±11.90 years; 63.33% were male. Mean NT-proBNP was 4559.50±801.65 pg/mL and mean LVEF was 34.45±11.19%. Reduced EF (≤40%) was present in 70%. NT-proBNP showed weak negative correlation with LVEF (r = -0.263, p = 0.021) and positive correlation with NYHA class (r = 0.401, p = 0.003). Discordance was observed in 30% of cases. Reduced EF (OR: 3.92, 95% CI: 1.71–8.97, p = 0.001) and NYHA III–IV (OR: 4.36, 95% CI: 1.98–9.62, p = 0.001) were strong predictors of elevated NT-proBNP. **Conclusion**: There is significant variability and partial discordance between NT-proBNP levels and left ventricular ejection fraction in patients with heart failure. Both parameters show a weak but significant relationship and often reflect different dimensions of cardiac dysfunction. Their combined interpretation improves diagnostic clarity and enhances clinical risk stratification.

Keywords: *Heart failure; NT-proBNP; Left ventricular ejection fraction; Discordance; Biomarkers; Echocardiography; NYHA functional class.*

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INTRODUCTION

Heart failure (HF) is a clinical syndrome characterized by a complex series of structural and/or functional cardiac abnormalities that lead to the heart's inability to pump sufficient blood to meet the metabolic needs of the body [1]. Left ventricular ejection fraction (LVEF), an established HF diagnosis with specific New York Heart Association (NYHA) is commonly used to assess systolic performance, whereas N-terminal pro–B-type natriuretic peptide (NT-proBNP) reflects myocardial wall stress and neurohormonal activation [2]. Both are common indices used in the field of HF assessment, but do not always agree, leading to variability and discordance that may impact diagnosis and management [3]. Heart failure is now a significant global public health challenge, impacting almost 64 million people worldwide, and associated with a rise in morbidity, mortality and healthcare expenditure [4]. The estimated prevalence of HF in the Southeast Asian region is 15% in adults, and this burden is increasing due to hypertension, diabetes, ischemic heart disease, and population ageing [5]. Although the treatment of heart failure has improved, the diagnosis of heart failure is still late, the diagnostic tools are not readily available, and access to advanced cardiac care is still poor in low- and middle-income countries [6]. NT-proBNP is released from the ventricular myocardium in response to increased wall stress and myocardial stretch due to pressure or volume overload [7]. High levels typically represent a decreased function of the ventricles and high intracardiac pressure [8]. LVEF, on the other hand, is the percentage of blood pumped out of the left ventricle during contraction, and is determined by echo [9]. HF can be present in patients with decreased, mildly decreased or normal EF, and NT-proBNP can range widely depending on EF [2]. Patients with high NT-proBNP levels and preserved LVEF and those with reduced LVEF may have similarly low levels of NT-proBNP, depending on obesity, renal function, age or the effects of medication [10]. The use of NT-proBNP in combination with the LVEF provides greater diagnostic and prognostic value in heart failure because of the incorporation of biomarker data of cardiac stress with structural cardiac function [11]. NT-proBNP testing is quick, simple and useful in emergency situations, whereas echocardiographic LVEF is direct measurement of cardiac structure and function [8]. Non-cardiac factors like renal dysfunction, advancing age, obesity and anemia-related conditions impact NT-proBNP, and echocardiographic LVEF assessment is inter observer dependent and technically/measurement dependent, which is problematic for clinical reproducibility [12,13]. Thus, differences between these values can make clinical interpretation difficult. NT-proBNP and LVEF are commonly used in heart failure evaluation, but they often show discordant results in clinical practice, leading to diagnostic uncertainty. This relationship is important to understand to enhance diagnostic clarity and contribute to better clinical decision making in heart failure, as both are limited in their ability and provide different perspective of cardiac function. The goal of this study was to determine the relationship and level of agreement between NT-proBNP and left ventricular ejection fraction (LVEF) in heart failure patients.

METHODS & MATERIALS

This cross-sectional observational study was conducted in the the Department of Medicine and Cardiology at Rangpur Medical College Hospital in Bangladesh over a period of 1 year from June 2019 to May 2020. The study aimed to evaluate the variability and discordance between NT-

proBNP levels and left ventricular ejection fraction (LVEF) in patients with heart failure. A total of 60 patients with clinically diagnosed heart failure were enrolled using a purposive sampling technique.

Inclusion Criteria

- Patients aged 20 years or older.
- Clinically diagnosed heart failure patients based on standard clinical and echocardiographic criteria.
- Patients with documented left ventricular ejection fraction (LVEF).
- Patients with available NT-proBNP measurements.

Exclusion Criteria

- Acute myocardial infarction at presentation.
- Severe valvular heart disease requiring immediate surgical intervention.
- End-stage renal disease on dialysis.
- Acute or chronic inflammatory or infectious conditions affecting NT-proBNP levels.
- Incomplete clinical, biochemical, or echocardiographic data.

Data Collection

Data were systematically collected using a structured and validated questionnaire. Baseline variables included age, gender, residence, smoking status, body mass index (BMI), and comorbid conditions such as hypertension, diabetes mellitus, ischemic heart disease, chronic kidney disease, atrial fibrillation, dyslipidemia, previous myocardial infarction, and dilated cardiomyopathy. Clinical assessment included NYHA functional class, systolic blood pressure, and heart rate.

Echocardiographic evaluation was performed to measure left ventricular ejection fraction (LVEF) along with left ventricular end-diastolic diameter, left atrial diameter, and pulmonary artery systolic pressure. NT-proBNP levels were measured using standard laboratory methods and categorized into clinically relevant groups.

Statistical Analysis

Statistical analysis was performed using SPSS software (version 23). Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were summarized as frequency and percentage. Pearson correlation was used to assess the relationship between NT-proBNP and echocardiographic parameters. Logistic regression analysis was applied to identify factors associated with elevated NT-proBNP levels, expressed as odds ratio (OR) with 95% confidence interval (CI). A p-value <0.05 was considered statistically significant.

RESULT

The present study included 60 patients diagnosed with heart failure. The majority of patients belonged to the 53–63 years age group (50.00%). The mean age was 57.88±11.90 years. Male patients predominated 63.33% compared to females (36.67%). Most participants were from rural areas (78.33%). Regarding smoking status, 66.67% were current smokers and 13.33% were former smokers. In terms of BMI, half of the patients (50.00%) were in the 18.5–24.9 kg/m² range, while (30.00%) were overweight (25–29.9 kg/m²), 13.33% were obese (>30 kg/m²), and 6.67% were underweight (<18.5 kg/m²) (*Table I*).

Table I

Baseline Socio-demographic Characteristics of Patients with Heart Failure (*n* = 60).

Baseline Characteristics	Frequency (n)	Percentage (%)
Age group (years)		
20-30	1	1.67
31-41	6	10.00
42-52	9	15.00
53-63	30	50.00
64-75	12	20.00
above 75	2	3.33
Mean age (years)	57.88±11.90	
Gender		
Male	38	63.33
Female	22	36.67
Residence		
Urban	13	21.67
Rural	47	78.33
Smoking status		
Current smoker	40	66.67
Former smoker	8	13.33
Never smoker	12	20
Body Mass Index (kg/m²)		
<18.5	4	6.67
18.5-24.9	30	50.00
25-29.9	18	30.00
>30	8	13.33

Hypertension was present in 45.00% patients, diabetes mellitus in 35.00%, ischemic heart disease in 30.00%, dyslipidemia in 26.67%, previous myocardial infarction in 23.33%. Regarding NYHA functional class, 48.33% patients were in Class III, 30.00% in Class II, and 21.67% in Class IV. The mean systolic blood pressure was 137.08±32.65 mmHg, and the mean heart rate was 96.42±14.18 beats per minute (*Table II*).

Table II
Clinical and Comorbid Characteristics of the Study Population (*n* = 60).

Clinical Variables	Frequency (n)	Percentage (%)
Hypertension	27	45.00
Diabetes mellitus	21	35.00
Ischemic heart disease	18	30.00
Chronic kidney disease	6	10.00
Atrial fibrillation	7	11.67
Dyslipidemia	16	26.67
Previous myocardial infarction	14	23.33
Dilated cardiomyopathy	12	20.00
NYHA Functional Class		
Class II	18	30.00
Class III	29	48.33
Class IV	13	21.67
Mean systolic BP (mmHg)	137.08±32.65	
Mean heart rate (beats/min)	96.42±14.18	

NT-proBNP levels were ≥6000 pg/mL in 23.33% patients, 3000–5999 pg/mL in 46.67% patients, 1000–2999 pg/mL in 23.33%, and <1000 pg/mL in 6.67%, with a mean value of 4559.50±801.65 pg/mL. Regarding LVEF, 70.00% patients had reduced EF (≤40%), 20.00% had mildly reduced EF (41–49%), and 10.00% had preserved EF (≥50%), with a mean LVEF of 34.45±11.19% (*Table III*).

Table III
Distribution of NT-proBNP Levels and Left Ventricular Ejection Fraction among Heart Failure Patients (*n* = 60).

Variables	Frequency (n)	Percentage (%)
NT-proBNP level (pg/mL)		
<1000	4	6.67
1000–2999	14	23.33
3000–5999	28	46.67
≥6000	14	23.33
Mean NT-proBNP (pg/mL)	4559.50±801.65	
Left Ventricular Ejection Fraction (LVEF)		
Preserved EF (≥50%)	6	10.00
Mildly reduced EF (41–49%)	12	20.00
Reduced EF (≤40%)	42	70.00
Mean LVEF (%)	34.45±11.19	

NT-proBNP showed a significant negative correlation with LVEF (r=-0.263, p=0.021). Significant positive correlations were observed with left ventricular end-diastolic diameter (r=0.318, p=0.011), left atrial diameter (r=0.276, p=0.029), pulmonary artery systolic pressure (r=0.344, p=0.007), and NYHA functional class (r=0.401, p=0.003) (*Table IV*).

Table IV
Correlation between NT-proBNP and Echocardiographic Parameters in Patients with Heart Failure.

Variables	Correlation coefficient (r)	P value
Left ventricular ejection fraction (%)	-0.263	0.021
Left ventricular end-diastolic diameter (mm)	0.318	0.011
Left atrial diameter (mm)	0.276	0.029
Pulmonary artery systolic pressure (mmHg)	0.344	0.007
NYHA functional class	0.401	0.003

The majority of patients 63.33% had high NT-proBNP with reduced EF, while 15.00% patients had high NT-proBNP with preserved or mildly reduced EF. Low or moderate NT-proBNP with reduced EF was observed in 6.67% patients, and 15.00% patients had low or moderate NT-proBNP with preserved or mildly reduced EF (*Table V*).

Table V
Discordance between NT-proBNP Levels and Left Ventricular Ejection Fraction Categories (*n* = 60).

NT-proBNP and LVEF Profile	Frequency (n)	Percentage (%)
High NT-proBNP with reduced EF	38	63.33
High NT-proBNP with preserved/mildly reduced EF	9	15.00
Low/moderate NT-proBNP with reduced EF	4	6.67
Low/moderate NT-proBNP with preserved/mildly reduced EF	9	15.00

Factors associated with elevated NT-proBNP levels are presented Reduced EF (≤40%) was significantly associated with elevated NT-proBNP (OR 3.92, 95% CI 1.71–8.97, p=0.001). NYHA Class III–IV also showed a strong association (OR 4.36,

95% CI 1.98–9.62, p = 0.001). Atrial fibrillation was significantly associated as well (OR 2.58, 95% CI 1.01–6.58, p=0.047). Although age ≥60 years (OR 1.84, p=0.083), chronic kidney disease (OR 2.11, p=0.112), and diabetes mellitus (OR 1.67, p=0.129) showed higher odds, these were not statistically significant (*Table VI*).

Table VI
Factors Associated with Elevated NT-proBNP Levels in Heart Failure Patients.

Characteristics	OR	95% C.I.	P value
Age ≥60 years	1.84	0.92–3.66	0.083
Reduced EF (≤40%)	3.92	1.71–8.97	0.001
Chronic kidney disease	2.11	0.84–5.32	0.112
NYHA Class III–IV	4.36	1.98–9.62	0.001
Diabetes mellitus	1.67	0.86–3.23	0.129
Atrial fibrillation	2.58	1.01–6.58	0.047

DISCUSSION

Heart failure is a complex clinical syndrome in which considerable variability and discordance may exist between circulating N-terminal pro–B-type natriuretic peptide (NT-proBNP) levels and left ventricular ejection fraction (LVEF), reflecting differences in cardiac dysfunction severity and underlying pathophysiological mechanisms [14]. The present cross-sectional study evaluated the variability and discordance between NT-proBNP levels and left ventricular ejection fraction (LVEF) among patients with heart failure. The majority of patients belonged to the 53–63 years age group (50.00%), with a mean age of 57.88±11.90 years. Male patients constituted 63.33% whereas females represented 36.67% of the study population. Rural residents accounted for 78.33% compared to 21.67% urban residents. Regarding smoking status, 66.67% were current smokers, 13.33% were former smokers, and 20.00% had never smoked. Body mass index analysis showed that 50.00% had normal BMI (18.5–24.9 kg/m²), 30.00% were overweight (25–29.9 kg/m²), 13.33% were obese (>30 kg/m²), and 6.67% were underweight (<18.5 kg/m²). Similar demographic patterns have been reported in heart failure registries where increasing age and male predominance are consistently associated with higher disease burden [15,16]. Hypertension was present in 45.00% of patients, diabetes mellitus in 35.00%, ischemic heart disease in 30.00%, dyslipidemia in 26.67%, previous myocardial infarction in 23.33%, dilated cardiomyopathy in 20.00%, atrial fibrillation in 11.67%, and chronic kidney disease in 10.00%. Regarding symptom severity, 48.33% belonged to NYHA Class III, followed by Class II (30.00%) and Class IV (21.67%). The mean systolic blood pressure was 137.08±32.65 mmHg, while the mean heart rate was 96.42±14.18 beats/min. Comparable studies have consistently demonstrated hypertension, diabetes, ischemic heart disease, and atrial fibrillation as major contributors to worsening ventricular dysfunction and increased NT-proBNP concentrations [17]. Studies by Januzzi et al. also noted that renal dysfunction and atrial fibrillation independently elevate natriuretic peptide concentrations irrespective of systolic impairment, due to reduced peptide clearance and increased atrial wall stress [18]. NT-proBNP levels between 3000–5999 pg/mL were observed in the largest proportion of patients (46.67%), followed by ≥6000 pg/mL (23.33%), 1000–2999 pg/mL (23.33%), and <1000 pg/mL (6.67%), with a mean NT-proBNP level of 4559.50±801.65 pg/mL. Regarding ventricular systolic function, 70.00% of patients had reduced EF (≤40%), 20.00% had mildly reduced EF (41–49%), and only 10.00% had preserved EF (≥50%), with a mean LVEF of 34.45±11.19%. A study by Luers et al. demonstrated significantly higher NT-proBNP levels among patients with reduced systolic function compared to preserved EF, supporting the role of ventricular wall stress in peptide release [19]. There is a statistically significant negative correlation between NT-proBNP and left ventricular ejection fraction (r=−0.263, p=0.021), indicating that lower LVEF was associated with higher NT-proBNP levels. However, the correlation strength was relatively weak, suggesting variability between ventricular systolic performance and biomarker elevation. Furthermore, NT-proBNP showed positive correlations with left ventricular end-diastolic diameter (r=0.318, p=0.011), left atrial diameter (r=0.276, p=0.029), pulmonary artery systolic pressure (r=0.344, p=0.007), and NYHA functional class (r=0.401, p=0.003). Similar observations have been reported in prior investigations showing that NT-proBNP reflects overall hemodynamic burden, myocardial wall stress, and filling pressure rather than isolated systolic function alone [17,20]. Substantial discordance was demonstrated between NT-proBNP levels and LVEF categories. While the majority of patients (63.33%) had high NT-proBNP with reduced EF, 15.00% exhibited high NT-proBNP despite preserved or mildly reduced EF. Conversely, 6.67% had low/moderate NT-proBNP despite reduced EF, whereas 15.00% had low/moderate NT-proBNP with preserved or mildly reduced EF. Previous studies have similarly shown that patients with preserved EF may still experience elevated ventricular filling pressures and myocardial stress, resulting in elevated natriuretic peptides despite relatively preserved systolic function. Conversely, obesity, pharmacotherapy, or early disease stages may contribute to lower NT-proBNP levels despite reduced EF [21-23]. Reduced EF (≤40%) was significantly associated with elevated NT-proBNP levels (OR: 3.92, 95% CI: 1.71–8.97, p=0.001). Similarly, NYHA Class III–IV patients demonstrated significantly higher odds of elevated NT-proBNP (OR: 4.36, 95% CI: 1.98–9.62, p=0.001), and atrial fibrillation was also significantly associated (OR: 2.58, 95% CI: 1.01–6.58, p=0.047). Although age ≥60 years (OR: 1.84, 95% CI: 0.92–3.66, p=0.083), chronic kidney disease (OR: 2.11, 95% CI: 0.84–5.32, p=0.112), and diabetes mellitus (OR: 1.67, 95% CI: 0.86–3.23, p=0.129) showed elevated odds, these associations did not reach statistical significance. Similar findings were observed in previous studies, where reduced ventricular function, worsening NYHA class, and atrial arrhythmias were major determinants of increased NT-proBNP levels and disease severity [20,24,25].

LIMITATIONS

This study has several limitations. It was conducted in a single tertiary care center with a relatively small sample size of 60 patients, which may limit generalizability to broader populations. The cross-sectional design prevents assessment of temporal changes and causal relationships between NT-proBNP and LVEF. Selection bias may be present due to purposive sampling. Additionally, potential confounding factors such as medication use, renal function variability, and duration of heart failure were not fully controlled, which could influence biomarker levels and echocardiographic findings.

CONCLUSION

The present study demonstrated a measurable variability and partial discordance between NT-proBNP levels and left ventricular ejection fraction in patients with heart failure. Although a significant inverse relationship was observed between NT-proBNP and LVEF, the correlation remained weak, indicating that both parameters reflect different aspects of cardiac dysfunction. A considerable

proportion of patients showed discordant profiles, particularly those with preserved or mildly reduced ejection fraction despite markedly elevated NT-proBNP levels. Reduced LVEF and higher NYHA functional class were significant predictors of elevated NT-proBNP, highlighting their combined prognostic value. These findings support the complementary use of NT-proBNP and LVEF for more accurate clinical assessment, risk stratification, and management of heart failure patients.

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CONFLICT OF INTEREST
None declared

ETHICAL APPROVAL
The study was approved by the Institutional Ethics Committee.

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