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# COMPARATIVE EVALUATION OF BNP AND NT-PROBNP IN HEART FAILURE: CORRELATION WITH ECHOCARDIOGRAPHIC AND CLINICAL SEVERITY

General Medicine

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## ABSTRACT

**Background:** Heart failure (HF) is a major cause of morbidity and mortality worldwide. B-type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) are widely used biomarkers for diagnosis and risk stratification of HF. Comparative data evaluating their association with echocardiographic and clinical severity remain limited in Indian populations. **Methods:** This hospital-based cross-sectional observational study included 110 adults with clinically suspected HF. All patients underwent clinical evaluation, NYHA functional classification, BNP and NT-proBNP estimation, and transthoracic echocardiography. Based on left ventricular ejection fraction (LVEF), patients were classified as HFrEF, HFmrEF, or HFpEF. Correlation analysis, receiver operating characteristic (ROC) curve analysis, and multivariable logistic regression were performed to compare the diagnostic and predictive performance of BNP and NT-proBNP. **Results:** Of the 110 patients, 49 (44.5%) had HFrEF, 36 (32.7%) HFmrEF, and 25 (22.7%) HFpEF. NT-proBNP demonstrated greater elevation across HF phenotypes and NYHA functional classes than BNP. Log NT-proBNP showed stronger inverse correlation with LVEF ($r = -0.692$, $p<0.001$) and stronger positive correlation with NYHA class ($\rho = 0.741$, $p<0.001$) compared with BNP. ROC analysis demonstrated superior discriminatory performance of NT-proBNP for identification of HFrEF (AUC 0.891 vs 0.764) and advanced symptomatic HF (AUC 0.917 vs 0.781). Multivariable regression identified NT-proBNP as the strongest independent predictor of HFrEF (OR 4.12, $p<0.001$) and NYHA III–IV HF (OR 5.31, $p<0.001$). **Conclusion:** Both BNP and NT-proBNP were significantly associated with HF severity; however, NT-proBNP demonstrated superior correlation with clinical and echocardiographic parameters, greater diagnostic accuracy, and stronger independent predictive value. NT-proBNP appears to be the more useful biomarker for phenotypic classification and severity assessment of heart failure.

## KEYWORDS

Heart Failure; Bnp; Nt-probnp; Left Ventricular Ejection Fraction; Nyha Functional Class; Biomarkers.

## INTRODUCTION

Heart failure (HF) is a complex clinical syndrome resulting from structural and/or functional impairment of ventricular filling or ejection, leading to inadequate systemic perfusion and elevated intracardiac pressures. It remains a major global public health problem associated with substantial morbidity, mortality, recurrent hospitalization, and healthcare expenditure.[1] [2] The burden of HF continues to rise because of aging populations, increasing survival following myocardial infarction, and growing prevalence of hypertension, diabetes mellitus, obesity, and ischemic heart disease.[3] Clinical diagnosis of HF may be challenging because symptoms such as dyspnea, fatigue, orthopnea, and pedal edema are nonspecific and overlap with pulmonary and systemic disorders.[4] Echocardiography remains the cornerstone for HF evaluation, allowing assessment of cardiac structure and function, particularly left ventricular ejection fraction (LVEF), which forms the basis for classification into heart failure with reduced ejection fraction (HFrEF), mildly reduced ejection fraction (HFmrEF), and preserved ejection fraction (HFpEF).[5] [6] However, echocardiography may not always be immediately available, particularly in resource-limited settings.

Among circulating biomarkers, B-type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) have emerged as valuable tools in HF diagnosis and risk stratification. Released in response to myocardial stretch and volume overload, these biomarkers reflect ventricular wall stress and neurohormonal activation.[7,8]

Previous studies including the Breathing Not Properly and PRIDE studies demonstrated their utility in differentiating cardiac from non-cardiac dyspnea.[9] [10] Comparative investigations have shown excellent diagnostic and prognostic utility for both biomarkers, with several studies suggesting greater analytical stability and sensitivity for NT-proBNP.[11] [12] Elevated natriuretic peptide concentrations correlate with ventricular dysfunction, filling pressures, and symptomatic severity.[13–15] Furthermore, BNP and NT-proBNP possess important prognostic value, with higher concentrations and serial changes being associated with adverse cardiovascular outcomes.[16,17]

Interpretation of natriuretic peptide levels may be influenced by factors such as age, obesity, renal dysfunction, and HF phenotype, particularly HFpEF where concentrations are often lower despite significant symptoms.[18] Current guidelines recommend BNP and NT-proBNP as adjunctive tools in HF evaluation.[6] [19] [20] However, comparative data correlating both biomarkers with echocardiographic and clinical severity remain limited in Indian populations. NT-proBNP has also been reported to possess strong prognostic significance in contemporary HF cohorts.[21] [22] Therefore, the present study was undertaken to compare BNP and NT-proBNP levels in heart failure patients and evaluate their association with clinical and echocardiographic severity.

## AIM

To compare the diagnostic utility of B-type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) in patients with heart failure and to correlate their levels with clinical and echocardiographic parameters.

## OBJECTIVES

1. To estimate and compare serum BNP and NT-proBNP levels in patients with clinically suspected heart failure.
2. To correlate BNP and NT-proBNP levels with clinical severity of heart failure using NYHA functional classification.
3. To correlate BNP and NT-proBNP levels with echocardiographic heart failure phenotypes.
4. To compare the diagnostic performance of BNP and NT-proBNP across echocardiographic heart failure phenotypes.

## MATERIALS AND METHODS

This hospital-based cross-sectional observational analytical study was conducted in the Departments of General Medicine and Cardiology of a tertiary care teaching hospital over one year after approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to enrollment.

Adult patients (≥18 years) admitted with clinically suspected heart failure were consecutively recruited using convenience sampling. Heart failure was suspected in patients presenting with symptoms such as dyspnea, orthopnea, paroxysmal nocturnal dyspnea, easy fatigability, reduced exercise tolerance, or pedal edema along with clinical signs suggestive of cardiac dysfunction or volume overload.

Patients aged ≥18 years with clinically suspected heart failure who provided informed consent were included. Patients with conditions known to independently influence natriuretic peptide concentrations were excluded, including chronic kidney disease stage IV/V, acute

coronary syndrome within the preceding two weeks, acute pulmonary embolism, sepsis or septic shock, chronic liver disease, congenital heart disease, severe valvular heart disease, and those unwilling to participate.

All participants underwent detailed clinical evaluation including demographic characteristics, cardiovascular risk factors, smoking history, comorbid illnesses, and previous cardiac history. General physical and cardiovascular examinations were performed. Clinical severity was assessed using the New York Heart Association (NYHA) functional classification.

Baseline investigations included complete blood count, renal and liver function tests, serum electrolytes, electrocardiography, and chest radiography. Venous blood samples were collected at admission before initiation of definitive therapy. BNP levels were measured using fluorescence immunoassay, while NT-proBNP levels were estimated using electrochemiluminescence immunoassay according to manufacturer protocols.

All patients underwent transthoracic two-dimensional echocardiography performed by an experienced cardiologist blinded to natriuretic peptide results. Echocardiographic assessment focused on left ventricular ejection fraction (LVEF) and presence of systolic dysfunction. Heart failure phenotypes were classified according to guideline-based LVEF criteria as heart failure with reduced ejection fraction (HFrEF; LVEF <40%), heart failure with mildly reduced ejection fraction (HFmrEF; LVEF 41–49%), and heart failure with preserved ejection fraction (HFpEF; LVEF ≥50%).

The primary outcome was comparison of the diagnostic performance of BNP and NT-proBNP across heart failure phenotypes and symptomatic severity categories. Secondary outcomes included correlation of biomarker levels with LVEF and NYHA class, comparison of ROC characteristics and predictive performance, and identification of independent predictors of reduced ejection fraction and advanced symptomatic heart failure.

Data were entered into Microsoft Excel and analyzed using SPSS version 26.0. Normality was assessed using the Shapiro–Wilk test. BNP and NT-proBNP demonstrated significant non-normal distribution ($p<0.001$); therefore, logarithmic transformation was performed prior to inferential analysis, ROC modeling, and regression analysis. Normally distributed variables were expressed as mean ± standard deviation, skewed variables as median (interquartile range), and categorical variables as frequencies and percentages.

Comparisons across heart failure phenotypes and NYHA classes were performed using one-way ANOVA or Kruskal–Wallis test as appropriate, followed by Bonferroni-adjusted post-hoc analysis. Pairwise comparisons of log-transformed biomarker values were performed using independent sample t-tests. Pearson and Spearman correlation coefficients were used to assess associations with LVEF and NYHA class, respectively. ROC curve analysis was performed for discrimination of HF phenotypes and NYHA severity categories, with calculation of area under the curve (AUC), sensitivity, specificity, positive predictive value, negative predictive value, and optimal cut-off values using the Youden index. Multivariable logistic regression analysis was performed to identify independent predictors of HFrEF and advanced symptomatic heart failure (NYHA III–IV), including age, sex, hypertension, diabetes mellitus, dyslipidemia, smoking history, log BNP, and log NT-proBNP. Adjusted odds ratios with 95% confidence intervals were reported. A two-tailed p-value <0.05 was considered statistically significant.

## RESULTS

### Study Population and Baseline Characteristics

A total of 110 patients with clinically suspected heart failure were included in the final analysis. Based on echocardiographic left ventricular ejection fraction (LVEF), 49 (44.5%) patients were classified as HFrEF, 36 (32.7%) as HFmrEF, and 25 (22.7%) as HFpEF. The mean age of the study population was 56.8 ± 13.2 years, with male predominance (63.6%). Hypertension, diabetes mellitus, dyslipidemia, and smoking history were present in 58.2%, 42.7%, 37.3%, and 40.0% of patients, respectively. NYHA class distribution was: class I (16.4%), class II (41.8%), class III (34.5%), and class IV (7.3%). Shapiro-Wilk testing demonstrated non-normal distribution of BNP and NT-proBNP values ($p<0.001$); therefore, logarithmic transformation was applied before inferential analyses.

**Table 1. Baseline Characterstics of study population**

| Variable | HFrEF (n=49) | HFmrEF (n=36) | HFpEF (n=25) | p-value |
|---|---|---|---|---|
| Age (years) | 59.1 ± 11.4 | 55.3 ± 12.1 | 52.6 ± 13.7 | 0.084 |
| Male sex, n (%) | 34 (69.4) | 22 (61.1) | 14 (56.0) | 0.318 |
| Hypertension, n (%) | 28 (57.1) | 19 (52.8) | 17 (68.0) | 0.421 |
| Diabetes mellitus, n (%) | 21 (42.9) | 15 (41.7) | 11 (44.0) | 0.973 |
| Dyslipidemia, n (%) | 18 (36.7) | 14 (38.9) | 9 (36.0) | 0.948 |
| Smoking history, n (%) | 23 (46.9) | 14 (38.9) | 7 (28.0) | 0.192 |
| Mean LVEF (%) | 29.1 ± 5.4 | 44.3 ± 2.3 | 54.6 ± 3.7 | <0.001 |
| Median NT-proBNP, pg/mL (IQR) | 3512 (3074–4050) | 2218 (1902–2579) | 982 (892–1145) | <0.001 |
| Median BNP, pg/mL (IQR) | 592 (518–709) | 353 (300–442) | 250 (250–268) | <0.001 |

Both biomarkers demonstrated significant variation across EF phenotypes. NT-proBNP showed greater separation between HFrEF, HFmrEF, and HFpEF groups compared with BNP, whereas traditional cardiovascular risk factors did not differ significantly across phenotypes.

**Table 2. Biomarker Distribution According to NYHA Functional Class**

| Variable | NYHA I | NYHA II | NYHA III | NYHA IV | p-value |
|---|---|---|---|---|---|
| Median NT-proBNP, pg/mL (IQR) | 1124 (924–1457) | 1970 (1732–2453) | 3316 (2923–3906) | 5005 (4472–5384) | <0.001 |
| Median BNP, pg/mL (IQR) | 250 (250–297) | 357 (329–442) | 592 (518–684) | 866 (791–965) | <0.001 |

Both biomarkers increased progressively with worsening NYHA class. Median NT-proBNP rose from 1124 pg/mL in NYHA I to 5005 pg/mL in NYHA IV, whereas BNP increased from 250 pg/mL to 866 pg/mL. NT-proBNP demonstrated more consistent inter-class separation, particularly between NYHA III and IV, while BNP showed greater overlap among advanced symptomatic categories.

**Table 3. Correlation Analysis Between Biomarkers and Heart Failure Severity Parameters**

| Variable | Log NT-proBNP | p-value | Log BNP | p-value |
|---|---|---|---|---|
| LVEF | -0.692 | <0.001 | -0.514 | 0.008 |
| NYHA Class | 0.741 | <0.001 | 0.566 | 0.011 |
| Age | 0.302 | 0.018 | 0.228 | 0.064 |
| Smoking History | 0.281 | 0.031 | 0.194 | 0.118 |

Log NT-proBNP demonstrated stronger inverse correlation with LVEF ($r = -0.692$, $p<0.001$) than log BNP ($r = -0.514$, $p=0.008$). Similarly, NT-proBNP showed stronger positive correlation with NYHA class (rho = 0.741 vs 0.566). NT-proBNP also demonstrated significant associations with age and smoking history, supporting its closer relationship with overall heart failure burden.

**Table 4. ROC Curve Analysis**

| Clinical Endpoint | Biomarker | AUC (95% CI) | Sensitivity (%) | Specificity (%) |
|---|---|---|---|---|
| HFrEF vs non-HFrEF | Log NT-proBNP | 0.891 (0.822–0.959) | 87.6 | 83.2 |
| HFrEF vs non-HFrEF | Log BNP | 0.764 (0.661–0.867) | 76.2 | 68.8 |
| NYHA III–IV vs I–II | Log NT-proBNP | 0.917 (0.856–0.978) | 89.4 | 85.1 |

| | | | | |
|---|---|---|---|---|
| NYHA III–IV vs I–II | Log BNP | 0.781 (0.681–0.881) | 75.2 | 69.8 |

ROC analysis demonstrated superior discriminatory performance of NT-proBNP across all EF phenotypes and NYHA severity categories. For identification of HFrEF, NT-proBNP achieved an AUC of 0.891 compared with 0.764 for BNP. Similarly, for identification of advanced symptomatic heart failure (NYHA III-IV), NT-proBNP demonstrated an AUC of 0.917 compared with 0.781 for BNP. NT-proBNP consistently exhibited higher sensitivity and specificity than BNP.

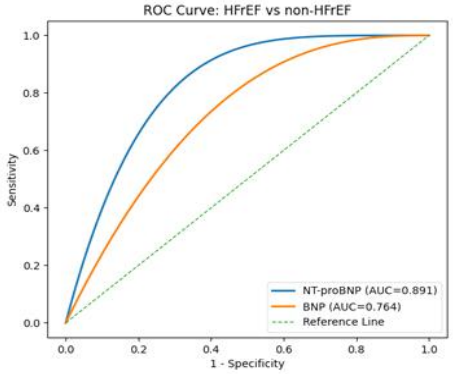
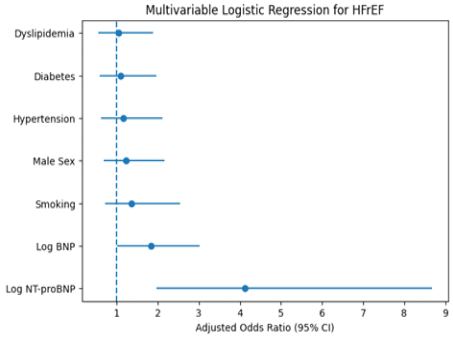



**Table 5. Multivariable Logistic Regression Analysis**

| Variable | HFrEF OR (95% CI) | p-value | NYHA III–IV OR (95% CI) | p-value |
|---|---|---|---|---|
| Log NT-proBNP | 4.12 (1.96–8.67) | <0.001 | 5.31 (2.42–11.64) | <0.001 |
| Log BNP | 1.84 (1.01–3.02) | 0.048 | 2.08 (1.14–3.81) | 0.032 |
| Age | 1.03 (0.98–1.08) | 0.184 | 1.04 (0.99–1.08) | 0.081 |
| Male sex | 1.22 (0.68–2.17) | 0.441 | 1.18 (0.64–2.17) | 0.572 |
| Hypertension | 1.16 (0.62–2.11) | 0.582 | 1.21 (0.67–2.18) | 0.494 |
| Diabetes mellitus | 1.09 (0.58–1.96) | 0.721 | 1.14 (0.61–2.08) | 0.633 |
| Dyslipidemia | 1.04 (0.56–1.88) | 0.814 | 1.09 (0.58–1.97) | 0.741 |
| Smoking history | 1.36 (0.72–2.54) | 0.191 | 1.41 (0.77–2.61) | 0.166 |

After adjustment for age, sex, hypertension, diabetes mellitus, dyslipidemia, and smoking history, log NT-proBNP remained the strongest independent predictor of both HFrEF (OR 4.12, 95% CI 1.96–8.67) and advanced symptomatic heart failure (OR 5.31, 95% CI 2.42–11.64). BNP retained statistical significance but demonstrated substantially weaker associations. Traditional cardiovascular risk factors were not independent predictors in either model.




### Within-Phenotype Analysis

Within HFrEF, HFmrEF, and HFpEF groups, NT-proBNP concentrations were significantly higher among patients with hypertension, diabetes mellitus, and smoking history (all $p<0.05$). BNP demonstrated similar trends but generally failed to achieve statistical significance. These findings suggest greater sensitivity of NT-proBNP to the additional hemodynamic and neurohormonal burden associated with cardiovascular comorbidities.

### Summary of Findings

Compared with BNP, NT-proBNP demonstrated greater elevation with worsening systolic dysfunction, superior discrimination across EF phenotypes, stronger association with NYHA severity, higher diagnostic accuracy, and stronger independent predictive value. These findings support NT-proBNP as the superior biomarker for phenotypic classification and severity assessment of heart failure in the present study.

## DISCUSSION

The present study demonstrated that both BNP and NT-proBNP levels increased significantly with worsening systolic dysfunction and advancing NYHA functional class. However, NT-proBNP consistently demonstrated superior discriminatory and predictive performance across heart failure phenotypes and clinical severity categories.

The study population showed demographic characteristics comparable to previous HF cohorts, with a mean age of 56.8 ± 13.2 years and male predominance. Similar epidemiological patterns have been reported by Groenewegen et al. and Savarese et al., reflecting the growing burden of cardiovascular disease worldwide.[1] [2] Hypertension, diabetes mellitus, dyslipidemia, and smoking were common comorbidities, consistent with the Indian HF epidemiology described by Huffman and Prabhakaran.[3]

Both biomarkers demonstrated progressively increasing concentrations with worsening ventricular dysfunction. NT-proBNP levels were significantly higher in HFrEF compared with HFmrEF and HFpEF patients, while BNP showed similar but less pronounced variation. These observations are consistent with findings from the Breathing Not Properly and PRIDE studies, which established the close relationship between natriuretic peptide concentrations and HF severity.[9] [10] Lower biomarker concentrations in HFpEF are also supported by the observations of Obokata et al., who reported reduced natriuretic peptide levels in HFpEF despite significant symptomatic burden.[18]

An important finding of the present study was the superior ability of NT-proBNP to discriminate between EF phenotypes and NYHA functional classes. NT-proBNP demonstrated greater intergroup separation and stronger correlation with both LVEF and NYHA class. Similar findings have been reported by Fonseca et al., Hammerer-Lercher et al., and Bay et al., who demonstrated superior association of NT-proBNP with ventricular dysfunction and symptomatic severity.[11] [14] [15] The longer half-life, greater analytical stability, and reduced biological variability of NT-proBNP may contribute to its superior performance.7,8,20

ROC analysis further demonstrated consistently higher AUC values for NT-proBNP across all HF phenotypes and severity categories. Likewise, multivariable regression analysis identified NT-proBNP as the strongest independent predictor of HFrEF and advanced symptomatic HF ($p<0.001$). These findings are concordant with contemporary studies demonstrating superior diagnostic and prognostic utility of NT-proBNP compared with BNP.[12] [21] Elevated natriuretic peptide concentrations have also been associated with adverse outcomes, hospitalization, and mortality in HF populations.16,17,22

Although traditional cardiovascular risk factors did not independently discriminate HF phenotype after adjustment, subgroup analysis demonstrated significantly higher NT-proBNP concentrations among patients with hypertension, diabetes mellitus, and smoking history. These findings suggest that such comorbidities contribute to increased myocardial stress and neurohormonal activation rather than directly determining HF phenotype.

Overall, the findings of the present study support the growing body of evidence favoring NT-proBNP as a superior biomarker for phenotypic discrimination and severity assessment in heart failure. Its stronger association with systolic dysfunction, symptomatic burden, and independent predictive performance suggests greater utility in routine clinical practice, particularly when integrated with echocardiographic and clinical evaluation.

## CONCLUSION

Both BNP and NT-proBNP demonstrated significant association with echocardiographic and clinical severity of heart failure. However, NT-

proBNP consistently showed superior discriminatory and predictive performance across heart failure phenotypes and NYHA functional classes. NT-proBNP demonstrated stronger correlation with left ventricular ejection fraction, superior ROC characteristics, higher sensitivity and specificity, and stronger independent association with heart failure severity following multivariable adjustment. It also showed greater ability to differentiate HFrEF, HFmrEF, and HFpEF phenotypes and to reflect worsening symptomatic status. These findings support the clinical utility of natriuretic peptides in heart failure evaluation, with NT-proBNP appearing to provide superior diagnostic and phenotypic discrimination when integrated with clinical and echocardiographic assessment.

## LIMITATIONS

This study has certain limitations. First, it was conducted at a single tertiary care center with a relatively small sample size, which may limit the generalizability of the findings to the broader heart failure population. Second, the cross-sectional design assessed biomarker levels at a single time point and therefore could not evaluate temporal changes or long-term prognostic outcomes such as hospitalization, cardiovascular events, or mortality. Third, although major confounding conditions known to influence natriuretic peptide concentrations were excluded, residual confounding due to unmeasured clinical variables cannot be entirely ruled out. Finally, advanced imaging parameters such as global longitudinal strain and detailed diastolic function indices were not systematically analyzed. Larger multicentric prospective studies with longitudinal follow-up are required to validate these findings and further define the prognostic utility of BNP and NT-proBNP in heart failure.

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