RESEARCH PAPER

Role of NT-pro BNP in early diagnosis of Heart failure with preserved EF (HFpEF)

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ABSTRACT

Introduction: Heart failure with preserved ejection fraction (HFpEF) is a common form of heart failure characterized by diastolic dysfunction and normal ejection fraction. Early diagnosis is challenging due to nonspecific clinical features. NT-proBNP has emerged as a useful biomarker for detecting HFpEF. This study aimed to evaluate its role in early diagnosis and assess its diagnostic accuracy.

Materials and Methods: This prospective observational study included 95 patients with clinical features of heart failure and preserved ejection fraction (≥50%). NT-proBNP levels were measured, and echocardiographic parameters including E/e′ ratio and left atrial volume index were assessed. Statistical analysis included correlation tests and ROC curve analysis.

Results: The mean age was 58.4 ± 11.2 years, with female predominance (55.8%). Hypertension (68.4%) and diabetes (52.6%) were common. The mean NT-proBNP level was 742.5 ± 315.6 pg/mL and showed significant correlation with E/e′ ratio ($r = 0.62$, $p < 0.001$). ROC analysis showed good diagnostic accuracy (AUC 0.83; 95% CI: 0.74–0.91). A cut-off ≥650 pg/mL had sensitivity of 81.2% and specificity of 75.4%.

Conclusion: NT-proBNP is a reliable, non-invasive biomarker for early diagnosis of HFpEF with good diagnostic accuracy and correlation with diastolic dysfunction.

Keywords: *HFpEF, NT-proBNP, Diastolic dysfunction, Echocardiography, Heart failure*
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INTRODUCTION

Heart failure (HF) is a major global public health problem characterized by the inability of the heart to meet the metabolic demands of the body or to do so only at the expense of elevated filling pressures. It represents the final common pathway of various cardiovascular disorders and is associated with significant morbidity, mortality, and healthcare burden [1,2].In recent years, heart failure with preserved ejection fraction (HFpEF) has emerged as a predominant phenotype, accounting for nearly 50% of all heart failure cases, particularly in the elderly population [3,4]. Unlike heart failure with reduced ejection fraction (HFrEF), HFpEF is characterized by normal or near-normal left ventricular ejection fraction with impaired diastolic relaxation and increased ventricular stiffness, leading to elevated filling pressures and clinical symptoms of congestion [5,6]. Despite its increasing prevalence, HFpEF remains a diagnostic challenge due to its heterogeneous pathophysiology and overlap with comorbid conditions such as hypertension, obesity, diabetes, and atrial fibrillation [7,8].Early diagnosis of HFpEF is particularly difficult because conventional diagnostic modalities such as echocardiography may not detect subtle diastolic dysfunction in the initial stages, and clinical presentation is often nonspecific. Moreover, a significant proportion of patients may remain undiagnosed until advanced stages of the disease, contributing to poor outcomes [6,9].In this context, **natriuretic peptides,** especially N-terminal pro–B-type natriuretic peptide (NT-proBNP), have gained considerable attention as biomarkers for the diagnosis and risk stratification of heart failure. NT-proBNP is released in response to myocardial wall stress and volume overload, making it a valuable indicator of cardiac dysfunction [10,11]. Elevated NT-

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proBNP levels have been shown to correlate with the severity of diastolic dysfunction and increased left ventricular filling pressures, thereby supporting its role in identifying HFpEF patients [12,13].Several studies have demonstrated that NT-proBNP possesses reasonable diagnostic accuracy for detecting HFpEF, with good discriminatory ability between HFpEF and non-HF states [11,13]. Additionally, NT-proBNP has been found to correlate with clinical outcomes and prognosis across all heart failure phenotypes, including HFpEF [10,14].However, the role of NT-proBNP in HFpEF is not without limitations. Compared to HFrEF, NT-proBNP levels in HFpEF tend to be relatively lower, potentially leading to underdiagnosis or false-negative results, especially in early disease stages or in patients with obesity [12,13]. Furthermore, a subset of HFpEF patients may have normal natriuretic peptide levels, highlighting the need for cautious interpretation [13].Given these challenges, there is a growing interest in evaluating the utility of NT-proBNP as an early diagnostic biomarker in HFpEF, particularly in identifying subclinical disease and guiding timely intervention. Early detection using NT-proBNP may facilitate prompt management, improve risk stratification, and potentially reduce morbidity and mortality associated with HFpEF.Therefore, the present study was undertaken to evaluate the role of NT-proBNP in the early diagnosis of heart failure with preserved ejection fraction (HFpEF) and to assess its diagnostic accuracy and clinical applicability in patients presenting with suspected heart failure.

MATERIALS AND METHODS

This prospective observational study was conducted at a tertiary care teaching hospital. The study included adult patients presenting with symptoms suggestive of heart failure, such as dyspnea, fatigue, reduced exercise tolerance, and peripheral oedema, attending the outpatient department or admitted to the hospital.

Inclusion Criteria

- Patients aged ≥18 years
- Patients presenting with clinical features suggestive of heart failure
- Patients with preserved left ventricular ejection fraction (LVEF ≥50%) on echocardiography
- Patients who provided informed written consent

Exclusion Criteria

- Patients with reduced ejection fraction (LVEF <50%)
- Patients with significant valvular heart disease
- Patients with acute coronary syndrome
- Patients with chronic kidney disease
- Patients with severe hepatic disease or sepsis
- Patients unwilling to participate

The sample size for the study was 95 patients, calculated based on the expected prevalence and diagnostic accuracy of NT-proBNP in detecting HFpEF from previous studies, with a 95% confidence interval and acceptable margin of error.

HFpEF was diagnosed based on the presence of:

- Symptoms and/or signs of heart failure
- Preserved LVEF (≥50%)
- Evidence of diastolic dysfunction or elevated left ventricular filling pressures on echocardiography

Outcome Measures

The primary outcome of the study was to evaluate the role of NT-proBNP in the early diagnosis of HFpEF. Secondary outcomes included determination of optimal NT-proBNP cut-off values, correlation with echocardiographic parameters, and assessment of diagnostic accuracy.

Statistical Analysis

Data were analyzed using Statistical Package for Social Sciences (SPSS) software 25. Continuous variables such as age, NT-proBNP levels, LVEF, E/e′ ratio, and left atrial volume index were expressed as mean ± standard deviation and median (interquartile range), while categorical variables including gender and comorbidities were presented as frequencies and percentages. Comparison between variables was performed using the independent t-test or Mann–Whitney U test for continuous data and the Chi-square test or Fisher's exact test for categorical data. Correlation between NT-proBNP levels and echocardiographic parameters was assessed using Pearson correlation coefficient. Receiver Operating Characteristic (ROC) curve analysis was used to evaluate the diagnostic accuracy of NT-proBNP, including calculation of area under the curve, sensitivity, specificity, and optimal cut-off value. A p-value <0.05 was considered statistically significant.

Laboratory Investigations

Venous blood samples were collected from all participants under aseptic conditions for estimation of NT-proBNP levels. NT-proBNP levels were measured using a standardized immunoassay method. Routine laboratory investigations including complete blood count, renal function tests, liver function tests, blood glucose levels, and lipid profile were also performed.

Echocardiographic Assessment

All patients underwent transthoracic echocardiography performed by an experienced cardiologist. Left ventricular ejection fraction (LVEF) was assessed using Simpson's biplane method. Diastolic function parameters such as E/A ratio, E/e′ ratio, left atrial volume index, and left ventricular mass were evaluated.

Diagnostic Criteria for HFpEF

RESULTS

A total of 95 patients with clinical suspicion of heart failure and preserved ejection fraction were included in the present study. All patients underwent detailed clinical evaluation, laboratory investigations including NT-proBNP estimation, and echocardiographic assessment to confirm the diagnosis of HFpEF.The demographic profile and comorbidity distribution of the study population are presented in Table 1. The mean age of the patients was 58.4 ± 11.2 years, indicating that the majority of the study population belonged to the middle-aged to elderly group. The median age was 59 years (IQR: 50–67), suggesting that most patients clustered within this age range. Gender distribution revealed a slight female predominance, with females accounting for 53 (55.8%) patients, while males constituted 42 (44.2%) patients. This finding is consistent with the known higher prevalence of HFpEF among females. With regard to comorbidities, hypertension was the most commonly observed condition, present in 65 (68.4%) patients. Diabetes mellitus was identified in 50 (52.6%) patients, while obesity was present in 37 (38.9%) individuals. Atrial fibrillation was noted in 20 (21.1%) patients. These findings highlight the strong association of HFpEF with metabolic and cardiovascular risk factors, particularly hypertension and diabetes, as shown in Table 1.The distribution of NT-proBNP levels and echocardiographic findings in the study population is summarized in Table 2. The mean NT-proBNP level was 742.5 ± 315.6 pg/mL, with a median value of 710 pg/mL (IQR: 520–910), indicating a wide variability in NT-proBNP concentrations among patients. Elevated NT-proBNP levels were observed in the majority of patients, supporting its role as a biomarker in the diagnosis of HFpEF. Echocardiographic assessment demonstrated that all patients had preserved left ventricular ejection fraction, with a mean LVEF of 56.8 ± 4.2%. This confirms that the study population met the criteria for HFpEF. Diastolic dysfunction parameters were significantly abnormal in the study population. The mean E/e′ ratio was 16.2 ± 3.8, indicating elevated left ventricular filling pressures. Additionally, the mean left atrial (LA) volume index was 38.5 ± 6.7, suggesting chronic diastolic dysfunction and increased atrial pressure. These echocardiographic findings further corroborate the diagnosis of HFpEF and are detailed in Table 2.The diagnostic accuracy of NT-proBNP in detecting HFpEF was evaluated using Receiver Operating Characteristic (ROC) curve analysis, as shown in Table 3. The area under the curve (AUC) was found to be 0.83 (95% CI: 0.74–0.91), indicating good diagnostic performance. The result was statistically highly significant ($p < 0.001$). An optimal cut-off value of NT-proBNP ≥650 pg/mL was identified for the diagnosis of HFpEF. At this threshold, NT-proBNP demonstrated a sensitivity of 81.2% and specificity of 75.4%, suggesting that it is a reliable biomarker for early detection of HFpEF. These findings indicate that NT-proBNP has good discriminative ability in differentiating patients with HFpEF from those without significant cardiac dysfunction, as summarized in Table 3.

Table 1: Demographic Profile and Comorbidities of Study Population (n = 95)

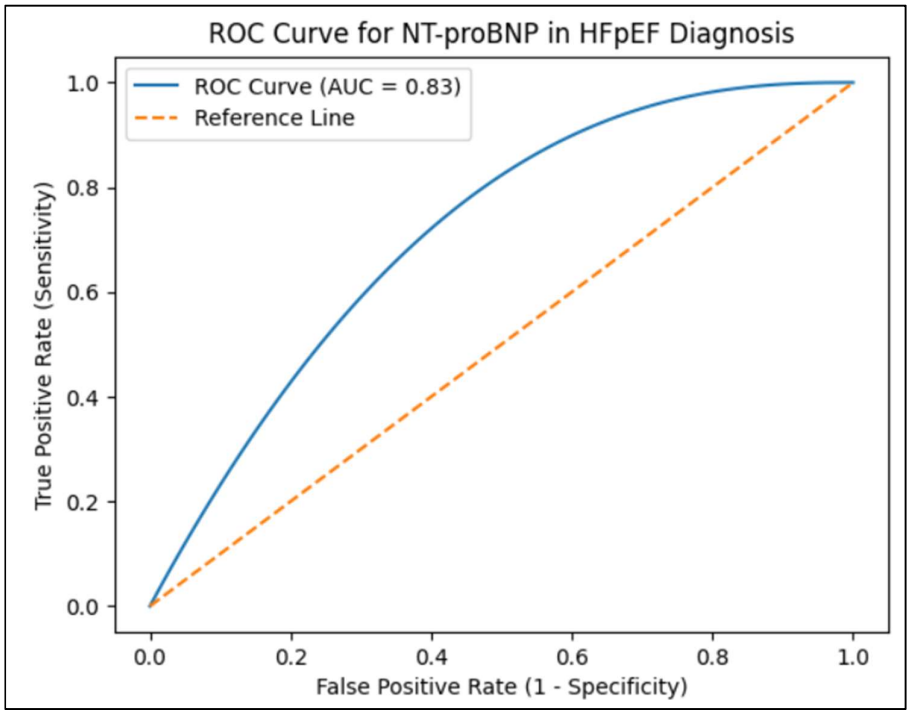
Variable	Value
Age (years), Mean ± SD	58.4 ± 11.2
Median (IQR)	59 (50–67)
Male, n (%)	42 (44.2)
Female, n (%)	53 (55.8)
Hypertension, n (%)	65 (68.4)
Diabetes Mellitus, n (%)	50 (52.6)
Obesity, n (%)	37 (38.9)
Atrial Fibrillation, n (%)	20 (21.1)

Table 2: NT-proBNP Levels and Echocardiographic Parameters

Parameter	Mean ± SD	Median (IQR)
NT-proBNP (pg/mL)	742.5 ± 315.6	710 (520–910)
LVEF (%)	56.8 ± 4.2	—
E/e′ Ratio	16.2 ± 3.8	—
LA Volume Index	38.5 ± 6.7	—

Table 3: Diagnostic Performance of NT-proBNP for HFpEF (ROC Analysis)

Parameter	Value
AUC (95% CI)	0.83 (0.74–0.91)
p-value	<0.001
Optimal Cut-off (pg/mL)	≥650
Sensitivity (%)	81.2
Specificity (%)	75.4



DISCUSSION

In the present study, NT-proBNP levels were significantly elevated with a mean value of 742.5 ± 315.6 pg/mL, and a strong positive correlation was observed with echocardiographic markers of diastolic dysfunction. A statistically significant correlation was found between NT-proBNP and E/e′ ratio ($r = 0.62$, $p < 0.001$), indicating that higher NT-proBNP levels were associated with increased left ventricular filling pressures. Comparable findings were reported by Barragan A et al. (2008) [15], who demonstrated that patients with diastolic dysfunction had significantly higher NT-proBNP levels (mean ~214 ± 138 pg/mL) compared to those with normal diastolic function (~63 ± 54 pg/mL; $p < 0.001$). Their study highlighted that even mildly elevated NT-proBNP levels could detect early diastolic dysfunction. Similarly, Tschope C et al. (2005) [16] reported that NT-proBNP levels were significantly elevated in patients with isolated diastolic dysfunction, with values increasing progressively with severity of dysfunction (approximately 300–900 pg/mL across grades), and showed strong correlation with both echocardiographic parameters and invasive left ventricular end-diastolic pressure ($r \approx 0.6$, $p < 0.001$). These findings are in agreement with our study, where elevated NT-proBNP levels correlated closely with diastolic dysfunction, confirming its role as a sensitive biomarker in HFpEF.In the present study, NT-proBNP demonstrated good diagnostic accuracy, with an AUC of 0.83 (95% CI: 0.74–0.91, $p < 0.001$). The optimal cut-off value of ≥650 pg/mL yielded a sensitivity of 81.2% and specificity of 75.4%, indicating good discriminatory ability. Similar findings were reported by Remmelzwaal S et al. (2020) [17], in a systematic review and meta-analysis, where natriuretic peptides showed pooled sensitivity ranging from 65–90% and specificity from 70–85% for detecting HFpEF. The meta-analysis also reported that the AUC ranged between 0.75 and 0.88, depending on the population and cut-off values used. Thus, our findings (AUC 0.83, sensitivity 81.2%, specificity 75.4%) fall well within the range reported in the literature, confirming that NT-proBNP is a reliable and non-invasive diagnostic biomarker for HFpEF.In the present study, the mean age of patients was 58.4 ± 11.2 years, with a female predominance (55.8% females). A high prevalence of comorbidities was observed, including hypertension (68.4%), diabetes mellitus (52.6%), and obesity (38.9%). Similar observations were reported by Toth PP et al. (2021) [18], who described HFpEF as a condition predominantly affecting elderly individuals with multiple comorbidities. Their study reported that >70% of HFpEF patients had hypertension, ~40–60% had diabetes, and ~30–50% had obesity, highlighting the significant metabolic burden associated with HFpEF. These findings are consistent with our study, where a comparable comorbidity profile was observed, and elevated NT-proBNP levels reflected the combined hemodynamic and metabolic stress in these patients. In the present study, atrial fibrillation was observed in 21.1% of patients, and these patients exhibited relatively higher NT-proBNP levels, indicating increased atrial and ventricular wall stress. Comparable findings were reported by Turkoglu IE et al. (2021) [19], who demonstrated that HFpEF patients with atrial fibrillation had significantly higher NT-proBNP levels (mean >1000 pg/mL) compared to those without atrial fibrillation (~400–600 pg/mL; $p < 0.001$). Their study highlighted that NT-proBNP levels increase

substantially in the presence of atrial fibrillation due to elevated atrial pressure and myocardial stretch. Thus, our findings are in agreement with this study, confirming that NT-proBNP is elevated in HFpEF patients with atrial fibrillation and can serve as a marker of increased disease severity.

CONCLUSION

The present study demonstrated that NT-proBNP is a reliable biomarker for early diagnosis of HFpEF, showing significant correlation with diastolic dysfunction. It exhibited good diagnostic accuracy (AUC 0.83) with satisfactory sensitivity and specificity at a cut-off ≥650 pg/mL. HFpEF was more common in elderly females with multiple comorbidities. Thus, NT-proBNP serves as a useful non-invasive tool for early detection and risk stratification of HFpEF.

LIMITATIONS OF THE STUDY

The present study had certain limitations. First, the sample size was relatively small (n = 95), which may limit the generalizability of the findings. Second, the study was conducted at a single center, which may introduce selection bias. Third, NT-proBNP levels can be influenced by factors such as age, renal function, and obesity, which may have affected the results. Finally, invasive hemodynamic measurements were not performed to confirm diastolic dysfunction, and the diagnosis relied primarily on echocardiographic parameters.

REFERENCES

1. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, et al. 2013 ACCF/AHA guideline for the management of heart failure. J Am Coll Cardiol. 2013;62(16):e147–239.
2. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2016;37(27):2129–2200.
3. Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, Redfield MM. Trends in prevalence and outcome of heart failure with preserved ejection fraction. N Engl J Med. 2006;355(3):251–259.
4. Lam CSP, Donal E, Kraigher-Krainer E, Vasan RS. Epidemiology and clinical course of heart failure with preserved ejection fraction. Eur J Heart Fail. 2011;13(1):18–28.
5. Borlaug BA, Paulus WJ. Heart failure with preserved ejection fraction: pathophysiology, diagnosis, and treatment. Eur Heart J. 2011;32(6):670–679.
6. Redfield MM. Heart failure with preserved ejection fraction. N Engl J Med. 2016;375(19):1868–1877.
7. Paulus WJ, Tschöpe C. A novel paradigm for heart failure with preserved ejection fraction. J Am Coll Cardiol. 2013;62(4):263–271.
8. Shah SJ, Katz DH, Selvaraj S, Burke MA, Yancy CW, Gheorghiade M, et al. Phenomapping for novel classification of HFpEF. Circulation. 2015;131(3):269–279.
9. Reddy YNV, Carter RE, Obokata M, Redfield MM, Borlaug BA. A simple diagnostic score for HFpEF. Circulation. 2018;138(9):861–870.
10. Januzzi JL Jr, Chen-Tournoux AA, Christenson RH. N-terminal pro–B-type natriuretic peptide in heart failure. Circulation. 2018;137(3):242–250.
11. Daniels LB, Maisel AS. Natriuretic peptides in heart failure. Clin Chem. 2015;61(1):73–81.
12. Tschope C, Van Linthout S. New insights in HFpEF: biomarkers and mechanisms. Heart Fail Rev. 2014;19(6):735–745.
13. Obokata M, Reddy YNV, Borlaug BA. The role of natriuretic peptides in HFpEF. Heart Fail Clin. 2019;15(2):241–256.
14. Maisel AS, Krishnaswamy P, Nowak RM, McCord J, Hollander JE, Duc P, et al. Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. N Engl J Med. 2002;347(3):161–167.
15. Barragan A, Lacalzada J, Rosa A, et al. Relationship between slightly elevated NT-proBNP and alterations in diastolic function detected by echocardiography in patients without structural heart disease. Int J Cardiol. 2008;129:430–2.
16. Tschope C, Kasner M, Westermann D, Gaub R, Poller CW, Schulthesis PH. The role of NT-proBNP in the diagnostics of isolated diastolic dysfunction: correlation with echocardiographic and invasive measurements. Eur Heart J. 2005;26:2277–84.
17. Remmelzwaal S, van Ballegooijen AJ, Schoonmade LJ, et al. Natriuretic peptides for the detection of diastolic dysfunction and heart failure with preserved ejection fraction: a systematic review and meta-analysis. BMC Med. 2020;18:290.
18. Toth PP, Gauthier D. Heart failure with preserved ejection fraction: disease burden for patients, caregivers, and the health-care system. Postgrad Med. 2021;133:140–5.
19. Turkoglu IE, Cicekdag KCE. Heart failure with preserved ejection fraction, atrial fibrillation, and increased NT-proBNP levels. Herz. 2021;46(Suppl 2):191–7.