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Original Research Article

# Correlation of NT Pro-BNP with Echocardiography as Index of Left Ventricular Diastolic Dysfunction in Elderly Patients: A Hospital Based Analytical Study

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**Abstract:**

**Background:** The main objective of the present study was to assess the significance of NT pro-BNP in identification of diastolic heart failure and its association with echocardiography.

**Methods:** Analytical and observational study conducted in a hospital setting on 65 individuals with diastolic heart failure who met the clinical inclusion criteria. The patients included in the study had an average age of 64.5 years, with a higher distribution of females. The patients received clinical assessment and echocardiography testing. Quantification of NT pro-BNP was performed using an automated analyzer. Patients were categorized into different levels of diastolic dysfunction based on echocardiography testing. The relevance of levels of NT pro-BNP and its link with the grade of diastolic heart failure was determined by statistical analyze.

**Results:** Statistically substantial elevations in serum NT pro-BNP levels were seen in individuals with diastolic heart failure, and these increases were directly correlated with the degree of diastolic dysfunction. The average concentration of NT pro-BNP rose from 361.079±140.649 pg/ml to 3570.001±436.989 pg/ml as the degree of diastolic dysfunction increased.

**Conclusion:** Serum NT-proBNP levels provide reliable diagnostic accuracy to detect diastolic heart failure and it correlates well with increasing severity of diastolic dysfunction as assessed by well-established modality of echocardiography.

**Keywords:** Diastolic heart failure; Diastolic dysfunction; Echocardiography; NT-proBNP.



## Introduction

A complex clinical syndrome, heart failure (HF) is caused by structural and functional impairment of ventricular filling or ejection of blood. This syndrome gives rise to a constellation of clinical symptoms and signs that result in a diminished quality of life and a reduced life expectancy. [1] Diastolic heart failure (DHF) is a clinical condition defined by the presence of heart failure symptoms and signs, along with a preserved ejection fraction (EF) and aberrant diastolic activity. [2]

The elderly population frequently develops left ventricular (LV) dysfunction as a consequence of multiple co-morbidities.[3] Diagnosing cardiac disorders in the elderly can be challenging due to distinct clinical manifestations that may significantly differ from those observed in younger patients with similar disorders. [4]This study looked at a substance called N-Terminal pro Brain Natriuretic Peptide (NT pro-BNP), which is a product of a hormone called Brain Natriuretic Peptide (BNP). [5] Diastolic dysfunction is commonly ascribed to heart failure occurring with normal or somewhat altered systolic function. Indeed, over 33% of patients who display symptoms and indications of congestive heart failure (CHF) demonstrate isolated diastolic dysfunction, a condition linked to a negative prognosis. [2] Clinical examination only is insufficient to accurately differentiate between systolic and diastolic heart failure. [6] Diastolic heart failure diagnosis is mostly established via the process of exclusion.

Given its capacity to detect or exclude abnormalities in the structure and function of the heart, echocardiography is a fundamental tool in the diagnostic assessment of patients experiencing difficulty breathing. [7] Early diastolic myocardial velocities (e') obtained from tissue Doppler

imaging, quantified at the mitral annulus; enable the evaluation of myocardial relaxation. The E/e' ratio is directly related to the left ventricular filling pressure. Echocardiographic evidence of left ventricular diastolic dysfunction may include a decreased stroke velocity (e' average >9 cm/s) or an elevated E/e' ratio (>15), or a combination of both. The existence of a minimum of two anomalous measures and/or atrial fibrillation enhances the probability of the accurate diagnosis. [8] B-type peptide (BNP) and its amino-terminal fragment (NT pro-BNP) are reliable indicators of heart failure (HF) in dyspneic patients. [8] Previous studies have demonstrated the accuracy of BNP in correlation with echocardiographic indices of diastolic function and right ventricular (RV) systolic function. However, the associations between NT pro-BNP and echocardiographic findings remain unclear. [9] Moreover, the extent to which measuring natriuretic peptides contributes to long-term prognostication, beyond the information obtained from echocardiography, is not well-established. This investigation was conducted to enhance pre-existing understanding of the integrated value of NT pro-BNP testing concerning the insights gained from echocardiography in dyspneic patients presenting to the emergency department. [5] Present study was conducted as a cross sectional study to assess the hypothesis that implementing a diagnostic strategy guided by the prompt measurement of NT pro-BNP levels would enhance the evaluation and management of elderly patients presenting with acute dyspnea to the emergency department (ED).

**Aims and Objectives:** The primary objective of the study was to test and establish a relationship between the levels of NT pro-BNP and all four grades (grade I to grade IV) of diastolic dysfunction as investigated by echocardiography. The secondary objective was to correlate NT pro-BNP with echo findings like EF, TAPSE, e', E/e', E/A.

## Material and Methods

The study was done as a cross sectional analytical study at the Department of Cardiology of MDM Hospital attached to Dr. S. N. Medical College, located in Jodhpur, Rajasthan, India.

**Inclusion And Exclusion Criteria:** Elderly patients (above 60 years of age) who presented with shortness of breath as primary symptom and/or admitted in department of cardiology with signs and symptoms suggestive of left ventricular diastolic dysfunction but a preserved ejection fraction (EF ≥50%), were recruited for the research after obtaining clearance from the institutional ethics committee and informed written consent from the patients. Under 60-year-old patients, or those with a history of acute myocardial infarction (lasting less than 7 days), unstable angina, serum creatinine levels above 2mg/dl, liver cirrhosis, haemoglobin levels below 10 g/dL, chronic obstructive pulmonary disease (COPD), sepsis, and atrial fibrillation.

**Sample Size Calculation:** It was done by employing Consecutive sampling method and the formula for calculating the sample size was $n = 2[Z(1-\alpha/2) + Z(1-\beta)]^2 x\sigma^2/d^2$. After considering the non-response rate of 10%, the minimum sample size required was 65.

## Methodology

Analyzed echocardiographic data includes isovolumic relaxation time (IVRT), mitral inflow, tissue doppler mitral annular velocity, and pulmonary venous patterns to evaluate diastolic dysfunction. The NTpro-BNP analysis was conducted using the Roche Diagnostics Cobas e-411 analyzer with ProBNP II[3]kit technology. This is an immunoassay designed to quantitatively determine the N-terminal pro B type natriuretic peptide in human blood and plasma in vitro. The method operates based on the principal of electrochemiluminescence. Analyzed samples consisted of human serum and plasma that had been treated with type K2-EDTA. Range of NT pro-BNP levels is between 5 and 35,000 pg/ml. Values below 5 were shown as <5pg/ml, while values over 35000pg/ml were indicated as > 35,000pg/ml. In patients aged 60-75 years and above 75 years, the cut off values were 900 pg/ml and 1800 pg/ml respectively. Extreme elevation was defined as values ≥3000pg/ml. [10]

**Statistical Analysis:** The categorical variables is expressed in numbers (%) and analysed by Chi square test and continuous variable were expressed in mean with Standard Deviation (SD) and analysed by t-test (for 2 groups) and by ANOVA test (for more than 2 groups). Pearson correlation coefficient was utilized for correlation. A p-value less than 0.05 was deemed statistically significant with a 95% confidence interval.

## Results

The current investigation documented a mean age of 64.5 years for the 65 cases, with a female predominance and a female to male ratio of 1.032. The present study included 65 patients, out of whom 41 individuals experienced dyspnoea during physical activity. Among these patients, 23 were female and 18 were male. A total of 19 individuals (29.23%) exhibited pedal oedema, whereas 6 individuals (9.23%) reported chest heaviness. Accordingly, the predominant first symptom seen was dyspnoea, followed by pedal oedema. Among the 65 individuals included in the current study, 18 (27.69%) were diagnosed with diabetes whereas 47 (72.30%) were not. [Table 1]

**Table 1: Distribution according to presenting complaints and history of diabetes mellitus**

| Presenting Complaints | N | % |
|---|---|---|
| Dyspnoea | 41 | 63.07 |
| Pedal oedema | 19 | 29.23 |
| Orthopnoea | 10 | 15.38 |
| Chest pain | 08 | 12.30 |
| Heaviness in chest | 06 | 9.23 |
| Nocturnal cough | 05 | 7.69 |
| Diabetes mellitus | 18 | 27.69 |

Among the 65 patients included in the study, the predominant chest X-ray observation was a normal chest X-ray in 36 patients, accounting for 55.38% from the total. The most pathological chest X-ray observation was cardiomegaly in 18 patients (27.69%), followed by the presence of pleural effusion in 6 patients (9.23%) and an increase in the broncho-vascular markings in 3 patients (4.61%). [Figure 1]

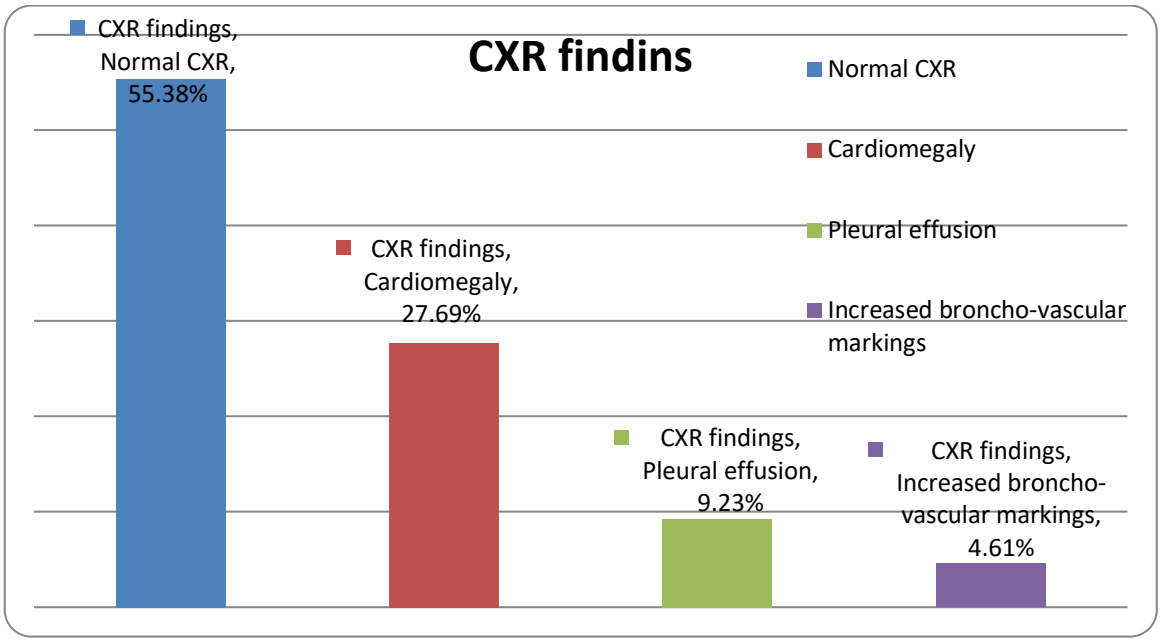


**Figure 1: Distribution of patients according to CXR findings**

In 21 individuals (32.30%), the predominant ECG observation in those with diastolic heart failure was manifestations of left ventricular hypertrophy. This was followed by sinus tachycardia (13 patients, 20.0%) and LAD (5 patients, 7.69%). Normal ECG was found in 32 patients (49.23%). [Figure 2]

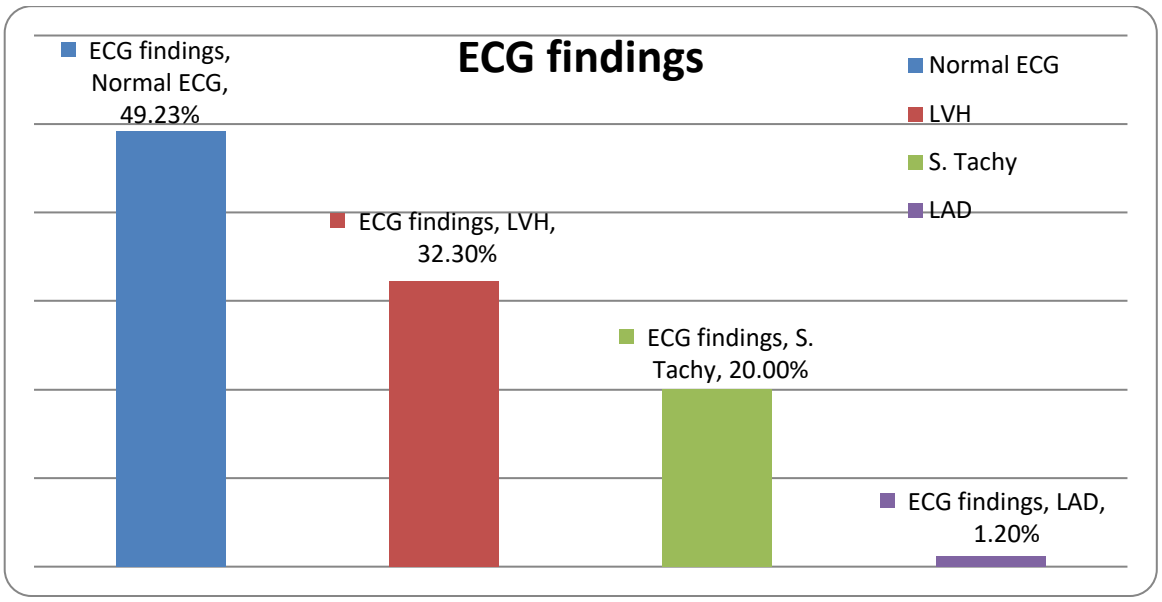


**Figure 2: Distribution of patients according to ECG findings**

Table 2 represents the comparison of mean NT-ProBNP according to diastolic dysfunction grades.

**Table 2: Comparison of mean NT-ProBNP according to diastolic dysfunction grades**

| Diastolic dysfunction grades | Mean NT-ProBNP | SD |
|---|---|---|
| I | 361.079 | 140.649 |
| II | 1618.229 | 540.979 |
| III | 2411.501 | 236.919 |
| IV | 3570.001 | 436.989 |

The present study compared participants with left ventricular hypertrophy (LVH) on electrocardiogram (ECG) with subjects without LVH in terms of mean levels of NT-proBNP using a student's t-test.

Levels of NT-proBNP were significantly greater in patients with left ventricular hypertrophy (LVH) compared to those without LVH ($p<0.001$).

The present work revealed a statistically significant difference ($p=0.008$) in the average levels of NT-proBNP between patients with systemic hypertension and non-hypertensive individuals. Statistical analysis revealed no significant difference ($p=0.71$) in the average levels of NT-proBNP between patients with diabetes and non-diabetics. Among the 65 patients diagnosed with diastolic heart failure, 32% (21 patients) were smokers. The average blood NT-proBNP levels in smokers and non-smokers were 1113.3 and 683.95 pg/ml, respectively. [Table 3]

**Table 3: Comparison of mean NT-ProBNP according to different parameters**

| Parameters | | Mean NT-ProBNP | SD | P-value |
|---|---|---|---|---|
| Gender | Male | 839.591 | 872.001 | 0.631 **(NS)** |
| | Female | 743.899 | 721.199 | |
| LVH on ECG | | 1352.629 | 783.479 | <0.001 **(S)** |
| Systemic HTN | | 925.079 | 844.559 | 0.008 **(S)** |
| Smokers | | 1113.299 | 674.382 | 0.006 **(S)** |

**NS- Non Significant, S- Significant**

## Discussion

Heart failure is a quite prevalent ailment in the current century. The estimated disease prevalence of heart failure in India ranges from 1.3 to 4.6 million, whereas the incidence is around 491,600-1.8 million. Indications of elevated filling pressures in patients with diastolic heart failure include an augmentation in left ventricular wall thickness and/or an enlargement of the left atrial (LA) size. Many patients exhibit further indications of reduced left ventricular filling or suction capacity, often known as diastolic dysfunction, which is widely acknowledged as the probable underlying cause of heart failure in these individuals (hence the name diastolic HF).[11]

The quantification of cardiac biomarkers has become a crucial supplement to the first and on-going assessments of patients with suspected or confirmed chronic heart failure. NT-proBNP and B-type natriuretic peptide (BNP) markers have become crucial in diagnosing and managing heart failure due to the challenges in determining the severity of the condition and delivering the best possible treatment in such instances. Cardiovascular biomarkers can detect structural alterations in the heart at an early stage. [12] Under normal cardiac conditions, the expression of the BNP gene mostly takes place in the atria. Nevertheless, the expression of the ventricular BNP gene is increased in disorders that impact the ventricles, such as severe heart failure.[13] B-type natriuretic peptide (BNP) has physiological effects including natriuresis/diuresis, peripheral vasodilation, and suppression of the rennin-angiotensin-aldosterone system (RAAS) and the sympathetic nervous system (SNS). [14] In comparison to BNP, NT-proBNP has a prolonged half-life and greater stability, accompanied by a seemingly reduced level of intra-patient variability. Grewal and colleagues discovered a strong association between NT-proBNP levels and diastolic heart failure, particularly when the starting threshold was set at 300pg/ml.[15] Hobbs et al observed increased levels of NT-proBNP, which, when excluding ventricular systolic failure, suggest diastolic dysfunction.[16]

In our investigation, hypertension was identified as the primary risk factor linked to diastolic heart failure. This outcome is consistent with the results reported by Panjiyar et al (78.94%) and McMurray et al (64%). [17,18] Given its compensatory thickening of the ventricular wall, hypertension is the most prevalent risk factor and primary antecedent to diastolic heart failure.

In the study conducted by Tschope et al, the levels of NT-proBNP showed a substantial increase in association with the severity of diastolic dysfunction. This ranged from impaired relaxation with an average of 151.6 pg/ml, pseudonormal filling with an average of 308.1 pg/ml, and

restrictive filling with an average of 2307.1 pg/ml. [19] Concisely, the current investigation revealed a statistically significant correlation between diastolic dysfunction and both hypertension and smoking. The average concentrations of serum NT-proBNP were greater in hypertension individuals than in normotensive patients. The present investigation indicates that there is no statistically significant link between diabetics and serum NT-proBNP levels. This observation might be ascribed to the non-diabetic group having a higher mean blood pressure. Statistically substantial increases in NT-proBNP levels were seen in individuals with diastolic heart failure, and these increases were found to be associated with the escalating severity of diastolic dysfunction. Diastolic dysfunction of grade-IV was associated with greater levels of NT-proBNP compared to grade-I diastolic dysfunction.

**Limitations in the study:** It was a single centre study and its statistical power could be increased with recruitment of more study subjects. As echocardiography findings are dependent on observer variations this can also theoretically affect the results.

## Conclusion

The diagnostic accuracy of serum NT-proBNP levels in detecting diastolic heart failure is accurate and consistently corresponds with the increasing degree of diastolic dysfunction as evaluated by the well-established method of echocardiography.

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