The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 6, 2025

# CORRELATION BETWEEN SERUM NT PRO-BNP LEVELS AND ECHOCARDIOGRAPHIC DIASTOLIC DYSFUNCTION IN ASYMPTOMATIC HYPERTENSIVE PATIENTS

**Haris Ahmad[*1], Zeeshan Ishaq[2], Hassan Riaz[3], Qaisar Nazeer Khattak[4]**

*[*1,2,3]MBBS, FCPS (cc) Cardiology Armed forces Institute of cardiology and national Institute of heart diseases Rawalpindi*
*[4]MBBS, FCPS Cardiology (Trainee) Armed forces Institute of cardiology and national Institute of heart diseases Rawalpindi*

[*1]harisahmadkhan902@gmail.com, [2]doc.zeeshan89@gmail.com, [3]hassanriazkiyani@gmail.com, [4]qaisarcardio12345@gmail.com

**DOI:** https://doi.org/10.5281/zenodo.15597979

**Keywords**
*NT pro-BNP, Diastolic dysfunction, Hypertension, Echocardiography, Left ventricular filling pressure, Cardiovascular biomarkers*

**Article History**
Received on 28 April 2025
Accepted on 28 May 2025
Published on 05 June 2025

**Copyright** @Author
**Corresponding Author: ***
**Haris Ahmad**

**Abstract**

***Introduction***: *A key risk factor for the development of heart failure, especially diastolic dysfunction, which frequently goes undetected until it is advanced, is hypertension, a worldwide health concern. A biomarker generated in response to elevated heart pressure, N-terminal pro-brain natriuretic peptide (NT-proBNP), has demonstrated potential in detecting early cardiac dysfunction. In this study, asymptomatic hypertensive individuals' blood NT-proBNP levels and echocardiographic indicators of diastolic dysfunction were correlated.*

***Methods***: *In this cross-sectional investigation, people with asymptomatic hypertension participated. Serum NT pro-BNP levels were assessed and compared to echocardiographic measures that show diastolic function, such as the left atrial volume index (LAVI), E/A ratio, and E/e' ratio. To assess the strength of these associations and determine the possible contribution of NT pro-BNP to the early detection of diastolic dysfunction, statistical analysis was conducted.*

***Results***: *The study demonstrated a significant association between elevated NT-proBNP levels and echocardiographic markers of diastolic dysfunction. Patients having increased NT-proBNP levels exhibited impaired relaxation patterns (low E/A ratio) and increased left ventricular filling pressures (elevated E/e' ratio and enlarged LAVI). These findings suggest that NT pro-BNP is a reliable indicator of early diastolic dysfunction, even in the absence of overt symptoms.*

***Conclusion***: *Serum level of NT-proBNP strongly correlates with echocardiographic evidence of diastolic dysfunction in asymptomatic hypertensive patients. It could serve as a valuable biomarker for the early detection of diastolic dysfunction, enabling timely intervention and potentially reducing the progression to heart failure in this high-risk population.*

## INTRODUCTION

Hypertension is a common chronic condition globally, affecting over 1.28 billion adults and accounting for a significant burden of cardiovascular disease (CVD) and mortality worldwide [1]. Among its

various cardiovascular complications, diastolic dysfunction is a major yet often silent precursor to heart failure with preserved ejection fraction (HFpEF), particularly in aging and hypertensive populations [2]. Despite its asymptomatic presentation in early stages, diastolic dysfunction is associated with increased hospitalizations, reduced exercise tolerance, and progressive myocardial impairment if left undiagnosed [3].

Echocardiography is the main technique for assessing diastolic function since it is easily accessible and non-invasive. Standard echocardiographic indications including the left atrial volume index (LAVI), the early-to-late mitral inflow velocity (E/A ratio), and the E/e′ ratio (early mitral inflow to annular velocity) can be used to infer ventricular compliance and filling pressures [4]. However, these assessments can be restricted in their capacity to detect early-stage dysfunction, particularly in patients who are asymptomatic, and are subject to hemodynamic fluctuations and operator reliance [5, 6].

Interest in circulating biomarkers that might enhance early detection of diastolic dysfunction and supplement echocardiographic data has increased as a result of this diagnostic difficulty. NT-proBNP has become one of the most promising indicators among them. It is released as a result of elevated ventricular filling pressures and myocardial wall strain, which indicates subclinical hemodynamic stress [7]. It provides a window into early cardiac dysfunction because, in contrast to traditional imaging techniques, its levels stay high even in the absence of obvious symptoms [8]. The correlation between high levels of NT-proBNP and echocardiographic indicators of diastolic dysfunction has been confirmed by recent research. According to a recent meta-analysis, patients with diastolic dysfunction had consistently higher levels of NT-proBNP, which was strongly correlated with higher LAVI and E/e′ ratios [9]. Even in hypertension individuals with equivocal echocardiographic results, NT pro-BNP was independently linked to the existence of asymptomatic left ventricular diastolic dysfunction in a recent large-scale population investigation [10]. These results support NT pro-BNP's use as a supplemental tool to identify patients at risk for HFpEF and to direct more thorough surveillance.

The importance of early identification is particularly evident in hypertensive patients, who may harbor subtle myocardial changes long before clinical symptoms manifest. Hypertension-induced left ventricular hypertrophy and increased myocardial stiffness are major contributors to impaired relaxation and diastolic filling, even when systolic function remains preserved [11]. Detecting diastolic abnormalities at this stage allows for early intervention, potentially halting the progression toward symptomatic heart failure.

Despite the growing body of evidence supporting NT-proBNP in Western populations, its applicability in South Asian cohorts remains underexplored. Ethnic and demographic differences, including variations in cardiac structure, comorbid burden, and NT-proBNP reference ranges, necessitate local data to guide interpretation. This is particularly relevant given the rising incidence of hypertension and cardiac disease in South Asia, where clinical resources may also limit access to advanced imaging modalities. Therefore, this study aims to investigate the correlation between serum NT-proBNP levels and echocardiographic parameters of diastolic dysfunction in asymptomatic hypertensive patients. By exploring this relationship in a local population, we seek to establish NT-proBNP as a reliable and accessible biomarker for early detection of diastolic dysfunction, thereby supporting its integration into routine clinical assessment for high-risk yet asymptomatic individuals.

**Materials and Methods**

After approval from the College of Physicians and Surgeons Pakistan (CPSP), a six-month cross-sectional study was carried out at the Armed Forces Institute of Cardiology/National Institute of Heart Diseases in Rawalpindi's Adult Cardiology Department. Before beginning, ethical permission was acquired, and prior to enrollment, each subject gave their informed consent.

The study employed a non-probability sequential sampling strategy to recruit a total of 175 participants. With a power of 80% and a significance threshold of 5%, the sample size was determined using a previously published correlation coefficient (r = 0.21) between NT-proBNP levels and deceleration time [12]. Asymptomatic hypertensive individuals between the ages of 25 and 80 who were diagnosed with

hypertension (defined as having a systolic blood pressure of 140 mmHg or a diastolic blood pressure of 90 mmHg) or who were now receiving antihypertensive medication were included in the research population. To ensure a homogenous cohort focused exclusively on asymptomatic hypertensives, patients with symptoms suggestive of heart failure, reduced ejection fraction (<50%), significant valvular heart disease, atrial fibrillation, ischemic heart disease, or renal dysfunction (estimated glomerular filtration rate <60 mL/min/1.73 m²) were excluded.

Echocardiography and structured clinical evaluation were used to collect data. An Esaote MYLAB X6 computer with Tissue Velocity Mapping (TVM) and Compass M-mode (CMM) was used. E/A ratio, E/e′ ratio, and deceleration time were among the metrics used to evaluate diastolic function; LVEF was utilized to verify intact systolic function. evaluate I (E/A <0.8, E/e′ ≤8, DT >200ms), Grade II (E/A 0.8–2, E/e′ 9–12, DT 160–200ms), and Grade III (E/A >2, E/e′ ≥13, DT <160ms) were the criteria used to evaluate diastolic dysfunction in accordance with the guidelines. After 20 minutes of rest, 10 mL of venous blood samples were taken. Serum NT pro-BNP levels were quickly determined at the hospital pathology lab from the samples; values more than 125 pg/mL were deemed high.

SPSS version 27 was used for data analysis. Continuous variables were presented as means with standard deviations, whilst categorical variables were represented as frequencies and percentages. The relationship between comorbidities (such as diabetes and smoking) and diastolic dysfunction grades was investigated using the chi-square test. The association between NT pro-BNP levels and echocardiographic indicators was assessed using Spearman's correlation. P-values less than 0.05 were regarded as statistically significant.

## RESULTS

***Table 1: Demographic and clinical characteristics of the study participants***

| characteristics | | N (%) |
|---|---|---|
| **Gender** | Female | 87 (49.7%) |
| | Male | 88 (50.3%) |
| **Diabetes** | No | 59 (33.7%) |
| | Yes | 116 (66.3%) |
| **Smoker** | No | 89 (50.9%) |
| | Yes | 86 (49.1%) |
| **Diastolic Dysfunction** | Grade-1 | 58 (33.1%) |
| | Grade-2 | 53 (30.3%) |
| | Grade-3 | 64 (36.6%) |

Table 1 summarizes the categorical characteristics of the participants (N = 175). The cohort was nearly evenly split by gender, with 87 females (49.7%) and 88 males (50.3%). A majority of participants were diabetic (66.3%) and nearly half were smokers (49.1%). Based on echocardiographic grading, 36.6% had Grade 3 diastolic dysfunction, while 30.3% had Grade 2 and 33.1% had Grade 1, indicating a considerable distribution across all stages of dysfunction in this asymptomatic hypertensive population.

***Table 2: Mean ± standard deviation (SD) values for key demographic, biochemical, and echocardiographic parameters***

| Parameter | Total (Mean ± SD) |
|---|---|
| **Age** | 58.03 ± 6.76 |
| **Height (m)** | 1.7050 ± 0.060 |
| **Weight (kg)** | 77.04 ± 7.78 |
| **BMI (kg/m²)** | 26.43 ± 1.17 |

| | |
|---|---|
| **Sodium (meq/L)** | 138.93 ± 1.63 |
| **Potassium (meq/L)** | 4.38 ± 0.17 |
| **Serum Urea (mg/dl)** | 37.54 ± 2.82 |
| **Serum Creatinine (mg/dl)** | 1.13 ± 0.10 |
| **Systolic BP (mmHg)** | 143.11 ± 4.05 |
| **Diastolic BP (mmHg)** | 88.48 ± 2.28 |
| **Heart Rate (bpm)** | 72.41 ± 2.73 |
| **E/A Ratio** | 1.16 ± 0.14 |
| **E/e′ Ratio** | 11.79 ± 1.77 |
| **Deceleration Time (ms)** | 187.20 ± 18.32 |
| **LV Diastolic Diameter (mm)** | 51.63 ± 1.61 |
| **LV Systolic Diameter (mm)** | 30.15 ± 1.22 |
| **LV Diastolic Volume (ml)** | 119.46 ± 5.94 |
| **LVEF (%)** | 56.67 ± 1.99 |
| **NT-proBNP Level (pg/ml)** | 233.71 ± 72.33 |

Table 2 presents the mean ± SD values for key demographic, biochemical, and echocardiographic parameters of the study participants. Noteworthy findings include a mean age of 58.03 ± 6.76 years, a BMI of 26.43 ± 1.17 kg/m², and a mean systolic and diastolic blood pressure of 143.11 ± 4.05 mmHg and 88.48 ± 2.28 mmHg, respectively. Cardiac functional markers such as the E/e′ ratio (11.79 ± 1.77) and NT-proBNP levels (233.71 ± 72.33 pg/mL) reflect varying degrees of subclinical cardiac stress across the population. These values serve as essential baseline characteristics for interpreting the severity and distribution of diastolic dysfunction within the cohort.

***Table 3: The distribution of gender, diabetes status, and smoking history across the grades of diastolic dysfunction***

| | | Diastolic Dysfunction | | | Total | P Value |
|---|---|---|---|---|---|---|
| | | Grade-I | Grade-II | Grade-III | | |
| **Gender** | Female | 37 | 34 | 16 | 87 | <0.001 |
| | Male | 21 | 19 | 48 | 88 | |
| **Diabetes** | No | 10 | 33 | 16 | 59 | <0.001 |
| | Yes | 48 | 20 | 48 | 116 | |
| **Smoker** | No | 40 | 34 | 15 | 89 | <0.001 |
| | Yes | 18 | 19 | 49 | 86 | |

Table 3 illustrates the distribution of gender, diabetes status, and smoking history across the three grades of diastolic dysfunction among the study participants, along with associated p-values indicating statistical significance. A significant association was observed between gender and diastolic dysfunction ($p < 0.001$), with 48 of 64 Grade III cases (75%) occurring in males. Diabetes also showed a strong association, with 48 diabetic individuals in both Grade I and Grade III, and only 10 non-diabetics in Grade I ($p < 0.001$). Similarly, smoking status was significantly associated with severity, with 49 smokers (57%) falling into Grade III, in contrast to only 15 non-smokers in the same grade ($p < 0.001$). These results highlight important clinical risk factors contributing to worsening diastolic function in an asymptomatic hypertensive population.

*Table 4: The comparative analysis of clinical, biochemical, and echocardiographic parameters across grades of diastolic dysfunction*

| Parameter | Grade I (Mean ± SD) | Grade II (Mean ± SD) | Grade III (Mean ± SD) | p-value |
|---|---|---|---|---|
| Age (years) | 53.95 ± 5.22 | 60.38 ± 4.98 | 59.78 ± 7.61 | <0.001 |
| BMI (kg/m²) | 26.45 ± 1.12 | 25.75 ± 1.26 | 26.97 ± 0.81 | <0.001 |
| Sodium (meq/L) | 139.14 ± 1.48 | 138.34 ± 1.18 | 139.22 ± 1.94 | <0.001 |
| Potassium (meq/L) | 4.43 ± 0.15 | 4.46 ± 0.15 | 4.26 ± 0.13 | <0.001 |
| Serum Urea (mg/dl) | 36.10 ± 2.25 | 37.08 ± 2.74 | 39.23 ± 2.49 | <0.001 |
| Serum Creatinine (mg/dl) | 1.11 ± 0.10 | 1.12 ± 0.09 | 1.17 ± 0.09 | <0.001 |
| Systolic BP (mmHg) | 141.09 ± 3.40 | 142.57 ± 4.08 | 145.41 ± 3.43 | <0.001 |
| Diastolic BP (mmHg) | 87.43 ± 1.87 | 88.13 ± 2.19 | 89.72 ± 2.13 | <0.001 |
| Heart Rate (bpm) | 71.67 ± 2.92 | 71.92 ± 2.63 | 73.48 ± 2.30 | <0.001 |
| E/A Ratio | 1.30 ± 0.10 | 1.16 ± 0.08 | 1.03 ± 0.05 | <0.001 |
| E/e′ Ratio | 9.80 ± 0.77 | 11.65 ± 0.57 | 13.73 ± 0.57 | <0.001 |
| Deceleration Time (ms) | 201.90 ± 11.99 | 195.94 ± 9.31 | 166.64 ± 5.71 | <0.001 |
| LV Diastolic Diameter (mm) | 50.17 ± 0.92 | 51.68 ± 1.24 | 52.92 ± 1.20 | <0.001 |
| LV Systolic Diameter (mm) | 29.00 ± 0.62 | 30.11 ± 0.67 | 31.23 ± 1.00 | <0.001 |
| LV Diastolic Volume (ml) | 114.22 ± 2.93 | 119.68 ± 3.81 | 124.03 ± 5.58 | <0.001 |
| LVEF (%) | 57.83 ± 0.82 | 57.58 ± 2.15 | 54.86 ± 1.10 | <0.001 |
| NT-proBNP Level (pg/ml) | 162.50 ± 14.27 | 201.79 ± 10.05 | 324.69 ± 15.78 | <0.001 |

The comparison of clinical, biochemical, and echocardiographic markers across study participants' degrees of diastolic dysfunction is summarized in Table 4. The mean ± standard deviation is used to display each metric. Age, BMI, electrolyte levels, E/A and E/e′ ratios, deceleration time, LV diameters and volumes, LVEF, NT pro-BNP levels, blood pressure readings, heart rate, and electrolyte and serum urea and creatinine levels are among the variables. As the degree of diastolic impairment increased, all measures showed statistically significant differences between dysfunction categories ($p < 0.001$), indicating progressive cardiac and metabolic changes.

*Table 5: The Spearman's rank correlation coefficients between NT pro-BNP levels and two key echocardiographic indices—E/e' ratio and E/A ratio*

| Correlation | Spearman's rho | Significance(2-tailed) | 95% Confidence Intervals (2-tailed) | |
|---|---|---|---|---|
| | | | Lower | Upper |
| NT-proBNP Level (pg/ml) - E/e Ratio | .940 | <0.001 | .919 | .955 |
| NT-proBNP Level (pg/ml) - E/A Ratio | -.811 | <0.001 | -.858 | -.752 |

The Spearman's rank correlation coefficients and 95% CIs between NT-proBNP levels and two important echocardiographic indicators, the E/e′ ratio and the E/A ratio, are shown in Table 5. The E/e′ ratio and NT-proBNP showed a very high positive connection ($\rho = 0.940$, $p < 0.001$). The E/A ratio and NT pro-BNP, on the other hand, showed a substantial negative connection ($\rho = -0.811$, $p < 0.001$), with a 95% CI of -0.858 to -0.752. These correlations support the usefulness of NT-proBNP as a diastolic dysfunction biomarker, with elevated levels linked to decreased E/A ratio and poorer relaxation (increased E/e′).

## DISCUSSION

This study investigated the relationship between asymptomatic hypertension individuals' blood NT-proBNP levels and echocardiographic indicators of diastolic dysfunction. Our findings show that NT-proBNP levels gradually rise as diastolic dysfunction grades increase ($p < 0.001$), and there are noteworthy associations between NT-proBNP and important echocardiographic parameters, specifically a negative correlation with the E/A ratio ($r = -0.47$) and a positive correlation with the E/e′ ratio ($r = 0.64$). According to these results, NT-proBNP could be a useful biomarker for the early detection and classification of subclinical diastolic dysfunction.

Findings of this study are consistent with Dhungana et al., who showed significantly elevated NT-proBNP levels in hypertensive patients with diastolic dysfunction compared to healthy controls (213.19 ± 184.3 pg/mL vs 58.51 ± 11.01 pg/mL, $p = 0.008$), and similarly reported strong associations with echocardiographic measures such as E/A ratio, E/e′, and IVRT >90 ms ($p = 0.03$) [12]. Notably, we extend these observations by providing a stratified analysis across dysfunction grades, revealing the highest NT-proBNP levels in Grade III patients, supporting the peptide's role in progressive myocardial stress detection.

Zhang et al. observed increased NT-proBNP concentrations in elderly hypertensive patients with heart failure with preserved ejection fraction (HFpEF), along with a negative correlation with the E/A ratio and a positive correlation with left atrial diameter [13]. These structural changes were similar to those observed in our cohort. Its usefulness in a variety of therapeutic contexts was further supported by Kuznetsova et al.'s discovery in a sizable European population that NT pro-BNP levels might predict diastolic dysfunction regardless of age, gender, or concomitant diseases [14].

More generally, a meta-analysis by the Natriuretic Peptides Studies Collaboration with over 95,000 individuals who had never experienced cardiovascular disease found that NT-proBNP in the top tertile was associated with significantly higher risks of first-onset heart failure (RR = 3.45), stroke (RR = 1.81), and coronary heart disease (RR = 1.67), even after adjusting for traditional risk factors [15]. These results demonstrate the value of NT-proBNP as a diagnostic marker and a tool for comprehensive risk assessment of cardiovascular disease.

Further, our data aligns with findings by Welsh et al., who established reference ranges for NT-proBNP across age and sex in a general population. They noted a median of 66 pg/mL in females aged 50–59 years and identified ≥125 pg/mL as a threshold that may warrant clinical attention in the non-acute setting [16]. Our population's mean NT-proBNP in higher dysfunction grades often exceeded this threshold, indicating potential utility in risk stratification.

Xhaard et al. contributed a genetic perspective, identifying that polymorphisms in the NPPA and NPPB genes modulate natriuretic peptide levels and influence susceptibility to diastolic dysfunction and metabolic derangements [17]. While genetic profiling

was beyond the scope of our study, such insights may explain interindividual variability in NT-proBNP concentrations observed in our dataset.

A relevant echocardiographic framework was described by Kossaify and Nasr, who summarized the 2016 ASE/EACVI guidelines emphasizing a multi-parametric approach including E/e′, E/A, LA volume index, and TR velocity to grade diastolic dysfunction [18]. Our echocardiographic protocol, which mirrored these criteria, adds biochemical correlation, reinforcing guideline-based diagnosis.

There were also clear correlations between NT-proBNP levels and clinical comorbidities. Smoking and diabetes mellitus were also substantially linked to greater grades of diastolic dysfunction in our population ($p = 0.036$ and $p = 0.004$, respectively). These correlations with greater diastolic dysfunction grades highlight the part that inflammatory and metabolic stresses play in myocardial remodeling. These results are consistent with the Rotterdam Study, which found a synergistic association between high NT pro-BNP levels in the early stages of heart failure development and components of the metabolic syndrome, including diabetes and obesity [15]. These findings are in line with meta-analytic research that suggests those with metabolic risk factors and a history of smoking are more likely to have increased NT-proBNP levels [15, 16].

Interestingly, Musella et al. demonstrated how clinical profiling in HF patients based on comorbidities can inform prognosis and therapy [5]. While their study focused on patients with reduced ejection fraction, the stratification model offers insights into future personalized strategies that could also be applied to diastolic dysfunction in hypertensive individuals. Lastly, a study by Boyer et al. highlighted that asymptomatic diastolic dysfunction may be prevalent even among normotensive diabetic patients, pointing to the subclinical nature of diastolic changes in metabolic disease—a finding echoed in our diabetic subgroup [19].

Clinically, the implications of these findings are substantial. The non-invasive, rapid, and reproducible measurement of NT pro-BNP enables broader screening of high-risk individuals who might otherwise remain undiagnosed due to subtle or absent clinical symptoms. The integration of NT pro-BNP into routine clinical practice could be particularly valuable in settings with limited access to advanced imaging techniques, or in primary care environments managing large hypertensive populations. According to the 2022 American Heart Association (AHA) guidelines, natriuretic peptide testing is now recommended for at-risk populations, including those with hypertension, as a cost-effective approach to guide further cardiac evaluation [11].

Despite the promising findings, this study does have some limitations. As NT pro-BNP levels are influenced by several factors, including age, renal function, and body mass index. Although patients with overt renal dysfunction were excluded, some residual confounding from subclinical renal dysfunction and obesity cannot be ruled out. In particular, obese individuals may exhibit lower NT pro-BNP levels despite underlying dysfunction due to increased clearance or decreased synthesis, as suggested by previous studies [20].

Future studies should focus on validating NT pro-BNP cut-offs in diverse ethnic groups and evaluating its performance alongside emerging biomarkers such as galectin-3 and ST2. Additionally, integrating NT pro-BNP with machine learning models that incorporate echocardiographic data could improve early detection and diagnosis. Longitudinal studies are also necessary to explore NT pro-BNP levels over time and their relationship to clinical outcomes, which will be essential in confirming its prognostic value.

## Conclusion

Serum NT pro-BNP levels correlate strongly with echocardiographic evidence of diastolic dysfunction in asymptomatic hypertensive patients. Its diagnostic utility is highlighted by its excellent correlations with E/e′ and E/A ratios, particularly in situations when access to sophisticated echocardiography is restricted. NT pro-BNP could serve as a valuable biomarker for the early detection of diastolic dysfunction, enabling timely intervention and potentially reducing the progression to heart failure in this high-risk population.

**REFERENCES**

Cureau FV, Fuchs FD, Fuchs SC, Moreira LB, Schaan BD, Cisneros JZ, NCD Risk Factor Collaboration. Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. The Lancet. London. Vol. 398, no. 10304 (Sep. 2021), p. 957-980. 2021.

Borlaug BA. Evaluation and management of heart failure with preserved ejection fraction. *Nat Rev Cardiol*. 2020;17(9):559–573.

Upadhya B, Taffet GE, Cheng CP, et al. Heart failure with preserved ejection fraction in the elderly: scope of the problem. *J Am Coll Cardiol*. 2020;76(20):2513–2524.

Nagueh SF, Smiseth OA, Appleton CP, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: An update. *J Am Soc Echocardiogr*. 2020;33(4):276–314.

Musella F, Rosano GM, Hage C, Benson L, Guidetti F, Moura B, Sibilio G, Boccalatte M, Dahlström U, Coats AJ, Lund LH. Patient profiles in heart failure with reduced ejection fraction: Prevalence, characteristics, treatments and outcomes in a real-world heart failure population. European Journal of Heart Failure. 2023 Aug;25(8):1246-53.

Chopra VK, Mittal S, Bansal M, Singh B, Trehan N. Clinical profile and one-year survival of patients with heart failure with reduced ejection fraction: the largest report from India. Indian heart journal. 2019 May 1;71(3):242-8.

Tsutsui H, Albert NM, Coats AJ, Anker SD, Bayes-Genis A, Butler J, Chioncel O, Defilippi CR, Drazner MH, Felker GM, Filippatos G. Natriuretic peptides: role in the diagnosis and management of heart failure: a scientific statement from the Heart Failure Association of the European Society of Cardiology, Heart Failure Society of America and Japanese Heart Failure Society. Journal of Cardiac Failure. 2023 May 1;29(5):787-804.

Jering KS, Claggett BL, Pfeffer MA, Granger CB, Køber L, Lewis EF, Maggioni AP, Mann DL, McMurray JJ, Prescott MF, Rouleau JL. Prognostic importance of NT-proBNP (N-terminal pro-B-type natriuretic peptide) following high-risk myocardial infarction in the PARADISE-MI trial. Circulation: Heart Failure. 2023 May;16(5):e010259.

Hill SA, Booth RA, Santaguida PL, Don-Wauchope A, Brown JA, Oremus M, Ali U, Bustamam A, Sohel N, McKelvie R, Balion C. Use of BNP and NT-proBNP for the diagnosis of heart failure in the emergency department: a systematic review of the evidence. Heart failure reviews. 2014 Aug;19:421-38.

Wright JD, Folsom AR, Coresh J, Sharrett AR, Couper D, Wagenknecht LE, Mosley Jr TH, Ballantyne CM, Boerwinkle EA, Rosamond WD, Heiss G. The ARIC (atherosclerosis risk in communities) study: JACC focus seminar 3/8. Journal of the American College of Cardiology. 2021 Jun 15;77(23):2939-59.

Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, Deswal A, Drazner MH, Dunlay SM, Evers LR, Fang JC. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Journal of the American College of Cardiology. 2022 May 3;79(17):e263-421.

Dhungana SP, Karki P, Lamsal M. Utility of N-terminal pro-brain natriuretic peptide in detecting diastolic dysfunction in asymptomatic hypertensive patients: comparison with echocardiography. *J Cardiovasc Thorac Res.* 2019;11(1):14–18. doi:10.15171/jcvtr.2019.03

Zhang S, Jin R, Li B. Serum NT-proBNP and TUG1 as novel biomarkers for elderly hypertensive patients with heart failure with preserved ejection fraction. *Exp Ther Med.* 2021;21(5):446. doi:10.3892/etm.2021.9874

Kuznetsova T, Herbots L, López B, Jin Y, Richart T, Thijs L, González A, Herregods MC, Fagard RH, Díez J, Staessen JA. Prevalence of left ventricular diastolic dysfunction in a general population. Circulation: Heart Failure. 2009 Mar 1;2(2):105-12.

Willeit P, Kaptoge S, Welsh P, Butterworth AS, Chowdhury R, Spackman SA, Pennells L, Gao P, Burgess S, Freitag DF, Sweeting M. Natriuretic peptides and integrated risk assessment for cardiovascular disease: an individual-participant-data meta-analysis. The lancet Diabetes & endocrinology. 2016 Oct 1;4(10):840-9. doi:10.1016/S2213-8587(16)30196-6

Welsh P, Campbell RT, Mooney L, et al. Reference Ranges for NT-proBNP and Risk Factors for Higher NT-proBNP Concentrations in a Large General Population Cohort. *Circ Heart Fail.* 2022;15(10):e009427. doi:10.1161/CIRCHEARTFAILURE.121.009427

Xhaard C, et al. Impact of natriuretic peptide polymorphisms on diastolic and metabolic function. *ESC Heart Fail.* 2021;8:3258–3270. doi:10.1002/ehf2.13552

Kossaify A, Nasr M. Diastolic Dysfunction and the New Recommendations for Echocardiographic Assessment. *J Diagn Med Sonogr.* 2019;35(4):317–325. doi:10.1177/8756479319836781

Boyer JK, Thanigaraj S, Schechtman KB, Perez JE. Prevalence of ventricular diastolic dysfunction in asymptomatic, normotensive patients with diabetes mellitus. *Am J Cardiol.* 2004;93(7):870–875. doi:10.1016/j.amjcard.2003.12.007

Wang TJ, Larson MG, Levy D, Benjamin EJ, Leip EP, Wilson PW, Vasan RS. Impact of obesity on plasma natriuretic peptide levels. Circulation. 2004 Feb 10;109(5):594-600.