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Brain Natriuretic Peptide (BNP) / N-Terminal Probnp And Its Role In Predicting Atrial Fibrillation

Aadhya Agarwal [1], Ajayta Chaudhary[2], Thuraya Abdulsalam A.A. Al-Azazi [3], Dr. S.B. Sharma [4], Dr. Manoj Kumar Nandkeoliar[5], Dr. Renu Chane[6*]

[1,2]2nd Year MBBS students, [3]Ph.D. Scholar, [4]Professor, [5] Emeritus Professor,
Department of Biochemistry, School of Medical Science & Research, Sharda University.

***Corresponding Author:**
Dr. Renu Chane
Associate Professor, Department of Biochemistry, School of Medical Sciences and Research, Sharda University, Gautam Budh Nagar, UP, India

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Abstract

Around the world, atrial fibrillation (AF) is the most prevalent prolonged cardiac arrhythmia and a leading cause of heart failure and stroke. In its management, timely prediction and prevention continue to be major obstacles. Secreted in response to cardiac strain, brain natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP) have been identified as putative indicators of the onset and recurrence of atrial fibrillation, and numerous studies have shown that these biomarkers are helpful in identifying high-risk patients since their higher levels occur before the start of AF. Furthermore, persistently elevated NT-proBNP levels after ablation or cardioversion were associated with a higher risk of recurrence, underscoring their relevance for therapeutic guidance and follow-up.

Keywords: Atrial Fibrillation (AF), brain natriuretic Peptide (BNP), N-terminal proBNP (NT-proBNP), Biomarkers

Introduction

Atrial fibrillation (AF) is a common supraventricular arrhythmia characterized by rapid, irregular atrial activity that leads to ineffective atrial contractions. It reduces quality of life and increases risks of stroke, heart failure, and death, imposing health and economic burdens worldwide. AF is the most prevalent persistent arrhythmia, with a rising prevalence through 2021 and projections through 2025. Holter monitoring in India shows a high paroxysmal AF prevalence (about 17.4%) among monitored adults, indicating underdiagnosis. Community studies report lower overall prevalence but higher rates among older people. These findings suggest that AF is under-recognized in India, underscoring the need for systematic screening and surveillance (1,2).

Early AF diagnosis and prediction, especially in high-risk individuals, can improve clinical outcomes. B-type natriuretic peptide (BNP) and its inactive fragment, N-terminal pro-BNP (NT-proBNP), have emerged as promising biomarkers for predicting the onset, recurrence, and prognosis of atrial fibrillation (AF) in recent years, due to their strong correlation with atrial stretch, remodeling, and myocardial wall stress. Early studies revealed a reversible relationship between BNP secretion and atrial pressure overload, with BNP levels sharply declining in patients with persistent AF if sinus rhythm is restored (3). BNP may be a valuable predictor of AF recurrence since it captures the dynamic state of atrial mechanical stress. In the acute phase of myocardial infarction, higher NT-proBNP levels were substantially linked with the occurrence of AF, showing subclinical atrial dysfunction even before arrhythmia manifestation(4). This further evidence supports the importance of NT-proBNP in predicting new-onset AF. The relevance of BNP in detecting silent AF in populations with

significant cardiovascular strain was also highlighted by studies in hemodialysis patients, which found it to be a reliable biomarker for AF detection (5).To better reflect long-term results, new NT-proBNP testing methods have also been proposed, such as total NT-proBNP. The prognostic utility of elevated total NT-proBNP levels beyond traditional criteria was highlighted by their independent association with recurrent AF (6). Similar results in patients with embolic stroke from an unknown cause showed that higher BNP levels may improve AF detection, allowing for an earlier identification in cases of cryptogenic stroke (7).

Additionally, BNP has shown good in forecasting results after interventional therapies, poorer success rates and recurrence after catheter ablation for AF were linked to higher pre-procedural BNP values and screening capability was further supported by the Find-AF Randomized Trial, which discovered that BNP elevation could predict the chance of identifying AF following stroke(8,9).Furthermore recent studies have confirmed the diagnostic consistency of NT-proBNP across different cardiac structures by showing that it accurately predicts the risk of clinical AF with and without left atrial enlargement (10). As a non-invasive diagnostic for post-ablation monitoring, NT-proBNP levels were also demonstrated to predict AF recurrence following cryoballoon pulmonary vein isolation (11).

In acute ischemic stroke, higher NT-proBNP has been linked to overestimation of core infarct size, suggesting that elevated BNP levels represent a wider range of cardiac-cerebral interactions than only AF [10]. Also the new predictive models that combine BNP with other biomarkers like angiotensin II, homocysteine, and inflammatory ratios have greatly enhanced the ability to predict early recurrence after AF ablation (12), highlighting BNP's continued significance as a key biomarker in AF risk assessment.

Overall , these studies illustrate that BNP and NT-proBNP are not merely passive reflections of cardiac stress but active indicators of atrial pathology. Their integration into clinical practice could refine AF prediction, guide therapeutic strategies, and improve prognostic assessment across diverse cardiovascular populations.

Atrial Fibrillation

Atrial fibrillation (AF) is the most common persistent arrhythmia, caused by rapid, uncoordinated electrical impulses in the atria that lead to an irregular ventricular rhythm. This results in reduced cardiac output, decreased ventricular filling, and ineffective atrial contractions. Risk factors include hypertension, ischemic heart disease, valve issues, age, obesity, and diabetes. Hemodynamic effects of AF, such as increased atrial pressure and atrial dilation, lead to structural changes, including fibrosis, which promote the condition's persistence in a self-sustaining cycle (13). Once viewed solely as an electrical phenomenon, AF is now recognized as a manifestation of atrial cardiomyopathy (AtCM)—a broader disease characterized by structural, functional, and molecular changes in the atrial myocardium. This shift highlights that AF often results from progressive atrial pathology rather than starting spontaneously.AtCM involves structural and functional changes such as fibrosis, myocyte hypertrophy, electrical instability, metabolic issues, and inflammation. These abnormalities often come before AF, persist even after sinus rhythm is restored, and independently raise the risk of blood clots. Importantly, AtCM is not uniform; its characteristics vary depending on factors like age, metabolic conditions, inflammation, genetics, and neurohormonal changes, creating a unique atrial substrate for each patient. Recognizing AtCM as the basis for both arrhythmia and thrombosis shifts the perception of AF from a temporary event to a sign of ongoing, widespread myocardial disease. This realization impacts treatment strategies: simply controlling AF isn't enough unless the underlying substrate is also targeted. Consequently, current treatments increasingly focus on preventing, reversing, or reducing atrial remodelling(14).

BNP/NT-PROBNP as a Predictor of Atrial Fibrillation

A cardiac hormone called B-type natriuretic peptide (BNP) is released from myocardial tissue in reaction to pressure overload, volume expansion, and wall stretch. BNP helps lower cardiac preload and afterload by promoting natriuresis, vasodilation, and inhibition of renin-angiotensin-aldosterone system . It is produced as the precursor proBNP, which undergoes enzymatic cleavage to produce active BNP and the more stable but inactive NT-proBNP (15).

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BNP represents reversible atrial mechanical stress, as early clinical findings showed that BNP levels dramatically decrease following sinus rhythm restoration (16). BNP is a worldwide diagnostic of cardiac stress because it can predict mortality and cardiovascular outcomes even in people without heart failure (17).BNP is useful for diagnosing and prognosticating AF. Higher pre-ablation BNP levels predict less success and increased recurrence following catheter ablation (8), and it aids in the identification of silent AF in hemodialysis patients (5). BNP was further confirmed as a screening measure for AF detection following an ischemic stroke by the Find-AF Randomized Trial (9).

The inactive segment created when proBNP is broken down in reaction to myocardial wall stress is known as NT-proBNP (N-terminal pro-B-type natriuretic peptide). Despite having no direct physiological activity, NT-proBNP is a better clinical biomarker for prolonged cardiac strain due to its longer half-life and increased stability (16). NT-proBNP is a powerful predictor of AF recurrence following cryoballoon ablation (11) and predicts AF risk even in the absence of left atrial hypertrophy (10)and, following cryoballoon ablation, is a reliable indicator of AF recurrence (11). The brain-heart systemic connection is reflected in elevated NT-proBNP in acute ischemic stroke (12). Early AF recurrence prediction is improved by multi-marker models that include NT-proBNP with inflammatory and neurohormonal indicators (13. NT-proBNP levels also indicate subclinical atrial dysfunction prior to the onset of arrhythmia and predict new-onset AF in the context of acute myocardial infarction (4).

While NT-proBNP is inert but more consistent represents chronic atrial remodeling and fibrosis, BNP is biologically active and mainly reflects acute atrial or ventricular stress (16). The NT-proBNP/BNP ratio is around 6:1 in heart failure with reduced ejection fraction, but it rises to approximately 8:1 in AF because of increased chronic atrial stretch and altered peptide clearance, which causes NT-proBNP to be disproportionately elevated (17,18).

Table 1: Summary of various Studies

S.No.	Author name and year	Methodology	Population studied	Result
1.	Yu et al. (2025)	Retrospective observational cohort study analyzing BNP tertiles, UR, and other factors for incident AF.	140 hemodialysis patients followed for 5 years	BNP independently predicts incident AF (HR 1.038 per 100 pg/mL)
2.	Bae et al.(2025)	Retrospective study identifying predictors for newly diagnosed AF during follow-up using logistic regression.	312 patients with ESUS	Markers of left atrial cardiopathy, including BNP>100pg/ml
3.	Zhou, Y., Cheng, Y., et al. (2025)	Logistic-regression model (BNP, Ang II, etc.)	279 (persistent	Elevated BNP among other markers predicts early recurrence

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			AF ablation)	
4.	Dong et al. (2024)	Retrospective cohort study using logistic regression to investigate NT-pro-BNPs effect on new-onset AF during hospitalization.	291 consecutive patients hospitalized for AMI	NT-pro-BNP was an independent risk factor.
5.	Kawaji et al. (2023)	Retrospective observational study analyzing baseline and 3-month follow-up BNP/NT-proBNP vs. recurrent AF/HF endpoint over 2.4 years.	1,750 patients undergoing initial AF ablation (TRANQUILIZE-AF Registry)	Low baseline BNP (<38.3 pg/mL) was independently associated with lower risks of recurrent AF (HR 0.63) and the composite HF endpoint (HR 0.17)
6.	Blessberger et al. (2022)	Single-center retrospective study assessing baseline NT-pro-BNP vs. AF relapse over a median of 3.8 years.	374 patients undergoing first-ever cryo-PVI (likely Germany)	Baseline NT-pro-BNP was associated with AF recurrence in univariate and multivariate models
7.	Zhao et al. (2021)	Observational study analyzing NT Pro-BNP adjusting for confounders.	1,243 patients with and without AF	NT Pro-BNP was a statistically significant predictor of AF, even without left atrial enlargement (LAD) (p < .001
8.	Staszewsky et al. (2021)	Serial biomarker measurements (Total NT-proBNP, NT-proBNP, Ang2, BMP10, etc.) and Cox regression over 12 months.	382 patients from the GISSI-AF trial in sinus rhythm with a history of AF	Total NT-proBNP & NT-proBNP predict recurrent AF (HR ≈ 1.19)

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9.	Wasse et al. (2019)	Prospective, randomized trial comparing Enhanced and Prolonged Holter Monitoring (EPM) vs. usual care; measured BNP at baseline and 3 months	373 acute ischemic stroke patients age approx. 60 years	BNP> 100pg/mL markedly Iproves detection of post stroke AF
10.	Beata Wożakowska-Kapłon et al (2010)	Measured BNP/NT-proBNP before and 24h after successful electrical cardioversion (EC), followed for 18 months.	43 patients with persistent AF undergoing cardioversion	Baseline BNP and NT-proBNP levels did not predict long-term sinus rhythm maintenance; plasma BNP decreased significantly 24h post-EC, but NT-proBNP did not
11	Moritz F. Sinner et al (2014)	Pooled-cohort analysis adding BNP/CRP to the CHARGE-AF risk score, assessed via C-statistic and NRI over a 5-year horizon.	18,556 individuals from ARIC, CHS, and FHS cohorts	BNP raises C-statistic to 0.790; HR 1.66 per SD increase

Discussion

The studies reveal several common patterns as well as notable differences in the predictive power of BNP and NT-proBNP in predicting the onset and recurrence of atrial fibrillation (AF).

The results of studies demonstrated that elevated levels of BNP or NT-proBNP preceded the onset or recurrence of AF, confirming their clinical utility as early biomarkers for identifying high-risk individuals (3-5). In both prospective and retrospective cohorts, higher peptide concentrations were consistently linked to an increased risk of AF, particularly in patients with structural heart disease or those who had had prior cardiac surgeries. This supports the idea that neurohormonal activation takes place prior to arrhythmic manifestation and highlights the fact that BNP/NT-proBNP is more than just a passive measure of cardiac strain.

Disparities were observed while evaluating prediction accuracy for a particular population,since cardiac surgery and post-ablation patients experience significant atrial remodelling and volume overload, the trustworthy associations were seen in these investigations (4, 8, 11). However, studies involving non-cardiac or systemic populations, such as those with acute stroke, chronic renal disease, or critical illness, also indicated that BNP/NT-proBNP elevation was an independent predictor of AF, albeit with a reduced sensitivity (5, 9, 12) the biomarker retains its predictive significance in a range of clinical contexts, its risk prediction thresholds may need to be adjusted.

The biochemical difference between BNP and NT-proBNP was an issue. It was observed that NT-proBNP was better for population screening and long-term prognostication because of its longer plasma half-life and higher analytical stability (4, 6, 11). However, BNP was useful for short-term monitoring because it more accurately indicated acute haemodynamic stress

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and instantaneous atrial distension (3-5). Therefore, the clinical context should determine which of BNP and NT-proBNP is used, with BNP being the recommended method for acute evaluation and NT-proBNP for chronic follow-up.

Recently innovative approaches have been introduced, such as the notion of "total NT-proBNP," which quantifies both the glycosylated and non-glycosylated peptide forms (6). This has given better diagnostic sensitivity for AF detection than traditional assays, indicating that circulating NT-proBNP quantities may be underestimated by typical immunoassays. Additionally, multimarker models that combine NT-proBNP with fibrotic or inflammatory markers like high-sensitivity troponin or Galectin-3 have improved prediction accuracy, signalling a shift towards integrative, precision-based risk algorithms (13).

Although there are some limitations like ,Comparability and standardisation between investigations are limited by test method and cut-off value variability (3, 5, 8), Generalisability was hampered by several investigations' small sample sizes and brief follow-up periods (6,10). The prediction of AF may be complicated by comorbid diseases such inflammation, obesity, and renal dysfunction that independently raise BNP (5,7, 12). Causal inference is limited by most research' observational design (4,9). Furthermore, the requirement for population-specific limits was highlighted by the infrequent analysis of ethnic and geographic differences in baseline BNP levels (11), but consistent results are in the favour of BNP role as a Predictor.

Conclusion

BNP and NT-proBNP consistently prove reliable biomarkers for predicting the onset, recurrence, and prognosis of atrial fibrillation. However, differences in assays, cut-off values, and patient profiles limit clinical standardization. Integrating multi-marker models and novel measures, such as total NT-proBNP may enhance predictive precision. Large-scale, prospective trials should be conducted to evaluate BNP-guided intervention strategies for AF prevention and management.

BNP and NT-proBNP serve as valuable, non-invasive biomarkers for early detection, risk stratification, and prediction of atrial fibrillation recurrence. Optimal results can be achieved by using individual cardiac monitoring.

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