

Are we using BNP and NT-proBNP only to diagnose or also to understand risk?

Why the prognostic value of natriuretic peptides may be underutilized in clinical practice

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For laboratory professionals and clinicians, confidence in the clinical diagnostic value of B-type natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP) is grounded in high-quality evidence and strong recommendations in major heart failure guidelines. Both biomarkers are recognized as valuable tools to aid in the diagnosis of heart failure by helping distinguish cardiac from non-cardiac causes of dyspnea. They are now embedded in routine clinical decision-making across acute care settings.^{1,2} Yet evidence and guideline support for BNP and NT-proBNP extend beyond diagnosis. These biomarkers also support risk stratification, help establish prognosis in hospitalized patients, and when measured before discharge, may clarify patient trajectory and post-discharge prognosis. The question is whether laboratories and clinicians are fully leveraging this prognostic value or whether diagnostic utility is overshadowing an equally important opportunity to guide risk-informed care?



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When a BNP or NT-proBNP test is ordered, the immediate focus is often diagnostic: Does this patient have heart failure? Increasingly, however, the literature suggests natriuretic peptides may

offer insight beyond diagnosis, including what the result suggests about short- and longer-term risk.¹ The distinction between diagnosis and risk assessment is clinically important.

A diagnosis helps clinicians understand what is happening today; risk assessment helps clinicians understand what may happen next. A growing body of evidence suggests that BNP and NT-proBNP may help inform both questions when interpreted in the appropriate clinical context.

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LEARNING OBJECTIVES

Upon completion of this article, the reader will be able to:

LEARNING OBJECTIVES

1. Identify the established diagnostic roles of BNP and NT-proBNP in the evaluation of patients with suspected heart failure.
2. Differentiate between the diagnostic and prognostic applications of natriuretic peptide testing.
3. Interpret key evidence-based findings regarding the prognostic significance of BNP and NT-proBNP concentrations, including their association with adverse cardiovascular outcomes and rehospitalization risk.



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We have become very good at using natriuretic peptides to diagnose heart failure

There is a reason BNP and NT-proBNP have become deeply embedded in cardiovascular care. The diagnosis of acute heart failure is rarely straightforward. Dyspnea is one of the most common reasons patients seek emergency care, yet its causes are remarkably diverse. Pulmonary disease, obesity, renal dysfunction, atrial fibrillation, and heart failure often

present with overlapping symptoms, creating diagnostic uncertainty when rapid treatment decisions are required.⁵

In this environment, natriuretic peptides have consistently demonstrated clinical value. In a prospective multicenter clinical trial involving patients presenting with suspected acute heart failure, NT-proBNP demonstrated strong diagnostic performance, with an area under the receiver operating characteristic curve (AUC) of 0.87.⁵ The PRECISE-HF study, which enrolled more than 2,300 patients presenting with suspected acute heart failure across 17 US emergency departments, also reported an AUC of 0.87.⁵ Perhaps most importantly, low NT-proBNP concentrations remain highly effective for excluding acute heart failure: In both studies, NT-proBNP concentrations below 300 ng/L demonstrated approximately 95% negative predictive value and 96% sensitivity for ruling out acute heart failure in patients presenting with dyspnea.^{5,6}

With BNP and NT-proBNP recognized as valuable tools for establishing a diagnosis of heart failure, the question arises: what other clinical uses can these markers support?

Diagnosis is only one part of clinical decision making

Consider two patients arriving in the emergency department with shortness of breath. Both are ultimately diagnosed with heart failure, receive appropriate treatment, and improve clinically, but their futures may differ dramatically. While one may remain stable for months, the other may return to the hospital within weeks, experience progressive deterioration, or suffer a major adverse cardiovascular event. Whereas diagnosis identifies disease, risk assessment identifies vulnerability. The distinction matters because healthcare is increasingly moving toward earlier intervention, risk-based management, and more personalized care pathways. As care shifts in this direction, biomarkers capable of providing insight into future outcomes, such as natriuretic peptides, become especially valuable.

The evidence suggests natriuretic peptides are also prognostic biomarkers

The 2023 scientific statement from the Heart Failure Association of the European Society of Cardiology, the Heart Failure Society of America, and the Japanese Heart Failure Society describes natriuretic peptides as biomarkers with

both diagnostic and prognostic value.¹ Importantly, the statement notes that higher BNP and NT-proBNP concentrations are associated with increased risk of adverse short- and long-term outcomes, including all-cause mortality and cardiovascular mortality.¹

This observation is not isolated. A meta-analysis examining 66 prospective studies involving more than 83,000 individuals found that each standard deviation increase in BNP or NT-proBNP concentration was associated with a 74% higher risk of major adverse cardiovascular events.³ One of the most compelling findings was that the prognostic relationship persisted not only in patients with heart failure, but also in populations without established heart failure.³

Taken together, these findings suggest BNP and NT-proBNP may provide clinically meaningful prognostic information beyond their well-recognized diagnostic role.

Viewed through this lens, BNP and NT-proBNP are not only diagnostic tests, but also indicators of clinical trajectory. Recognizing this broader role may help laboratories communicate the clinical value and limitations of these biomarkers more effectively.

The signal persists in contemporary heart failure care

One criticism often directed at biomarker studies is that treatment paradigms evolve. Heart failure management today looks very different from it did a decade ago, with substantial expansion of guideline-directed medical therapy, including ARNI and SGLT2 inhibitor therapies. Importantly, NT-proBNP continues to demonstrate prognostic relevance within this contemporary treatment landscape. In a contemporary cohort of patients with heart failure with reduced ejection fraction, NT-proBNP concentrations ≥ 1858 pg/mL were independently associated with more than a twofold increase in the risk of 90-day mortality or heart failure rehospitalization.⁴ Similarly, the PRECISE-HF study demonstrated that higher NT-proBNP concentrations were associated with shorter major adverse cardiovascular event-free survival: patients with NT-proBNP concentrations ≥ 1000 ng/L experienced significantly greater rates of adverse cardiovascular outcomes during follow-up.⁶ These findings suggest that NT-proBNP may help identify patients who remain vulnerable after diagnosis has been established.

The opportunity may be larger than heart failure

Historically, BNP and NT-proBNP have been viewed through the lens of heart failure diagnosis and management. Their biological relationship to myocardial wall stress and ventricular dysfunction is well established.⁷ However, if elevated concentrations consistently identify individuals at greater risk of future cardiovascular events regardless of heart failure status, then the clinical value of these biomarkers may be broader than previously appreciated.³ These observations suggest that natriuretic peptide results may provide clinically relevant information about future cardiovascular risk.

Turning results into clinical insight requires context

Healthcare systems today face increasing pressure to improve outcomes while managing constrained resources, and laboratory medicine is evolving accordingly. Historically, laboratories were expected to generate accurate results. Increasingly, they are also expected to support clinically actionable insights. For laboratories, this shift is not simply about increasing testing volume or adding another assay to a menu. It is about helping clinicians extract greater clinical value from laboratory information that already exists. Natriuretic peptides may represent one of the clearest examples of that opportunity. The evidence increasingly suggests that BNP and NT-proBNP may provide information relevant to diagnosis and future cardiovascular risk.⁵ The opportunity is to interpret existing natriuretic peptide results within the appropriate clinical context and to communicate both their diagnostic role and the potential information they may provide about future cardiovascular risk. As with any biomarker, BNP and NT-proBNP results should be interpreted in conjunction with the patient's overall clinical presentation, applicable clinical guidelines, and the intended use of the specific assay being used.⁵

As access to natriuretic peptide testing continues to expand, laboratories may be increasingly positioned to support both diagnostic and risk-informed clinical decision-making.⁵

Context still matters

Recognizing prognostic value does not eliminate the need for thoughtful interpretation. In fact, it makes interpretation even more important. Age, obesity,



chronic kidney disease, atrial fibrillation, and pre-existing heart failure all influence natriuretic peptide concentrations.⁵ For example, obesity may suppress natriuretic peptide concentrations, while atrial fibrillation and renal dysfunction may elevate them independent of acute

decompensated heart failure.⁵ Recent analyses in patients with chronic kidney disease suggest that adjusted NT-proBNP thresholds may preserve diagnostic performance.⁹

These findings reinforce an important principle: clinical insight comes not from the biomarker alone but from interpreting the result within the appropriate clinical context. While the laboratory provides the result, its greatest value emerges when that result is integrated with the patient's overall clinical presentation, comorbidities, and risk profile.

Are we fully using what BNP and NT-proBNP are telling us?

The laboratory community has spent years helping clinicians answer one important question: Is heart failure contributing to this patient's presentation? The evidence reviewed here suggests natriuretic peptides may simultaneously be answering another: What does this result suggest about this patient's future cardiovascular risk?

This question aligns with a broader transformation occurring across healthcare. As medicine increasingly emphasizes prevention, risk stratification, and personalized management, the value of laboratory testing may be measured not only by its ability to identify disease but also by its ability to illuminate future risk. Viewed through that lens, BNP and NT-proBNP may represent more than diagnostic biomarkers. They may represent an opportunity to advance clinical capabilities by transforming laboratory data into clinically actionable insights.

The future conversation surrounding natriuretic peptides may focus less on whether they can aid in heart failure diagnosis and more on how consistently healthcare systems, clinicians, and laboratories use the prognostic information these biomarkers may provide. 

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This article discusses published evidence regarding BNP and NT-proBNP as biomarkers. The clinical performance, indications for use, and intended applications of any specific BNP or NT-proBNP assay may vary. Healthcare professionals should consult the applicable Instructions for Use, product labeling, and local clinical guidelines when interpreting results. References to BNP and NT-proBNP in this article do not constitute additional claims for any specific Beckman Coulter assay beyond its cleared, approved, or intended use.



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