COLLEGE of AMERICAN PATHOLOGISTS

B-Type Natriuretic Peptide (BNP) or N-Terminal-ProBNP (NT-proBNP) for Clinicians

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SYNOPSIS AND RELEVANCE

BNP is frequently used in the evaluation of dyspnea and to assess risk and prognosis of patients with congestive heart failure (CHF). Rational use of BNP or NT-proBNP can improve patient care by:

1. Helping to differentiate dyspnea in patients caused by pulmonary dysfunction from dyspnea caused by CHF.
2. Stratifying risk and prognosis in patients with CHF.
3. Avoiding confusion or misinterpretation of fluctuating BNP or NT-proBNP levels due to change in fluid status or biologic variation by decreasing unnecessary repeat testing before pharmacologic therapy of CHF can show effectiveness.

INSIGHTS

1. BNP or NT-proBNP is useful to predict morbidity and mortality in congestive heart failure (CHF).
2. BNP or NT-proBNP is useful to differentiate pulmonary causes of dyspnea from cardiac causes of dyspnea (CHF).
3. Repeat or serial BNP or NT-proBNP levels are of dubious value in inpatients.

BACKGROUND

B-type natriuretic peptide (BNP) is a member of a family of four natriuretic peptides, stored as a polypeptide precursor, proBNP, in secretory granules in cardiac ventricles. After proBNP is secreted in response to volume overload and resulting myocardial stretch, it is cleaved to a biologically inert N-terminal fragment NT-proBNP and a biologically active hormone, BNP. BNP results in natriuresis, diuresis, and reduction in blood pressure through vasodilation.

Guidelines from the American College of Cardiology and American Heart Association recommend use of plasma BNP or NT-proBNP measurements to assess risk and prognosis in patients with known heart failure.[1] For example, measurement of BNP in heart failure patients at discharge provides prognostic information about risk of death and readmission within 6 months. In addition, BNP may be used to differentiate between cardiac and non-cardiac causes of dyspnea of uncertain etiology, and as a diagnostic adjunct when the clinical diagnosis of heart failure is uncertain, especially in the acute care setting.

Plasma BNP concentrations can vary with the assay used (due to different manufacturer antibodies) and there is no simple conversion factor to compare BNP and NT-proBNP levels.[2] Optimal reference intervals should account for age, gender, and body mass index (or other measure of body composition) as well as renal function. Elevated natriuretic peptide levels should be interpreted in the context of other clinical information; they may lend weight to the diagnosis of CHF but should not be used in isolation to diagnose heart failure. New dual drug therapies, sacubitril/valsartan (Entresto), that include an angiotensin receptor neprilysin inhibitor (ARNI) (sacubitril) combined with an angiotensin receptor blocker (valsartan) are aimed at reducing the risk of cardiovascular death and hospitalization for patients with CHF and reduced ejection fraction. Since BNP is degraded by neprilysin, treatment with ARNI causes elevation of BNP levels. Some have recommended use of NT-proBNP because of the effect of neprilysin inhibition on BNP levels,[3] while other studies have recommended monitoring both BNP and NT-proBNP.[4] However, the clinical and analytical studies are limited, and the diversity of both BNP and NT-proBNP assays used in clinical laboratory practice have not been adequately evaluated to provide an evidence-based conclusion regarding the appropriate assay to use when a patient is treated with ARNI.[5] BNP and NT-proBNP should never be ordered together during CHF treatment or with ARNI, and either BNP or NT-proBNP have shown comparable prognostic performance in the PARADIGM-HF (Prospective Comparison of ARNI with ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure) trial.

The use of serial measurements of plasma BNP or NT-proBNP to manage patients with heart failure remains debatable and is not, as yet, validated or recommended for routine care. A number of factors confound the use

of plasma BNP or NT-proBNP for monitoring in heart failure, including wide biological variation, lack of appropriate target values, failure to show an impact on morbidity or mortality, and questionable impact on clinical management. Nevertheless, if serial measurements are used for heart failure management, the minimum time interval needed to observe any correlation with outcome and plasma BNP or NT-proBNP values from therapy is at least 2 to 4 weeks in outpatients, and several clinical trials have used serial measurements every 12 weeks. For inpatients, a commonly accepted interval for BNP or NT-proBNP testing is once per admission.

Population studies also show that an elevation in plasma BNP or NT-proBNP has predictive value for the development of heart failure or other cardiovascular events in patients with stable angina and acute coronary syndrome.[6] However, there are no guidelines or recommendations for routinely using BNP or NT-proBNP for this purpose. It has also been reported that measurement of BNP and NT-proBNP is of little value for predicting the prognosis of, or monitoring the clinical status of, critically ill patients.[7]

This information may be used to guide utilization practices; specifically, to assess the indications for, and frequency of, plasma BNP or NT-proBNP testing. For example, frequent (eg, daily) monitoring of plasma BNP or NT-proBNP in inpatients would be difficult to justify as an appropriate clinical practice. In this case, an intervention may be warranted to control unnecessary testing. As one example, Lum[8] reported on the use of a protocol that required cardiologist approval for repeat BNP measurements that successfully reduced unnecessary testing. Others have seen benefit from the implementation of clinical decision support tools to reduce unnecessary BNP testing, as well as several other analytes.[9]

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