

Using B-Type Natriuretic Peptide (BNP) in Heart Failure

Approximately 5 million adults have congestive heart failure (CHF) in the US, and approximately 550,000 new cases of heart failure are diagnosed in this country every year. The incidence of CHF increases dramatically in the elderly population: Approximately 10% of men and women older than 75 years have the disease. Cardiovascular disease (CVD) remains the leading cause of death in both men and women in the United States, and CHF remains the most common cause of hospitalization in patients older than 65. Recent statistics from the American Heart Association (AHA) indicate that CHF-related mortality rose 35% from 1992 to 2002. The high disease prevalence and high mortality associated with CHF mandate aggressive diagnostic and management strategies. The revised American College of Cardiology/AHA heart failure guidelines incorporate a new classification system to more readily identify high-risk patients and to direct primary and secondary prevention efforts.

ACC/AHA Heart Failure Stages

Stage	Description
A	Patients without structural heart disease but at increased risk to develop heart failure. Risk factors include hypertension, diabetes mellitus, coronary artery disease, and family history of heart disease. Treatment recommendations include management of hypertension and/or lipids, smoking cessation, regular exercise, limitation of alcohol intake, ACE inhibitor therapy as appropriate.
B	Patients with structural heart disease but no heart failure symptoms. Risk factors include LV hypertrophy, MI, left bundle branch block, diminished LV contractility, and asymptomatic valve disease. Treatment recommendations include all Stage A recommendations, ACE inhibitors and/or beta blockers as appropriate.
C	Patients with structural heart disease with past or current heart failure symptoms (exertional dyspnea, peripheral edema, fatigue). Correlates with NYHA Heart Failure Class I, II, and III. Treatment recommendations include all Stage A and B recommendations, ACE inhibitors, beta blockers, diuretics, digoxin, cardiac resynchronization therapy, implantable cardioverter defibrillator if appropriate, and sodium restriction.
D	Patients with refractory end-stage heart failure (heart failure symptoms at rest despite maximal medical therapy). Correlates with NYHA Heart Failure Class IV. Treatment recommendations include all Stage A, B, and C recommendations, positive inotropes, heart transplant, ventricular assist device, hospice care.

Heart Failure Pathophysiology

CHF occurs when the heart cannot meet the body's metabolic demands because of a structural or functional problem. In *diastolic heart failure*, patients have normal ventricular pumping function but impaired ventricular relaxation. By contrast, *systolic heart failure* arises from ventricular pump dysfunction, which frequently occurs after a myocardial infarction (MI). The ventricles lose the ability to contract and empty effectively, causing volume and pressure overload in these heart chambers. Systolic heart failure causes the ventricles to distend, which leads to the release of neurohormones. The natriuretic peptides are among the newest groups of neurohormones to be studied.

Natriuretic Peptides

Both atrial natriuretic peptide (ANP) and b-type natriuretic peptide (BNP) appear to play an important role in CHF. Both of these peptides cause natriuresis and vasodilation, and they inhibit the renin-angiotensin system. BNP has been reported to be a more sensitive, stable, and reliable marker of left ventricular (LV) dysfunction than is ANP. BNP is stored in heart tissue; it begins as a precursor called pro-BNP. Pro-BNP is released into the blood in response to increased wall stress caused by ventricular pressure and volume overload. Once pro-BNP enters the blood, it is converted into BNP, its active hormone, and an inactive metabolite called N-terminal pro-BNP. BNP and its inactive metabolite can be measured in the blood and are stable markers, BNP has a half-life of about 20

minutes. N-terminal pro-BNP has a slower clearance from the body and the half-life is about 90 minutes.

When a patient develops decompensated heart failure with volume and pressure overload in the left ventricle, the pressures measured inside the heart (ie, LV end-diastolic pressure, pulmonary capillary wedge pressure, and right atrial pressure/central venous pressure) increase, and the LV ejection fraction and left ventricular stroke work index decreases. Using an invasive catheter routinely to measure intracardiac pressures is usually not desirable because of the cost and increased risk. Serum BNP levels have been found to correlate with elevated heart pressures and decreased myocardial contractility obtained during an episode of acute heart failure.

Measuring and Interpreting BNP Values in Heart Failure

Several different tests are available to measure serum BNP levels; therefore, nurse practitioners (NPs) should ascertain which particular test is used in their practice facility. The Elecsys® pro-BNP Immunoassay actually measures N-terminal pro-BNP, whereas the Biosite Triage® Test, Abbott AxSYM Test, and the Bayer ADVIA Centaur Test measures BNP itself. All test results are reported in pg per mL. Several studies comparing BNP and N-terminal BNP reveal similar sensitivity, specificity, and diagnostic accuracy.

Normal BNP levels vary with age and sex. Mean normal BNP levels with the Biosite Triage Test are 26 pg per mL for persons aged 55 to 64, 31 pg per mL for those aged 65 to 74, and 63 pg per mL for those aged 75 years or older. Women tend to have slightly higher normal BNP levels, as well as higher BNP levels in all heart failure stages, than do men in all age ranges. It is not known why BNP levels are higher in the elderly and in women. In elderly patients, cardiac hypertrophy and a stiffer left ventricle wall, which are part of the normal aging process, are likely contributory. With regard to women, it has been suggested that female hormones may cause the higher BNP levels reported. This area needs further investigation, but present data suggest that nurses should consider a patient's age and sex when interpreting BNP results.

Patients with severe LV dysfunction, as compared with those with milder forms of CHF, have a greater volume overload and more ventricular stretching, and have been found to have higher serum BNP levels.

BNP Levels with Different Heart Failure Classes

CHF Class/Stage	BNP Levels (pg/mL)
Mild (NYHA Class I)	83-152
Mild to moderate (NYHA Class II)	235-322
Moderate to severe (NYHA Class III)	459-590
Severe (NYHA Class IV)	960-1119

(NYHA = New York Heart Association)

LV systolic dysfunction is associated with higher BNP levels than is diastolic dysfunction and/or right ventricular systolic dysfunction. Patients with isolated LV diastolic dysfunction will usually have BNP levels between 300 and 480 pg per mL, whereas patients with LV systolic dysfunction usually have BNP levels between 550 and 820 pg per mL. Patients with both systolic and diastolic LV dysfunction can have BNP levels between 800 and 1300 pg per mL or higher, depending on disease severity. As BNP levels increase, the positive predictive value for diagnosing systolic heart failure also increases. BNP by itself does not differentiate between systolic and diastolic heart failure. A patient with a presumed normal ejection fraction who presents with CHF and moderately elevated BNP levels is very likely to have diastolic heart failure. An echocardiogram should be performed for a definitive diagnosis. The n-terminal pro-BNP Investigation of Dyspnea in the Emergency Department (PRIDE) Study reported a higher sensitivity for diagnosing isolated diastolic heart failure with NT pro-BNP rather than BNP. Other diseases, can cause ventricular dilatation and stretch, and lead to elevated BNP levels.

BNP Levels with Different Diseases

Disease	BNP Levels (pg/mL)
Severe aortic valve stenosis	100-350
Acute pulmonary embolus	100-500
Acute MI	100-400
Pulmonary hypertension	300-500
Right-sided heart failure	300-600
LV diastolic dysfunction	300-480
Acute decompensated LV heart failure/systolic heart failure	>800

Differentiating Between Cardiac and Pulmonary Dyspnea

One of the most important indications for measuring BNP levels is to aid in distinguishing between cardiac dyspnea and pulmonary dyspnea. In many cases, patients with CHF present with nonspecific signs and symptoms that can delay diagnosis and treatment. Serum BNP results may be extremely useful in this regard: Numerous studies have demonstrated that the BNP test is very rapid, useful, and reliable in differentiating between cardiac dyspnea and pulmonary dyspnea, even in patients with a history of chronic obstructive pulmonary disease (COPD).

The “Breathing Not Properly” Study was a large multicenter investigation involving patients who presented to an emergency department (ED) with acute dyspnea. A serum BNP level was obtained to assist in differentiating between heart failure and pulmonary disease. In this study, a BNP level of 100 pg per mL or higher was 90% sensitive and 73% specific for diagnosing CHF. The negative predictive value of heart failure in patients with a BNP level less than 50 pg per mL was 96%. Researchers also evaluated a subgroup of patients with COPD but no *prior* history of heart failure who presented with dyspnea: The mean BNP value was 587 pg per mL in those who had heart failure and 108 pg per mL in those without heart failure. These findings demonstrate that BNP is useful in diagnosing CHF even in patients with pre-existing pulmonary disease.

BNP is most informative and useful in patients with very low or very high serum levels. The greatest advantage of BNP is its *high negative predictive value* of heart failure: That is, if a patient’s serum BNP is less than 80 pg per mL, then the likelihood that he or she does *not* have CHF is greater than 90%. Although acute heart failure is very unlikely in patients with a BNP level less than 100 pg per mL, it is possible that the BNP level was measured too early (<1 hour after the onset of acute symptoms) and simply did not have enough time to become elevated. Thus, nurses may need to obtain serial BNP levels in patients who present very early after the onset of acute dyspnea. Furthermore, low BNP levels may occur in patients with CHF who do not have ventricular dysfunction (eg, those with mitral stenosis or acute mitral regurgitation). A BNP level of 100 to 400 pg per mL indicates that the patient may have mild heart failure, right-sided heart failure, pulmonary hypertension, severe aortic stenosis, acute pulmonary emboli, or an acute MI. If the BNP level exceeds 400 pg per mL, then heart failure is highly likely, but the patient should also be evaluated for severe renal disease.

Using BNP Levels to Guide CHF Management

Obtaining BNP levels during hospitalization for CHF not only can optimize treatment decisions and shorten length of stay, but it can also provide useful prognostic information. If BNP levels rise during hospitalization, patients are more likely to be readmitted within 30 days of discharge and/or have a higher mortality rate. By contrast, if BNP levels decline during hospitalization, patients are less likely to experience an adverse event, be readmitted to the hospital, or die within 1 year. One study found that if the BNP level before discharge was less than 230 pg per mL, patients were less likely to be readmitted within 12 months. Another study in patients younger than 65 years found that if the BNP level were less than 132 pg per mL on hospital discharge, the patient had a better event-free survival and fewer adverse events.

Clinical Implications

Serial BNP levels should be obtained in patients hospitalized with CHF in order to monitor response to therapy: The BNP level just before discharge is the one variable most strongly associated with readmission and mortality. The higher the BNP level just prior to hospital discharge, the earlier the patient may be readmitted or suffer an adverse cardiovascular event. The optimal discharge BNP level has not yet been established; additional research studies are warranted. The most important goal is to get the BNP level to decrease during hospitalization as much as possible; the greater the decrease, the better the patient outcome. One recent study found that when BNP guided therapy was used to manage elderly heart failure patients the total treatment cost was \$2,030 less than when BNP was not used.

Conclusion

BNP is a valuable test for nurses to use to complement their clinical assessment skills. Nurses can have a tremendous impact on improving both short-term and long-term patient outcomes by utilizing BNP monitoring.

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