OBJECTIVES:

1. Describe the optimal approaches to the diagnosis of acute decompensated heart failure (ADHF).
2. Describe the role of brain natriuretic peptide (BNP) in evaluating patients with ADHF.

INTRODUCTION

To determine optimal therapy for patients with acute decompensated heart failure (ADHF), the emergency physician must be able to confidently diagnose patients with heart failure. This requires knowledge of the diagnostic methods used to identify patients with heart failure as well as knowledge of the different etiologies of this disease.

Heart Failure Etiology

The potential etiologies of ADHF are multifactorial. They can be broadly divided into two major categories: (1) the underlying etiology of the heart failure (the baseline cause of dysfunction), and (2) the etiology of the acute precipitant that resulted in worsening from the chronic compensated state. For some patients, particularly those presenting for the first time, these two components may be identical. Coronary artery disease and chronic hypertension are the two most common causes of heart failure; however there are a myriad of other medical conditions that can also result in heart failure. They include dilated, hypertrophic, and restrictive cardiomyopathies; myocarditis; pericardial tamponade; valvular heart disease; and secondary effects of pulmonary diseases or metabolic disorders. Approximately 80% of patients presenting to the emergency department with ADHF have a prior diagnosis of heart failure so determining the etiology of the underlying (baseline) heart failure can usually be obtained by asking the patient or reviewing the medical records.

When the etiology of the underlying heart failure is not known, investigation of the underlying etiology is important to determine whether there is a reversible component of the disease; however, this is usually beyond the scope of the emergency physician. There causes are, however, several etiologies for heart failure that the emergency physician should be aware of, as they may require modification of initial therapy. These are severe aortic stenosis, idiopathic hypertrophic subaortic stenosis or hypertrophic obstructive cardiomyopathy, and pulmonary hypertension. Identification of patients with these conditions is important because aggressive preload and afterload reduction can lead to cardiovascular collapse since these patients cannot increase their forward blood flow through the fixed mechanical lesion (eg, a flow-restricted aortic valve).

Reliance upon clinical impression alone leads to diagnostic uncertainty because the signs and symptoms of heart failure are relatively nonspecific.
Separate and distinct from the initial etiology is the cause of the acute precipitant. Heart failure can be exacerbated by worsening of the underlying condition, by medication or dietary noncompliance, or by development of new or complicating medical conditions such as ischemia, dysrhythmias, pulmonary embolus, or infection.

**Diagnosis of Acute Decompensated Heart Failure**

The diagnosis of ADHF has traditionally been challenging. Reliance upon clinical impression alone leads to diagnostic uncertainty because the signs and symptoms of heart failure are relatively nonspecific. Studies have shown that the inter-rater reliability of heart failure signs, such as an S3, or even the presence or absence of rales, is not very good. Key symptoms such as shortness of breath are nonspecific in patients with comorbidities such as reactive airway disease. Likewise, routine laboratory tests, electrocardiograms, and radiographs cannot be relied upon to always guide an accurate and appropriate diagnosis.

Despite these challenges, diagnostic capabilities in heart failure have improved in recent years with recognition of the role that B-type natriuretic peptide (BNP) plays in the disease. In addition to being a pump, the heart is an endocrine organ that functions together with other physiological systems to control fluid volume. The myocardium produces natriuretic peptides, one of which is B-type natriuretic peptide (BNP), a hormone with diuretic, natriuretic, and vascular smooth muscle relaxing actions. BNP is a natural antagonist for the sympathetic nervous system and the renin-angiotensin-aldosterone axis. BNP is secreted in response to wall stretch, ventricular dilation and/or increased filling pressures. Measurement of endogenous BNP is thus a clinically reasonable way to assess whether a particular patient has heart failure.

The Breathing Not Properly study was a multinational study of 1,586 patients who presented to emergency departments with shortness of breath. It showed that BNP levels alone were more accurate predictors of the presence or absence of heart failure than any historical factors, physical findings, or laboratory values.\(^1\)\(^2\) In fact, BNP was more accurate than emergency physician estimates of the likelihood of heart failure. BNP levels were much higher in patients who were subsequently diagnosed with heart failure than in those diagnosed with noncardiac dyspnea (675 pg/dL vs. 110 pg/dL). A BNP cutoff value of 100 pg/dL had a sensitivity of 90% and a specificity of 76% for differentiating heart failure from other causes of dyspnea, and a cutoff of 50 pg/mL had a negative predictive value of 96%. Without knowledge of BNP levels, emergency physicians had a 43% indecision rate in trying to make a diagnosis. BNP levels added significantly to the clinical impression, as it was found that clinical decision-making in conjunction with BNP levels could have reduced the diagnostic indecision rate to 11%. In multivariate analyses, BNP levels always contributed to the diagnosis, even after taking into account findings from the history and physical examination. Thus, the Breathing Not Properly trial demonstrated that BNP levels have significant clinical utility for both the diagnosis and risk stratification of heart failure patients in the emergency department.\(^1\)\(^2\) Both diastolic and systolic dysfunction are associated with high BNP levels of more or less the same degree.\(^3\)

BNP must be used with caution in certain populations. Although BNP can help differentiate pulmonary from cardiac etiologies of dyspnea, some types of lung disease, such as cor pulmonale and pulmonary embolism have elevated BNP levels; however BNP is not usually elevated to the same high level as it is in patients with ADHF. In a subgroup of patients with a history of reactive airway disease in the Breathing Not Proper trial, in 417 subjects with a history of asthma or chronic obstructive pulmonary disease without a history of heart failure, 21% were found to have newly discovered ADHF. Only 37% were identified in the ED, while a BNP >100 pg/mL identified 93%\(^4\). Additionally, BNP levels >100 pg/mL provided diagnostic information beyond that obtained from individual chest radiographic indicators.\(^5\)
There is a significant inverse relationship between body weight (BMI) and BNP levels. Thin patients with heart failure are more likely to have elevated BNP values in the absence of heart failure. Conversely, obese patients are more likely to have lower levels of BNP for any given severity of heart failure. As a result, BNP levels should be used with caution in patients with obesity, unless of course baseline BNP values are known. When baseline levels are known in obese patients, it would be reasonable to use the baseline level to determine if the current BNP is elevated or not, thereby allowing the obese patient to be followed for a new acute decompensation.

The Breathing Not Proper Trial demonstrated that BNP is useful for the diagnosis of ADHF in the ED. The REDHOT Study suggests that BNP might also be useful to improve triage and disposition of patients who present to the ED with heart failure. This trial demonstrated a “disconnect” between the physician perception of the severity of heart failure and the actual BNP value. In the first phase, 464 patients visiting EDs with complaints of breathing difficulty had BNP measurements taken on arrival. Physicians were blinded to BNP results; however inclusion in the trial required a BNP > 100 pg/ml. Patients discharged from the ED had higher BNP levels than those admitted to the hospital (976 pg/ml vs 766 pg/ml). With respect to the admitted patients, 11% had BNP levels < 200 pg/ml, which is indicative of less severe ADHF: most of these patients were perceived to have class III or IV heart failure. Mortality for these patients was 0% at 30 days and only 2% at 90 days, suggesting that patients with heart failure and low levels of BNP might have been safe for discharge. With respect to patients that were actually discharged, 78% had BNP levels >400 pg/mL. At 90 days, mortality was 9%. There was no mortality for those discharged with BNP levels <400 pg/mL. This suggests that use of BNP in the ED might also help determine which well appearing patients are at high risk for a bad outcome over the short term (90 days). It also suggests that when the clinician thinks the patients is safe for discharge but the BNP level is over 400 pg/ml, the clinician may wish to reconsider the disposition decision. Almost one in ten patients with these characteristics had died at 90 days. Thus, although the REDHOT trial did not demonstrate that admitting these patients to the hospital would alter the outcome, the clinician may wish to think carefully about the decision to discharge this cohort of patients (BNP > 400 pg/ml).

Elevations of BNP are useful for assessing risk stratification and prognosis in patients with heart failure. BNP levels are related to changes in limitations of physical activities and functional status. Harrison et al. followed 325 patients for 6 months after an index visit to the ED for dyspnea. Higher BNP levels were associated with a progressively worse prognosis. The relative risk of 6-month ADHF admission or death in patients with BNP levels >230 pg/mL was 24 times the risk of patients with levels less than 230 pg/mL. When combined with troponin I, both troponin I and BNP alone and in combination predict survival in ADHF. Both together have additive prognostic risk.
The utility of BNP to diagnose ADHF is well established however, it’s ability to drive treatment is still under study. REDHOT II is a randomized controlled trial comparing treatment and outcomes of patients where therapy is guided by serial BNP measurements in the experimental group. This study, which should complete enrollment soon, should shed some light on the utility of BNP to guide treatment.

Due to the large volume of data on the clinical utility of BNP, consensus panel guidelines were published last year. These recommendations state:

1. For patients presenting to emergency services with dyspnea, a history, physical examination, chest x-ray, and ECG should be performed together with laboratory measurements that include BNP.
2. As BNP levels rise with age and are affected by gender, comorbidity, and drug therapy, the plasma BNP measurement should not be used in isolation from the clinical context.
3. If the BNP level is <100 pg/mL, then heart failure is highly unlikely (negative predictive value, 90%).
4. If the BNP level is >500 pg/mL, then heart failure is highly likely (positive predictive value, 90%).
5. For BNP levels between 100–500 pg/mL, one should consider the following conditions in the differential diagnosis:
   a. Baseline BNP value due to stable underlying dysfunction
   b. Right ventricular failure from cor pulmonale
   c. Acute pulmonary embolism
   d. Renal failure
6. Patients may present with ADHF with normal BNP levels or with BNP levels below what would be expected can occur in the following situations:
   a. Flash pulmonary edema (<1–2 hours)
   b. Heart failure up-stream from the left ventricle (i.e., acute mitral regurgitation from papillary muscle rupture)
   c. Obese patients (body mass index [BMI] >30 kg/m²)

REFERENCES


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