

# BRAIN NATRIURETIC PEPTIDE AND HEART FAILURE

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## Introduction

Clinicians are increasingly using biochemical markers to diagnose and monitor disease. Thyroid function tests provide a good example. Could brain natriuretic peptide (BNP) become a marker of heart failure as thyroid-stimulating hormone (TSH) is to thyroid disease?

BNP is a 32 amino acid peptide secreted chiefly from the cardiac ventricles in response to ventricular strain associated with pressure and volume overload. Although found mainly in heart muscle, it was isolated originally from porcine brain. Hence its name. On secretion, proBNP, the storage form of BNP, is split into the inactive N-terminal-proBNP and the endocrinologically active BNP. The active moiety promotes natriuresis, diuresis and vasodilatation. The blood concentration of BNP is raised in patients with cardiac disease, particularly with cardiac failure.

Plasma BNP and N-terminal-proBNP can be measured rapidly by radioimmunoassay or immunoradiometric assay. Reliable 20 minute near patient testing is also available. These technical advances have made the routine use of BNP practical.

## BNP as an aid to diagnosis of heart failure

The reliability of a clinical diagnosis of heart failure is poor, especially in primary care. Recent guidelines recommend that the clinical diagnosis of heart failure should be backed up by objective confirmation of underlying cardiac dysfunction. Echocardiography is the safest and most practical method of confirming dysfunction. However, there are huge numbers of suspected new cases of heart failure each year in Ireland. The overstretched diagnostic services cannot meet the need if all cases of suspected heart failure are referred for echocardiography. Might BNP help detect those patients most likely to benefit from imaging?

Several groups have shown the value of measuring BNP concentration in patients admitted to hospital with acute breathlessness. Although the diagnosis of heart failure in such circumstances is not as difficult as when patients have milder symptoms, BNP can help discriminate between those with breathlessness caused by heart failure from other causes.<sup>1</sup> In addition, rapid measurement of BNP using a BNP rapid assay kit in patients presenting to the Accident and Emergency Department can distinguish dyspnoea due to congestive heart failure from acute shortness of breath from lung disorders.<sup>2,3</sup>

BNP does not replace echocardiography. A normal BNP concentration virtually excludes left ventricular dysfunction, but a high concentration merely indicates the presence of

some cardiac problem which requires further cardiac evaluation. The high negative predictive value of BNP is most helpful in excluding the diagnosis of heart failure.

## BNP as a prognostic marker for patients with heart failure

Measurement of BNP levels at the Accident and Emergency Department accurately predicts future cardiac risk in patients who have acute dyspnoea due to congestive heart failure<sup>3</sup> and helps in assessing the prognosis.

Preliminary work from a few large population-based studies suggest that plasma BNP and N-terminal-proBNP concentrations are both highly associated with survival and the risk of rehospitalisation for heart failure patients. If these data are confirmed, it is likely that clinicians will use BNP measurement to help target more intensive treatment and follow up the patients most at risk of death or hospitalisation.

## A better way to assess control of the syndrome?

Monitoring patients with heart failure has been difficult, partly because of the absence of a biochemical marker for the early detection of deterioration. Increasing fluid retention is a late sign of worsening cardiac function and often needs hospital admission for restabilisation.

## Is BNP likely to be this marker?

With the advent of near patient testing for BNP, it might be possible for a patient with heart failure to monitor their disease just as patients with diabetes check their blood sugar. After appropriate education, many patients could adjust their medication using serial measurements. In one study, treatment guided by BNP measurements was compared to standard clinical assessment. Total cardiovascular events were reduced and the time taken before further admission to hospital was increased.<sup>4</sup>

## Other possible uses of BNP in heart failure

It has been suggested that BNP may play a role in modulating cardiac function, vascular function and fluid status in congestive heart failure.<sup>5,6</sup> This suggests a therapeutic potential for natriuretic peptides.

Nesiritide is a recombinant form of BNP. In one trial, a 24 hour infusion produced rapid and sustained haemodynamic improvement in patients with acute heart failure. The authors suggest that BNP may become a first-line therapy in such patients.<sup>7</sup>

Further evidence for its effectiveness in this situation is

provided by the results of the Vasodilatation in the Management of Acute Congestive Heart Failure Study. In this study, nesiritide was compared to nitroglycerin infusion over a three hour period. Nesiritide demonstrated superior haemodynamic and symptomatic improvement. On this basis, nesiritide was approved for treatment of acute decompensated heart failure.

### **Brave new world?**

BNP has changed from a research tool to a clinically useful test. In the near future, primary care physicians will use BNP to help confirm a clinical diagnosis of heart failure and assess the need for further cardiac assessment. Cardiologists will use it to evaluate prognosis and to monitor response to treatment. Serial measurements may allow earlier adjustment of therapy to prevent deterioration and reduce hospital admission.

### **References**

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