Plasma Brain Natriuretic Peptide Level: Marker for Heart Failure and Cardiovascular Disease

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Brain natriuretic peptide (BNP), also called B-type natriuretic peptide, is a member of structurally related neurohormones, the natriuretic peptides. This family also includes atrial natriuretic peptide (ANP) and C-type natriuretic peptide (CNP). BNP has recently gained a lot of popularity as a marker for diagnosis and management of heart failure. It has also been investigated as a prognostic marker in various other conditions. BNP, a 32 amino acid protein, was first isolated from porcine brain and therefore it is called brain natriuretic peptide. In human, BNP is mainly synthesised and secreted from the cardiac ventricles as a response to increased myocyte stretch following volume expansion and pressure overload and is metabolised by neutral endopeptidase into inactivated fragments. The precursor of BNP, pro-BNP is stored in secretory granules in myocyte. After being synthesised in the ventricle, pro-BNP is cleaved by a protease into its biologically active form, BNP, and N-terminal (NT)-proBNP, the biologically inactive amino portion. Compared to BNP, NT-proBNP has a longer half-life (60 to 120 min vs 15 to 20 min) and is more stable. NT-proBNP provides much the same information as BNP and its measurement is not affected by the administration of exogenous BNP. Assays for NT-proBNP are now available commercially. NT-proBNP or BNP is considered superior to ANP as potential diagnostic marker of acute heart failure because it is specific to the ventricles and the secretion of BNP occurs more rapidly in acute overload. BNP has effects on vasodilatation, natriuresis, diuresis and plays an important role in congestive heart failure as a counter-regulatory hormone. Plasma BNP or NT-proBNP level is increased in patients with heart failure and correlates with pulmonary capillary wedge pressure, left ventricular end-diastolic pressure, left ventricular ejection fraction and functional class.

Plasma NT-proBNP or BNP level as a marker for diagnosis and management of heart failure

Studies have shown that plasma levels of BNP facilitate rapid diagnosis of heart failure in acute care setting. The Breathing Not Properly study, included 1586 patients, showed that plasma BNP level was increased in heart failure patients presented with dyspnea. At a BNP level > 100 pg/ml, BNP had a sensitive of 90% and specificity of 73% to distinguish between heart failure and other causes of dyspnoea. BNP did better than all other clinical variables and clinical judgement of the emergency room physicians to diagnosis heart failure. Data from another study showed that rapid measurement of BNP in the emergency department, use in conjunction with other clinical information, improved the evaluation and treatment of patients with acute dyspnoea and reduced the time to discharge and total cost of treatment.

Measuring plasma BNP or NT-proBNP can also be used to screen for left ventricular dysfunction in the primary care setting in patients suspected of having heart failure. A local study was recently been conducted at the Pamela Youde Nethersole Eastern Hospital involving 50 Chinese patients suspected to have heart failure. Unpublished preliminary data showed that NT-proBNP levels were inversely related to left ventricular ejection fraction. Using a cutoff value of 100 pg/ml, the sensitivity and specificity to identify left ventricular systolic or diastolic dysfunction were greater than 90%. The negative predictive value was also over 90%, suggesting that patients with low levels could be ruled out from having left ventricular dysfunction and thus reduce excessive referrals for evaluating left ventricular function by echocardiogram. Indeed, the US FDA has approved NT-proBNP and BNP to be used as an aid for heart failure diagnosis and recent European guidelines of chronic heart failure has also included its use. BNP level is increased in patients with isolated diastolic heart failure and correlates with the severity of diastolic dysfunction. Accuracy of BNP for diagnosis of isolated diastolic heart failure approaches that for diagnosis of heart failure due to systolic dysfunction.

BNP level also becomes an important prognostic marker for patients with heart failure. Higher BNP level at the time of hospital admission in patients with decompensated heart failure is associated with poorer prognosis and can be used to identify patients who require more aggressive monitoring and treatment. There is some evidence to suggest that BNP levels may be used to guide heart failure therapy because BNP level decreases after optimisation of heart failure treatment. In one study, patients with heart failure were randomised to receive treatment guided by plasma NT-proBNP or by symptoms. ACE inhibitors and diuretics were used more frequently in the plasma-BNP-guided group during a mean follow-up of 9.5 months. Significantly fewer events were observed in the BNP-guided therapy group as well.
Emerging roles of plasma BNP level in other conditions

More recently, the prognostic implications of BNP and NT-proBNP have also been extended to patients with acute coronary syndrome (ACS). Data from a study in patients with ACS showed that baseline higher NT-proBNP level was associated with higher event rates. It is postulated that transient ischemia can induce BNP synthesis via an increase in wall stress. The levels of BNP and NT-proBNP may reflect the size or severity of the myocardial ischemia.

BNP level may be used as a marker of long-term mortality in patients with stable coronary disease. A study showed that the median NT-pro-BNP level was significantly lower among patients with stable coronary heart disease who survived than among those who died after a median follow-up of 9.2 years.

NT-proBNP or BNP may be used for screening of left ventricular hypertrophy (LVH) and diastolic dysfunction in patients with hypertension. It has been shown that in patients with hypertension, plasma BNP levels are significantly higher if LVH or diastolic dysfunction is present.

Prevalence of left ventricular diastolic dysfunction is high in diabetic patients. It has been shown that BNP is elevated in type 2 diabetic patients with microalbuminuria. Therefore, BNP may be used as a potential marker of diastolic dysfunction in type 2 diabetes. Moreover, Steno-2 Study showed that high plasma NT-proBNP is a major risk marker for cardiovascular disease in patients with type 2 diabetes and microalbuminuria. The study demonstrated a significant and independent correlation between plasma NT-proBNP levels and the future risk of cardiovascular disease, cardiovascular mortality and hospitalisation for congestive heart failure.

Last but not least, BNP level has been investigated as a cardiovascular risk assessment marker in the general population. A study conducted in 3346 asymptomatic persons without heart failure after a mean follow-up of 5.2 years and adjustment for other cardiovascular risk factors, BNP and NT-proBNP levels were found to be associated with increase in the risk of death, heart failure, atrial fibrillation, stroke and transient ischemic attacks. Another study also showed that NT-proBNP is a powerful predictor for mortality and the occurrence of first cardiovascular events in older individuals without cardiovascular disease, and appears more efficient than C-reactive protein and urinary albumin/creatinine ratio.

In conclusion, a simple blood test has emerged to aid in the diagnosis and management of patients with heart failure. More and more data suggest that measurement of BNP or NT-proBNP may aid in the early detection of cardiovascular disease. Further studies will provide more information on the value of using BNP or NT-proBNP as a cardiovascular risk assessment marker.

References: