BNP and NT-proBNP: Markers of Cardiac Failure and Tools for Risk Stratification

BNP (B type natriuretic peptide) is a hormone released by ventricular myocytes in response to cardiac stretch, as may occur in cardiac failure. BNP acts in a concerted way to ameliorate cardiac failure by enhancing diuresis, increasing renal sodium excretion and inhibiting the renin aldosterone and sympathetic nervous systems. Recombinant BNP has recently been developed for therapeutic purposes.

In the myocyte, the hormone precursor pro-BNP is split into the active hormone BNP and an inactive (but more stable) fragment, N terminal proBNP (NT-proBNP) (Figure 1). BNP is then co-secreted with equimolar quantities of NT-proBNP. Assays are now available for both of these peptides and clinical outcome research has shown that they have similar utility in most settings. We have opted to offer NT-proBNP as it is more stable than BNP and this is a significant advantage especially in the outpatient setting. NT-proBNP has also been shown to have the best power for separating healthy individuals from those with mild cardiac failure.

Many studies have now been done on the clinical utility of BNP and NT-proBNP measurement. The best accepted use is as a diagnostic tool for the evaluation of acute dyspnea, specifically to decide whether the cause of the dyspnea is cardiac or respiratory (or cardiac failure superimposed on respiratory pathology).

In the PRIDE study of 600 emergency department patients with acute dyspnea, NT-proBNP was shown to be highly sensitive and specific for the diagnosis of acute cardiac failure (92% sensitivity and 85% specificity); levels also correlated with its severity.

Studies done on patients with non-acute cardiac failure show that both peptides reliably predict cardiac failure and left ventricular ejection fractions of less than 40% and that the grade of cardiac failure correlates with hormone level. Successful therapy of cardiac failure lowers NT-proBNP levels.

The use of BNP and NT-proBNP measurement in risk stratification of patients is another rapidly growing research area. Congestive cardiac failure has a 5 year survival of around 50% and thus risk stratification is very pertinent in this setting to identify patients requiring intensive intervention.

- Elevated NT-proBNP levels in outpatients with congestive cardiac failure have been shown to predict both mortality and future hospital admission rates.
- Patients presenting with acute cardiac failure post myocardial infarct are also reliably risk stratified by NT-proBNP into a group at increased risk of mortality and complications.
- In patients with severe cardiac failure awaiting transplantation, NT-proBNP predicted mortality and requirement for urgent transplantation. NT-proBNP is in fact a better predictor of adverse outcomes in severe left ventricular failure than left ventricular ejection fraction and the previous “gold standard” predictor, maximal oxygen extraction.
- Furthermore, successful therapy of cardiac failure and consequent reduction of NT-proBNP is shown to be associated with a reduction in future mortality and complication risk.
Extending the prognostic theme further, recent studies have shown that NT-proBNP elevation predicts mortality in situations without clinical evidence of cardiac failure, i.e. in acute coronary syndromes and in stable coronary heart disease, and there is now evidence that low-level BNP elevations (i.e. below the range associated with cardiac failure) predicts adverse outcomes in asymptomatic well individuals; this is likely to also hold for NT-proBNP.

Despite its excellent sensitivity and specificity for cardiac failure in the clinical setting, other conditions may elevate these peptides; namely pulmonary embolus and acute coronary syndromes per se. NT-proBNP may be elevated by renal failure and results need to be interpreted with caution in its presence.

BNP and NT-proBNP reagents are rather expensive, but now have Medicare item numbers and receive a rebate BUT ONLY FOR THE “Quantitation of BNP or NT-proBNP for the diagnosis of heart failure in patients presenting with dyspnoea to a hospital Emergency Department”. Patients who do not fulfil these criteria will be charged to cover laboratory costs (currently $50 per test).