

Natriuretic Peptides in Diagnosis of Heart Failure: Is it the End of Road?

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In the initial years of launch of natriuretic peptides as a diagnostic test for heart failure, the impression was that they will bring ease to practice by reliably differentiating heart failure from other diagnoses or simply stating, cardiac dyspnea from the non-cardiac causes. However, after many years of use of natriuretic peptides in clinical practice, do we still think so?

Brain natriuretic peptide (BNP) is released from myocytes in response to myocardial strain/stress. It can also be released by neurohumoral stimuli, in response to heart failure. By this concept, use of natriuretic peptides in diagnosing heart failure looks lucrative. But when we see current literature, the list of conditions associated with increased BNP levels include more than 20 cardiac and non-cardiac conditions beside heart failure. These include old age, hypertension, pulmonary hypertension, atrial fibrillation, acute coronary syndrome, cardiomyopathies, valvular heart diseases, chronic obstructive pulmonary disease (COPD), pulmonary embolism, sepsis, renal failure and anemia [1].

BNP levels are increased in elderly. In the BED study, among patients with age more than 80 years, BNP levels were significantly higher in those with cardiac causes of dyspnea as compared to pulmonary causes, but, on its own BNP showed poor discriminative ability [2].

As compared to controls, patients of chronic kidney disease undergoing hemodialysis have been found to have very high plasma NT-proBNP levels (> 300 times). These patients had no clinical evidence of heart failure. Surprisingly, these high levels had no correlation with left ventricular systolic dysfunction [3]. BNP levels are increased in patients with cirrhosis. The levels increase irrespective of presence of LV systolic dysfunction. The levels are higher in patients with decompensated hepatic failure and those with worse Child-pugh class [4].

Patients with COPD are also found to have high NT-proBNP levels in absence of LV systolic dysfunction. The increase in peptide levels was not associated with severity of COPD or presence of other comorbid conditions, though it predicted longer hospital stay for these patients [5]. Presence of chest infection, pulmonary embolism, pulmonary hypertension and right ventricular failure may cause increase in BNP levels in these patients. NT-pro BNP levels are increased in patients with severe sepsis and septic shock. The rise may be related to systolic or isolated diastolic dysfunction which is not uncommonly seen in such patients. Relatively higher levels are associated with increased mortality in these patients [6].

In current clinical practice, old age, anemia, acute coronary syndrome, atrial fibrillation, renal failure, severe infections, liver failure, COPD and pulmonary hypertension are frequently present conditions in patients of heart failure. All these conditions can cause rise of natriuretic peptides independent of heart failure. Therefore, specificity of natriuretic peptides in diagnosing heart failure becomes questionable in a large proportion of patients with suspected heart failure who have these comorbidities. Conceptually also, specificity of na-

triuretic peptides in diagnosing heart failure should be low. Diastolic dysfunction causes increase stress on myocytes which in turn causes release of these peptides. Diastolic dysfunction may be associated with a large number of clinical conditions beside heart failure. These include hypertension, myocardial ischemia, severe infections, sepsis, chronic hypoxia, renal failure, obesity, old age, cardiomyopathies, pulmonary hypertension etc.

Early on, this limitation of natriuretic peptides was noticed and it was stressed that these tests have a high negative predictive value than positive predictive value for detection of heart failure [7]. In clinical scenarios where expert cardiac opinion is not readily available, the 'point of care' NT-proBNP has a specificity of 44 - 74% in diagnosing heart failure which is dismally low for the purpose of triage [8]. Therefore, in a given individual patient, reliance on natriuretic peptides for diagnosing heart failure can be awfully misleading. We must look for alternatives which can give quicker and reliable results. Hand-held 'point of care' cardiac ultrasounds may fill this position but needs to be tested in large scale trials.

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