Should brain natriuretic peptides be measured in patients with aortic valve disease?

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This editorial refers to ‘Relation of N-terminal pro B-type natriuretic peptide to progression of aortic valve disease’† by Weber et al., on page 1023

Close to 3% of the population over the age of 65 suffers from significant aortic valve disease, a figure likely to rise in our aging population. The current guidelines reflect the ample evidence supporting surgical intervention in symptomatic patients.1 However, optimal treatment of asymptomatic patients with severe disease remains undetermined. The risk of surgical intervention outweighs the risk of sudden cardiac death in asymptomatic patients with severe aortic stenosis (AS), but determining whether a given patient is truly asymptomatic may be difficult. Patients may not recognize their symptoms because of the insidious nature of the disease or the patients’ inactivity may preclude the development of symptoms. Exercise stress testing is gaining acceptance in the assessment of patients with severe AS, because it provides an objective assessment of functional and symptomatic status. However, it is performed in <6% of such patients, reflecting the established teaching that severe AS is a contraindication to the exercise stress test.2

There is a need for a reliable method to risk stratify asymptomatic patients with severe aortic valvular disease. Brain natriuretic peptide (BNP), a 32 amino acid peptide which is released from ventricular myocardium in response to ventricular pressure and volume load, could potentially fill this role. Its levels are elevated in a variety of cardiovascular disorders such as myocardial infarction, congestive heart failure, and pulmonary hypertension. Recent studies have demonstrated that serum BNP is also elevated in patients with valvular AS.3–6 Lim et al.4 showed that serum BNP was a strong independent predictor of clinical outcome in both symptomatic and asymptomatic patients with AS. A serum BNP value of >66 pg/mL predicted the development of symptoms in the following year in patients with severe AS, with a sensitivity of 84% and a specificity of 82%. Similar observations have also been reported by Bergler-Klein et al.5

Weber et al.7 examined the use of N-terminal pro B-type natriuretic peptide (NT-proBNP) in patients with aortic valve disease including AS, aortic regurgitation (AR), and aortic valve replacement (AVR). They prospectively followed 109 patients with AS, 37 patients with AR, and 22 patients with AVR for a median of 335 days. In the medically treated patients including 37 AS, 23 AR, and 22 AVR patients, 70% (58 patients) showed a progression in their disease which was associated with a significant increase in the serum NT-proBNP. In the 21 patients who had no progression in their disease, the serum NT-proBNP levels did not change significantly. In patients with AS, the baseline BNP levels correlated well with functional class as well as the mean transvalvular gradients. Changes in the serum NT-proBNP also correlated with the changes in the mean transvalvular pressure gradient as well as the changes in left ventricular mass during the follow-up period.

There have only been few studies evaluating utility of BNP in patients with isolated chronic AR, showing a direct correlation between serum BNP level and severity of AR, as well as presence of symptoms.8,9 In the subgroup of patients with AR (37 patients), Weber et al.7 also showed a strong correlation between AR severity and NT-proBNP levels. In both patients with AS or AR, valve surgery led to a significant drop in NT-pro BNP, but it is noteworthy that patients who did not have clinical improvement following AVR had no decrease in NT-pro BNP. Furthermore, smaller prosthetic valves were associated with higher transvalvular gradients and higher NT-pro BNP levels.7

The findings of Weber et al. suggest that NT-proBNP may have a useful role in the management of patients...
with AS or AR. With increasing NT-pro BNP levels, progression of aortic valve disease should be suspected and surgery should be considered. Following AVR, a drop in NT-proBNP levels predicts clinical improvement, whereas persistent elevation after surgery may suggest prosthesis mismatch. However, there are limitations in using BNP to assist in decision making in patients with aortic valve disease. Higher levels are seen with advancing age, in female patients, in patients with diminished creatinine clearance, and in patients with pulmonary embolism. Elevations in BNP are also seen in a number of other cardiac conditions such as arrhythmias, mitral regurgitation, significant coronary artery disease, and congestive heart failure. Many of these conditions are not uncommon in patients with aortic valve disease. Individual values may be misleading because of the significant overlap of these measurements between patients with and without progression of aortic valve disease, and in patients with serial measurements what constitutes a meaningful change needs to be better defined. Finally, there is no consensus as to which form of BNP (BNP or NT-proBNP) is of superior utility in aortic valve disease. Although these markers show similar changes with respect to disease severity, they have different properties. For instance, NT-proBNP has a longer plasma half-life than BNP and its plasma concentrations are considerably higher.10

In conclusion, recent studies including the one by Weber et al. show that BNP may be a useful biomarker for the assessment of the functional significance of AS and AR.3–9 Further studies are needed to determine which form of BNP is superior, to provide a more precise range of values that correlates with severity and symptom development and to define what constitutes a significant rise in BNP level that should lead to the consideration of surgical intervention. Until these studies become available, BNP levels should not be routinely measured in patients with aortic valve disease. These patients should have careful follow-up to look for the development of symptoms or ventricular dysfunction according to the published guidelines.

References