The Use of B-Type Natriuretic Peptides in Coronary Artery Disease

Utile or Futile?*

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B-type natriuretic peptides (BNP and N-terminal [NT]-proBNP) have been shown to be extremely helpful in the diagnosis, prognosis, and monitoring of therapy of patients with heart failure (HF) (1). These neurohormones are predominantly secreted from the left and the right cardiac ventricle in response to cardiac stress. The BNP s can be seen as quantitative markers of HF summarizing the extent of systolic and diastolic left ventricular dysfunction, valvular dysfunction, and right ventricular dysfunction (1).

Inspired by the overwhelming success in HF, several recent studies have addressed the use of BNP in the diagnosis, prognosis, and management of patients with coronary artery disease (CAD) (2–13).

Diagnosis of stable CAD. In patients with stable CAD, BNP s are associated with the presence of myocardial ischemia, and angiographic disease severity (2–4). These findings have lead to the hypothesis that myocardial ischemia is a major trigger for the release of BNP s, and measurement of either baseline levels or exercise-induced increase of BNP s might be clinically helpful in the diagnosis of myocardial ischemia and CAD. Larger studies including consecutive patients with suspected myocardial ischemia referred for stress testing confirmed the association between BNP s and myocardial ischemia. However, the diagnostic accuracy of BNP s for the detection of myocardial ischemia (~65%) was only moderate. Still, the combination of exercise electrocardiogram (ECG) and BNP s seemed to slightly improve diagnostic accuracy when compared with exercise ECG alone (5–7). The availability of more accurate noninvasive tests like perfusion imaging and stress echocardiography might determine whether the diagnostic accuracy of BNP s in this indication is high enough to justify clinical use. Importantly, recent evidence suggested that selection bias and comorbidity significantly influence the accuracy of BNP s to diagnose stable CAD (8).

Diagnosis of acute coronary syndrome (ACS). Cardiac troponins (T and I) are currently the gold standard for the diagnosis of myocardial infarction (MI). Unfortunately, cardiac troponin is undetectable by current assays in peripheral blood within the first 3 to 6 h after the onset of chest pain in MI (“troponin-blind” period). Preliminary data suggested that BNP s might be clinically helpful in the early diagnosis in patients with chest pain and no ST-segment elevation. In a large series of consecutive patients, the BNP median level at presentation was 204 pg/ml in MI, 78 pg/ml in unstable angina, and 28 pg/ml in patients without ACS (9). At presentation, BNP was >100 pg/ml in ~70% of patients subsequently diagnosed with MI, while cardiac troponin was elevated in only ~50% of these patients initially. The specificity of BNP for MI was 69%. Several ongoing studies will further elucidate the role of BNP s in conjunction with novel high sensitivity cardiac troponin assays and possibly other markers including myeloperoxidase for the early diagnosis of ACS.

Prognosis of stable CAD and ACS. Multiple large cohort studies have consistently shown that BNP s are powerful predictors of death in patients with stable CAD or ACS (10–12). Already 6 years ago, the TIMI (Thrombolysis In Myocardial Infarction) study group demonstrated that after adjustment for independent predictors of the long-term risk of death, patients in the 4th quartile of BNP had nearly 6 times the risk of death as compared with patients in the 1st quartile. A single measurement of BNP s provides powerful information for use in risk stratification across the spectrum of CAD. This finding suggests that cardiac neurohormonal activation may be a unifying feature among CAD patients at high risk for death. The data from the PEACE (Prevention of Events with Angiotensin Converting Enzyme Inhibition) trial published in this issue of the Journal extend this observation to low-risk stable CAD patients (12). The BNP s are also powerful predictors for the development of HF and for the presence of impaired left ventricular systolic function. The accuracy of BNP s to detect a left ventricular ejection fraction of below 30% was about 80% (11). In contrast, BNP s do not seem to predict future nonfatal MI (10–12).

Management of CAD. The key question still remains to be addressed. How should BNP s influence patient management? Is there a specific medication or intervention that should be initiated based on elevated levels of BNP s? Obviously, BNP s can only be used in conjunction with other clinical information to guide management in patients with suspected or proven CAD. Despite this caveat, many clinicians including this editorialist had hoped that B-type natriuretic peptides might
help to target angiotensin-converting enzyme (ACE) inhibitors in CAD. As BNP s are closely associated with impaired left ventricular function and cardiac stress, those patients with elevated BNP s should derive particular benefit of ACE inhibitors. Unfortunately, neither the data from the PEACE trial nor the data from the HOPE (Heart Outcomes Prevention Evaluation) study (S. Blankenberg, personal communication, March 4, 2007) support this hypothesis. In both randomized controlled trials, no significant interaction between levels of BNP s and benefit from ACE inhibition was found.

High-risk patients with non–ST-segment elevation ACS seem to derive maximal benefit from an early revascularization strategy (13,14). Could BNP s, therefore, be useful in the selection of initial ACS management? In the FRISC (Fragmin and fast Revascularization during InStability in Coronary artery disease) study, the mortality benefit from an early invasive strategy after non–ST-segment elevation ACS was slightly greater when BNP s were higher. However, no interaction between BNP s and the benefit of early revascularization was observed in the TACTICS (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy) study.

As BNP s predict both left ventricular systolic dysfunction and the risk of sudden cardiac death, it is reasonable to assume that BNP s might be helpful to achieve a higher cost effectiveness in our patient selection for implantation of a defibrillator (15,16). Additional studies are necessary to verify this hypothesis.

In conclusion, BNP s are very attractive tools also in CAD. However, we still have to learn how to make the best clinical use of the information provided.

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