Plasma Brain Natriuretic Peptide Levels Indicate the Distance From Decompensated Heart Failure

To the Editor:

We read with great interest the recent article by Tang et al. on plasma brain natriuretic peptide (BNP) levels in ambulatory patients with established chronic symptomatic systolic heart failure. They concluded that both symptomatic and asymptomatic patients present with a wide range of plasma BNP levels and that this heterogeneity may preclude the use of plasma BNP levels for deciding therapy and monitoring response. We agree with the analysis of their results; however, we disagree with their interpretation.

BNP increases not only in response to pressure or volume loads, but also in response to neurohumoral factors and cytokines, independently of hemodynamic load. The clinical implications of increased plasma BNP levels differ depending on the underlying condition. For example, elevated BNP levels can mean increased filling pressure in dilated cardiomyopathy, the development of ventricular remodeling in myocardial infarction of recent onset, and left ventricular hypertrophy in hypertension. Plasma BNP levels are also influenced by many factors, including age, renal function, and arrhythmias.

Because heart failure has diverse causes and patients have various clinical characteristics, we must analyze the meaning of increased BNP levels in individual patients. Nevertheless, measurement of plasma BNP remains important in heart failure, because decompensated heart failure does not occur in the absence of elevated plasma BNP levels. In patients with heart failure, symptoms are often very subjective and unrelated to cardiac status. Exercise capacity in heart failure is known not to correlate with cardiac function. In contrast, plasma BNP is secreted mainly from the ventricles and correlates with cardiac indices in heart disease; BNP markedly increases in decompensated heart failure. Thus, it seems reasonable to assume that the plasma BNP level in heart failure is inversely related to the distance from decompensated heart failure. For example, in patients with low BNP levels, the distance from decompensated heart failure is far; such patients are at low risk for the development of decompensated heart failure. In patients with high BNP levels, the distance is very close to decompensated heart failure, which easily develops even without symptoms. Intensive medical therapy should be considered in such patients. In patients with low BNP levels, including those with severe symptoms, intensive medical therapy would probably not be beneficial. Thus, medical therapy based solely on patients’ symptoms may be cost ineffective. Medical therapy based on the more objective indices such as plasma BNP levels is more likely to lead to a better outcome and more efficient use of valuable resources.

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Response

We agree with the comments of Drs Nishikimi and Matsuoka that elevated plasma B-type natriuretic peptide (BNP) levels can be due to many factors beyond pressure and volume loads, although the evidence remains observational in nature. We also agree with many investigators that plasma BNP or N-terminal proBNP testing is highly valuable as an aid to the diagnosis, management, and risk stratification of patients with heart failure. However, whereas the average plasma BNP levels are likely to be higher in a population of patients who develop worsening heart failure signs and symptoms than those who will not, the same may not be true when clinically assessing individual patients. Our observations caution the use of a single cutoff plasma BNP or N-terminal–proBNP level as part of the “diagnostic” criteria for chronic heart failure, mainly because of their biological variability or other confounding factors, which can be dependent on the clinical setting. Furthermore, in our experience in the heart failure intensive care unit at the Cleveland Clinic, we have observed a wide variation of plasma BNP levels in patients admitted for decompensated heart failure requiring hemodynamically guided therapy. Some of them (particularly those with idiopathic dilated cardiomyopathy) can even be in the lower ranges around or below 100 pg/mL by the Biosite assay, and may not correlate closely with changes in intracardiac filling pressures. These bedside observations, however, do not undermine the usefulness of the BNP or N-terminal proBNP assays, but simply point out that like all diagnostic tests, the validity of the test results have to complement clinical findings and other test measurements to define a disease process.

In our opinion, viewing plasma BNP level simply as a marker of “wellness” and basing therapeutic decisions on this measurement, although attractive, are far too simplified. Given the current level of evidence, we believe that intensive medical therapy should be considered in all patients with chronic heart failure and should not be limited to those with higher plasma BNP levels. Patients with higher plasma BNP levels may benefit from closer follow-up and more attention to treatable causes or comorbidities. The hypothesis that medical therapy based on plasma BNP levels “is more likely to lead to a better outcome and more effective use of valuable resources” is currently being tested in several randomized clinical trials. Our data would suggest that the baseline or “dry” BNP or N-terminal proBNP levels may vary greatly among patients with heart failure, and thus, a BNP-guided therapy approach may require highly individualized targets.

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