

Letters to the Editor

Reports of Heart Failure Trials and the Dissociation With the Prevailing Clinical Practice

The report (1) and editorial (2) in a recent issue of the *Journal* on N-terminal pro-B-type natriuretic peptide (NT-proBNP) in the management of patients with heart failure (HF) led to the conclusion that B-type natriuretic peptide has not fulfilled original expectations, although NT-proBNP provided advanced detection of events and enhanced medication use. The editorial pointed out that although NT-proBNP did not improve events, this could partially reflect the need for a larger study, adoption of individualized NT-proBNP targets, timing of the sampling for the nadir of NT-proBNP, and threshold percentage rise in NT-proBNP for up-titrating therapy. They also recommended consideration of the patients' age, other factors influencing BNP, systolic dysfunction, and use of individual patient data in meta-analyses.

Trials of HF should include, along with the parameters under study, a minimum of information currently used in the management of patients. The cornerstone of the assessment of a patient with HF is the history and physical examination (pulmonary rales, elevated mean jugular venous pressure, and peripheral edema [PERED]), although these conditions are insensitive and do not correlate with hemodynamics (3). PERED is often undetected until the patient has accumulated approximately 10 l of fluid (4). Body weight (BW) is used in all clinical encounters with patients with HF, and it should be a study variable in HF trials. Did the researchers have BW measurements of their patients? If so, what was the correlation between the BW and NT-proBNP percentage perturbations? The quoted "negative" study (3) included a "positive" correlation ($r = 0.82$) of proportional pulse pressure (systolic blood pressure [SBP] – diastolic blood pressure [DBP]/SBP) with cardiac index. The mean SBP and DBP in Table 1 (1) were not statistically significant, although individual patient values are needed to calculate proportional pulse pressure.

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REFERENCES

- Eurlings LW, van Pol PE, Kok WE, et al. Management of chronic heart failure guided by individual N-terminal pro-B-type natriuretic peptide targets: results of the PRIMA (Can Pro-Brain-Natriuretic Peptide Guided Therapy of Chronic Heart Failure Improve Heart Failure Morbidity and Mortality?) study. *J Am Coll Cardiol* 2010;56:2090–100.
- Troughton RW, Frampton CM, Nicholls MG. Biomarker-guided treatment of heart failure: still waiting for a definitive answer. *J Am Coll Cardiol* 2010;56:2101–4.
- Stevenson LW, Perloff JK. The limited reliability of physical signs for estimating hemodynamics in chronic heart failure. *JAMA* 1989;261:884–8.
- Fauci AS, Braunwald E, Kasper DL, et al., editors. *Harrison's Principles of Internal Medicine*. 17th edition. New York, NY: McGraw-Hill Medical Publishing Division, 2008:231–6.

Reply

We would like to thank Dr. Madias for his valuable comments on our study (1) assessing the effect of N-terminal pro-B-type natriuretic peptide (NT-proBNP)-guided therapy in the management of chronic heart failure (HF). As rightfully indicated, quantification of fluid retention by physical examination is troublesome, and the correlation between symptoms and severity of cardiac dysfunction is poor. Trials such as the PRIMA (Can Pro-brain-natriuretic peptide guided therapy of chronic heart failure Improve heart Failure morbidity and mortality?) study (1) have been performed in order to assess the additive value of serial BNP or NT-proBNP measurements at the outpatient management of HF patients.

Dr. Madias asks for data on body weight (BW). This was not initially reported as we felt that with outpatient visits occurring at an interval of up to 3 months, the value of reporting outpatient BWs with such wide intervals would be quite limited.

However, we did collect data on BW at index admission, at discharge, and at every outpatient visit during the follow-up period of our study. During the index hospitalization because of acute HF, BW decreased with a median value of 4.48 kg (interquartile range: 1.8 to 6.2 kg). The change in BW during index admission correlated weakly, yet significantly, with changes in NT-proBNP levels ($r = 0.144$, $p = 0.016$). At the outpatient clinic, there was no statistically significant correlation between changes in BW and NT-proBNP levels.

In addition, Dr. Madias expresses an interest in possible correlations between the proportional pulse pressure (PPP) and NT-proBNP. We failed to find any correlation between PPP and NT-proBNP (correlation between PPP and NT-proBNP at admission: $r = 0.019$, $p = 0.723$; at discharge: $r = 0.035$, $p = 0.532$; and at 2-week follow-up: $r = 0.023$, $p = 0.689$).

We also did not find a correlation in the subgroups of patients with left ventricular systolic dysfunction HF or those with preserved left ventricular systolic function HF.

In conclusion, Dr. Madias rightfully points out the value of physical examination in the management of outpatient HF with special emphasis on BW. In the PRIMA study, changes in BW during the index admission correlated weakly, yet statistically significantly, with NT-proBNP (1). No correlation was found between outpatient NT-proBNP values and either BW or PPP, which for the latter may be explained by the fact that PPP seems to reflect cardiac output, a parameter correlating poorly with BNP (2).

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REFERENCES

1. Eurlings LW, van Pol PE, Kok WE, et al. Management of chronic heart failure guided by individual N-terminal pro-B-type natriuretic peptide targets: results of the PRIMA (Can Pro-brain-natriuretic peptide guided therapy of chronic heart failure IMprove heart fAilure morbidity and mortality?) study. *J Am Coll Cardiol* 2010;56:2090–100.
2. Kazanegra R, Cheng V, Garcia A, et al. A rapid test for B-type natriuretic peptide correlates with falling wedge pressures in patients treated for decompensated heart failure: a pilot study. *J Card Fail* 2001;7:21–9.