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EDITORIAL COMMENT

NT-proBNP

The Gold Standard Biomarker in Heart Failure*

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The concept of the heart as an endocrine organ emerged with the discovery of the atrial natriuretic peptide (ANP) by de Bold et al. (1) in 1981, followed later by the discovery of B-type remodeling of the heart, and metabolic disease (2,3). Reduced bioavailability in early hypertension and asymptomatic heart failure (HF) (Stage B), as well as an increased concentration of biologically inactive

hypoxia. Measurement of natriuretic peptide now is common as an endpoint in HF trials, and the use of natriuretic peptides for diagnosis and prognosis purposes is guideline supported. Additionally, a large study to evaluate the efficacy of NT-proBNP to guide HF therapy is underway (GUIDE-IT [Guiding Evidence Based Therapy Using Biomarker Intensified Treatment in Heart Failure] trial) (10).

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In this issue of the *Journal*, Zile et al. (11) report findings of the prognostic value of NT-proBNP in the PARADIGM-HF trial. As the authors state, the PARADIGM-HF trial represented an unprecedented opportunity to investigate the prognostic robustness of NT-proBNP in a large (>8,000 subjects), international, and randomized trial with positive outcomes for HF-related mortality and morbidity. Indeed, the clinically significant reduction in hospitalization and death with ARNi therapy compared with enalapril is speculated to be in part secondary to the shifting of a neurohumoral profile dominated by the renin-angiotensin-aldosterone system to one more weighted toward the natriuretic peptide/cGMP system with beneficial organ and cellular protective properties secondary to inhibition of NEP, as well as coblockade of AT1R.

The principal objective of the Zile et al. study (11) was to test the hypothesis that the degree of change in NT-proBNP would parallel changes in death and hospitalization. This is an important question in part as the HF community strives to develop surrogate endpoints for HF trials. The investigators defined NT-proBNP levels in a subset of patients in the PARADIGM-HF trial (n = 2,080) and 62% of those subjects (n = 1,292) had an NT-proBNP above 1,000 pg/ml and follow-up NT-proBNP levels at 1 and 8 months. Impressively, as early as at 1 month, the NT-proBNP decreased below 1,000 pg/ml in 24% of participants, and the reduction from above to below 1,000 pg/ml was associated with improved outcomes when compared with participants whose levels