Brain natriuretic peptide in heart failure: an improving prognosis?

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This editorial refers to ‘Using BNP to develop a risk score for heart failure in primary care’† by D. Adlam et al., on page 1086

Over the last half century heart disease has undergone a dramatic and technology-driven transformation, from a condition that typically manifested itself as an acute and often fatal episode into a disease that in many cases is becoming survivable. The downside of this inexorable march towards progress is that although overall mortality from heart disease is falling, the prevalence of conditions such as heart failure (HF) is increasing. In Europe alone there are an estimated 10 million patients with HF.1 Being the final common pathway for many types of heart disease, HF has a poor prognosis and relapse and repeated hospitalization are both commonplace and costly.2 HF has become a major challenge not only to the medical profession but also to society in general.

Conventional pharmacotherapy (diuretics, β-blockers, angiotensin-converting enzyme inhibitors, etc.) can reduce both hospital admissions and, to a lesser extent, mortality.1 The logical consequence of the convergence of increasing prevalence of the disease in an ageing population with therapeutic advances which reduce hospitalization, has been for the management of HF to increasingly become the responsibility of those working in primary care.

Many patients present with non-specific symptoms and co-morbidity. To compound these diagnostic challenges, facilities such as ultrasonography are not universally accessible in the primary care sector, hindering the diagnosis and management of HF in this setting. Primary care decision-making would be enhanced by the development of a reliable test that provides at a minimum as good an assessment tool as does echocardiography. Ideally, such a test would lend itself to multifaceted applications in terms of not only diagnosis but also screening, management, dose adjustment, and evaluation of prognosis.

Recent decades have seen episodic enthusiasm for various biochemical and biophysical markers for HF. The initial excitement and promise of plasma levels of atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) were soon tempered by suspicion and unease. Concerns were raised over issues such as disease-specificity and technical aspects of these assays, and confusion as to what constitutes a ‘normal’ level in the face of potential confounding factors such as age, obesity, gender, and renal disease.3,4 Indeed, the popularity of these biomarkers has waxed and waned over the years, reminiscent of the clinical course of HF in many patients.

Of all the candidates for a HF biomarker, plasma BNP has weathered these challenges better than most and is now coming of age not only as a diagnostic tool but also as a predictor of rehospitalization and mortality. This neurohormone is released by myocytes in cardiac ventricles during pressure or volume overload and acts to regain homeostasis by direct vasodilatory action on arteries and veins, by opposing the action of vasoconstrictive and sodium-retaining neurohormones and by working with ANP to promote diuresis and natriuresis.5 Consistent with our understanding of these activities, intravenous injections of nesiritide, a genetically-engineered (and ruinously expensive) version of BNP improve both the haemodynamic deficiencies and the symptoms seen with HF.2

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A recent meta-analysis concluded that elevated plasma BNP levels were an accurate predictor (more so than ANP) of impaired left ventricular ejection fraction: pooled diagnostic odds ratio 11.6 (95% CI 8.4–16.1). This relationship was nearly three times as strong when clinical criteria were used to diagnose HF, supporting an additional role for BNP as an indicator of 'diastolic' HF.

The majority of evidence supporting a diagnostic role for BNP has come from specialist or secondary care settings. Caution is needed in translating these developments into the primary care setting where the prevalence, severity and case-mix of disease can be so different. In this instance the experience in primary care is promising. Following from the pioneering work of Cowie et al. in London, our own study of 155 elderly patients in UK general practice led us to propose that plasma levels of BNP could be of value in screening for HF in primary care. Other work, mostly in the USA and UK, support the concept of using plasma BNP levels outside of acute settings to diagnose and monitor HF.

In a retrospective study, Adlam et al. from Nottingham used historic data from patients in UK primary care to generate a prognostic scoring system for HF. The authors propose a model that includes plasma BNP levels, age, gender, and clinical information such as ECG status and previous history of stroke. Importantly, plasma BNP levels are used as a continuous variable within this formula, avoiding some of the previous arguments as to the cut-off value for 'normality'. There could be initial concern about the data quality in this study. For example, the ECG data were classified as normal or abnormal by a single general practitioner. However, we consider this to be a strength of the study: this is a straightforward pragmatic approach that uses the information that is readily available in primary care, now the major setting for HF management. There is an obvious need for this work to be confirmed prospectively and in ethnically and otherwise diverse populations, but the prognostic scoring approach, available to any family doctor, is likely to facilitate the future management of HF in primary care.

If HF is to be cared for outside of hospitals, then we need an individualized evidence base, not one simply transferred over from research in secondary and tertiary care, for our patients. A recent and controversial editorial in the Lancet challenged the need for (and value of) primary care research, likening it to a 'lost cause'. The study by Adlam et al. illustrates how research conducted in a community setting can make an invaluable contribution to the evidence base underpinning patient care. The prognosis is looking good both for BNP as a biomarker for HF and for primary care research as a discipline in its own right.

References