Assessing prognosis in heart failure: you can see a lot if you look, but more if you look again

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This editorial refers to ‘Usefulness of clinical and NT-proBNP monitoring for prognostic guidance in destablized heart failure outpatients†’ by D.A. Pascual-Figal et al., on page 1011

The management of an individual patient should encompass not only consideration of the diagnosis and appropriate treatment, but also assessment of prognosis. This is particularly so in the case of the patient suffering from a condition which may reasonably be expected to have an impact on life expectancy and on quality of life. Chronic heart failure (CHF) certainly meets these criteria, having an impact on prognosis as severe as that of many of the common malignancies and on quality of life as severe as other chronic conditions.

Current national and international guidelines, including those of the European Society of Cardiology, recognize that assessment of prognosis should be a part of the standard management of the patient with CHF. However, these same guidelines recognize the inherent difficulty of this process. A variety of factors contribute to this difficulty: varying aetiology, frequent co-morbidity, and, perhaps most importantly, huge inter-individual variability in disease progression and outcome. Although CHF is chronic, it is also a condition in which significant proportions of patients experience an apparently ‘sudden’ death, a fact almost certainly contributing to our difficulty in assessing individual patient prognosis.

For the reasons above, and others, physicians are in general uncomfortable with the process of prognostication in CHF. While for many patients the outcome is relatively benign, CHF is regarded as a ‘malignant’ condition. This may lead us to overestimate, as well as underestimate, the risk of adverse outcome. For example, in a study of primary care physicians in Switzerland, the estimated probability of death within 1 year for patients with CHF was double that actually observed in the cohort. This was estimated probability of death within 1 year for patients with CHF.

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Any estimate of prognosis represents the summation of information considered at one point in time but perhaps gathered a longer period. However, it is important to consider that CHF is a condition for which prognosis changes, and indeed may be changed by the intervention of the physician. We know that therapy can improve the outlook for populations of patients with CHF and we must remember that for angiotensin-converting enzyme (ACE) inhibitors, aldosterone receptor antagonists, and cardiac resynchronization therapy (CRT), evidence of symptomatic and survival benefit was established first in patients with more advanced disease. However, it is extremely difficult for the physician to gain meaningful information regarding the effect on prognosis of pharmacological, or indeed device, therapy in an individual patient with CHF. To date we have lacked the ability to identify patients who may benefit most from treatment, in the way of oestrogen receptor or HER2 receptor status in the treatment of breast cancer. Similarly we have lacked a biomarker which may allow assessment of disease activity and response to therapy, as does monitoring of prostate-specific antigen in prostatic cancer.

Pascual-Figal et al. describe the prognostic utility of serial monitoring of plasma N-terminal pro B-type natriuretic peptide (NT-proBNP). In a population of outpatients with destabilized CHF, the authors compared the prognostic utility of a structured clinical disease severity score (CDSS) with that of NT-proBNP. The attending physician amended pharmacological therapy with the aim of achieving clinical stabilization of CHF, again assessed in a structured fashion. The assessed outcomes were cardiovascular death or hospitalization due to heart failure. The patients had advanced CHF, with mean left ventricular ejection fraction (LVEF) < 30%, with most patients being in New York Heart Association (NYHA) class III. The patients appear to have been well treated, with an ACE inhibitor [or angiotensin receptor blocker (ARB)] and β-blocker being prescribed in all, spironolactone in 65%, and digoxin in 41%. Patients were followed-up intensively, weekly for 4 weeks and then at 3, 6, and 12 months.

There are three main findings from the study. First, the authors report that while baseline clinical score was predictive of prognosis, the relative (percentage) change in this was not. Secondly, and in contrast to the findings with clinical score, baseline NT-proBNP

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did not predict prognosis, while the relative (percentage) change did. Thirdly, greater prognostic information was obtained from consideration of the combination of baseline clinical disease score and the change in plasma NT-proBNP. In this study, there was no difference in baseline plasma NT-proBNP levels between patients destined to experience an event during follow-up compared with those who did not. However, in the latter group, plasma NT-proBNP fell by an average of >20% by 1 week and by >30% by 2 weeks. In contrast, for patients experiencing cardiovascular death or heart failure hospitalization during the subsequent 12 months, NT-proBNP fell by only 10% by 1 week, a change which showed very little change thereafter.

Is this information clinically useful? Well, potentially, yes. In the absence of information on the change in NT-proBNP, baseline clinical score was highly predictive of outcome, a reassuring finding for the clinician. The study also suggests that in a group of patients with decompensated CHF, a single assessment of NT-proBNP may not be predictive of outcome. This may appear to fly in the face of perceived wisdom regarding the natriuretic peptides, but I suggest that this is due to the fact that in this population, NT-proBNP was uniformly elevated (the minimum baseline concentration was >1800 pg/mL), removing much of the discriminatory value of this variable. However, when we look a second and more times at NT-proBNP, we learn much more, and quite quickly.

It appears that we can identify patients destined to have a particularly poor prognosis, as indicated by the failure of NT-proBNP to fall by more than a small percentage. However, it is not entirely clear what we might do with this information. Although the patient population was apparently well treated, we are not told what doses of ACE inhibitor/ARB or β-blocker were prescribed at baseline. Moreover, the changes in therapy instituted in the treatment of the patients are not detailed; in terms of pharmacological therapy, we do not know where the patients started and finished. However, as the patients in this study had to present with clinical evidence of fluid overload, it may be surmised that modification of diuretic therapy was required frequently. This would be consistent with the findings of the recent STARS BNP trial, which demonstrated the prognostic benefit of frequently. This would be consistent with the findings of the recent STARS BNP trial, which demonstrated the prognostic benefit of daily use of NT-proBNP. The authors do not report the positive or negative predictive value of changes in NT-proBNP. Both are likely to be low, as event rates were high even for patients with greater falls in plasma natriuretic peptide levels.

Nonetheless, the study by Pascual-Figal et al. is an important addition to the literature pertaining to the clinical utility of plasma natriuretic peptide levels in CHF. Physicians caring for patients with CHF may have available a tool which may provide useful information on individual patient response to treatment. In considering prognosis, we should not simply ‘fire and forget’ in terms of therapy, but we should look, and look again. We may learn a lot.

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References


