Prognostic stratification in heart failure: what’s the point?

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Despite advances in medical and surgical management, the prognosis of patients with heart failure and left ventricular systolic dysfunction remains generally poor. Clinical progression and prognosis are, however, highly variable and do not correlate well with measures of systolic function. Several parameters have been shown to predict prognosis, including age, NYHA class, heart rate, and neurohormone concentrations\[^{[1]}\], but despite its poor correlation with ejection fraction, peak oxygen uptake (VO\(_2\) max) is generally recognized to be one of the best prognostic indicators\[^{[2]}\], as is per cent of predicted VO\(_2\) max, which is less dependent on age, weight and gender\[^{[3]}\].

Doppler echocardiographic parameters of left ventricular filling, whilst limited by variables such as heart rate, age and loading conditions are also of prognostic value. E wave deceleration time (Dt) has been shown to be a powerful, independent predictor of outcome in patients with heart failure and impaired systolic function, and a deceleration time of less than 125 ms conveys prognostic information additional to other echocardiographic or clinical variables\[^{[4]}\]. Transmitial flow velocity profiles have also been used to identify patients who are at increased risk\[^{[5,6]}\]. A restrictive transmitial flow pattern is defined as an E/A ratio ≥2 or an E/A ratio between 1 and 2 when the E wave deceleration time is ≤140 ms. Non-restrictive patterns are defined as E/A ratios of ≤1 or between 1 and 2 if the E wave deceleration time is greater than 140 ms. Using the combination of E/A ratio and Dt, all patients can be grouped as restrictive or non-restrictive\[^{[5]}\]. However, transmitial flow patterns are dynamic phenomena that may change rapidly within the same patient in response to alterations in loading conditions or drug treatment. Assessment of changes in the transmitial flow patterns after load manipulation can be used to further stratify patients into high or low risk subgroups. A patient whose transmitial flow pattern remains restrictive after manipulation of loading conditions, has a worse prognosis than one whose transmitial flow pattern changes from restrictive to non-restrictive. A continuum exists, with fixed restrictive patterns conveying the worst and fixed non-restrictive the best prognosis\[^{[7,8]}\].

In this issue, Tabet et al\[^{[9]}\] prospectively compare the prognostic value of left ventricular filling patterns with peak oxygen consumption during exercise (VO\(_2\) max) in 100 men with heart failure and impaired systolic function. Patients were divided into groups based on transmitial flow patterns and E wave deceleration time, with a third group consisting of patients with fused E and A waves due to tachycardia (fusion group). Whilst E wave deceleration time (Dt) correlated strongly with maximal exercise capacity (r=0.65), per cent predicted VO\(_2\) max remained the strongest predictor of death or transplantation. Doppler parameters of left ventricular filling did exceed the prognostic power of ejection fraction and left ventricular dimensions; however, further stratification of the three patient groups using the response of transmitial flow patterns to load manipulation and the isovolumetric relaxation time\[^{[7]}\] may have improved the predictive power of left ventricular filling parameters.

It is unfortunate that neurohormone levels were not included in this study as they have been shown to be extremely good prognostic indicators over and above conventional parameters in patients with heart failure and left ventricular systolic dysfunction\[^{[10]}\]. Brain natriuretic peptide (BNP) and atrial natriuretic peptide (ANP) are released as a response to increased atrial and ventricular wall stretch, are related to left ventricular filling pressures\[^{[11]}\] and are markers of the severity of heart failure. Patients with restrictive transmitial velocity patterns have higher ANP and BNP levels than patients with non-restrictive patterns, and the close relationship of neurohormone levels with diastolic Doppler indices of left ventricular filling\[^{[12]}\] suggests that transmitial velocity profiles may simply be a marker of the degree of neurohormone activation in patients with heart failure\[^{[11]}\].

Knowledge of neurohormone levels, transmitial flow velocities, percent predicted VO\(_2\) max and various other parameters is useful to allow prediction of survival in patients with heart failure, although this is of little value unless patient management is improved as a consequence.

Treatment for chronic heart failure is increasingly complex, management of individual patients is often difficult and polypharmacy a potential problem. Current practice uses clinical evaluation, physician preference and patient adherence rather than objective clinical measures to guide drug selection, and dosage and risk-profiling currently has little role in individual treatment plans. There is, however, recent evidence to suggest that heart failure treatment can be better tailored to individual patients and that such strategies improve patient outcomes. Troughton et al\[^{[13]}\]
randomized patients with heart failure to treatment guided by standard clinical assessment or treatment guided by neurohormone levels. They showed a significant reduction in total cardiovascular events in patients whose treatment was altered on the basis of neurohormone levels compared to clinical judgement. A similar study used BNP levels to titrate vasodilator therapy in patients with heart failure and showed a decrease in resting heart rate and a more profound inhibition of the renin angiotensin aldosterone system in the group using neurohormone levels to guide treatment compared to empirical therapy\textsuperscript{[14]}. It has been reported previously that patients with raised neurohormone levels benefit most from the addition of beta-blockade to their existing treatment\textsuperscript{[15]} and raised renin levels predict patients in whom ACE inhibitor treatment is likely to be of greatest value\textsuperscript{[16]}.

Thus, rather than being used simply to assess timing and suitability of heart transplantation, parameters which identify adverse prognosis could be of value in tailoring treatment regimes to individual patients. Evidence from clinical trials supports the application of several types of drugs in heart failure, including ACE inhibitors, beta-blockers, spironolactone and digoxin. A minority of patients will actually take such cumbersome combinations in recommended doses. The above studies suggest methods of patient profiling which may lead to selection and individualization of treatment, avoiding polypharmacy and improving patient outcomes. For many years, oncologists have used staging investigations to apply the most appropriate treatment to each individual with a diagnosis of cancer. Perhaps it is time for more accurate patient profiling and heart failure staging to be studied and considered as a means of tailoring heart failure treatment more effectively.

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References


\textsuperscript{[14]} Murdoch D, McDonagh T, Byrne J \textit{et al.} Titration of vasodilator therapy in chronic heart failure according to plasma brain natriuretic peptide concentration: Randomized comparison of the haemodynamic and neuroendocrine effects of tailored versus empirical treatment. Am Heart J 1999; 138: 1126–32.
