EDITOR'S CHOICE

Systematic review with meta-analysis

B-type natriuretic peptide-guided therapy for chronic heart failure reduces all-cause mortality compared with usual care but does not affect all-cause hospitalisation or survival free of hospitalisation

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Commentary on: **Porapakkham P**, Porapakkham P, Zimmet H, *et al.* B-type natriuretic peptide-guided heart failure therapy: A meta-analysis. *Arch Intern Med* 2010;**170**:507–14.

Despite advances in drug and device therapy, after admission and treatment for acute heart failure (HF), 30% of patients are readmitted and 10% die within 90 days. This partly reflects imperfect implementation of proven therapies with surveys indicating only a minority of patients receive target doses of effective medications.

The gap in guiding HF treatment

In turn, this reflects the absence of an objective measure of adequacy of treatment. After overt signs and symptoms of cardiac decompensation resolve, the clinician has no clear guide for titration of therapy. Plasma B-type natriuretic peptide (BNP/NTproBNP) levels may fill this gap. BNP/NTproBNP independently indicate prognosis at all grades of HF and parallel response to effective therapies. Hence, they may allow individual tailoring of treatment with the possibility of better outcomes.

Porapakkham and colleagues have conducted a meta-analysis of prospective randomised controlled trails comparing BNP-guided therapy with standard care. In eight trials including 1726 patients, all-cause one year mortality was reduced by BNP-guided treatment (RR 0.76, 95% CI 0.63 to 0.91, p=0.003). In patients under 75 years of age (data from two trials), mortality was more clearly reduced (RR 0.52, 95% CI 0.33 to 0.82, p=0.005) while no benefit was observed in the those over 75 years (RR 0.94, 95% CI 0.71 to 1.25, p=0.70). The authors concluded that B-type peptide-guided therapy reduces all-cause mortality with chronic HF compared with usual clinical care especially in patients younger than 75 years.

Information left out of the report

Constrained by its methodology, the report does not adequately convey much important information to readers who are advised to read the originally published information on the eight trials. Four are included in the absence of full publication, from abstracts and presentations that is without full data and without peer-review. This along with the absence of individual patient data meta-analysis weakens this report. Conversely, at least two relevant reports that were fully published before the publication date of this report[1 2] are not referenced.

In contradistinction to the statement from Porapakkham and colleagues that all studies were performed in patients with left ventricular fraction (LVEF) less than 50%, the NT-proBNP-Assisted Treatment To Lessen Serial Cardiac Readmissions and Death (BATTLESCARRED) trial recruited patients at all levels of LVEF. This was also the design of Trial of Intensified versus standard Medical therapy in Elderly patients with Congestive Heart Failure (TIME-CHF) although recruitment of patients with preserved ejection fraction (EF) was limited, and the published report was confined to impaired systolic function. This is an important point as older patients are more likely to have HF with preserved EF, a group without proven effective treatment, perhaps partly explaining the lack of efficacy of BNP guidance in those over 75 years in BATTLESCARRED. The full report also makes it clear that older patients were much more at risk of intolerance to medications and were far less able to achieve target drug doses.

The current report does not provide any insight into possible effects on HF admissions. TIME-CHF, the largest trial to date, showed a clear reduction in HF admissions overall (p=0.008) and a similar trend was observed in the BATTLESCARRED study, but in both trials the benefit was driven by benefit to those under 75 years. STARS BNP, the other sizeable, fully published trial, showed benefits largely confined to reductions in death from HF and admission for HF. The authors' lack of access to analysable data on this important end point could be balanced by fuller discussion of findings reported in the individual trials. Lack of effect on all-cause hospital admissions is no surprise given the dual effects of common significant comorbidity, and the fact that the intensified monitoring and follow-up attending BNP-guided therapy makes admission of the decompensating patient more likely than in the less closely scrutinised patient receiving 'usual care'. Trials of multi-disciplinary HF management may reduce all-cause mortality, without necessarily affecting other end points.[3]

The remaining need for data

The need remains for further trials of BNP-guided treatment adequately powered to define interactions of this treatment strategy with age and systolic function, to define the most effective drug escalation algorithms and to define target peptide levels.

Take home message

The evidence indicates every physician caring for patients with HF should take an interest in their B-type peptide levels. In patients under 75 years, continuing elevation of peptide levels appears to warrant escalation of treatment if this is feasible.

Competing interests None.

References

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