

Declarative title

Natriuretic peptide guided therapy for management of patients with heart failure does not show improvement compared to medical therapy for a composite outcome of first heart failure hospitalisation and cardiovascular mortality.

Context

Natriuretic peptides (NPs), a collective term for B-type natriuretic peptide (BNP) and N (or amino)-terminal pro-B-type natriuretic peptide (NT-proBNP), are released by the myocardium in response to pressure or fluid overload. In patients with heart failure (HF) the NP levels are raised. NP testing is currently used in diagnosis and prognosis, but its role in guiding HF treatment remains uncertain. The guidelines do not currently recommend NP guided treatment. Previous clinical trials and meta-analyses have researched NP-guided treatment with mixed results (1-6). Felker et al, in the GUIDE-IT study, aimed to resolve this uncertainty by testing the role of NP-guided therapy in the largest study to date.

Methods

GUIDE-IT was a multicentre randomised control trial testing the efficacy of NP-guided therapy (NT-proBNP) compared to medical therapy alone in patients with HF who had a left ventricular ejection fraction (LVEF) of $\leq 40\%$. 894 (of 1100 planned patients) were randomised in a 1:1 manner using a computer-generated method and followed up for a median 15 months. Assessment for each group of patients was the same in terms of planned visits and therapy recommendations following the American Heart Association (AHA)/ American College of Cardiology (ACC) practice guidelines, except with the addition of NP measurements for the NP-guided group. In this group, a level of less than 1000 pg/mL NT-proBNP was targeted. The primary outcome was a composite of time to first HF hospitalisation or cardiovascular mortality.

Findings

This study was stopped early due to futility as recommended by the study's data and safety monitoring board. The study found no significant improvement in time to first HF hospitalisation or cardiovascular mortality between the NP-guided therapy (n=164) and medical therapy alone (n=164) groups (hazard ratio 0.98, confidence interval 0.79-1.22, p-value 0.88). Both groups intensified HF therapy, with no significant difference between the two. Secondary clinical outcomes (first HF hospitalisation, total hospitalisations, all-cause mortality, days alive and not hospitalised for cardiovascular reasons, adverse events) were not significantly different between the groups.

Commentary

Overall the GUIDE-IT study methods were robust. The groups were well balanced at baseline. However, whilst the outcome assessors were blinded, the study clinicians and patients were not, and this could have added bias to the findings.

The GUIDE-IT study showed no effect for the primary composite outcome and on the basis of this outcome the study was stopped early. The authors suggest that the lack of effect,

but increased levels of HF therapy, may be due to an increased intensity of visits and monitoring of all patients. Furthermore, any potential benefit of NP-guided therapy was minimal because patients were already at high risk of heart failure. However, a LVEF of <40% is similar to the majority of studies previously examining this research question (3). We consider this study comparable to previous studies in the field. Nevertheless, no previous study has used this composite outcome to allow direct comparison of findings.

Implications for practice

Felker et al did not comment on implications for practice. However, readers could conclude that any plausible effects of NP-guided therapy are unlikely to be worthwhile. Nevertheless, the effects on individual outcomes, specifically mortality and hospitalization, whilst not significant in this trial, are of comparable magnitude to those observed in the recent Cochrane review and meta-analysis (3). We would like to see the GUIDE-IT study findings, with > 400 more patients than any previous study, added to this existing body of evidence before any final conclusions are drawn on the effectiveness of this intervention.

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800 words

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Competing interests

None

Funding

This article presents independent research funded by the National Institute for Health Research (NIHR) under its Programme Grants for Applied Research Programme (Reference Number RP-PG-1210-12003). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.