B-type natriuretic peptide-guided heart failure therapy

CRD summary
This review compared the effect of B-type natriuretic peptide (BNP)-guided drug therapy with usual care in patients with chronic heart failure. The authors concluded that BNP-guided therapy reduced all-cause mortality, especially in patients younger than 75 years. This was a reasonably well-conducted review, but the uncertain quality of included trials and concerns regarding generalisability warrant some cautious interpretation.

Authors' objectives
To evaluate the effect of B-type natriuretic peptide (BNP)-guided drug therapy on cardiovascular outcomes in patients with chronic heart failure.

Searching
MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and ClinicalTrials.gov were searched from 1966 to 2008. Search terms were reported. Bibliographies of retrieved articles were handsearched. Abstracts of five scientific meetings (reported in the paper) were searched.

Study selection
Randomised controlled trials (RCTs) that compared BNP-guided drug treatment with usual clinical care in at least 20 outpatients with a history of heart failure were eligible for inclusion in the review. There were no inclusion criteria for outcomes, other than that each had to be reported in more than one study. All-cause mortality, all-cause hospitalisation, survival free of any hospitalisation, number of days alive in non-hospitalised patients and percentage of patients with subsequently-adjusted heart failure medication and their achievement of target dose were assessed. Included trials comprised patients graded as New York Heart Association class II or greater and with left ventricular ejection fraction less than 50%. Mean age of patients ranged between 18 to 85 years. Most participants were men. The BNP level and its precursor (N-terminal pro-BNP) were used to guide treatment with diuretics, aldactone, beta-blockers, angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) in the included trials. Criteria used to determine target treatment levels varied (reported in the paper). Two reviewers independently selected the trials for inclusion.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Data were extracted to enable the calculation of relative risks (RR) and 95% confidence intervals (CI) for the outcomes of interest. Two reviewers independently extracted the data.

Methods of synthesis
Relative risks and 95% CIs were pooled in a fixed-effect meta-analysis (Mantel-Haenszel method). Heterogeneity was assessed using the $X^2$ test and was considered statistically significant at $p=0.05$. Subgroup analyses were conducted to explore differential effects of treatment on younger (<75 years) and older (>75 years) patients. Sensitivity analysis was carried out to examine the impact of excluding selected trials. Publication bias was assessed visually in a funnel plot.

Results of the review
Eight RCTs (n=1,726 patients, sample size range 41 to 499) were included in the meta-analysis. Mean duration of follow-up was 17 months (range three to 24 months).

A statistically significant lower risk of all-cause mortality was reported following BNP-guided treatment (RR 0.76, 95% CI 0.63 to 0.91; eight trials). The effect size was influenced by one trial that contributed nearly 50% of the weight. When this trial was excluded in the sensitivity analysis, relative risk became non-significant (RR 0.76, 95% CI 0.58 to 1.00).
In a subgroup analyses of two trials, all-cause mortality remained significantly lower in younger patients (<75 years) who received BNP-guided treatment (RR 0.52, 95% CI 0.33 to 0.82). There was no difference in outcome between modes of care in older patients. There were no statistically significant differences between groups for hospitalisation (three trials) and survival free of any hospitalisation (two trials).

There was no statistically significant heterogeneity in any of the analyses. Publication bias was considered not to be influential.

Other results outside the meta-analysis showed no statistically significant differences in terms of number of days alive and not hospitalised (two trials). Patients in the BNP-guided treatment group were more likely to have their heart failure medications (ACE inhibitors and beta-blockers) increased (two trials). Twice as many patients in the BNP-guided treatment group reached their target treatment levels compared with those who received usual care (two trials).

**Authors' conclusions**

BNP-guided drug therapy reduced all-cause mortality in patients with chronic heart failure compared with usual clinical care, especially in patients younger than 75 years.

**CRD commentary**

The review question was clear. Detailed inclusion criteria were stated for all aspects except for outcomes. A range of outcomes was available for measurement, although not all were eligible for meta-analysis. It was noteworthy that there was a disparity between eligible patients with a history of heart failure and results that appeared to apply to those with the chronic condition. The search strategy included some relevant sources. There was no indication that unpublished material was sought. Publication bias was assessed and considered to be insignificant, despite some observed asymmetry in the funnel plots. Study selection and data extraction were carried out with sufficient attempts to minimise error and bias. However, the absence of any formal quality assessment of included trials limited interpretation of the reliability of the findings. Study details were adequately provided. The chosen method of synthesis appeared to be appropriate given the absence of statistical heterogeneity, although the chosen level of significance could have resulted in underestimation and some clinical variation was apparent. This was a reasonably well-conducted review, but the uncertain quality of included trials and potential concerns about the generalisability of findings mean that some caution is required when interpreting the reliability of the authors' conclusions.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that larger trials with careful matching of age, sex and other clinical variables were needed. Continued outcome measurement of hospitalisation for heart failure and other expected benefits of BNP-guided treatment was recommended.

**Funding**

None reported.

**Bibliographic details**


**PubMedID**

20308637

**DOI**

10.1001/archinternmed.2010.35

**Original Paper URL**

http://archinte.ama-assn.org/cgi/content/abstract/170/6/507
**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Biomarkers /blood; Heart Failure /blood /mortality /therapy; Humans; Natriuretic Peptide, Brain /blood; Randomized Controlled Trials as Topic; Treatment Outcome

**AccessionNumber**
12010001703

**Date abstract record published**
24/03/2010

**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.