Meta-analysis: effect of B-type natriuretic peptide testing on clinical outcomes in patients with acute dyspnea in the emergency setting
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CRD summary
This review concluded that knowledge of B-type natriuretic peptide test values moderately reduced length of hospital and intensive unit care stay in patients presenting with acute dyspnoea in emergency settings, but did not affect admission rates or mortality. Given the limitations highlighted by the authors and variation between the included trials, the authors’ conclusions should be interpreted with some caution.

Authors’ objectives
To assess the effects of knowledge of B-type natriuretic peptide tests on clinical outcomes in patients presenting with acute dyspnoea in an emergency setting.

Searching
MEDLINE and EMBASE were searched without language restrictions between 1996 and July 2010 for relevant diagnostic studies published in an international peer-reviewed journal. Search terms were not reported, but the full search strategy was available from the authors. Reference lists of relevant studies and reviews were manually searched, and experts in the field contacted.

Study selection
Randomised controlled trials (RCTs) that compared B-type natriuretic peptide or N-terminal proB-type natriuretic peptide testing plus routine testing and clinical assessment versus routine testing and clinical assessment to diagnose heart failure in patients presenting with acute shortness of breath in the emergency setting were eligible for inclusion. Eligible trials were required to report on at least one of the following primary outcomes: hospital admission rate, length of hospital stay, and in-hospital mortality. Secondary outcomes included intensive care unit admission rates, length of included intensive care stay, 30-day mortality, and 30-day readmission.

The included trials were conducted in Switzerland, Canada, The Netherlands, USA, and Australia. The mean age of included patients ranged between 58.2 and 74 years; just over half of them were men. Where reported, between 17 and 40% of patients had a history of heart failure, between 24 and 45% had a history of chronic obstructive pulmonary disease, and 50 to 72% had a history of smoking. Emergency patient management was undertaken by specialists or rotating junior medical officers.

Two reviewers independently screened studies for inclusion, with disagreements resolved by discussion or referral to a third author if necessary.

Assessment of study quality
Two reviewers independently assessed trial quality according to the Cochrane Collaboration guidelines, including criteria on randomisation, allocation concealment, blinding, missing data, absence of selective reporting and other bias, and comparability of participant characteristics at baseline. An overall score was not reported.

Data extraction
Two reviewers independently extracted means and standard deviations (SDs) for continuous outcome data to calculate mean differences (MDs) and 95% confidence intervals (CIs). Rates for dichotomous data were extracted to calculate odds ratios (ORs) and 95% confidence intervals. Primary authors were contacted for further data, where necessary.

Methods of synthesis
Random-effects models were used to pool mean differences, odds ratios and their 95% confidence intervals, weighted by the inverse of the variance. Statistical heterogeneity was assessed using the $I^2$ statistic.
Sensitivity analyses were undertaken to assess the robustness of the findings by removing each trial individually, and by analysing trials by the specific biomarker used (data not provided).

**Results of the review**

Five RCTs (n=2,513 patients; range 452 to 612) were included in the review. All RCTs reported adequate randomisation. Four RCTs reported adequate allocation concealment. None of the RCTs were double blind, but two were blind to participants and three were blind to outcome assessors. All RCTs adequately addressed missing data, absence of selective reporting and other bias.

Knowledge of the B-type natriuretic peptide test reduced the length of hospital stay (MD -1.22 days, 95% CI -2.31 to -0.14; five RCTs) and length of critical care unit stay (MD -0.56 days, 95% CI -1.06 to -0.05; four RCTs). However, significant statistical heterogeneity was reported for both outcomes. There was a reduction in critical care unit admissions in favour of knowledge of B-type natriuretic peptide (OR 0.72, 95% CI 0.55 to 0.95; four RCTs).

No statistically significant differences were found for hospital mortality (five RCTs), 30-day mortality (four RCTs), 30-day and 60-day mortality combined (five RCTs), hospital admission rates (five RCTs), or 30-day readmission (four RCTs).

Sensitivity analyses did not significantly alter the results.

**Authors’ conclusions**

Knowledge of B-type natriuretic peptide test value in patients presenting with dyspnoea of suspected cardiac origin in the emergency department moderately reduced the length of hospital and intensive unit care stay, but did not affect hospital and critical care admission rates or mortality.

**CRD commentary**

The review question was supported by clearly defined inclusion criteria. The literature search was somewhat limited using only two databases and, although there were no language restrictions, only full publications were sought, so potentially relevant data may have been missed. The authors undertook each stage of the review process in duplicate, reducing the potential for reviewer error and bias.

Appropriate criteria were used to assess trial quality, with the majority of RCTs fulfilling most criteria. Statistical heterogeneity was reported for some outcomes (although data were not presented). The authors acknowledged the clinical and methodological heterogeneity among trials, but it was questionable whether pooling of the results was appropriate. Sensitivity analyses examined possible changes in effect size by removing individual trials, but whether or not there was any accompanying effect on statistical heterogeneity was not reported. The authors also acknowledged the small number of trials and small sample size, and wide confidence intervals for some outcomes.

Given the limitations highlighted by the authors and the issues relating to heterogeneity, the authors' conclusions should be interpreted with some degree of caution.

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

**Practice:** The authors stated that the benefit of shortening the length of stay is most likely to be seen in settings with longer hospitalisation. Significant benefit will be harder to demonstrate in settings in which hospital stay is shorter.

**Research:** The authors stated that future research should focus on developing recommendations on the use of B-type natriuretic peptide as a quantitative value and provide more information on how to interpret B-type natriuretic peptide in patients with different characteristics and several comorbidities, including heart failure.

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