

Review: B type natriuretic peptide consistently predicts death and cardiovascular events in heart failure

Doust JA, Pietrzak E, Dobson A, *et al*. How well does B-type natriuretic peptide predict death and cardiac events in patients with heart failure: systematic review. *BMJ* 2005;**330**:625.

Clinical impact ratings IM/Ambulatory care ★★★★★☆☆ Internal medicine ★★★★★☆☆ Cardiology ★★★★★☆☆ Emergency medicine ★★★★★☆☆

Q In patients with heart failure (HF), how well does B type natriuretic peptide (BNP) or its precursor form, N terminal pro-brain natriuretic peptide (NT-proBNP), predict mortality and morbidity?

METHODS



Data sources: Medline and EMBASE/Excerpta Medica (January 1994 to March 2004) and reference lists.



Study selection and assessment: studies in any language were selected if they evaluated the prognostic value of BNP in patients with heart failure. Studies were excluded if patients had had recent myocardial infarction or if endpoints were not clearly clinical. Study quality was assessed (ie, patient selection, completeness of follow up, and blinding).



Outcomes: death, cardiac death, sudden death, or other cardiovascular events.

MAIN RESULTS

19 studies assessed the relation between BNP concentrations and death or cardiovascular events in patients with HF, and 5 studies assessed the same relation in asymptomatic persons. The studies were done in various clinical settings and used various BNP tests.

Patients with HF: 4 of 5 studies using continuous measures were pooled using a random effects model. The relative risk of death per 100 pg/ml of BNP in patients with HF was 35% (95% CI 22% to 49%). The inclusion of the fifth study led to statistically significant heterogeneity. 7 studies used dichotomous measures to assess the relation between BNP and death. Different cutpoints were used, and some studies did not adjust for other risk factors. However, a consistently increased risk of death was associated with increased concentrations of BNP. The largest study showed a hazard ratio for death of 2.10 (CI 1.79 to 2.42) for patients with BNP concentrations >97 pg/ml. A similar relation was seen in studies assessing the relation between BNP concentrations and cardiovascular events (3 used continuous measures; 7 used dichotomous measures).

Asymptomatic patients: 5 studies showed a relation between increased BNP concentrations and increased risk of death. The 2 largest studies used low cutpoint scores: for ≥ 17.9 pg/ml, the hazard ratio for death was 2.2 (CI 1.2 to 3.8); for >20.0 pg/ml in men and >23.3 pg/ml in women, the hazard ratio for death was 1.6 (CI 1.1 to 2.4). 3 studies showed a relation between increased BNP concentrations and increased risk of cardiovascular events. In the largest study, the hazard ratio for cardiovascular events was 1.8 (CI 1.1 to 2.9) for a cutpoint BNP concentration >20.0 pg/ml in men and >23.3 pg/ml in women. 35 multivariable models included BNP or NT-proBNP to predict survival, cardiac death, readmission, or cardiac events. BNP or NT-proBNP had the smallest p value in 23 of these models and was the only predictor that reached statistical significance in 9 models.

For correspondence: Dr J Doust, University of Queensland, Herston, Queensland, Australia. doust@sph.uq.edu.au

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CONCLUSION

In patients with heart failure, higher concentrations of B-type natriuretic peptide or its precursor form, N-terminal pro-brain natriuretic peptide, are consistently associated with increased risk of death or cardiovascular events.

Abstract and commentary also appear in ACP Journal Club.

Commentary

BNP is a neurohormone secreted mainly by the ventricles of the heart in response to wall stretching, ventricular dilation, and/or increased ventricular pressures. Previous studies have shown that elevated plasma concentrations of BNP may be useful in the diagnosis of HF, especially in patients with acute dyspnoea.¹ In such a setting, BNP concentrations <100 pg/ml have a 90% predictive value for the absence of HF, and concentrations >500 pg/ml have a 90% predictive value for the presence of HF. BNP concentrations between 100 and 500 pg/ml are somewhat less helpful, and other tests may be needed for diagnosis.¹ However, these results are not generalisable to stable HF, where a significant proportion (20–50%) of symptomatic though well treated and compensated patients may have concentrations <100 pg/ml.

Worse left ventricular (LV) dilation, greater elevation of LV filling pressures, and more LV remodelling should all lead to higher concentrations of BNP. Therefore, BNP concentrations would be expected to be a marker of HF severity.

Doust *et al* provide a rigorous review and synthesis of the prognostic importance of BNP concentrations. Using studies of HF, almost all of which were in patients with systolic HF, and studies of asymptomatic populations, they confirmed the consistent association between higher concentrations of BNP and increased risk of death and cardiovascular events. Although large studies have identified cutpoints above which the risk is increased, the cutpoint values have varied widely among studies. In addition, when dealing with individual patients, a single cutpoint value may be difficult to use because of biological variation in BNP concentrations, including higher concentrations in older patients, women, or patients with renal insufficiency and lower concentrations in obese patients. In patients who have mild to moderate elevations in BNP, those who have no or only a minimal lowering of BNP in response to HF therapy may also represent a subset with worse prognosis.

Further studies will determine whether more aggressive treatment of patients with persistently elevated concentrations of BNP is beneficial—that is, whether BNP concentrations can be used to follow the effects of and titrate therapy for HF.

Anita Deswal, MD, MPH
Michael E DeBakey VA Medical Center
Houston, Texas, USA

¹ Maisel AS, Krishnaswamy P, Nowak RM, *et al*. Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. *N Engl J Med* 2002;**347**:161–7.