

B-type natriuretic peptide testing in the emergency setting for managing acute dyspnea

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Key words BNP, acute dyspnea, Epistemonikos, GRADE

Abstract

Introduction

The performance of B-type natriuretic peptide to accurately diagnose dyspnea of cardiac origin has been widely proved. However, its impact in clinical practice is less clear.

Methods

We searched in Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others. We extracted data from the systematic reviews, reanalyzed data of primary studies, conducted a meta-analysis and generated a summary of findings table using the GRADE approach.

Results and conclusions

We identified two systematic reviews including five studies overall, of which all were randomized trials. We concluded the use of B-type natriuretic peptide for the management of acute dyspnea in the emergency setting probably leads to a small reduction in the need for hospitalization. Additionally, it may slightly reduce mortality and intensive care unit admission, but the certainty of the evidence is low.

Problem

BNP (brain natriuretic peptide or B-type natriuretic peptide) is a polypeptide, originally found in the brain, which is secreted by ventricular cardiomyocytes in response to the stretching of myocardial fibers due to an increased hydrostatic pressure. Therefore, its levels increase in heart failure, especially when there is a reduced left ventricular ejection fraction. Its function is to promote diuresis and natriuresis, and thus to lower blood pressure. Given its correlation with heart failure, it constitutes a diagnostic method in dyspnea of cardiac origin, with high sensitivity and specificity when used in conjunction with classic methods for the diagnosis of heart failure: symptoms, physical examination, chest radiography and electrocardiogram. However, it is not clear whether the addition of this test to the management of acute dyspnea leads to changes in the clinical decisions that will ultimately translate into benefits for these patients.

Key messages

- The use of BNP in the management of acute dyspnea in the emergency setting may slightly reduce mortality and intensive care unit admission (low certainty of evidence).
- The use of BNP in the management of acute dyspnea in the emergency setting probably leads to a small reduction of hospital admission (moderate certainty of evidence).
- We are uncertain whether the use of BNP in the management of acute dyspnea in the emergency setting has any impact on readmission as the certainty of the evidence has been assessed as very low.

Methods

We searched in Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others, to identify systematic reviews and their included primary studies. We extracted data from the identified reviews and re-analyzed data from primary studies included in those reviews. With this information, we generated a structured summary denominated FRISBEE (Friendly Summary of Body of Evidence using Epistemonikos) using a pre-established format, which includes key messages, a summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies when it is possible, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

About the body of evidence for this question

What is the evidence. See evidence matrix in Epistemonikos later	We found two systematic reviews ^{1,2} , which included five primary studies ³⁻⁷ , all corresponding to randomized controlled trials.
What types of patients were included*	All trials included patients that presented acute dyspnea in an emergency setting. The mean age ranged from 58 to 74 years across the different trials, with a small predominance of male participants. Three trials ^{3,5,6} , reported that 17% to 40% of the patients included had past medical history of heart failure. Four trials ³⁻⁶ , reported that 24 to 45% of included patients had chronic obstructive pulmonary disease, and four trials ³⁻⁶ , reported past history of tobacco use in 28 to 50% of patients.
What types of interventions were included*	Three trials evaluated the use of BNP ^{4,6,7} and two trials measured Pro-BNP ^{3,5} . All trials compared against routine evaluation, which included general blood exams, electrocardiogram and chest x-rays.
What types of outcomes were measured	The trials evaluated multiple outcomes, which were grouped by the systematic reviews as follows: <ul style="list-style-type: none"> • Hospital admission • Intensive care unit admission • Length of hospital stay • In-hospital mortality • Mortality (at 30 days) • Readmission (at 30 or 60 days) <p>The mean follow up time for the trials was 30 days, with a range from 30 to 60 days.</p>

* The information about primary studies is extracted from the systematic reviews identified, unless otherwise specified.

Summary of Findings

The information on the effects of BNP in the management of acute dyspnea in the emergency setting is based on five randomized trials³⁻⁷ that included 2488 patients.

All trials reported hospital admissions (2488 patients), three trials evaluated mortality (at 30 days) (1524 patients) and intensive care unit admissions (1541 patients)⁴⁻⁶ and two trials evaluated readmission (848 patients)^{4,5}.

The summary of findings is as follows:

- The use of BNP in the management of dyspnea in the emergency setting may slightly reduce mortality at 30 days (low certainty of evidence).
- The use of BNP in the management of acute dyspnea in the emergency setting probably slightly reduces hospital admissions (moderate certainty of evidence).
- The use of BNP in the management of acute dyspnea in the emergency setting may slightly reduce intensive care unit admissions (low certainty of evidence).
- We are uncertain whether the use of BNP test in the management of acute dyspnea in the emergency setting has any impact on readmissions as the certainty of the evidence has been assessed as very low.

BNP in the management of acute dyspnea				
Patients	Acute dyspnea in the emergency setting			
Intervention	BNP testing			
Comparison	Traditional evaluation of acute dyspnea (routine evaluation which includes general blood exams, electrocardiogram, and chest x-rays)			
Outcome	Absolute effect*		Relative effect (95% CI)	Certainty of evidence (GRADE)
	WITHOUT BNP	WITH BNP		
	Difference: patients per 1000			
Mortality (at 30 days)	87 per 1000	75 per 1000	RR 0.86 (0.61 to 1.21)	⊕⊕○○ ¹ Low
	Difference: 12 patients less (Margin of error: from 34 less to 18 more)			
Hospital admission	763 per 1000	733 per 1000	RR 0.96 (0.91 to 1.00)	⊕⊕⊕○ ¹ Moderate
	Difference: 30 patients less (Margin of error: 0 to 69 less)			
Intensive care unit admission	132 per 1000	100 per 1000	RR 0.76 (0.58 to 0.99)	⊕⊕○○ ^{1,2} Low
Outcome sin información	Difference: 32 patients less (Margin of error: 1 to 55 less)		--	
Readmission	83 per 1000	77 per 1000	RR 0.93 (0.59 to 1.46)	⊕○○○ ^{1,2} Very low
	Difference: 6 patients less (Margin of error: 34 less to 38 more)			
Margin of error: 95% confidence interval (CI). RR: Risk ratio. GRADE: Evidence grades of the GRADE Working Group (see later). *The risk WITHOUT BNP is based on the risk in the control group of the trials. The risk WITH BNP (and its margin of error) is calculated from relative effect (and its margin of error). ¹ The certainty of the evidence was downgraded in one level due to imprecision, since decisions at both ends of the confidence interval would vary. For the outcomes mortality and readmission, two levels were downgraded since the decisions would vary substantially at each end of the confidence interval. ² The certainty of the evidence was downgraded in two levels due to inconsistency, since the trials presented results with opposite direction.				

Follow the link to access the interactive version of this table ([Interactive Summary of Findings – iSoF](#))

About the certainty of the evidence (GRADE)*



High: This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.



Moderate: This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate.



Low: This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.



Very low: This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

* This concept is also called 'quality of the evidence' or 'confidence in effect estimates'.

† Substantially different = a large enough difference that it might affect a decision

Other considerations for decision-making

To whom this evidence does and does not apply

These results are applicable to patients with acute dyspnea of possible cardiac origin, in which an early identification of heart failure could change the clinical decisions.

It does not apply to patients with advanced renal insufficiency, acute myocardial infarction or evidence of recent trauma.

About the outcomes included in this summary

The outcomes presented in the summary of findings table were mortality, hospital admission, intensive care unit admission and readmission, which are critical for decision-making according to the authors of this article.

Three trials did not differentiate readmission from secondary admission^{3,5,6}.

This summary did not address the difference between the skills of physicians from different centers, which could affect the impact of BNP use in clinical outcomes. One of the trials⁶ did analyze the difference between experienced versus less experienced physicians.

The evaluated intervention is the use of BNP in common clinical practice. The incorporation of guidance or protocols for the treatment of heart failure could eventually lead to different results.

Balance between benefits and risks, and certainty of the evidence

The use of BNP in the management of acute dyspnea in the emergency setting may lead to a small benefit in mortality, hospital and intensive care unit admission. Its use does not present risks, thus, the balance between risks and benefits could be slightly favorable.

Resource considerations

The cost of using BNP is variable as are the possible saved costs derived from mortality reduction, and hospital and intensive care unit admission. Given that the certainty of these outcomes is moderate and low, it is difficult to adequately estimate the balance between costs and benefits. It is reasonable to perform a formal economic evaluation in

centers where this test is to be incorporated.

None of the identified studies reported a formal cost or cost-benefit analysis.

What would patients and their doctors think about this intervention

Considering the small magnitude of the benefit and the existing uncertainty, it is likely that the decisions of different clinicians regarding BNP use will vary substantially.

Moreover, in contexts with resource constraints, it is possible that the clinical decision will lean against its use.

Differences between this summary and other sources

The conclusions obtained by this analysis are similar to those presented in the systematic reviews identified.

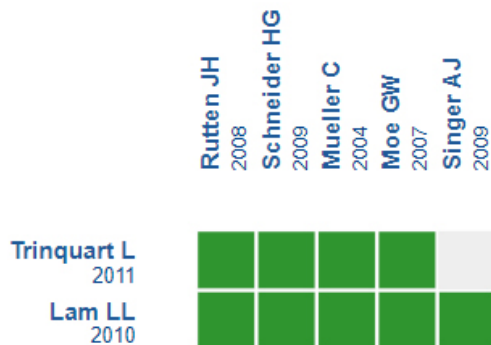
Could this evidence change in the future?

The probability that future evidence changes the conclusions of this summary is moderate due to the uncertainty associated to the critical outcomes for decision-making.

We identified two ongoing trials on this topic in the International Clinical Trials Registry Platform of the World Health Organization^{8,9}, which could provide new information.

How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.



An evidence matrix is a table that compares systematic reviews that answer the same question. Rows represent systematic reviews, and columns show primary studies. The boxes in green correspond to studies included in the respective revisions. The system automatically detects new systematic reviews including any of the primary studies in the matrix, which will be added if they actually answer the same question.

Follow the link to access the **interactive version**: [B-type natriuretic peptide testing for managing acute dyspnea at emergency settings](#)

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Notes

The upper portion of the matrix of evidence will display a warning of “new evidence” if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier.

After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated notifications any time new evidence potentially relevant for the question appears.

This article is part of the Epistemonikos Evidence Synthesis project. It is elaborated with a pre-established methodology, following rigorous methodological standards and internal peer review process. Each of these articles corresponds to a summary, denominated FRISBEE (Friendly Summary of Body of Evidence using Epistemonikos), whose main objective is to synthesize the body of evidence for a specific question, with a friendly format to clinical professionals. Its main resources are based on the evidence matrix of Epistemonikos and analysis of results using GRADE methodology. Further details of the methods for developing this FRISBEE are described here (<http://dx.doi.org/10.5867/medwave.2014.06.5997>)

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database

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