Annals of Internal Medicine | ARTICLE

B-Type Natriuretic Peptide Testing, Clinical Outcomes, and Health Services Use in Emergency Department Patients With Dyspnea

A Randomized Trial

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Background: B-type natriuretic peptide (BNP) is used to diagnose heart failure, but the effects of using the test on all dyspneic patients is uncertain.

Objective: To assess whether BNP testing alters clinical outcomes and health services use of acutely dyspneic patients.

Design: Randomized, single-blind study. Patients were assigned to a treatment group through randomized numbers in a sealed envelope. Patients were blinded to the intervention, but clinicians and those who assessed trial outcomes were not.

Setting: 2 Australian teaching hospital emergency departments.

Patients: 612 consecutive patients who presented with acute severe dyspnea from August 2005 to March 2007.

Intervention: BNP testing (n = 306) or no testing (n = 306).

Measurements: Admission rates, length of stay, and emergency department medications (primary outcomes); mortality and readmission rates (secondary outcomes).

Results: There were no between-group differences in hospital admission rates (85.6% [BNP group] vs. 86.6% [control group]; difference, −1.0 percentage point [95% CI, −6.5 to 4.5 percentage points]; P = 0.73), length of admission (median, 4.4 days [interquartile range, 2 to 9 days] vs. 5.0 days [interquartile range, 2 to 9 days]; P = 0.94), or management of patients in the emergency department. Test discrimination was good (area under the receiver-operating characteristic curve, 0.87 [CI, 0.83 to 0.91]). Adverse events were not measured.

Limitation: Most patients were very short of breath and required hospitalization; the findings might not apply for evaluating patients with milder degrees of breathlessness.

Conclusion: Measurement of BNP in all emergency department patients with severe shortness of breath had no apparent effects on clinical outcomes or use of health services. The findings do not support routine use of BNP testing in all severely dyspneic patients in the emergency department.

Primary Funding Source: Janssen-Cilag.

Ann Intern Med. 2009;150:365-371. www.annals.org
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ClinicalTrials.gov registration number: NCT00163709.

A total of 10% to 15% of all emergency department presentations are due to shortness of breath, secondary to heart failure or lung disease. Approximately 80% of patients with acute heart failure syndromes present through the emergency department (1), with dyspnea as the chief symptom (2). The incidence of heart failure is reaching epidemic proportions in the Western world (3). In Europe, up to 2% of the population has symptomatic heart failure (4) (1.5% to 2% in Australia [5]). The incidence of heart failure increases with age; approximately 10% of persons older than 65 years and more than 50% of those older than 85 years have heart failure (6, 7). With an aging population and greater survival from disease processes leading to heart failure, the burden of this disease on the health care system will only increase.

Plasma B-type natriuretic peptide (BNP) measurement in patients who present with shortness of breath could improve diagnosis and management. B-type natriuretic peptide is a 32 AA peptide hormone released from the cardiac muscle cells in response to increased ventricular filling pressure and volume expansion (8). Some observational studies have suggested excellent sensitivity and specificity for this test in diagnosing heart failure (9–15).

However, only 1 trial of moderate size (450 patients) has randomly assigned patients to undergo BNP testing or not (16). In the study, investigators in Switzerland reported that the use of the BNP test reduced hospital and intensive care unit (ICU) admissions by 10% and further reduced the median time to discharge. Death and readmissions of these patients were not altered. B-type natriuretic peptide testing markedly reduced costs ($1800 per patient), mainly because of the reduction in hospital and ICU admissions. The U.S. Food and Drug Administration approved the BNP test, and it is widely marketed throughout the United States and Europe.

Swiss emergency care systems differ from Anglo-American health systems, and it is not known whether this influences the extent to which BNP testing may affect the decision to admit patients. It is not known how the test will affect patient management and admission rates when it is done in the central laboratory and patients are assessed

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Table 1. **Baseline Demographic and Clinical Characteristics and Vital Signs**

Characteristic	BNP Group (n = 306)	Control Group (n = 306)
Age, *y*		
Mean (SD) [range]	74 (11) [42–98]	73 (11) [40–98]
Median (IQR)	76 (66–82)	75 (65–81)
Men, *n (%)*	166 (54)	162 (53)
Smoking status, *n (%)*		
Current	43 (25)	35 (22)
Former	181 (59)	185 (61)
Medical history, *n (%)*		
Hypertension	170 (56)	138 (45)
Heart failure	123 (40)	97 (32)
Ischemic heart disease	129 (42)	124 (41)
Atrial fibrillation	93 (30)	79 (26)
COPD or asthma	202 (66)	186 (61)
Diabetes mellitus	61 (20)	60 (20)
Renal failure	32 (11)	37 (12)
Symptoms, *n (%)*		
Orthopnea	76 (25)	48 (16)
Cough	153 (50)	152 (50)
Sputum	79 (26)	81 (27)
Fever	36 (12)	44 (14)
Ankle swelling	41 (13)	54 (18)
Physical examination findings, *n (%)*		
Crackles on auscultation	168 (55)	173 (57)
Increased jugular venous pressure	81 (28)	88 (30)
Wheeze on auscultation	84 (28)	86 (28)
Third heart sound	5 (2)	11 (4)
Displaced apex beat	54 (19)	36 (13)
Mean vital signs (SD) [range]		
Heart rate, *beats/min*	95 (24) [46–178]	97 (23) [50–175]
Systolic blood pressure, *mm Hg*	143 (30) [70–269]	141 (28) [70–240]
Diastolic blood pressure, *mm Hg*	73 (18) [30–155]	73 (18) [23–140]
Respiratory rate, *breaths/min*	25 (6) [6–46]	25 (8) [12–62]
Oxygen saturation, %	95 (5) [73–100]	95 (7) [42–100]
Site, *n (%)*		
The Alfred*	199 (65)	207 (68)
The Northern Hospital†	107 (35)	99 (32)

BNP = B-type natriuretic peptide; COPD = chronic obstructive pulmonary disease; IQR = interquartile range.
* Prahran, Victoria, Australia.
† Epping, Victoria, Australia.

Wales, Australia. The funding source had no role in the design, conduct, data analysis, or reporting of this study or in the decision to submit the manuscript for publication.

RESULTS

We recruited 799 patients; 187 of whom were excluded (Figure 1). The main reasons were decline to consent (n = 135), met exclusion criteria (n = 20), transfer within 24 hours (n = 19), or incomplete sample collection (n = 13). Ten patients in the BNP group had no BNP measurement because of laboratory error but we included them in the analysis. Our final study group was 612 patients randomly assigned to either the BNP group (n = 306) or the control group (n = 306). Follow-up data were available from all 612 patients. The 2 groups were similar in age, sex, smoking history, frequency of ischemic heart disease, and history of chronic obstructive pulmonary disease (Table 1). About 20% in both groups were diabetic, and 10% had a history of renal impairment. Hypertension and a history of heart failure were more frequent in the BNP group. Patients in the BNP group reported orthopnea more frequently, whereas about 50% of patients had cough, and 25% in both groups had sputum production. Both groups had similar dyspnea grades, heart rates, blood pressure, and oxygenation status (Table 1). The initial respiratory rate was increased to a similar extent in both groups.

Most patients were admitted to the hospital (Table 2). Admission rates were 85.6% in the BNP group and 86.6% in the control group (difference, −1.0 percentage point [CI, −6.5 to 4.5 percentage points]; P = 0.73). Accounting for stratification by hospital site (using the Mantel–Haenszel test) did not alter the result (odds ratio, 0.93 [CI, 0.59 to 1.5]; P = 0.74). Admissions to the ICU (1% [BNP group] vs. 3% [control group] [CI for difference, −4% to 0.4%]) and critical care unit (12% vs. 16% [CI for difference, −9% to 2%]) also did not differ, although we had limited power to detect a difference in ICU admissions. The results were unchanged after adjustment for history of hypertension, history of heart failure, and hospital site. B-type natriuretic peptide measurement did not alter hospital length of stay. The median total admission time was 4.4 days (interquartile range [IQR], 2 to 9 days) in the BNP group and 5.0 days (IQR, 2 to 9 days) in the control group (P = 0.94). Analysis of admission rates and length of stay by site did not show a difference. Review of the patient medications and treatment initiated in the emergency department for shortness of breath revealed no significant differences between groups (Table 3). Knowledge of BNP levels did not change the use of bronchodilators, diuretics, vasodilators, antibiotics, steroids, angiotensin-converting enzyme inhibitors, and noninvasive ventilation, and use of appropriate heart failure medication was not increased in patients with heart failure in the BNP group versus the control group (data not shown).

The overall 30-day mortality rate was 6.9% in the control group and 6.5% in the BNP group (P = 0.87) and varied by hospital (8% at The Alfred and 4% at The Northern Hospital in both groups). Readmission rates were 15% in the BNP group and 18% in the control group (P = 0.27), again higher at The Alfred than at The Northern Hospital (20.1% [BNP group] and 24.6% [control group] vs. 5% and 4%). Patients discharged from the emergency department directly had the same readmission

readmission and death. We achieved complete follow-up of all study participants.

Trained research assistants, who were not blinded to the group assignment, collected baseline demographic characteristics, admission rates, length of hospital stay, and clinical information from hospital records.

Two physicians made the final diagnosis of heart failure; one was a cardiologist. The physicians had access to additional information, including case notes; results of blood tests; electrocardiography and chest radiography reports; and clinical course during inpatient stay, including response to treatment, transthoracic echocardiography results, and pulmonary function test results. We did not blind physicians to the group assignment, but we did blind them to the BNP results. Reviewers defined heart failure on the basis of the definition from the European Society of Cardiology working group on heart failure diagnostic criteria (18), as well as an algorithm for the diagnosis of heart failure.

The reviewers determined whether heart failure caused the presentation to the emergency department with dyspnea or not. If the 2 independent reviewers agreed, their diagnoses were taken as the final diagnosis. When they disagreed, a third physician reviewed all available data and made the final diagnosis. The degree of agreement between the 2 reviewers was substantial in both the BNP and control groups (κ = 0.79 [95% CI, 0.78 to 0.83] and 0.82 [CI, 0.78 to 0.86], respectively).

Statistical Analysis

Prespecified outcomes were the hospital admission rate, the length of hospital stay, and any change in management in the 2 groups. With a sample size of 300 patients in each group, we calculated an 80% power to detect an absolute reduction of 10 percentage points (80% to 70%) in hospital admission rates and a relative reduction of 20% (8.0 to 6.4 days) in hospital length of stay, assuming tests were 2-sided and P values were 0.05. Statistical analysis was done by intention to treat in all patients who consented after randomization. Demographic characteristics, clinical characteristics, and baseline vital signs in the BNP and control groups are reported in counts and percentages or means (SDs), as appropriate. We compared admission rates by using Pearson chi-square and Fisher exact tests. We used the Mantel–Haenszel test to compare admission rates with and without the BNP test and stratified by hospital site. We compared length of admission between the 2 groups by using the 2-sample Wilcoxon rank-sum (Mann–Whitney) test. In addition, we did multivariate logistic regression to investigate the probability of hospital admission and length of stay. Covariates included a history of hypertension, history of heart failure, and hospital site. We compared the type of medication administered in the emergency department (number of patients and percentage) between the BNP and control groups by using the Pearson chi-square test. We compared clinical characteristics between patients with and without heart failure by using the Pearson chi-square test. We quantified agreement between the 2 reviewers by using the Cohen statistic. We did all statistical analyses by using Intercooled Stata, version 9.0, software package (Stata Corporation, College Station, Texas).

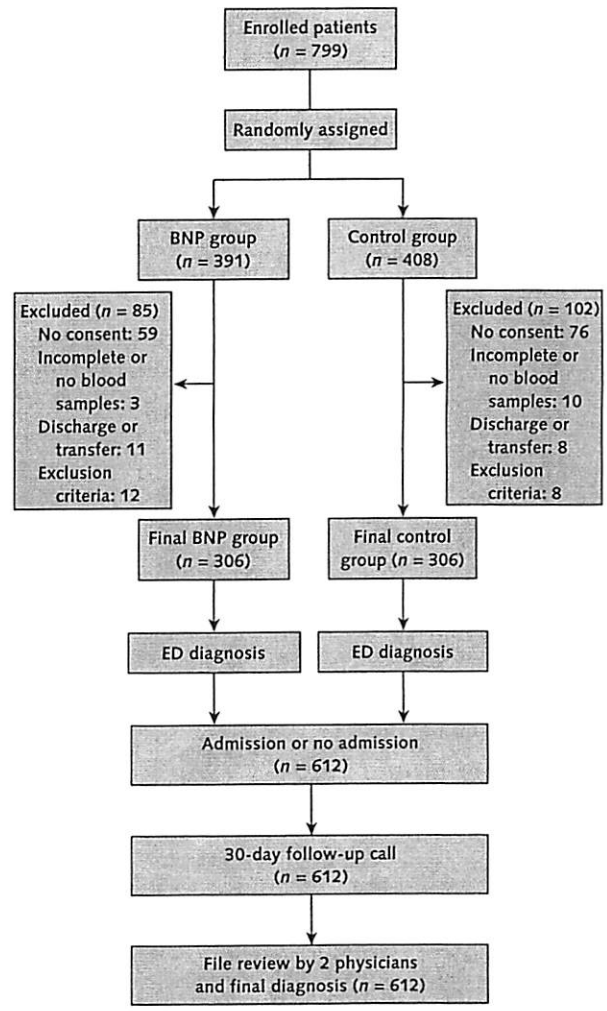
Ethical Issues

The Alfred and The Northern Hospital ethics committees and the Monash University Standing Committee on Ethics in Research Involving Humans approved this study. A trained research assistant obtained consent from all participating patients or their next of kin within 24 hours of presentation to the emergency department.

Role of the Funding Source

The study was supported by an unrestricted educational grant from Janssen-Cilag, North Ryde, New South

Figure 1. Study flow diagram.



BNP = B-type natriuretic peptide; ED = emergency department.

Context

Serum levels of B-type natriuretic peptide (BNP) increase in patients with decompensated heart failure, and BNP testing is commonly done to distinguish cardiac from noncardiac causes of dyspnea.

Contribution

In this randomized trial, BNP testing did not reduce health services use or improve health outcomes for dyspneic patients who visited emergency departments.

Caution

Patients were sick enough that the test itself was unlikely to change treatment decisions or outcomes.

Implication

The practice of measuring BNP in all dyspneic patients to see if heart failure is a cause of their symptoms may not be justified.

—The Editors

with results of chest radiography, electrocardiography, and laboratory testing, which are all available to the treating emergency physician.

We investigated whether patients who presented with shortness of breath would be managed differently and hospitalization rates would be altered if BNP was measured. We did a randomized, controlled trial of BNP testing in 2 busy, university-based, teaching hospital emergency departments.

METHODS

Design Overview

This study on BNP in shortness of breath was a randomized, controlled, single-blind trial investigating the effect of BNP testing on admission rates, length of hospital stay, and management of patients who presented to the emergency department with shortness of breath as the main symptom. We blinded patients to the intervention but did not blind clinicians or those who assessed trial outcomes.

Setting and Participants

We conducted the study in the emergency departments of The Alfred (Prahan, Victoria, Australia; a tertiary referral center with 45 000 patient attendances per year), and The Northern Hospital (Epping, Victoria, Australia; a metropolitan hospital with 70 000 patient attendances per year). We enrolled patients who presented with severe shortness of breath as the main symptom from August 2005 to March 2007. We included only patients who presented with the primary symptom of shortness of breath and were triaged to category 1 to 3 (severe illness acuity requiring assessment by a physician immediately to within 30 minutes after arrival). Exclusion criteria were age younger than 40 years, dyspnea secondary to trauma, cardiogenic shock, and a creatinine level greater than 250 μmol/L (>2.82 mg/dL). We further excluded patients who were transferred to another hospital within 24 hours of presentation because of difficulty with follow-up.

A registrar or consultant clinically assessed all patients in the emergency department. Routine investigations included blood tests, chest radiography, and electrocardiography. We ordered transthoracic echocardiography and pulmonary function tests within 30 days of presentation when possible.

Randomization and Interventions

Emergency department staff enrolled patients in the study at presentation. Patients were randomly assigned to have BNP tested (BNP group) or not tested (control group) before consent. Consent for use of patient data and follow-up and further involvement in the trial was obtained within 24 hours.

We blinded patients to the intervention. Allocation to the BNP and control group was by random numbers (from computer-generated, random-number tables) in a sealed envelope. The randomization was stratified by site.

We collected 10 mL of the patient's blood in tubes containing EDTA and sent it to the hospital laboratory. Patients randomly assigned to the BNP group had BNP analyzed, and the result was provided with other blood test results within 60 minutes. We measured BNP by using the Abbott AxSYM MEIA Automated Immunoassay (Abbott, Chicago, Illinois). The measurable range of the BNP assay is 15 to 4000 ng/L. The assay has a functional sensitivity of 20 ng/L (coefficient of variation, 20%) and is calibrated against the Triage B-Type Natriuretic Peptide test (Biosite, San Diego, California) (9). The diagnostic value of detecting heart failure by using this BNP assay has been documented (17).

Four education sessions during the study period familiarized emergency department staff with BNP, its role in the diagnosis of heart failure, and the current literature in the field. The BNP test had been done at the main study hospital for 5 years if requested from the cardiology department; but if other physicians requested the test, a chemical pathologist needed to approve it. Each physician who treated an enrolled patient received a written guideline on the treatment of acute heart failure and chronic obstructive pulmonary disease, as well as the BNP nomogram published by McCullough and coworkers (10). We advised physicians that a BNP level less than 100 ng/L made the diagnosis of heart failure unlikely, whereas a BNP level greater than 500 ng/L made heart failure likely.

Outcomes and Follow-up

Primary outcomes were hospital admission rate, length of stay, and change in patient management. Secondary outcomes were 30-day mortality and readmission rates. We contacted all patients or next of kin after 30 days about

Table 2. Admission Rates and Length of Hospital Stay

Variable	Admissions, *n* (%)		Between-Group Difference (95% CI), *percentage points**	Median Length of Stay (IQR), *d*		*P* Value†
	BNP Group (*n* = 306)	Control Group (*n* = 306)		BNP Group (*n* = 306)	Control Group (*n* = 306)	
All units	262 (85.6)	265 (86.6)	−1.0 (−6.5 to 4.5)	4 (2–9)	5 (2–9)	0.93
ICU	4 (1.3)	10 (3.3)	−2.0 (−4.3 to 0.4)	2 (2–5)	4 (2–6)	0.44
CCU	38 (12.4)	48 (15.7)	−3.3 (−8.8 to 2.3)	4 (2–6)	3 (1–7)	0.28
General ward	220 (71.9)	207 (67.7)	4.2 (−3.0 to 11.5)	5 (3–10)	5 (3–9)	0.69

BNP = B-type natriuretic peptide; CCU = critical care unit; ICU = intensive care unit; IQR = interquartile range.
* Statistical analysis by Pearson chi-square test, 2-sample *t* test, and Fisher exact test (ICU). All *P* values were greater than 0.100.
† Statistical analysis by Wilcoxon rank-sum (Mann–Whitney) test.

rate, regardless of whether BNP was tested (8 of 36 [BNP group] vs. 7 of 34 [control group]; $P = 0.89$).

Heart failure was the final diagnosis in 44.8% ($n = 274$) of all patients who participated in the trial (148 [48.4%] patients in the BNP group and 126 [41.2%] patients in the control group). Patients with heart failure were on average 6 years older (mean age, 77 years [SD, 10.8] [range, 45 to 98 years] vs. 70.8 years [SD, 11.5] [range, 40 to 94 years]; $P < 0.001$) than those without. Patients with heart failure were more likely to have a history of hypertension, heart failure, ischemic heart disease, and atrial fibrillation. A history of chronic obstructive pulmonary disease was more frequent in the patients without heart failure (Table 4). Consistent with the final diagnosis, symptoms and signs of heart failure were more frequent in the heart failure group.

Patients in the BNP group with a final diagnosis of heart failure had markedly elevated BNP values compared with those without heart failure (median, 830 ng/L [IQR, 391 to 1425 ng/L] vs. 99 ng/L [IQR, 46 to 180 ng/L]) (Figure 2).

When compared with the final adjudicated diagnosis of heart failure, BNP discriminated accurately between patients with and without heart failure (area under the receiver-operating characteristic curve [AUC], 0.87 [CI, 0.83 to 0.91]).

Table 3. Treatment Initiated in the Emergency Department

Medication	BNP Group (*n* = 306), *n* (%)	Control Group (*n* = 306), *n* (%)	Between-Group Difference (95% CI), *percentage points**
Bronchodilator	122 (39.8)	112 (36.6)	3.2 (−4.5 to 11.0)
Diuretic	110 (36.0)	109 (35.6)	0.4 (−7.3 to 8.0)
Vasodilator	52 (17.0)	47 (15.4)	1.6 (−4.2 to 7.5)
Antibiotic	100 (32.7)	112 (36.6)	−3.9 (−11.5 to 3.6)
Steroid	80 (26.1)	65 (21.2)	4.9 (−1.8 to 11.7)
Morphine	17 (5.6)	17 (5.6)	0 (−3.6 to 3.6)
Digoxin	8 (2.6)	8 (2.6)	0 (−2.5 to 2.5)
Amiodarone	0 (0)	2 (0.7)	−0.7 (−1.6 to 0.3)
ACE inhibitor	3 (1.0)	3 (1.0)	0 (−1.6 to 1.6)
Noninvasive ventilation	43 (14.1)	30 (9.8)	4.3 (−0.9 to 9.4)

ACE = angiotensin-converting enzyme; BNP = B-type natriuretic peptide.
* Statistical analysis by Pearson chi-square test and 2-sample *t* test. All *P* values were greater than 0.100.

Discussion

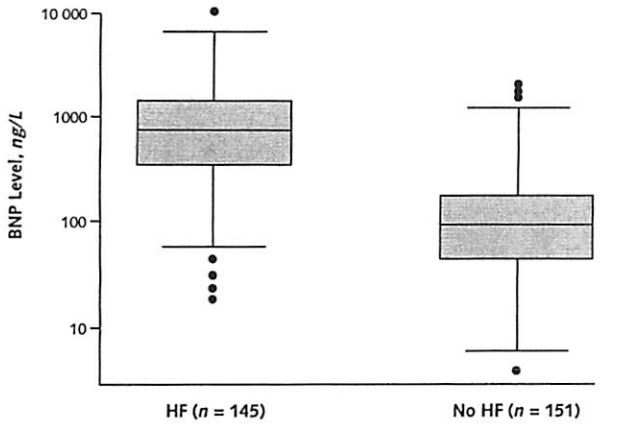
In this randomized study of 612 patients, clinician knowledge of BNP values in patients who presented with shortness of breath to the emergency department did not reduce the probability of hospital admission or alter management or length of hospital stay. Therefore, these data do

Table 4. Clinical Characteristics of Patients With a Final Diagnosis of Heart Failure or No Heart Failure

Characteristic	Heart Failure (*n* = 274 [44.8%]), *n* (%)	No Heart Failure, (*n* = 338 [55.2%]), *n* (%)	*P* Value*
Trial assignment†			
BNP group	148 (54)	158 (47)	–
Control group	126 (46)	180 (53)	–
Medical history			
Hypertension	173 (63)	135 (40)	<0.001
Heart failure	163 (60)	57 (17)	<0.001
Ischemic heart disease	162 (60)	91 (27)	<0.001
Atrial fibrillation	110 (40)	62 (19)	<0.001
COPD or asthma	156 (57)	232 (69)	0.003
Diabetes mellitus	63 (23)	58 (17)	0.072
Renal failure	49 (18)	20 (6)	<0.001
Symptoms			
Orthopnea	86 (31)	38 (11)	<0.001
Cough	111 (41)	194 (57)	<0.001
Sputum	49 (18)	111 (34)	<0.001
Fever	24 (9)	56 (17)	0.004
Ankle swelling	63 (23)	32 (10)	<0.001
Physical examination findings			
Crackles on auscultation	204 (75)	137 (41)	<0.001
Increased jugular venous pressure	136 (52)	33 (10)	<0.001
Wheeze on auscultation	64 (23)	106 (31)	0.028
Third heart sound	10 (4)	6 (2)	0.148
Displaced apex beat	68 (27)	22 (7)	<0.001

BNP = B-type natriuretic peptide; COPD = chronic obstructive pulmonary disease.
* Statistical analysis by Pearson chi-square test.
† Percentages in the BNP and control groups were calculated by using the trial group denominator ($n = 306$).

Figure 2. BNP values in patients who presented to the emergency department with shortness of breath and had a final diagnosis of HF or no HF.



BNP = B-type natriuretic peptide; HF = heart failure.

not support routine use of BNP testing in all patients who present to the emergency department with shortness of breath.

We did a systematic search of MEDLINE using the terms *heart failure*, *emergency service*, *natriuretic peptides*, *BNP*, *NT-proBNP* [*N*-terminal fragment of prohormone BNP], *shortness of breath*, and *randomized, controlled trial* to identify all trials evaluating the use of BNP testing in emergency department settings. We identified 1 trial that looked at the effect of BNP testing (16) and 2 trials that investigated the use of NT-proBNP testing (19, 20) in patients who present to the emergency department with shortness of breath.

The previous trial of BNP (16) evaluated the use of a point-of-care BNP testing device and found that it reduced hospital and ICU admission rates, time to treatment, and length of hospital stay. Because results of a point-of-care assay are usually available within 20 minutes, the observed effects might have been due to the fact that the physicians received the BNP result earlier, reassessed patients faster, and administered the correct medications sooner and avoided incorrect medications. Hospitalization rates in our study (85%) were similar to that of the other trials' control groups (85%), but length of stay in that trial (8.0 days [BNP group] and 11 days [control group]) was almost twice that found in our trial (4.4 days [BNP group] and 5.0 days [control group]), so there may have been a greater opportunity for reductions in hospitalizations and lengths of stay. The BNP test that we studied was done in a central laboratory within 60 minutes, but we did not measure time to medication initiation. The use of correct medication for heart failure was not improved in the BNP group compared with the control group.

Similar to our findings, neither of the 2 trials that investigated NT-proBNP testing in patients who presented to the emergency department with shortness of breath (19, 20) showed decreased admission rates. One trial (20) showed reduced hospital stay, whereas the other found a reduction in readmission rates after hospitalization (19). The sample in our trial was older than the sample in the trial that found a reduction in hospital stay, and the hospitalization rates seen in our study were higher than those in both NT-proBNP trials (57% to 58% [19] and 62% to 67% [20]). Mortality rates were lower than those in the other BNP study (6.5% to 7% vs. 10% to 12%) (16) but were similar to those in the NT-proBNP studies (4.5% to 5.5% [19] and 6% to 8% [20]). Use of BNP did not alter the mortality rate during follow-up after presentation in any previous study. The availability of BNP or NT-proBNP testing did not alter admission rates or length of stay in our trial or the other trial with qualified emergency physicians in the emergency departments (19).

We did BNP testing by using a previously validated technique on routine laboratory equipment (17). Test discrimination was good (AUC, 0.87 [CI, 0.83 to 0.91]) and similar to that in other large studies using BNP (9) and NT-proBNP (19) in the emergency department.

Our study has several limitations. Our results may be limited to patients with severe shortness of breath because we included only patients in emergency department triage category 1 to 3. We excluded 187 patients after randomization before consent, but we enrolled all attendees to the emergency department. We did not stratify by physician, but we do not believe this is likely to affect the trial findings because of the number of clinicians involved and their standardized approach to care. We did our study at only 2 academic centers in Australia, and the findings might not be generalizable to other settings, perhaps especially centers with less experienced staff. Slightly more patients with a history of heart failure were in the BNP group. It is not clear whether this could have influenced our results, but our findings reflect adjustments for imbalances in hypertension and a history of heart failure. Chung and colleagues (21) reported that BNP discriminated less well in patients with a history of heart failure, but test accuracy was higher in our trial (AUC, 0.87 vs. 0.75). A total of 60% of our patients had chronic obstructive pulmonary disease and lung disease causing right heart failure and pulmonary hypertension, which can elevate BNP (22), but this did not seem to affect the accuracy of the BNP test in our population. B-type natriuretic peptide testing has been shown to increase accuracy of heart failure diagnosis in general practitioners (23), but we lack data for improved management. Finally, although indiscriminate BNP testing of all patients who presented to the emergency department with shortness of breath did not alter admission rates or length of stay, there might be subgroups that would benefit from the test. In a meta-analysis, Wang and coworkers (24) showed that a high level of clinical suspicion for heart failure has a high positive likelihood ratio (9.9), and BNP

might not help in that situation. Furthermore, in a retrospective analysis of the PRIDE study (ProBNP Investigation of Dyspnea in the Emergency Department), Green and colleagues' data (25) indicate that NT-proBNP might be especially helpful, if the clinical certainty is low. Further investigations are required in this regard.

In summary, our study demonstrated that routine use of a BNP assay in all patients who presented with severe dyspnea to an emergency department does not improve admission or discharge decisions or improve initial treatment planning. The value of clinical decision making, in conjunction with established routine investigations, should be emphasized. Our findings do not support routine use of the BNP assay in all patients who present with shortness of breath to the emergency department.

From Alfred Health, Prahran, and Royal Melbourne Hospital, Parkville, Victoria, Australia.

Grant Support: By an unrestricted educational grant from Janssen-Cilag to Drs. Schneider and Krum.

Potential Financial Conflicts of Interest: *Grants received*: H.G. Schneider (Janssen-Cilag), H. Krum (Janssen-Cilag).

Reproducible Research Statement: *Study protocol*: Available from Dr. Schneider (e-mail, schneiderh@alfred.org.au). *Statistical code and data set*: Not available.

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Current author addresses and author contributions are available at www.annals.org.

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BNP testing, clinical outcomes and health service use in ED patients with dyspnoea
Annals Intern Med 2009; 150:365 – 371

1. **Provide a summary of this paper (max 200 words, short bullet points are acceptable) (6)**

2. **Why did the authors feel it was necessary to undertake this study? (1)**

3. **The following quote is taken from the 'Methods' section of the paper:**
   'a randomized, controlled, single-blind trial' External / Internal validity

   a) How was randomization achieved and what purpose does it serve? (1)
   b) Who was 'blinded' and was this the correct subgroup to blind to the test results? – Explain your answer (1)
   c) What was the control intervention and was why was it used? (1)

4. **What was the role of written guidance on the management of acute heart failure and COPD? (1)**

5. **The following quote is taken directly from the paper:**
   " the degree of agreement between the 2 reviewers was substantial in both the BNP and control groups (k=0.79 [95% CI 0.78 to 0.83] and 0.82 [CI 0.78 to 0.86] respectively"

   random = 0

   a) What is the 'k' (kappa score) and why is it used (1) should be >0.6
   b) Explain the meaning of [95% CI 0.78 to 0.83] (1)

6. **Why is the 'intention to treat' principle for data interpretation used? (1)** to account for crossover / drop out
   to protect allocation concealment

7. **What is the purpose of a sample size calculation? (1)** to prevent Type 2 error

8. **Where the groups comparable at baseline and suggest how the presentation of this data could be improved (1)**

9. **The following quote is taken directly from the paper**
   "Admission rates were 85.6% in the BNP group and 86.6% in the control group (difference, -1.0 percentage point [CI, -6.5 to 4.5 percentage points] P= 0.73"

   What is the role of the p value? (1) = probability of effect occurring by chance

10. **What is meant by the terms median and 'interquartile range'? (1)**

11. **What is meant by the term positive likelihood ratio? (1)**

12. What is the weakness of performing subgroup analysis? (1)

13. How could this study be improved? (4)

Total (24)
Pass mark 15