ORIGINAL INVESTIGATION

Cost-effectiveness of B-Type Natriuretic Peptide Testing in Patients With Acute Dyspnea

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Background: B-type natriuretic peptide (BNP) is a quantitative marker of heart failure that seems to be helpful in its diagnosis.

Methods: We performed a prospective randomized study (B-Type Natriuretic Peptide for Acute Shortness of Breath Evaluation) including 452 patients who presented to the emergency department with acute dyspnea to estimate the long-term cost-effectiveness of BNP guidance. Participants were randomly assigned to a diagnostic strategy involving the measurement of BNP levels (n=225) or assessment in a standard manner (n=227). Nonparametric bootstrapping was used to estimate the distribution of incremental costs and effects on the cost-effectiveness plane during 180 days of follow-up.

Results: Testing of BNP induced several important changes in management of dyspnea, including a reduction in the initial hospital admission rate, the use of intensive care, and total days in the hospital at 180 days (median, 10 days [interquartile range, 2-24 days] in the BNP group vs 14 days [interquartile range, 6-27 days] in the control group; *P*=.005). At 180 days, all-cause mortality was 20% in the BNP group and 23% in the control group (*P*=.42). Total treatment cost was significantly reduced in the BNP group ($7930 vs $10 503 in the control group; *P*=.004). Analysis of incremental 180-day cost-effectiveness showed that BNP guidance resulted in lower mortality and lower cost in 80.6%, in higher mortality and lower cost in 19.3%, and in higher or lower mortality and higher cost in less than 0.1% each. Results were robust to changes in most variables but sensitive to changes in rehospitalization with BNP guidance.

Conclusion: Testing of BNP is cost-effective in patients with acute dyspnea.

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THE CLINICAL DIAGNOSIS OF heart failure (HF) may be difficult,[1-4] particularly in patients presenting with acute dyspnea in the emergency department (ED). Clinical history, physical examination, electrocardiography, and chest radiography may provide valuable clues as to whether HF is the cause of acute dyspnea.[1,2] However, after review of this information, physicians are left with considerable diagnostic uncertainty in up to 50% of patients.[4-6] Misdiagnosis of HF can lead to morbidity and increased resource utilization.

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Recently, B-type natriuretic peptide (BNP) has been suggested to be helpful in this setting. Levels of BNP are reliably elevated in the setting of HF and significantly increase the accuracy of the clinical evaluation.[4-10] The randomized B-Type Natriuretic Peptide for Acute Shortness of Breath Evaluation (BASEL) study showed that more rapid and more accurate diagnosis results in a reduction in the rate of hospitalizations, time to discharge, and initial treatment cost.[11] Therefore, BNP testing may confer improvements in both the costs and the effectiveness of treatment of patients with acute dyspnea. We planned and prospectively performed long-term cost-effectiveness analyses of BNP testing in patients enrolled in the BASEL study.

METHODS

PATIENT POPULATION

The design and primary results of the BASEL study have been previously reported.[11,12] Briefly, 452 patients presenting to the ED with acute dyspnea were enrolled in this randomized, controlled single-blind trial. Exclusion criteria included trauma, severe renal disease, and cardiogenic shock. Groups were assigned with the use of a computer-generated randomization scheme in a 1:1 ratio without stratification. A total of 225 patients were randomly assigned to be examined with a diagnostic strategy that included rapid measurement of BNP levels, and 227 were assigned to be examined with the conventional diagnostic strategy.

PROCEDURES

All patients underwent an initial clinical assessment that included clinical history taking, physical examination, electrocardiography, pulse oximetry, blood tests, and chest radiography. The study investigators neither were directly involved in patient care nor had any influence on the decision to admit or discharge patients. The study was carried out in accordance with the principles of the Declaration of Helsinki and approved by the local ethics committee. Written informed consent was obtained from all participating patients.

During the initial evaluation, venous blood was collected in tubes containing potassium EDTA. The BNP was measured with the use of a rapid fluorescence immunoassay (Biosite Inc, San Diego, Calif). In the BNP-guided group, the BNP level was considered in the context of the clinical information obtained and the physicians' clinical impression.[11,12] We used 2 BNP cutoff levels (rule out, 100 pg/mL; rule in, 500 pg/mL) to separate HF from other causes of acute dyspnea. In patients with a BNP level less than 100 pg/mL, HF was considered unlikely and alternative causes of dyspnea had to be pursued. In patients with a BNP level greater than 500 pg/mL, HF was considered very likely and rapid therapy with diuretics, nitroglycerin, and angiotensin-converting enzyme inhibitors was recommended. Patients in the control group were examined and treated according to the most recent clinical guidelines.[1,2]

SURVIVAL AND RESOURCE USE

We obtained data on survival from the time of randomization to the end of study follow-up and on the use of specific health care resources. Patients were contacted 6 months after the initial presentation by telephone interview. In addition, referring physicians were contacted. The calculation of total days in the hospital and total cost of treatment included all hospitalizations after the initial presentation to the ED. Because ratios of costs to charges have not been defined for most of the services and departments at our institution, hospital charges were used as the most appropriate estimate of the true costs.[13,14] To avoid an imbalance due to differences in reimbursement or charges associated with different types or classes of insurance, charges were standardized according to the actual rates for patients with general insurance who were living in Basel, Switzerland. Expenses for hospital care were primarily determined by the intensity of care and the length of stay. The following cost weights applied: for the first 3 days in hospital, $575 per day; for every additional day, $383; for outpatient visits, $286; for visits of less than 24 hours but with stay overnight in the ED, $381; and for every hour in the intensive care unit, $86. Total cost of treatment also included cost of cardiovascular and pulmonary medication calculated according to standard rates in Switzerland in 2003. Other medication was not included in this cost analysis because differences would be more likely due to differences in baseline medical conditions than related to BNP testing. For the cost of BNP testing, the reimbursement amount for the measurement of BNP in Switzerland ($47) in 2002 was used. Because of the short follow-up period, cost during follow-up was not deflated. All end points were assessed in a blinded fashion by physicians who were not involved in patient care, with the use of all medical records pertaining to each patient. To address the possibility that tailoring of resources may be cost-effective initially but may result in large secondary costs due to recurrent symptoms and hospitalizations or potentially even increased mortality, cost-effectiveness analysis was performed at 180 days of follow-up.

COST-EFFECTIVENESS ANALYSIS

Cost-effectiveness analysis evaluates and compares both costs and effects of alternative therapies. We estimated effects (mean mortality rate) and the mean cost per patient for the BNP and control groups. Mean cost was calculated by multiplying each resource use component by the unit cost and summing the results for each patient; we then calculated the mean across all patients. Recent developments in economic methods emphasize the importance of quantifying uncertainty about the incremental cost-effectiveness ratio by examining the joint density of cost and effect differences.[15-17] Nonparametric bootstrap analysis was used to estimate 95% confidence intervals for differences in average costs and for the incremental cost-effectiveness ratios presented (each of these simulations using 5000 bootstrap samples drawn from the original data set), and also to assess the shape of the joint sampling distribution of the differences in average individual costs and effects between the 2 groups.[15-17] Uncertainties surrounding costs, benefits, and cost-effectiveness were represented by confidence ellipses in the "cost-effectiveness plane."[15-17] The presentation of cost-effectiveness results as cost-effectiveness ratios with 95% confidence interval is inappropriate, since confidence intervals of costs (ie, the numerator of the cost-effectiveness ratio) and effects (ie, the denominator of the cost-effectiveness ratio) are multiplied, and also insufficient, since the interpretation of cost-effectiveness ratios depends on the quadrants of the cost-effectiveness plane into which incremental costs and effects fall.[17-19] For example, in the assessment of a less efficient but cheaper new treatment strategy (represented in the lower left quadrant of the cost-effectiveness plane), a numerically high cost-effectiveness ratio would be favorable, whereas in the assessment of a more expensive but more efficient strategy (upper right quadrant), the opposite is true.[17-19] The remaining quadrants represent situations where the evaluated strategy is more expensive and less effective (dominated; upper left quadrant) or less expensive and more effective (dominant; lower right quadrant). This taken into account by an additional graphic representation of the bootstrapping results in the cost-effectiveness plane, with 95% and 50% confidence ellipses describing their degree of uncertainty. To assess the robustness of the results, sensitivity analyses were performed for changes in the duration of the initial hospitalization, expense for BNP testing, time in the intensive care unit, cost of long-term medication, and rehospitalization days with BNP guidance. The statistical analyses were performed with the SPSS/PC (version 13.0; SPSS Inc, Chicago, Ill) and SAS/PC (version 8.2; SAS Institute Inc, Cary, NC) software packages. A statistical significance level of .05 was used. All data were analyzed on an intention-to-treat basis. Comparisons were made by means of the t test, Mann-Whitney test, Fisher exact test, and χ^2 test as appropriate. Costs were compared by bootstrap t tests. All hypothesis testing was 2 tailed. These analyses were prespecified in the BASEL study protocol. The economic analysis was conducted in Swiss francs and then converted to US dollars by using the average actual currency conversion rate during the trial period.

RESULTS

Baseline demographic and clinical characteristics were well matched between the 2 groups (**Table 1**). Mean age was 71 years. In the BNP group, BNP levels were less than 100 pg/mL in 80 patients (36%), 100 to 500

Table 1. Baseline Characteristics in the BNP and Control Groups*

Characteristic	BNP Group (n = 225)	Control Group (n = 227)
Age, mean (SD), y	70 (16)	71 (15)
Women, No. (%)	93 (41)	97 (43)
History, No. (%)		
Coronary artery disease	113 (50)	112 (49)
Arterial hypertension	113 (50)	124 (55)
Diabetes mellitus	47 (21)	56 (25)
COPD	75 (33)	65 (29)
Asthma	17 (8)	12 (5)
Pneumonia	30 (13)	28 (12)
Pulmonary embolism	18 (8)	13 (6)
Other pulmonary or pleural disease	20 (9)	26 (11)
Any pulmonary disease	119 (53)	107 (47)
Depressive disorder	15 (7)	21 (9)
Stroke or peripheral vascular disease	40 (18)	49 (22)
Chronic kidney disease	56 (25)	56 (25)
Deep vein thrombosis	19 (8)	22 (10)
Symptoms, No. (%)		
Dyspnea†		
Slight hill	32 (14)	33 (15)
Level ground	125 (56)	132 (58)
At rest	66 (29)	58 (26)
Paroxysmal nocturnal dyspnea	79 (35)	87 (38)
Nocturia	60 (27)	76 (33)
Chest pain	76 (34)	78 (34)
Coughing	101 (45)	123 (54)
Expectoration	72 (32)	87 (38)
Fever	59 (26)	50 (22)
Vital status, mean (SD)		
Systolic blood pressure, mm Hg	146 (29)	145 (28)
Diastolic blood pressure, mm Hg	85 (17)	86 (19)
Heart rate, beats/min	96 (23)	99 (26)
Temperature, °C	37.6 (1.0)	37.4 (1.0)
Signs, No. (%)		
Tachypnea (>20/min)	106 (47)	104 (46)
Elevated jugular venous pressure	32 (14)	32 (14)
Hepatojugular reflux	25 (11)	24 (11)
Rales	103 (46)	104 (46)
Wheezing	55 (24)	45 (20)
Hyperresonant percussion	22 (10)	17 (7)
Dullness	20 (9)	26 (11)
Cyanosis	14 (6)	19 (8)
Lower-extremity edema	73 (32)	83 (37)
Laboratory tests, mean (SD)		
Hemoglobin, g/dL	13.5 (2.2)	13.4 (3.1)
Serum creatinine, mg/dL	1.28 (0.67)	1.31 (0.61)
Serum albumin, g/L	34 (6)	33 (5)
Final discharge diagnosis, No. (%)‡		
Acute heart failure	101 (45)	116 (51)
Exacerbated COPD/asthma	51 (23)	25 (11)
Pulmonary embolism	10 (4)	11 (5)
Pneumonia	32 (14)	30 (13)
Anxiety disorder	7 (3)	9 (4)
Other disease§	26 (12)	33 (15)
Unknown cause	8 (4)	12 (5)

Abbreviations: BNP, B-type natriuretic peptide; COPD, chronic obstructive pulmonary disease.

SI conversion factor: To convert creatinine to micromoles per liter, multiply by 88.4.

*There were no significant differences between the BNP group and the control group.

†Four patients in the BNP group and 2 patients in the control group had dyspnea only while walking up a steep incline.

‡*P* = .05 for the overall comparison of discharge diagnoses.

§Including interstitial lung disease, pneumothorax, pleural effusion, sepsis, and anemia.

Table 2. Outcomes in the BNP and Control Groups

Variable	BNP Group (n = 225)	Control Group (n = 227)	*P* Value
Initial hospital visit			
Total days in hospital, median (IQR)	8 (1-16)	10 (5-18)	.002
If admitted, median (IQR)	11 (6-19)	13 (8-21)	.06
Total treatment cost, mean (SD), $	5410 (6804)	7264 (7363)	.006
All-cause mortality, No. (%)	13 (6)	21 (9)	.21*
At 90 d			
Total days in hospital, median (IQR)	9 (1-19)	13 (6-24)	.001
Days in hospital for dyspnea	8.5 (1-19)	12 (6-23)	.001
Medication cost, mean (SD), $	173 (137)	173 (127)	.98
Total treatment cost, mean (SD), $	6499 (7518)	9037 (8314)	.001
All-cause mortality, No. (%)	32 (14)	36 (16)	.69*
At 180 d			
Total days in hospital, median (IQR)	10 (2-24)	14 (6-27)	.005
Days in hospital for dyspnea	9 (1-20)	13 (6-24)	.003
Medication cost, mean (SD), $	328 (253)	326 (267)	.92
Total treatment cost, mean (SD), $	7930 (8805)	10 503 (10 176)	.004
All-cause mortality, No. (%)	44 (20)	52 (23)	.42*

Abbreviations: BNP, B-type natriuretic peptide; IQR, interquartile range.
*Fisher exact test.

pg/mL in 64 patients (28%), and greater than 500 pg/mL in 80 patients (36%). Testing of BNP induced several important changes in patient treatment. Heart failure was the final discharge diagnosis in 45% of patients in the BNP group and 51% of patients in the clinical group (*P*=.19). Exacerbation of obstructive pulmonary disease was considered the cause of acute dyspnea more often in the BNP group than in the clinical group (23% vs 11%; *P*=.001) (**Table 2**). Follow-up was complete in 451 (99.8%) of 452 patients (**Figure 1**). Cost data were available equally in both groups. Detailed data on outcomes and use of specific resource in the hospital and during follow-up are summarized in **Tables** 2, **3**, and **4**.

During the initial presentation to the ED, the use of BNP levels significantly reduced the need for hospitalization and intensive care: 75% of patients in the BNP group were hospitalized, as compared with 85% of those in the control group (*P*=.008), and 15% of patients in the BNP group required admission to the intensive care unit, as compared with 24% of those in the control group (*P*=.01) (Table 3). Moreover, the use of BNP levels reduced the need for ventilatory support and the number of echocardiographic procedures performed during the initial presentation. Patients assigned to the BNP group spent significantly fewer days in the hospital than did patients in the control group (median, 8 days [interquartile range, 1-16 days] vs 10 days [interquartile range, 5-18 days]; *P*=.002) (Table 2). Total initial treatment cost was significantly reduced in the BNP group ($5410 vs $7264

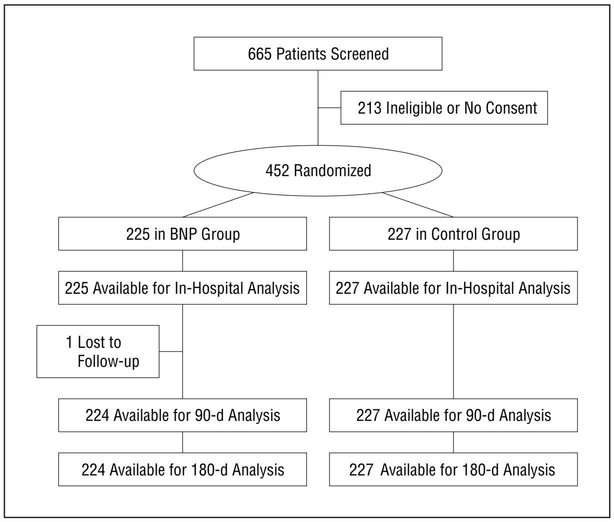

Figure 1. Patient flow through trial.

Table 3. Use of Specific Resources in the BNP and Control Groups*

Variable	BNP Group (n = 225)	Control Group (n = 227)	*P* Value
During initial hospital visit			
Intensive care	33 (15)	54 (24)	.01
Time in ICU, mean (SD) [median], h	10 (40) [0]	18 (47) [0]	.01
Mechanical ventilation (intubation)	2 (1)	8 (4)	.11
Noninvasive ventilation	13 (6)	20 (9)	.22
Any ventilatory support†	14 (6)	28 (12)	.03
Pulmonary artery catheter	0	5 (2)	.06
Coronary angiography	12 (5)	20 (9)	.15
Echocardiography	91 (40)	112 (49)	.06
Holter ECG	8 (4)	11 (5)	.49
Exercise ECG	8 (4)	10 (4)	.64
Myocardial perfusion SPECT	6 (3)	9 (4)	.44
During 180-d follow-up			
Coronary angiography	7 (3)	7 (3)	>.99
Echocardiography	33 (15)	38 (17)	.55
Holter ECG	8 (4)	6 (3)	.58
Exercise ECG	14 (6)	11 (5)	.52
Myocardial perfusion SPECT	14 (6)	12 (5)	.67

Abbreviations: BNP, B-type natriuretic peptide; ECG, electrocardiogram; ICU, intensive care unit; SPECT, single photon emission computed tomography.

*Values are expressed as number (percentage) of patients unless otherwise indicated.

†Mechanical ventilation (intubation) or noninvasive ventilation.

Table 4. Specific Drugs Used in the Intensive Care Unit* and at Hospital Discharge

Variable	BNP Group	Control Group	*P* Value
In intensive care unit	n = 33	n = 54	
Nitroglycerin IV	15 (45)	11 (20)	.01
Nitroglycerin oral or transdermal	8 (24)	8 (15)	.27
ACE inhibitors†	16 (48)	22 (41)	.48
Loop diuretics IV	25 (76)	31 (57)	.08
Thrombolysis	1 (3)	2 (4)	>.99
Antibiotics	14 (42)	26 (48)	.60
Vasopressors or inotropic agents	2 (6)	9 (17)	.20
Insulin IV	4 (12)	6 (11)	>.99
At hospital discharge	n = 212	n = 206	
Diuretics	128 (60)	128 (62)	.71
β-Blockers	71 (33)	96 (47)	.006
Nitroglycerin	44 (21)	43 (21)	>.99
ACE inhibitors†	113 (53)	120 (58)	.31
Digoxin	12 (6)	16 (8)	.39
Amiodarone	26 (12)	21 (10)	.50
Aspirin	72 (34)	74 (36)	.67
Anticoagulation	84 (40)	93 (45)	.25
Inhaled bronchodilators	62 (29)	45 (22)	.08
Inhaled corticosteroids	40 (19)	30 (15)	.24
Oral corticosteroids	45 (21)	36 (17)	.33

Abbreviations: ACE, angiotensin-converting enzyme; BNP, B-type natriuretic peptide; IV, intravenous.

*Within the first 24 hours.

†Or angiotensin receptor blockers.

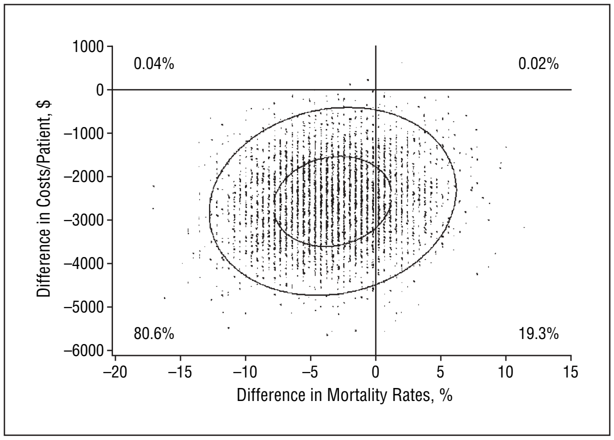

Figure 2. Results for incremental 180-day cost-effectiveness of B-type natriuretic peptide (BNP) guidance from 5000 bootstrap replications. The outer ellipse defines the 95% confidence region for true incremental cost-effectiveness of BNP guidance compared with only clinical guidance. The inner ellipse defines the 50% confidence region. The center of the ellipse represents our point estimate of incremental costs and effects. Each percentage indicates the estimated probability that the incremental cost-effectiveness of BNP guidance obtained from a bootstrap sample lies in that quadrant. In 80.6% of bootstrapping replications, BNP guidance was less expensive and resulted in lower mortality; in 19.3% it was less expensive and resulted in higher mortality. In less than 0.1% of replications was BNP guidance more expensive and associated with either higher or lower mortality. Comparison of mortality, *P* = .42; comparison of costs (bootstrap *t* test), *P* = .004.

in the control group; *P* = .006). The reduction in total treatment cost was mainly driven by the significant reduction in days in the hospital.

At 180 days, all-cause mortality was 20% in the BNP group and 23% in the control group (*P* = .42) (Table 2). Patients assigned to the BNP group spent significantly fewer days in the hospital than those in the control group (median, 10 days [interquartile range, 2-24 days] vs 14 days [interquartile range, 6-27 days]; *P* = .005). Total treatment cost was significantly reduced in the BNP group ($7930 vs $10 503 in the control group; *P* = .004). Again, the reduction in total treatment cost was mainly driven by the reduction in days in the hospital. Results for incremental 180-day cost-effectiveness of BNP guidance are displayed in **Figure 2**.

As shown in **Table 5**, the cost-effectiveness of BNP guidance was robust to changes in several variables, but

Table 5. Sensitivity Analyses: Effect of Changes in Variables on Differences in Initial and 180-Day Total Treatment Cost*

	Initial Total Treatment Cost		180-d Total Treatment Cost	
Variable	**Change, $/Patient**	***P* Value**	**Change, $/Patient**	***P* Value**
Duration of initial hospitalization† (both groups), %				
−10	−1665	.006	−2385	.005
−20	−1475	.006	−2198	.006
−30	−1285	.006	−2010	.007
Cost per day in hospital, $‡				
−150	−1377	.008	−1785	.006
As in this trial	−1854	.006	−2573	.004
+150	−2332	.005	−3362	.004
+300	−2808	.005	−4150	.004
Cost for outpatient visit, $§				
−100	−1864	.006	−2583	.004
As in this trial	−1854	.006	−2573	.004
+100	−1844	.006	−2564	.004
+200	−1834	.006	−2554	.004
Cost for intensive care, $/h				
−25	−1668	.005	−2387	.005
As in this trial	−1854	.006	−2573	.004
+25	−2042	.007	−2759	.004
+50	−2229	.008	−2945	.004
Expense for BNP testing, $				
100	−1801	.007	−2520	.005
47 (as in this trial)	−1854	.006	−2573	.004
25	−1876	.005	−2595	.004
10	−1891	.005	−2610	.004
Time in ICU with BNP guidance, h‖				
+1	−1769	.008	−2487	.006
+3	−1597	.02	−2316	.01
+5	−1426	.03	−2144	.02
Cost of long-term medication with BNP guidance, %				
−25	−1854	.006	−2654	.003
As in this trial	−1854	.006	−2573	.004
+25	−1854	.006	−2491	.006
+50	−1854	.006	−2409	.008
+100	−1854	.006	−2245	.01
Rehospitalization days with BNP guidance¶				
−1	−1854	.006	−3421	<.001
As in this trial	−1854	.006	−2573	.004
+1	−1854	.006	−1725	.06
+2	−1854	.006	−877	.33
+3	−1854	.006	−30	.97

Abbreviations: BNP, B-type natriuretic peptide; ICU, intensive care unit.

*Positive values indicate that BNP guidance is more expensive; negative values indicate that BNP guidance is less expensive.

†In patients hospitalized, assuming an equal reduction in high-cost units and low-cost units, as well as no change in those treated as outpatients.

‡Assuming no change in outpatient cost.

§Assuming no change in inpatient cost.

‖On average for all patients in the BNP group, assuming no change in the overall time to discharge.

¶On average for all patients in the BNP group initially discharged alive, assuming an average total cost of $900 per day.

sensitive to changes in rehospitalization days with BNP guidance.

Subgroup analysis showed that the benefit of BNP testing to reduce total treatment cost at 180 days was particularly evident in patients with a history of coronary artery disease ($8566 vs $12 194 in the control group; $P = .005$) and in patients with a history of pulmonary disease ($8876 vs $12 408 in the control group; $P = .01$).

COMMENT

We performed cost-effectiveness analyses of BNP testing in patients presenting to the ED with acute dyspnea. To address the fact that tailoring of resources may very well be cost-effective initially but result in large secondary costs due to recurrent symptoms and potentially even increased mortality, cost-effectiveness analyses were performed at 180 days of follow-up. As our major finding, we report that BNP testing is cost-effective. The use of BNP levels significantly reduced total treatment cost. This reduction was driven by significantly fewer days spent in the hospital in the BNP group. A large part of this reduction in days in the hospital and cost occurred during the initial presentation and was fully maintained at 180 days. Sensitivity analyses demonstrated that this observation was robust to changes in most variables but sensitive to changes in rehospitalization with BNP guidance. Subgroup analysis showed that the benefit of BNP testing was particularly evident in patients with a history of either coronary artery disease or pulmonary disease. We extrapolate that the impact of BNP testing observed in our study also applies to patients presenting to North American hospitals. Beyond doubt, North American hospitals differ in several aspects from European hospitals. However, as disease prevalence,[1-3] patient characteristics,[1-3,5,6,20] treatment strategies,[1-3,5,6,20] and total cost of treatment[1-3] are remarkably similar, this extrapolation seems justified. In 1997, an estimated $5501 was spent for every hospital discharge diagnosis of HF in North America.[1-3] Estimated total 1-year treatment cost was $5037 in patients with stage II chronic obstructive pulmonary disease and $10 812 in patients with stage III chronic obstructive pulmonary disease.[21] Moreover, our results should apply in all major health care systems. In a health care system in which reimbursements are governed by a system of diagnosis related groups (DRGs), similar cost savings should arise as the DRGs are generally higher for HF than for chronic obstructive pulmonary disease. In nations with nationalized health care, the reductions in total days in the hospital will release resources for other patients and may therefore result in a reduction in waiting periods for elective in-hospital procedures.

These long-term follow-up data are reassuring given recent criticism regarding the value of BNP testing in clinical medicine, and they considerably extend the evidence regarding the cost-effectiveness of this marker.[22-24] The use of BNP levels in patients presenting to the ED with acute dyspnea has several beneficial effects on patient treatment that, in summary, lead to reduction in resource utilization and significantly improved cost-effectiveness. First, the use of BNP levels significantly increases diagnostic accuracy.[5,6,9,10,25] This reduces the number of patients incorrectly diagnosed and therefore incorrectly treated. Second, the use of BNP levels allows more rapid diagnosis and therefore more rapid initiation of the appropriate therapy.[11] Third, more rapid initiation of the appropriate therapy results in more favorable short-term patient outcome as quantified by a reduction in the need for hospital admission or intensive care. This finding is supported by recent data from ADHERE (Acute Decompensated Failure National Registry) showing that early use of intravenous nitroglycerin or nesiritide may improve in-hospital outcomes.[26] Early diagnosis of HF by means of BNP seems to expedite effective drug treatment, as in the intensive care unit intravenous nitroglycerin was used more often in the BNP group. Given the enormous public health burden of HF,[1-4] this is of paramount importance.

Little is known regarding the cost-effectiveness of most diagnostic tests currently used in clinical practice. This lack of data also applies to the measurement of troponin in patients with acute chest pain, the measurement of D-dimers in patients with suspected pulmonary embolism,[27] and tests performed in the screening for cancer including prostate-specific antigen in elderly men,[28] among others. Obviously, it would be far more difficult for a single diagnostic test performed at a unique point in patient presentation to impact on mortality or total cost of disease than it would, for example, for prolonged medical therapy or prolonged benefit from implantation of a defibrillator or pacemaker.[29] The use of BNP levels also seems to provide the potential for cost savings in other indications. These include the screening of asymptomatic left ventricular dysfunction[30] and the optimization of medical therapy in patients with chronic HF.[31]

In the BASEL study, BNP testing reduced the rate of hospital admission, the rate of admission to intensive care, and the time to discharge. No indication was found that the early benefits in the BNP group were counterbalanced by worse outcome or higher resource utilization during follow-up. This is of particular interest, as the use of BNP affected not only the initial resource utilization, including intensive care and echocardiography, but also the quantitative distribution of diagnoses, with a higher detection rate of exacerbated obstructive pulmonary disease in the BNP group. Accordingly, β-blockers were prescribed less often at hospital discharge in the BNP group.

The BASEL study included unselected consecutive patients presenting with acute dyspnea. Recent data[5,6] suggested that BNP levels are most useful in patients with an intermediate clinical probability of HF. Whether restricting BNP measurements to patients in this subgroup would yield medical and economic long-term benefits similar to those observed in this study is unknown. Moreover, the approach used in the BASEL study has obvious logistical advantages. Delaying the venipuncture for BNP until the physician has collected all clinical data to determine whether an individual patient in fact has an intermediate clinical probability of HF would significantly increase the time to the correct diagnosis and, accordingly, the time to appropriate treatment in patients who might benefit the most from BNP testing. Because BNP testing is noninvasive, simple, and inexpensive, measuring BNP directly at presentation in all patients with acute dyspnea seems to be a reasonable strategy. Moreover, in addition to the diagnostic utility, BNP levels do provide valuable prognostic information in patients with HF. The action resulting from this prognostic information may have contributed to the improved outcomes of the patients in the BNP group.[32]

A particular strength of our study is that the study population was highly representative of the elderly population of patients with acute dyspnea in clinical practice.[1-3] The mean age was 71 years, nearly half the patients were women, and coexisting conditions were common. The rapid and accurate differentiation of HF from other causes of acute dyspnea and corresponding long-term management of HF in such patients is often difficult.

Several limitations apply to this study. First, resource use was limited to key items collected in the BASEL study. Second, the results are generalizable only to patients presenting to the ED. It is unknown to what extent the effects of BNP testing observed in this setting can be extrapolated to patients presenting to physicians in private practice. Initial experience is promising but requires confirmation by additional studies.[25] Third, the interpretation of BNP levels was based on the data available when the study protocol was devised. More recent data have suggested that 200 to 225 pg/mL rather than 100 pg/mL is the most appropriate lower cutoff value in patients with renal disease.[20,33] In contrast, the presence of obesity seems to require the use of lower cutoff values.[34,35]

In conclusion, this study in patients presenting to the ED with acute dyspnea demonstrates that rapid BNP testing is cost-effective during the initial hospital encounter as well as at 180 days.

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