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BRAIN NATRIURETIC PEPTIDE IN THE EVALUATION OF EMERGENCY DEPARTMENT DYSPNEA: IS THERE A ROLE?

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Abstract

Background—Acute decompensated congestive heart failure (ADCHF) is a common etiology of dyspnea in emergency department (ED) patients. Delayed diagnosis of ADCHF increases morbidity and mortality. Two cardiac biomarkers, N-terminal-pro brain natriuretic peptide (NT-proBNP) and brain natriuretic peptide (BNP) have demonstrated excellent sensitivity in diagnostic accuracy studies, but the clinical impact on patient-oriented outcomes of these tests remains in question.

Clinical Question—Does emergency physician awareness of BNP or NT-proBNP level improve ADCHF patient-important outcomes including ED length of stay, hospital length of stay, cardiovascular mortality, or overall health care costs?

Evidence Review—Five trials have randomized clinicians to either knowledge of or no knowledge of ADCHF biomarker levels in ED patients with dyspnea and some suspicion for heart failure. In assessing patient-oriented outcomes such as length-of-stay, return visits, and overall health care costs, the randomized controlled trials fail to provide evidence of unequivocal benefit to patients, clinicians, or society.

Conclusion—Clinician awareness of BNP or NT-proBNP levels in ED dyspnea patients does not necessarily improve outcomes. Future ADCHF biomarker trials must assess patient-oriented outcomes in conjunction with validated risk-stratification instruments.

Keywords

natriuretic peptide; congestive heart failure; outcomes; cost-effectiveness

CASE REPORT

An 85-year-old man appearing younger than his stated age presents to your Emergency Department (ED) with progressively increasing dyspnea associated with a nonproductive cough. On review of systems, he notes no associated fever or viral symptoms, orthopnea, paroxysmal nocturnal dyspnea, or edema. His past medical history includes hypertension and myocardial infarction 20 years prior. He appears comfortable, with stable vital signs, no obvious jugular venous distension, hepatojugular reflux, S3, wheezing or rales, and an electrocardiogram with lateral T-wave flattening unchanged compared with 6 years prior. While the chest X-ray study is pending, you peer at your “undifferentiated dyspnea” physician order set. Brain natriuretic peptide (BNP) is an option, so you contemplate whether it will enhance your diagnostic accuracy or, more importantly, improve your patient’s outcome.

CLINICAL QUESTION

Does emergency physician awareness of BNP or N-terminal-pro brain natriuretic peptide (NT-proBNP) level improve acute decompensated congestive heart failure (ADCHF) patient-important outcomes including ED length of stay (LOS), hospital LOS, cardiovascular mortality, or overall health care costs?

CONTEXT

ED patients presenting with undifferentiated dyspnea are commonly encountered. The broad differential diagnosis includes acute coronary syndrome, chronic obstructive pulmonary disease (COPD), asthma, pneumonia, pulmonary embolism, and ADCHF. When clinicians remain uncertain of the cause of dyspnea in the ED, patients have longer hospital LOS, as well as increased morbidity and mortality (1). Congestive heart failure (CHF) incidence increases from 5% in those over age 65 years to 15% in those over age 85 years (2). An increasingly aging ED demographic means that acute care physicians will be caring for greater numbers of CHF patients in coming decades (3). Today, 80% of acute CHF patients present through the ED, and dyspnea is their predominant chief complaint (4). Heart failure is associated with an annual mortality of 18.7% and an estimated direct plus indirect cost of \$39.2 billion in the United States alone (5). Only 45–60% of patients survive 5 years after the initial diagnosis of CHF (6).

Delayed diagnosis of CHF has been associated with increased mortality (1). Unfortunately, history and physical examination alone are often insufficient to rule in or rule out CHF (7,8). A decade ago, BNP and NT-proBNP were proposed as potentially valuable diagnostic tests to augment the clinical diagnosis of ADCHF (9). Meta-analysis of BNP diagnostic accuracy studies yielded a negative likelihood ratio of 0.18 (95% confidence interval [CI] 0.13–0.23) for all testing methods with better diagnostic performance for enzyme-linked immunosorbent assay than for radioimmunosorbent assays (10). Januzzi et al. demonstrated a negative likelihood ratio of 0.12 for NT-proBNP using age-related cutoff points to define abnormal levels (11). BNP and NT-proBNP seem to be interchangeable, without clinically meaningful differences in overall accuracy (12).

Some observational trials have suggested that ADCHF biomarker testing in the ED is cost effective (13). Others have demonstrated an association with increased ADCHF treatment delays when BNP levels were not immediately assessed (14). Although observational trials, which are often industry-sponsored, evaluating biomarkers like BNP and NT-proBNP, have shown promise to improve clinicians’ diagnostic accuracy for ADCHF in the ED, the role of these biomarkers in the acute management of dyspnea remains undefined and somewhat contentious (15,16). Additionally, serum levels of these biomarkers can be elevated by non-

ADCHF conditions like pulmonary hypertension, left ventricular hypertrophy, renal failure, acute coronary syndrome, atrial dysrhythmia, sepsis, and lung cancer (17). Nonetheless, the American College of Emergency Physician clinical policy provides Level B recommendations that “the addition of a single BNP or NT-proBNP measurement can improve the diagnostic accuracy compared to standard clinical judgment alone in ED patients” using BNP < 100 pg/dL or NT-proBNP < 300 pg/dL to rule out CHF and BNP > 500 pg/dL or NT-proBNP > 1000 pg/dL to rule in the diagnosis (18). This recommendation is based largely upon studies of diagnostic accuracy and one single-center randomized trial.

Although BNP/NT-proBNP testing might help discriminate ADCHF from other causes of dyspnea, it can also paradoxically increase diagnostic uncertainty or increase confirmatory testing-related evaluations on low-risk populations (19). Additionally, because clinicians with high certainty for the likelihood of CHF are generally quite accurate, the optimal pre-test probability threshold requiring BNP/NT-proBNP testing is unknown (Figure 1) (19,20). A continuing problem in assessing the diagnostic performance of BNP/NT-proBNP is that the optimal cutoff points to distinguish normal from abnormal BNP/NT-proBNP vary from study to study without any well-accepted laboratory threshold to date (21). Furthermore, age, gender, renal impairment, and obesity-related thresholds to differentiate normal from abnormal BNP/NT-proBNP levels remain heterogeneous or poorly defined from study to study (16,22–25).

EVIDENCE SEARCH

Because you are interested in the patient-oriented evidence that matters (i.e., clinical outcomes) rather than diagnostic accuracy of CHF biomarkers, you will be evaluating diagnostic randomized controlled trials (RCTs) that blind the control group of clinicians to the BNP result. You first turn to BestBETs (<http://www.bestbets.org/>), entering the search term “BNP” and identify two incomplete reviews. Next you search using PubMed Clinical Queries, selecting diagnostics (broad, sensitive search) for “congestive heart failure” and then combine that search with a search for “natriuretic peptide,” yielding 2732 citations, which you don’t have time to review right now. Therefore, you apply several limitations to these search results (humans, RCT) and obtain 91 citations that you are able to quickly peruse to identify three ED-based RCTs. Again, because your clinical question resides in the overlap between diagnostics and therapeutics, you conduct another search using PubMed Clinical Queries therapy (broad, sensitive) for “congestive heart failure” and combine the results with the previous search results for “natriuretic peptide” to identify 47 citations, including an additional two RCTs (Figure 2).

EVIDENCE REVIEW

Use of B-type Natriuretic Peptide in the Evaluation and Management of Acute Dyspnea, 2004 (26)

Population—Subjects were all adult patients presenting to the ED of the University Hospital in Basel, Switzerland between May 2001 and April 2002 with non-traumatic acute dyspnea. In total, 665 consecutive patients were screened and 452 enrolled in the trial, with mean age 71 years and no clinically or statistically significant differences between the treatment and control groups for all measured prognostic variables.

Study design—This was an industry-sponsored, prospective, randomized, controlled, single-blind study with group allocation accomplished using a computer-generated randomization scheme in a 1:1 ratio without stratification (27–29). All patients were evaluated in standard fashion including history, physical examination, electrocardiography, pulse oximetry, blood tests, and chest radiography. Although outpatient echocardiography

and pulmonary-function tests were recommended for discharged or admitted ED patients, the research protocol did not mandate these interventions. At the time of the initial evaluation, B-type natriuretic peptide was measured in those patients allocated to the intervention arm with the use of a rapid fluorescence immunoassay (Biosite Diagnostics, San Diego, CA) within 15 min (30). In the intervention arm, the BNP result was incorporated into the entire clinical scenario with the general guideline that a level below 100 pg/mL made the diagnosis of heart failure unlikely, whereas a level above 500 pg/mL made heart failure the most likely diagnosis. Clinicians for patients in the control group did not have access to BNP levels because they were not routinely available at the time this study was conducted. In subjects in whom heart failure was deemed the most likely diagnosis for both groups, rapid therapy with diuretics, nitroglycerin, angiotensin-converting enzyme inhibitors, and morphine was advocated. All data were analyzed according to the intention-to-treat principle.

Primary outcome—The primary outcomes were time to discharge and the cost of treatment. Secondary outcomes assessed included in-hospital and 30-day mortality. Time to discharge was defined as the interval from ED presentation to discharge, excluding those who died in the hospital. Hospital charges were used to estimate true costs, including the reimbursement rate for BNP in Switzerland at that time (\$47). All endpoints were assessed by physicians blinded to the allocation arm and not involved in the patient's care with access to all medical records pertaining to that patient.

Exclusion criteria—Exclusion criteria included renal disease (creatinine > 2.8 mg/dL), cardiogenic shock, or patients requesting a transfer to another hospital.

Main results—Eighty percent of the control group were admitted after the ED evaluation (compared to 75% of the BNP group; $p = 0.008$) and the control group were more often admitted to an intensive care unit (ICU; 24% vs. 15%; $p = 0.01$). The BNP group had a shorter interval between presentation and initiation of appropriate therapy (63 min vs. 90 min; $p = 0.03$) and a shorter hospital LOS (median 8 days vs. 11 days). Total treatment costs were significantly less in the BNP group (\$5410 vs. \$7264; $p = 0.006$). No differences were noted in inpatient (6% BNP group vs. 9% control group; $p = 0.19$) or non-admitted 30-day (4% vs. 3%; $p = 1.0$) mortality.

N-terminal Pro-B-type Natriuretic Peptide Testing Improves the Management of Patients with Suspected Acute Heart Failure 2007 (31)

Population—Patients were adults over age 18 years presenting to one of seven Canadian EDs between December 2004 and December 2005 with dyspnea of suspected cardiac origin. After 534 subjects were screened, 500 were randomized and 97% had 60-day follow-up information available. The subjects were predominantly white, with mean age 70 years and mean body mass index 28 kg/m². The final diagnosis was acute heart failure in 46% and over one-third had a prior history of left ventricular dysfunction, and over one-half had resting dyspnea, but most lacked other signs or symptoms traditionally associated with congestive heart failure. There were no significant differences between groups.

Study design—This was an industry-sponsored, randomized, controlled, double-blind, prospective multicenter study. Each center generated a randomization schedule in blocks of four contained in a sealed envelope that was available only to the research coordinator at each locale. After enrollment but before randomization, baseline demographics, medical history, and clinical findings were documented in addition to standard test results including electrocardiogram, chest X-ray study, and routine blood tests. NT-proBNP was also collected at this time on all subjects using the Elecsys 1010, 2100, or E170 proBNP

immunoassay (Roche Diagnostics, Indianapolis, IN) (32), but only clinicians in the intervention arm had access to the results after randomization. Based upon the N-Terminal Pro-BNP Investigation of Dyspnea in the Emergency Department (PRIDE) study, physicians were provided a threshold value of NT-proBNP > 450 pg/mL below age 50 years or > 900 pg/mL above age 50 years to rule in the diagnosis of heart failure, whereas a value < 300 pg/mL ruled out the diagnosis of heart failure (32). No management protocols were reported as part of this trial. Physicians in both groups were asked to estimate the likelihood that heart failure was the etiology of the patient's complaints before randomization. The diagnosis of heart failure occurred when two cardiologists evaluated all clinical data except the NT-proBNP results 60 days after enrollment.

Primary outcome—The primary outcomes were the duration of the initial ED evaluation and the total direct medical costs of treatment. Secondary outcomes included hospital LOS, and inpatient and 60-day mortality, as well as rehospitalization rates.

Exclusion criteria—Exclusion criteria included serum creatinine > 2.8 mg/dL, acute myocardial infarction, malignant disorders, and obvious etiology of dyspnea, including pneumothorax or chest wall trauma.

Main results—The median duration of the ED evaluation was 5.6 h in the NT-proBNP group and 6.3 h in the usual care group ($p = 0.03$), and fewer patients in the intervention group were re-admitted at 60 days (13% vs. 20%; $p = 0.05$). Total medical costs in the NT-proBNP group were also significantly reduced (\$6129 vs. \$5180; $p = 0.02$). No significant differences in initial hospitalizations, hospital LOS, ICU admissions, or inpatient/outpatient mortality were noted between the two groups. The investigators also conducted an a priori subset analysis of the group of patients in which clinicians estimated the likelihood of CHF between 20% and 80% (intermediate probability cohort consisting of 219 subjects). In this subset of patients, duration of ED evaluation (5.4 vs. 7.5 h; $p < 0.01$) and total expenses (\$5126 vs. \$6541; $p = 0.08$) were more strikingly in favor of the NT-proBNP group. When comparing the receiver operating characteristic area under the curve, unaided clinical gestalt was 0.83 (95% CI 0.80–0.84) and improved to 0.90 (95% CI 0.90–0.93) when physicians were made aware of the NT-proBNP results.

N-terminal Pro-brain Natriuretic Peptide Testing in the ED: Beneficial Effects on Hospitalization, Costs, and Outcome 2008 (33)

Population—Subjects were adult patients with a chief complaint of acute dyspnea presenting between December 2004 and February 2006 to the Erasmus Medical Center ED in Rotterdam, Netherlands. During this 14-month interval, 29,000 ED visits occurred with 785 dyspnea patients, from which 477 were randomized, with mean age 59 years. No significant prognostic imbalances were noted between the intervention and control groups. The pre-test probability of acute heart failure was high in 15%, indefinite in 21%, and unlikely in 59% of the population. The patients enrolled had pre-existing cardiac disease (20%), pulmonary disease (35%), or both (24%), and two-thirds of them had been referred to the ED by their primary care physician. The ED evaluation was by an emergency physician in 24%, internal medicine specialist in 24%, cardiologist in 18%, and by a pulmonary physician in 32%. Nine patients in the intervention and 8 patients in the control group were lost to follow-up.

Study design—This was a non-industry-sponsored RCT. Patients were randomized 1:1 without stratification using a computer-generated scheme with allocation blinded to the treating clinician via use of a sealed, opaque envelope. There is no clear statement of blinding for the outcome assessors. At admission, NT-proBNP level was determined using

the Elecsys 2010 analyzer (Roche Diagnostics) (34). The NT-proBNP level was provided only to physicians in the intervention group, with the guidance that a level below 93 pg/mL for males and 144 pg/mL for females ruled out heart failure, whereas levels above 1017 pg/mL ruled in the diagnosis (35–37). Clinicians from both groups rated the probability of acute heart failure from 1% to 100% using a visual analogue scale before the sample was sent to the laboratory but after the rest of their work-up. Clinicians in the intervention group then incorporated the NT-proBNP level with the history, physical examination, other laboratory tests, chest X-ray study, electrocardiogram, and, as indicated, computed tomography. Most echocardiograms and pulmonary function testing was performed during the subsequent hospitalization or as outpatient procedures. All analyses were by the intention-to-treat principle. The investigators do not describe their criterion standard for establishing the diagnosis of acute heart failure. In addition, they do not directly assess the impact of the NT-proBNP result on post-test probability judgments in the intervention group.

Primary outcome—The primary outcome was time to discharge. Secondary outcomes included costs and ED LOS, as well as hospital and ICU admission rates. Thirty-day outcomes were assessed by medical record review and telephone contact. The cost of one NT-proBNP test used was \$34. Inpatient costs were computed based upon the national averages for a general ward (\$612/day) or an ICU (\$2165/day) for a university hospital. For diagnostic evaluations, the prices as charged to health insurance companies were used.

Exclusion criteria—Exclusion criteria included trauma or cardiogenic shock, dialysis-dependent renal failure, or inability to consent the patient.

Main results—The NT-proBNP group had significantly shorter median hospital LOS (1.9 days vs. 3.9 days; $p = 0.04$) with a trend towards decreased overall costs (\$4984 vs. \$6352, mean difference \$1364, with 95% CI–\$246–\$3215). The cost-effectiveness plane demonstrated a trend for reduced costs without increasing mortality, with the strongest savings on those with cardiac dyspnea (\$2627 per patient). No differences were noted in hospitalization rates or ED LOS. Additionally, no differences were noted in inpatient or outpatient 30-day mortality rates between the groups. Among the 105 patients with indeterminate pre-test probability (25%–75% chance of acute heart failure), NT-proBNP was low in 20%, indefinite in 23%, and high in 56% using the investigators predefined thresholds.

B-type Natriuretic Peptide Testing, Clinical Outcomes, and Health Services Use in ED Patients with Dyspnea: A Randomized Trial 2009 (38)

Population—Population included adult patients over age 40 years presenting with severe dyspnea to one of two Australian EDs in Prahran or Epping, Victoria between August 2005 and March 2007. During this time, 612 patients were randomized, with the control group of emergency physicians blinded to the BNP result. Hypertension and prior history of CHF were more common in the BNP group, who also reported orthopnea more frequently. Otherwise, the two groups did not differ significantly in other important prognostic variables including age, gender, smoking history, ischemic heart disease, COPD, dyspnea severity grades, initial blood pressure, or oxygenation. Acute CHF was the diagnosis in 45%, and 85% of patients overall were admitted.

Study design—This was an industry-sponsored, randomized, single-blinded trial. Patients were randomized to the intervention or control group by computer-generated random-number tables in a sealed envelope with randomization stratified by site. BNP was measured within 60 min using the Abbott AxSYM MEIA Automated Immunoassay (Abbott Diagnostics, Abbott Park, IL) (39,40). At the study hospitals, only cardiologists had the

capability to order a BNP outside the study protocol without a pathologist's approval. During the study, ED staff received four educational sessions to update them on the diagnostic accuracy and potential effectiveness of BNP testing in the setting of potentially cardiogenic dyspnea. Physicians were advised that a BNP < 100 ng/L made the diagnosis of heart failure unlikely, whereas a BNP > 500 ng/L made heart failure likely (41). All emergency physicians received written guidelines on the treatment of acute heart failure and COPD at the onset of the study. Two physicians (including one cardiologist) established the diagnosis of CHF with access to all clinical data except the BNP result using the European Society of Cardiology guidelines (42). Outcome assessors were not blinded to patients' group allocation assignment, but they were blinded to the BNP result.

Primary outcome—The primary outcomes were hospital admission rates, LOS, and change in patient management. Secondary outcomes were 30-day mortality and readmission rates.

Exclusion criteria—Exclusion criteria included age under 40 years, dyspnea related to trauma or cardiogenic shock, creatinine > 2.8 mg/dL, or transfer to another hospital within 24 h of presentation.

Main results—There were no differences between BNP and controls for any of the primary or secondary outcomes. Admission rates (85% BNP vs. 87% controls), ICU admissions (1% vs. 3%), length of stay (median 4.4 days vs. 5.0 days), 30-day mortality (6.5% vs. 6.9%), and re-admission rates (15% vs. 18%) did not differ statistically between the two groups. These results were not changed when analyzed by hospital site. Logistic regression performed to adjust for differences in pre-existing hypertension or CHF history or hospital site did not alter the outcomes either. Clinicians informed of BNP results did not demonstrate any differences in their use of bronchodilators, diuretics, vasodilators, steroids, angiotensin-converting enzyme inhibitors, or noninvasive positive pressure ventilation. The median BNP for no CHF was 99 ng/L, vs. 830 ng/L for those with CHF.

Rapid ED Heart Failure Outpatients Trial (REDHOT II): A Randomized Controlled Trial of the Effect of Serial B-type Natriuretic Peptide Testing on Patient Management 2009 (43)

Population—Subjects included adult patients over age 18 years presenting to one of 10 academic and community EDs between November 2004 and September 2006 with signs or symptoms of CHF requiring acute therapy. Initially, 480 patients were randomized, but 33 were excluded due to missing data and another 62 were lost to follow-up, so 385 were included in this analysis. The overall population had mean age of 64 years and were 50% male; 83% were admitted and 5% went to an observation unit from the ED. No significant prognostic differences between the treatment and the control groups were noted. The mean BNP level was about 1100 pg/mL. Only 7.5% of patients had BNP testing on day 2, and on the day of hospital discharge only 21% had central laboratory BNP testing obtained.

Study design—This was a prospective, convenience-sampling, industry-sponsored, randomized, non-blinded clinical trial. Randomization occurred at a central location using a computer-generated random-numbers table stratified by study site. Allocation was revealed to all parties once the opaque envelopes containing group assignment were opened. In the intervention group, patients had BNP testing at baseline and 3, 6, 9, and 12 h after enrollment. Additional BNP levels were obtained daily until discharge for admitted patients or at ED discharge if more than 2 h since the last BNP level. BNP results were made available to one of the patient's physicians in the intervention group. In the control group, routine BNP testing was not performed. BNP testing used the triage BNP point-of-care test and physicians were not given standardized instructions on how to alter therapy based on

BNP levels. Trained research nurses and assistants abstracted demographic and clinical data via medical record review and scripted telephone follow-up. There is no clear statement of an intention-to-treat analysis.

Primary outcome—The primary outcome was the hospital LOS. Secondary outcomes included in-hospital and 30-day mortality rates, as well as readmission rates for cardiac-related diseases within 30-days. Logistic regression analysis was performed to adjust for potential confounding variables including age, gender, blood urea nitrogen, serum creatinine, systolic blood pressure, heart rate, and whether or not BNP was obtained.

Exclusion criteria—Exclusion criteria included BNP < 100 pg/mL, acute myocardial infarction, acute coronary syndrome with > 1 mm ST-segment deviation, dialysis-dependent renal failure, hemodialysis within the previous month, or enrollment in another drug trial.

Main results—There was no significant difference in initial mean BNP level between the control group (1178 pg/mL) and the BNP group (1118 pg/mL). No differences were noted between the BNP and control groups for LOS, in-hospital mortality, 30-day mortality, or return visit rates. The investigators also assessed the use of CHF medications during admission and at discharge, noting no differences between the two groups. Multivariate logistic regression modeling demonstrated that admitted patients with reduced blood pressure and heart rates had longer LOS, but LOS was not independently associated with BNP testing, age, gender, or renal function. BNP testing was not independently associated with mortality or unplanned 30-day revisit rates on further logistic regression modeling.

CONCLUSION

Fryback and Thornbury described six levels of diagnostic test quality: 1) technical quality of test information; 2) diagnostic accuracy; 3) change in the referring physician's diagnostic thinking; 4) change in the patient management plan; 5) change in patient outcomes; and 6) societal costs and benefits (44). Randomized trials of new diagnostic tests to demonstrate improved patient outcomes are often not performed because they are not required for marketing approval and can be expensive to conduct (45). Although diagnostic accuracy studies for new tests may suffice if the new test has equal sensitivity but superior specificity or a better safety profile than the old test, many new tests have superior sensitivity so they detect a new spectrum of disease. Unfortunately, clinicians may not be able to confidently extrapolate improved detection with better patient outcomes (45).

BNP and NT-proBNP are ADCHF biomarkers with well-described diagnostic accuracy that should logically extrapolate to improved patient outcomes within the context of frequently delayed diagnoses in ED patients with multiple confounding comorbidities (10,11). However, the randomized trial evidence presented in this manuscript is inconclusive. Although Mueller et al. and Moe et al. demonstrated decreased ED LOS and overall hospital costs when the biomarkers were made available to clinicians, Rutten et al., Schneider et al., and Singer et al. did not demonstrate any such benefits in similarly designed randomized trials (26,31,33,38,43). One key to this heterogeneity was identified in the Schneider trial in which undifferentiated severe dyspnea patients were recruited for indiscriminate BNP testing (38). Although emergency physicians may not be innately Bayesian, the appropriate use of BNP/NT-proBNP probably requires a logical estimate of ADCHF pre-test probability along with a diagnostic and therapeutic threshold beyond which further testing will be discontinued (20,46). One diagnostic model has been derived to force clinicians to incorporate age, pre-test probability, and NT-proBNP to derive a post-test probability of ADCHF (47). In addition, multiple diagnostic and prognostic decision tools have been developed for clinicians to risk-stratify acute dyspnea patients for ADCHF in ED settings

(48–51). Future trials of ADCHF biomarkers should assess the impact and cost-effectiveness of testing when used in conjunction with these or future validated risk-stratification instruments. Another source of heterogeneity and challenge in this research is the lack of a valid and reliable definition of CHF. In the meantime, clinicians, patients, and policy-makers cannot be confident that knowledge of BNP or NT-proBNP levels will improve outcomes or reduce costs when evaluating ED patients with dyspnea.

COMMENTARY BY DR. PETER ROSEN

My problem with all of these studies is that it is impossible to believe that the only variable in the diagnosis and management of these patients was a single BNP level obtained in the ED. Moreover, we don't know the emergency medicine expertise of the caring physicians, whether there was any direct training in emergency medicine, or how much experience beyond training.

Furthermore, the problem to be studied is unlikely to be present in the kind of case presented above. Where the BNP is likely to be useful is in the patient presenting with a distracting diagnosis based upon physical examination. For example, we have all seen patients inappropriately treated for asthma because they were wheezing, even though they were elderly, had no prior asthma history, and were having wheezing induced by early pulmonary edema. This is the kind of patient who is going to suffer from having a delay in recognition and treatment for congestive failure. Yet, the very physician who would benefit from a laboratory test to direct thinking towards the correct diagnosis is likely to be the one who will either not order a BNP level, being sure of the diagnosis of asthma, or who will pay no attention to the result, being sure of the diagnosis of asthma.

The other place where a BNP level would help is the COPD patient who is failing from cor pulmonale, whose failure is presumed to be an acute-superimposed-upon-chronic respiratory failure, most likely due to mucous plugging. This is another patient in whom the appearance of CHF will not be obvious, and in whom a high BNP level would help.

A third class of patient is the one with chronic bronchitis, who clinically seems to be having a flare of infectious bronchitis, or possibly a chronic cough induced by tobacco consumption. This kind of patient would benefit from a BNP determination, and again help in the recognition of failure induced by something other than pure cardiac disease.

Yet these are the very groups of patients who often have no BNP determination, and therefore continue to be misassessed, and mistreated, whereas the test is routinely demanded for patients who are already being considered as heart failure patients.

Given the results of the studies above, even though I have some concerns about the methodologies of all the studies, I would suggest that we abandon the routine obtaining of a BNP level for patients deemed to be having a CHF flare-up, and instead consider it in all dyspnea patients that we don't believe are having CHF.

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Figure 1.
Clinical decision thresholds for diagnostic testing and therapy (20).

Background:
The purpose of this study was to determine the effect of a teaching intervention on the knowledge and skills of emergency medicine residents in the management of patients with acute respiratory distress syndrome (ARDS). The study was conducted in a teaching hospital in the United States.

Methods:
The study was a prospective, controlled trial. The intervention group received a teaching intervention consisting of a series of lectures, case studies, and a simulation exercise. The control group received no intervention.

Results:
The intervention group showed a significant improvement in knowledge and skills compared to the control group. The improvement was most pronounced in the areas of patient assessment, diagnosis, and management.

Conclusion:
The teaching intervention was effective in improving the knowledge and skills of emergency medicine residents in the management of patients with ARDS.

Keywords:
ARDS, emergency medicine, teaching intervention, knowledge, skills.

Figure 2.
Evidence-based medicine teaching points.