

# Does This Dyspneic Patient in the Emergency Department Have Congestive Heart Failure?

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## CLINICAL SCENARIOS

### Case 1

A 70-year-old woman with a history of a previous myocardial infarction and heart failure presents to the emergency department (ED) with a 2-day history of dyspnea at rest, orthopnea, and paroxysmal nocturnal dyspnea. Physical examination reveals an elevated jugular venous pressure, a third heart sound (S<sub>3</sub>) gallop (positive LR=11; 95% CI, 4.9-25.0); (4) the chest radiograph showing pulmonary venous congestion (positive LR=12.0; 95% CI, 6.8-21.0); and (5) electrocardiogram showing atrial fibrillation (positive LR=3.8; 95% CI, 1.7-8.8). The features that best decreased the probability of heart failure were the absence of (1) past history of heart failure (negative LR=0.45; 95% CI, 0.38-0.53); (2) the symptom of dyspnea on exertion (negative LR=0.48; 95% CI, 0.35-0.67); (3) rales (negative LR=0.51; 95% CI, 0.37-0.70); (4) the chest radiograph showing cardiomegaly (negative LR=0.33; 95% CI, 0.23-0.48); and (5) any electrocardiogram abnormality (negative LR=0.64; 95% CI, 0.47-0.88). A low serum BNP proved to be the most useful test (serum B-type natriuretic peptide <100 pg/mL; negative LR=0.11; 95% CI, 0.07-0.16).

### Case 2

A 65-year-old previously healthy man with a 30 pack-year smoking history presents to the ED with a 3-week history of dyspnea on exertion and at rest, associated with productive cough and sputum. Physical examination reveals bilateral rales and wheezing. The chest radiograph reveals pulmonary venous congestion and a pattern of interstitial edema. An ECG shows lateral ST-segment depression.

### Case 3

A 60-year-old man with a history of chronic obstructive pulmonary dis-

**Context** Dyspnea is a common complaint in the emergency department where physicians must accurately make a rapid diagnosis.

**Objective** To assess the usefulness of history, symptoms, and signs along with routine diagnostic studies (chest radiograph, electrocardiogram, and serum B-type natriuretic peptide [BNP]) that differentiate heart failure from other causes of dyspnea in the emergency department.

**Data Sources** We searched MEDLINE (1966-July 2005) and the reference lists from retrieved articles, previous reviews, and physical examination textbooks.

**Study Selection** We retained 22 studies of various findings for diagnosing heart failure in adult patients presenting with dyspnea to the emergency department.

**Data Extraction** Two authors independently abstracted data (sensitivity, specificity, and likelihood ratios [LRs]) and assessed methodological quality.

**Data Synthesis** Many features increased the probability of heart failure, with the best feature for each category being the presence of (1) past history of heart failure (positive LR=5.8; 95% confidence interval [CI], 4.1-8.0); (2) the symptom of paroxysmal nocturnal dyspnea (positive LR=2.6; 95% CI, 1.5-4.5); (3) the sign of the third heart sound (S<sub>3</sub>) gallop (positive LR=11; 95% CI, 4.9-25.0); (4) the chest radiograph showing pulmonary venous congestion (positive LR=12.0; 95% CI, 6.8-21.0); and (5) electrocardiogram showing atrial fibrillation (positive LR=3.8; 95% CI, 1.7-8.8). The features that best decreased the probability of heart failure were the absence of (1) past history of heart failure (negative LR=0.45; 95% CI, 0.38-0.53); (2) the symptom of dyspnea on exertion (negative LR=0.48; 95% CI, 0.35-0.67); (3) rales (negative LR=0.51; 95% CI, 0.37-0.70); (4) the chest radiograph showing cardiomegaly (negative LR=0.33; 95% CI, 0.23-0.48); and (5) any electrocardiogram abnormality (negative LR=0.64; 95% CI, 0.47-0.88). A low serum BNP proved to be the most useful test (serum B-type natriuretic peptide <100 pg/mL; negative LR=0.11; 95% CI, 0.07-0.16).

**Conclusions** For dyspneic adult emergency department patients, a directed history, physical examination, chest radiograph, and electrocardiography should be performed. If the suspicion of heart failure remains, obtaining a serum BNP level may be helpful, especially for excluding heart failure.

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ease (COPD) and previous myocardial infarction presents to the ED with a 2-week history of worsening dyspnea on exertion and cough. Physical

examination reveals an elevated jugular venous pressure, bilateral wheezing, and bilateral lower extremity edema. The chest radiograph shows

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normal results. An ECG shows Q waves inferiorly.

### WHY IS THIS QUESTION IMPORTANT?

Heart failure is a major public health concern. A heart failure epidemic affects more than 15 million people in North America and Europe, and an additional 1.5 million new cases are diagnosed every year.<sup>1-5</sup> It is the most costly cardiovascular disorder in western countries, accounting for an estimated total direct annual expenditure of more than \$24 billion in the United States in 2001.<sup>6,7</sup> Failure to diagnose heart failure increases mortality, delays hospital discharge, and increases treatment costs.<sup>8,9</sup>

Dyspnea, an uncomfortable sensation of breathing<sup>10</sup> or an awareness of respiratory distress,<sup>11</sup> is the cause for more than 2.5 million clinician visits per year in the United States.<sup>12</sup> A number of disorders cause dyspnea including congestive heart failure, COPD, asthma, deconditioning, metabolic acidosis, anxiety, upper airway obstruction, and neuromuscular weakness. Identifying patients with heart failure among the other causes allows early institution of appropriate symptomatic and evidence-based therapies.

It is not always possible (nor feasible) to promptly evaluate every patient with dyspnea with tests of cardiac function (echocardiography, nuclear scans, or cardiac catheterization). This challenges physicians who must identify heart failure based on history, physical examination, and rapidly available investigations (eg, chest radiograph, electrocardiogram ECG, B-type natriuretic peptide [BNP]). Therefore, the purpose of this review was to identify the most useful symptoms, signs, and tests in diagnosing the clinical syndrome of heart failure in dyspneic patients presenting to the ED. By the syndrome of heart failure, we mean an overall clinical diagnosis of heart failure as the cause of dyspnea (irrespective of etiology, systolic, or diastolic dysfunction), using information from many sources including history, physical examination, chest radiograph, ECG, serum chemistries, and

**Table 1.** Physiological Categories and Mechanisms Causing Dyspnea in Heart Failure\*

Category	Mechanisms†
Increased respiratory drive	Increased left ventricular end diastolic pressure → pulmonary venous congestion → stimulation of pulmonary J receptors (transmitted by vagal afferents to brain)
	Pulmonary venous congestion → ventilation/perfusion mismatch, shunt‡ → hypoxemia → stimulation of central and peripheral chemoreceptors
Increased work of breathing	Pulmonary venous congestion → reduced lung compliance → increased airways resistance → increased elastic and resistive work of breathing → mismatch between afferent information from upper airway, lower airway, chest wall mechanoreceptors, and efferent signals to respiratory muscles
Weakness of respiratory pump muscles	Activation of catabolic factors → myopathy (structural, biochemical, functional abnormalities of skeletal respiratory muscles) → reduced respiratory muscle efficiency and endurance → mismatch between afferent mechanoreceptors and efferent signals to respiratory muscles
Psychological	Anxiety, depression → altered central perception

\*Adapted from Murray and Nadel *Textbook of Respiratory Medicine*,<sup>13</sup> Harrison's *Principles of Internal Medicine*,<sup>14</sup> American Thoracic Society Dyspnea Consensus Statement,<sup>15</sup> *Heart Disease*,<sup>16</sup> and Manning and Schwartzstein.<sup>10</sup>  
†Arrows denote one mechanism leading to another.  
‡Occurs when blood moves through the lung without coming into contact with oxygenated air.

one or more confirmatory tests of cardiac function.

### Pathophysiology of Dyspnea in Heart Failure

Multiple pathophysiological mechanisms have been hypothesized to modulate the sensation of dyspnea in patients with symptomatic heart failure (TABLE 1).

A previous review in The Rational Clinical Examination series assessed the usefulness of the clinical examination in predicting decreased left ventricular ejection fraction or increased filling pressure.<sup>17</sup> Our current review extends the previous report by focusing on the prediction of the clinical syndrome of heart failure in dyspneic patients. This clinical focus is useful because not every patient with left ventricular dysfunction and/or high filling pressures on objective cardiac testing will be subjectively dyspneic; furthermore, patients with a reduced ejection fraction may be dyspneic from causes other than heart failure.<sup>18-20</sup> Therefore, the use of the syndrome of heart failure takes into account a patient's subjective sensation and findings on routine investigations, in addition to objective cardiac testing. One previous literature review

has reported on the use of the clinical examination for discriminating causes of dyspnea; however, it was not restricted specifically to the syndrome of heart failure, and summary measures of sensitivity, specificity, and likelihood ratios (LRs) were not reported.<sup>21</sup>

We included serum BNP testing in this review because recent evidence suggests that it is useful in diagnosing heart failure.<sup>22</sup> BNP is a neurohormone that is secreted almost exclusively from the ventricles in response to pressure and volume overload that produces natriuresis, diuresis, and smooth muscle relaxation.<sup>23</sup> There is also emerging evidence that BNP is useful in prognosticating cardiovascular mortality in both acute and chronic heart failure.<sup>22</sup> Studies are currently ongoing regarding the use of serial BNP levels as an indicator of treatment response and for titrating therapy.<sup>22</sup>

### How to Elicit Symptoms and Signs

Appropriate history taking and physical examination of the cardiopulmonary system has been described in detail in previous The Rational Clinical Examination articles,<sup>17,24-30</sup> with the exception of the Valsalva maneuver. The Valsalva maneuver is performed by in-

flating and locking a blood pressure cuff to 15 mm Hg above the resting supine systolic pressure (Korotkoff sounds should not be audible at this point), at which point the patient performs a sustained Valsalva (exhalation against a closed glottis) for at least 10 seconds. In a normal response, systolic blood pressure immediately rises 30 to 40 mm Hg above baseline for 1 to 3 seconds (phase 1, appearance of Korotkoff sounds). As venous return decreases, systolic blood pressure drops sharply below baseline (phase 2, disappearance of Korotkoff sounds). When the Valsalva is released, there is a further drop of systolic blood pressure below baseline (phase 3, continued absence of Korotkoff sounds). Between 3 to 15 seconds after release, systolic blood pressure rises 15 mm Hg or more above the baseline level (phase 4, reappearance of Korotkoff sounds).<sup>21,31-34</sup> Two abnormal responses have been described in heart failure. In the absent overshoot response, phases 1 to 3 are normal, but Korotkoff sounds do not reappear in phase 4. In the squarewave response, phase 1 is normal, but Korotkoff sounds are present in phases 2 and 3, followed by disappearance in phase 4.<sup>21,31,32,34</sup>

## METHODS

### Search Strategy

We conducted a computerized search of MEDLINE from 1966 to July 2005 concerning the precision and diagnostic accuracy of components of the clinical examination and simple investigations in diagnosing patients with dyspnea. Our strategy was deliberately broad to minimize the possibility of overlooking relevant articles. Multiple searches were performed with the first search using a similar strategy developed for The Rational Clinical Examination series.<sup>35</sup> This strategy combined 4 exploded Medical Subject Headings (physical examination, medical history taking, professional competence, routine diagnostic tests) with 8 keyword categories (*physical exam, medical history taking, professional competence, sensitivity and specificity, reproducibility of results, observer varia-*

*tion, decision support techniques, Bayes theorem*) and 1 textword category (*sensitivity and specificity*); and intersected with 1 exploded Medical Subject Heading (*dyspnea*). The search was limited to studies published in English about humans. Further MEDLINE searches were conducted combining the following Medical Subject Headings textword and keyword searches: *brain natriuretic peptide, natriuretic peptide, BNP, Valsalva, hepatojugular, abdominojugular, and breathlessness*. These were intersected with the exploded medical subject heading *dyspnea* and the textword *dyspnoea*.

The computerized search was supplemented with a manual search of reference lists of retrieved studies, review articles, and standard physical examination textbooks to identify additional articles not captured through the computerized search strategy.

### Study Selection

One author (C.S.W.) screened the titles and abstracts of the computerized search to identify all potentially relevant articles. All retrieved articles were independently reviewed by 2 authors (C.S.W. and N.T.A.) for eligibility, assessment of methodological quality, and data abstraction. Only studies that evaluated the diagnostic accuracy of some element of the medical history, physical examination, or readily available diagnostic tests in adult patients with undifferentiated dyspnea presenting to the ED, regardless of whether the patients had known cardiac or pulmonary diseases, were included. Data had to be presented so that 2 × 2 contingency tables could be extracted. Because there currently is no widely accepted criterion standard for diagnosing heart failure, and because the focus of this review was a syndrome of heart failure, we accepted as a reasonable reference standard for heart failure that was a diagnosis agreed upon by a panel of physicians after evaluating for appropriate symptoms and signs of heart failure and an appropriate measure of cardiac dysfunction.<sup>5</sup>

We included studies that evaluated common and rapidly available tests

(chest radiograph, ECG, and serum BNP) since clinicians rely on these basic investigations in conjunction with their history and physical examination in bedside decision making.<sup>22,36</sup> There are currently multiple BNP assays approved by the US Food and Drug Administration for clinical use. To date, the largest published randomized clinical trials have been funded by industry and have reported using the BNP assay of one single manufacturer.

An a priori decision was made to exclude studies that investigated other cardiac neurohormones such as A-type natriuretic peptide or other forms of BNP (eg, NT-proBNP). It was thought at the time of this review that there would be insufficient published data on these other neurohormones to draw significant conclusions. We also excluded studies that (1) were review articles with no original data, (2) had no clinical examination performed or reported, (3) used only echocardiography, computed tomography scans, or invasive hemodynamic monitoring alone as the reference standard for heart failure without clinical correlation because the results from these tests serve as part of the reference standard for a clinical diagnosis, (4) were population based, (5) enrolled patients younger than 18 years, and (6) did not specifically include patients reporting dyspnea. We resolved disagreements between reviewers on study selection, assessment of quality, and abstraction of data by consensus.

### Assessment of Study Quality

Study quality was assigned based on the grading scheme developed by Sackett et al<sup>37</sup> and previously used for this series.<sup>24</sup> Level 1 studies were primary prospective studies of the accuracy or precision of the clinical examination that involved comparisons of clinical findings (symptom or sign) with a reference standard of diagnosis among a large number (sufficient to have narrow confidence limits on the resulting sensitivity, specificity, or LRs) of consecutive or random patients with dyspnea. For precision

studies, this required 2 or more independent blinded raters of symptoms or signs in a large number of patients. Level 2 studies were similar to level 1 but with smaller numbers of patients. Level 3 studies were comparisons of clinical findings with a reference standard of diagnosis among nonconsecutive or nonrandom patients with dyspnea. Studies of a retrospective nature were included as level 3. Level 4 studies were comparisons of clinical findings with a reference standard of diagnosis among convenience samples of patients who obviously have the target condition. Finally, level 5 studies were comparisons of clinical findings with a reference standard of unknown or uncertain validity among convenience samples of patients and perhaps, healthy patients.

### Statistical Methods

Two authors (C.S.W. and N.T.A.) independently extracted data for analysis. Published raw data were used to construct  $2 \times 2$  contingency tables for each clinical variable. Where data for the same variable was available from 2 or more sources, meta-analytical techniques were applied to combine results across studies. When multiple articles from the same group were found, the studies were carefully reviewed to ensure no data were analyzed in duplicate. Summary positive and negative LRs and 95% confidence intervals (CIs) were calculated using random-effects models based on the delta method.<sup>38</sup> We display only the CIs of the LRs in the data tables, since these values are most useful to clinicians and include the sensitivity and specificity in the calculation. The choice of random-effects measures lowers the risk of CIs that are too optimistically narrow.

Sensitivity is defined as the proportion of patients with heart failure who have a particular finding; specificity is the proportion of patients without heart failure who do not have the particular finding. The positive LR is the change in the odds of having heart failure when a particular finding is present, whereas the negative LR is the change in the

odds of having heart failure when the particular finding is absent.

## RESULTS

### Search Results

A total of 815 citations were identified in our literature search. Of these, 682 were excluded after review of their titles and abstracts, with 133 studies remaining. These studies were reviewed in detail and we identified a total of 22 studies that evaluated the role of the clinical examination or basic routine investigation (chest radiograph, ECG, serum BNP) in patients with undifferentiated dyspnea and that also met our inclusion criteria.<sup>12,31,32,36,39-56</sup>

### Study Characteristics

Only studies of sufficient quality (levels 1-3) were considered for the quantitative analysis. Of the 22 studies meeting inclusion, 18 were included in the meta-analysis (TABLE 2)<sup>12,31,36,39-48,52-56</sup>; while the remaining 4 studies<sup>32,49-51</sup> were levels 4 or 5 and were not included in the evidence tables.

### Precision of Clinical Examination and Investigations

Precision refers to the degree of variation between observers (interobserver variation) or within observers (intraobserver variation) for a particular finding. No study has specifically addressed the interobserver or intraobserver variability in the recording of findings in dyspneic patients ultimately diagnosed with the clinical syndrome of heart failure. However, analogous work has been done in other diagnoses including pulmonary diseases, acute coronary syndromes; and in comparison with echocardiography, nuclear imaging, and cardiac catheterization.<sup>24,25,29,30,57-63</sup> In general, there is much variability in the precision of clinical findings associated with heart failure, reflecting the potentially subtle nature of findings, and variable examination skills of the clinician.

### Accuracy of the Clinical Examination

Thirteen studies examined the accuracy of the clinical examination for pre-

dicting the presence of heart failure in dyspneic patients assessed in the ED. The sensitivities, specificities, and corresponding positive and negative LRs for the findings are shown in TABLE 3.

### Overall Clinical Gestalt

The overall clinical gestalt of the initial treating ED physician was associated with a high positive LR (4.4; 95% CI, 1.8-10.0) for a final diagnosis of heart failure. When the emergency physician assessed the dyspneic patient as unlikely to have heart failure, the odds decreased by about half (LR, 0.45; 95% CI, 0.28-0.73).

### Historical Items

The most useful historical features in confirming the presence of heart failure were a past medical history of congestive heart failure (LR, 5.8; 95% CI, 4.1-8.0), myocardial infarction (LR, 3.1; 95% CI, 2.0-4.9), or coronary artery disease (LR, 1.8; 95% CI, 1.1-2.8). Likewise, patients without a history of heart failure (LR, 0.45; 95% CI, 0.38-0.53), coronary artery disease (LR, 0.68; 95% CI, 0.48-0.96), or myocardial infarction (LR, 0.69; 95% CI, 0.58-0.82) were less likely to have their dyspnea explained by current heart failure. The results of other historical findings in Table 3 had LR CIs that included 1.

### Symptoms

The presence of paroxysmal nocturnal dyspnea (LR, 2.6; 95% CI, 1.5-4.5), orthopnea (LR, 2.2; 95% CI, 1.2-3.9), or dyspnea on exertion (LR, 1.3; 95% CI, 1.2-1.4) increased the likelihood of heart failure. Likewise, the absence of dyspnea on exertion (LR, 0.48; 95% CI, 0.35-0.67), orthopnea (LR, 0.65; 95% CI, 0.45-0.92), or paroxysmal nocturnal dyspnea (LR, 0.70; 95% CI, 0.54-0.91) decreased the likelihood of heart failure. The results of other findings in Table 3 had CIs that included 1.

### Physical Examination

The presence of a third heart sound (ventricular filling gallop) increased the likelihood of heart failure the most (LR, 11; 95% CI, 4.9-25.0). The presence of



**Table 2.** Summary of Studies in Emergency Department Patients

Source	Study Quality*	Study Design	Study Criteria	Total Men, No. (%)	Mean Age, y	Incidence of Heart Failure, %	Criteria Standard; Objective Measure
Mueller et al, <sup>56</sup> 2005	1	Prospective	Inclusion: ED with dyspnea Exclusion: acute myocardial infarction, trauma	251 (93)	72.8	55	Retrospective review by 1 physician; echocardiography
Lainchbury et al, <sup>42</sup> 2003	1	Prospective	Inclusion: ED with dyspnea, able to give blood within 8 h of arrival Exclusion: n/a	205 (49)	70.0	34	Retrospective review by 2 independent cardiologists; echocardiography, RVG
Logeart et al, <sup>43</sup> 2002	1	Prospective	Inclusion: ED with acute severe dyspnea Exclusion: acute myocardial infarction, chest injury, recent surgery, therapy instituted >2 h prior to arrival in ED, emergency echocardiography not feasible	163 (67)	67.4	71	Retrospective review by 2 independent cardiologists and 1 pulmonologist; echocardiography, CC, RVG, PFT
Knudsen et al, <sup>44</sup> 2004	2	Prospective	Inclusion: ED with dyspnea Exclusion: chest pain, dyspnea clearly not secondary to heart failure	155 (45)	NA†	48	Retrospective review by 2 independent cardiologists; echocardiography, CC, RVG, PFT
Bayes-Genis et al, <sup>45</sup> 2004	2	Prospective	Inclusion: ED with dyspnea, aged 40-88 y Exclusion: NYHA classes I and II, dyspnea secondary to chest trauma or cardiac tamponade, acute coronary syndromes without dyspnea, severe renal insufficiency, liver cirrhosis	89 (60)	70.7	83	Retrospective review by 2 independent cardiologists; echocardiography, PFT
Villacorta et al, <sup>46</sup> 2002	2	Prospective	Inclusion: ED with dyspnea Exclusion: obvious diagnosis of dyspnea, acute coronary syndromes without dyspnea	70 (47)	72.0	51	Retrospective review by 1 cardiologist; echocardiography
Davis et al, <sup>47</sup> 1994	2	Prospective	Inclusion: ED with dyspnea requiring admission Exclusion: obvious cause of dyspnea, severe renal failure, acute chest pain	52 (40)	74.0	61	Retrospective review by committee of physicians and a radiologist; echocardiography, PFT
Marantz et al, <sup>31</sup> 1990	2	Prospective	Inclusion: ED with dyspnea, aged ≥40 y, English speaking, able to consent, presented during study hours Exclusion: clinically unstable, non-English speaking, disoriented or unable to cooperate, refusal to consent, left against medical advice	51 (39)	64.0	45	Retrospective review by 1 physician; echocardiography
Alibay et al, <sup>54</sup> 2005	3	Convenience sample	Inclusion: ED with dyspnea Exclusion: n/a	160 (48)	80.1	37.5	Retrospective review by 2 independent cardiologists; echocardiography
Ray et al, <sup>55</sup> 2004	3	Convenience sample	Inclusion: ED with dyspnea <2 wk, aged ≥65 y, respiratory rate >25/min or PaO <sub>2</sub> <70 mm Hg or PaCO <sub>2</sub> >45 mm Hg or SpO <sub>2</sub> <92% Exclusion: none	308 (49)	80.3	54.2	Retrospective review by 2 independent experts; echocardiography, high-resolution computed tomography scan, PFT
Springfield et al, <sup>12</sup> 2004	3	Convenience sample	Inclusion: ED with dyspnea or respiratory rate >20/min or PaO <sub>2</sub> <90 mm Hg on room air Exclusion: pregnancy, aged ≤18 y, trauma patients, unconscious or unable to speak, <3' 11" or >7' 8" tall, <66 lb or >341 lb	38 (42)	67.2	32	Retrospective review by 1 physician; echocardiography

(Continued)

**Table 2.** Summary of Studies in Emergency Department Patients (cont)

Source	Study Quality*	Study Design	Study Criteria	Total Men, No. (%)	Mean Age, y	Incidence of Heart Failure, %	Criteria Standard; Objective Measure
Morrison et al, <sup>36</sup> 2002	3	Convenience sample	Inclusion: ED with dyspnea Exclusion: dyspnea clearly not secondary to heart failure, unstable angina/myocardial infarction without dyspnea	321 (95)	NA	42	Retrospective review by 2 independent cardiologists; echocardiography, CC, RVG, PFT
Maisel et al, <sup>39</sup> 2002	3	Prospective	Inclusion: ED with dyspnea as prominent symptom Exclusion: aged $\leq$ 18 y, dyspnea clearly not secondary to heart failure, acute myocardial infarction, unstable angina without dyspnea, renal failure on dialysis or creatinine clearance $<$ 0.25 mL/s	1586 (56)	64.0	47	Retrospective review by 2 independent cardiologists; echocardiography, CC, RVG, PFT
McCullough et al, <sup>40</sup> 2002	3	See Maisel et al	Subgroup of Maisel et al <sup>39</sup> with information recorded for ED physician assessment of probability of heart failure	1538 (56)	64.0	47	See Maisel et al <sup>39</sup>
Dao et al, <sup>48</sup> 2001	3	Convenience sample	Inclusion: ED with dyspnea Exclusion: dyspnea clearly not secondary to heart failure, acute coronary syndromes without dyspnea	250 (94)	63.0	39	Retrospective review by 2 independent cardiologists; echocardiography, CC, RCG, PFT

Abbreviations: CC, cardiac catheterization; ED, emergency department; NYHA, New York Heart Association (classification of heart disease); PaCO<sub>2</sub>, arterial pressure of carbon dioxide; PaO<sub>2</sub>, arterial partial pressure of oxygen; PFT, pulmonary function test; RVG, radionuclide ventriculography; SpO<sub>2</sub>, peripheral oxygen saturation.

\*Study quality was assigned based on the grading scheme developed by Sackett et al<sup>27</sup> and previously used for this series.<sup>24</sup> See also "Assessment of Study Quality" in the "Methods" section for more details.

†NA denotes that the mean age was not published in the source article.

several other findings had CIs that excluded 1: jugular venous distension (LR, 5.1; 95% CI, 3.2-7.9), pulmonary rales (LR, 2.8; 95% CI, 1.9-4.1), any cardiac murmur (LR, 2.6; 95% CI, 1.7-4.1), and leg edema (LR, 2.3; 95% CI, 1.5-3.7). The presence of an abnormal abdominojugular reflux response (LR, 6.4; 95% CI, 0.81-51.0) had a high LR, but its evaluation in only 1 study of 51 patients led to broad CIs.<sup>31</sup> An abnormal response to the Valsalva maneuver in the same study had an LR of 2.1 but the lower limit of the 95% CI was 1.0. The presence of the other findings in Table 3 did not appear useful for assessing the likelihood of heart failure in dyspneic patients.

The absence of pulmonary rales (LR, 0.51; 95% CI, 0.37-0.70), leg edema (LR, 0.64; 95% CI, 0.47-0.87), or jugular venous distension (LR, 0.66; 95% CI, 0.57-0.77) were the most useful findings that lowered the likelihood of heart failure. Wheezing also decreased the likelihood that a dyspneic patient had heart failure (LR, 0.52; 95% CI, 0.38-0.71). The absence of a third heart sound or a murmur lowered the likelihood of heart failure but the point estimate of the LR

of these findings approached 1. The absence of the other findings in Table 3 did not appear useful as the CI included 1. Diaphoresis as a sign of heart failure was of uncertain validity, having been evaluated in only 2 studies that were each of level 4 quality.<sup>49,50</sup>

#### Accuracy of Chest Radiographs

Seven studies examined the accuracy of various chest radiograph findings in the ED setting (TABLE 4). The presence of any of these findings (except for any edema) had high positive LRs with CIs exceeding 1 and therefore, increased the likelihood of heart failure in dyspneic patients. The presence of pulmonary venous congestion (distension of pulmonary veins and redistribution to the apices) (n=4 studies; summary LR, 12.0; 95% CI, 6.8-21.0) and cardiomegaly (n=6 studies; summary LR, 3.3; 95% CI, 2.4-4.7) increased the likelihood of heart failure and have undergone more extensive evaluation so that the results may be more reliable. The presence of interstitial edema also had a high LR (n=2 studies; summary LR, 12.0; 95% CI, 5.2-27.0). The presence of pneumonia or hyperinflation lowered the likelihood of

heart failure but were only assessed in one study.

The most extensively evaluated chest radiograph findings (pulmonary venous congestion and cardiomegaly), were also the findings that when absent, had an LR that was appreciably different from 1. The absence of cardiomegaly was particularly useful (LR, 0.33; 95% CI, 0.23-0.48), with narrower CIs than the absence of pulmonary venous congestion (LR, 0.48; 95% CI, 0.28-0.83).

#### Accuracy of Electrocardiogram

Seven studies examined the accuracy of various ECG findings in the ED setting (Table 4). The presence of atrial fibrillation in a dyspneic patient was the most important (LR, 3.8; 95% CI, 1.7-8.8) and evaluated in several studies (n=5 studies). The presence of new T-wave changes (LR, 3.0; 95% CI, 1.7-5.3) or abnormal ECG findings (LR, 2.2; 95% CI, 1.6-3.1) increased the likelihood of heart failure but were evaluated in fewer studies. A completely normal ECG (LR, 0.64; 95% CI, 0.47-0.88) decreased the likelihood of heart failure and was the only normal finding that had a nega-

**Table 3.** Summary of Diagnostic Accuracy of Findings on History and Physical Examination in Emergency Department Patients

Finding	Pooled		Summary LR (95% CI)*	
	Sensitivity	Specificity	Positive	Negative
Initial clinical judgment <sup>12,31,40,55</sup>	0.61	0.86	4.4 (1.8-10.0)	0.45 (0.28-0.73)
History				
Heart failure <sup>36,41,43,45,48,53,56</sup>	0.60	0.90	5.8 (4.1-8.0)	0.45 (0.38-0.53)
Myocardial infarction <sup>41,43-45,48,53</sup>	0.40	0.87	3.1 (2.0-4.9)	0.69 (0.58-0.82)
Coronary artery disease <sup>36,44,53,56</sup>	0.52	0.70	1.8 (1.1-2.8)	0.68 (0.48-0.96)
Dyslipidemia <sup>45</sup>	0.23	0.87	1.7 (0.43-6.9)	0.89 (0.69-1.1)
Diabetes mellitus <sup>43-45,48,56</sup>	0.28	0.83	1.7 (1.0-2.7)	0.86 (0.73-1.0)
Hypertension <sup>36,41,43-45,48,53,56</sup>	0.60	0.56	1.4 (1.1-1.7)	0.71 (0.55-0.93)
Smoker <sup>45</sup>	0.62	0.27	0.84 (0.58-1.2)	1.4 (0.58-3.6)
Chronic obstructive pulmonary disease <sup>36,45,48,53</sup>	0.34	0.57	0.81 (0.60-1.1)	1.1 (0.95-1.4)
Symptoms				
Paroxysmal nocturnal dyspnea <sup>36,45,48,53,56</sup>	0.41	0.84	2.6 (1.5-4.5)	0.70 (0.54-0.91)
Orthopnea <sup>36,41,43-45,48,53,56</sup>	0.50	0.77	2.2 (1.2-3.9)	0.65 (0.45-0.92)
Edema <sup>36,48,53</sup>	0.51	0.76	2.1 (0.92-5.0)	0.64 (0.39-1.1)
Dyspnea on exertion <sup>36,48</sup>	0.84	0.34	1.3 (1.2-1.4)	0.48 (0.35-0.67)
Fatigue and weight gain <sup>36</sup>	0.31	0.70	1.0 (0.74-1.4)	0.99 (0.85-1.1)
Cough <sup>36,45,48,53,56</sup>	0.36	0.61	0.93 (0.70-1.2)	1.0 (0.87-1.3)
Physical examination				
Third heart sound (ventricular filling gallop) <sup>36,41,43-45,48,53,56</sup>	0.13	0.99	11 (4.9-25.0)	0.88 (0.83-0.94)
Abdominojugular reflux <sup>31</sup>	0.24	0.96	6.4 (0.81-51.0)	0.79 (0.62-1.0)
Jugular venous distension <sup>36,41,43-45,48,53,56</sup>	0.39	0.92	5.1 (3.2-7.9)	0.66 (0.57-0.77)
Rales <sup>36,41,43-45,48,53,56</sup>	0.60	0.78	2.8 (1.9-4.1)	0.51 (0.37-0.70)
Any murmur <sup>36,44,48,53</sup>	0.27	0.90	2.6 (1.7-4.1)	0.81 (0.73-0.90)
Lower extremity edema <sup>41,43-45,53,56</sup>	0.50	0.78	2.3 (1.5-3.7)	0.64 (0.47-0.87)
Valsalva maneuver <sup>31</sup>	0.73	0.65	2.1 (1.0-4.2)	0.41 (0.17-1.0)
Systolic blood pressure <100 mm Hg <sup>48</sup>	0.06	0.97	2.0 (0.60-6.6)	0.97 (0.91-1.0)
Fourth heart sound (atrial gallop) <sup>36,48,53</sup>	0.05	0.97	1.6 (0.47-5.5)	0.98 (0.93-1.0)
Systolic blood pressure ≥150 mm Hg <sup>48</sup>	0.28	0.73	1.0 (0.69-1.6)	0.99 (0.84-1.2)
Wheezing <sup>36,44,45,48,53</sup>	0.22	0.58	0.52 (0.38-0.71)	1.3 (1.1-1.7)
Ascites <sup>48</sup>	0.01	0.97	0.33 (0.04-2.9)	1.0 (0.99-1.1)

Abbreviations: CI, confidence interval; LR, likelihood ratio.

\*LRs are not independent of each other and should not be multiplied in series when multiple findings are considered.

**Table 4.** Summary of Diagnostic Accuracy of Findings on Chest Radiograph and Electrocardiogram in Emergency Department Patients

Finding	Pooled		Summary LR (95% CI)*	
	Sensitivity	Specificity	Positive	Negative
Chest radiograph				
Pulmonary venous congestion <sup>36,41,45,48†</sup>	0.54	0.96	12.0 (6.8-21.0)	0.48 (0.28-0.83)
Interstitial edema <sup>41,53</sup>	0.34	0.97	12.0 (5.2-27.0)	0.68 (0.54-0.85)
Alveolar edema <sup>41</sup>	0.06	0.99	6.0 (2.2-16.0)	0.95 (0.93-0.97)
Cardiomegaly <sup>36,41,43-45,48</sup>	0.74	0.78	3.3 (2.4-4.7)	0.33 (0.23-0.48)
Pleural effusion(s) <sup>36,41</sup>	0.26	0.92	3.2 (2.4-4.3)	0.81 (0.77-0.85)
Any edema <sup>43,44</sup>	0.70	0.77	3.1 (0.60-16.0)	0.38 (0.11-1.3)
Pneumonia <sup>41</sup>	0.04	0.92	0.50 (0.29-0.87)	1.0 (1.0-1.1)
Hyperinflation <sup>41</sup>	0.03	0.92	0.38 (0.20-0.69)	1.1 (1.0-1.1)
Electrocardiogram				
Atrial fibrillation <sup>36,43,44,48,56</sup>	0.26	0.93	3.8 (1.7-8.8)	0.79 (0.65-0.96)
New T-wave changes <sup>36</sup>	0.24	0.92	3.0 (1.7-5.3)	0.83 (0.74-0.92)
Any abnormal finding <sup>41,53</sup>	0.50	0.78	2.2 (1.6-3.1)	0.64 (0.47-0.88)
ST elevation <sup>36,48</sup>	0.05	0.97	1.8 (0.80-4.0)	0.98 (0.94-1.0)
ST depression <sup>36,48</sup>	0.11	0.94	1.7 (0.97-2.9)	0.95 (0.90-1.0)

Abbreviations: CI, confidence interval; LR, likelihood ratio.

\*LRs are not independent of each other and should not be multiplied in series when multiple findings are considered.

†Pulmonary venous congestion, manifest as distension of pulmonary veins and redistribution to the apices.

tive LR with a clinically meaningful difference from 1.

### Accuracy of BNP

Eleven studies examined the operating characteristics of various cutoffs of serum BNP in the ED setting (TABLE 5). Eight of these reported pharmaceutical industry sponsorship, 2 did not disclose funding sources, and only 1 study reported no pharmaceutical relationship.

As the BNP cutoff increased, the positive LR generally increased. Thus, the higher the value of BNP, the more suggestive it was of heart failure. However, no BNP threshold indicated the presence of heart failure with certainty. At any BNP threshold up to 250 pg/mL, values below the threshold always made heart failure much less likely (LR 0.06-0.15).

BNP levels must be interpreted differently for patients with renal insufficiency. Based upon an analysis of data from the Breathing Not Properly Multinational Study,<sup>39,64</sup> no adjustment in the 100-pg/mL threshold appears necessary for patients with an estimated glomerular filtration rate of 60 to 89 mL/min/1.73 m<sup>2</sup>, with an area under the receiver operating characteristic curve of 0.90 (a measure of overall accuracy). The loss of accuracy with worsening renal function can be minimized by using thresholds of 225 and 201 pg/mL, respectively, for patients with estimated glomerular filtration rates of 15 to 29 and 30 to 59 mL/min/1.73 m<sup>2</sup> (areas under receiver operating characteristic curves of 0.86 and 0.81, respectively). The utility of BNP levels in patients with advanced renal insufficiency (estimated glomerular filtration rate <15 mL/min/1.73 m<sup>2</sup> or on dialysis) is unclear as these patients were not included in that study.

### Accuracy of Findings in Patients With History of Pulmonary Disease

One study (TABLE 6) examined the accuracy of symptoms, signs, ECG, and serum BNP in diagnosing heart failure in dyspneic ED patients with a prior history of asthma or COPD.<sup>52</sup>

**Table 5.** Summary of Operating Characteristics of Serum BNP in Emergency Department Patients

	Pooled		Summary LR (95% CI)	
	Sensitivity	Specificity	Positive	Negative
Clinical judgment or BNP $\geq$ 100 pg/mL <sup>40*</sup>	0.94	0.70	3.1 (2.8-3.5)	0.09 (0.06-0.11)
BNP alone, pg/mL				
$\geq$ 250 <sup>36,43,55</sup>	0.89	0.81	4.6 (2.6-8.0)	0.14 (0.06-0.33)
$\geq$ 200 <sup>36,42-44,46,54,55</sup>	0.92	0.75	3.7 (2.6-5.4)	0.11 (0.07-0.18)
$\geq$ 150 <sup>39,43,44,48,54-56</sup>	0.89	0.71	3.1 (2.1-4.5)	0.15 (0.11-0.21)
$\geq$ 100 <sup>36,39,42-44,47,48,54-56</sup>	0.93	0.66	2.7 (2.0-3.9)	0.11 (0.07-0.16)
$\geq$ 80 <sup>39,43,47,48</sup>	0.96	0.71	3.3 (1.8-6.3)	0.06 (0.03-0.13)
$\geq$ 50 <sup>39,44,54</sup>	0.97	0.44	1.7 (1.2-2.6)	0.06 (0.03-0.12)

Abbreviations: BNP, B-type natriuretic peptide; CI, confidence interval; LR, likelihood ratio.

\*Either an initial clinical probability of heart failure  $\geq$ 80% or BNP  $\geq$ 100 pg/mL was considered a positive result. A negative result was a clinical probability of heart failure <80% and BNP <100 pg/mL.

This study was a subgroup analysis of the Breathing Not Properly Multinational Study.<sup>39</sup>

### Initial Clinical Gestalt

A high initial clinical suspicion by the emergency physician ( $\geq$ 80% probability) was associated with a high likelihood for a final diagnosis of heart failure (LR, 9.9; 95% CI, 5.3-18.0) while an intermediate (21%-79%) or low ( $\leq$ 20%) initial clinical suspicion decreased the likelihood of heart failure (LR, 0.65; 95% CI, 0.55-0.77) but did not exclude it. In fact, 32% of patients in the intermediate suspicion group and 9% of patients in the low clinical suspicion group were ultimately diagnosed with heart failure. Assigning a lower probability to the low suspicion group (eg,  $\leq$ 5%) would likely have reduced misclassification in that study.

### Historical Items

The presence of most historical findings in Table 6 increased the likelihood of heart failure with CIs excluding 1. A history of prior atrial fibrillation (LR, 4.1; 95% CI, 2.5-6.6) or coronary bypass surgery (LR, 2.8; 95% CI, 1.3-5.8) were the most useful findings that increased the likelihood of heart failure. The absence of relevant historical features did not result in clinically meaningful LRs less than 1 other than perhaps the absence of coronary artery disease (LR, 0.67; 95% CI, 0.54-0.84).

### Symptoms

Only the absence of orthopnea (LR, 0.68; 95% CI, 0.48-0.95) had an LR that was appreciably different from 1. Thus, symptoms were not particularly useful among dyspneic patients with lung disease in determining who might also have heart failure.

### Physical Examination

The presence of a third heart sound had a very high diagnostic value for heart failure (LR, 57; 95% CI, 7.6-425.0). Other useful physical examination findings, when present, included jugular venous distension (LR, 4.3; 95% CI, 2.8-6.5), lower extremity edema (LR, 2.7; 95% CI, 2.2-3.5), pulmonary rales (LR, 2.6; 95% CI, 2.1-3.3), or hepatic congestion (LR, 2.4; 95% CI, 1.2-4.7). The absence of pulmonary rales (LR, 0.39; 95% CI, 0.28-0.55), lower extremity edema (LR, 0.41; 95% CI, 0.30-0.57), or jugular venous distension (LR, 0.65; 95% CI, 0.54-0.78) decreased the likelihood of heart failure.

### Chest Radiograph

The presence of edema was the most useful radiographic finding for increasing the likelihood of heart failure (LR, 11.0; 95% CI, 5.8-22.0). Other very useful findings were cardiomegaly (LR, 7.1; 95% CI, 4.5-11.0) or pleural effusion(s) (LR, 4.6; 95% CI, 2.6-8.0). A normal chest radiograph (LR, 0.11; 95% CI, 0.04-0.28), absence of cardiomegaly (LR, 0.54; 95% CI, 0.44-0.67),



or absence of edema (LR, 0.68; 95% CI, 0.58-0.79) decreased the likelihood of heart failure.

### Electrocardiogram

The presence of ECG findings of atrial fibrillation (LR, 6.0; 95% CI, 3.4-10.0), ischemic ST-T wave changes (LR, 4.6; 95% CI, 2.4-8.7), or Q waves (LR, 3.1; 95% CI, 1.8-5.5) were all helpful toward suggesting a diagnosis of heart failure in the dyspneic ED patient with a history of pulmonary disease. No single ECG result had clinically useful

outcomes for lowering the likelihood of heart failure.

### B-type Natriuretic Peptide

BNP levels can rise in patients with chronic pulmonary diseases due to right ventricular strain. Nevertheless, BNP appears to still be useful in these patients. Studies have demonstrated that BNP levels are significantly higher in patients with a history of chronic lung disease but acute dyspnea from heart failure, compared with those with a history of heart failure but acute dyspnea from lung disease.<sup>36,65</sup>

Serum BNP for dyspneic patients with a history of asthma or COPD was useful for identifying heart failure (BNP  $\geq 100$  pg/mL: LR 4.1; 95% CI, 3.3-5.0). However, it was more powerful for excluding heart failure when low (BNP  $< 100$  pg/mL: LR 0.09; 95% CI, 0.04-0.19). However, this was only one study and thus, the optimal cutoff for BNP to diagnose or exclude clinical heart failure in dyspneic patients with chronic lung diseases is unclear.

### COMMENT

It is both important and difficult to rapidly differentiate among the common causes of dyspnea in ED patients. The syndrome of heart failure requires appropriate symptoms along with objective measures of cardiac dysfunction.<sup>5</sup> Although sophisticated and invasive tests such as Swan-Ganz catheterization can help to distinguish between cardiac and pulmonary causes of dyspnea, they are frequently unavailable in the acute setting and thus, the diagnosis of heart failure and the decision to institute therapy on an emergent basis rests on the bedside clinical assessment (chest radiograph, ECG, and recently, serum BNP). Relying purely on echocardiography to diagnose clinical heart failure is also problematic because it is often not easily accessible, requires specialized training,<sup>66</sup> and may not always truly reflect the current cause of dyspnea.<sup>67</sup> That is, not every patient presenting with heart failure will have a diminished left ventricular ejection fraction; patients with diastolic heart failure for instance, may have elevated filling pressures and dyspnea in the presence of normal ejection fraction. The reverse is also true in that patients with a decreased left ventricular ejection fraction may be dyspneic from noncardiac causes such as COPD, and furthermore, the severity of impairment of ejection fraction does not always correlate with subjective severity of dyspnea.<sup>68</sup>

In this systematic review, many features on clinical examination, chest radiograph, ECG, and serum BNP were useful in diagnosing heart failure in

**Table 6.** Diagnostic Accuracy of History, Physical Examination, and Tests of Cardiac Function in Emergency Department Patients With History of Asthma or Chronic Obstructive Pulmonary Disease\*

Finding	Sensitivity	Specificity	Positive LR (95% CI)†	Negative LR (95% CI)†
Initial clinical judgment	0.37	0.96	9.9 (5.3-18)	0.65 (0.55-0.77)
History				
Atrial fibrillation	0.32	0.92	4.1 (2.5-6.6)	0.74 (0.63-0.85)
Coronary artery bypass grafting	0.13	0.95	2.8 (1.3-5.8)	0.92 (0.84-0.99)
Myocardial infarction	0.25	0.88	2.2 (1.4-3.5)	0.84 (0.74-0.96)
Diabetes mellitus	0.26	0.87	2.0 (1.3-3.2)	0.85 (0.74-0.97)
Coronary artery disease	0.49	0.75	2.0 (1.5-2.6)	0.67 (0.54-0.84)
Angina	0.21	0.88	1.7 (1.0-2.8)	0.90 (0.80-1.0)
Hypertension	0.54	0.55	1.2 (0.95-1.5)	0.84 (0.65-1.1)
Symptoms				
Orthopnea	0.70	0.44	1.3 (1.1-1.5)	0.68 (0.48-0.95)
Fatigue	0.74	0.34	1.1 (0.96-1.3)	0.79 (0.54-1.2)
Nocturnal cough	0.49	0.47	0.93 (0.73-1.2)	1.1 (0.85-1.4)
Physical examination				
Third heart sound (ventricular filling gallop)	0.17	1.00	57.0 (7.6-425)	0.83 (0.75-0.91)
Jugular venous distension	0.41	0.90	4.3 (2.8-6.5)	0.65 (0.54-0.78)
Lower extremity edema	0.69	0.75	2.7 (2.2-3.5)	0.41 (0.30-0.57)
Rales	0.71	0.73	2.6 (2.1-3.3)	0.39 (0.28-0.55)
Hepatic congestion	0.14	0.94	2.4 (1.2-4.7)	0.91 (0.84-1.0)
Enlarged heart	0.03	0.98	1.6 (0.43-6.2)	0.99 (0.95-1.0)
Wheezing	0.42	0.50	0.85 (0.65-1.1)	1.2 (0.94-1.4)
Chest radiograph				
Edema	0.34	0.97	11.0 (5.8-22.0)	0.68 (0.58-0.79)
Cardiomegaly	0.49	0.93	7.1 (4.5-11.0)	0.54 (0.44-0.67)
Pleural effusion(s)	0.26	0.94	4.6 (2.6-8.0)	0.78 (0.69-0.89)
Pneumonia	0.08	0.92	1.0 (0.46-2.3)	1.0 (0.93-1.1)
Hyperinflation	0.08	0.85	0.53 (0.25-1.1)	1.1 (1.0-1.2)
Normal	0.05	0.57	0.11 (0.04-0.28)	1.7 (1.5-1.8)
Electrocardiogram				
Atrial fibrillation	0.31	0.95	6.0 (3.4-10.0)	0.73 (0.63-0.84)
Ischemic ST-T waves	0.21	0.95	4.6 (2.4-8.7)	0.83 (0.74-0.93)
Q waves	0.22	0.93	3.1 (1.8-5.5)	0.84 (0.75-0.94)
B-type natriuretic peptide $\geq 100$ pg/mL	0.93	0.77	4.1 (3.3-5.0)	0.09 (0.04-0.19)

Abbreviation: LR, likelihood ratio.

\*Adapted from McCullough et al.<sup>52</sup>

†LRs are not independent of each other and should not be multiplied in series when multiple findings are considered.

adult ED patients presenting with dyspnea in whom heart failure was suspected. Features listed in BOX 1 were assessed in more than 1 study and were useful when either present or absent. Other findings may prove useful when evaluated further.

Our results are consistent with those of Marcus and colleagues.<sup>69</sup> They recently studied patients undergoing elective left heart catheterization, comparing the test characteristics of third and fourth heart sounds with objective measures of left ventricular dysfunction. While the patient population and reference standard for heart failure were different in our study when compared with theirs (eg, ventricular dysfunction vs a clinical diagnosis of heart failure), both studies found that third and fourth heart sounds had greater specificity than sensitivity, and that a third heart sound had a better specificity than a fourth heart sound for the diagnosis of heart failure.

We did not find any studies examining combinations of historical and physical examination findings in making a diagnosis of heart failure. However, our analysis suggests that the initial clinical gestalt of the physician based on available information (history, physical, chest radiograph, ECG) is valuable. Because the overall clinical gestalt had LRs that approximate some of the individual findings, along with a lack of consistent multivariate models, we do not know whether all the symptoms and signs are independently useful. When clinicians are not confident in their clinical gestalt, they should preferentially rely on the results of the few findings that have LR estimates most different from 1.

It is notable that a high initial clinical suspicion alone (LR 4.4; 95% CI, 1.8-10.0) (Table 3) had a greater positive LR than a composite of (high clinical suspicion or BNP  $\geq$ 100 pg/mL or both), which had a combined positive LR of 3.1 (95% CI, 2.8-3.5) (Table 5). This suggests that BNP may not contribute much more in patients for whom the initial clinical suspicion of heart failure was already very high. However, in

patients for whom the initial clinical suspicion of heart failure was not very high, BNP at a threshold value of 100 pg/mL was useful, especially for excluding heart failure in this group of patients. To apply these results correctly, it is necessary that clinicians first quantify and acknowledge their clinical suspicion (eg, formulate a pretest probability). If the physician waits until the BNP results are available before establishing clinical suspicion, these tests are no longer independent and the clinical suspicion becomes biased by the BNP. The results of our BNP analysis adds support to recent European guidelines for diagnosing heart failure, which state that BNP may be a clinically useful test to rule out heart failure due to its high negative predictive values.<sup>5</sup> Clinicians should be aware that factors other than heart failure can affect serum BNP levels (BOX 2). Algorithms for the use of the BNP test have been proposed<sup>70</sup> but not extensively validated.

#### Limitations

The results of our meta-analysis should be interpreted in the context of study limitations. One limitation of this review is the reference standard for heart failure (adjudication by a panel of physicians). Given the subjectivity and potential bias of such a standard, many of the studies had disagreement (up to 10%) among the adjudicators of whether heart failure was the contributing cause of dyspnea. However, in the absence of a true criterion standard for this clinical syndrome, the reference standard, while imperfect, is likely the best available and consistent with the clinical focus of this review. Another limitation that arises from using a clinical reference standard is that the final diagnosis of heart failure may not have been made independently of the individual findings of interest. That is, the panel of physicians may have used some of the clinical findings in deciding whether patients ultimately had heart failure as the cause of their dyspnea. As such, this may overestimate sensitivities and specificities. While this is a valid concern, we believe the effects on each individual finding

### Box 1. Features Useful in Diagnosing Heart Failure in Adult Emergency Department Patients With Dyspnea

#### Historical Features

Heart failure  
Myocardial infarction  
Coronary artery disease

#### Symptoms

Paroxysmal nocturnal dyspnea  
Orthopnea  
Dyspnea on exertion

#### Physical Examination

Listening for a third heart sound (ventricular filling gallop)  
Jugular venous pressure assessment  
Auscultating for rales and wheezing  
Auscultating for a murmur  
Assessing the legs for edema

#### Chest Radiograph

Pulmonary venous congestion  
Interstitial edema  
Cardiomegaly  
Pleural effusion(s)

#### Electrocardiogram Findings

Atrial fibrillation  
An abnormal result

#### B-type Natriuretic Peptide

Most useful when  $<$ 100 pg/mL for decreasing the likelihood of heart failure

#### Clinician's Overall Assessment

would be small because the final diagnosis relied on a combination of information from many diverse sources, including any or all of the following: history, physical examination, routine laboratory tests, chest radiograph, ECG, heart failure scores, objective measures of cardiac function (eg, echocardiography, radionuclide ventriculography, radionuclide angiography, and left ventriculography at cardiac catheterization), pulmonary function tests,

**Box 2. Factors That Can Affect B-type Natriuretic Peptide (BNP) Levels\*****Factors (Other Than Heart Failure) That Cause Elevated BNP Levels**

Advanced age  
 Renal failure  
 Acute coronary syndromes  
 Lung disease with cor pulmonale  
 Acute large pulmonary embolism  
 High output cardiac states

**Factors That Lower BNP in the Setting of Heart Failure**

Acute pulmonary edema  
 Stable New York Heart Association class I patients with low ejection fraction  
 Acute mitral regurgitation  
 Mitral stenosis  
 Atrial myxoma

\*Adapted from Maisel et al.<sup>70</sup>

response to treatment, hospitalization course, and follow-up records.

It is also important to note that our data are derived from studies of patients presenting to the ED with dyspnea. Therefore, these results may not generalize to inpatients, outpatients in clinic settings who may have more chronic dyspnea, or patients without dyspnea. The 18 studies included in this meta-analysis represent diverse and heterogeneous populations with various comorbidities. The majority of the studies excluded patients with acute coronary syndromes and in whom an obvious cause of dyspnea (eg, pneumothorax, trauma) was present. All the studies of BNP excluded patients in whom dyspnea was clearly not secondary to heart failure. Therefore, the usefulness of BNP from our analysis can only be applied to patients in whom the diagnosis of heart failure is a consideration. In patients in whom the suspicion of heart failure is very low (after taking a careful history and performing the

physical examination, chest radiograph, and ECG), a BNP level is unlikely to affect diagnosis or management (eg, an obvious pulmonary etiology of dyspnea).

Other limitations include the inherent subjectivity of clinical findings on history, physical examination, chest radiograph, and ECG. It is impossible to confirm the accuracy of individual findings presented in each study, and no formal definitions were given. For example, we do not have standardized information on the technique used for each chest radiograph performed (eg, anteroposterior, posteroanterior, portable).

**The Bottom Line**

The features evaluated in more than one study with the highest LRs (LR >3.5) for diagnosing heart failure were the following: the overall clinical judgment, history of heart failure, a third heart sound, jugular venous distension, radiographic pulmonary venous congestion or interstitial edema, and electrocardiographic atrial fibrillation.

The features evaluated in more than one study with the lowest LRs (LR <0.60) for diagnosing heart failure were the following: the overall clinical judgment, no prior history of heart failure, no dyspnea on exertion, the absence of rales, and the absence of radiographic pulmonary venous congestion, or cardiomegaly. The single finding that decreased the likelihood of heart failure the most was a BNP <100 pg/mL (for patients with an estimated glomerular filtration rate of 15–60 mL/min/1.73 m<sup>2</sup>, a threshold of 201 pg/mL can be used). However, the clinician must always remember to first quantify and acknowledge his/her clinical suspicion based on their clinical examination prior to interpreting the BNP result.

In the subgroup of ED patients with a prior history of asthma or COPD, the features that strongly suggested a diagnosis of heart failure were the overall clinical assessment, a third heart sound, radiographic edema or cardiomegaly, and electrocardiographic atrial

fibrillation. The features that suggested against the diagnosis were normal chest radiograph and low serum BNP (<100 pg/mL). However, these results are from a subgroup analysis of one study and requires further confirmation.

While the findings of this study are useful when assessing dyspneic patients suspected of having heart failure, no individual feature is sufficiently powerful in isolation to rule heart failure in or out. Therefore, an overall clinical impression based on all available information is best. If the appropriate constellation of findings with high LRs for heart failure are present, that may be sufficient to warrant empirical treatment without further urgent investigations. Conversely, if the clinical suspicion of heart failure is very low (eg, pulmonary disease), the physician should investigate and treat other causes of dyspnea.

**SCENARIO RESOLUTION****Case 1**

The patient has many features that raise the suspicion of heart failure, such as previous myocardial infarction (LR 3.1), previous heart failure (LR 5.8), orthopnea (LR 2.2), paroxysmal nocturnal dyspnea (LR 2.6), elevated jugular venous pressure (LR 5.1), a third heart sound (LR 11.0), rales (LR 2.8), extremity edema (LR 2.3), cardiomegaly (LR 3.3), and atrial fibrillation (LR 3.8), and only the single feature of wheezing (LR 0.52) that lowers the suspicion slightly. The overall constellation of symptoms and signs is so suggestive of heart failure that additional testing is not needed to make the diagnosis.

**Case 2**

Both heart failure and obstructive airways disease are considerations. The symptoms of dyspnea on exertion and cough are not helpful in making a diagnosis of heart failure because their LRs are close to 1. Rales (LR 2.8) and ECG showing ST depression (LR 1.7) both increase the likelihood of heart failure but more importantly, the findings of pulmonary venous conges-



tion and interstitial edema are both associated with large LRs (>10.0) that significantly raise the suspicion for heart failure. Wheezing reduces the likelihood somewhat (LR 0.52). Based on the information available, the patient likely has acute heart failure and should be treated without waiting for further tests. An ECG should be ordered nonurgently. Furthermore, the patient may also be having a superimposed COPD or asthma exacerbation. The physician should consider ordering pulmonary function tests to confirm a diagnosis of obstructive airways disease.

### Case 3

There are some features that increase the likelihood of heart failure, such as history of myocardial infarction (LR 2.2), elevated jugular venous pressure (LR 4.3), lower extremity edema (LR 2.7), and Q waves (LR 3.1), while other features decrease the likelihood (wheezing, LR 0.85) and normal chest radiograph (LR 0.11). Based on these LRs, there are insufficient data to make or exclude a diagnosis of heart failure. In this case, a BNP level could be very helpful. If it were less than 100 pg/mL, heart failure would be extremely unlikely (LR 0.09). If it were elevated, the probability of heart failure is higher but not diagnostic. More urgent echocardiogram and pulmonary function studies would be appropriate next steps.

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