Assessing the breathless patient

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Abstract

Breathlessness can be caused by many pathologies, and correctly identifying those patients who have heart failure can be a challenge in day-to-day practice in both the acute and chronic setting. The approach to the breathless patient should rely on good history taking and clinical examination, supplemented by investigations that help include or exclude particular diagnoses. The measurement of the plasma concentration of natriuretic peptides can be a very useful additional test, helping to rule out heart failure. If the levels are elevated, heart failure is not proven but is much more likely, and further investigation (typically including echocardiography and a specialist opinion) is required. The current European Society of Cardiology guidelines recommend a decision cut point of 125 pg/mL for N-terminal pro–B-type natriuretic peptide (NT-proBNP) and 35 pg/mL for B-type natriuretic peptide (BNP) in the chronic setting, and 300 pg/mL for NT-proBNP and 100 pg/mL for BNP in the acute setting. Recently published US guidelines are also strongly supportive of the use of natriuretic peptide testing to rule out heart failure as the cause of breathlessness. ■ *Heart Metab*. 2017;74:4-7

Keywords: diagnosis; heart failure; natriuretic peptide

Primary care/clinic setting

The diagnosis of heart failure can be challenging. In primary care, patients may present with symptoms of gradual-onset breathlessness, fatigue, or ankle swelling,[1] but these symptoms are not specific to heart failure, and many patients have several comorbidities.[2,3] Making a timely and accurate diagnosis is key to identifying the underlying cause and starting potentially life-saving therapy. Most studies from general practice suggest that the diagnosis is only confirmed in around 30% of cases of suspected heart failure—which is appropriate, as the index of suspicion should be high.[4]

An individual meta-analysis of nine prospective studies reported that certain clinical features were highly specific for heart failure, including added heart sounds (99%), hepatomegaly (97%), history of myocardial infarction (89%), orthopnea (89%), and elevated jugular venous pressure (70%).[4] Most of those features are not highly sensitive and so are helpful when present but may be absent in many patients with heart failure.

Clinical decision rules can help a clinician to decide whether a patient is likely to have a particular diagnosis. Several have been developed for heart failure arising in primary care.[4,5] A decision rule based on meta-analysis was developed, suggesting that a patient presenting in primary care with symptoms that might be due to heart failure should be referred directly for echocardiography if they had one of the following: a history of myocardial infarction, basal crepitations, or ankle edema (in a man). Otherwise, an N-terminal pro–B-type natriuretic peptide (NT-proB-

Abbreviations

BNP: B-type natriuretic peptide; **ECG:** electrocardiogram; **ESC:** European Society of Cardiology; **NICE:** National Institute for Health and Care Excellence; **NP:** natriuretic peptide; **NPV:** negative predictive value; **NT-proBNP:** N-terminal pro–B-type natriuretic peptide

NP) test should be performed, and depending on the NT-proBNP level, the patient should have echocardiography.[4] This clinical decision rule was prospectively tested in 28 general practices and found to be less good than a simple cut off based on natriuretic peptides alone.[1] At a decision cut point of plasma NT-proBNP under 125 pg/mL, the sensitivity for heart failure was 94% (95% confidence interval [CI], 88%-98%), and specificity was 49% (95% CI, 42%-56%), with an area under the receiver operating characteristics (AUROC) curve of 0.72.

The National Institute for Health and Care Excellence (NICE) in England currently recommends a primary care decision cut point of greater than or equal to 400 pg/mL for NT-proBNP and of greater than or equal to 100 pg/mL for B-type natriuretic peptide (BNP),[6] but in the recent general practice prospective validation study,[1] the sensitivity at this decision cut point was only 77%, albeit with a high specificity of 92%. Nearly all such patients will have heart failure (or other serious cardiovascular/renal problems), but up to 1 in 5 patients with heart failure may be missed. This is not ideal for a test to be used in primary care to rule out heart failure and further cardiological investigation. However, a Swiss study using similar cut points reported that the use of BNP testing in primary care leads to increased diagnostic certainty, less diagnostic work-up, and an accelerated initiation of appropriate treatment.[7]

An electrocardiogram (ECG) can also be used to rule out heart failure—a completely normal ECG is unlikely in a patient with heart failure (negative predictive value around 90% for systolic heart failure).[8] However, ECG abnormalities become more common with advancing age, and the ECG is therefore not useful as a "rule in" test in the target population. Some ECG abnormalities may give a clue as to the etiology of heart failure (eg, myocardial infarction, atrial fibrillation) or indications for therapy (eg, anticoagulation for atrial fibrillation, cardiac resynchronization therapy for a broad QRS complex), adding value to this test.

The current European Society of Cardiology (ESC) guidelines provide an algorithm for the diagnosis of heart failure in the "nonacute" setting (*Figure 1*).[9] The
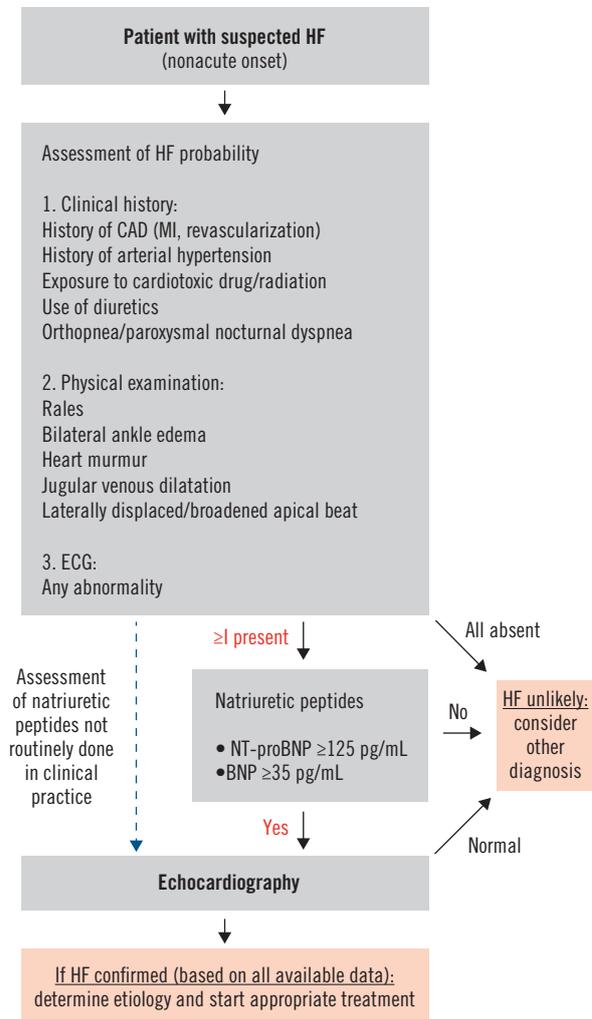

Fig. 1 *Diagnostic algorithm for heart failure in a nonacute setting recommended by the European Society of Cardiology.*
Abbreviations: *BNP, B-type natriuretic peptide; CAD, coronary artery disease; ECG, electrocardiogram; HF, heart failure; MI, myocardial infarction; NT-proBNP, N-terminal pro–B-type natriuretic peptide.*
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guidelines state that if there is nothing on clinical history, examination, or ECG to suggest heart failure, then other diagnoses should be pursued (at least initially). If there is a suggestive history, or an abnormal examination or ECG, then natriuretic peptides (NPs) should be measured "where available," and if the NT-proBNP level is greater than or equal to 125 pg/mL (or BNP ≥ 35

pg/mL), then echocardiography should be performed to confirm the clinical diagnosis of heart failure. Such imaging provides information on global and regional ventricular function, chamber volumes, wall thickness, and valve function, and can identify pulmonary hypertension.

In routine practice, general practitioners may be reluctant to rely on their own cardiovascular examination or ECG interpretation and may wish to measure plasma NPs, even when they can find no abnormality on examination. In England, NICE makes the point that echocardiographic interpretation may not be straightforward and that a general practitioner should refer for "echocardiography AND a specialist assessment."[6] This is likely to be particularly valuable for patients who have heart failure with preserved ejection fraction or due to valve disease.

The most recent North American guidelines also suggest that the NPs are useful in patients presenting with dyspnea to "support a diagnosis or exclusion of heart failure," awarding it the highest possible level of recommendation.[10] In the chronic ambulatory setting, the guideline states that NPs provide incremental diagnostic value to clinical judgment, particularly when the etiology of dyspnea is unclear. In the emergency setting, the NP value is included as a high-sensitivity "rule out" test, rather than for specificity, as there are many other causes of raised NPs. (*Table I*)

Cardiac
Heart failure, including right ventricular dysfunction
Acute coronary syndrome
Heart muscle disease, including left ventricular hypertrophy
Valvular heart disease
Pericardial disease
Atrial fibrillation
Myocarditis
Cardiac surgery
Cardioversion
Cancer chemotherapy with drugs that affect cardiac function or metabolism

Noncardiac
Advancing age
Anemia
Renal failure
Obstructive sleep apnea
Pneumonia
Pulmonary hypertension
Critical illness
Bacterial sepsis

Table I *Causes of elevated plasma natriuretic peptide concentrations.*

The acute setting

Breathlessness is a common symptom in those presenting in the emergency room or coronary care unit.

Similarly to the more chronic setting, diagnosis should be based upon a thorough history (assessing symptoms, previous cardiovascular history, and potential cardiac and noncardiac precipitants) and a physical examination, including looking for signs of congestion and/or hypoperfusion. Further information from the ECG, chest radiograph, blood work, and echocardiography can be useful. Early diagnosis is key to early treatment and better outcome.

The current ESC guidelines make several recommendations regarding diagnostic investigations in the acute setting (*Figure 2*).[9] All patients should have NPs measured on presentation to help distinguish cardiac from noncardiac causes of breathlessness. The high sensitivity of NPs is emphasized (good for a "rule out" test, with BNP <100 pg/mL or NT-proBNP <300 pg/mL making heart failure unlikely, except in some patients with end-stage decompensated heart failure, "flash" pulmonary edema, or right-sided heart failure). A recent meta-analysis suggests that at these cut points, the NPs have sensitivities of over 95% and negative predictive values of over 94%.[11] Raised levels do not necessarily confirm the diagnosis as there are many causes of elevation (*Table I*).

The guidelines state that routine hemodynamic evaluation with a pulmonary artery catheter is not indicated but may be helpful in selected unstable patients with an unknown reason for deterioration.[9] Despite much work on other biomarkers in heart failure, none other than the NPs have found their way into routine clinical practice, except for cardiac troponin, which is elevated in acute coronary syndrome but also in many patients with heart failure or pulmonary embolism.[12,13] Interestingly, and in contrast to the chronic heart failure guideline, NICE recommends the same cut points in the acute setting as the ESC guidelines.[14]

The benefit of the measurement of NPs in the diagnostic work-up of patients presenting with breathlessness in the acute setting has been further demonstrated by a shorter and less expensive inpatient length of stay in a randomized trial in Switzerland.[15]

Conclusions

Careful history taking and physical examination remain at the core of the diagnosis of heart failure, in both the acute and chronic settings. Measurement of plasma NPs provide useful rule out information: nor-

Recommendations	Class[a]	Level[b]
Upon presentation, a measurement of plasma natriuretic peptide level (BNP, NT-proBNP or MR-proANP) is recommended in all patients with acute dyspnea and suspected AHF to help in the differentiation of AHF from noncardiac causes of acute dyspnea.	I	A
At admission, in all patients presenting with AHF, the following diagnostic tests are recommended: a. 12-lead ECG; b. chest X-ray to assess signs of pulmonary congestion and detect other cardiac or noncardiac diseases that may cause or contribute to the patient's symptoms; c. the following laboratory assessments in the blood: cardiac troponins, BUN (or urea), creatinine, electrolytes (sodium, potassium), glucose, complete blood count, liver function tests, and TSH.	I I I	C C C
Echocardiography is recommended immediately in hemodynamically unstable AHF patients and within 48 hours when cardiac structure and function are either not known or may have changed since previous studies.	I	C

[a]Class of recommendation. [b]Level of evidence.

Fig. 2 *Recommendations from the European Society of Cardiology regarding applied diagnostic measurements in the acute setting.*
Abbreviations: *AHF, acute heart failure; BNP, B-type natriuretic peptide; BUN, blood urea nitrogen; ECG, electrocardiogram; MR-proANP, mid-regional pro–A-type natriuretic peptide; NT-proBNP, N-terminal pro–B-type peptide; TSH, thyroid stimulating hormone.*
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mal levels make heart failure unlikely, although there is some debate about the critical decision cut points. Raised NP concentrations should trigger a search for cardiovascular/renal pathologies, and further blood tests and echocardiography are likely to be required. The ECG should also be mandatory because it may help to rule out heart failure, provide clues as to etiology of heart failure, or may indicate key treatment choices. A chest radiograph is generally of most value to exclude other pathologies that may contribute to symptoms. Adoption of the current approach recommended in the ESC guideline is likely to improve both the accuracy and speed of diagnosis and enable early commencement of targeted therapy. ■

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