Diagnosis of heart failure

J G F Cleland

There is no doubt that many patients with clinically important ventricular dysfunction and symptoms suggestive of heart failure, such as exertional breathlessness, are not treated until overt signs of fluid retention are apparent. There is growing evidence that such patients benefit from a variety of treatments. However, a large proportion of patients who have developed signs of fluid retention or become breathless are treated with diuretics without real consideration of the underlying cause. More detailed diagnosis is required to establish that heart failure is the cause of symptoms and to ascertain the cause of heart failure itself.

The most commonly abused treatment for heart failure in the UK are the loop diuretics (4% of the population), while in Germany it is digoxin (3% of the population). It is a matter for debate which of these two treatments is most toxic when used inappropriately. The fact remains that many patients who have heart failure and who would benefit from treatment with an ACE inhibitor do not receive the most beneficial treatment. It is likely that inadequate diagnosis is a major factor in undertreatment.

The above considerations result in two “heart failure rules of halves” (fig 1). Rule 1 is that while about half of the patients with left ventricular systolic dysfunction (3–8% of the adult population) are receiving treatment for heart failure, half of them are receiving inappropriate treatment. Rule 2 is that only about half of the patients being treated for heart failure (about 3–4% of the population using prescription data) have confirmed left ventricular dysfunction, and among these patients half or less are being treated appropriately. These data highlight the ample scope for improving the diagnosis and management of heart failure.

Diagnostic process

The diagnostic process in heart failure has five components (table 1), each of which is important in determining the optimum treatment for that individual. These five components are not exhaustive; there is an added aim of predicting which patients are going to develop heart failure, which serves two purposes. First, if a patient is in a high risk group for developing heart failure then the onset of typical symptoms make a diagnosis of heart failure likely. Second, anticipating the occurrence of heart failure would allow the introduction of interventions that may help to prevent the onset of heart failure. ACE inhibitors, antihypertensive treatment, and lipid lowering agents have all been shown to reduce the risk of developing heart failure in at risk populations, and it is likely that β blockers will confer similar benefit.

Definition of heart failure

Classic definitions of heart failure based on cardiac output and filling pressures are derived from the physiology laboratory. While contributing to the understanding of heart failure they have limited practical use as, currently, only a few patients undergo haemodynamic evaluation. Furthermore, treatment to improve the haemodynamic markers of heart failure has not, so far, been shown to alter outcome. Consequently, there has been a move towards a more practical and clinically useful definition of heart failure.

A definition such as that adopted by the European Society of Cardiology (table 2) is more appropriate to clinical practice, although inevitably the clinician must still decide whether exertional breathlessness is more severe than might be expected in health, on the importance of any underlying cardiac dysfunction as a cause of symptoms, and if any response to treatment is genuine or just a placebo effect.

Ascertaining that the patient has heart failure

Table 3 summarises the studies showing the inaccuracy of a clinical diagnosis of heart failure. Diagnosis of heart failure by a non-specialist appears to be wrong in up to 50% of cases when made by clinical means alone. It is likely that the specialist would not fare much better without resort to further tests. A survey of US cardiologists indicated that they felt that they could diagnose only advanced heart
Diagnosis of heart failure

Table 1 Diagnostic aims in heart failure

<table>
<thead>
<tr>
<th>Objective</th>
<th>Symptoms of heart failure</th>
<th>Retrospective</th>
<th>Objective signs or chest radiography or echocardiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference</td>
<td>1 Echocardiography and 6 months follow up</td>
<td>Men 16.2</td>
<td>Diagnosis unlikely (%) Diagnosis probable (%)</td>
</tr>
<tr>
<td>2 Echocardiography</td>
<td>Women 47.1</td>
<td>Women 13.7*</td>
<td>Men 56.8*</td>
</tr>
<tr>
<td>3 Objective signs or chest radiography or echocardiography</td>
<td>Men 37</td>
<td>Men 63</td>
<td></td>
</tr>
<tr>
<td>4 Echocardiography</td>
<td>Women 73</td>
<td>Women 27</td>
<td></td>
</tr>
</tbody>
</table>

Numbers do not make 100% as some patients were classified as possible heart failure.

SIGNS

Although cardiologists can attain a high degree of agreement on the presence of raised jugular venous pressure, displaced apex beat, pulmonary crepitations or the presence of a third heart sound under study conditions, it is likely that interobserver agreement is lower among non-specialists and in the routine clinic setting (see table 6). Peripheral oedema, pulmonary crepitations, and tachycardia are usually absent and jugular venous pressure is often normal in well treated heart failure, even if severe. Pulmonary crepitations and ankle oedema, although common signs, are not specific to heart failure.

When several signs are present, a clinical diagnosis of heart failure may be made with some confidence. Although a clinical diagnosis reached in this way may be specific, it is likely to be insensitive, especially for patients with milder degrees of heart failure who might obtain greater benefit from treatment. The subjective component of the examination and the inability to make a permanent direct record with which to convince others who have not seen the patient, are further major weaknesses of relying on clinical features alone.

Although symptoms and signs are important, as they alert the observer to the possibility that heart failure exists, the clinical suspicion of heart failure must be confirmed by more objective tests.

HOSPITAL DIAGNOSIS

In the UK, approximately 30% of patients with heart failure are admitted to hospital within each 12 month period, and about 74% of patients with heart failure in the community at any time will have been seen by a hospital.
Table 6  Interobserver reproducibility of physical signs in heart failure19–22

<table>
<thead>
<tr>
<th>Sign</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>Peripheral oedema</td>
<td>10 to 80</td>
</tr>
<tr>
<td>Raised jugular vein pressure</td>
<td>20 to 85</td>
</tr>
<tr>
<td>Displaced apex</td>
<td>35 to 72</td>
</tr>
<tr>
<td>Murmur</td>
<td>No data</td>
</tr>
<tr>
<td>Third heart sound</td>
<td>51 to 81</td>
</tr>
<tr>
<td>Pulmonary crepitations</td>
<td>10 to 88</td>
</tr>
</tbody>
</table>

Results depend on whether cardiologists or non-cardiologists are studied. Reproducibility of all signs is < 50% when three or more observers are studied.

ELECTROCARDIOGRAPHY

A normal ECG is uncommon in patients with heart failure and, if present, it suggests that a diagnosis of heart failure should be reviewed carefully (table 7).21–23 Left and, to a lesser extent, right bundle branch block are also markers for an increased risk of ventricular dysfunction, at least in a population with coronary artery disease.24 ST segment elevation on treadmill exercise is also a marker of poor ventricular function.25 However, a recent report suggests that 8% or more of patients with heart failure may have a normal ECG.25 This area clearly requires further research before a normal ECG can be used confidently as a substitute for lack of evidence of important cardiac dysfunction on echocardiography.23

CHEST RADIOGRAPHY

There is a poor relation between heart size on x-ray and left ventricular function.26–29 The presence of cardiomegaly undoubtedly supports a diagnosis of heart failure, especially if it is associated with upper lobe venous dilatation, although the latter is a poor guide to the simultaneous pulmonary capillary wedge pressure.30–32 A normal sized heart associated with clinical evidence suggesting chronic heart failure indicates that the diagnosis should be reviewed. Interobserver agreement in the interpretation of pulmonary congestion on x-ray is only modest.33 In patients who have suffered a myocardial infarction, prediction of left ventricular ejection fraction using clinical information has so far proved to be inaccurate even when combined with ECG and chest x-ray results.31–33 However, chest radiography is useful in helping to exclude pulmonary disease as a cause for symptoms.

PULMONARY FUNCTION

Measurements of lung function are used to exclude respiratory causes of breathlessness, although the presence of pulmonary disease does not exclude co-existent heart failure. Epidemiological studies suggest that there is a strong association between chronic obstructive airways disease and ischaemic heart disease, which is one of the principal causes of heart failure.34 Pulmonary function tests may predict those at greater risk of heart failure.35–37 Peak expiratory flow rate and forced expiratory volume in one second are reduced in heart failure, but not to the same extent as in symptomatic obstructive airways disease. In patients presenting with severe breathlessness and wheeze, a peak expiratory flow rate < 200 l/min suggests a diagnosis of asthma rather than acute pulmonary oedema.40

ECHOCARDIOGRAPHY

Echocardiography should be used routinely for the optimal diagnosis of heart failure.10 The test is widely available, simple, and safe. The interpretation of echocardiographic measures of diastolic ventricular function is complex, and although no practically useful Doppler echocardiographic guidelines are yet available for diagnosing diastolic heart failure, this is an active area of research.41–42 Atrial fibrillation reduces the reliability of these measurements and, in approximately 10% of patients, adequate transthoracic echocardiographic images cannot be obtained. It is also pertinent to mention that ejection fraction is based on two rather inaccurate measurements of volume, which are prone to calculation errors. This makes the accuracy and reproducibility of this variable poor.

NUCLEAR CARDIOLOGY

Nuclear angiography provides a simple assessment of global left and right ventricular systolic function, and of myocardial perfusion.14 Images may be obtained in patients in whom echocardiography is not possible. Myocardial perfusion imaging, at rest and during or after exercise, allows the presence and extent of ischaemia to be evaluated. The disadvantages

Table 7  Relation between ECG findings and congestive heart failure

<table>
<thead>
<tr>
<th>Reference</th>
<th>Patient population</th>
<th>ECG findings</th>
<th>No CHF (%)</th>
<th>CHF/LVD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>CASS registry</td>
<td>Normal (n = 4034)</td>
<td>92</td>
<td>0.6*</td>
</tr>
<tr>
<td>22</td>
<td>Echocardiography</td>
<td>Normal (n = 275)</td>
<td>98</td>
<td>2</td>
</tr>
<tr>
<td>23</td>
<td>Referrals with CHF from community practice</td>
<td>Normal (n = 34)</td>
<td>65</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abnormal (n = 166)</td>
<td>47 (n = 16)</td>
<td>53 (n = 18)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Normal (n = 166)</td>
<td>11 (n = 19)</td>
<td>89 (n = 147)</td>
</tr>
</tbody>
</table>

*Ejection fraction < 35%.

CHF, congestive heart failure; LVD, left ventricular dysfunction.
of nuclear angiography are that it is of minimal use for the assessment of valve function, it does not measure ventricular hypertrophy, and its availability is more restricted than for echocardiography. Reproducibility of ventricular volumes is only moderate and the patient is exposed to radiation. The latter limits the frequency with which studies can be performed.

Nuclear angiography is also relatively expensive. Despite these limitations, radionuclide but not echocardiography derived ejection fraction has been shown to predict prognosis in multivariate analysis in heart failure populations.43

EXERCISE TESTING
Reduced exercise performance, when the limiting symptoms are breathlessness or fatigue, is characteristic of but not specific to heart failure. Therefore, exercise testing is of limited value in the diagnosis of heart failure in clinical practice. Accurate assessment of functional capacity requires that the patient is familiar with what is required and that the observer has the required expertise. A normal exercise test in a patient not receiving treatment for heart failure excludes heart failure as a diagnosis. Pharmacological treatment and exercise training may improve exercise performance in patients with a definite diagnosis of heart failure, but rarely restore it to normal. In patients with an established diagnosis, exercise performance is a useful way of assessing the severity of the condition and possibly of monitoring its progress.

A pronounced fall in arterial oxygen saturation during exercise usually suggests the presence of pulmonary disease,44 although small falls in arterial oxygen tension during exercise in patients with heart failure without evidence of pulmonary disease have been noted.44 45

Measurement of oxygen consumption during exercise as well as being a research tool, is a potentially useful guide to prognosis and the need for transplantation. In clinical terms it can help determine whether exercise is limited by cardiorespiratory or by other factors. However, data relating the severity of heart failure to peak exercise oxygen consumption are inadequate, especially for women. Correcting oxygen uptake for age, sex, and weight may enhance the prognostic value of the exercise test.46

CARDIAC CATHETERISATION
Invasive investigation is generally not required to establish the diagnosis of chronic heart failure but may be important in elucidating the cause. Heart failure may exist in the presence of a normal cardiac output and filling pressures at rest, at least in treated patients.14 15 Conversely, resting cardiac output may be depressed and filling pressure raised in patients with cardiac dysfunction who do not have symptoms of heart failure. Reduced cardiac output and raised pulmonary capillary wedge pressure during exercise may be caused by reversible myocardial ischaemia and are not specific to heart failure, whereas a normal haemodynamic response to maximum exercise excludes heart failure as the cause of symptoms.

Exclusion of diastolic dysfunction by non-invasive means may be difficult. Diastolic heart failure in the absence of major systolic dysfunction should generally be confirmed by invasive haemodynamic study. Invasive measurement of cardiac output and filling pressures may also be helpful in supporting or excluding heart failure in the presence of pulmonary or hepatic disease.

NEUROENDOCRINE EVALUATION
The best candidates for neuroendocrine markers for diagnostic evaluation of heart failure in individual patients are the natriuretic peptides. Atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) increase early in the course of cardiac dysfunction before the onset of symptoms. N-terminal ANP is an inactive byproduct of the ANP prohormone and its presence may reflect the presence and severity of ventricular dysfunction more accurately than ANP itself.47 48 It has the added advantages of stability, being relatively slow (several hours) to respond to physiological stimuli in vivo, and of being chemically stable in vitro.49

There is growing evidence that BNP may be an even better marker of left ventricular dysfunction than N-terminal ANP. BNP changes more rapidly than N-terminal ANP in vivo but is of similar stability in vitro.

There may be a role for natriuretic peptides not only for diagnosis but also for therapeutic monitoring as natriuretic peptides have been shown to reflect cardiac filling pressure.50 However, potential new treatments such as the neutral endopeptidase inhibitors increase plasma concentrations of ANP and BNP, which could invalidate their use for therapeutic monitoring. N-terminal ANP is not similarly affected.51

A raised plasma concentration of one of the natriuretic peptides associated with appropriate symptoms, in the absence of renal failure, strongly suggests a diagnosis of heart failure. A normal plasma concentration of natriuretic peptides in a patient receiving treatment does not necessarily refute a diagnosis of heart failure, as normal concentrations may reflect the effects of treatment.52 Plasma concentrations of natriuretic peptides increase to a modest extent with age and increase significantly in patients with renal failure. Thus natriuretic peptide concentrations should always be interpreted in conjunction with serum creatinine.

Determining the cause of heart failure
In many cases of heart failure, further investigations to disclose or confirm the underlying cause are warranted. However, many patients with heart failure are frail and elderly and this may limit therapeutic options such as surgery. If surgery or angioplasty are not options then there is little profit in undertaking coronary angiography. While investigations to determine whether heart failure is present should be a clinical routine, the investigation of the underlying cause of heart failure should be tailored to answering important questions that
will determine optimal management of individual patients.

Some diagnoses require sophisticated investigations. For example, coronary angiography is required to exclude coronary artery disease in patients with suspected dilated cardiomyopathy. Such complicated investigations are not indicated in all patients. In many cases, the optimum approach is to record the diagnosis as uncertain and then highlight the diagnostic suspicion rather than attribute the diagnosis to an aetiology without adequate evidence that may lull subsequent carers into a false sense of security.

Heart failure is the final common pathway of many diseases. Correctable causes of heart failure are rare individually but as a group contribute to a population that, considering the malignant prognosis of heart failure, is worthwhile identifying and treating. Determining the cause of heart failure is important for the selection of appropriate drug treatment. Most recent therapeutic developments, including ACE inhibitors, β blockers, and digoxin, have shown efficacy only in patients with concomitant left ventricular systolic dysfunction, the presence of which needs to be established by investigation.

**HISTORY AND EXAMINATION**

The patient’s history of disease, such as myocardial infarction, alcohol intake, and drug treatment, is of paramount importance in determining the cause of heart failure. Symptoms also establish the presence of common concomitant disease, for instance a history of intermittent claudication is probably the best available symptomatic marker for renal artery stenosis. However examination is not sensitive to determining whether the patient has heart failure, it can give valuable clues to its cause, especially valve disease, and important associated diseases.

Most patients with heart failure are over the age of 65 years and multiple co-existing degenerative diseases are commonly present that have implications for how heart failure should be managed. For example, loop diuretics may precipitate urinary retention in patients with prostatic hypertrophy. Fifty per cent of patients with intermittent claudication have renal artery stenosis; ACE inhibitors should be used with caution in such patients. Anaemia may exacerbate pre-existing heart failure. While a raised haematocrit suggests that breathlessness may be caused by pulmonary disease or cyanotic (congenital) heart disease. Measurement of serum urea or creatinine is essential for the differential diagnosis from renal failure, which may induce all the features of heart failure secondary to volume overload, and for subsequent management of heart failure.

Urine analysis is useful in detecting proteinuria and glycosuria, thereby alerting the clinician to the possibility of underlying renal problems or diabetes mellitus, conditions that may contribute to or complicate heart failure.

Heart failure due to thyrotoxicosis is frequently associated with rapid atrial fibrillation and may be the presenting feature of thyrotoxicosis in the elderly. Hypothyroidism may also present as heart failure.

**CARDIAC FUNCTION TESTS**

The ECG is crucial in confirming heart rhythm; however, ECG abnormalities in patients with heart failure often do not point to any specific underlying cause. The presence of Q waves suggest myocardial infarction but in the absence of an appropriate history this needs to be confirmed by other investigations, such as echocardiography.

The shape of the cardiac silhouette may suggest a specific diagnosis as may calcification in valves, myocardium or pericardium. However, echocardiography is required to differentiate reliably between dilatation of cardiac chambers, hypertrophy, and pericardial effusion. This technique is invaluable in assessing the integrity of the cardiac valves and gives important insights into the nature and severity of ventricular and atrial dysfunction.

Myocardial perfusion imaging at rest and during or after exercise, allows the presence and extent of ischaemia to be evaluated. Rest redistribution myocardial imaging with thallium or newer isotopes has a valuable role to play in the detection and management of a non-contracting but viable myocardium (hibernating or stunned myocardium). The full importance of detecting hibernating myocardium awaits proper documentation of its prevalence and management. No controlled trials exist to support observational experience and current opinion that such patients should be revascularised.

Provocation of angina during exercise testing is not conclusive evidence of epicardial coronary disease, but in a patient with known coronary disease it does suggest reversible ischaemia. ST segment changes are frequently difficult to interpret in patients with heart failure as the resting ECG is usually abnormal. ST segment elevation is associated with poor ventricular function. Imaging studies, most commonly and reliably by radionuclide techniques, currently offer the best method for defining ischaemia in this setting.

Haemodynamic studies are sometimes required to assess the importance of valve lesions or to assess formally systolic and diastolic function. However, their role in both settings has diminished with the development of echocardiography. Coronary angiography is required to exclude coronary disease when a diagnosis of dilated cardiomyopathy is being considered. Angiography will also be required in patients with heart failure and evidence of myocardial ischaemia if coronary revascularisation is considered a treatment option.

Endomyocardial biopsy, although a useful research tool, is of limited clinical use. In experienced hands, patients with unexplained myocardial dysfunction should be considered for biopsy to exclude infiltrative or inflammatory disease, such as amyloidosis, haemochromatosis or myocarditis.
Diagnosis of heart failure has been shown repeatedly. The ability to achieve such standards be no lower standard for diagnosis in the community. The tests summarised in table 8 are the minimum requirements expected for a hospital diagnosis of heart failure. Ideally there should be no lower standard for diagnosis in the community. The ability to achieve such standards has been shown repeatedly.

<table>
<thead>
<tr>
<th>Symptoms of heart failure</th>
<th>Normal ECG</th>
<th>Improvement of symptoms in response to treatment</th>
<th>Medical history (past and current) and examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal cardiac function (usually determined by echocardiography)</td>
<td>Cardiomegaly on chest radiography</td>
<td>Reduced exercise test duration (Lung disease)</td>
<td>Biochemistry</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Raised plasma natriuretic peptide*</td>
<td>Urine analysis</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Haematology</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Chest radiography</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pulmonary function tests (Lung disease)</td>
</tr>
</tbody>
</table>

Tests in bold are considered to be the minimum necessary for the confirmation of a diagnosis of heart failure, for an initial attempt at determining its principal cause, and for excluding additional or alternative conditions as a cause of symptoms.

**Full diagnostic potential still under review, may be normalised by treatment and is increased in old age and by renal dysfunction.**

Conclusions

The tests summarised in table 8 are the minimum requirements expected for a hospital diagnosis of heart failure. Ideally there should be no lower standard for diagnosis in the community. The ability to achieve such standards has been shown repeatedly.

### References

16. Spiteri MA, Connelly DR, Clarke SW. Reliability of eliciting diagnostic potential still under review, may be normalised by treatment and is increased in old age and by renal dysfunction.

### Table 8 A simplified plan for the diagnosis of heart failure (adapted from ESC guidelines)

<table>
<thead>
<tr>
<th>Necessary</th>
<th>Opposed</th>
<th>Supports</th>
<th>Excludes alternative and/or helps determine cause</th>
</tr>
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<tr>
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<td></td>
<td></td>
<td>Pulmonary function tests (Lung disease)</td>
</tr>
</tbody>
</table>

Lancet 1996;348:1387–88

42. Davie DP, Weston AR, Hughes JMB, et al. Effects of increased inspired oxygen concentrations on exercise per-


