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HEART FAILURE (HF) IS A COMPLEX CLINICAL SYNDROME RESULTING FROM THE IMPAIRED ability of the heart to cope with the metabolic needs of the body, resulting in breathlessness, fatigue and fluid retention. It is a progressive disease characterised by high rates of hospitalisation. The National Heart Failure Audit in England and Wales in 2012/2013 reported that 5% of all emergency hospitalisations were related to heart failure, with 11% inpatient mortality and 26% of those discharged dead within the follow-up period.3 At present HF affects nearly one million people in the UK.3,4 Studies suggest that approximately half these patients have normal, or near normal, left ventricular ejection fraction (LVEF) and are classified as heart failure with preserved ejection fraction (HFpEF).5

The prevalence of HFpEF in studies has been reported as 40-71%.1 This variation reflects both the current challenges in accurately diagnosing HFpEF and that different LVEF cutoffs (varying from > 40% to > 55%) have been used. In 2007, the average number of patients on a practice list in England was 6,487 which would equate to around 50 patients with HFpEF per practice. However, the true overall prevalence of HFpEF in the community has estimated to be higher, with each practice likely to have approximately 200 patients with HFpEF.6

PATHOPHYSIOLOGY
The exact pathophysiology of HFpEF remains uncertain although increased left ventricle passive stiffness is consistently reported.7 Patients often have overlapping comorbidities and it has only recently been convincingly demonstrated that HFpEF represents more than the sum of all its comorbidities and is a condition in its own right.9 HFpEF is likely to be caused by: diastolic dysfunction, impaired systolic function on exercise, abnormal ventricular-arterial coupling, inflammation and endothelial dysfunction, chronotropic incompetence, altered myocardial energetics and peripheral skeletal.
HFpEF was initially referred to as diastolic HF as opposed to systolic HF that corresponded with HFrEF (heart failure with reduced ejection fraction). However, diastolic dysfunction has been shown not to be unique to HFpEF. Furthermore, newer imaging techniques have confirmed that systolic function in HFpEF patients is not completely normal, with reduced long axis function and extensive but subtle changes on exercise. HFpEF is the accepted name, although preserved implies that the left ventricular ejection fraction was known previously and is unchanged, which is not always the case.\textsuperscript{10}

### RISK FACTORS

Large epidemiological studies have found that HFpEF patients are likely to be older women with a history of hypertension.\textsuperscript{5,11,12} Other cardiovascular risk factors, such as diabetes mellitus, atrial fibrillation and coronary artery disease are prevalent in the HFpEF population, see figure 1, pxx. Non-cardiovascular comorbidities, renal impairment, chronic lung disease, liver disease, hypothyroidism and anaemia, consistent with an elderly population have also been reported.\textsuperscript{13}

### PRESENTATION

Clinical symptoms and signs in HFpEF are often nonspecific although the primary symptoms of HF are breathlessness, fatigue and fluid retention.

Patients often find their exercise tolerance is limited by fatigue and breathlessness. Fluid overload can result in weight gain, peripheral oedema, or swelling of the ankles and legs, as well as abdominal congestion, resulting in impaired absorption and contributing to renal dysfunction.

Depression is common in heart failure, with a prevalence of 20-40%.\textsuperscript{14} Patients with heart failure and depression have been found to have increased morbidity and mortality with impaired quality of life, when compared with heart failure patients without depression.\textsuperscript{15,16}

The New York Heart Association (NYHA) functional classification provides an easy way to classify patients depending on their physical limitations, see table 1, above.\textsuperscript{17} Criticisms of the classification system focus on difficulties defining the difference between slight and marked limitation\textsuperscript{18} with low reproducibility values between clinicians.\textsuperscript{19} However, the NYHA classification system provides a rapid assessment of exercise capacity that is easy to communicate and has been well documented to predict prognosis.\textsuperscript{20,21}

### Table 1

<table>
<thead>
<tr>
<th>The New York Heart Association functional classification system</th>
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<td>Class</td>
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### FIGURE 2

Symptoms to consider in the medical history in a patient with suspected HFpEF
both indicate fluid overload.

Hepatomegaly and ascites indicate poor cardiac output and patient’s volume status. Cool extremities allow assessment of the pressure and the presence of peripheral oedema. Anorexia, weight loss and early satiety suggest fluid overload, whereas rapid weight gain is suggestive of fluid overload.8 Several large-scale trials have demonstrated neutral results although there were no universal entry criteria and so different populations have been studied. Recent heart failure guidelines have concluded that “no treatment has yet been shown convincingly to reduce mortality or morbidity in patients with HFrEF”.12

The medical history needs to include previous cardiac disease such as coronary artery disease and atrial fibrillation, as well as previous episodes of hospitalisation. Other cardiovascular risk factors and family history should be documented.

ASSESSMENT

Despite significant advances in medical imaging, the cornerstone in the assessment of HF remains a thorough medical history and physical examination, see figure 2, opposite. There is still no single diagnostic test for HFrEF.

The medical history needs to include previous cardiac disease such as coronary artery disease and atrial fibrillation, as well as previous episodes of hospitalisation. Other cardiovascular risk factors and family history should be documented.

‘Rapid weight gain is suggestive of fluid overload’

The duration of symptoms is relevant as are the extent of symptoms such as chest pain, breathlessness and exercise limitation. It is useful to classify patients according to the NYHA functional assessment. Rapid weight gain is suggestive of fluid overload, whereas anorexia, weight loss and early satiety suggest cardiac cachexia that is associated with an adverse prognosis.22

The physical examination needs to include the patient’s BMI and weight, heart rate and rhythm, lying and standing blood pressure and auscultation to rule out valvular disease and pulmonary congestion.

Estimating the jugular venous pressure and the presence of peripheral oedema allows assessment of the patient’s volume status. Cool extremities indicate poor cardiac output and perfusion. Hepatomegaly and ascites both indicate fluid overload.

CONFIRMING DIAGNOSIS

Recent guidelines have been published to improve the diagnosis of HFrEF, see table 2, above.12,13 Echocardiography is clearly critical in the diagnosis of HFrEF, but not all GPs have access to this and most have to refer patients to their local cardiology departments.

Before referral an ECG can be performed to check for heart rate and rhythm, as well as any suggestion of previous ischaemic disease, left ventricular hypertrophy or atrial enlargement. Blood tests for full blood count, serum electrolytes including magnesium and calcium, renal function, thyroid function, glucose, liver function, fasting lipid profile and NT-proBNP, see box 1, below, can all add important information to the early assessment of a patient with suspected HFrEF.

Patients with heart failure should be referred to heart failure nurses and have follow-up with local cardiology services, as these have both been shown to reduce mortality.2

Once the patient has been referred to cardiology, it is likely that further specialist investigations will be undertaken, such as cardiac magnetic resonance imaging, coronary angiography, computer tomography coronary angiography, exercise testing and lung function tests.

‘Anorexia, weight loss and early satiety suggest cardiac cachexia’

MANAGEMENT

Given the uncertainty in diagnoses and pathophysiology it is not surprising that there have been no evidence-based HFrEF therapies beyond treatment directed at comorbidities and diuretics for fluid overload.8 Several large-scale trials have demonstrated neutral results although there were no universal entry criteria and so different populations have been studied. Recent heart failure guidelines have concluded that “no treatment has yet been shown convincingly to reduce mortality or morbidity in patients with HFrEF”.12

The recommendations include managing breathlessness and fluid overload with diuretics, managing heart rate control and treating myocardial ischaemia and hypertension.25

Drug therapy

Loop diuretics and thiazides are effective for the rapid relief of

Box 1

NT-proBNP testing

BNP or its amino-terminal cleavage equivalent (NT-proBNP) is generated by cardiomyocytes in the context of numerous triggers, most notably myocardial stretch. Assays for both BNP and NT-proBNP are increasingly used to establish the presence and severity of HF. Either can be used in patient care settings as long as their respective absolute values are not used interchangeably.1 The value of natriuretic peptide testing is particularly significant when the aetiology of dyspnoea is unclear, and if BNP is normal it is unlikely that the patient has heart failure.

Patients with HFrEF have lower levels of BNP than HFrEF patients. However, for a given BNP level, the prognosis (risk of all-cause mortality and HF hospitalisation) is similar in both HFrEF and HFrEF patients.2

LONG-TERM OUTCOMES

Studies suggest that the mortality rate in HFrEF patients is substantial ranging from 10 to 30%, with higher rates in epidemiological studies than clinical trials.24 Mortality rates are clearly higher than controls matched for age and comorbidities25 and may be as high as mortality rates in HFrEF.33 In clinical trials, sudden death and HF death are the leading causes of cardiovascular death.26 Survival has improved in HFrEF over the past 10 to 20 years although no change has been observed for HFrEF patients.

Table 2

<table>
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<tr>
<th>Diagnostic criteria in HFrEF</th>
<th>American College of Cardiology/ American Heart Association, 2013 1</th>
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<tr>
<td>1 Symptoms and signs typical of heart failure</td>
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<tr>
<td>2 Normal, or only mildly reduced LVEF</td>
<td>2 Normal LVEF</td>
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<tr>
<td>3 Relevant structural heart disease left ventricular hypertrophy, atrial enlargement</td>
<td>3 No significant valvular abnormalities on echocardiography</td>
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<td>4 ± diastolic dysfunction</td>
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Heart failure affects nearly one million people in the UK, half of these patients have normal, or near normal left ventricular ejection fraction and are classified as heart failure with preserved ejection fraction (HFpEF).

Newer imaging techniques have confirmed that systolic function in HFpEF patients is not completely normal, with reduced long axis function and extensive but subtle changes on exercise. Patients are likely to be older women with a history of hypertension. Other cardiovascular risk factors, such as diabetes mellitus, atrial fibrillation and coronary artery disease are prevalent in the HFpEF population.

Clinical symptoms and signs in HFpEF are often nonspecific although the primary symptoms are breathlessness, fatigue and fluid retention. Fluid overload should be assessed as these have both been shown to reduce mortality. Breathlessness and fluid overload should be managed with diuretics, heart rate controlled and treating depression is important in these patients.

There is still no single diagnostic test for HFpEF and the cornerstone in the assessment remains a thorough medical history and physical examination. The duration and extent of the symptoms are relevant and it is useful to classify patients according to the NYHA functional assessment. Rapid weight gain is suggestive of fluid overload, whereas anorexia, weight loss and early satiety suggest cardiac cachexia that is associated with an adverse prognosis.

Physical examination should include the patient’s BMI and weight, heart rate and rhythm, lying and standing blood pressure and auscultation to rule out valvular disease and pulmonary congestion. Estimating the jugular venous pressure and the presence of peripheral oedema allows assessment of the patient’s volume status.

Patients with heart failure should be referred to heart failure nurses and have follow-up with local cardiology services. As these have both been shown to reduce mortality. Breathlessness and fluid overload should be managed with diuretics, heart rate controlled and myocardial ischemia and hypertension treated. Loop diuretics and thiazides are effective for the rapid relief of symptoms and may improve quality of life, although they do not reduce morbidity or mortality. There is some evidence that thiazide diuretics may reduce morbidity and mortality in older hypertensive patients.

‘Loop diuretics and thiazides are effective for the rapid relief of symptoms’

CONCLUSION

The prevalence of HF is expected to increase by 25% by 2030 and approximately half of all HF patients have HFpEF. HFpEF represents a collection of different conditions and current imaging and physiological research is seeking to understand this better and improve characterization. Symptoms and signs of heart failure are central to the diagnosis of HFpEF. Currently no treatments have convincingly been shown to reduce mortality or morbidity in these patients with comparable outcome data to HFpEF.

Improved characterisation of HFpEF will enable future trials to define inclusion criteria, ensuring that similar patients are being studied.

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