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Management of heart failure with preserved ejection fraction

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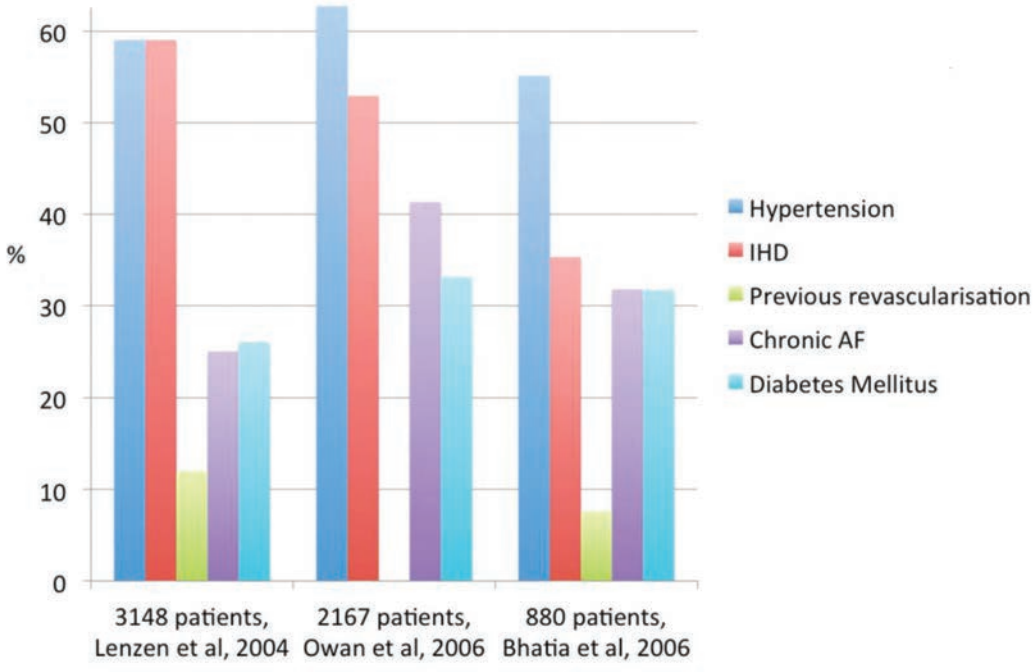


FIGURE 1
Risk factors in three HFpEF studies involving 6,195 patients[12,5,11]

What are the risk factors for HFpEF?

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]

How should diagnosis be confirmed?

The prevalence of HFpEF in HF 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 over 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 been estimated to be higher, so each practice could have up to 200 patients with HFpEF.[6] This means it is important for all clinicians to consider HFpEF when seeing patients with signs and symptoms of heart failure.[6]

'Patients with heart failure and depression have increased morbidity and mortality'

What are the management approaches?

PATHOPHYSIOLOGY

The exact pathophysiology of HFpEF remains uncertain although increased left ventricle passive stiffness is consistently reported.[7,8] 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 »

Table 1

The New York Heart Association functional classification system

Class	NYHA functional classification
I	Patients have cardiac disease but without limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnoea
II	Patients have cardiac disease resulting in slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnoea
III	Patients have cardiac disease resulting in marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation, or dyspnoea
IV	Patients have cardiac disease resulting in inability to carry out any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases

energetics and peripheral skeletal muscle metabolism and perfusion, pulmonary hypertension and renal insufficiency.[8]

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.[10]

RISK FACTORS

Large epidemiological studies have found that HFpEF patients are likely to be older women with a history of hypertension.[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, p21.

Non-cardiovascular comorbidities, renal impairment, chronic lung disease, liver disease, hypothyroidism and anaemia, consistent with an elderly population have also been reported.[13]

PRESENTATION

Clinical symptoms and signs in HFpEF are often nonspecific although the primary symptoms of HF are fatigue, breathlessness 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 also renal dysfunction.

Depression is common in heart failure, with a prevalence of 20-40%.[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.[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.[17] Criticisms of the classification system focus on difficulties defining the difference between slight and marked limitation[18] with low reproducibility values between clinicians.[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.[20, 21]

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, below. There is still no single diagnostic test for HFpEF.

The medical history needs to include

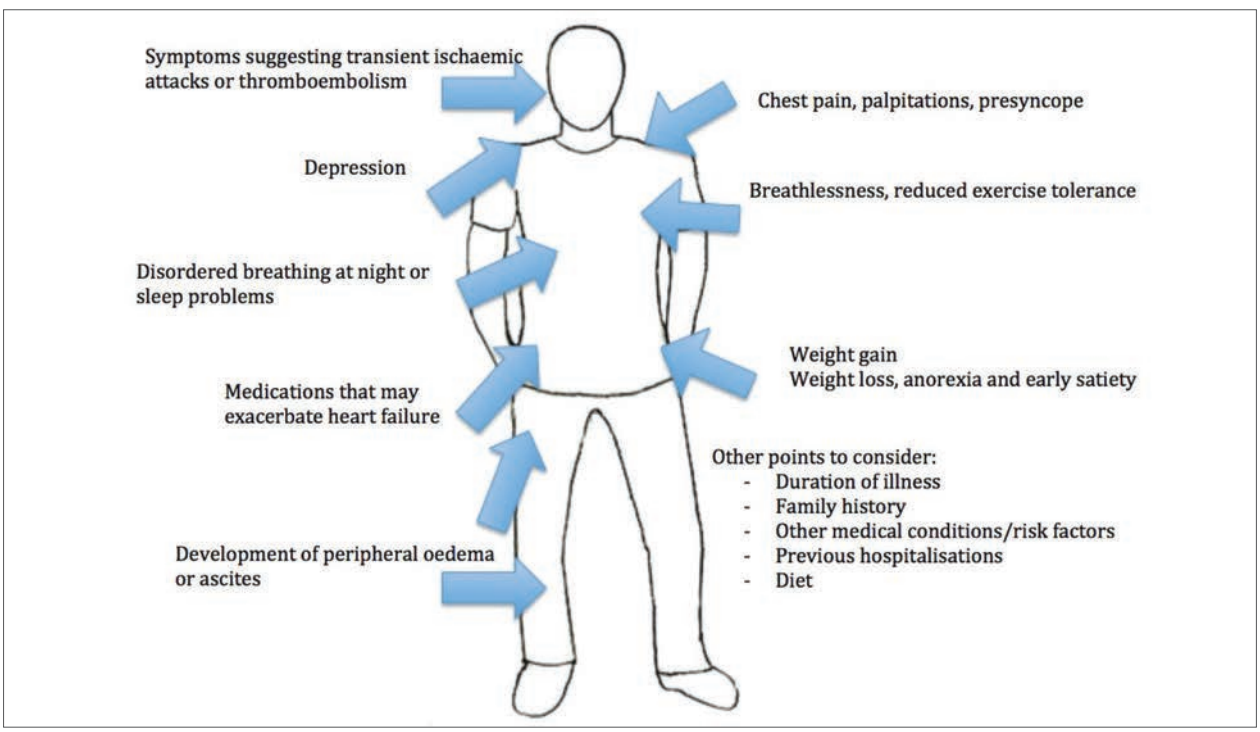


FIGURE 2
Symptoms to consider in the medical history in a patient with suspected HFpEF

Table 2

Diagnostic criteria in HFpEF

European Society of Cardiology, 2012[23]	American College of Cardiology/ American Heart Association, 2013[1]
1 Symptoms and signs typical of heart failure **2** Normal, or only mildly reduced LVEF **3** Relevant structural heart disease left ventricular hypertrophy, atrial enlargement **4** ± diastolic dysfunction	**1** Symptoms and signs typical of heart failure **2** Normal LVEF **3** No significant valvular abnormalities on echocardiography

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.

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]

'Rapid weight gain is suggestive of fluid overload'

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 HFpEF, see table 2, above.[1,23] Echocardiography is clearly critical in the diagnosis of HFpEF, but not all GPs have access to this and most have to refer patients to their local cardiology department.

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 HFpEF.

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.[3]

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.

LONG-TERM OUTCOMES

Studies suggest that the mortality rate in HFpEF 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 comorbidities[25] and may be as high as mortality rates in HFrEF.[5,11] 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 HFpEF patients.

MANAGEMENT

Given the uncertainty in diagnoses and pathophysiology it is not surprising that there have been no evidence-based HFpEF 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 HFpEF'.

'Anorexia, weight loss and early satiety suggest cardiac cachexia'

The recommendations include managing breathlessness and fluid overload with diuretics, managing heart rate control and treating myocardial ischaemia and hypertension.[23]

Drug therapy

Loop diuretics and thiazides are effective for the rapid relief of symptoms and may improve quality of life, although do not reduce morbidity or mortality.[27] There is some evidence that thiazide diuretics may reduce morbidity and mortality in older hypertensive patients.[28,29] There is no such evidence for loop diuretics. Identifying and treating depression is important in these patients. »

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 heart failure. 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 HFpEF have lower levels of BNP than HFrEF patients. However, for a given BNP level, the prognosis (risk of all-cause mortality and heart failure hospitalisation) is similar in both HFpEF and HFrEF patients.[2]

key points

SELECTED BY
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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 can result in weight gain, peripheral oedema, or swelling of the ankles and legs, as well as abdominal congestion.

Depression is common in heart failure, with a prevalence of 20-40%. 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. Identifying 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 ischaemia 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.

We welcome your feedback

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CONCLUSION

The prevalence of HF is expected to increase by 25% by 2030[30] 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 characterisation.

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

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 HFrEF.

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

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