# Guidelines for management of Heart Failure patients with preserved Ejection Fraction (HFpEF)

*(This document may be of interest to patients and carers, but is intended for Primary Care Drs, Nurses and Pharmacists)*

## Introduction

Approximately 50% of patients with the clinical syndrome of heart failure have normal (>50% - Heart failure with preserved ejection fraction - HFpEF) or mildly reduced ejection fraction (40-50% - Heart failure with mid-range ejection fraction – HFmrEF). These patients have similar symptoms and prognosis as patients with Heart failure with reduced ejection fraction (HRrEF), but their treatment options are different and much more limited. HFmrEF and HFpEF are both life-limiting conditions.

## Investigations

Symptoms consistent with heart failure are unexplained breathlessness (particularly orthopnoea and paroxysmal nocturnal dyspnoea), oedema (including ascites and pleural effusion) and cachexia. Breathlessness is very common and the most common cause is deconditioning, i.e. being unfit owing to lack of exercise.

NICE guidance recommends considering an alternate cause of symptoms if NT-proBNP is less than 400 pg/ml, referring for routine Echocardiogram (within 6 weeks) if NT-proBNP is 400-2000 pg/ml and referring for urgent Echocardiogram (within 2 weeks) if NT-proBNP >2000 pg/ml. A treatment plan will be provided after the Echocardiogram and selected patients will be offered a Cardiology appointment (Hospital or Community Heart Failure Service).

All patients should have a 12 –lead ECG and standard blood tests (FBC, U&E, TSH, Liver function, Calcium, Glucose, HBA1C, Random lipid profile).

If HFpEF is confirmed then urinary Bence Jones protein and serum electrophoresis should be performed to assess for AL amyloid.

## Diagnosis

HFpEF is difficult to diagnose and is prone to over and under diagnosis. The main symptom is breathlessness, but this is non-specific as 50% of people over the age of 80 report breathlessness as a symptom. Symptoms are not reliable in making a diagnosis. Diagnosis is based on at least 3 of the following groups of features:

1. Clinical evidence of fluid overload:
    a. pitting oedema, ascites
    b. raised jugulovenous pulse
    c. pleural effusions
    d. pulmonary oedema)

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2. Cardiac investigations showing cardiac insufficiency:
   a. Moderate to severe valve dysfunction on echo
   b. Arrhythmia (atrial fibrillation or atrial flutter)
   c. Severe coronary artery disease
   d. Definite diastolic dysfunction confirmed by a Cardiologist (diastolic indices vary with age and many echocardiograms report diastolic variants that are normal for age)
   e. Right ventricular impairment and/or pulmonary hypertension

3. Elevated NT-BNP level (>2000 pg/ml or >4000 pg/ml if over 90 years old)

4. Response to treatment i.e. there should be at least a short-term improvement with diuretic treatment. If a patient doesn't respond to treatment then consider whether diuretic dose is sufficient or if diagnosis is correct

Mild anaemia, deconditioning, lung disease, renal failure, musculoskeletal disorders, liver cirrhosis, dependent oedema, drug side-effects, ischaemic heart disease and anxiety can masquerade as HFpEF and often co-exist with HFpEF. Common drug side-effects include oedema from calcium channel blockers and nonsteroidal anti-inflammatory drugs, excessive rate control of atrial arrhythmias and excessive control of hypertension.

Patients with valve disorders, coronary disease or arrhythmias that cannot be corrected or are not worth correcting because of low probability that correction will improve quality or duration of life, are often classified as HFpEF.

**Treatment**

Many trials have been carried out with medication used for heart failure with reduced ejection fraction and only Empagliflozin has been shown to reduce cardiovascular hospitalisation and death. The mainstay of treatment is holistic care of the patient, fluid management, rate control of arrhythmias and blood pressure control. Once the diagnosis is confirmed echocardiographic surveillance is usually not required (see 'Surveillance').

- Holistic care involves optimal treatment of all the related and unrelated comorbidities associated with HFpEF. Recognition of when treatment is not working is important. The hallmarks are oedema refractory to treatment, hypotension and declining renal function. Reversible causes should be sought, but if none are found then early discussion of end-of-life planning and referral to Palliative and Supportive Services is recommended.

- Fluid management is used to control oedema, ascites, pleural effusions and pulmonary oedema. Diuretic treatment without evidence of fluid overload clinically or on chest X ray is usually unsuccessful.

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Strategies to treat and prevent fluid overload are:

- Fluid restriction to 1.5l/day, but with leniency as quality of life is our main aim
- Loop diuretics:
  - Furosemide 20mg – 160mg/day
  - Bumetanide 1-6mg/day
- Mineralocorticoid antagonists (MRA). Very useful for right heart failure, ascites and when loop diuretics cause low potassium:
  - Spironolactone 12.5mg – 200mg/day
  - Eplerenone 12.5-50mg/day
- Thiazide diuretics
  - Bendroflumethiazide 2.5-10mg/day
  - Indapamide 2.5mg/day
- Potassium sparing diuretics used when MRAs are not tolerated
  - Amiloride 2.5-10mg/day

Empagliflozin 10mg OD (sodium glucose cotransporter 2 inhibitor or SGLT2I) is not yet NICE approved, but is likely to have similar guidance to the Area Prescribing Committee (APC) guidance for Dapagliflozin (the Dapagliflozin trial DELIVER has not completed). 'The heart failure specialist should prescribe the Dapagliflozin/ Empagliflozin for at least 1 month. Ensuring that the patient's heart failure is stable (particularly in relation to eGFR) and the patient is benefitting from treatment before transfer of care to the primary care prescriber.'

- Liver disease or eGFR < 20 ml/min are contraindications to SGLT2I for patients with heart failure
- There is a diuretic and hypoglycaemic effect so consider reducing diuretic and/or diabetes medication before starting SGLT2I.

Monitoring or renal function is important especially after changes in treatment. A degree of renal impairment should be accepted provided eGFR is stable >30ml/min and the patient is not overdiuresed i.e. no oedema and hypotensive.

- Renal function should be measured 2-4 weeks after any change in medication and then again at 3 months
- Patients should be assessed after dose changes and hospitalisation to prevent overdiuresis
- If treatment is stable and eGFR >30 then check U&E 6 monthly otherwise 3 monthly
- Some patients with cardiorenal and renocardiac failure will have a treatment plan based on lower eGFR as advised by Cardiologist or Nephrologist
- Arrhythmia control
  - AF rate control should be 60-100/min. Rate control is only needed if rate >100/min at rest.

- Betablockers are preferable to calcium channel blockers
- If patient is too hypotensive (Systolic < 110) to tolerate betablockers or calcium channel blockers then use digoxin
- Blood pressure control. High blood pressure promotes diastolic dysfunction and low blood pressure reduces renal perfusion. Systolic BP 110-150 is acceptable.
- ACE Inhibitors and ARBs can be used for BP control, but can cause renal impairment and have no prognostic benefit with HFpEF
- Most patients who are adequately diuresed do not need additional antihypertensives
- Calcium channel blockers cause oedema especially at higher doses

## Guidelines for management of Heart Failure patients with mildly reduced (HFmrEF)

HFmrEF is a recent classification for patients who may have some prognostic benefit from disease modifying treatments such as ACE Inhibitors, Sacubutril-Valsartan and betablockers and MRAs even though trial evidence is not definitive. The SGLT2I, Empagliflozin is effective treatment for HFmrEF.

### Diagnosis

Patients have ejection fraction 40-49% combined with another cardiac abnormality such as moderate valve dysfunction, arrhythmia or ischaemic heart disease.

### Treatment

Treatment is a composite of HFpEF and HFrEF (Heart failure with reduced ejection fraction) treatment. ACE Inhibitors and betablockers should be used if possible (as described in NICE Guidance for HFrEF), but one often has to accept doses lower than target because of hypotension and renal impairment. Sacubutril-Valsartan may be used for HFmrEF especially when hypertension is the cause, but should be initiated by a Heart Failure Specialist as per the Shared Care protocol.

Evidence from the Ashford and St Peter's Heart Failure Cohort Study shows the same poor prognosis for this group as for HFrEF and HFpEF and so holistic care as described above is important.

### Surveillance tests for HFpEF and HFmrEF

- Patients with valve disease who may be suitable for valve intervention in the future should have echocardiographic surveillance. This depends on the type of valve problem and the patient's functional status.
  - Aortic stenosis that is moderate usually will be monitored yearly
  - A Cardiologist should advise if moderate or severe mitral regurgitation should be monitored based on whether the patient will tolerate and benefit from valve intervention
  - Tricuspid regurgitation is usually not monitored

  - Patients whose frailty precludes invasive intervention do not require valve monitoring
- ECG should be performed if there is marked clinical deterioration
  - Treat any new arrhythmia. AF should be treated in Primary Care with rate control and anticoagulation. Bradycardias and ventricular arrhythmias should be referred to Arrhythmia service.
  - Refer for echo if develops new bundle branch block
- Renal function monitoring is as for HFpEF
- NT-proBNP is useful for diagnostic screening, but not recommended for routine monitoring once a diagnosis is made.

**Renocardiac failure and liver cirrhosis**

Advanced renal failure causing fluid overload owing to inability to excrete fluid mimics HFpEF and less often HFmrEF. The hallmark is renal dysfunction and symptoms out of keeping with mild abnormalities of cardiac function. NT-proBNP is usually very high and not useful for distinguishing renal from cardiac failure. It is incorrect to classify this as Heart Failure although treatment can be similar for patients with renal failure who decide against renal replacement treatment.

Liver cirrhosis predominantly causes ascites, but can cause peripheral oedema and pleural effusions. NT-proBNP is not useful in distinguishing from heart failure, but liver imaging and liver function tests are useful. Treatment is managed by Gastroenterologists/Hepatologists, but generally higher doses of Spironolactone are used.

If the patient remains symptomatic despite optimal medical therapy, please refer for Specialist HF Nurse assessment (csh.spareferrals@nhs.net) or Cardiology Department, Ashford and St Peter's NHS Foundation Trust


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| Dr Ian Beeton<br>Cardiologist<br><br>ASPH | Sister Deborah McCarthy<br>Community Heart Failure Specialist Nurse<br>CSH Northwest Surrey | Sister Tracey Bradshaw<br>Acute Heart Failure Specialist Nurse<br>ASPH |


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