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OVERVIEW OF HEART FAILURE

- **Heart failure is associated with significant morbidity and mortality; the prevalence is increasing**
- **Measures to prevent heart failure are an important consideration to reduce morbidity and mortality**
- **The symptoms of heart failure may be difficult to distinguish from symptoms of other conditions, which may also co-exist with heart failure**
- **Patients with elevated natriuretic peptides require echocardiography to confirm a diagnosis of heart failure**

INTRODUCTION

Heart failure (HF) is a clinical syndrome, caused by cardiac dysfunction, which is characterised by signs and symptoms (e.g. dyspnoea, oedema and fatigue).[1] It is a global pandemic affecting approximately 23 million people.[2] **HF occurs in up to 2% of the adult population in developed countries, rising to ≥10% in those aged >70 years.**[3-5] The prevalence of HF has increased in the last 20 years, due in part to an ageing population, improved survival following coronary events, increased prevalence of risk factors (e.g. hypertension, diabetes and atrial fibrillation [AF]) and prolonged survival of patients with HF on effective therapy.[4,6]

HF is associated with significant morbidity and mortality resulting in increased risk of hospitalisation and significant reduction of all aspects of quality of life (QoL);[7-9] it is also a financial burden for healthcare systems.[7] **HF is the most common cardiovascular reason for hospitalisation for people >60 years of age**;[6] in Ireland there are approximately 5,800 hospital admissions with HF annually.[5] There have been modest improvements in mortality for people with HF over the last 20 years, however the 5-year survival rate is close to 50%.[2,4,8,10,11] The diagnosis of HF can be challenging, as it frequently co-exists with other conditions (e.g. the prevalence of undiagnosed HF in patients ≥65 years with concomitant chronic obstructive pulmonary disease [COPD] is 20%).[12] Factors associated with an increased risk of morbidity and mortality include older age, female sex, co-morbidities, increased severity of HF and poor socioeconomic status.[2,8-10]

Patients with established HF tend to gradually deteriorate over time.[1,5] Timely diagnosis of HF is important in order to optimise evidence-based therapies, to reduce mortality and to improve outcomes.[1,11] This, the first of two bulletins, will give an overview of HF including the diagnosis and management. The second bulletin will focus on the pharmacological management of chronic HF.

CLASSIFICATION

There are a number of ways to classify HF. The 2016 European Society of Cardiology (ESC) guideline classifies HF into three categories based on the left ventricular ejection fraction (LVEF) following echocardiography; HF with reduced EF (HFrEF), HF with preserved EF (HFpEF) and HF with mid-range EF (HFmrEF) (table 1).[3] **It is important to distinguish between the different types of HF; current pharmacological therapies have a strong evidence base for patients with HFrEF, but not for those with HFpEF.**[3,13]

Table 1: European Society of Cardiology heart failure categories[3]

Category of HF	Abbreviation	Left ventricular EF %	Additional criteria to meet diagnosis
Heart failure with reduced EF (also known as systolic heart failure)	HFrEF	<40	Symptoms +/- signs*
Heart failure with mid-range EF	HFmrEF	40-49	Symptoms +/- signs* ↑ levels of NPs and either relevant structural heart disease (LVH +/- LAE) or diastolic dysfunction
Heart failure with preserved EF (also known as diastolic heart failure)	HFpEF	≥50	Symptoms +/- signs* ↑ levels of NPs and either relevant structural heart disease (LVH +/- LAE) or diastolic dysfunction

EF – ejection fraction; NP – natriuretic peptides; LVH – left ventricular hypertrophy; LAE – left atrial enlargement
*signs may not be present in the early stages of HF and in patients treated with diuretics

HF can also be classified by the time course of the development of symptoms.[14] **Acute HF** (AHF) refers to the rapid onset or worsening of symptoms and/or signs of HF; it typically requires hospitalisation.[13,14] AHF may be precipitated

by events such as the onset of an arrhythmia, acute myocardial dysfunction (e.g. ischaemic, inflammatory, or toxic), acute valvular insufficiency or pericardial tamponade.[14] **Chronic HF** is a longer term syndrome, which is described as "stable" if the patient's condition has not deteriorated requiring hospital admission within the previous year.[5] A patient with stable chronic HF may deteriorate slowly or suddenly; the latter is described as "**acute decompensated HF**".[3,15] The New York Heart Association (NYHA) classifies HF according to a patient's symptoms (table 2).

Table 2: New York Heart Association (NYHA) classification of heart failure[16]

Class	Patient Symptoms
I	No limitation of physical activity: no symptoms*
II	Slight limitation of physical activity: comfortable at rest but ordinary physical activity causes symptoms*
III	Marked limitation of physical activity: comfortable at rest but less than ordinary activity causes symptoms*
IV	Breathless at rest: unable to carry out any physical activity without discomfort

* symptoms = undue breathlessness, palpitations or fatigue

AETIOLOGY AND PATHOPHYSIOLOGY

HF is caused by structural and/or functional cardiac abnormalities that result in a reduced cardiac output and/or elevated intra-cardiac pressure.[3,13,17] HF may occur due to: 1) a diseased myocardium (e.g. ischaemic heart disease [IHD], toxic damage, immune mediated and inflammatory damage, infiltration, metabolic derangements and genetic abnormalities), 2) abnormal loading conditions (e.g. hypertension, valve and myocardial structural defects, pericardial and endomyocardial defects) and 3) arrhythmias.[3,14] **The most common causes of HF are IHD, hypertension and diabetes.[18]** HFrEF and HFpEF seem to have different epidemiological and aetiological profiles, however the symptoms are similar; all-cause mortality is generally higher in patients with HFrEF than those with HFpEF.[3,6]

Patients with HFrEF have an underlying condition (e.g. myocardial infarction, cardiomyopathy or valve disease) that affects ventricular contraction and ejection.[6,14,18] This results in cardiac enlargement leading to weak contraction, elevated filling pressures and increased peripheral resistance, resulting in an inadequate cardiac output.[14]

Patients with HFpEF have impaired relaxation and ventricular filling during diastole, however left ventricular systolic function is relatively preserved.[14,18] Patients tend to be older, female sex, and have more co-morbidities (e.g. hypertension, diabetes, AF, anaemia, obesity and COPD) than patients with HFrEF.[3,6,19] HFpEF occurs in approximately 50% of patients with HF.[3,6,19] The causes of death and hospitalisation in patients with HFpEF are more likely to be non-cardiovascular than in those with HFrEF.[3]

Compensatory mechanisms occur in patients that develop HF, in an attempt to maintain tissue perfusion.[18] This includes neurohormonal activation with activation of the sympathetic nervous system and the renin-angiotensin-aldosterone system (RAAS), resulting in enhanced cardiac contractility, sodium and fluid retention and peripheral vasoconstriction.[17,18] **While initially beneficial, over time these compensatory mechanisms lead to progressive ventricular remodelling, resulting in worsening HF.[17,18]** Ventricular distension results in the release of natriuretic peptides (NPs), (including B-type NP [BNP] and N-terminal proBNP [NT-proBNP]), which partially counteract RAAS, and stimulate vasodilatation and natriuresis.[14,17,18] **Elevated BNP is thought to be one of the first signs of HF;** it is useful in the diagnosis or exclusion of HF, and in the assessment of HF severity.[14,18,20,21] **There is an emerging role for the use of NPs to target individuals who would benefit most from HF prevention strategies.[22-24]**

HEART FAILURE PREVENTION

The prevention of HF is an important aspect to consider in order to reduce morbidity and mortality from HF.[3,6] HF can be delayed or prevented by modifying risk factors for cardiovascular disease (CVD).[3,25] **Adherence to healthy lifestyle factors such as no smoking, regular exercise, healthy weight, moderate alcohol intake and healthy diet is associated with a lower risk of developing HF.[6,25]** The initiation of, or an increase in physical activity, even in late middle age, has been shown to lower HF risk.[6]

Patients with established CVD should be appropriately treated to potentially prevent future HF events.[3,25] For example, **reducing BP decreases the risk of HF by as much as 40%.[3,6]** Initiation of an angiotensin-converting enzyme inhibitor (ACEI), a beta blocker, a mineralocorticoid receptor antagonist (MRA) and a statin following a myocardial infarction, especially when it is associated with LV systolic dysfunction, reduces the risk of hospitalisation for HF and mortality.[3,6] Type 2 diabetes mellitus (T2DM) is a risk factor for the development of HF.[6,25] Recently, sodium-glucose co-transporter-2 (SGLT2) inhibitors (e.g. empagliflozin, canagliflozin and dapagliflozin) have been shown to improve outcomes (including reduced HF hospitalisations and mortality) in T2DM patients;[3,6,26] **it is recommended that SGLT2 inhibitors should be considered for T2DM patients with established CVD or at high CV risk for the prevention of HF related outcomes.[21,25]** Recent evidence suggests that SGLT2 inhibitors may reduce hospitalisations and death in patients with HFrEF without diabetes, however further research is required.[27]

DIAGNOSIS

A thorough clinical history and physical examination is required in patients with symptoms and signs of HF (table 3), especially those with risk factors including coronary artery disease and hypertension.[3] The symptoms of HF may be difficult to differentiate between HF and other conditions (e.g. pulmonary disease), which may also co-exist with HF.[3,12]

Table 3: Symptoms and signs typical of HF[3]

Symptoms of heart failure	Signs of heart failure
Typical symptoms include: • Breathlessness, orthopnoea, paroxysmal nocturnal dyspnoea, reduced exercise tolerance, fatigue, tiredness, increased time to recover after exercise and ankle swelling	More specific signs include: • elevated jugular venous pressure, hepatojugular reflux, third heart sound and laterally displaced apical impulse
Less typical symptoms include: • nocturnal cough, wheezing, bloated feeling, loss of appetite, confusion (especially the elderly), depression, palpitations, dizziness and syncope	Less specific signs include: • weight gain, weight loss (in advanced heart failure), tissue wasting, cardiac murmur, peripheral oedema, pulmonary crepitations, reduced air entry and dullness at lung bases and tachycardia

It is important to consider the patient's 1) history, 2) physical examination and 3) ECG in those presenting with suspected HF (table 4).[13] **If these three factors are normal, HF is highly unlikely and an alternative diagnosis should be considered.[3,13]** If at least one factor is abnormal, NPs such as BNP or NT-proBNP should be measured to identify patients who need echocardiography, to confirm a diagnosis of HF.[3,13,22] If NPs are not available and there is a high index of suspicion that HF is present, a trial of therapy with loop diuretics and management of any other CV risk factors is appropriate while awaiting assessment.[13] Measurement of NPs should also be considered in patients presenting with symptoms suggestive of worsening HF.[22]

Table 4: Diagnostic algorithm for non-acute heart failure[3,13]

Patient with suspected heart failure (non-acute onset)

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Assessment of probability includes:

1. History
   - history of ischaemic heart disease
   - history of hypertension or diabetes
   - exposure to cardiotoxic drugs/radiation
   - use of diuretics
   - orthopnoea/paroxysmal nocturnal dyspnoea
2. Physical examination
   - pulmonary crepitations
   - bilateral ankle oedema
   - heart murmur
   - elevated jugular venous pressure
   - displaced apex beat
3. ECG
   - any abnormality

↓

if there is ≥ one of the above present assess natriuretic peptides if available

Guidelines recommend different thresholds of NPs at which HF is considered unlikely in the non-acute setting; for example the ESC recommends a threshold of NT-proBNP <125pg/ml (sensitivity of 94%), while the UK National Institute for Health and Care Excellence (NICE) recommends a NT-proBNP level of <400pg/ml (sensitivity of 75%).[3,15,28] NP measurements should always be used in conjunction with all other clinical information.[22] **The higher the level of NP, the higher the likelihood that the patient's symptoms are caused by HF.[22]** Elevated NPs will not confirm a HF diagnosis**,** as NPs may also be elevated in patients with increasing age, AF, pulmonary disease, sepsis and renal failure.[3,25] Factors associated with reduced NP levels include obesity, African or African-Caribbean origin, or treatment with therapies including diuretics, beta blockers and RAAS inhibitors.[3,15,20,25] **Patients with elevated NPs above the specified threshold require echocardiography to confirm a diagnosis of HF**; this gives information on chamber volumes, ventricular systolic and diastolic function, wall thickness, valve function and pulmonary hypertension.[3,10] **It is important to identify the underlying cardiac cause of HF as this determines the treatment for the individual patient** (e.g. specific pharmacological therapy for HFrEF and valve repair for valve disease).[3] Other investigations that should also be considered to evaluate possible aggravating factors and/or alternative diagnoses include chest x-ray(CXR), renal, hepatic and thyroid function, cholesterol, full blood count, HbA1c, urinalysis, peak flow or spirometry.[15,10,25] Other investigations that may also be useful include coronary angiography and cardiopulmonary exercise testing.[1]

MANAGEMENT

The goals of management of a patient with HF are to 1) improve the patient's clinical status, functional capacity and QOL, 2) prevent hospitalisation and 3) reduce mortality.[3]

Patients with HF should have a treatment plan, and their management should be a shared responsibility between healthcare professionals (HCPs), the patients and/or their carers.[13,29] **A shared and effective multidisciplinary team of HCPs including a hospital specialist, GP, HF nurse, practice nurse, pharmacist and dietician is essential in the management of HF.[10,15,29]** Stable HF patients can be cared for in primary care with ready access to specialist and multidisciplinary team (MDT) services, thereby reducing the risk of hospitalisation.[5,10,15] GPs play a key role in the diagnosis, long-term management of patients with stable HF, onward referral to specialist services for unstable patients and end-of-life care for patients with HF.[5,10]

A Heart Failure Model of Care was developed by the National Clinical Programme for HF in 2012,[29] which led to the establishment of programmes including hospital HF programmes, General Practice Virtual Consultation Services

(between GPs and cardiologists) for HF patients, a prevention programme for HF and a community diagnostic clinic.[30-33] Further details are available on www.hse.ie/eng/about/who/cspd/ncps/heart-failure/.

NON-PHARMACOLOGICAL MANAGEMENT

Non-pharmacological management is an essential strategy for all patients with HF. Lifestyle modifications such as smoking cessation, avoidance of excessive alcohol, weight loss and exercise are recommended.[1,12,13,17,25,34] Immunisation against influenza and pneumococcus is also advised.[1,12,13,17,34] Salt rich foods should be avoided, however salt restriction has not been shown to improve outcomes.[1]

Patients and their carers should be given access to support programmes to enable them to increase their knowledge and skills in improving their self-care.[13] Improved self-care has been associated with improved outcomes in HF.[13] Early patient recognition of changes in signs and symptoms (e.g. reduced exercise tolerance, shortness of breath and weight gain), with the patient taking appropriate action (e.g. taking an extra diuretic dose or contacting their HCP), have shown benefit in those with HF.[13] **The website heartfailurematters.org is a useful resource on HF for patients and their carers**.[13]

PHARMACOLOGICAL MANAGEMENT

The pharmacological management of chronic HF will be covered in the next bulletin(NMIC 2019, Volume 25, No. 6).

ACUTE HEART FAILURE

Acute heart failure (AHF) may occur as a new onset of HF or as an acute decompensation of chronic HF.[3] **AHF is a life-threatening condition, associated with a high risk of mortality and rehospitalisation;[3,6,35]** it is a common cause of hospitalisation in those aged ≥65 years.[3,6] **Patients with AHF require early assessment and treatment of AHF and any underlying condition**, such as acute **C**oronary syndrome, **H**ypertension emergency, **A**rrhythmia, acute **M**echanical cause and **P**ulmonary embolism (**CHARM**).[3] Other factors that may precipitate AHF include renal impairment, infection and non-adherence to existing HF medications.[3,6]

Management: Patients require rapid transfer to hospital for assessment; evidence suggests the importance of "time to therapy" in AHF,[35-37] therefore all patients with AHF should receive appropriate therapy as soon as possible.[35] The use of non-invasive monitoring (e.g. pulse oximetry, BP, respiratory rate), oxygen therapy (if oxygen saturation <90% or on clinical judgement) and initiation of medical treatment while awaiting transfer and/or in the ambulance may be appropriate.[35]

The signs and symptoms in a patient with AHF reflect fluid overload or less often reduced cardiac output. Patients may be classified as 1) **warm and wet** (e.g. well perfused and congested), 2) **warm and dry** (compensated, well perfused without congestion), 3) **cold and dry** (hypoperfused without congestion) and 4) **cold and wet** (hypoperfused and congested).[3] **The majority of patients with AHF have normal or elevated BP with signs and symptoms of congestion.[3,35]** Up to 8% of patients are hypotensive and hypoperfused, which is associated with poor prognosis.[3,35] Investigations required include ECG, echocardiography, CXR and NPs; other investigations such as angiography may also be required. **Higher levels of NPs on admission are usually associated with a greater risk of adverse outcomes.[20,25]**

Patients with signs of fluid overload are treated with IV and oral loop diuretics to relieve their symptoms;[3,17] early treatment (within 100 minutes) with diuretics is associated with reduced mortality.[36] **The dose of diuretic used should be limited to the smallest amount necessary to provide adequate clinical effect.[35]** A furosemide bolus at least equivalent to the oral dose of diuretics used in the patient with CHF is recommended or 40 mg IV furosemide for patients with new onset HF or those not on maintenance diuretics.[35,38] Diuretics should be avoided in patients with signs of hypoperfusion.[3] Vasodilators may be given if the systolic BP is ≥110 mmHg.[35] In general, the routine use of opioids is not recommended.[35,37] Other therapies including inotropes and/or vasopressors may also be required in patients who are hypoperfused.[3,6]

Patients should not be discharged until they are stable; they should be established on evidence-based medications (see the next bulletin) and have stable renal function for at least 24 hours.[3,6,15] **There is a need for close follow-up and monitoring following hospital discharge, as this is a high-risk period and a major aim is to prevent readmission.[6]** If possible the patient should be enrolled in a disease management programme; **there is a need for timely communication between primary and secondary care.[3,6,10]** A MDT approach with close collaboration between all members of a HF team has been shown to reduce further HF hospitalisation and improve survival in patients discharged from hospital.[6] Patients with persistently elevated NP levels may need closer follow-up to reduce the risk of hospitalisation.[25] The patient should be advised to be aware of signs of decompensation following discharge.[3,10]

USEFUL RESOURCES

Heart Failure Matters website (Practical information on heart failure for patients, families and caregivers provided by the Heart Failure Association of the European Society of Cardiology) – www.heartfailurematters.org
ICGP Heart Failure in General Practice guideline and appendix (March 2019) accessible on www.icgp.ie
National Clinical Programme (NCP) HF www.hse.ie/eng/about/who/cspd/ncps/heart-failure/
Heart Failure - Irish Heart Foundation – www.Irishheart.ie
St Vincent's Screening to Prevent Heart Failure http://stophf.ie/
The Summary of Product Characteristics (SmPC) for individual medicines is available on www.hpra.ie and www.medicines.ie

List of references available on NMIC website. Date of preparation: Dec 2019

Overview of Heart Failure – bulletin 1 references 3rd February 2020

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