Cardiology update: Heart failure

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Consultant Cardiologist
Outline

Heart failure definitions

Diagnosing heart failure

Treatment of chronic heart failure

- Pharmacological
- Non-pharmacological
- Acute heart failure
- NICE Guidelines October 2014
Heart failure

Heart failure is a condition in which the heart does not pump enough blood to meet all the needs of the body. It is caused by dysfunction of the heart due to muscle damage (systolic or diastolic dysfunction), valvular dysfunction, arrhythmias or other rare causes.
HF Incidence and Prevalence

Prevalence

- Worldwide, 22 million\(^1\)

Incidence

- Worldwide, 2 million new cases annually\(^1\)

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\(^1\) World Health Statistics, World Health Organization
## Diagnosis of heart failure

<table>
<thead>
<tr>
<th>The diagnosis of HF-REF requires three conditions to be satisfied:</th>
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<tbody>
<tr>
<td>1. Symptoms typical of HF</td>
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<tr>
<td>2. Signs typical of HF(^a)</td>
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<tr>
<td>3. Reduced LVEF</td>
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<td>2. Signs typical of HF(^a)</td>
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<td>3. Normal or only mildly reduced LVEF and LV not dilated</td>
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<tr>
<td>4. Relevant structural heart disease (LV hypertrophy/LA enlargement) and/or diastolic dysfunction (see Section 4.1.2)</td>
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</table>

HF = heart failure; HF-PEF = heart failure with ‘preserved’ ejection fraction; HF-REF = heart failure and a reduced ejection fraction; LA = left atrial; LV = left ventricular; LVEF = left ventricular ejection fraction.

\(^a\)Signs may not be present in the early stages of HF (especially in HF-PEF) and in patients treated with diuretics (see Section 3.6).
## Symptoms and signs

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
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<tbody>
<tr>
<td>Breathlessness</td>
<td>Elevated jugular venous pressure</td>
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<tr>
<td>Orthopnoea</td>
<td>Hepatojugular reflex</td>
</tr>
<tr>
<td>Paroxysmal nocturnal dyspnoea</td>
<td>Third heart sound (gallop rhythm)</td>
</tr>
<tr>
<td>Reduced exercise tolerance</td>
<td>Laterally displaced apical impulse</td>
</tr>
<tr>
<td>Fatigue, tiredness</td>
<td>Cardiac murmur</td>
</tr>
<tr>
<td>Ankle swelling</td>
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Aetiology of Heart Failure

- Ischaemic Heart Disease
- Hypertension
- Dilated Cardiomyopathy (familial, viral)
- Valvular Disease
- Toxins (e.g. alcohol or cytotoxic drugs)
- Prolonged Arrhythmias
Left Ventricular Dysfunction

**Systolic:** Impaired contractility / ejection

- Approximately 70% of heart failure patients have systolic dysfunction\(^1\)

**Diastolic:** Impaired filling / relaxation

\(^1\) Lilly, L. *Pathophysiology of Heart Disease*. Second Edition
Diagnosing heart failure

- Take a detailed history and perform a clinical examination

- Previous MI
  - Within 2 weeks: Specialist assessment and Doppler echocardiography
  - Within 6 weeks: Consider measuring serum natriuretic peptides if levels not known

- No previous MI
  - Measure serum natriuretic peptides
    - Within 2 weeks: High levels or Raised levels
      - High levels: Specialist assessment and Doppler echocardiography
      - Raised levels: Investigate other diagnoses
        - Raised levels: Investigate other diagnoses
          - Other cardiac abnormality
          - Heart failure due to left ventricular systolic dysfunction
          - Heart failure with preserved ejection fraction
          - Heart failure unlikely, other diagnosis
B-type Natriuretic Peptide

- First isolated in 1988 from Porcine brain
- Mainly found in ventricular myocardium
- Cardiac hormone
- Belongs to a family of natriuretic peptides (ANP, CNP, urodilatin)
- Main stimulus for secretion is myocardial wall stress
- Synthesised as pro-BNP which is cleaved to BNP (active) and NT-proBNP (inactive)
BNP in patients with heart failure according to NYHA class

Adapted from Wieczorek et al.
Role of BNP and NT-proBNP in clinical routine: key points

• BNP and NT-proBNP are reliable biomarkers, reflecting myocardial stress

• Both markers are stable in whole blood and can be measured in clinical routine using fully automated assays

• The diagnostic performance of BNP and NT-proBNP is comparable and there is no meaningful difference

• The particular strength of BNP and NT-proBNP is to rule out heart failure in patients with shortness of breath

• Both markers provide prognostic information in patients with heart failure, coronary artery disease, and valvular heart disease
Treating heart failure

Heart failure

Heart failure with preserved ejection fraction

Manage comorbid conditions such as high blood pressure, ischaemic heart disease and diabetes mellitus in line with NICE guidance

Heart failure due to left ventricular systolic dysfunction\(^1\)

Offer both ACE inhibitors and beta-blockers licensed for heart failure as first-line treatment

Consider an ARB if intolerant of ACE inhibitors

Specialist assessment

Offer rehabilitation and education, and diuretics for congestion and fluid retention

Consider hydralazine in combination with nitrates if intolerant of ACE inhibitors and ARBs

If symptoms persist despite optimal first-line treatment, seek specialist advice and for second-line treatment consider adding:

- an aldosterone antagonist licensed for heart failure (especially in moderate to severe heart failure\(^3\) or MI in past month) or
- an ARB licensed for heart failure\(^4\) (especially in mild to moderate heart failure\(^5\)) or
- hydralazine in combination with nitrates (especially in people of African or Caribbean origin\(^6\) with moderate to severe heart failure\(^3\))

Consider an ICD where appropriate\(^2\)

If symptoms persist consider:

- CRT (pacing with or without a defibrillator)\(^7\)
- digoxin
Management I: General Measures

Lifestyle:
- Weight reduction
- Discontinue smoking
- Avoid alcohol excess
- Exercise

Medical:
- Treat HTN, diabetes, arrhythmias
- Anticoagulation
- Immunization
- Sodium / fluid restriction
Management II

Diuretics
ACE Inhibitors / ARAs
Beta-Blockers
Aldosterone Antagonists (Spironolactone)
Digoxin
Devices (cardiac resynchronization, ICD)
Pharmacological treatment of heart failure due to LV systolic dysfunction

New diagnosis

Start ACE inhibitor and titrate upwards
Or ARA if ACE-intolerant

Add beta-blocker and titrate upwards
Providing no contraindication and patient is stable.
Usually as outpatient.

Add spironolactone
If patient remains moderately to severely symptomatic (NYHA III/IV)

Seek specialist advice for further options

Add Diuretic
Diuretic therapy is likely to be required in most cases

Add Digoxin
Sinus Rhythm
Only if symptomatic despite ACE-inhibitor and beta-blocker

Atrial Fibrillation
Use as first line therapy

NICE guidelines 2003
Pharmacological therapy (HEF-REF)

Current therapy (better than placebo)

- ACE-I (CONSENSUS and SOLVD Treatment)
- Beta blockers (COPERNICUS, MERIT-HF, CIBIS II)
- MRA (RALES and EMPHASIS-HF)
Next step

Ongoing symptoms

- LVEF <35%
- Sinus rhythm with HR >75 (NICE guidelines)
- Add Ivabradine ($I_f$ inhibitor)
Ivabradine

SHIFT trial (2010) (HR>70)

NICE Guidance: Ivabradine is recommended as an option for treating chronic heart failure for people:

- with NYHA class II to IV stable chronic heart failure with systolic dysfunction and
- who are in sinus rhythm with a heart rate of 75 bpm or more and
- who are given ivabradine in combination with standard therapy including beta-blocker therapy, ACE inhibitors and aldosterone antagonists, or when beta-blocker therapy is contraindicated or not tolerated and
- with a left ventricular ejection fraction of 35% or less.

Ivabradine should only be initiated after a stabilisation period of 4 weeks on optimised standard therapy with ACE inhibitors, beta-blockers and aldosterone antagonists.
The future…
Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure

PARADIGM-HF

BACKGROUND
We compared the angiotensin receptor–neprilysin inhibitor LCZ696 with enalapril in patients who had heart failure with a reduced ejection fraction. In previous studies, enalapril improved survival in such patients.

METHODS
In this double-blind trial, we randomly assigned 8442 patients with class II, III, or IV heart failure and an ejection fraction of 40% or less to receive either LCZ696 (at a dose of 200 mg twice daily) or enalapril (at a dose of 10 mg twice daily), in addition to recommended therapy. The primary outcome was a composite of death from cardiovascular causes or hospitalization for heart failure, but the trial was designed to detect a difference in the rates of death from cardiovascular causes.

RESULTS
The trial was stopped early, according to prespecified rules, after a median follow-
Design of the trial

Enrolled broad-spectrum with HF-REF (10521)

Superiority over ACE-I (Enalapril used as evidence-based)

Active run in period (to test they could tolerate both)

1. Enalapril 10mg BD – proven to reduce mortality in SOLVD-treatment trial
2. LCZ696 200mg BD – equivalent of Valsartan 160mg BD to test incremental benefit of Neprilysin inhibition after angiotension system blockade

Randomised (8339)

Tolerability during run-in (some dropped out during run in – more during Enalapril part)

Followed for median of 27 months (stopped early due to benefit of LCZ696)
Results

Primary endpoint: CV death or hospitalisation for heart failure

20% reduction in risk of primary end point in LCZ696 group

NNT = 21
Device Therapy for heart failure:

1. Cardiac Resynchronization (CRT, biventricular pacing)

2. Implantable Cardiac Defibrillators (ICD$s$)
## Terminology

<table>
<thead>
<tr>
<th>CRT</th>
<th>= cardiac resynchronisation therapy</th>
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<tr>
<td>CRT – P</td>
<td>= pacing alone (no defib)</td>
</tr>
<tr>
<td></td>
<td>= ‘low energy’</td>
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<tr>
<td>CRT – D</td>
<td>= biventricular pacing with defib</td>
</tr>
<tr>
<td></td>
<td>= ‘high energy’</td>
</tr>
<tr>
<td>ICD (AICD)</td>
<td>= implantable cardiac defib</td>
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</tbody>
</table>
What is CRT?
All-Cause Mortality (CARE-HF)

HR 0.64 (95% CI 0.48 to 0.85)

p = .0019

CRT

Medical Therapy

Number at risk

<table>
<thead>
<tr>
<th></th>
<th>CRT</th>
<th>Medical Therapy</th>
</tr>
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<tbody>
<tr>
<td>409</td>
<td>376</td>
<td>365</td>
</tr>
<tr>
<td>351</td>
<td>321</td>
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<td>213</td>
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<td>89</td>
<td>71</td>
<td>8</td>
</tr>
<tr>
<td>8</td>
<td>5</td>
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Prognosis in Heart Failure

- 5-year mortality rate is 50%
- Median survival following diagnosis is 1.7 years for men and 3.2 years for women
- In people diagnosed with heart failure, sudden death occurs at 6 to 9 times the rate of the general population
LVEF and SCD Incidence

Modes of Death

NYHA II

- CHF: 64%
- Other: 24%
- Sudden Death: 12%

- n = 27

NYHA III

- CHF: 59%
- Other: 15%
- Sudden Death: 26%

- n = 103

NYHA IV

- CHF: 56%
- Other: 33%
- Sudden Death: 11%

- n = 27


Chelsea and Westminster Hospital
NHS Foundation Trust
Treatments to Reduce SCD

Correcting Ischemia
- Revascularization
- Beta-blocker

Preventing Plaque Rupture
- Statin
- ACE inhibitor
- Aspirin

Stabilizing Autonomic Balance
- Beta-blocker
- ACE inhibitor

Improving Pump Function
- ACE inhibitor
- Beta-blocker

Prevention of Arrhythmias
- Beta-blocker
- Amiodarone

Terminating Arrhythmias
- ICDs
- AEDs

Prevent Ventricular Remodeling and Collagen Formation
- Aldosterone receptor blockade

Implantable Defibrillators (1989-2001)

209 cc
113 cc
80 cc
80 cc
72 cc
54 cc

62 cc
49 cc
39.5 cc
39 cc
39.5 cc
39 cc
39.5 cc
36 cc
Device therapy - NICE

Implantable cardioverter defibrillators (ICDs), cardiac resynchronisation therapy (CRT) with defibrillator (CRT-D) or CRT with pacing (CRT-P) are recommended as treatment options for people with heart failure who have left ventricular dysfunction with a left ventricular ejection fraction of 35%.
# NICE - CRT – June 2014

<table>
<thead>
<tr>
<th>QRS interval</th>
<th>NYHA 1</th>
<th>NYHA II</th>
<th>NYHA III</th>
<th>NYHA IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;120 ms</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>120-149ms without LBBB</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>CRT-P</td>
</tr>
<tr>
<td>120-149ms with LBBB</td>
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<td>CRT-D</td>
<td>CRT-P or CRT-D</td>
<td>CRT-P</td>
</tr>
<tr>
<td>150ms +/- LBBB</td>
<td>CRT-D</td>
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<td>CRT-P or CRT-D</td>
<td>CRT-P</td>
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</table>
Management of co-morbidities

- Anaemia
- Angina
- Asthma/COPD
- Cachexia
- Cancer
- Depression
- Diabetes mellitus
- Erectile dysfunction
- Gout

- Hyperlipidaemia
- Hypertension
- Iron deficiency
- Kidney dysfunction
- Obesity
- Prostatic obstruction
- Sleep disturbance/ sleep disordered breathing
Acute heart failure

Acute heart failure can present as new-onset heart failure in people without known cardiac dysfunction, or as acute decompensation of chronic heart failure.
Diagnosis, assessment and monitoring

- History
- Examination
- ECG
- CXR
- Blood tests
- BNP (<100ng/L) or NT-pro-BNP (<300ng/L)
In people presenting with new suspected acute heart failure with raised natriuretic peptide levels perform transthoracic Doppler 2D echocardiography to establish the presence or absence of cardiac abnormalities.

In people presenting with new suspected acute heart failure, consider performing transthoracic Doppler 2D echocardiography within 48 hours of admission to guide early specialist management.
Initial pharmacological treatment

Offer intravenous diuretic therapy to people with acute heart failure. Start treatment using either a bolus or infusion strategy.

For people already taking a diuretic, consider a higher dose of diuretic than that on which the person was admitted unless there are serious concerns with patient adherence to diuretic therapy before admission.

Closely monitor the person's renal function, weight and urine output during diuretic therapy.

Do not routinely offer nitrates to people with acute heart failure.

If intravenous nitrates are used in specific circumstances, such as for people with concomitant myocardial ischaemia, severe hypertension or regurgitant aortic or mitral valve disease, monitor blood pressure closely in a setting where at least level 2 care can be provided.
Consider inotropes or vasopressors in people with acute heart failure with potentially reversible cardiogenic shock. Administer these treatments in a cardiac care unit or high dependency unit or an alternative setting where at least level 2 care
Non-pharmacological

Do not routinely use non-invasive ventilation (continuous positive airways pressure [CPAP] or non-invasive positive pressure ventilation [NIPPV]) in people with acute heart failure and cardiogenic pulmonary oedema.

If a person has cardiogenic pulmonary oedema with severe dyspnoea and acidaemia consider starting non-invasive ventilation without delay.
Do not routinely offer ultrafiltration to people with acute heart failure.

Consider ultrafiltration for people with confirmed diuretic resistance.
Treatment after stabilisation

In a person presenting with acute heart failure who is already taking beta-blockers, continue the beta-blocker treatment unless they have a heart rate less than 50 beats per minute, second or third degree atrioventricular block, or shock.

Start or restart beta-blocker treatment during hospital admission in people with acute heart failure due to left ventricular systolic dysfunction, once their condition has been stabilised – for example, when intravenous diuretics are no longer needed.

Ensure that the person’s condition is stable for typically 48 hours after starting or restarting beta-blockers and before discharging from hospital.

Offer an angiotensin-converting enzyme inhibitor (or angiotensin receptor blocker if there are intolerable side effects) and an aldosterone antagonist during hospital admission to people with acute heart failure and reduced left ventricular ejection fraction. If the angiotensin-converting enzyme inhibitor (or angiotensin receptor blocker) is not tolerated an aldosterone antagonist should still be offered.
Follow-up

Management after the acute phase should be as per chronic HF management

Importance of specialist heart failure team input
Cardiac rehabilitation

• Offer a supervised group exercise-based rehabilitation programme designed for patients with heart failure

• Ensure the patient is stable and does not have a condition or device that would preclude an exercise-based rehabilitation programme.

• Include a psychological and educational component in the programme.

• The programme may be incorporated within an existing cardiac rehabilitation programme
Any questions?