The Syndrome of Heart Failure

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Why is palliative care / advanced care planning important?

- 682,298 heart failure coded admissions in England and Wales 2014 - 2015
- In-patient mortality around 10%
- Post discharge mortality 28% at one year, so 38% mortality at one year if admitted with heart failure
(National Heart Failure audit 2015)

“Looking after end-stage heart failure is not rocket science. It is much more difficult. The trajectory of a rocket is predictable: the course of heart failure is not. Patients are not made of metal, and it matters what happens to them.”

Quote from preface to second edition of Heart Failure and Palliative Care: a team approach (2015)

Barriers to having ‘the conversation’

- Uncertainty regarding prognosis
- Concern that hope will be taken away
- Complexity of ensuring whole team are in agreement
- Emergency situations

- Difficult for heart failure nurses to access advanced communication skills training
- Are we sure that everything that can be done has been done?
What are the issues for palliative care clinicians in heart failure?

• Uncertain trajectory of illness compared with cancer – are we there yet? “Prognostic paralysis”, can be overcome through a problem approach, rather than prognostic approach
• Concerns about lack of cardiac expertise
• Difficulty of discussing end of life issues when life expectancy uncertain (honesty and hope)
• Can we cope with the numbers?

Common Symptoms

- Lack of energy
- Breathlessness
- Feeling drowsy
- Dry mouth
- Numbness/tingling in hands/feet
- Difficulty sleeping
- Worrying
- Cough
- Feeling sad
- Pain
- Change in taste
- Weight loss


- 62–70%
- 56–63%
- 52%
- 50–73%
- 48–55%
- 44–47%
- 44–50%
- 40–45%
- 38–43%
- 38–52%
- 25–50%
- 15–52%

General points

- On average each person with heart failure experiences 9–12 symptoms, half relating symptom distress
- High risk of depression and anxiety, loss of roles, feelings of guilt because they might ‘look well’ but just don’t have the energy to do what they used to, e.g. mow the lawn
- Poorly controlled co-morbidities makes the heart failure worse e.g. diabetes, hypertension, COPD
- Infections make heart failure worse
- NSAIDs account for 17% of admissions with heart failure decompensation

Cardiovascular Disease Outcomes Strategy

- People with cardiovascular disease and their carers felt abandoned after acute sector treatment
- They felt they needed emotional and practical support that was not forthcoming
- They did not receive the information they needed to live as well as possible with their condition
- Some services were inappropriately targeted e.g. exercise classes
- 62% of patients with cardiovascular disease die in hospital, though the large majority would like to die in their place of residence (DH 2013, chapter 5)

Prognostication

• There are over 300 prognostic markers in heart failure, BUT...
• Notoriously difficult because ‘heart failure’ includes a very varied group of patients with significant comorbidities
• Around half will die suddenly, for the remaining group a gradual decline with multiple acute decompensation episodes, like “the pattern of a flat stone skimming across water”

Drivers for improved palliative and end of life care in heart failure

• European Society for Cardiology – task force for the diagnosis and treatment of heart failure (2016). Identified gaps in evidence, including this as an issue that deserves to be addressed in future clinical research
• Increasing involvement of palliative care expertise and services in chronic disease management
• All Party Parliamentary Group: Focus on Heart Failure (2016). 10 recommendations – 2 regarding the need for advanced communication skills and advanced care planning
Epidemiology

• 1-2% of adult population in developed countries
• > 10% among people > 70 years
• People > 65 years presenting to primary care with dyspnoea on exertion, one in six will have heart failure
• Most deaths are due to cardiovascular causes, mainly sudden death and worsening heart failure

(European Society of Cardiology 2016)

Aetiology

• Ischaemic heart disease
• Toxins – e.g. alcohol, anthracyclines, NSAID
• Immune mediated/ inflammation – e.g. bacteria, viruses, HIV, myocardiitis
• Infiltration – e.g. Amyloidosis, sarcoidosis
• Metabolic derangements – e.g. thyroid disease, thiamine deficiency
• Genetic – e.g. Hypertrophic cardiomyopathy, muscular dystrophies
• Hypertension
• Structural defects – e.g. valve disease
• Pericardial & endomyocardial pathologies – e.g. constrictive pericarditis
• High output states e.g. severe sepsis
• Volume overload – e.g. renal failure
• Arrhythmias

Definition of Heart Failure Syndrome

• Typical symptoms – dyspnoea, fatigue, leg swelling
• Signs – elevated JVP, pulmonary crepitations, peripheral oedema
• Caused by structural and/or functional cardiac abnormality on imaging
• Resulting in reduced cardiac output and/or elevated pressures within the heart

Identification of underlying cardiac problem is crucial as this determines specific treatments

(European Society of Cardiology, 2016)

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Comparison

Lung Cancer

• Cancer trajectory with clearer terminal phase. Able to plan
• Swinging between hope and despair
• Cancer takes over life and becomes main concern
• Relatives anxious
• Financial benefits available
• Care prioritised as ‘cancer’ and later as ‘terminally ill’

(Johnson et al 2002)

Heart Failure

• Gradual decline punctuated by episodes of acute deterioration. Sudden, unexpected death with no distinct terminal phase
• Daily grind of hopelessness
• Much co-morbidity to cope with, heart often not main issue
• Relatives isolated and exhausted
• Less access to benefits with uncertain prognosis
• Less priority as ‘chronic disease’ and less priority later as uncertain if yet ‘terminally ill’

Quality of Care

• NICE guidelines 2003 (No.5) – partial update 2010 (No.108) and Acute heart failure (No.187) 2014
• Annual national heart failure audit of all acute admissions in England and Wales (NICOR)
• Quality Standard 103: Acute heart failure (December 2015) — BNP +/- echo; heart failure team input within 24 hours; evidence based medicines & review within 2 weeks
• Quality Standard 109: Chronic heart failure (February 2016) — assessment within 2 weeks if BNP elevated or previous MI; evidence based medicines & review within 2 weeks

Pathophysiology

• In order to maintain cardiac output/blood pressure:
  1. Neurohormonal activation, thus
  2. Salt and water retention
  3. Peripheral vasoconstriction
  4. Myocardial cell damage -apoptosis
  5. Adverse remodelling, risk of LV aneurysm and thrombus formation

(European Society of Cardiology, 2014)
Is challenging, particularly in context of high BMI and COPD. New categorisation in 2016:

- Heart failure symptoms +/- signs with reduced ejection fraction < 40% (HFrEF)
- Heart failure symptoms +/- signs with mid range ejection fraction 40-49% (HFrEF)
- Heart failure symptoms +/- signs with preserved ejection fraction 50% + (HFpEF)

NB symptom severity links to skeletal muscle fitness, not ejection fraction

NYHA Class

Class I
Patients with cardiac disease but without resulting in limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation (rapid or pounding heart beat), dyspnoea (shortness of breath), or anginal pain.

Class II (Mild)
Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnoea, or anginal pain.

Class III (Moderate)
Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnoea, or anginal pain.

Class IV (Severe)
Patients with cardiac disease resulting in the inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

NYHA Functional Classification

Treatment – Heart Failure with reduced Ejection Fraction (HFrEF)

- Diuretics – to reduce oedema, a loop diuretic initially, but if resistant, a thiazide e.g. Metolazone or Bendroflumethiazide may be used for brief periods in addition. Reduce breathlessness and improve exercise performance
- ACE Inhibitor – eg Ramipril, Enalapril, reduces production of Angiotensin II (vasoconstrictor) and by inhibiting the enzyme kininase II, block the breakdown of the vasodilator bradykinin. Reduces myocardial oxygen demand. Increase life expectancy and quality of life, reduce hospitalisation and symptoms

Beta-blockers – reduce heart rate and risk of arrhythmias. Negative inotrope, thus reducing myocardial oxygen demand. Bisoprolol, Carvedilol or Nebivolol. Increases life expectancy and reduce need for hospitalisation.

Aldosterone antagonists – reduces salt and water retention. Spironolactone or Eplerenone. Increases life expectancy and reduces need for hospitalisation.

Ivabradine – reduces heart rate by inhibiting the ‘funny channel’ in the sinus node so must be in sinus rhythm. No effect on blood pressure. Improved prognosis in heart failure if heart rate is < 75

Coronary revascularisation remains contentious and should be considered carefully in each individual

Treatment – Heart Failure with reduced Ejection Fraction (HFrEF)

- Digoxin – in AF, or resistant to treatments already listed. Positive inotrope, negative chronotrope. Reduces hospitalisation
- Angiotensin Receptor Blockers (ARB) – e.g. Valsartan, Candesartan. Only if intolerant of ACE inhibitors. Reduce mortality and hospitalisation
- Amiodarone – for ventricular tachycardia. Specialist initiation only.
- Anticoagulants – for AF, history of thromboembolism, left ventricular aneurysm, or intracardiac thrombus
- Aspirin and statin – only in the presence of atherosclerotic arterial disease
- Isosorbide & Hydralazine – only if intolerant of ACE-inhibitor or ARB, specialist initiation only
What's new in treating HFrEF?
PARADIGM-HF study (2014)

- **ENTRESTO**: Valsartan and neprilysin inhibitor Sacubitril simultaneously blocks the renin–angiotensin–aldosterone system (RAAS) and augments endogenous natriuretic peptides and other vasoactive substances by blocking the enzyme that degrades them (ARNI). Compared to Enalapril 10 mg BD.
- Neprilysin increases concentration of natriuretic peptides (includes ANP, BNP & urodilatin – secreted by heart, vasculature, kidney & central nervous system in response to cardiac wall stress)
- Effect: vasodilatation & natriuresis, inhibition of RAAS, reduce sympathetic drive, antiproliferative & antihypertrophic effects

**HEART (PUMP) FAILURE**

**INOTROPES** (Digoxin)
- Cardiac output
- Peripheral resistance

**VASODILATORS**
- nitrate, hydralazine

**BETA-BLOCKERS**
- O2 demand but not in acute failure
- Peripheral & Pulmonary oedema

**ANGIOTENSIN II** stimulates
- Vasoconstriction & release of Aldosterone
- Aldosterone causes Na (& H2O) retention

**ALDOSTERONE ANTAGONIST**
- Spironolactone, Eplerenone

**ACE inhibitors/ARB**
- or ARNI

**Rationale for Cardiac Resynchronisation Therapy (CRT)**
- Dyssynchrony may be between left and right ventricles or between the septum and the left ventricular free wall
- 20 – 30% of people with heart failure might benefit
- Must be on maximum tolerated medical therapy yet still symptomatic before considered for it
- Picked up clinically with bundle branch block on ECG
- Only approximately 2/3 of patients have symptomatic benefit
- Costs around £20,000 including follow-up care

**Treatment in HFrEF and HFpEF – includes diastolic dysfunction, right heart failure**
- Diuretics
- Treat the co-morbidities – e.g. hypertension, diabetes, arrhythmias, COPD, anaemia, thyroid disease, sleep disordered breathing
- First line oral hypoglycaemic drug should be Metformin. A recent trial of Empagliflozin showed a reduction in body weight, probably by inducing glycosuria and osmotic diuresis. It was associated with reduced hospitalisations for heart failure and cardiovascular mortality

**What is end-stage heart failure?**
- Advanced age
- Refractory symptoms despite optimal therapy
- > 3 hospital admissions with decompensation in < 6 months
- Dependent for > 3 activities of daily life
- Cardiac cachexia
- Resistant hyponaesthesia
- Albumin <25 g/litre
- Multiple shocks from ICD
- A co-morbidity conferring a poor prognosis, e.g. terminal cancer

(Connelly et al 2010 in Ashton-Clarkson & Thackwray 2012)
Triggers for a palliative approach

Deterioration despite optimally tolerated therapy
• Increased functional dependence
• Progressive fatigue
• Recurring hospitalisations
• Emotional distress
• Carer exhaustion
• Patient request

(O’Leary et al 2009 in Ashton-Clarkson & Thackwray 2012)

General points

• Even in the dying phase it is appropriate to treat the heart failure for comfort
• Treatment of co-morbidities also need attention
• Try to continue medications provided symptom relief outweighs the drug related adverse effects
• If someone is falling, check that it was not a mechanical trip before presuming it was due to hypotension and stopping heart failure medications

What should be avoided?

• Tricyclic antidepressants (interactions, anticholinergic effects)
• Non-steroidal anti-inflammatories, steroids, COX 2 inhibitors (fluid retention)
• Cyclizine (hypotension)
• Domperidone (QT prolongation)
• Glitazones (increased mortality risk)
• Verapamil (contra-indicated in heart failure)
• Adding Angiotensin Receptor Blocker to ACE-inhibitor (hypotension and hyperkalaemia)

Fluid balance

• Helpful to have a ‘dry weight’
• Advised to seek advice if gain 2 kg or more over 3 days
• Aim for 0.5–1 kg weight loss/day
• Can be up to 5 litres of fluid overload before noticed by most patients
• If very hot and sweaty, diarrhoea or vomiting, safest to stop diuretics until resolved as high risk of acute renal failure. (‘Sick day rules’)

General points

• The extent of fatigue and breathlessness can be hard for the person to articulate and difficult for us as clinicians to understand.
• Active treatment alongside palliation of symptoms is the ideal, they should not be mutually exclusive

References

ACE-Inhibitors/ ARBs (in HFrEF)

- Continue if possible as they help reduce symptoms of dyspnoea and fatigue.
- If cough side-effect, switch from ACE-inhibitor to ARB
- Hypovolaemia, hypotension, deteriorating renal function will require down-titration
- A blood pressure of 80 systolic is acceptable unless also dizzy/feeling very unwell or renal function markedly worsening
- Try taking before bed instead of in the morning with all other medications
- Risk of hyperkalaemia, especially with deteriorating renal function
- Alternative in renal impairment is Hydralazine 25 mg TDS and ISMO 10 mg

Beta-blockers (in HFrEF)

- Try to continue as they reduce myocardial oxygen demand and thus dyspnoea and breathlessness, unless real problem with dizziness, hypotension, cold peripheries
- Try to reduce rather than stop if possible
- Prioritise over other blood pressure lowering agents if the person has frequent angina or recurrent VF
- Best avoided in isolated right heart failure – usually makes HF worse
- Ivabradine as an alternative to reduce heart rate if in sinus rhythm

Aldosterone Antagonists (also known as MRAs – Mineralocorticoid Receptor Antagonists)

- Spironolactone has gynaecomastia as side-effect, is so switch to Eplerenone
- Helpful in all categories of heart failure in addition to loop and thiazide/thiazide type diuretics
- Risk of hyperkalaemia (allow potassium to rise to 5.5)

Digoxin

- For relief of dyspnoea and fatigue in HFrEF in addition to standard therapy if no longer helping. Positive inotropic effect, negative chronotropic effect and promotes natriuresis
- May be ultimately instead of ACE-inhibitor and Beta-blocker
- Hypokalaemia potentiates its effect, so take care
- Risk of toxicity, serum level aim 0.5 – 0.8 ng/ml
- Improves symptoms, reduces hospitalisations but does not improve mortality rates
- For fast atrial fibrillation if Beta-blocker cannot be tolerated

Anticoagulation

- If unable to take oral medication consider low dose molecular weight heparin
- If prognosis clearly < 6/12, could halve the CHADSVASC risk score – discuss the risk with the patient.
  (see European Society of Cardiology guidelines on Atrial Fibrillation this week)
- Oral anticoagulants (e.g. Apixaban - least renally excreted NOAC), less risk of haemorrhagic stroke than with warfarin but increased risk of GI bleed
- Reduced dose (2.5 mg BD) if > 80 years, renal impairment or < 60 kg body weight
- No reversal agent for oral anticoagulant although one apparently in development – very expensive
### Diuretics
- Subcutaneous furosemide is widely used when venous access too difficult, no randomised controlled trial yet
- Needs to be tailored to the individual, eg diuretics would continue at the expense of an ACE inhibitor if the person had gross peripheral oedema, very heavy oedematous legs contribute to falls.
- Bumetanide has better bioavailability if gut oedema (40 mg furosemide = 1 mg Bumetanide)
- Inhaled furosemide – pilot study in progress
- Hyponatraemia is usually due to haemodilution but can sometimes be due to over-diuresis
- In diuretic resistance, IV furosemide and 20 minutes after start of infusion give Metolazone
- Extreme caution with Metolazone due to electrolyte disturbances, usually 2.5 mg alternate days at first as delayed diuresis and can be dramatic when it happens

### Oedema
- Pulmonary oedema – increased blood pressure within the lungs
- Peripheral oedema – increased right heart pressures, usually secondary to increased left heart pressure
- Low albumin/anaemia
- Dependent oedema

### Dyspnoea
- **Reduced cardiac output:** reduced systolic ventricular function, hypertension, coronary artery disease, valve disease, ‘stiff’ heart
- ‘Air hunger’ or dyspnoea on exertion, or both
- Orthopnoea
- Paroxysmal nocturnal dyspnoea
- Pulmonary congestion – white frothy sputum
- Pulmonary hypertension (prevalence 40 – 70%)

### Dyspnoea
- Arrhythmia (usually AF, reported prevalence 15–30%)  
- Anaemia (prevalence > 33%) – ACE inhibitors, poor nutrition, renal disease, iron deficiency contribute
- Deconditioning
- Inflammatory mediators linked to pathogenesis and progression of chronic heart failure. Cytokine activity triggers skeletal muscle wasting (cardiac cachexia) that leads to stimulation of the respiratory centre and thus increased respiratory rate
- COPD (reported prevalence in HF range 9–41%)

### Nausea, anorexia and constipation
- Ascites – feeling bloated
- Liver congestion
- Gut/ intestinal oedema – leading to release of toxins from the bowel, reduced perfusion, reduction in ability to digest food and absorb nutrients and also medications
- Reduced physical activity

### Fatigue
- Reduced cardiac output (5 litres/minute), myocardial oxygen demand exceeds supply
- Gross oedema – extra weight to move around
- Anaemia
- Hypothyroidism
- Chronic lack of good quality sleep (need to sleep upright, nocturia – better renal perfusion supine, not able to be active during the day to get physically tired, coughing, anxiety/fear)
- Sleep disordered breathing – obstructive sleep apnoea, central sleep apnoea, ie cyclical hypoxaemia & sympathetic activation (prevalence 50% in chronic heart failure), Cheyne Stokes respirations – in the last 6 months of life
- Poorly controlled diabetes (prevalence 34 – 44%)
- Beta-blockers
Cognitive impairment

- Reduced cardiac output/ hypoxia
- Possibly acute delirium in decompensation episodes
- Biochemistry derangement
- Extreme frailty/ cachexia
- Anxiety/ Depression – due to cytokine release, depletes tryptophan and hence serotonin, also social isolation
- Cerebrovascular disease

Pruritus
- The mechanism is not clear in heart failure, sometimes thinned epidermis of the elderly contributes