Heart failure: classification and pathophysiology

Simon G Pearse

Martin R Cowie

Abstract

Heart failure (HF) is a clinical syndrome in which there are characteristic signs and symptoms, such as oedema, breathlessness and fatigue, due to an underlying abnormality of cardiac function. Understanding the cause of the cardiac dysfunction and the body's response to it are essential in effective management. Despite improved knowledge of the pathophysiology and a growing range of therapeutic options, HF remains a serious condition with considerable morbidity and mortality. HF is a global problem, although the common aetiologies vary between the developed and developing world. HF can present acutely, for example as a consequence of an acute myocardial insult, or in its chronic form in which acute decompensation may occur with an identifiable precipitant. Cardiac dysfunction triggers the activation of an array of neurohormonal compensatory mechanisms that may ultimately become deleterious to cardiac function. The consequences include sodium and fluid retention, excess sympathetic tone, altered breathing patterns, arrhythmia, and an inflammatory state with immune activation. Significant recent advances in pharmacological, surgical and device therapy ameliorate these responses, improving survival and quality of life.

Keywords Heart failure; pathophysiology; renin-angiotensin system; sympathetic nervous system

What's new?

- The prognosis of chronic heart failure (CHF) has improved in the past decade, probably as a result of wider use of drug therapy which modifies the neurohormonal response to cardiac dysfunction
- Electrical device therapy can further improve prognosis and quality of life for selected patients with high risk of sudden death and/or evidence of electrical dyssynchrony
- The likelihood of hospital admission can be reduced by careful chronic disease monitoring and management by a multidisciplinary team
- The syndrome of heart failure with preserved left ventricular systolic function (HFPEF) is increasingly recognized, although effective therapy for this group of patients is still lacking
- There is increasing awareness of the complications of heart failure, such as sleep-disordered breathing and anaemia, with an increasing evidence base for treatment of these conditions

Definition

HF is a clinical diagnosis in which there are symptoms (breathlessness, fatigue, oedema and/or orthopnoea) and signs (elevated venous pressure, pulmonary crackles, displaced apex beat), with evidence of abnormal cardiac function on investigation.[1] It should be stressed that HF is a clinical syndrome rather than merely an abnormality found on cardiac imaging.

Historically, cardiac dysfunction has been quantified with reference to left ventricular ejection fraction (LVEF), usually derived from echocardiography, with values of more than 50–60% accepted as normal. However, it is now well recognized that the HF syndrome can present where LVEF is in the normal range, but there is significant impairment of diastolic relaxation or filling (heart failure with preserved ejection fraction [HFPEF]). Diagnosis of HFPEF can be difficult but population studies suggest that up to 50% of cases of incident HF occur with a 'normal' LVEF, particularly in the elderly.[2] Abnormalities of cardiac rhythm, valve function, or congenital structural or functional abnormalities can also lead to the heart failure syndrome.

Aetiology

HF is a syndrome rather than a complete diagnosis and the underlying cause of the cardiac dysfunction should always be determined. The major aetiologies are detailed in Table 1. In the developed world, ischaemic heart disease and hypertension remain the leading causes. Rates of hypertensive heart failure are declining with improved management of blood pressure in primary care. The prevalence of HF due to degenerative valve disease (chiefly aortic stenosis) is likely to increase as the population ages.

There are few data for developing countries but rheumatic heart disease continues to be a major health problem, particularly in Africa and Asia. Chagas' disease remains an important cause of HF in South America. In African and African-American populations, hypertension remains the main aetiology of HF in almost half of all cases.

Pathophysiology

The two main categories of HF are HFREF (HF with reduced ejection fraction) and HFPEF (HF with preserved ejection fraction). The body's responses to these two types of left ventricular abnormalities may be very similar, but the evidence base for therapy is much better established for the former.

In **HFREF** ('systolic' HF), the disease process affects contraction of the heart muscle. This may be regional (e.g. following a myocardial infarction) or global (as seen in dilated cardiomyopathy or chronic mitral regurgitation). The result is that, although the heart may fill well during diastole, the failing myocardium is unable to eject sufficient blood during systole. This leads to dilatation of the heart and stretching of the muscle

Simon G Pearse *MRCP is a Clinical Research Fellow in Cardiology at the Royal Brompton Hospital, London, UK. Competing interests: none declared.*

Martin R Cowie *MD MSc FRCP FRCP (Ed) FESC is Professor of Cardiology at Imperial College London and Honorary Consultant Cardiologist at the Royal Brompton Hospital, London, UK. Competing interests: Dr Cowie provides consultancy advice to several companies developing or producing diagnostics, devices or drugs for heart failure.*

Causes of heart failure: general classification

- Coronary artery disease
- Intrinsic myocardial disease
  - Dilated cardiomyopathy
  - Hypertrophic cardiomyopathy
  - Restrictive cardiomyopathy
  - Arrhythmogenic right ventricular cardiomyopathy
- Valvular heart disease
  - Congenital
  - Age-related/calcific
  - Infective endocarditis
  - Immunological (e.g. rheumatic fever)
  - Collagen disease (e.g. Marfan's syndrome)
  - Neoplastic (metastases, carcinoid syndrome)
- Congenital heart disease
- Hypertension
  - Systemic and pulmonary
- Arrhythmias and cardiac conduction disturbances
  - Tachyarrhythmias
  - Bradyarrhythmias
  - Intraventricular conduction disturbance
- High-output cardiac failure
  - Anaemia
  - Thyrotoxicosis
  - Pregnancy
  - Arteriovenous fistula
  - Liver cirrhosis
  - Paget's disease
  - Renal cell carcinoma
- Pericardial disease
  - Constrictive pericarditis
  - Pericardial effusion with tamponade

Reproduced from: Cowie MR, Poole-Wilson PA. Pathophysiology of heart failure.[3] With kind permission of Springer Science + Business Media.

Table 1

fibres. According to Starling's law, there is an initial increase in the force of contraction that helps to restore cardiac output. Eventually, however, this compensatory mechanism starts to fail and cardiac output falls, with progressive dilatation of the ventricle.

A similar process is seen in valvular disease. Regurgitant lesions cause volume overload of the ventricles whereas valve stenosis causes pressure loading. In addition, mitral stenosis causes high pulmonary pressures, leading to right ventricular failure while impairing diastolic filling of the left ventricle. The plasticity of the cardiac chambers in response to an abnormal pressure or volume load, with a change in shape, size and function, accompanied by changes at the cellular level, is termed 'remodelling'. Some of the changes observed are shown in Table 2.

In **HFPEF ("diastolic" HF)**, systolic function is preserved but there is impairment of cardiac filling during diastole. This can be visualized using Doppler echocardiography to assess flow through the mitral valve and ventricular wall movement during diastole. HFPEF becomes increasingly common with advancing age, and is typically associated with a history of hypertension or diabetes.

The end result of either HFREF or HFPEF is a fall in cardiac output, or an inadequate increase on exercise. This leads to under-perfusion of organs and activation of the baroreceptors, triggering a complex neurohumoral response. This response has the effect of increasing heart rate and blood pressure with salt and water retention — a response that is perhaps appropriate in the short term to maintain organ perfusion, but in the longer term this causes further cardiac damage.

Typically, as the syndrome progresses, left ventricular end-diastolic pressure increases, and both the ventricle and atrium enlarge. Back pressure into the pulmonary veins increases, leading to extravasation of fluid into the alveoli — pulmonary oedema. Ultimately, pulmonary artery pressure rises and the right ventricle may fail.

It is increasingly recognized that many patients with hypertrophic or dilated cardiomyopathy (where the underlying cause is not obvious clinically) have an underlying genetic defect of proteins of the sarcolemma, cell nuclear or surface membrane, or connecting proteins. Although single gene defects have been identified in many families, the situation is complex as there appears to be modification by other genes, epigenetic processes, and the environment. Specific therapies targeted at these gene defects are not yet available.

Sympathetic nervous system

Falling pressure at the baroreceptors in the carotid bodies and aortic arch leads to increased sympathetic and decreased parasympathetic nervous system activity. High concentrations of plasma noradrenaline are found in patients with heart failure, particularly in more advanced stages. The increase in sympathetic tone results in an increased heart rate and stroke volume (the volume of blood ejected from the left ventricle with each beat) and this acts to maintain cardiac output. Sympathetic activity also causes peripheral vasoconstriction, renin release, and sodium and water retention. The increased preload acts to increase cardiac output via the Starling mechanism. However, excessive vasoconstriction increases afterload, thereby increasing the work of the failing heart, the output of which subsequently begins to deteriorate. Catecholamines may also be directly toxic to the myocardium, and increase the likelihood of arrhythmia, such as atrial fibrillation or ventricular tachycardia.

Renin–angiotensin–aldosterone system (RAAS)

Under-perfusion of the juxtaglomerular apparatus of the kidney leads to upregulation of the renin–angiotensin–aldosterone pathway (Figure 1). Renin, which cleaves two amino acids from angiotensinogen to form angiotensin I, is released into the blood. Angiotensin I is then further cleaved by angiotensin-converting enzyme (ACE), particularly prevalent in the lungs, to form angiotensin II (ATII). The net result is arterial vasoconstriction, myocyte apoptosis, polydipsia, noradrenaline release with increased sensitivity of the vasculature to its actions, and vasopressin release. ATII also stimulates the release of aldosterone from the adrenal cortex. This mineralocorticoid acts on the distal convoluted tubules and collecting ducts of the kidney to enhance sodium and water reabsorption, and potassium

Abnormalities of the failing heart

- Macroscopic
  - Loss of muscle mass
  - Alteration in chamber size and shape (dilation and/or hypertrophy)
  - Incoordinate contraction and abnormal timing of contraction
- Microscopic
  - Myocyte changes (cell thinning, lengthening, hypertrophy, necrosis, apoptosis)
  - Disorganized muscle fibre orientation and myocyte slippage
  - Extracellular matrix inflammatory cell infiltrate, fibroblast expansion, and fibrosis
- Intracellular
  - Disorganized cytoskeleton
  - Impaired cell-to-cell communication (gap junctions)
  - Contractile protein structural and functional derangements
  - Deranged excitation—contraction coupling and calcium homeostasis
  - Reduced efficiency of intracellular signal-transduction pathways
  - Altered energy metabolism
  - Regression to de-differentiated 'fetal' gene expression pattern

Reproduced from: Cowie MR, Poole-Wilson PA. Pathophysiology of heart failure.[3] With kind permission of Springer Science + Business Media.

Table 2

secretion into the urine. The final result is increasing blood pressure and vascular resistance with water and salt retention leading to high pre- and after-load. In the short term these mechanisms act to maintain cardiac output and organ perfusion, but in the longer term they accelerate cardiovascular dysfunction.

Other hormones

Arginine vasopressin concentration is usually high in heart failure, thought to be secondary to reduced distension of the carotid baroreceptors. This causes translocation of aquaporin two receptors into the membranes of the collecting ducts in the kidney with subsequent water reabsorption, and contributes to the hyponatraemia seen in heart failure — a poor prognostic sign.

Atrial natriuretic peptide (ANP) is stored in the atria (and to a lesser extent in the ventricles) and is released in response to atrial distension. *B-type natriuretic peptide (BNP)* is synthesized in the ventricles and released in heart failure (along with NT-proBNP, a by-product of its cleavage from a precursor protein). BNP assays are a useful marker of heart failure. These peptides partially counteract the RAAS — they are vasodilators, and diuretics because they increase sodium secretion in the kidneys — and they also attenuate noradrenaline release.

The *endothelins* are a group of peptides that are powerful vasoconstrictors, also stimulating aldosterone release and sodium and water retention in the kidney. Endothelin concentrations are high in heart failure. Likewise, regulation of *nitric oxide*, the major vasodilator found in the vasculature, is impaired in heart failure, contributing to endothelial dysfunction.

The activation of these multiple neurohormonal systems triggers the syndrome that is recognized clinically: tachycardia, peripheral oedema, venous congestion, pulmonary oedema, cool peripheries and hyponatraemia (Figure 2). The atria and ventricles dilate and functional mitral (or tricuspid) regurgitation due to distortion of the valve rings and papillary muscles may ensue.

The clinical syndromes of acute and chronic heart failure

HF can present with gradually increasing breathlessness, fatigue and oedema or it may present acutely, either de novo or in an acute-on-chronic picture. Causes of heart failure are listed in Table 1.

Acute HF is characterized by a rapid onset of signs and symptoms due to cardiac dysfunction. There may be pulmonary oedema due to back pressure into the lungs from the failing left ventricle. Once plasma oncotic pressure is exceeded, extravasation of fluid occurs and hypoxia may ensue. Jugular venous pressure may be raised, reflecting elevated right ventricular filling pressure. The patient may be tachycardic, agitated, clammy and peripherally cyanosed due to the actions of the sympathetic nervous system. If there is significant organ hypoperfusion, confusion and renal failure may occur and the patient is said to be in cardiogenic shock — a condition with a particularly poor prognosis.

Chronic HF may present more insidiously with fatigue, breathlessness and a more gradual build-up of fluid in the lungs and periphery. In advanced stages, the patient may lose lean body mass and become cachectic. Many patients present first with an acute episode of HF, followed, if they survive, by evidence of ongoing 'chronic' HF. An acute 'decompensation' can then occur, where the syndrome rapidly becomes worse.

Treatment aims to stabilize the patient, correct the maladaptive compensatory mechanisms and treat the underlying cause of the cardiac dysfunction. This is discussed elsewhere.

Ventricular dyssynchrony

With ventricular dilatation and dysfunction, especially in the presence of a left bundle branch block pattern on the ECG, dyssynchrony may occur. This is due to disruption of the normal fast-conducting His—Purkinje system and results in uncoordinated contraction of different regions of the heart. This may be atrioventricular, interventricular or intraventricular, or a combination of all three. There is a strong evidence base for the benefit of cardiac resynchronization therapy (CRT) in such patients, in addition to optimal medical therapy. CRT involves pacing both ventricles (with leads in the right ventricle and coronary sinus) to restore coordinated contraction.

Atrial fibrillation and other arrhythmia

Raised atrial pressure is common and predisposes to AF, the onset of which may result in the development of acute HF.[4] Less commonly, chronic, rapid and irregular cardiac contraction may lead to structural changes in myocytes and the development of a 'tachycardia-associated' cardiomyopathy.

Ventricular arrhythmias are also frequent in patients with HF. The underlying cause is likely to be micro re-entry circuits set up by a combination of factors, including raised sympathetic nervous system and RAAS activity, myocardial necrosis and fibrosis,

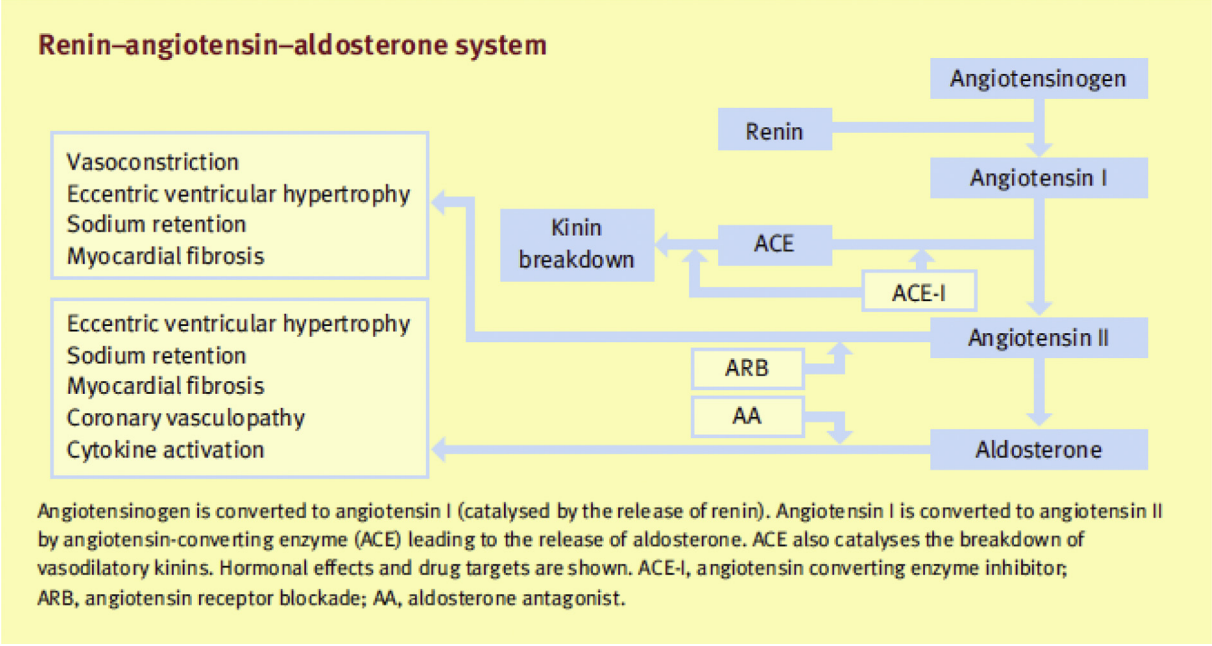


Figure 1

repolarization abnormalities, frequent ectopy, and electrolyte abnormalities. Sudden, presumed arrhythmic, death is relatively common in patients with heart failure, particularly in those with milder symptoms.[5] Those with more advanced symptoms usually die of progressive pump failure. The risk of sudden cardiac death can be reduced by neurohormonal antagonists, such as β-blockers and aldosterone antagonists, or by device therapy with cardiac resynchronization and/or implantable cardiac defibrillators.

Renal dysfunction

Many patients with HF have at least moderate renal impairment. This is usually the result of an ageing kidney with low perfusion and high venous pressure, but pre-existing damage as a result of diabetes or hypertension may exacerbate this problem.[6] Renal perfusion may worsen with intense diuretic therapy, hypotension, and RAAS antagonism.

A vicious cycle of progressive cardiac and renal dysfunction (the cardiorenal syndrome) has been recognized and is associated with a particularly poor prognosis.

Anaemia

Many patients with moderate-to-severe HF develop anaemia of chronic disease or functional iron deficiency. The mechanism appears to relate to changes in iron handling and sensitivity of the red blood cell precursors to erythropoietin. Chronic renal dysfunction also contributes through reduced erythropoietin production. Trials of intravenous iron replacement in those with iron deficiency have led to improvement in symptoms and reduced need for hospitalization,[7] although the additional use of

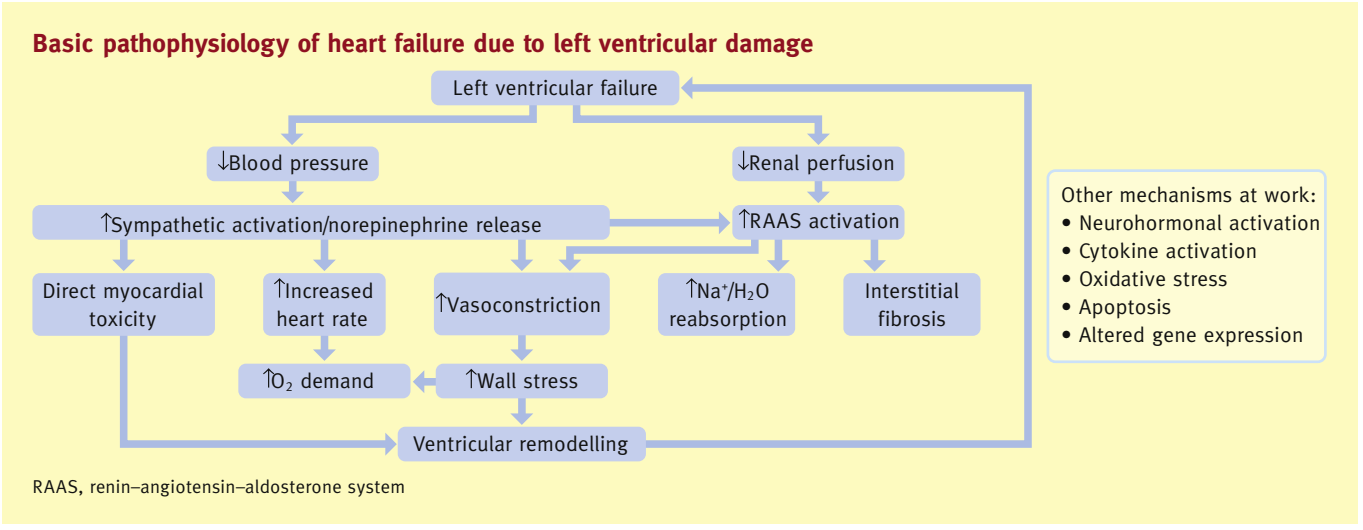
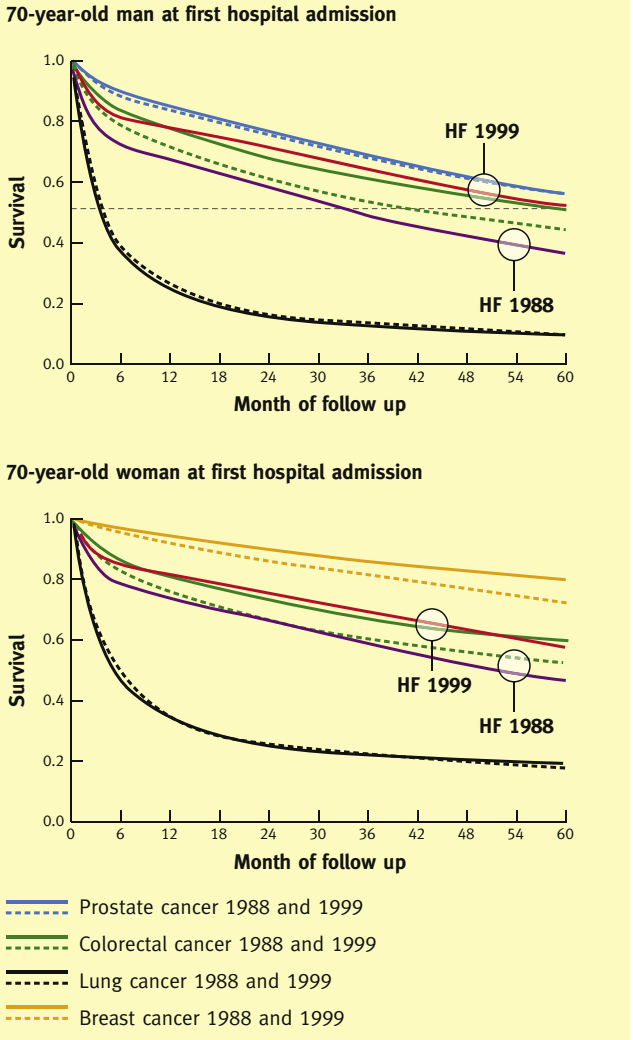


Figure 2

Five-year Kaplan-Meier survival curves from first hospital admission with heart failure and common types of cancer in Sweden – 1988 and 1999 cohorts



Reproduced with permission from: Stewart S, Ekman I, Ekman T et al. Circ Cardiovasc Qual Outcomes 2010; **3**: 573–80.[13]

Figure 3

synthetic erythropoietin may be harmful. Other causes of anaemia in patients with heart failure, such as poor diet or gastrointestinal blood loss, should not be overlooked.

Cardiac cachexia and metabolic abnormalities

Severe HF can cause a general loss of fat, lean and bony tissue, associated with a particularly poor prognosis. Cachexia is usually associated with neurohormonal and immunological changes, including raised plasma concentrations of adrenaline, noradrenaline, cortisol, renin, aldosterone and inflammatory cytokines, including tumour necrosis factor (TNF)-α, interleukins 1 and 6, interferon-γ and transforming growth factor (TGF)-β. The mechanism of such immune activation is not clear but may be related to endotoxin absorption from the oedematous gut.[8] High uric acid concentrations are also common, which may cause gout.

Skeletal muscle abnormalities

In HF there is loss of bulk (wasting), impaired intrinsic perfusion, increased (and earlier) fatigue, and underlying abnormal histology and metabolism of skeletal muscle. Patients with HF and substantial skeletal muscle wasting demonstrate exaggerated release of catabolic cytokines and resistance to growth hormone. Physical inactivity, anorexia and poor intestinal absorption are also likely to have a role, along with insulin resistance (loss of anabolic function) and raised concentrations of TNF-α and noradrenaline. Exercise training in carefully selected patients with stable mild-to-moderate CHF may improve symptoms and exercise tolerance.[9]

Sleep-disordered breathing

Around 50% of patients with advanced heart failure suffer from sleep-disordered breathing (SDB). Obstructive sleep apnoea (OSA), due to loss of pharyngeal muscle tone, is common but central sleep apnoea (CSA) becomes predominant in patients with more severe failure. In this syndrome, there is an exaggerated chemoreceptor response to arterial carbon dioxide ($PaCO_2$) largely due to excess sympathetic activity. As $PaCO_2$ rises in the blood during sleep, there is relative hyperventilation. In addition, receptors in the lungs are stimulated by pulmonary oedema to induce hyperventilation. Prolonged circulation time between the lungs and the chemoreceptors results in a lag phase and over-correction in the homeostatic mechanism that control $PaCO_2$. This drives the $PaCO_2$ below the apnoeic threshold, causing cessation of breathing (apnoea). As $PaCO_2$ rises, the cycle of hyperventilation and apnoea begins again. A particularly cyclical type of CSA is termed 'Cheyne–Stokes respiration' and is a poor prognostic sign.

Prognosis

The prognosis of HF is poor. UK data demonstrate a 6-month mortality rate of 30%, and over 40% of patients do not survive 18 months from the time of diagnosis.[10] This prognosis is worse than many common malignancies, such as breast or colorectal cancer (Figure 3).[13] Recent data from North America and Europe suggest that survival may be improving,[11] but overall prognosis remains severe, with 5-year mortality rates of around 50%.[12]

Hospitalization

Each year, 0.2% of the UK population are hospitalized for HF, accounting for 4–5% of all adult medical admissions. The average length of hospital stay is 9.5 days, second only to stroke admissions. HF is associated with high rates of repeat admission – approximately one-third of patients are re-admitted within 12 months of initial hospital discharge. Chronic disease monitoring, both by the patient and the heart failure medical/nursing team, can reduce the risk of hospitalization and improve prognosis.[14]

Cost

HF accounts for around 2% of healthcare expenditure in Europe and North America; up to 75% of this relates to the cost of hospitalization.

Future trends

As survival from cardiac disease continues to improve, the prevalence of heart failure will increase significantly in the

coming decades. With primary angioplasty for myocardial infarction, more comprehensive secondary prevention measures following MI, improved outcomes for patients with congenital and valvular heart disease and an ageing population, many experts talk of a 'heart failure epidemic' due to more individuals living with damaged hearts at risk of HF. In addition, the growing range of effective therapies available for patients with heart failure — including drugs, pacing therapies, rehabilitation and surgery — have resulted in improved prognosis and greater longevity. Closer chronic disease monitoring, allowing early detection of deterioration and access to a multidisciplinary healthcare team, is also likely to improve prognosis and reduce the need for hospitalization in the increasing number of people living with this condition. ◆

REFERENCES

1 McMurray JJV, Adamopoulos S, Anker SD, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012. *Eur Heart J* 2012; **33:** 1787–847.

2 Owan TE, Hodge DO, Herges RM, et al. Trends in prevalence and outcome of heart failure with preserved ejection fraction. *N Engl J Med* 2006; **355:** 251–9.

3 Cowie MR, Poole-Wilson PA. Pathophysiology of heart failure. In: Rosendorff C, ed. Essential cardiology. 3rd edn. New York: Springer, 2013.

4 Cleland JGF, Swedberg K, Follath F, et al. The EuroHeart failure survey programme — a survey on the quality of care among patients with heart failure in Europe: Part 1: patient characteristics and diagnosis. *Eur Heart J* 2003; **24:** 442–63.

5 Mehta PA, Dubrey SW, McIntyre HF, et al. Mode of death in patients with newly diagnosed heart failure in the general population. *Eur J Heart Fail* 2008; **10:** 1108–16.

6 Damman K, Navis G, Smilde TDJ, et al. Decreased cardiac output, venous congestion and the association with renal impairment in patients with cardiac dysfunction. *Eur J Heart Fail* 2007; **9:** 872–8.

7 Okonko DO, Grzeslo A, Witkowski T, et al. Effect of intravenous iron sucrose on exercise tolerance in anemic and nonanemic patients with symptomatic chronic heart failure and iron deficiency FERRIC-HF: a randomized, controlled, observer-blinded trial. *J Am Coll Cardiol* 2008; **51:** 103–12.

8 Von Haehling S, Lainscak M, Springer J, Anker SD. Cardiac cachexia: a systematic overview. *Pharmacol Ther* 2009; **121:** 227–52.

9 O'Connor CM, Whellan DJ, Lee KL, et al. Efficacy and safety of exercise training in patients with chronic heart failure: HF-ACTION randomized controlled trial. *JAMA* 2009; **301:** 1439–50.

10 Cowie MR, Wood DA, Coats AJS, et al. Survival of patients with a new diagnosis of heart failure: a population based study. *Heart* 2000; **83:** 505–10.

11 Mehta PA, Dubrey SW, McIntyre HF, et al. Improving survival in the 6 months after diagnosis of heart failure in the past decade: population-based data from the UK. *Heart* 2009; **95:** 1851–5.

12 Levy D, Kenchaiah S, Larson MG, et al. Long-term trends in the incidence of and survival with heart failure. *N Engl J Med* 2002; **347:** 1397–402.

13 Stewart S, Ekman I, Ekman T, et al. Population impact of heart failure and the most common forms of cancer — a study of 1 162 309 hospital cases in Sweden (1988 to 2004). *Circ Cardiovasc Qual Outcomes* 2010; **3:** 573–80.

14 McAlister FA, Stewart S, Ferrua S, McMurray JJJV. Multidisciplinary strategies for the management of heart failure patients at high risk for admission: a systematic review of randomized trials. *J Am Coll Cardiol* 2004; **44:** 810–9.

FURTHER READING

British Heart Foundation statistics website. www.heartstats.org.

Clark AL. Almanac 2013: heart failure. *Heart* 2013; **99:** 1562–6.

Dar O, Cowie M. The epidemiology and diagnosis of heart failure. In: Fuster V, Walsh RA, Harrington RA, eds. Hurst's The Heart. 13th edn. New York: McGraw Hill, 2011.

Gheorghiade M, Pang PS. Acute heart failure syndromes. *J Am Coll Cardiol* 2009; **53:** 557–73.

McMurray JJV, Adamopoulos S, Anker SD, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012. *Eur Heart J* 2012; **33:** 1787–847.

McMurray J, Petrie M, Swedberg K, et al. Heart failure. In: Camm AJ, Luscher TF, Serruys PW, eds. The ESC Textbook of Cardiovascular Medicine. 2nd edn. Oxford: Oxford University Press, 2009.

Mosterd A, Hoes AW. Clinical epidemiology of heart failure. *Heart* 2007; **93:** 1137–46.

Practice points

- Heart failure is a multisystem syndrome in which the underlying cardiac abnormality must be determined and the systemic response understood to achieve effective treatment
- The prevalence of HF is rising, mainly as a result of the ageing population and improved treatment of the acute manifestations of coronary artery disease
- Coronary artery disease (often associated with hypertension) is the single most common cause of HF in the developed world
- HF can result from systolic or diastolic dysfunction of the left (and/or right) ventricular myocardium, valve disease, arrhythmia, congenital heart disease, pericardial disease, or a combination of these problems
- HF is associated with a poor prognosis, with an 18-month mortality of at least 40%, although this has improved in the past decade
- Better understanding of the pathophysiology of HF caused by LV systolic dysfunction has led to effective therapies, including drugs and pacing devices. Optimal management of diastolic heart failure is less certain
- HF can be associated with ventricular dyssynchrony and cardiac arrhythmias, which can be treated with electrical devices in addition to appropriate pharmacological therapy
- HF is often associated with renal dysfunction, anaemia, skeletal muscle abnormalities, cachexia and sleep-disordered breathing — these are markers of a poor prognosis