Heart failure: classification and pathophysiology

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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

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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

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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

