Management of heart failure

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This short review will concentrate on concepts and issues pertinent to the management of heart failure patients in modern clinical practice, with emphasis on aspects of therapy that have not been highlighted in more recent review articles (eg Ref 1). More comprehensive reviews are to be found in specific textbooks on heart failure (eg Ref 2).

Definition of heart failure

Heart failure has either eluded definition or the attempts at definition have not met with general approval by different professional groups[3]. Many proposals by clinicians have confused the word 'definition' of heart failure with 'diagnosis'. Perhaps the best definition proposed so far is that by William Osler[4], who stated a century ago that:

> the reserve force is lost, and with it the power of meeting the demands exacted in maintaining the circulation during severe exertion.

This emphasises a hallmark of heart failure well known to many physicians, namely intolerance to severe exertion. In mild to moderate chronic heart failure, the patient is usually relatively asymptomatic at rest but becomes increasingly symptomatic as exertion increases. In very severe failure, even at maximal stimulation, the heart is unable to maintain the requisite circulation to ensure prolonged survival[5,6]. An important concept in clinical management is that heart failure, whatever the cause, represents a condition of erosion of reserve cardiac function.

Adopting this conceptual framework provides a better perspective and a more rational approach to management. Thus, correction of remediable cardiac defects would revert the reserve function of the heart towards normal (Fig 1), and perhaps thereby obviate the need for heart failure medication (eg diuretics, angiotensin converting enzyme (ACE) inhibitors and beta-blockers).

It also allows differentiation of true heart failure from *relative* heart failure. An example of the latter is the so-called 'high output' heart failure, in which the arteriovenous shunting in the systemic circulation means that a full use of cardiac reserve is required to supply adequate blood flow to the metabolising tissues, while the blood flow through the shunts is effectively wasteful. The demands on the heart may be so excessive that symptoms of heart failure ensue despite the heart itself being structurally and functionally normal. Provided that the heart has not reached a decompensated state, correction of the volume overload leads to the resolution of heart failure. Similarly, in severe hypertension, the demands on the heart may become so excessive that the normal cardiac reserve fails to provide the requisite output, resulting in heart failure symptoms; these also vanish if the pressure overload is removed. A helpful analogy is that a human heart with a normal reserve cannot be expected to maintain the circulation of a giraffe or an elephant. Therapy in these circumstances should be directed towards normalising the excessive load, not towards stimulating the heart.

Treatment considerations based on pathophysiology

Primary defects

The initiating event in heart failure is damage or malfunction affecting any component part(s) of the cardiac structure which results in impairment of function leading to symptoms. The damage may affect the myocardium (through infarction or myocarditis), the valvular apparatus(es), the pacemaker and/or conducting tissues, and the pericardium. Such malfunctions constitute the primary defects in heart failure.

Treatment of primary defects. Having established the presence of heart

Key Points

- **Heart failure should never be considered as a final diagnosis**
- **Excessive load on a normal cardiac pump may result in clinical features of congestion or low output. This is *relative* heart failure and treatment should be directed primarily at reducing the load**
- **The therapeutic strategy should be to alleviate symptoms, preserve pump function, prolong life and avoid iatrogenic complications**
- **Diuretics remain essential for rapid and sustained relief of symptoms and improved quality of life**
- **Electrolyte imbalance is a frequent complication of diuretic therapy and should be closely monitored and corrected, ideally maintaining serum K^+ around 4.5 mmol/l with addition of K-sparing diuretics**
- **ACE inhibition and beta blockade improve prognosis but the doses need careful adjustment to optimise effects on quality and quantity of life, especially in the older heart failure population with disabling symptoms**

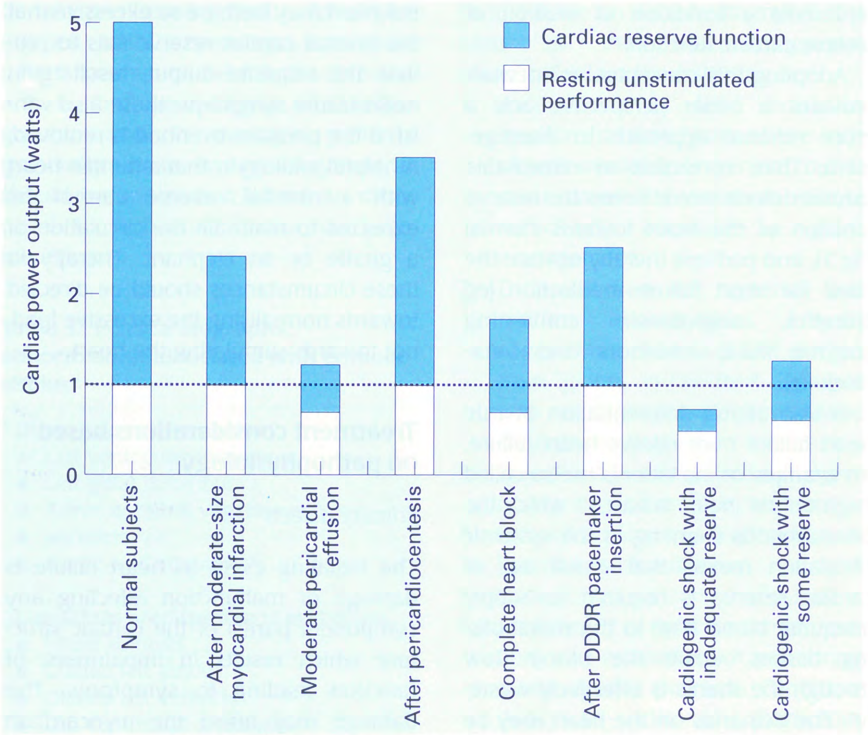

Fig 1. Reserve function of normal and diseased hearts. Cardiac performance is represented by the cardiac power output (CPO) (useful work output per second) (dashed horizontal line = baseline resting power output of an average-sized normal adult human). With effective treatment, such as pericardiocentesis or pacing, cardiac function may be improved towards normality (DDDR = rate-responsive dual chamber cardiac pacing).

failure, a rational approach to management is critically dependent on the aetiology, particularly when the cause is remediable, whether through surgical or medical interventions. These include valve repair or replacement, closure of septal defects, pericardiocentesis, pericardiectomy, pacemaker insertion, cardioverter/defibrillator implantation, coronary bypass surgery or angioplasty, or medical therapy using anti-arrhythmic, anti-ischaemic or cardioprotective agents.

Not all primary defects, however, are amenable to corrective treatment. These include:

- systolic left ventricular dysfunction secondary to myocardial infarction (the most common defect in Western societies).
- idiopathic dilated cardiomyopathy, which accounts for a smaller proportion of cases of systolic dysfunction and can be diagnosed if specific forms of heart muscle disease have been excluded.
- diastolic ventricular dysfunction, often linked to left ventricular hypertrophy; it usually results from chronic hypertension but may also be also secondary to rarer forms of myocardial infiltration.
- systolic and diastolic dysfunction, which frequently coexist particularly with underlying ischaemic heart disease.
- various systemic diseases, such as diabetes mellitus, dysthyroidism, amyloidosis, sarcoidosis, haemochromatosis and beri-beri, which may also present with heart failure.

Treatment objectives in these situations should be aimed at dealing with the underlying causes in an attempt to preserve cardiac function through preventing further damage.

Cardiologists are increasingly aware of the possibility of patients with hibernating myocardium[7,8] or silent ischaemia[9] presenting with heart failure symptoms such as dyspnoea on exertion. Treatment is achieved bascially by relief of ischaemia and coronary stenoses, when feasible, in preference to standard heart failure therapy (see below).

Secondary defects

The persistence of heart failure secondary to the above primary defects triggers secondary defects via compensatory mechanisms and neurohumoral activation: the worse the heart failure, the greater the extent of such activation. The sympathetic and renin-angiotensin-aldosterone systems are the key ones activated, although there is also release of other factors, including vasopressin, endothelins and natriuretic peptides[10]. This activation initially tends to maintain systemic arterial pressure (through vasoconstriction) and cardiac output (through fluid retention and the Starling effect), respectively increasing the afterload and preload to the failing ventricle. However, detrimental effects are also triggered, the most important being arrhythmia and ongoing myocardial apoptosis[11], necrosis[12,13] and fibrosis[14]. The ability of ACE inhibitors and beta-blockers to suppress these detrimental effects is probably a major reason for their beneficial effects on prognosis in heart failure trials.

With the persistence of cardiac failure, symptoms of congestion, dyspnoea, hypoperfusion and fatigue become evident, with the added disadvantages of increased ventricular loading, renal hypoperfusion and dysfunction, pulmonary congestion, hypoxia (when pulmonary oedema is severe), gut oedema leading to malabsorption (eg of medication), malnutrition, cachexia and endotoxaemia[15].

Treatment of secondary defects. Fluid retention and concomitant congestion should be treated with diuretics. There is no evidence that the latter are beneficial in terms of prognosis but, in view of their marked symptomatic and functional benefits, it is considered

unethical to withhold diuretics from congestive cardiac failure patients. Loop diuretics have been shown to improve exercise ability by more than 90%[16], while other therapeutic approaches achieve much less[17,18].

It is accepted that diuretics are the first-line therapy for heart failure. The European Working Group Guidelines[19] even recommend a trial of loop diuretic therapy as a guide to the diagnosis of heart failure. In all the ACE inhibitor, beta-blocker and angiotensin-receptor blocker trials in heart failure that showed survival benefits, therapy at recruitment included diuretics[20–23].

The compensatory arterial vasoconstriction imposes higher afterload on the heart; this can be treated by arterial vasodilators, but with varying effects, for example:

- alpha-adrenergic blockers neither improve exercise tolerance[24] nor prognosis[25]
- ACE inhibitors do not usually improve exercise tolerance[17], but can markedly improve prognosis in more severe cardiac failure[20,21,26]
- preferential vasodilation with dopaminergic (DA_1) agonism, using low-dose dopamine or dopexamine, may help renal and splanchnic hypoperfusion[27–29]
- venodilators (eg nitrates) are effective in relieving excessive cardiac preload[30].

The therapeutic strategy should be directed towards optimising the beneficial compensatory mechanisms, without the accompanying deleterious effects (Table 1). If treatment of the primary defect is either awaited or ruled out, management may be directed towards palliative (symptomatic relief) or preventive/prophylactic therapy to slow the rate of progression of heart failure and avert sudden death, while avoiding iatrogenic complications.

Tertiary defects

Therapy directed at the secondary defects is necessary, but may itself be problematic and it requires great skill to implement. Powerful loop diuretics are highly effective at relieving congestion but, especially in combination with metolazone or other thiazides, they can produce detrimental effects, such as hypokalaemia, hypomagnesaemia and hyponatraemia (all of which are arrhythmogenic), overdehydration, renal

Table 1. Management of heart failure based on pathophysiology.

Defects	Management
Primary (cause of cardiac pump dysfunction)	
Pericardial effusion	Pericardiocentesis
Pericardial constriction	Pericardiectomy
Valvular disease	Valve repair/replacement
Valve stenosis	Valvotomy/valvuloplasty, valve replacement
Intracardiac shunts	Repair of shunts
Heart block	Pacemaker insertion
Myocardial ischaemia/hibernation	Coronary revascularisation
Significant primary arrhythmia	Cardioversion, ablation, AICD, antiarrhythmics, treat ischaemia
Secondary (partly through neurohumoral activation)	
Fluid retention and congestion	Fluid restriction, diuretics, venodilators
Vasoconstriction	Vasodilators, ACE inhibitors, A II blockers
Flow redistribution	ACE inhibitors, low-dose dopamine, inotropes
Neurohumoral abnormality	ACE inhibitors, beta-blockers, A II blockers
Organ hypoperfusion	Inotropes, fluid infusion if required
Arrhythmia	Correct tertiary defects, treat myocardial ischaemia, anti-arrhythmics
Tertiary (secondary to therapeutic attempts)	
Electrolyte imbalance	Monitor biochemistry, correct imbalance, potassium-sparing diuretics, ACE inhibitors
Arrhythmia	Avoid pro-arrhythmic agents, correct electrolyte imbalance
Ongoing myocardial injury	ACE inhibitors, beta-blockers, avoid excessive inotropes
Organ hypoperfusion	Adjust diuretics dosage, judicious fluid replacement
Maldistribution of flow	Avoid alpha-adrenergic inhibitors
Skeletal muscle deconditioning	Avoid bed rest, exercise rehabilitation

A II = angiotensin II
ACE = angiotensin-converting enzyme
AICD = artificial implantable cardioverter defibrillator

dysfunction (especially in combination with ACE inhibitors), and further activation of the renin-angiotensin-aldosterone system with its attendant harm. Preservation of renal function in patients with heart failure is vitally important because heart failure is virtually impossible to treat medically without functioning kidneys. Haemodialysis or haemofiltration is invasive and not well tolerated by these patients.

Hypokalaemia and hypomagnesaemia. Hypokalaemia is a well known side effect of diuretic therapy. Potassium supplementation is frequently prescribed, but often fails to correct the accompanying hypomagnesaemia (which is also arrhythmogenic)[31]. Measurement of serum magnesium does not reflect the more important cellular hypomagnesaemia which is much more difficult to measure[32]. Replacement therapy for both hypokalaemia and hypomagnesaemia is necessary if patients are severely deficient or in the presence of troublesome arrhythmia. Combination therapy with potassium-sparing diuretics (which are also magnesium-sparing) is indicated, but close monitoring of electrolytes is essential in renal dysfunction.

There is a current misconception that potassium-sparing therapy must be stopped when an ACE inhibitor is added to loop diuretic therapy, but in fact ACE inhibitors are relatively weakly potassium-sparing, and are thus unlikely to counterbalance the potassium and magnesium losses by loop diuretics, except in renal dysfunction. The potassium-sparing diuretics should therefore be continued, adjusting the dose to maintain the serum potassium at about 4.5 mmol/l. The recently presented RALES II study confirms that spironolactone added to ACE inhibitor therapy confers a significant survival benefit of 27% (American Heart Association meeting, November 1998; unpublished data). Spironolactone can cause gynaecomastia and mastalgia in men, and amiloride or triamterene may be used instead.

Hyponatraemia. Hypokalaemia and hypomagnesaemia are relatively straightforward to correct but hyponatraemia is very difficult to manage in heart failure. It often occurs when the patient is still congested. Continuing high doses of diuretics usually exacerbate the hyponatraemia, while withholding diuretics or sodium replacement worsens the congestion. Stringent fluid restriction may be necessary, but is poorly tolerated. Treatment with a specific vasopressin (V_2) antagonist is required but such an agent is not yet available. In severe hyponatraemia, dialysis or haemofiltration may be necessary. It is therefore vital to try to avoid the onset of hyponatraemia both by monitoring electrolytes assiduously and by careful use of diuretic therapy.

Renal dysfunction and failure. Overdiuresis and relative dehydration may reduce the preload too much, thereby exacerbating systemic vasoconstriction and hypoperfusion of vital organs, one manifestation of which is increased serum urea and creatinine. If protracted, the renal dysfunction may progress to renal failure. Prompt treatment is required by reducing diuretic dosage and, if necessary, fluid replacement. In some patients, it may be necessary to compromise, allowing a small amount of oedema to avoid overdiuresis and to preserve renal function.

Treatment of tertiary effects. The beneficial effects of ACE inhibitors on prognosis are well known[20,21,26], but their impact on renal function and quality of life less so[33]. In unilateral renal artery stenosis, ACE inhibitor and angiotensin II receptor (AII) blockade can cause chemical autonephrectomy, and simply monitoring serum urea and creatinine levels may not reveal any renal impairment if the contralateral kidney is functioning satisfactorily. In significant bilateral renal stenosis, these drugs will cause renal failure. It is now considered inexcusable not to check serum urea and creatinine before and after initiation of either ACE inhibitors or AII blockers. If renal artery stenosis is suspected, prior investigation is necessary before their administration.

Like other arterial vasodilator agents, ACE inhibitors and AII blockers are antihypertensive, so overvasodilatation may occur leading to dizziness and potential syncope, especially in hypotensive patients with severe heart failure. This may arise subclinically during exercise, thus compromising exercise ability[34]. Cough may sometimes also be dose-related to some extent.

High-dose ACE inhibitors are recommended on prognostic grounds (ATLAS study, presented at the American College of Cardiology Meeting, March 1998; unpublished data), but this should be balanced against the likely impacts on quality of life. An aggressive approach may not be in the best interests of patients whose quality of life is further compromised by high-dose therapy.

Until recently, beta-adrenergic blockers were considered to be contraindicated in heart failure because of their negative inotropic and chronotropic effects. They are now accepted as effective treatment[22,23] because, on balance, their beneficial cardiopreserving properties are more prominent in heart failure. Slow introduction and careful titration of dose upwards is essential, and readjustment of other concurrent medication may be necessary.

Acute versus chronic heart failure

One fundamental pathophysiological difference between acute and chronic heart failure that is relevant to management is often overlooked. In acute failure (in the presence of pulmonary or systemic oedema) or in cardiogenic shock, the circulation is inadequate to meet the requirements for tissue metabolism at rest, even when the compensatory mechanisms are fully activated and all the cardiac reserves are exhausted[6]. In contrast, in ambulatory chronic heart failure patients, the circulation is adequate at rest, and the cardiac reserve becomes

exhausted only during varying degrees of exertion.

This difference explains why some treatments prove effective only in acute failure *or* in chronic failure. For instance, positive inotropic agents, which are useful in acute failure and cardiogenic shock, have not been beneficial in chronic heart failure[35–39]. Similarly, beta-blockade and ACE inhibitors are not helpful in cardiogenic shock and may be detrimental in acute failure. It is therefore vitally important to apply specific therapy to the appropriate subcategories of heart failure. (A summary of the management of acute heart failure is shown in Table 2).

Table 2. Management of acute heart failure

• Oxygen therapy	PEEP if wheezy; ventilate if pCO_2 >7 kPa
• Analgesic and anxiolytic	Beware respiratory depression of diamorphine
• Reduce preload	Patch or iv nitrates, loop diuretics, inodilators
• Promote diuresis	iv diuretics, low-dose dopamine, dopexamine
• Pre-shock syndrome	Recognition, prophylactic treatment, prevent deterioration into shock
• Treat cause	Diagnosis Control arrhythmia and heart rate Lower blood pressure if hypertensive Seek surgically treatable conditions

iv = intravenous
PEEP = positive end-expiratory pressure

Systolic versus diastolic heart failure

Similarly, therapy beneficial in systolic heart failure may not prove effective in diastolic heart failure. Most of the large randomised controlled trials of therapeutic agents apply to systolic heart failure (with low left ventricular ejection fractions as an inclusion criterion)[20–22]. There are no data showing that ACE inhibition or beta-blockade is conclusively beneficial in patients with primarily diastolic heart failure, partly because methods for diagnosing diastolic heart failure are not, in general, clinically applicable[19]. (For a proposal of practical therapeutic strategies to deal with diastolic heart failure, see Ref 40.)

Quality versus quantity of life

Determination of life or death is simple and unambiguous, so it is easier to obtain definitive outcome data about *quantity* of life as opposed to *quality* of life. Large-scale clinical trials investigating the effects of ACE inhibitors and beta-blockers are conclusive about survival benefits, but less so about their impact on quality of life, symptom scores and exercise capacity[17,33,41,42]. In applying these trial results to clinical practice, therefore, it is important to consider the total well-being of patients. For instance, the prime concern of patients of advanced age with very poor quality of life is often not so much about years of life remaining but rather about the expected quality of those years.

The initiation of any therapy to extend life is basically an act of faith: the prescriber of that therapy believes that it will prolong life. There is no direct way of proving or disproving that a certain prescription actually prolongs the life of any individual patient being treated, unless the timing of death can be predicted definitely. Surrogate end-points are not reliable. In contrast, if the aim of the therapy is to improve quality of life, it can be adjusted and readjusted either depending on symptoms experienced by an individual patient or through objective evaluation of exercise capacity. It may therefore be argued that, despite the lack of data on positive survival benefits, prescribing diuretics, digoxin or other agents to improve symptoms and other aspects of quality of life is justifiable provided that due attention is paid to the patient's well-being.

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