Heart failure management

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Patients with heart failure have a shorter life expectancy and experience symptoms that can reduce their quality of life. Their management involves three key elements: addressing lifestyle issues (see Box 1, p121), optimising drug therapy and using non-pharmacological interventions appropriately. The aims of treatment are to:

- Reduce the risk of mortality
- Delay disease progression
- Control symptoms
- Improve quality of life

From a cardiologist’s point of view, there is always a strong focus on reducing the risk of mortality for patients diagnosed with cardiovascular diseases. However, this must be balanced against the needs and wishes of patients who are often more concerned with day-to-day symptom control to allow them to carry out the normal activities of living (see section on diuretic treatment, p125). Clinicians should therefore pay as much attention to quality-of-life issues as they do other, more robust, end-points.

The prognosis for heart failure patients has been revolutionised over the past two decades by the introduction of several drug classes targeting the two biological pathways implicated in progression of the disease:

- The renin-angiotensin-aldosterone system (RAAS)
- The sympathetic nervous system

Activation of the RAAS

A fall in cardiac output causes stimulation of the RAAS. In an attempt to improve blood pressure and renal perfusion, this causes peripheral vasoconstriction, sodium and water retention, and stimulation of the sympathetic nervous system. Although this may be beneficial in the short term, it results in increased myocardial workload, which can exacerbate chronic heart failure and lead to further disease progression.

Medicines that block the RAAS have been shown to improve long-term prognosis and day-to-day quality of life significantly. Figure 1 (p122) shows the RAAS and how particular medicines affect it.

ACE inhibitors The central role of angiotensin-converting enzyme (ACE) inhibitors in managing all classes of heart failure is well established. ACE inhibitors block the conversion of angiotensin I to angiotensin II, the latter causing many of the effects of RAAS stimulation. ACE inhibitors have been shown to improve heart failure outcomes in several clinical studies. A meta-analysis has concluded that ACE inhibitors reduce mortality and cardiovascular hospital admissions by around 35% in patients with heart failure caused by left-ventricular systolic dysfunction. According to National Institute for Health and Clinical Excellence guidelines (“Management of chronic heart failure in adults in primary and secondary care”), all patients with impaired left-ventricular systolic function should be considered for treatment with an ACE inhibitor,

SUMMARY

Heart failure is a complex syndrome requiring multiple interventions to optimise outcomes. Drug therapy, in particular with ACE inhibitors and beta-blockers, is the mainstay of treatment for most patients and significantly reduces mortality and morbidity.

Care should be taken to manage patients holistically to ensure lifestyle issues are addressed and symptoms are controlled alongside optimising drug therapies to improve outcome. Clinicians managing heart failure also need to ensure that comorbidities are addressed and consider whether other, non-pharmacological interventions would be beneficial.

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regardless of whether or not they are experiencing symptoms (see Figure 2, p124).

Initiating ACE inhibitors for patients with heart failure rarely presents a major challenge in clinical practice. Doses should start low and be titrated up over a few weeks until they reach the doses used in clinical studies. In the “Assessment of treatment with lisinopril and survival” (ATLAS) study, higher doses of lisinopril (32.5–35mg daily) reduced hospital admissions significantly when compared with low doses (2.5–5mg daily), and displayed a trend towards reduced mortality.2

A low initial dose is necessary to avoid first-dose hypotension. However, this problem is uncommon with longer-acting agents (eg, ramipril, lisinopril). Hypotension itself is not a contraindication to treatment; ACE inhibitors can be initiated safely for patients with a systolic blood pressure as low as 85–90mmHg. However, serum creatinine must be monitored cautiously for these patients to ensure renal perfusion has not been compromised.

ACE inhibitors should be avoided for patients with bilateral renal artery stenosis and those with a history of angioedema — a rare but serious adverse effect caused by accumulation of bradykinin during therapy. Patients with aortic stenosis should be referred for specialist review before starting ACE inhibitor treatment.

Raised creatinine is not a contraindication to therapy, but generalists may opt to refer patients with a history of significant renal dysfunction (serum creatinine >200µmol/L) to a specialist heart failure service or renal consultant for initiation of treatment.

**Monitoring** Renal function should be monitored before and within a month of starting therapy, and when changing doses, and at least six-monthly thereafter. A rise in creatinine is expected when an ACE inhibitor is initiated, but the action taken should be determined according to the magnitude of the rise (see Box 2, p122).

Hyperkalaemia is a potential problem during therapy. However, cessation of ACE inhibitor treatment should only be considered if serum potassium is >6mmol/L. Mildly raised potassium levels (5–6mmol/L) can often be managed by dietary modifications — patients should be advised not to eat foods containing high levels of potassium (eg, bananas, tomatoes and citrus fruits).

Patients often complain of a dry, irritating cough, which is caused by bradykinin accumulation. Although this troublesome side effect can fade over time, or disappear if an alternative ACE inhibitor is prescribed, it often persists and causes substantial disruption to patients and their partners, particularly if it occurs at night. In this circumstance, clinicians should consider switching the patient to an angiotensin-II receptor blocker (ARB).

Other adverse effects of ACE inhibitors include hypotension (which may limit how far the dose can be titrated), voice changes and rashes.

**Angiotensin receptor blockers** ARBs reduce RAAS activity by blocking the angiotensin-II receptor site. The evidence base to support using ARBs to treat heart failure is weaker than for ACE inhibitors, with three key clinical trials informing practice.

The “Losartan heart failure survival” (ELITE-II) study tested whether losartan was superior to captopril in patients with heart failure, but failed to demonstrate this.3 The “Valsartan heart failure trial” (Val-HeFT), which investigated the addition of valsartan to standard heart failure therapy, demonstrated a reduction in hospital admissions but not in overall mortality.4 Finally, the “Candesartan in heart failure assessment of reduction in mortality and morbidity” (CHARM) study considered candesartan as an alternative treatment for patients intolerant to ACE inhibitors and, in its second arm, candesartan in addition to standard treatment, including an ACE inhibitor.5,6 It reported that using candesartan resulted in a significant reduction in
mortality and morbidity in both arms, although the benefit was small for patients already taking ACE inhibitors.

The place of ARBs in the treatment of heart failure remains debatable. Because ACE inhibitors and ARBs have not been compared in a robust head-to-head study, current evidence supports the use of ACE inhibitors wherever possible. However, an ARB should be considered for any patient unable to tolerate ACE inhibitors.

The question remains as to whether ARBs should be added to ACE inhibitor therapy to improve outcomes further. The impact that prescribing this extra medicine might have on adherence should be considered. Most clinicians in the UK do not prescribe ARBs and ACE inhibitors together routinely to treat heart failure if ACE inhibitor therapy is optimised and symptoms are well controlled. At the time of writing, candesartan is the only ARB licensed for the treatment of chronic heart failure in the UK.

Aldosterone antagonists The third class of medicines used to block the effects of RAAS stimulation are the aldosterone antagonists, in particular spironolactone. The evidence base for spironolactone relies on the results from the “Randomized aldosterone evaluation study” (RALES), published in 1999. In this placebo-controlled study of patients with severe heart failure, all-cause mortality was 35% in the low-dose spironolactone group, compared with 46% in the placebo group ($P=0.0001$).7 Those in the treatment group were also less likely to be admitted to hospital.

Spironolactone is now used to treat patients with severe chronic heart failure-related symptoms and those with frequent episodes of acute fluid overload. NICE endorses the use of spironolactone for patients who remain symptomatic despite optimal treatment with ACE inhibitors and beta-blockers. For this indication, spironolactone is prescribed at a low dose (25mg daily initially, increasing to 50mg daily after a few weeks if symptoms persist).

**Monitoring** Hyperkalaemia is common among patients prescribed aldosterone antagonists. If it occurs, the dose of spironolactone may need to be reduced to 25mg on alternate days (or 12.5mg daily). If the potassium level still remains raised, treatment will need to be stopped. Advice on avoiding food containing high levels of potassium should be given whenever hyperkalaemia occurs. Some patients experience a decline in renal function; serum creatinine and electrolytes should be checked within one week of starting treatment, then again after four, eight and 12 weeks, and every three to six months thereafter. Spironolactone should be stopped if serum creatinine rises above 200µmol/L.

Gynaecomastia can occur during spironolactone treatment (because of the drug’s effect on androgen and progesterone receptors), which might necessitate cessation of treatment if it proves troublesome for the patient. Those patients who have responded well to spironolactone could be considered for treatment with eplerenone, a newer aldosterone antagonist, although this medicine is not licensed to treat chronic heart failure. Other adverse effects of spironolactone include nausea, vomiting and diarrhoea.

**Sympathetic nerve activity** As well as stimulating RAAS activity a fall in cardiac output stimulates baroreceptors, which leads to activation of the sympathetic nervous system. This increases the rate and force of myocardial contraction and, hence, increases cardiac output. As with activation of the RAAS, this response is helpful in the short term but, in the long term, increases the pressure on an already failing heart and raises the risk of arrhythmias and episodes of ischaemia. Despite these deleterious effects, patients with chronic heart failure become dependent on this sympathetic overdrive to maintain their cardiac output. Therefore, blockade of this system must be undertaken slowly and cautiously to avoid precipitating an acute deterioration in heart failure status.

**Beta-blockers** Beta-adrenoceptor blockers are the only class of medicines used to suppress sympathetic activity in
the management of chronic heart failure. They have been studied in several clinical trials and have shown to reduce mortality due to heart failure by about a third, which includes a significant reduction in the risk of sudden cardiac death. NICE recommends that all patients with symptomatic heart failure due to left ventricular systolic dysfunction (New York Heart Association classes II–IV) should be prescribed a beta-blocker regardless of whether or not they are experiencing symptoms.

Beta-blockers must be started at lower doses than those used to treat angina or hypertension (eg, bisoprolol at 1.25mg daily, carvedilol at 3.125mg daily and nebivolol at 1.25mg daily). The licences for these medicines advise that only clinicians with experience of managing heart failure should initiate beta-blocker therapy. Doses should be titrated slowly over at least two to three months, as determined by the patient's response — the aim being to attain a resting heart rate of 50–60 beats/min.

Heart failure symptoms can be exacerbated during the initiation and dose-titration phases as the body adjusts to a slower heart rate and reduced force of cardiac contraction. Patients should be informed that increased breathlessness or ankle swelling is not uncommon during the first few days of treatment and be advised of what to do if these symptoms become pronounced or troublesome. This can include increasing their diuretic dose temporarily to help control these symptoms, or seeking help from their GP or local heart failure team. Patients with significant symptoms after dose titration may need to have their next dose escalation delayed for several weeks to allow such effects to stabilise or, occasionally, may need their dose to be stepped back down.

**Contraindications** Beta-blockers are contraindicated for patients with severe bronchial asthma or severe chronic obstructive pulmonary disease, evidence of current significant fluid overload, sinus bradycardia (heart rate <50beats/min) or symptomatic hypotension (systolic blood pressure <90mmHg).

Although mild-to-moderate reversible airways disease is not an absolute contraindication to beta-blocker use in heart failure, affected patients should be referred to a specialist heart failure service where lung function can be assessed fully and, if appropriate, a cardioselective beta-blocker introduced cautiously.

Heart rate and blood pressure should be checked before, and within one month of, starting beta-blocker treatment. Before starting treatment for patients with a heart rate below 60beats/min, an electrocardiogram (ECG) should be obtained to exclude heart block.
Comorbidities
Atrial fibrillation (AF) exacerbates the symptoms of heart failure and ventricular rate control is therefore important for patients with this condition. Such patients should be optimised on beta-blockers and considered for treatment with digoxin. Direct current cardioversion may be used to achieve sinus rhythm, with amiodarone added to improve success rates for patients who fail to cardiovert initially.

Digoxin may improve symptom control and reduce hospital admissions for patients in sinus rhythm with ongoing symptoms. However, the data to support this treatment predate the routine use of beta-blockers.

It is essential to ensure intensive control of blood pressure (in hypertensive patients), blood glucose (in diabetic patients) and angina. Treatments such as statins and aspirin should be prescribed for the primary and secondary prevention of cardiac events as appropriate.

Diuretic treatment
The most common symptoms of heart failure are breathlessness (due to pulmonary congestion and peripheral oedema), ankle swelling and abdominal distension. Therefore, the management of day-to-day symptoms relies primarily on the appropriate use of diuretic medicines. Loop diuretics, such as furosemide or bumetanide, promote substantial diuresis in most patients. Furthermore, doses of these medicines can be titrated up or down according to the patient’s diuretic needs.

Patients are usually advised to weigh themselves daily — on waking and after voiding — and can be taught to manage their own diuretic doses according to daily fluctuations in weight.

Some patients are prone to sudden episodes of fluid overload that are resistant to oral loop diuretics despite dose increases. A hospital admission is often necessary for such patients to be treated with intravenous diuretics, since 500ml to 1L of fluid may need to be removed per day.

Alternatively, the addition of a thiazide or thiazide-type diuretic (eg, metolazone) to loop diuretic treatment can lead to profound diuresis, and must be approached with caution. Most clinicians prescribe a low dose of metolazone (2.5–5mg every other day) to encourage a controlled diuresis and reduce the risk of causing renal dysfunction.

Some primary care providers and hospital day-case centres now prescribe courses of intermittent metolazone or administer loop diuretic infusions to reduce the need for hospital admission for patients with chronic, resistant fluid overload. Such patients must be instructed to restrict their fluid intake to approximately 1L per day and limit their salt intake.

Monitoring During long-term treatment with diuretics, patients’ renal function should be monitored every six months. Particular attention should be paid to serum levels of sodium, creatinine and potassium due to the risk of precipitating hypokalaemia, renal dysfunction and hypouricaemia. Care should also be taken to avoid overdose, which can present as excessive thirst alongside raised serum creatinine and, in particular, raised urea.

In some patients it is difficult to achieve adequate diuresis to control heart failure symptoms without precipitating renal failure and hyperkalaemia, so a suitable compromise will need to be reached. Other problems that can occur as a result of treatment with diuretics include hypotension, tiredness and gout.

Conclusion
Heart failure management is best addressed by a multi-disciplinary team approach. The team should include cardiologists, GPs, nurses and pharmacists.

Non-pharmacological interventions
There are several non-pharmacological interventions that can help to manage heart failure. These include:

- Revascularisation — percutaneous coronary intervention or coronary artery bypass surgery aim to reperfuse the damaged myocardium in selected patients with ischaemic heart disease
- Chronic resynchronisation therapy (CRT) — biventricular pacemakers can be implanted to improve myocardial pump function in patients with class III or IV heart failure and evidence from an electrocardiogram of ventricular dyssynchrony despite optimal drug treatment
- Implantable cardiac defibrillators — these reduce the risk of sudden cardiac death by delivering low- or high-voltage electrical impulses to the heart if ventricular tachycardia or ventricular fibrillation occurs.
- They are used primarily in ischaemic patients with left ventricular dysfunction and previous evidence of ventricular tachycardia
- Ventricular assist devices — although used relatively infrequently, these implantable pumps are used to support the left ventricle and maintain cardiac output in patients awaiting an intervention, such as heart transplantation, or to allow the myocardium time to recover following an acute event

Heart transplantation can also be considered for patients with end-stage heart failure (life expectancy of 12–18 months and class III or IV heart failure) that is refractory to medical therapy and CRT.

References