Improving treatment of systolic heart failure

People with systolic heart failure should be treated with angiotensin-converting enzyme (ACE) inhibitors and heart failure specific beta blockers to reduce morbidity and mortality. The most recent NPS clinical audit in heart failure patients suggests these guidelines are being followed. But there are still areas where treatment is not optimal. This NPS News outlines ways to further improve the treatment of systolic heart failure.

Use an ACE inhibitor in all grades of systolic heart failure

ACE inhibitors reduce mortality and morbidity in people with symptomatic and asymptomatic left ventricular systolic dysfunction.\textsuperscript{1-5} NPS audit data shows that almost everyone (90%) with systolic heart failure who does not have a contraindication for treatment with an ACE inhibitor or an angiotensin II-receptor antagonist is taking one. However, a considerable number were using an ACE inhibitor dose that was below the recommended target range (Table 1). ACE inhibitors have proven survival benefits at the doses used in randomised controlled trials; attempt to titrate doses to reach this range.\textsuperscript{4,5} Diuretic doses may need to be altered if patients experience worsening renal function or hypotension.\textsuperscript{6} If reaching the target dose level of the ACE inhibitor is difficult because of intolerable adverse effects, titrate to the highest tolerated dose as this may still be beneficial.\textsuperscript{6,7} Angiotensin II-receptor antagonists also reduce mortality and morbidity but are no more effective than ACE inhibitors.\textsuperscript{8-11} They are an acceptable alternative for people unable to tolerate ACE inhibitors.\textsuperscript{5}

Most people with symptomatic heart failure will also require diuretic therapy.

Table 1: Recommended daily dose of ACE inhibitors\textsuperscript{12,13}

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting dose</th>
<th>Target maintenance dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>captopril</td>
<td>6.25 mg three times daily</td>
<td>25–75 mg twice daily</td>
</tr>
<tr>
<td>enalapril</td>
<td>2.5 mg daily</td>
<td>10–20 mg twice daily</td>
</tr>
<tr>
<td>fosinopril</td>
<td>5–10 mg daily</td>
<td>20–40 mg daily</td>
</tr>
<tr>
<td>lisinopril</td>
<td>2.5 mg daily</td>
<td>20–40 mg daily</td>
</tr>
<tr>
<td>perindopril arginine</td>
<td>2.5 mg daily</td>
<td>5–10 mg daily</td>
</tr>
<tr>
<td>perindopril erbumine</td>
<td>2 mg daily</td>
<td>4–8 mg daily</td>
</tr>
<tr>
<td>quinapril</td>
<td>5 mg daily</td>
<td>20–40 mg daily</td>
</tr>
<tr>
<td>ramipril</td>
<td>2.5 mg daily</td>
<td>5–10 mg daily</td>
</tr>
</tbody>
</table>
Box 1: New York Heart Association (NYHA) grading for heart failure symptom severity

<table>
<thead>
<tr>
<th>Class</th>
<th>Symptom Description</th>
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<tbody>
<tr>
<td>I – Asymptomatic</td>
<td>No limitations in normal physical activity</td>
</tr>
<tr>
<td>II – Mild</td>
<td>Slight limitation of physical activity. Ordinary physical activity results in fatigue, palpitation, dyspnoea or angina pectoris.</td>
</tr>
<tr>
<td>III – Moderate</td>
<td>Marked limitation of physical activity. Less than ordinary activity results in symptoms.</td>
</tr>
<tr>
<td>IV – Severe</td>
<td>Unable to carry out any physical activity without discomfort. Symptoms present at rest.</td>
</tr>
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Add beta blockers in stable systolic heart failure

Mortality and hospital admissions can be reduced among people with stable heart failure if certain beta blockers (carvedilol, bisoprolol and metoprolol extended release) are added to an ACE inhibitor and a loop diuretic. 14–16 Recently, a fourth beta blocker, nebivolol*, has been approved for this indication. Nebivolol reduces the risk of a composite outcome of death or cardiovascular hospitalisation in people aged ≥ 70 years. 17

Start low, go slow

Beta blockers may initially worsen heart failure symptoms. 5,12,18 Start people with stable heart failure on a low dose once they are clinically euvolaemic and increase the dose slowly (every 2–4 weeks) to target (Table 2). Wait before increasing the dose if heart failure symptoms worsen, or if bradycardia or symptomatic hypotension is present — these side effects are often transitory. 5,12,13,19

Cardioselective (beta,-selective) beta blockers should not be routinely withheld from people with both heart failure and COPD. 20 They may be used with caution in patients with mild to moderate asthma — short term use (up to 4 weeks) of cardioselective beta blockers does not appear to cause adverse respiratory effects among these people. 21

Combined ACE inhibitors and angiotensin II-receptor antagonists benefit uncertain

Seek specialist advice if considering the combination of an ACE inhibitor and an angiotensin II-receptor antagonist. 12 Meta-analyses show there is no mortality benefit in combining an ACE inhibitor with an angiotensin II-receptor antagonist in people with heart failure but it may reduce heart failure hospitalisations. 22–24 However, many of the patients included in these meta-analyses were not using beta blockers. Thus the benefit of starting an angiotensin II-receptor antagonist in people who are already using an ACE inhibitor and a beta blocker is uncertain.

Combined ACE inhibitors angiotensin II-receptor antagonists may increase risk

Combining an ACE inhibitor and an angiotensin II-receptor antagonist increases the risk of worsening renal function, hyperkalaemia and symptomatic hypotension and significantly more people stop treatment because of adverse effects. 23,25,26

Table 2: Recommended daily dose of beta blockers12,13

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting dose</th>
<th>Target maintenance dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>bisoprolol</td>
<td>1.25 mg once daily</td>
<td>10 mg once daily</td>
</tr>
<tr>
<td>carvedilol†</td>
<td>3.125 mg twice daily</td>
<td>25 mg twice daily†</td>
</tr>
<tr>
<td>metoprolol extended release</td>
<td>23.75 mg once daily</td>
<td>190 mg once daily</td>
</tr>
<tr>
<td>nebivolol</td>
<td>1.25 mg once daily</td>
<td>10 mg once daily</td>
</tr>
</tbody>
</table>

† Not a beta,-selective beta blocker.
‡ 50 mg twice daily in people > 85 kg with mild to moderate heart failure.

* Nebivolol is TGA indicated for the treatment of heart failure as an adjunct to standard therapies in patients 70 years or older.
Aldosterone antagonists may help those who remain symptomatic

If people taking an ACE inhibitor (or angiotensin II-receptor antagonist) and a beta blocker are still symptomatic, Australian guidelines recommend spironolactone for severe symptoms. While guidelines suggest consideration of eplerenone for mild symptoms it is not TGA approved* for this indication. Although a trial of spironolactone has not been conducted in people with mild symptoms it is possible that it may have the same cardiovascular benefits as eplerenone.27,28

Beware of hyperkalaemia

Combining an aldosterone antagonist with an ACE inhibitor or an angiotensin II-receptor antagonist increases the risk of hyperkalaemia. Do not use an aldosterone antagonist in people with severe renal impairment or in those taking both an ACE inhibitor and an angiotensin II-receptor antagonist.6,12 Monitor potassium concentrations frequently; every week for the first month, then monthly for 2 months, then every 3 months and when indicated clinically.12

Trials suggest benefits

Two large trials of aldosterone antagonists (spironolactone and eplerenone) in people with systolic heart failure found significant reductions in mortality and rates of hospitalisation.29,30 In the first trial, spironolactone improved cardiovascular outcomes in people with moderate to severe heart failure (NYHA class III or IV) who were already taking a loop diuretic, an ACE inhibitor and digoxin. Beta blockers were not widely used for heart failure when this trial was conducted.29 More recently, eplerenone improved cardiovascular outcomes in people with mild symptomatic heart failure (NYHA class II) patients who were already using ACE inhibitors (or angiotensin II-receptor antagonists), beta blockers and, if indicated, a diuretic. However, while this group had mild symptoms they were still at high risk of cardiovascular events as all had been hospitalised because of a cardiovascular event in the previous 6 months.30,31 It is unclear whether mildly symptomatic patients who are not at such high risk would benefit from the addition of eplerenone.

Remember to regularly review all medicines

From NPS audit data, 20% of patients with systolic heart failure take a medicine or medicines that can exacerbate heart failure — most commonly a COX-2 selective NSAID. Commonly used medicines to avoid, if possible, include:
- conventional and COX-2 selective NSAIDs
- thiazolidinediones (e.g. rosiglitazone or pioglitazone)
- corticosteroids (e.g. hydrocortisone, prednisone, fluticasone)
- anti-arrhythmic medicines (except for heart failure specific beta blockers and amiodarone)
- non-dihydropyridine calcium-channel blockers (e.g. verapamil or diltiazem)
- tricyclic antidepressants.5,12

Plan end of life care for those with advanced disease

Advanced age, NYHA class IV symptoms, repeated hospitalisations, poor renal function, cardiac cachexia, low sodium concentration and refractory hypotension requiring withdrawal of medical therapy are indicators that a person may be at high risk of dying within 12 months.5 Care of these people is aimed at improving end of life quality. Reassess all current medicines but do not withdraw heart failure specific medicines (ACE inhibitors, beta blockers, diuretics) unless there is intolerance as these medicines improve symptoms.5,32 Additional medicines to alleviate pain, anxiety and dyspnoea (e.g. diuretics, opioids, sedatives) may be needed.5

* Eplerenone is TGA indicated for use in people who have evidence of heart failure and left ventricular impairment within 3 to 14 days of an acute myocardial infarction.
Address lifestyle factors that exacerbate heart failure

Lack of physical activity, poor diet, excessive consumption of fluids and being overweight can exacerbate heart failure. Advise patients to quit smoking, avoid drinking more than 2 L of fluid per day and to limit or stop caffeine and alcohol intake. A dietitian can help plan a diet high in fibre and low in sodium and saturated fat. Encourage patients to weigh themselves every morning to monitor fluid retention. Let them know they should contact a health professional immediately if they gain or lose more than 2 kg over 2 days.

Exercise-based rehabilitation significantly reduces hospitalisations from heart failure, improves quality of life and does not increase mortality in people with stable systolic heart failure. Refer everyone to a heart failure specific physical activity program if available. Encourage people with NYHA class I or II symptoms to walk for at least 10 to 30 minutes on most days. Other low to moderate intensity exercises include cycling on a stationary bicycle, light weights and stretching. Patients should exercise to a level that allows them to carry on a normal conversation.

Self-management resources for patients

Encourage patients to call the Heart Foundation on 1300 362 787 to obtain a copy of the Living Well with Chronic Heart Failure booklet. This is designed to help people with chronic heart failure better understand and manage their condition.

Ask patients or carers to bring in this booklet, or download the associated information sheet, and discuss its contents with them (link to this available at www.nps.org.au/news_75).

Use the Heart Foundation’s Heart Health Information Service (1300 362 787) to find, and refer patients to, heart failure specific management programs in their local area.

References


Citations available online at www.nps.org.au/news_75