

Improving outcomes in chronic heart failure

by early detection, drug therapy and patient support

Chronic heart failure is a progressive disease mostly affecting people over the age of 65 years.¹⁻³ The prevalence increases sharply with age from approximately 1% in people 50 to 59 years to over 10% in those 80 years and older.⁴ The true prevalence may be higher given the likely extent of undiagnosed cases.^{1,4,5} This issue of *NPS News* highlights the importance of early detection and patient support to maximise the benefits of drug therapies at all stages of chronic heart failure.

Identify, diagnose and intervene early

Early detection and management of heart failure is important, but despite this it is an under-diagnosed disease — symptoms can be non-specific and the clinical findings subtle (see Table 1). Suspect heart failure in people with signs and symptoms that may include unexplained shortness of breath, fatigue, exercise limitation, weight gain and fluid retention, especially in the elderly.

Identify people at high risk of developing heart failure such as those with diabetes, obesity, ischaemic heart disease and hypertension, and those who are taking drugs that may exacerbate heart failure (see examples on page 5). Consider further investigation (e.g. ECG, chest X-ray) as all such patients may have asymptomatic disease.⁶

Confirm with an echocardiogram

Refer all patients with suspected heart failure for an echocardiogram. This confirms a diagnosis and determines the underlying structural or functional abnormality.⁶⁻⁸

Refer patients to a cardiologist, especially if the diagnosis, prognosis or treatment is uncertain.⁶ Specialist input may be especially warranted for younger patients (< 65 years).

Table 1: New York Heart Association (NYHA) grading system for severity of heart failure symptoms⁶

NYHA grading	Symptoms
Class I Asymptomatic	No limitations in normal physical activity
Class II Mild	Slight limitation of physical activity. Ordinary physical activity results in fatigue, palpitation, dyspnoea or angina pectoris
Class III Moderate	Marked limitation of physical activity. Less than ordinary activity results in symptoms
Class IV Severe	Unable to carry out any physical activity without discomfort. Symptoms present at rest

Systolic or diastolic dysfunction?

Heart failure is widely recognised as being caused by left ventricular systolic dysfunction (systolic heart failure) but it may also be due to diastolic dysfunction (heart failure with preserved systolic function) or a combination of both (see Box 1).⁶ About half of all those with heart failure have diastolic dysfunction.⁹ Prognosis is poor in both types of heart failure; both groups have 5-year survival rates of less than 50%.^{10,11} There is insufficient evidence to guide treatment in diastolic heart failure so current approaches include treating the underlying causes of heart failure, managing coexisting conditions and controlling symptoms.⁶

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Box 1: Characteristics of systolic heart failure and heart failure with preserved systolic function (diastolic heart failure)^{3,6}

Systolic heart failure	Diastolic heart failure
<ul style="list-style-type: none"> • Reduced left ventricular ejection fraction (< 40%) 	<ul style="list-style-type: none"> • Relatively normal (preserved) left ventricular ejection fraction (≥ 40%)
<ul style="list-style-type: none"> • Ventricle unable to ‘pump’ with enough force during systole (impaired diastolic function often coexists) 	<ul style="list-style-type: none"> • Ventricle unable to relax sufficiently to allow normal filling during diastole
<ul style="list-style-type: none"> • More common in men than women, frequently in those ≥ 65 years 	<ul style="list-style-type: none"> • Rare in young patients and those without a history of hypertension; more common in women
<ul style="list-style-type: none"> • Risk factors include hypertension and ischaemic heart disease 	<ul style="list-style-type: none"> • Risk factors include hypertension, coronary heart disease, diabetes, vascular disease and left ventricular hypertrophy
<ul style="list-style-type: none"> • Good evidence for effective treatment 	<ul style="list-style-type: none"> • Limited evidence for treatment

Flag patients at high risk of mortality and morbidity for frequent review

Evaluate people with heart failure more frequently if they are at high risk of premature mortality, morbidity and hospital readmissions. These include people with heart failure who have at least 2 of the following risk factors:

- Age ≥ 65 years
- NYHA Class III or IV symptoms
- Comorbidities
- Left ventricular ejection fraction (LVEF) ≤ 30%
- Living alone or remote from specialist medical services
- Depression
- Language barrier (e.g. non English speaking)
- Lower socio-economic status
- Significant renal dysfunction (estimated glomerular filtration rate < 60 mL/min/1.73m²).⁶

Frequent monitoring and follow-up in high-risk patients (especially the elderly) may detect preventable causes of worsening heart failure and prevent hospital admission (see Box 2).

Box 2: Preventable causes of worsening heart failure and hospital admission^{6,12}

- Inadequate or inappropriate medical treatment
- Lack of patient knowledge about heart failure, treatment and their medication
- Inadequate patient response to, or recognition of, relapse of their condition
- Non-adherence with medications or non-drug therapy
- Poor social support

A search of electronic records can help identify high-risk patients who may benefit from a medication review. Tools that extract data from prescribing software may be helpful. NPS is including some heart failure indicators into two of the available data extraction tools that search computer records. This initiative will assist GPs in improving the quality of their prescribing for heart failure.

People at highest risk of premature death from heart failure gain the greatest benefit from treatment.^{13,14} However these may be the least likely to receive appropriate drug therapy.¹⁵ Barriers to optimal prescribing in heart failure include uncertainty about diagnosis, and concern about safety and tolerability, especially for elderly patients with coexisting conditions who are receiving multiple medications.^{16,17}

Consider the goals of treatment (improving symptoms and function versus improving prognosis) for patients with significant coexisting conditions (e.g. cognitive impairment, cancer, renal impairment).⁷ Target doses for heart failure medications may not be tolerated by these people.

Targeted education and multidisciplinary support improve outcomes

Enabling patients with heart failure to play an active role in self-management has been shown to improve clinical outcomes.¹⁸⁻²¹ Provide patients with comprehensive education and multidisciplinary support, including:

- regular medication review
- checking compliance with therapies
- information and strategies to monitor and control fluid balance
- information about how to make some long-term lifestyle changes
- reinforcing the benefits of therapies and health-related behaviours
- mechanisms for intensive follow-up.^{18,19,22-26}

A structured patient education and support program — focussing on the relationships between heart failure, medications, diet and other health behaviours — was found to significantly reduce the relative risk of hospital readmission or death by 30% (RR 0.69, CI 8% to 48%) after 1 year compared with regular care.²¹

General practitioners can help patients self-manage their condition by providing the Heart Foundation's 'Living well with chronic heart failure' information sheet and action plan, and discussing its contents with the patient or carer. Providing written information together with self-management advice may be more effective than either alone in improving a patient's understanding of their condition and its treatment.²⁷ The Heart Foundation's information sheet includes some tips on controlling symptoms (including side effects of medications) and answers common questions asked by patients (this is available for download at www.heartfoundation.org.au/chf). This resource can also be printed out through prescribing software from GP desktops. Encourage patients to call the Heart Foundation's Heart Health Information Service on 1300 362 787 to obtain a copy of the entire *Living Well with Chronic Heart Failure* booklet.

Refer patients to a specialised program, if possible within their community. The Heart Health Information Service has a database of heart failure management programs available in Australia and this can be used to find programs for your patients.

ACE inhibitors are first-line therapy for chronic heart failure

ACE inhibitors reduce mortality and morbidity at any grade of systolic heart failure (see Table 2), even in patients with asymptomatic disease.²⁸⁻³⁰ Start with a low dose and titrate upwards slowly, doubling the dose at no less than 2-weekly intervals except under close supervision. Titrate patients to a target dose that has proven survival benefits or maintain them at their maximally tolerated dose indefinitely, unless problems arise.^{7,8}

The Heart Foundation and Cardiac Society of Australia and New Zealand *Guidelines for the Prevention, Detection and Management of Heart Failure in Australia* (2006) includes figures outlining pharmacological treatment of all grades of systolic heart failure (these are available for download at www.heartfoundation.org.au/chf).



These NPS materials form part of a joint program with the Heart Foundation of Australia and the NHMRC National Institute of Clinical Studies to improve the management of heart failure.

ACE inhibitors continued...

Table 2: Recommended starting and target doses of ACE inhibitors in patients with heart failure*^{31,32}

ACE inhibitor	Starting dose	Target maintenance dose
captopril	6.25 mg three times daily	25–75 mg twice daily (maximum 150 mg daily)
enalapril	2.5 mg daily	10–20 mg twice daily
fosinopril	5–10 mg daily	20–40 mg daily
lisinopril	2.5 mg daily	20–40 mg daily
perindopril arginine	2.5 mg daily	5 mg daily (up to 10 mg for reduction of risk of cardiovascular events in patients with established coronary artery disease without heart failure)
perindopril erbumine	2 mg daily	4 mg daily (up to 8 mg for reduction of risk of cardiovascular events in patients with established coronary artery disease without heart failure)
quinapril	5 mg daily	20–40 mg daily
ramipril	2.5 mg twice daily	5–10 mg daily
trandolapril	0.5 mg daily	2–4 mg daily

* Smaller starting doses and slower dose titration may be required for frail patients.

Angiotensin II-receptor antagonists are an effective alternative in ACE inhibitor intolerance

Angiotensin II-receptor antagonists improve mortality and morbidity in patients with symptomatic heart failure (class II to IV) compared with placebo.^{33–35} They appear to have similar efficacy to ACE inhibitors.^{35–38} As such, they are an effective alternative in patients unable to tolerate ACE inhibitors due to kinin-mediated adverse effects (such as a troublesome cough).^{6,8,39}

There is conflicting evidence on the benefits of combining an ACE inhibitor with an angiotensin II-receptor antagonist in people with heart failure. This combination may be considered, at the recommendation of a cardiologist, as one of several options for individual patients who remain symptomatic despite optimal ACE inhibitor therapy.^{6,7,39,40}

Be aware that the combination of an ACE inhibitor and an angiotensin II-receptor antagonist is associated with significant increases in the risk of medication discontinuation due to adverse effects including worsening renal function, hyperkalaemia and symptomatic hypotension⁴¹, patients also require more frequent monitoring. Specialist input may be required if initiating complex combination therapies.

Diuretics only provide symptom relief

Diuretics are not appropriate as monotherapy and should only be used to relieve symptoms of fluid overload in combination with standard heart failure therapies with proven survival benefits.⁶

Role of aldosterone antagonists and digoxin

Low-dose spironolactone improves survival in severe heart failure⁴² and can be considered for people who remain symptomatic despite optimal doses of an ACE inhibitor and diuretics.⁶ Spironolactone may cause hyperkalaemia and worsening renal function when added to an ACE inhibitor or angiotensin II-receptor antagonist, and close monitoring is required.⁴³

Eplerenone is recommended early in addition to standard therapy (ACE inhibitor and beta blocker) for myocardial infarction complicated by symptomatic heart failure.⁶

Digoxin reduces hospitalisations for worsening heart failure but has no clear effects on mortality.⁴⁴ Digoxin has a role in treating patients with persistent symptomatic heart failure despite optimal doses of ACE inhibitors and diuretics⁴⁵ and in controlling ventricular rate in patients with heart failure and atrial fibrillation.⁶

Use heart-failure-specific beta blockers in all stabilised patients

Adding a heart-failure-specific beta blocker (bisoprolol, carvedilol or controlled-release metoprolol) to an ACE inhibitor has significant additional mortality and morbidity benefits in patients with stable symptomatic heart failure.^{46–49}

Do not initiate beta blockers in patients who are haemodynamically unstable until they are stabilised with appropriate doses of an ACE inhibitor, angiotensin II-receptor antagonist or other medications. Be alert for additional hypotensive effects when beta blockers are used with other drugs that cause hypotension.

Use heart-failure-specific beta blockers with efficacy proven in clinical trials (carvedilol, bisoprolol, metoprolol SR). These beta blockers appear to have equal efficacy.⁵⁰

Heart-failure-specific beta blockers are recommended for asymptomatic patients after myocardial infarction.^{6,39,52} Their role in asymptomatic disease outside this context has not been adequately studied.

Table 3: Recommended starting and target doses of beta blockers in patients with heart failure in Australia^{*31,32,51}

Beta blocker	Starting dose*	Target maintenance dose
bisoprolol	1.25 mg daily	10 mg daily
carvedilol	3.125 mg twice daily	25 mg twice daily
metoprolol CR	23.75 mg daily	190 mg daily

* Smaller starting doses and slower dose titration may be required for frail patients.

Specialist advice should always be sought before starting a beta blocker in patients with:

- severe heart failure
- bradycardia (< 50 beats per minute)
- symptomatic hypotension
- recent exacerbation of heart failure which may or may not have necessitated hospital admission.^{7,53}

Avoid drugs that exacerbate heart failure

Avoid, if possible, drugs that can exacerbate heart failure, including:

- anti-arrhythmic drugs (except for heart failure specific beta blockers and amiodarone)
- non-dihydropyridine calcium-channel blockers (e.g. verapamil, diltiazem)
- tricyclic antidepressants (e.g. amitriptyline, nortriptyline, doxepin)
- conventional non-steroidal anti-inflammatory drugs (NSAIDs)
- COX-2 selective NSAIDs (e.g. celecoxib)
- thiazolidinediones (e.g. rosiglitazone and pioglitazone)

- corticosteroids (e.g. hydrocortisone, prednisone)
- oncology drugs (e.g. anthracyclines, trastuzumab)
- clozapine
- tumour necrosis factor antagonists (e.g. infliximab, etanercept).^{6,7,32}

Look for potentially serious drug interactions

Regularly review medication lists and consider potentially serious drug interactions when initiating new therapies, especially for elderly patients and those with renal impairment.³²

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