2011 Update to National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand *Guidelines for the prevention, detection and management of chronic heart failure in Australia, 2006*

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Chronic heart failure (CHF) is a complex and lethal clinical syndrome accounting for an increasing number of Australian hospital separations (up more than 7% from 1998–99 to 2007–08)[1] and more than 2700 deaths in Australia in 2008.[2]

This article summarises recent updates to the National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand *Guidelines for the prevention, detection and management of chronic heart failure in Australia, 2006*.[3] In some cases, new evidence strengthens the recommendations made in the guidelines; in others, it provides new approaches to current recommended practice. The grades of recommendation used here reflect the two highest grades in the 2006 guidelines (A: rich body of high-quality randomised controlled trial [RCT] data; and B: limited body of RCT data or high-quality non-RCT data).

In all cases, patient circumstances and clinical judgement should guide the interpretation of these findings. The updated version of the guidelines will be made available on the National Heart Foundation of Australia website (http://www.heartfoundation.org.au).

ABSTRACT

- Chronic heart failure (CHF) is a complex and lethal clinical syndrome accounting for an increasing number of Australian hospital separations and more than 2700 Australian deaths in 2008.
- In 2006, the National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand published *Guidelines for the prevention, detection and management of chronic heart failure in Australia, 2006*.
- Results from recently published clinical trials provide additional information to be considered in the prevention, detection and management of CHF. In some cases, this new evidence strengthens recommendations previously made in the 2006 guidelines; in others, it provides new approaches to current recommended practice.
- Areas in which there have been significant new developments include:
  - Use of B-type natriuretic peptide (BNP) or N-terminal proBNP plasma level measurement in guiding treatment of CHF
  - New pharmacological approaches to the treatment of systolic heart failure
  - Drugs to avoid or use with caution in CHF
  - Treatment of cardiac arrhythmias in patients with CHF
  - Multidisciplinary care and post-discharge management programs.
- While patient circumstances and clinical judgement should guide the interpretation of these findings in the clinical context, this update, together with the 2006 guidelines, provides current clinical guidance on CHF.

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Diagnosis

Diagnostic investigations

Natriuretic peptides

The 2006 guidelines reported that titration of drug therapy according to plasma levels of N-terminal pro B-type natriuretic peptide (proBNP) had been associated with reduced cardiovascular events in a small study.[4]

Large RCTs have evaluated this strategy (using plasma levels of either BNP or N-terminal proBNP) compared with standard therapy for patients with CHF.[4-7] Recent meta-analyses reported a significant reduction in all-cause mortality for patients with CHF and low ejection fractions that was associated with titrating therapy based on natriuretic peptide levels, but no significant effect on all-cause hospitalisation.[8,9] While further studies are in progress, none are very large, and these early conclusions are unlikely to change.

Plasma natriuretic peptide level-guided therapy should be confined to CHF patients with systolic dysfunction who are felt not to have responded adequately to conventional management (Grade B recommendation). The cost-effectiveness of this approach remains uncertain, and more definitive trials are required to fully establish the role of hormone level measurement in guiding CHF treatment.

Non-pharmacological management

Physical activity and rehabilitation

Regular physical activity is strongly advised for people with CHF, with benefits including a reduction in physical deconditioning, symptoms and neurohormonal abnormalities, as well as improvements in functional capacity.[3]

Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training (HF-ACTION) showed that aerobic exercise, in addition to usual care, resulted in improvements in self-reported health status, including quality of life, in patients with heart failure and a left-ventricular ejection fraction (LVEF) $\leq 35\%$.[10] A retrospective analysis of the study (adjusted for prognostic factors) showed that patients who exercised as instructed achieved modest but significant benefits in terms of clinical outcomes (including all-cause mortality or hospitalisation and cardiovascular mortality or hospitalisation for CHF).[11]

The evidence supporting the benefits of regular physical activity in people with CHF, particularly among middle-aged patients with

systolic heart failure, has strengthened in recent years. The recommendation in the 2006 guidelines that all patients be referred to a specifically designed physical activity program, if available, stands (Grade A recommendation).

Uncertainty remains about the benefit of physical activity in older patients and those with CHF associated with preserved left-ventricular systolic function.

Pharmacological therapy

Treatment of symptomatic systolic heart failure

β-Blockers

The 2006 guidelines recommended use of β-blockers that have been evaluated in large-scale CHF trials, unless not tolerated or contraindicated, for all patients with systolic CHF who remain mildly to moderately symptomatic despite appropriate doses of an angiotensin-converting enzyme inhibitor (ACEI). Such β-blockers were also recommended for patients with symptoms of advanced CHF.

More recently, nebivolol (a selective β1 receptor antagonist) has been approved for use in Australia for the treatment of stable CHF. It has been found to be safe and effective in elderly patients with either relatively preserved or impaired ejection fraction,[12-14] and may be considered an appropriate β-blocker for treating stable CHF in patients aged 70 years or older (Grade B recommendation).

Angiotensin II receptor antagonists

Angiotensin II receptor antagonists (ARAs) can be used as an alternative for patients who do not tolerate ACEIs due to kinin-mediated adverse effects (eg, cough), and they should also be considered for reducing morbidity and mortality in patients with systolic CHF who remain symptomatic despite receiving ACEIs.[3]

A recent study demonstrated that a higher dose of an ARA (losartan) is superior to a lower dose in reducing death or admission for heart failure for patients with systolic CHF who do not tolerate ACEIs.[15] These findings suggest that maximising renin–angiotensin system (RAS) blockade provides additional clinical benefit in such patients, and reinforces existing guideline recommendations to aim for target doses of RAS blockers as used in the major clinical outcome trials, if possible.

Aldosterone antagonists

The 2006 guidelines indicated that aldosterone receptor antagonists such as spironolactone may provide benefit by reducing all-cause mortality and symptoms in patients with advanced CHF.

A study of the selective aldosterone antagonist eplerenone in patients with systolic heart failure and mild (New York Heart Association [NYHA] Class II) symptoms was recently halted when it reached a prespecified threshold for benefit with regard to the study's primary composite end point of cardiovascular mortality and hospitalisation for heart failure.[16]

Aldosterone blockade with eplerenone should therefore be considered in patients with systolic heart failure who still have mild (NYHA Class II) symptoms despite receiving standard therapies (ACEIs, β-blockers) (Grade B recommendation).

Polyunsaturated fatty acids

A recent trial showed a small reduction in mortality and hospital admissions for cardiovascular reasons for patients with CHF who were treated with omega-3-acid ethyl esters versus placebo (in addition to usual therapy in both arms of the trial).[17] Symptomatic CHF patients in this study were primarily, but not exclusively, those with an LVEF ⩽ 40%.

Based on this evidence, polyunsaturated fatty acids should be considered as a second-line agent for patients with CHF who remain symptomatic despite standard therapy, which should include ACEIs (or ARAs) and β-blockers if tolerated (Grade B recommendation).

Direct sinus node inhibitors

A study of the direct sinus node inhibitor ivabradine versus placebo has recently demonstrated improvements in terms of the primary composite end point of cardiovascular mortality and hospitalisation for heart failure in patients with symptomatic systolic heart failure, sinus rhythm (heart rate ⩾ 70 beats/min) and recent hospitalisation for heart failure.[18] This benefit was largely due to a reduction in hospitalisations, and was additional to patients already being on the highest tolerated dose of background β-blockers (although only 26% were being treated with the target dose). A similar earlier study, using a heart rate cut-off of 60 beats/min in sinus rhythm, had failed to show an impact on its primary end point.[19]

It is therefore recommended that direct sinus node inhibition with ivabradine be considered for CHF patients with impaired systolic function and a recent hospitalisation for heart failure who are in sinus rhythm, where their heart rate remains ⩾ 70 beats/min despite efforts to maximise dosage of background β-blockers (Grade B recommendation).

Iron

Iron deficiency is common in patients with CHF, and is usually associated with anaemia. A recent study has demonstrated reduced symptoms and improved submaximal exercise tolerance and quality of life with use of intravenous ferric carboxymaltose (in addition to standard therapies) in iron-deficient patients with CHF.[20]

Iron deficiency should be looked for and treated in patients with CHF to reduce symptoms and improve exercise tolerance and quality of life (Grade B recommendation).

Drugs to avoid or use with caution in CHF

The 2006 guidelines listed a number of drugs to be avoided in treating patients with CHF. Based on recent trial evidence, the following drugs should be added to that list.

- Dronedarone: associated with increased mortality in patients with NYHA Class IV CHF, or in those with NYHA Class II–III CHF with a recent decompensation requiring hospitalisation,[21] and is contraindicated in such patients.
- Trastuzumab: associated with the development of reduced LVEF and heart failure.[22] It is contraindicated in patients with symptomatic heart failure or reduced LVEF (< 45%). Baseline and periodic evaluation of cardiac status including assessment of LVEF should occur if used in patients for whom it is not contraindicated.
- Tyrosine kinase inhibitors such as sunitinib: associated with hypertension, reduced LVEF and heart failure.[23] The risk–benefit profile of these agents needs to be considered for patients with a history of symptomatic heart failure or cardiac disease. Baseline and periodic evaluation of LVEF should be considered in patients treated with these agents, especially in the presence of cardiac risk factors.

- Moxonidine (sustained release): associated with increased mortality in patients with heart failure and is contraindicated in such patients.[24]

While the 2006 guidelines suggested that metformin should be avoided in patients with CHF, it appears to be safe in recent analyses of patients with heart failure, except in cases of concomitant renal impairment.[25]

Outpatient treatment of advanced systolic heart failure

Positive inotropic agents

The 2006 guidelines suggested several inotropic agents (including dobutamine and dopamine) for short-term use in patients with acute haemodynamic compromise. In addition, it was suggested that levosimendan (a calcium-sensitising inotropic agent) may be superior to dobutamine in the treatment of advanced heart failure, although there was a lack of evidence to confirm the place of levosimendan in the management of decompensated CHF.

Further studies have suggested that levosimendan may improve clinical status and haemodynamic parameters in patients with acutely decompensated CHF.[26,27] However, the Survival of Patients With Acute Heart Failure in Need of Intravenous Inotropic Support (SURVIVE) study showed no improvements in survival at 180 days with levosimendan compared with dobutamine in acute decompensated heart failure, although secondary analyses showed a small improvement in survival at 7 and 30 days.[28]

Levosimendan is available in Australia on a compassionate-use basis. It should be reserved for patients who do not respond to dobutamine or for those in whom dobutamine is contraindicated because of arrhythmia or myocardial ischaemia.

Devices

Biventricular pacing

The 2006 guidelines stated that biventricular pacing, or cardiac-resynchronisation therapy (CRT), should be considered in patients who fulfil all the following criteria:

- NYHA Class III–IV symptoms despite optimal medical therapy
- Dilated heart failure with an ejection fraction ⩽ 35%
- QRS duration ⩾ 120 ms
- Sinus rhythm.

Three RCTs have reported favourable effects of CRT on left-ventricular remodelling in patients with relatively asymptomatic or mildly symptomatic heart failure associated with left-ventricular systolic dysfunction and a wide QRS complex.[29-31] One of these trials found that prophylactic CRT in combination with an implantable cardioverter defibrillator (ICD) resulted in a 34% reduction in risk of death or heart failure events, with the benefit driven by a 41% reduction in heart failure events.[29] All patients had a history of heart failure symptoms, with the majority being symptomatic at the time of enrolment. A significantly greater benefit was observed in patients with a QRS duration ⩾ 150 ms. There was no difference in mortality; however, the study was not powered to determine this.

A more recent study reported a significant 25% reduction in risk of death and a 32% reduction in hospitalisation for heart failure with combined ICD–CRT, compared with ICD therapy alone, in patients with mild to moderately symptomatic systolic heart failure associated with a wide QRS complex. A significant benefit was seen in patients with NYHA Class II symptoms.[32] Although there were more early adverse events with combined ICD–CRT, including lead dislodgement and coronary sinus dissection, a greater benefit was seen in patients with a QRS duration ⩾ 150 ms and in the presence of a left bundle branch block pattern.[32]

In addition to the 2006 recommendations for CRT, for patients in whom implantation of an ICD is planned to reduce the risk of sudden death, it is reasonable to also consider CRT to reduce the risk of death and heart failure events if the LVEF is ⩽ 30% and the QRS duration is ⩾ 150 ms (left bundle branch block morphology), with associated mild symptoms (NYHA Class II) despite optimal medical therapy (Grade A recommendation).

Surgery

Surgical ventricular reconstruction

At the time of writing the 2006 guidelines, a number of methods to restore normal mass-to-volume ratio in patients with severe left-ventricular dilatation were under investigation, including left-ventricular free-wall excision.

A recent trial examined whether the routine addition of surgical ventricular reconstruction to coronary artery bypass grafting (CABG) decreases rates of death or hospitalisation for cardiac causes, compared with CABG alone. The study demonstrated that the reduction in left-ventricular volumes that occurred with the combined approach was not associated with a clinical benefit,[33] suggesting that routine addition of surgical ventricular reconstruction to CABG to restore left-ventricular volume should not be recommended as a treatment for CHF.

Acute exacerbations of CHF

Management of decompensated CHF

Non-invasive assisted ventilation

Continuous positive airway pressure (CPAP) and bilevel positive airway pressure (BiPAP) ventilation have a well defined role in management of acute pulmonary oedema, but there has been limited trial evidence to support their use in decompensation. Their use in this context has been largely confined to the overlap syndrome, where pulmonary oedema and poor oxygenation are dominant clinical issues in decompensation.[3]

A recent meta-analysis has suggested that both CPAP and BiPAP ventilation reduce the need for invasive ventilation in patients with acute pulmonary oedema.[34] CPAP is generally the first-line modality, but BiPAP is useful in patients with coexistent type II respiratory failure with hypercapnoea as well as acute pulmonary oedema. A subsequent RCT found that, although the use of non-invasive ventilation was associated with a reduction in symptoms and metabolic disturbance, there was no significant difference in 7-day mortality.[35]

In light of available data, both CPAP and BiPAP ventilation should be considered in the management of acute exacerbations of CHF, particularly acute pulmonary oedema (Grade A recommendation).

Heart failure with preserved systolic function

Suggested treatments for heart failure with preserved systolic function (HFPSF), or diastolic heart failure, have focused on aggressive risk-factor modification, including blood pressure reduction and glycaemic control.[3]

A study evaluating the effects of perindopril (an ACEI) in patients with HFPSF, reported in 2006, had insufficient power to determine its effects on long-term morbidity and mortality.[36] A later study found that angiotensin II receptor blockade with irbesartan did not improve outcomes for patients with HFPSF.[37]

There are still no conclusive data regarding the efficacy of any drug class in treating HFPSF.

Treatment of associated disorders

Cardiac arrhythmia

Atrial fibrillation

The 2006 guidelines indicated that pharmacotherapy remains an important mainstay for patients with CHF who develop atrial fibrillation (AF), although episodic electrical cardioversion may be required for those who experience symptomatic deterioration. Anti-arrhythmic therapy usually requires amiodarone, or occasionally sotalol, and long-term anticoagulation is required unless an acute, reversible cause of AF can be identified. If sinus rhythm cannot be maintained for prolonged periods, the guidelines advised that therapy should be directed at controlling ventricular response rate (with digoxin, β-blockers or amiodarone) and reducing thromboembolic risk with warfarin. While it was noted that electrophysiological ablation prevents recurrence of atrial flutter in about 95% of cases, the role of curative ablation for AF was considered controversial.

A large multicentre trial involving patients with CHF, an LVEF ⩽ 35% and a history of AF recently showed that the control of ventricular rate with the use of digoxin and β-blockers, and the use of warfarin anticoagulation, was easier than and as effective on the primary end point of death from cardiovascular causes as therapy designed to restore and maintain sinus rhythm.[38]

Another small study found that pulmonary vein isolation therapy for AF in patients with CHF resulted in a high rate of freedom from AF, with improved symptomatic status, exercise tolerance and LVEF.[39] For patients with CHF due to left-ventricular systolic dysfunction associated with drug-resistant symptomatic AF, the study demonstrated the superiority of a rhythm-control strategy based on pulmonary vein isolation compared with a ventricular rate-control strategy based on atrioventricular node ablation with biventricular pacing.

Rate control (rather than rhythm control), together with warfarin anticoagulation, is the preferred method of treating patients with CHF and AF if their condition permits this (Grade B recommendation). The role of atrioventricular node ablation and pulmonary vein isolation for these patients requires further research, and no specific recommendation can be made at this stage.

Post-discharge management programs

Multidisciplinary programs of care targeting high-risk patients with CHF after acute hospitalisation prolong survival, improve quality of life, and are cost-effective in reducing hospital stays.[3]

Recent systematic reviews and meta-analyses have highlighted the broad elements common to the most effective multidisciplinary programs. These are described in detail in a National Heart Foundation of Australia publication.[40]

Telemonitoring has been found to be associated with reduced all-cause mortality, and a recent Cochrane review found that both structured telephone support and telemonitoring reduced CHF-related hospitalisations, improved quality of life and reduced health care costs.[41] However, several recently reported trials (including one involving 1653 patients with CHF in the United States[42]) have found no benefits with respect to rehospitalisation or survival, relative to usual care.

All patients hospitalised for heart failure should have post-discharge access to best-practice multidisciplinary CHF care that is linked with health services, delivered in acute and subacute health care settings. Priority should be given to face-to-face management of patients with CHF. The application of remote management assisted by structured telephone support and telemonitoring should be considered for those patients who do not have ready access to a CHF management program (Grade A recommendation).

Summary

While patient circumstances and clinical judgement should guide the interpretation of these findings in the clinical context, this update, together with the 2006 guidelines, provides current clinical guidance for the prevention, detection and management of CHF in Australia. The National Heart Foundation of Australia website (http://www.heartfoundation.org.au) provides further information on managing patients with CHF and access to relevant physician and patient resources.

Competing interests

Many members of the guidelines writing panel have received paid honoraria for work performed on behalf of manufacturers of therapies described in the guidelines. However, no members of the writing panel stand to gain financially from their involvement in the guidelines.

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