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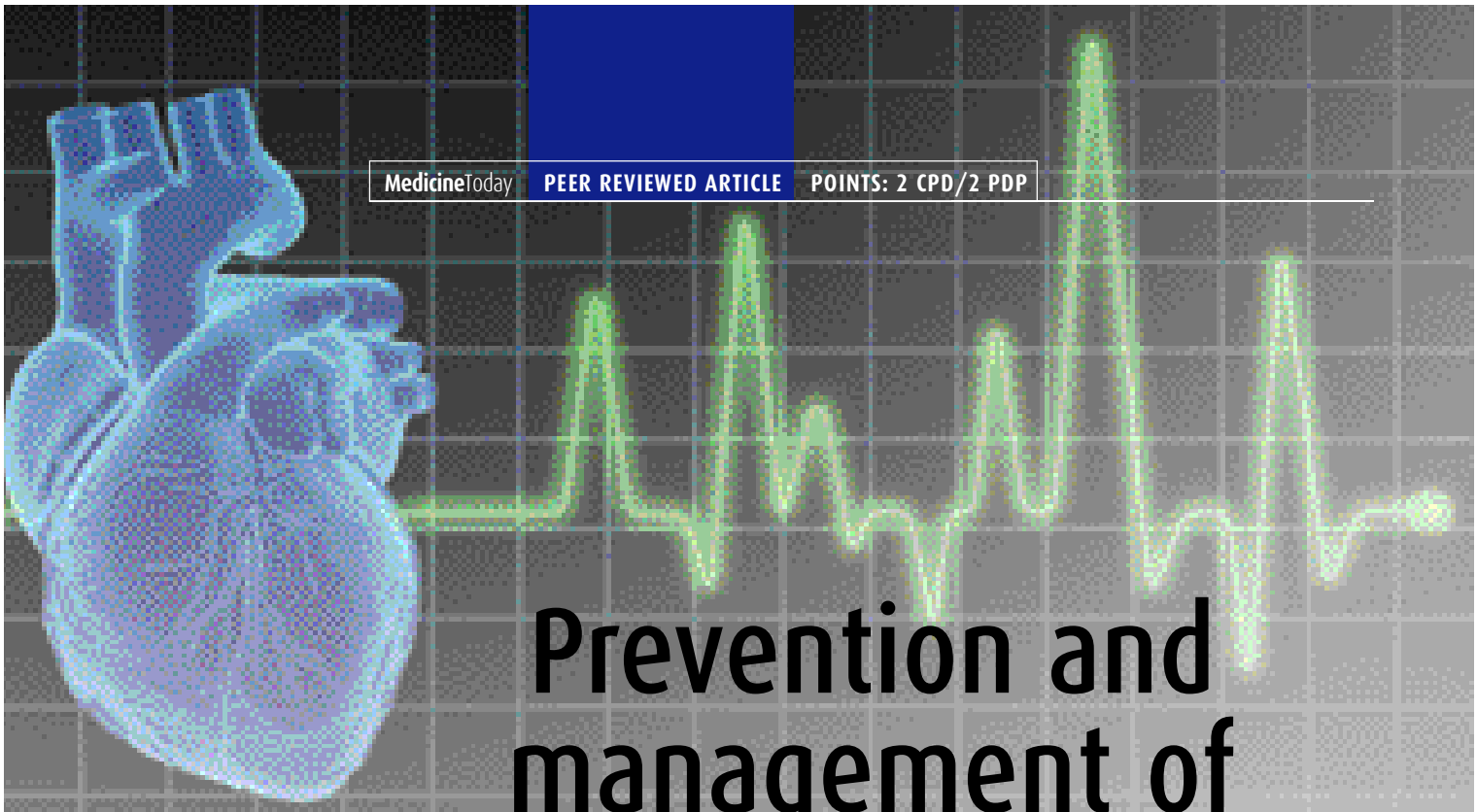

Prevention and management of heart failure

Heart failure is associated with substantial morbidity and mortality. Lifestyle and behavioural modification to reduce cardiovascular disease risk factors are important in preventing the condition, and the pharmacological management is guided by the findings on echocardiography.

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Heart failure affects more than 300,000 Australians and about 30,000 new cases are diagnosed each year. The healthcare costs associated with heart failure were estimated at a staggering $1 billion in the year 2000, a considerable proportion of this spent on heart failure hospitalisations.[1] Chronic heart failure is common in the elderly, with one in 10 people aged over 60 years

IN SUMMARY

- **Bedside clinical assessment and chest x-ray may allow a diagnosis of heart failure but do not allow the diagnosis to be ruled out.**
- **The echocardiogram is the single most useful investigation to confirm or rule out the diagnosis of heart failure and to guide management.**
- **Plasma natriuretic peptides are useful when the diagnosis is uncertain and an echocardiogram cannot be arranged in a timely fashion.**
- **ACE inhibitors (or angiotensin receptor blockers) and ß-blockers are the gold standard for treating systolic heart failure, with aldosterone antagonists providing added benefit if symptoms persist.**
- **Implantable cardioverter defibrillators and cardiac resynchronisation therapy provide added benefit in selected patients.**
- **Multidisciplinary heart failure disease management programs should be offered to patients recently hospitalised with heart failure.**

presenting to a general practitioner having the condition.[2] Despite treatment advances over the past two decades, many patients remain burdened with debilitating symptoms and a five-year survival rate as low as 30 to 50%.[3] Consequently, prevention is as important as treatment of symptomatic heart failure.

What is heart failure?

The National Heart Foundation of Australia defines chronic heart failure as 'a complex clinical syndrome with typical symptoms (e.g. dyspnoea, fatigue) that can occur at rest or on effort that is characterised by objective evidence of an underlying structural abnormality or cardiac dysfunction that impairs the ability of the ventricle to fill with [diastolic heart failure] or eject [systolic heart failure] blood.'[4]

Patients with systolic heart failure typically have a dilated left ventricle with reduced contractility (i.e. left ventricular ejection fraction (LVEF) 40% or less; Figure 1). In contrast, patients with diastolic heart failure, who constitute about one-third of cases, are usually elderly with a normal sized left ventricle and preserved contractility (i.e. LVEF more than 40%) associated with impaired left ventricular (LV) filling. Several other terms have been used to subclassify heart failure, including left and right heart failure, which refer to pulmonary and systemic venous congestion respectively. These terms have limited clinical application. For example, although right heart failure can occur in the setting of chronic lung disease, pulmonary vascular and thromboembolic disease and right heart pathology, the most common cause is raised pulmonary arterial pressure due to pulmonary venous or 'left-sided' congestion often caused by LV dysfunction.

Epidemiology – the growing iceberg

Approximately one in five people aged 40 years will develop heart failure at some point in their life.[5] Although heart failure is more common in the elderly, affecting more than 10% of octogenarians, it may occur at any age.[6] Despite improved treatment of coronary artery disease and hypertension, the age-adjusted incidence of heart failure remains little changed in the past few decades.[3]

It is likely that the heart failure burden will increase further with the ageing population, increasing prevalences of diabetes and obesity, and with the improved survival of patients with heart failure. Patients with symptomatic heart failure represent only the tip of the iceberg, with a large number of individuals with asymptomatic LV dysfunction remaining unrecognised and a larger number at risk of developing LV dysfunction in the future (Figure 2).[6]

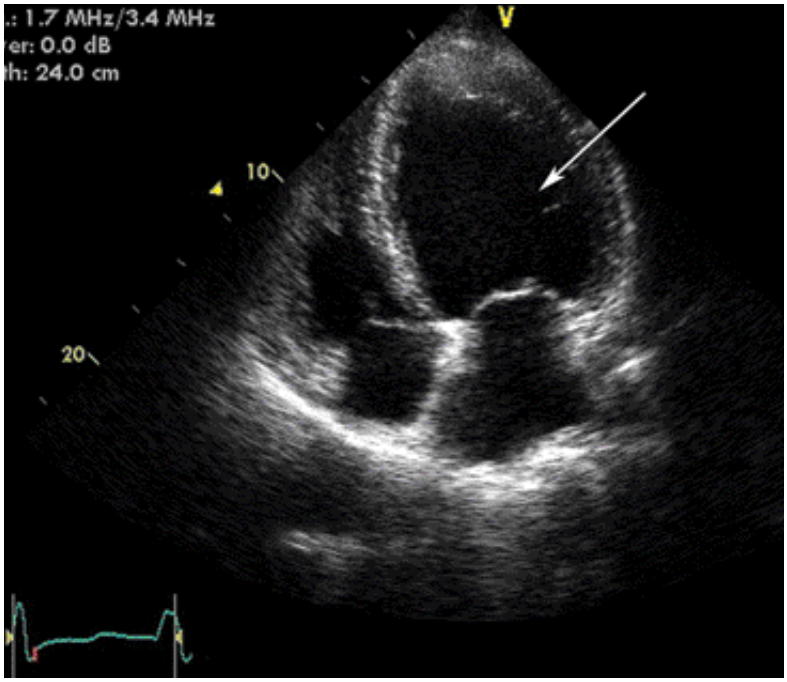

Figure 1. An echocardiogram from a patient with dilated cardiomyopathy. This still-frame image of a four-chamber view shows a dilated left ventricle (arrow).

Pathophysiology

Heart failure is characterised by neurohormonal activation, release of pro-inflammatory cytokines and adverse LV remodelling. The failing left ventricle initially maintains stroke volume at the expense of higher end diastolic pressure and volume (the Frank-Starling law of the heart – the greater the volume of blood entering the heart during diastole [end-diastolic volume], the greater the volume of blood ejected during systolic contraction [stroke volume] and vice versa). Ultimately, the reduced cardiac output leads to sympathetic activation and renal hypoperfusion, which activates the renin–angiotensin–aldosterone system (RAAS) causing volume expansion (Figure 3).

Sympathetic stimulation, angiotensin II and vasopressin cause peripheral vasoconstriction, which along with volume expansion maintains

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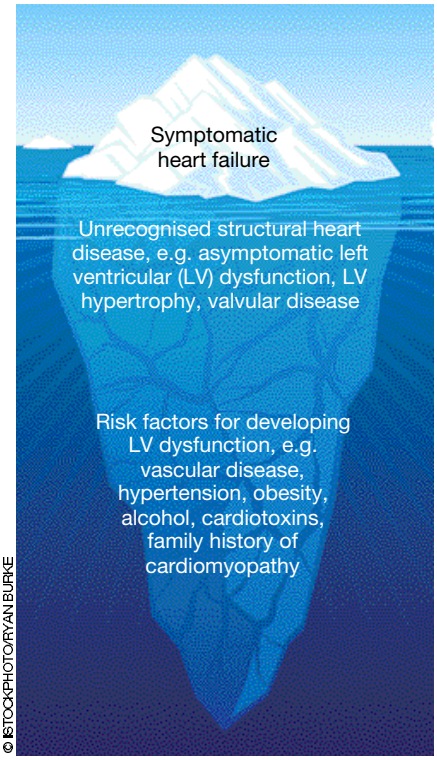

Figure 2. Patients with symptomatic heart failure form only the tip of the iceberg. Beneath the surface are individuals with unrecognised structural heart disease and individuals with risk factors for developing LV dysfunction in the future.

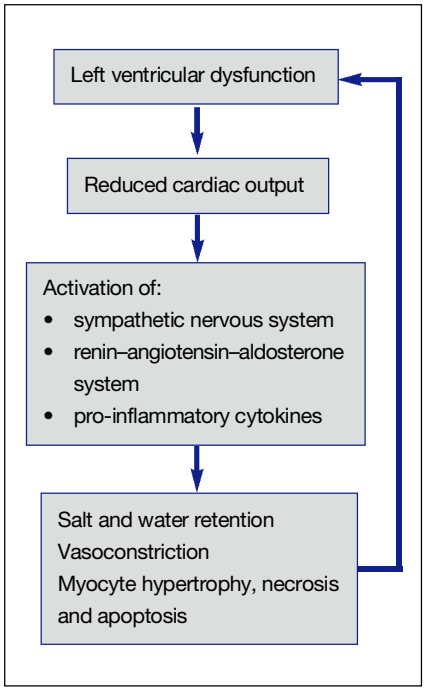

Figure 3. The vicious cycle of neurohormonal and cytokine activation in the progression of heart failure.

Table 1. Clinical features of heart failure

Symptoms

- Dyspnoea
- Fatigue
- Nocturnal cough
- Orthopnoea
- Paroxysmal nocturnal dyspnoea
- Lower limb swelling
- Abdominal swelling; epigastric discomfort

Signs

- Tachycardia
- Displaced apex beat; cardiac murmur; gallop rhythm
- Basal inspiratory crackles
- Elevated venous pressure
- Peripheral oedema
- Hepatomegaly, with or without ascites
- Pleural effusion

blood pressure and perfusion of vital organs at least in the short term. In the longer term, however, chronic neurohormonal activation induces fibrosis and myocyte hypertrophy and apoptosis, with consequent maladaptive LV remodelling. The left ventricle dilates, hypertrophies and attains a more spherical shape with a further deterioration in function.

Diagnosing heart failure

The signs and symptoms of heart failure are listed in Table 1. The usual clinical scenario is a patient who presents with dyspnoea, exercise intolerance or unexplained leg swelling.

Although most patients with heart failure will complain of dyspnoea, this symptom also occurs in many other conditions. If the dyspnoea is worse when the patient is lying flat and can be avoided by sleeping in a more upright position (orthopnoea) or if it occurs in the early hours of the morning and settles with sitting upright (paroxysmal nocturnal dyspnoea), the clinician may be more confident that the patient has heart failure. However, these symptoms tend to occur at a later stage.

Similarly, although certain clinical signs are relatively specific for the diagnosis (e.g. raised jugular venous pressure, gallop rhythm), these also tend to occur at a later stage and can be difficult to demonstrate. Indeed, a normal physical examination does not allow the diagnosis of heart failure to be excluded.

Further investigations are therefore required in all patients with suspected heart failure; these include an electrocardiogram (ECG), a chest x-ray and an echocardiogram (Table 2 and Figure 1). If an echocardiogram cannot be arranged in a timely fashion and the diagnosis is not clear, measurement of plasma natriuretic peptides (B-type, natriuretic peptide [BNP] or the N-terminal prohormone of BNP [NT-proBNP]) improves diagnostic accuracy (the diagnosis of heart failure is unlikely if the level of either of these peptides is low).[4]

If there is doubt about the diagnosis or the patient is younger than age 65 years, specialist referral should be considered (see the box on page 60). A diagnostic algorithm is provided on page 62.

The causes of heart failure

Heart failure is the end manifestation of various cardiovascular diseases, most commonly coronary artery disease and hypertension. When a patient presents with heart failure, the clinician should establish the mechanism and cause of the heart failure and identify whether any precipitating or aggravating factors are relevant.

Table 2. Investigations for heart failure

Electrocardiography
- Usually abnormal
- May provide additional information about the cause of heart failure (e.g. previous myocardial infarction, arrhythmias)

Chest x-ray
- May allow a diagnosis of heart failure or alternative pathology; however, a normal x-ray does not exclude the diagnosis of heart failure

Echocardiography
- The single most useful investigation in patients with suspected heart failure
- Confirms the diagnosis and provides anatomical and functional information to guide management

Full blood count, serum electrolyte, renal and liver function
- Anaemia can exacerbate or cause heart failure
- Renal failure and electrolyte abnormalities may occur as a consequence of drug therapy; measurements should be performed in stable patients every six months
- Hepatic congestion may cause elevated liver enzymes

Thyroid function test
- Thyroid dysfunction is an uncommon cause of heart failure
- Thyrotoxicosis may also precipitate arrhythmias (e.g. atrial fibrillation)

Natriuretic peptides (BNP/NT-proBNP)
- Useful in excluding heart failure in patients with undifferentiated clinical features, especially if the echocardiogram cannot be arranged in a timely manner
- Less useful in patients with clear-cut features of heart failure who should proceed directly to echocardiography

Cardiac catheterisation
- Coronary angiography should be considered in patients with angina or suspected coronary artery disease
- Endomyocardial biopsy is rarely performed and is indicated in unexplained acute rapidly progressive heart failure; it is also helpful in heart failure with suspected infiltrative disease (e.g. amyloidosis, sarcoidosis)

Assessment of myocardial ischaemia and viability
(e.g. stress nuclear study, stress echocardiogram, cardiac MRI, PET)
- Useful to determine whether revascularisation should be considered in patients with coronary artery disease and left ventricular dysfunction
- May also be considered in patients with unexplained exertional dyspnoea and a normal resting echocardiogram to rule out ischaemia

Respiratory function tests
- Useful to exclude respiratory disease

ABBREVIATIONS: BNP = B-type natriuretic peptide; MRI = magnetic resonance imaging; NT-proBNP = N-terminal prohormone BNP; PET = positron emission tomography.

When to refer

Specialist referral should be considered for most patients with heart failure. Early referral should be offered if there are any of the following circumstances, especially if the patient is geographically isolated:

- uncertain diagnosis
- age younger than 65 years
- complex management issues (e.g. difficulty starting or uptitrating β-blockers)
- acute decompensation
- refractory symptoms.

Early referral is also appropriate for evaluation of those patients being considered for revascularisation or device implantation.

The single most useful test to confirm the diagnosis and determine the mechanism and in some cases the cause of heart failure is the echocardiogram. The mechanisms can be broadly divided into whether the patient has a myopathic process (by far the most common, and can be further subdivided into systolic and diastolic heart failure), valvular heart disease (e.g. aortic stenosis or mitral regurgitation) or a rare cause such as pericardial disease or high-output failure.

The myopathic causes of heart failure are given in Table 3. Coronary artery disease and hypertension can each lead to heart failure either as a result of reduced LV contractility (systolic heart failure) or abnormal LV filling with delayed relaxation or increased stiffness (diastolic heart failure). Precipitating and aggravating factors for heart failure that should be considered are listed in Table 4.

Heart failure prevention

The prevention of heart failure involves the prevention of cardiovascular disease by the recognition and treatment of cardiovascular risk factors (i.e. hypertension, dyslipidaemia, diabetes, obesity and smoking). Secondary prevention in patients with established vascular disease reduces the risk of ischaemic events that will predispose the patient to adverse LV remodelling.

Asymptomatic LV systolic dysfunction is associated with a fivefold risk of dying or developing heart failure.[7] If identified, there is good evidence that angiotensin

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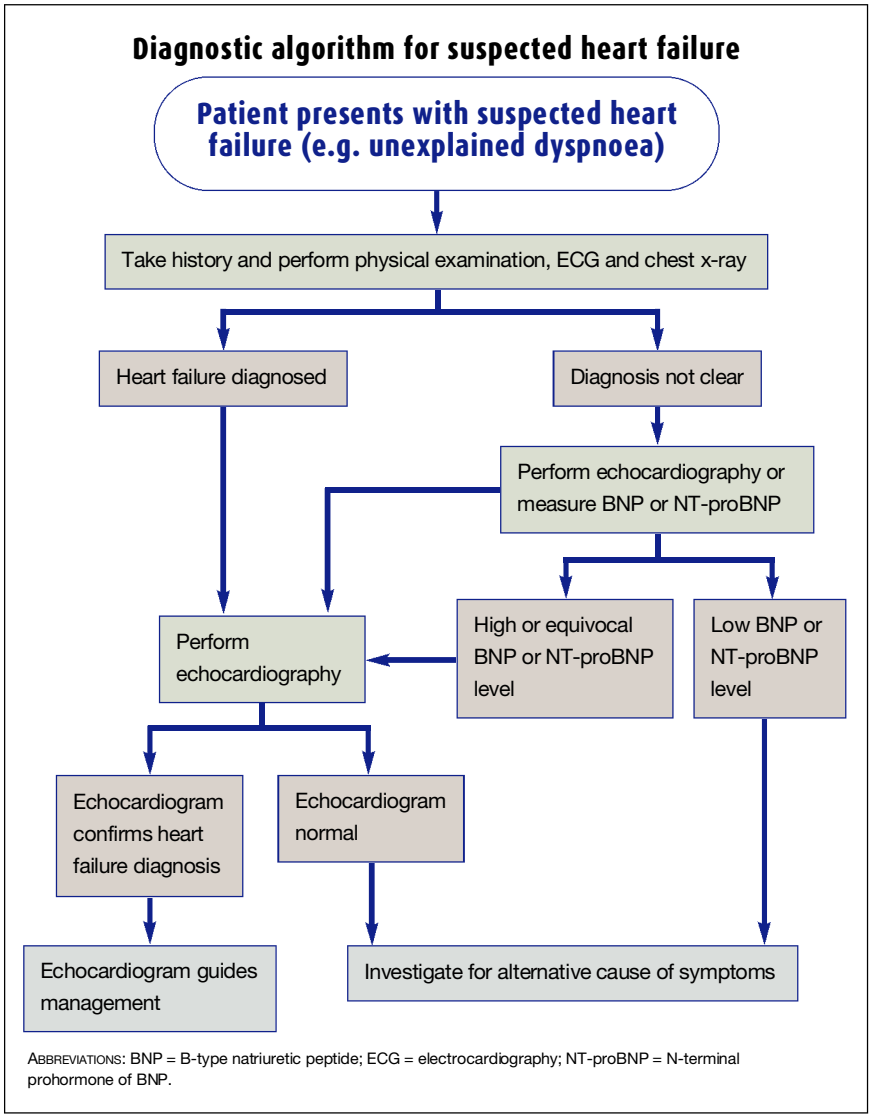

ABBREVIATIONS: BNP = B-type natriuretic peptide; ECG = electrocardiography; NT-proBNP = N-terminal prohormone of BNP.

converting enzyme (ACE) inhibitors reduce this risk; most guidelines also advocate the use of β-blockers.[4] Although there are specific high-risk groups where serial echocardiography is currently recommended (e.g. first-degree relatives of patients with familial dilated cardiomyopathy), there are many other high-risk groups (e.g. patients with chronic hypertension, previous myocardial infarction, peripheral vascular disease, diabetes or heavy alcohol exposure) where serial screening for asymptomatic LV dysfunction remains controversial. Given the limited availability of standard echocardiography, the acceptable screening test remains contentious, although natriuretic peptides and hand-held echocardiography hold the most promise for widespread screening in high-risk individuals.[8,9]

Treatment of heart failure

Nonpharmacological treatment

Lifestyle and behavioural modification are central to the successful management of patients with heart failure (Table 5).

Salt (sodium) restriction and attention to fluid balance is necessary in all patients. Patients should be instructed to weigh themselves every morning after going to the toilet and before getting dressed or eating breakfast. They should seek advice if their weight increases or decreases by more than 2 kg over two days. Some patients may be instructed to self-regulate a flexible diuretic dose. All clinically stable patients should be considered for referral to a supervised physical activity program, aiming for 10 to 30 minutes of moderate intensity physical activity on most days of the week.

Multidisciplinary heart failure disease management programs co-ordinated by heart failure nurses promote self-management. They have been shown to be effective in reducing hospitalisation and mortality, especially in patients recently hospitalised with heart failure.

Pharmacological treatment

The management of patients with heart failure is guided by the findings on echocardiography. If the patient has significant primary valvular disease, surgical or percutaneous intervention (e.g. valve replacement, mitral valvuloplasty) will usually be required. If the echocardiogram reveals LV systolic dysfunction (LVEF 40% or less) as the likely cause of heart failure, there is high-level evidence that neurohormonal blocking agents (i.e. β-blockers, ACE inhibitors, aldosterone antagonists, angiotensin receptor blockers) will improve LV function and reduce symptoms, hospitalisation and mortality.[4] Unfortunately, these medications are still underprescribed in clinical practice and many patients often remain on inadequate doses.

A pharmacological treatment algorithm is provided on page 68.

ACE inhibitors and β-blockers

Regardless of symptoms, ACE inhibitors should be prescribed to all patients with LV systolic dysfunction (LVEF 40% or less). Once considered contraindicated, β-blockers are now mandatory for all

patients with symptomatic systolic heart failure provided there are no contraindications and the patient is euvolaemic. Among the available β-blockers, only bisoprolol, carvedilol, controlled-release metoprolol and nebivolol have been shown to have a prognostic benefit. They should be started at low doses and uptitrated every two to four weeks.

Generally, the aim with using ACE inhibitors and β-blockers to treat heart failure is to achieve target doses (i.e. the doses shown to be clinically effective in randomised controlled studies) of drug therapy rather than specific blood pressures and heart rates. Indeed, provided the renal function is stable and the patient is not suffering from symptomatic hypotension, low-normal blood pressures are preferred (i.e. systolic blood pressures below 120 mmHg), especially in patients with systolic heart failure. Similarly, although specific heart rates are not mandated, the aim is to get the heart rate to around 55 to 65 beats per minute.

A patient's vital signs and volume status should be monitored as these drugs are uptitrated. If the doses that were shown to be clinically effective in the randomised controlled studies cannot be reached then the maximum doses tolerated by the patient should be used.

Angiotensin receptor blockers and aldosterone antagonists

Angiotensin receptor blockers are an alternative for patients who do not tolerate ACE inhibitors (often due to cough). In patients who remain symptomatic despite ACE inhibitors, β-blockers and diuretics, addition of either spironolactone (a nonselective aldosterone antagonist) or an angiotensin receptor blocker should be considered; however, serum potassium levels and renal function should be closely monitored.

The selective aldosterone antagonist eplerenone has been shown to decrease mortality when commenced in the immediate postmyocardial infarction period in patients with heart failure and LV systolic dysfunction.

Table 3. Aetiology of heart failure due to heart muscle dysfunction

Systolic heart failure	Diastolic heart failure
Common causes	
Coronary artery disease Hypertension	Hypertension Coronary artery disease Diabetes Obesity
Less common causes	
Dilated cardiomyopathy (idiopathic, familial, ethanol, chemotherapeutic agents, other drugs, tachycardia-mediated, metabolic, nutritional, HIV, peripartum) Myocarditis	Hypertrophic cardiomyopathy Restrictive cardiomyopathy (infiltrative, e.g. amyloidosis)

Diuretics, digoxin, nitrates and omega-3 fatty acids

Diuretics, digoxin and nitrates are useful symptomatic treatments, although they have not been shown to decrease mortality.

Loop diuretics (e.g. frusemide) are the most effective drugs to treat congestion. They are usually required in the initial management of patients with symptoms or signs of congestion, although the dose may be reduced once the patient is euvolaemic to facilitate the uptitration of ACE inhibitors and other vasodilator therapy. The dose of diuretic can also be adjusted depending on the patient's volume status, which is guided by daily weight measurements.

Digoxin reduces hospitalisation in patients with severe symptoms without added mortality benefit. It is also a useful ventricular rate-controlling agent for atrial fibrillation.

The combination of hydralazine and nitrate may provide marginal benefit in patients in whom ACE inhibitors and angiotensin receptor blockers are contraindicated. Omega-3 fatty acid supplementation has a modest mortality benefit in addition to standard therapy.[10]

Treatment of persisting oedema

In patients with persisting oedema despite the treatments already discussed, further

Table 4. Precipitating and aggravating factors for heart failure

- Nonadherence to fluid intake, salt restriction and drug therapy
- Arrhythmia (e.g. atrial fibrillation)
- Myocardial ischaemia/infarction
- Cardiac depressant or salt-retaining drug (e.g. nondihydropyridine calcium channel blockers, corticosteroids, NSAIDs, glitazones) use
- Ethanol or illicit drug (e.g. cocaine) use
- Infection
- Renal failure
- Pulmonary thromboembolism
- High-output states (e.g. anaemia, thyrotoxicosis)

options are increasing the dose of loop diuretic or adding spironolactone (if not already commenced), a nitrate or a thiazide diuretic.

In refractory cases, the patient may be admitted to hospital for intravenous loop diuretic infusions or short-term infusions of positive inotropic agents, with close monitoring of electrolyte levels and renal function. These patients generally have a poor prognosis.

Treatment of diastolic heart failure

Treatment of diastolic heart failure (LVEF more than 40%) remains largely empirical. Current treatment concentrates on decreasing congestion, treating ischaemia and risk factor modification (i.e. treating hypertension and diabetes).

Devices

Cardiac devices are costly and invasive. Nevertheless, in carefully selected patients they offer improvement in symptoms, quality of life and mortality.[4] About 50% of patients with heart failure die suddenly, usually due to a ventricular arrhythmia. Survivors of ventricular fibrillation and unstable ventricular tachycardia with no correctable cause should receive an implantable cardioverter defibrillator (ICD). Primary prophylactic ICD therapy should also be considered for patients with a LVEF of 35% or less despite medical therapy to reduce the risk of sudden cardiac death.

Some patients with heart failure have dyssynchronous LV contraction (more common in patients with a broad QRS complex, especially left bundle branch block), which is associated with an adverse prognosis. Cardiac resynchronisation therapy using a biventricular pacemaker to resynchronise LV contraction is recommended for patients with systolic heart failure (LVEF 35% or less) associated with a QRS width of 120 milliseconds or greater who remain severely symptomatic despite medical therapy.

Treatment of exacerbations of heart failure

Precipitating or aggravating factors should be identified and treated in patients who present with an exacerbation of heart failure (Table 4). Medical therapy will usually need to be adjusted, which will often involve increasing the dose of diuretic therapy in the first instance, and adjusting other treatments once the patient is stabilised. Generally, the patient's usual heart failure therapy, including β-blockers, is continued during exacerbations. However, if the patient is hypotensive, the β-blocker dose may need to be reduced or temporarily suspended, with the aim of restarting it once the patient's clinical state has improved.

Some patients with decompensated heart failure will need to be admitted to hospital for stabilisation. Treatment options include high-flow oxygen, intravenous morphine, diuretics, vasodilators and/or inotropes, noninvasive or invasive ventilation, and mechanical support with intra-aortic balloon pumps or LV assist devices.

Treatment of end-stage heart failure

Cardiac transplantation is the treatment of choice in selected patients with refractory heart failure. Five-year survival rates may be as high as 65 to 75% with careful patient selection. Ventricular assist devices may be used as a bridge to transplant. Domiciliary inotrope infusions are also an option.

In patients with severe refractory symptoms that are resistant to optimal pharmacological and nonpharmacological therapy, interdisciplinary palliative care should be considered.

Patient information sheet

The patient information sheet on chronic heart failure, 'Living well with chronic heart failure', can be downloaded from the National Heart Foundation of

Table 5. Nonpharmacological treatments for heart failure*

- Exercise training program in clinically stable patients
- Referral to a multidisciplinary heart failure disease management program in high-risk patients such as those recently hospitalised with heart failure
- Treatment of obstructive sleep apnoea
- Bed rest during acute decompensation
- Dietary sodium restriction (less than 2 g/day)
- Avoidance of excess fluid intake
- Limiting of alcohol intake to less than one to two standard drinks a day or total abstinence in patients with alcoholic cardiomyopathy
- Smoking cessation
- Daily weighing, with seeking of medical advice if rapid weight gain or loss
- Regular influenza and pneumococcal vaccination
- Avoidance of high-altitude travel destinations
- Avoidance of phosphodiesterase-5 inhibitor (e.g. sildenafil) use in patients receiving nitrates
- Weight loss for obese patients
- Diet low in saturated fat and high in fibre†
- Limiting of caffeinated beverages intake to less than two cups a day
- Pregnancy should generally be avoided

* Based on 'Guidelines for the prevention, detection and management of people with chronic heart failure in Australia 2006.'[4]

† In the cachectic phase, a high-calorie and high-protein diet with no restriction of fat intake may be encouraged.

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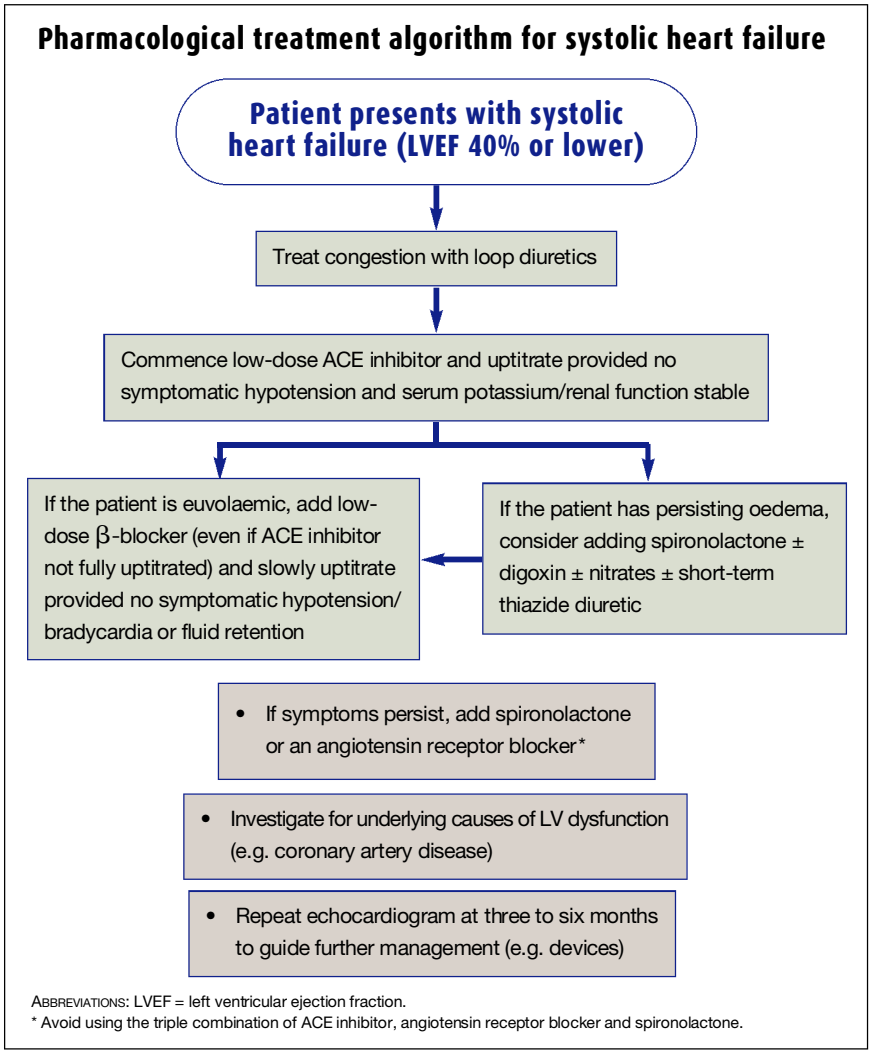

Australia's website (http://www.heartfoundation.org.au/SiteCollectionDocuments/CHF%20IS-346%20Info%20Sheet%20Living%20Well%20CHF.pdf).

Conclusion

Heart failure occurs as an end result of numerous conditions, especially coronary artery disease and hypertension. Although bedside clinical assessment may allow the diagnosis of heart failure, a normal examination and chest x-ray does not exclude the diagnosis, hence further investigation with echocardiography is recommended. These patients generally have a poor quality of life and high mortality, especially if the diagnosis is not made in a timely fashion.

It is important to identify the mechanism and cause of heart failure to correctly guide management. Lifestyle and behavioural modification to reduce cardiovascular disease risk factors are central to the successful management of patients with heart failure. ACE inhibitors, angiotensin receptor blockers, β-blockers and aldosterone antagonists improve symptoms and reduce the risk of hospitalisation and death in patients with systolic heart failure, with device therapy providing added benefit in selected patients. Furthermore, multidisciplinary heart failure disease management programs should be considered in all patients recently hospitalised with heart failure. MT

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A list of references is available on request to the editorial office.

Further reading

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The full version of these guidelines, by the National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand, is available online at: http://www.heartfoundation.org.au/SiteCollectionDocuments/CHF%202006%20Guidelines%20NHFA-CSANZ%20WEB.pdf (accessed May 2010).

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