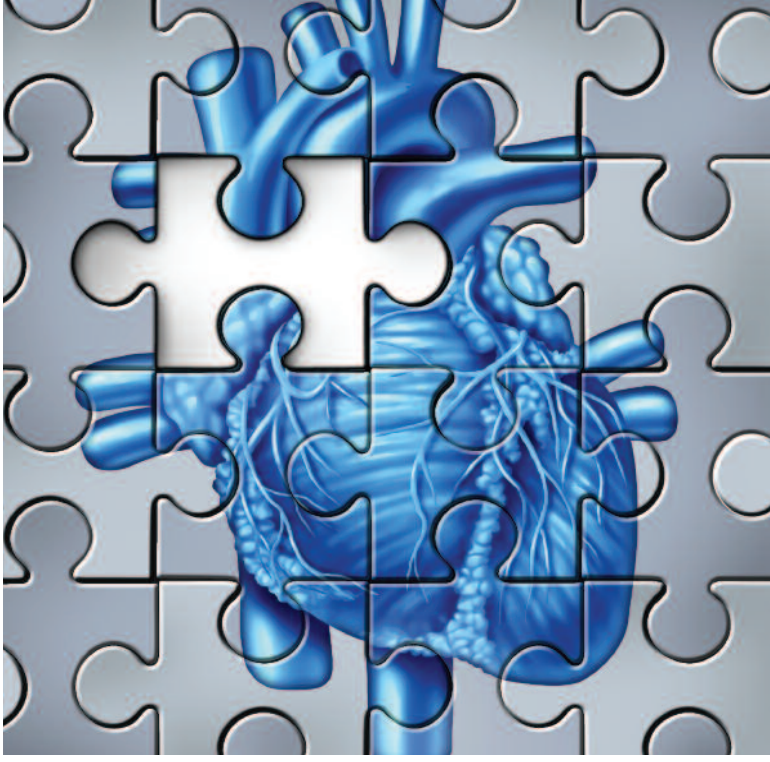
FEATURE

Management of chronic heart failure: a pill too far?



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Chronic heart failure is an increasingly common condition associated with high mortality, poor quality of life and recurrent hospitalisation. Management involves identification and treatment of reversible causes and the use of nonpharmacological, medical and device therapies.

Key points

- **Chronic heart failure is a common, costly and debilitating disease, which has a higher mortality than that of most cancers.**
- **All patients suspected of having heart failure should be seen at least once by a cardiologist to help guide therapy and investigate for ischaemia, valvular or pericardial disease.**
- **Patients with heart failure should undergo echocardiography for diagnosis and to help guide treatment.**
- **Measurement of plasma B-type natriuretic peptide levels is often useful in the diagnosis of heart failure and to guide therapy in difficult cases.**
- **All patients with heart failure should be treated with ACE inhibitors and beta blockers unless contraindicated.**
- **Aldosterone antagonists are useful in patients who are resistant to treatment, whereas digoxin and diuretics are mainly used for symptom control as they do not improve long-term survival.**
- **Regular exercise, patient support programs and cardiac devices play an important role in further managing patients with heart failure.**

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Heart failure has been defined as: 'a complex clinical syndrome with symptoms (dyspnoea, fatigue) that can occur at rest or on exercise, and are the result of an underlying structural or functional cardiac abnormality that impairs the ability of the heart to fill with or eject blood'.[1]

Chronic heart failure (CHF) affects more than 300,000 people in Australia, with over 30,000 new cases diagnosed annually. The prevalence has been increasing as the Australian population ages and the management of heart failure improves, leading to more patients living with CHF but having more advanced disease.[2] CHF is associated with significant morbidity, mortality and hospitalisations making it not only a common condition but also one that consumes significant health resources. From the time of diagnosis, median survival is less than four years with 65% of patients dying within five years.[3] However, recent advances in the understanding of the pathophysiology of CHF and development of therapies, particularly angiotensin converting enzyme (ACE) inhibitors and beta blockers, have improved mortality and reduced symptoms and hospitalisation, but outcomes are still poor. Accurate diagnosis and use of medications shown to be effective will improve this bleak outlook for patients with CHF.

CHF may occur as a result of systolic heart failure (SHF) or heart failure with preserved ejection function (HFPEF). SHF is a clinical syndrome in which patients' symptoms are due to reduced left ventricular contraction (left ventricular ejection fraction [LVEF] <50%). In HFPEF (previously known as diastolic heart failure), patients have

New York Heart Association functional classification

Class I – asymptomatic left ventricular dysfunction
Class II – symptoms with normal activities
Class III – symptoms with less than normal activities
Class IV – symptoms at rest

normal systolic function yet still have symptoms of CHF. In HFPEF, the ejection fraction may be normal but the stroke volume and cardiac output are reduced due to decreased ventricular filling secondary to abnormal left ventricular relaxation. One-third to two-thirds of cases of CHF are due to HFPEF.[4,5] The prognosis of patients with HFPEF has been shown to be better than that of patients with SHF.[5] Despite improvements in the prognosis of SHF in the past two decades, there has been little improvement in the prognosis of HFPEF. Predictors of poor prognosis in CHF are shown in the box below.

Epidemiology

By the age of 40 years, the lifetime risk of developing CHF is approximately one in five.[6] CHF affects 2.5% of Australians aged 55 to 64 years and 8.2% of those aged over 75 years.[2] CHF is the eighth most common cause of death in Australia,[7] CHF caused 4000 deaths and was a contributory cause in a further 20,000 deaths in 2007.[2] CHF led to approximately 43,000 hospitalisations in 2006-7 in Australia, with many more as a secondary diagnosis.[2]

Severity of CHF is graded according to the New York Heart Association (NYHA) functional classification (see the box on page 14).[8] Annual mortality is approximately 5% for patients with NYHA class I and more than 50% for class IV.

Clinical assessment

History

Patients with CHF may be described as having predominantly left or right ventricular failure. Symptoms of left ventricular failure include exertional dyspnoea and orthopnoea with paroxysmal nocturnal dyspnoea occurring later. Right ventricular failure leads to lower limb oedema with ascites developing later. Other symptoms include cough, (particularly when supine), fatigue, nausea and anorexia (due to reduced cardiac output, hepatic congestion and bowel oedema). The box below lists the physical signs of CHF.

A history should be taken to identify the aetiology of CHF, including myocardial infarction, risk factors for coronary artery disease, hypertension, excessive alcohol intake, antecedent viral illness and prior rheumatic fever or murmurs (see the box below). The causes of decompensation in established CHF should also be elucidated (see the box on page 16). A family history of cardiomyopathy, heart failure or sudden death should be enquired about.

Investigation

A full blood count may demonstrate anaemia or a leucocytosis infection, which may precipitate CHF decompensation. Electrolyte and renal function measurements help to guide diuretic therapy. Elevated gamma glutamyl transpeptidase and alkaline phosphatase levels may suggest hepatic congestion. Thyroid function tests, autoimmune screen for connective tissue disease, iron studies for haemochromatosis and viral serology may help identify the cause of CHF. Urine dipstick to exclude obvious infection is also helpful.

Brain natriuretic peptide (BNP) is released by ventricular myocardium in response to pressure or volume stress, and its measurement may assist in the exclusion of CHF decompensation.[1] A BNP level of less than 100 ng/mL makes a diagnosis of CHF very unlikely. A BNP level of more than 400 ng/mL is consistent with decompensated or severe established CHF, with the test becoming

Predictors of poor prognosis in patients with CHF

- Renal impairment
- Resting tachycardia
- Left bundle branch block
- Anaemia
- Secondary pulmonary hypertension
- Elevated levels of aldosterone
- Elevated levels of endothelin
- Elevated levels of uric acid
- Low sodium levels
- Hypotension not due to medication
- High plasma B-type natriuretic peptide
- Significant valvular dysfunction
- Elevated levels of angiotensin II
- Elevated levels of adrenaline
- Elevated levels of tumour necrosis factor alpha

Physical signs of heart failure

Signs of heart failure

- Elevated jugular venous pressure
- Basal inspiratory crepitations
- Ankle oedema
- Third heart sound
- Hypotension not due to medication

Signs of severe heart failure

- Markedly elevated jugular venous pressure
- Crepitations beyond the mid-zones of the lungs
- Oedema above the mid tibia
- Pulsatile hepatomegaly
- Ascites
- Weight gain, greater than 1.5 kg in a 48-hour period

Causes of chronic heart failure

Common

- Ischaemic heart disease
- Hypertension
- Valvular heart disease
- Idiopathic dilated cardiomyopathy

Less common

- Diabetic cardiomyopathy
- Myocarditis
- Congenital heart disease
- Drugs (alcohol or chemotherapeutic agents, e.g. anthracyclines)
- HIV infection
- Peripartum cardiomyopathy
- Thyroid disease (hypothyroidism or hyperthyroidism)
- Infiltrative conditions (sarcoidosis, amyloidosis)
- Connective tissue diseases
- Iron overload
- Arrhythmia or tachycardia-induced cardiomyopathy

more specific if the result is very high. However, levels between 100 and 400 ng/mL are difficult to interpret. BNP levels may rise in people with renal impairment, pulmonary embolism, pulmonary hypertension or lung disease with associated right heart strain, or in those with a history of CHF who present with other illnesses (e.g. sepsis). In general practice, measurement of BNP levels may be useful to exclude heart failure if the level is below 100 ng/mL, but otherwise its place is somewhat limited when clinical parameters are also taken into account. Regular BNP testing is not recommended for prognostic reasons or to guide treatment, except in specialised clinics.

A chest x-ray can assess for pulmonary congestion and pleural effusions, whereas cardiomegaly and upper lobe diversion are features of established CHF. ECG may identify prior myocardial infarction (Q-waves, delayed or early R-wave progression in the precordial leads) or left ventricular hypertrophy. The ECG can detect arrhythmia (including atrial fibrillation with a rapid ventricular response that can cause decompensation of CHF), which may complicate CHF. An ECG may also demonstrate left bundle branch block, which is an indication for biventricular pacing.

Echocardiography is the gold-standard investigation in CHF.[9] All patients with shortness of breath should have an echocardiography. It assesses ventricular size, contractility and diastolic function (e.g. mitral E/A ratio and E/e' ratio). Echocardiography may identify valvular heart disease, left ventricular hypertrophy, pulmonary hypertension or regional wall motion abnormalities suggesting coronary artery disease (CAD). An echocardiography can assess response to therapy by serial measurement of LVEF.

CAD should be considered in all newly diagnosed patients with CHF because it is a potentially reversible cause of CHF. Revascularisation (coronary stent or bypass grafting) improves ventricular function and prognosis. Coronary angiography should be considered if there is clinical suspicion of CAD (i.e. angina, risk factors, or echocardiographic or ECG evidence of silent myocardial infarction). If there is a low likelihood of CAD, then noninvasive imaging should be undertaken (e.g. stress echocardiogram, CT coronary angiography or nuclear perfusion scan).

Causes of exacerbations in patients with CHF

- Ischaemia
- Infections, particularly respiratory, urinary tract or cellulitis
- Arrhythmias (most commonly atrial fibrillation)
- Valvular dysfunction (e.g. acute mitral regurgitation)
- Lack of compliance with medication or cessation of medication (particularly frusemide)
- Lack of adherence to salt and fluid restriction
- Commencement of drugs that worsen heart failure
- Renal failure leading to fluid overload
- Anaemia
- Pulmonary embolus
- Thyroid imbalance (hypothyroidism or hyperthyroidism)

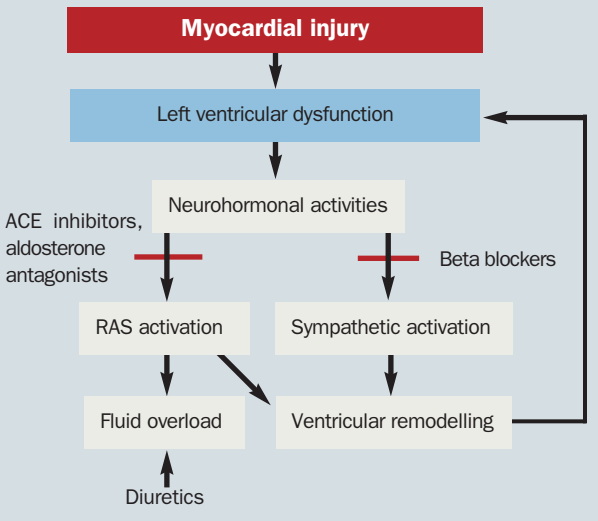

Figure. Neurohormonal activation in CHF and therapeutic targets.
Abbreviations: ACE = angiotensin converting enzyme; CHF = chronic heart failure.

Management

Management of CHF aims to improve prognosis and quality of life and to reduce the number of hospitalisations. Management involves identification and treatment of reversible causes and use of nonpharmacological, medical and device therapies.

Fluid retention in CHF is initiated by low cardiac output and activation of the renin–angiotensin–aldosterone system and the sympathetic nervous system, which is detrimental to ventricular structure and function. Diuretics reduce fluid overload and enable patient stabilisation and symptom relief. ACE inhibitors, angiotensin receptor blockers (ARB) and beta blockers target these pathways (see Figure).

Many treatments for CHF promote vasodilatation and relative bradycardia to enhance ventricular function. It is recommended to slowly achieve a target heart rate of 55 to 60 beats per minute and systolic blood pressure of 105 to 110 mmHg.[10] It is preferable for all patients with CHF to see a cardiologist, at least once, to help guide therapy and to identify those who require revascularisation, biventricular pacing or an implantable defibrillator.

About 80% of sudden deaths, pulmonary oedema and myocardial infarctions occur between 3 am and 8 am. The use of once-daily ACE inhibitors, ARBs, beta blockers and nitrates at night may improve outcomes by antagonising the diurnal surges in adrenaline, noradrenaline, angiotensin II, cortisol and melatonin, which contribute to the high risk in the early morning period.

A summary of medications to avoid in patients with CHF is listed in the box on page 18.

Medications to avoid in patients with CHF

- Calcium channel blockers
- NSAIDs and COX-2 inhibitors
- Corticosteroids
- Antiarrhythmic agents (except beta blockers and amiodarone)
- Tricyclic antidepressants
- Clozapine
- Thiazolidinediones (pioglitazone, rosiglitazone)
- Tumour necrosis factor-alpha receptor antagonists
- Dronedarone
- Trastuzumab
- Tyrosine kinase inhibitors
- Moxonidine

All of the above medications have been shown to increase mortality, worsen symptoms or increase arrhythmia in patients with chronic heart failure (CHF).

Nonpharmacological measures for CHF

- Sodium restriction <2 g/day
- Fluid restriction 1.5 L/day (1.2 L in severe CHF)
- Daily weight measurements at home
- Alcohol cessation in patients with alcohol-related cardiomyopathy (<20 g/day with two alcohol-free days in other patients)
- Smoking cessation
- Identification and treatment of comorbid conditions (e.g. sleep apnoea, iron deficiency/anaemia, depression)
- Regular physical activity and bed rest only during exacerbations of CHF
- Vaccination against influenza and pneumococcus
- Enrolment in a CHF program:
  - early identification of symptoms and signs of CHF deterioration
  - development of a CHF action plan and flexible diuretic regimen
  - uptitration of CHF therapy, especially beta blockers and ACE inhibitors
  - patient and carer education about CHF and its management
  - advanced care planning
  - increased access to a heart failure specialist for: referral to a cardiothoracic surgeon or to an electrophysiologist; echocardiography; and consideration of more advanced care (e.g. heart transplantation, left ventricular assist device)

Abbreviations: ACE = angiotensin converting enzyme; CHF = chronic heart failure.

Nonpharmacological management

Patients who are hospitalised with CHF should be enrolled in a CHF program, which involves visiting the patient in hospital, uptitrating the doses of beta blockers and ACE inhibitors, regular telephone follow up, cardiac rehabilitation and follow up in a heart failure clinic (see the box on this page). These CHF programs have been shown to improve quality of life, survival and reduce hospitalisations,[11] and are often overseen by nurse-directed, multidisciplinary heart failure programs. These programs also involve education, counselling, supervised exercise programs tailored to the patient's exercise tolerance and home visits to ensure compliance.

Patient outcomes are also improved when a cardiologist participates in outpatient CHF management due to optimal uptitration of the pharmacological therapies.[12] For patients with CHF who live in rural or remote areas, telemonitoring or simple telephone follow up may reduce hospital readmission and improve symptoms.

Target doses of ACE inhibitors in CHF

Ramipril 10 mg/day
Perindopril 10 mg/day
Enalapril 20 mg twice daily
Fosinopril 20 mg/day
Lisinopril 10 mg/day
Trandolapril 4 mg/day
Captopril 25 mg three times daily

Abbreviations: ACE = angiotensin converting enzyme; CHF = chronic heart failure.

Pharmacological management

ACE inhibitors and ARBs

Use of ACE inhibitors, if not contraindicated, is mandatory in all patients with CHF, even in asymptomatic patients, because they reduce mortality and hospitalisation and improve symptoms.[1] Use of ACE inhibitors reduces the risk of myocardial infarction in patients with CHF by 20%, cardiovascular death by 26% and overall mortality by 16%.[13] ACE inhibitors should be started at low doses and uptitrated over three to four weeks to the highest tolerated dose. Renal function and electrolyte levels should be checked two weeks after commencement, then after one month and then three to six monthly. ACE inhibitors should be discontinued if potassium levels exceed 5.5 mmol/L or creatinine levels increase by more than 20% from baseline. Reasons for discontinuation include cough (20% of patients), symptomatic hypotension and renal or electrolyte disturbance. Daytime hypotension may be reduced by taking ACE inhibitors at night. Target doses of ACE inhibitors in patients with CHF are shown in the box to the left of this page.

Improvements in mortality, hospitalisation and symptoms have been shown to be similar in patients with CHF who are taking ARBs or ACE inhibitors.[1] ARBs should be considered only in patients intolerant of ACE inhibitors because of cough or in addition to ACE inhibitors in patients with CHF who remain symptomatic or hypertensive. Caution should be exercised in combining ACE inhibitors and ARBs in patients with renal impairment or diabetes. Titration of ARBs and measurement of renal function and electrolyte levels are carried out in the same way as with ACE inhibitors. An elevated level of angiotensin II is a marker of poor prognosis in patients with CHF, but this is not routinely measured in general practice and is influenced by most therapies that treat CHF.

Table. Beta blocker dose titration in CHF

Week	Carvedilol	Bisoprolol	Nebivolol	Extended-release metoprolol
0–2	3.125 mg twice daily	1.25 mg/day	1.25 mg/day	23.75 mg/day
2–4	6.25 mg twice daily	2.5 mg/day	2.5 mg/day	47.5 mg/day
4–6	12.5 mg twice daily	5 mg/day	5 mg/day	95 mg/day
6 onwards	25 mg twice daily*	10 mg/day	10 mg/day	190 mg/day

*The dosage of carvedilol may be increased to 50 mg twice daily in patients who weigh more than 85 kg.

Beta blockers

Beta blockers are indicated in all patients with CHF and inhibit the adverse effects of sympathetic activation. They improve both mortality and morbidity (by approximately 34% when combined with an ACE inhibitor).[1] Beta blockers for CHF available in Australia include carvedilol, bisoprolol, nebivolol and extended-release metoprolol.[1] Beta blockers should be commenced at low doses after the patient is euvolaemic, and uptitrated over one to two months (see Table). Patients should be haemodynamically stable with a systolic blood pressure of more than 85 mmHg, without postural drop, minimal peripheral oedema and no pulmonary crackles before beta blockers are prescribed. Rapid uptitration may lead to adverse effects and inappropriate discontinuation. The dose of beta blocker should be reduced if the heart rate falls below 55 beats per minute. Hypotension can be treated by reducing the dose of diuretics or other vasodilators, rather than reducing the dose of the beta blocker.

Side effects of beta blockers include hypotension, fatigue, bronchoconstriction in patients with reversible airways obstruction (>15% improvement in forced expiratory volume in 1 second with bronchodilators), depression, insomnia and mild initial worsening of CHF symptoms. Nonvasodilatory beta blockers (bisoprolol or extended-release metoprolol) may be helpful in patients with postural hypotension. Cardioselective beta blockers (e.g. bisoprolol, nebivolol) are tolerated by over 85% of patients with chronic obstructive pulmonary disease (COPD) without reversible airways obstruction. Patients with true asthma or taking corticosteroid treatment for COPD may not tolerate beta blockers. Nebivolol has been shown to be effective in patients over 70 years of age, regardless of ejection fraction.[14]

Aldosterone antagonists

Aldosterone antagonists, such as spironolactone or eplerenone, have been shown to improve mortality and morbidity in all grades of CHF including postmyocardial infarction left ventricular dysfunction.[1] Eplerenone is a selective aldosterone antagonist and does not cause gynaecomastia, which can occur with spironolactone. Monitoring of electrolyte levels and renal function (one week, then one month, then three monthly checks after initiation) is important as aldosterone antagonists may cause hyperkalaemia. These drugs are contraindicated in patients with significant renal impairment (glomerular filtration rate of less than 30 mL/min). Low doses of spironolactone (e.g. 25 mg once or twice weekly) are useful in combination with ACE inhibitors, ARBs or other diuretics, especially for patients with refractory peripheral oedema or hypertension.

Diuretics

Diuretics treat congestive symptoms by preventing sodium accumulation and reducing plasma volume, venous return and cardiac preload. They do not have a long-term mortality benefit.[1] In patients who are volume overloaded, a reasonable goal is a weight reduction of 1 kg/day. Once patients are euvolaemic, the dose of diuretics may be reduced, especially if this will allow initiation of drugs with a proven mortality benefit (e.g. beta blockers and ACE inhibitors).

Digoxin

Digoxin improves symptoms of CHF (fatigue, dyspnoea and exercise intolerance) and reduces hospitalisations in patients with persistent symptoms, despite use of the above mentioned therapies, but has no effect on mortality.[1] Digoxin is particularly valuable in patients with atrial fibrillation. Low doses are recommended (e.g. 62.5 µg/day or every two to three days) in patients with renal impairment.

Other drug therapies

Nitrates and hydralazine provide vasodilatation in patients who are intolerant of ACE inhibitors and ARBs. Nitrates reduce nocturnal dyspnoea, peripheral oedema, secondary pulmonary hypertension and myocardial ischaemia via venodilatation, improve venous capacitance and reduce right ventricular preload.[3,13] Nitrate patches are less well absorbed in patients with CHF due to poor peripheral perfusion. Isosorbide mononitrate is commenced at 30 mg every night, titrating to 60 mg and later 120 mg over one to two weeks. Use of hydralazine reduces nitrate tolerance, improves nitrate sensitivity and controls hypertension in patients with CHF who are not adequately controlled using first-line medications. Hydralazine is commenced at 12.5 mg twice daily, and increased to a maximum of 100 mg three times daily over one to two months.

Amiodarone has not been shown to improve mortality, but may control ventricular arrhythmia and atrial fibrillation in patients

with CHF. Complications include thyroid dysfunction, pulmonary fibrosis, hepatic dysfunction, corneal deposits, peripheral neuropathy, photosensitivity and skin discolouration.[15] Amiodarone should be initiated by a specialist or in consultation with a specialist.

Warfarin, dabigatran, rivaroxaban or apixaban are indicated for use in patients with CHF who have atrial fibrillation or cardiac thrombus.[1] Currently, warfarin is the only one of these anticoagulants reimbursed by the PBS for this indication. (Rivaroxaban, dabigatran and apixaban have all received recent PBAC recommendations for atrial fibrillation.) Patients with ischaemic cardiomyopathy should receive aspirin.[3] There is no strong evidence, however, for the use of anticoagulants or antiplatelets in patients with nonischaemic cardiomyopathy.

The sinus node inhibitor, ivabradine, has been shown to reduce the combined endpoint of cardiovascular mortality and heart failure hospitalisation in patients with CHF and a resting heart rate of more than 70 beats per minute. It has also been shown to reduce overall mortality in patients with CHF and a heart rate of more than 77 beats per minute.[16] Ivabradine is not currently available on the PBS. (However, it has recently been approved by both the TGA and PBAC for use in patients with heart failure and a heart rate of more than 77 beats per minute.)

Omega-3 ethyl esters 1000 mg/day has been shown to lead to a 9% reduction in mortality in patients with CHF.[17]

Management of refractory CHF

Patients with systolic dysfunction and NYHA class III and IV symptoms who do not respond to optimal medical therapy or who experience a rapid recurrence of symptoms may require hospitalisation for intensive management. A five-day course of intravenous inotropic therapy (dobutamine or dopamine) may provide temporary relief of symptoms and prolong the time to the next admission without mortality benefit. Left ventricular assist device implantation or cardiac transplantation may be considered in this group. Unfortunately, the waiting time for patients on the transplant list is considerable.

Device therapies

Patients with CHF who have experienced cardiac arrest or ventricular arrhythmias have a high risk of recurrent events. An implantable cardioverter defibrillator in patients with an LVEF of less than 35%, for both primary and secondary prevention of ventricular arrhythmia, leads to a reduction in mortality in both of these settings.[1] Cardiac dyssynchrony is seen in approximately one-third of patients with CHF and leads to further impairment of left ventricular function, abnormal remodelling and secondary mitral regurgitation.

Pacing the left and right ventricles simultaneously with cardiac resynchronisation therapy has shown to improve symptoms, functional capacity, CHF hospitalisations and mortality. The criteria for cardiac resynchronisation therapy are an LVEF of less than 35%, evidence of cardiac dyssynchrony (QRS duration >120 ms) and left bundle branch block.[1]

Left ventricular assist devices were developed initially for use as a bridge to cardiac transplantation in patients with severe heart failure and have been successful in achieving this aim. However, the results of a number of trials, including the randomization evaluation of mechanical assistance for the treatment of congestive heart failure (REMATCH) trial, have demonstrated that these devices are effective as destination therapy in experienced centres.[18]

Newer devices, such as the HeartMate II, Ventrassist and DeBakey devices, may be able to prolong life as well as improve quality of life. Complications of left ventricular assist devices include infections and haemorrhagic complications.[19]

Management of HFPEF

There is limited effective treatment for patients with HFPEF. No single drug can selectively enhance myocardial relaxation without inhibiting left ventricular function. Guidelines suggest to control systolic and diastolic hypertension (regression of left ventricular wall thickness on echocardiography is a therapeutic goal that may improve diastolic function), control ventricular rate in atrial fibrillation, and treat congestion with diuretics and coronary revascularisation in patients with CHF and ischaemia.[11]

Patients with stiff left ventricles and diastolic dysfunction are susceptible to excessive preload reduction, which can lead to underfilling of the left ventricle, a fall in cardiac output and hypotension (leading to weakness, presyncope and syncope). Thus, diuretics or venodilators, such as nitrates and ACE inhibitors, must be used judiciously.

Management of coexistent conditions

Several conditions may cause patients with CHF to have continued symptoms despite improvements in cardiac status. These comorbidities should be optimised to improve response to CHF therapy.

COPD

Hypoxia and hypercapnoea should be avoided in patients with CHF and use of inhaled anticholinergic agents and inhaled corticosteroids are recommended. Beta agonists may induce tachycardia and diminish the effects of beta blockers. Digoxin may have a role in patients with poor right ventricular function.

Obstructive sleep apnoea

Use of nocturnal continuous positive airway pressure masks is strongly recommended in patients with CHF and obstructive sleep apnoea to reduce hypoxia, sympathetic tone, arrhythmia and secondary pulmonary hypertension.

Iron deficiency/anaemia

Iron is an important substrate in muscle function, including cardiac muscle function. Patients with CHF who are iron deficient have elevated levels of hepcidin, which reduces oral iron absorption and uptake. Intravenous iron infusions are recommended for patients

with a transferrin saturation of less than 20% or ferritin level of less than 30 µg/L. Iron infusions have been shown to improve exercise capacity and quality of life.[20] Haemoglobin levels should be maintained above 100 g/L.

Erythropoiesis-stimulating agents (e.g. darbepoetin, erythropoietin) may benefit patients with CHF who have anaemia related to renal impairment as these medications improve quality of life, and their effect on survival in those with CHF has been evaluated. Treatment of mild, asymptomatic anaemia using darbepoetin in patients with CHF has recently been shown to have no benefit.[21]

Some trials have suggested overly aggressive correction of anaemia may be harmful, particularly in patients with chronic kidney disease, and a haemoglobin level of 110 to 120 g/L should be targeted.[22]

Atrial fibrillation

The ventricular response to atrial fibrillation should be controlled in patients with CHF and atrial fibrillation to maximise ventricular filling time and optimise stroke volume. Patients with heart rates of more than 80 beats per minute should be treated with rate-lowering agents such as beta blockers, digoxin and amiodarone, if necessary. Calcium channel blockers may worsen cardiac function.

Pulmonary hypertension

Left ventricular dysfunction is one of the most common causes of pulmonary hypertension. Treating CHF aggressively will reduce the risk of developing pulmonary hypertension, and the addition of nitrates and hydralazine will reduce the degree of secondary pulmonary hypertension. Endothelin receptor antagonists have not been shown to improve outcomes in patients with CHF.[23,24]

Depression

Some symptoms of depression can mimic CHF. Use of tricyclic antidepressants may increase the risk of arrhythmia and prolong the QT interval. Selective serotonin reuptake inhibitors and many of the newer agents and the atypical antipsychotics used for depression appear to be safe to use in patients with CHF.

Obesity

Obesity may increase afterload and predispose to left ventricular hypertrophy. Obesity will increase exertional dyspnoea and measures at weight reduction should be attempted. Increased abdominal girth will cause elevation of the diaphragm and reduced lung capacity. Cachexia is a poor prognostic indicator in patients with advanced CHF.

Thyroid dysfunction

Patients with CHF and hyperthyroidism are more prone to tachycardia and arrhythmia, particularly atrial fibrillation and even ventricular tachycardia. Hyperthyroidism should be treated aggressively. Hypothyroidism causes fluid retention, bradycardia and fatigue but should be very carefully and slowly corrected to avoid tachycardia and arrhythmia. Amiodarone may lead to hypothyroidism or hyperthyroidism.

Renal impairment

CHF may worsen renal function due to renal hypoperfusion or the toxic effects of drugs. Renal impairment may lead to fluid retention, which can exacerbate heart failure and should be treated carefully. It is easier to remove excess fluid with use of a diuretic than to attempt to correct acute renal failure. Urinary tract infections may cause deterioration of renal function and may also cause an exacerbation of CHF and should be excluded.

Arthritis

Patients with CHF and arthritis should avoid use of NSAIDs and corticosteroids, if possible, as they cause fluid retention and increases in blood pressure. NSAIDs may also exacerbate renal impairment or predispose to peptic ulcer disease. Some NSAIDs have also been shown to increase cardiovascular mortality in patients with ischaemic heart disease and are best avoided in these patients. Omega-3 fatty acids, paracetamol, joint injections, surgery, analgesics or glucosamine may be used if indicated.

Gout

As with arthritis, patients with CHF and gout should avoid using NSAIDs and corticosteroids. Colchicine is safe to use for acute exacerbations of gout. There is epidemiological data showing that the higher the uric acid level, the higher the mortality in patients with CHF.[25] Uric acid is also negatively inotropic. Use of allopurinol to reduce uric acid levels may be beneficial in patients with advanced heart failure, although this has not been proven in clinical trials.

Summary

CHF is an increasingly common condition associated with high mortality, poor quality of life and recurrent hospitalisation. Accurate diagnosis, treatment of reversible causes and institution of proven medical and device therapies are crucial.

Affected patients often require combinations of medications, regular review and liaison with multidisciplinary team members because they are often elderly with multiple medical problems. Modern therapies, including ACE inhibitors, beta blockers, diuretics (if necessary), spironolactone, nitrates and angiotensin receptor antagonists, can reduce the burden of this lethal, expensive and debilitating disease. **CT**

References

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

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