Clinical review

Recent developments

Management of chronic heart failure

Martin R Cowie, Alex Zaphiriou

Cardiac Medicine, National Heart and Lung Institute, Faculty of Medicine, Imperial College, London SW3 6LY Martin R Cowie professor of cardiology Alex Zaphiriou clinical research fellow

Correspondence to: M R Cowie m.cowie@ic.ac.uk

BMJ 2002;325:422-5

Heart failure is a complex syndrome that results from any structural or functional cardiac disorder that impairs the ability of the heart to function as a pump. It has a major impact on longevity and quality of life. One to two per cent of the general population of developed countries have heart failure, and the average age at diagnosis is 76 years. Although the steady rise in hospital admissions for heart failure has slowed recently, the management of heart failure still accounts for 1-2% of healthcare expenditure in the United Kingdom and other countries in the developed world.² Improvements in cardiac imaging and new biochemical assays have made diagnosis more straightforward. Major changes in treatment have resulted from a better understanding of the pathophysiology of heart failure and the results of large clinical trials. Improving outcomes now increasingly depends on improved communication between healthcare professionals, education of patients and carers, and better chronic disease management.

Sources and search criteria

We searched the PubMed database for publications on the diagnosis and treatment of chronic heart failure in adult humans. We also consulted recent international guidelines to develop an overview of the evidence based management of heart failure.

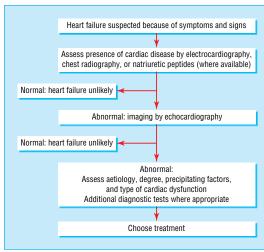


Fig 1 Algorithm for the diagnosis of heart failure (based on the most recent guidelines from the European Society of Cardiology)³

Recent developments

Transthoracic echocardiography is the key investigation to confirm the underlying structural and functional abnormalities of the heart

Patients with heart failure due to left ventricular systolic dysfunction should be treated with a diuretic, an angiotensin converting enzyme inhibitor, and a β blocker (unless contraindicated)

Patients with more severe symptoms should also be prescribed spironolactone

Monitoring of the control of the heart failure syndrome and blood biochemistry is essential to reduce the risk of complications and decompensation

High quality and timely communication between patients and all the healthcare professionals involved in their care is essential

Diagnosis

Heart failure is usually associated with dyspnoea, fatigue, and fluid retention. Symptoms alone cannot be relied on in making the diagnosis: a careful history and physical examination need to be supplemented by further tests. Diagnosis requires consideration of the underlying abnormality of the heart, the severity of the syndrome, the aetiology, the precipitating and exacerbating factors, the identification of concomitant disease relevant to management, and an estimation of prognosis. Figure 1 shows the algorithm for the diagnosis of heart failure currently recommended by the European Society of Cardiology.³

Any condition that damages the heart can lead to heart failure. The most common cause in the developed world is coronary heart disease, although hypertension often coexists.¹⁴ Such patients usually have obvious abnormalities of the systolic function of the left ventricle. Identification of any reversible cause of damage to the heart (for example, chronic alcohol misuse) is particularly important.

The following investigations should be carried out in a patient with suspected heart failure:



- Twelve lead electrocardiography
- Chest radiography
- Blood biochemistry (including urea, creatinine, glucose, electrolytes), haemoglobin, thyroid and liver function tests, and blood lipids
- Urinalysis to detect proteinuria or glycosuria
- Cardiac imaging—usually a transthoracic echocardiogram, which can rapidly provide detailed information about the structure and function of the cardiac chambers, valves, and pericardium.

These tests will help not only to confirm the clinical diagnosis but also to exclude other pathologies that may masquerade as heart failure, such as renal failure or severe anaemia. They may also identify comorbidities that can influence management. In most cases the above investigations will rapidly confirm the clinical diagnosis of heart failure. Some cases may be more difficult, however, and the input of a specialist may be needed.

It has been noted that if the electrocardiogram is completely normal then heart failure due to left ventricular systolic dysfunction is unlikely.⁵ The plasma concentration of B type natriuretic peptide may be even more useful, in that heart failure (due to any cause) is unlikely if this blood test result is normal.⁶ Both tests may, therefore, be very helpful as "rule out" tests in the differential diagnosis of patients presenting with dyspnoea or effort intolerance. If either test is (or both tests are) abnormal further cardiac investigation is likely to prove worth while. Unfortunately, testing for B type natriuretic peptide is not widely available, but the development of relatively cheap and rapid assays for both B type natriuretic peptide and *N*-terminal pro-B type natriuretic peptide should facilitate its adoption.

A minority of patients with heart failure, particularly among elderly patients, have no obvious valvular or systolic impairment of the heart and are assumed to have "diastolic" abnormalities that account for the syndrome. This is more likely if the patient has a history of hypertension. A definitive diagnosis can only be made by cardiac catheterisation, but the echocardiogram may give some pointers towards this diagnosis. The appropriate treatment for these patients is not known, but several clinical trials are ongoing. In the meantime, such patients are usually treated with angiotensin converting enzyme inhibitors and diuretics.

Treatment

Heart failure is characterised by neurohormonal activation that initially helps to maintain circulatory function but is ultimately harmful to the heart. Modern treatment aims to control symptoms and prolong life by blocking the neurohormonal activation and controlling the fluid retention.

Lifestyle management

Lifestyle changes can have an important impact. Ready to cook meals and convenience foods contain large amounts of salt and may increase the dose of diuretic needed to control fluid retention. All patients should be discouraged from adding salt to their food and should try to reduce the amount of salt they add during cooking. Severe salt restriction (<2 g/day) is rarely necessary. Regular aerobic exercise should be encouraged, as it improves peripheral muscle function

and exercise tolerance in patients with heart failure.⁸ Annual vaccination against influenza is a sensible precaution. If alcohol is the cause of the heart failure then abstinence is essential. Smoking cessation should be encouraged.

Drugs

Diuretics are the most effective means of removing fluid retention, and their introduction often produces rapid symptomatic relief.9 Most patients with heart failure need at least a small dose of regular diuretic. On its own such treatment exacerbates neurohormonal activation, and modern treatment of heart failure due to systolic dysfunction of the left ventricle thus demands the use of two other types of drug: an angiotensin converting enzyme inhibitor and a β blocker. The angiotensin converting enzyme inhibitor should be introduced at a low dose and titrated upwards over several weeks to the doses shown to be effective in clinical trials, while symptoms, blood pressure, and renal function are monitored (table) This can be safely accomplished in primary care, provided the patient is not hypotensive or on high dose diuretic treatment. Once the patient is stable on this treatment a β blocker such as carvedilol, bisoprolol, or metoprolol can be added-again starting at a low dose and titrating upwards gradually over several weeks, with close supervision of the control of the heart failure syndrome.¹⁰ Until recently, β blockers were considered to be contraindicated in heart failure, but recent trials have shown that they can markedly improve survival and are safe to introduce, w1-w3 provided a "start low, go slow" policy is used. 11 This can be very labour intensive and may be best managed by a nurse specialist.12

The valsartan heart failure trial found that patients did not live longer if the angiotensin II receptor blocker valsartan was added to conventional treatment with an angiotensin converting enzyme inhibitor. However, this study did show a reduction in the risk of admission to hospital for worsening heart failure.¹³ Ongoing trials will help to clarify the role of this class of drugs, but current evidence indicates that they are no more effective than angiotensin converting enzyme inhibitors in reducing mortality in patients with heart failure due to left ventricular systolic dysfunction. Most doctors would, however, now consider using angiotensin II receptor blockers for patients who develop an intractable cough on angiotensin converting enzyme

Recommended starting and maintenance dose ranges for selected angiotensin converting enzyme inhibitors and $\boldsymbol{\beta}$ blockers used in clinical trials for the treatment of heart failure

Drug	Starting dose	Maintenance dose
Angiotensin converting enzyme inhibitors		
Captopril	6.25 mg three times daily	25-50 mg three times daily
Enalapril	2.5 mg once daily	10 mg twice daily
Lisinopril	2.5 mg once daily	5-20 mg once daily
Perindopril	2 mg once daily	4 mg once daily
Ramipril	1.25-2.5 mg once daily	2.5-5 mg twice daily
Trandolapril	1 mg once daily	4 mg once daily
β blockers		
Bisoprolol	1.25 mg once daily	10 mg once daily
Carvedilol	3.125 mg twice daily	25 mg twice daily
Metoprolol tartrate	5 mg three times daily	50 mg three times daily
Metoprolol succinate CR	12.5-25 mg once daily	200 mg once daily

inhibitors, rather than the previously favoured combination of oral hydralazine and nitrate.

Spironolactone at a dose of 25-50 mg once daily reduces mortality in patients with moderate or severe symptoms due to systolic heart failure.¹⁴ Its benefit in other patient groups is unclear.

Digoxin has an important role in the symptomatic treatment of patients with heart failure and atrial fibrillation. There is no evidence, however, that digoxin improves survival in patients in sinus rhythm. 15 It may reduce the risk of admission to hospital, but its toxicity has to be considered, especially in elderly patients. Patients with atrial fibrillation are particularly complicated and usually benefit from specialist assessment. Formal anticoagulation with warfarin should be considered in order to reduce the risk of thromboembolism.

Drugs that interact with anti-failure drugs or increase fluid retention—such as non-steroidal anti-inflammatory agents; diltiazem, verapamil, or short acting dihydropyridine calcium antagonists; lithium; and parenteral corticosteroids—should be avoided. Tricyclic antidepressants may increase the risk of arrhythmia. It is essential to educate patients about their drug treatment and which over the counter medicines they should avoid.

Cardiac surgery

Heart transplantation can transform a very sick patient, but owing to the shortage of donor organs and the general level of comorbidity in many patients with heart failure this is not an option for the vast majority. Xenotransplantation using a genetically modified pig heart remains a distant prospect. The design of implantable mechanical assist devices is improving, and these provide a "bridge" to transplantation or may

Additional educational resources

Task Force for the Diagnosis and Treatment of Chronic Heart Failure, European Society of Cardiology. Guidelines for the diagnosis and treatment of chronic heart failure. *Eur Heart J* 2001;22:1527-60. www.escardio.org/Scinfo/Guidelines/diagnosis.pdf

Hunt SA, Baker DW, Chin MH, Cinquegrani MP, Feldman AM, Francis GS, et al. ACC/AHA guidelines for the evaluation and management of chronic heart failure in the adult: executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2001;104:2996-3007. www.acc.org/clinical/guidelines/failure/hf_index.htm

McMurray J, Pfeffer MA. New therapeutic options in congestive heart failure: parts I and II. *Circulation* 2002;105:2099-106, 2223-8

Patient information

The British Heart Foundation (14 Fitzhardinge Street, London W1H 6DH; tel: 020 7935 0185; fax: 020 7486 5820; email: internet@bhf.org.uk) publishes patient information leaflets. Its website is useful for basic questions about heart failure and other cardiovascular conditions: www.bhf.org.uk

The Hertfordshire Primary Care Research Network has designed a very patient friendly website with much useful information and with patient stories to illustrate relevant points; www.heartsforlife.co.uk

The Cardiomyopathy Association (40 The Metro Centre, Tolpits Lane, Watford WD1 8SB; tel: 01923 249977; fax: 01923 249987; email: cmaassoc@aol.com) will be a useful source of information for patients with heart failure who have cardiomyopathy. The website has many useful links: www.cardiomyopathy.org

The National Heart, Lung and Blood Institute has a large website with useful information about heart failure and good links to other sites: www.nhlbi.nih.gov/health/public/heart/other/hrtfail.htm

tide a patient over until recovery from myocarditis. Some patients have survived several years with such devices.¹⁶

Around 10% of new cases of heart failure in the United Kingdom are primarily due to valve disease, although this proportion is likely to be much higher in developing countries. Valve surgery can replace or repair damaged cardiac valves; the timing of such procedures is critical, and specialist assessment is needed.

Many patients with a heart damaged by coronary artery disease may have clinically important recovery of cardiac function after revascularisation by coronary artery bypass surgery, even in the absence of angina. Specialised imaging is needed to detect "hibernating" myocardium—muscle that is still alive but not contracting and has the potential to recover after revascularisation. The operative risk for such patients may, however, be considerable.

Implantable pacemakers and defibrillators

Traditionally, pacemakers were used for patients with symptomatic bradycardia, but recent research indicates that a new form of pacing in which the timing between atrial and ventricular contraction and the pattern of ventricular activation is optimised (biventricular pacing) may improve symptoms for selected patients with heart failure. Is 19,w4,w5 Half of all deaths in patients with heart failure are sudden—the mode of death is arrhythmic in most such cases. Automatic internal cardiac defibrillators are increasingly considered for patients with heart failure at high risk of sudden death—for example, patients with a previous cardiac arrest or episodes of sustained ventricular tachycardia. Anti-arrhythmic treatment on its own is less effective at preventing sudden death in this group of patients. 20,w6-w10

Disease monitoring

Patients with heart failure are often elderly and frail, and changes in treatment should be monitored closely. Traditionally, this has been achieved by clinical examination (noting the extent of fluid retention, jugular venous pressure, and lung auscultatory findings) supplemented by checking of blood biochemistry. A recent randomised study suggested that adding serial measurement of plasma concentration of N-terminal pro-B type natriuretic peptide to clinical assessment facilitates tighter control of the heart failure syndrome and reduces cardiovascular events in outpatients with heart failure.21 Use of teams of experienced heart failure physicians and nurses reliably reduces the rate of admission to hospital in patients with heart failure.²² The key element is likely to be the close contact in the community between the nurse and the patient (or carer), enabling early identification of clinical deterioration. Patients can monitor their weight and can be educated to adjust the dose of diuretic at an early stage of decompensation. Flow of information between healthcare sectors and between professionals should be fast and efficient.

Communication with the patient and carer

"Heart failure" has strongly negative connotations for lay people, who equate it with "cardiac arrest." Feedback from focus groups of patients and carers shows that an

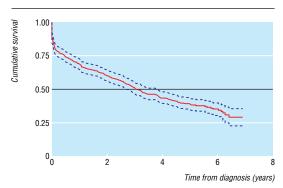


Fig 2 Cumulative survival of 552 incident cases of heart failure identified in the London heart failure studies 1995-8. Kaplan-Meier estimates with 95% pointwise confidence bands (authors' own data)

early and frank discussion of the diagnosis and treatment options is greatly appreciated. Such discussion will also improve patients' understanding of the disease and empower them (and their carers) to take a more active role in management. Healthcare professionals should be sensitive to the information needs of their patients and should tailor the method and content of their communications appropriately. Skills in palliative care are an important component of good management in the terminal stages of the condition, and communication is particularly crucial at this point.

Prevention

Prevention is most definitely better than cure. Despite modern treatments, survival after a diagnosis of heart failure in the United Kingdom averages three years (fig 2). Measures for preventing coronary heart disease,23 both in clinical practice and at the population level, are likely to reduce the risk of heart failure or at least delay its onset. Once cardiac damage has occurred, typically from a heart attack, the risk of developing frank heart failure can be reduced by treatment with an angiotensin converting enzyme

Key ongoing clinical trials

- CHARM (candesartan in heart failure—assessment of reduction in mortality and morbidity)-investigating the clinical efficacy of candesartan in reducing mortality and morbidity in three groups of patients: those with left ventricular systolic function treated with an angiotensin converting enzyme inhibitor, those with systolic dysfunction intolerant of an angiotensin converting enzyme inhibitor, and those with non-systolic heart failure. Reporting 2003-4
- CARE-HF (cardiac resynchronisation in heart failure)-large multicentre randomised study to evaluate the long term effects of cardiac resynchronisation on mortality and morbidity in patients with heart failure. Approximately 800 patients followed for 18 months. Reporting 2004
- UK natriuretic peptide study—a pragmatic multicentre UK study of the diagnostic value of measuring plasma B type natriuretic peptide (or *N*-terminal pro-B type natriuretic peptide) in patients presenting to primary care with a suspected diagnosis of heart failure. Approximately 300 patients will be recruited. Reporting 2003

inhibitor and β blocker.²⁴ Hypertension is an important causative factor and should be treated appropriately.

We thank Mike Kirby and Stephen Lynch for comments on an earlier version of this manuscript.

Competing interests: MRC is the clinical expert adviser for the national clinical guideline on the management of heart failure commissioned by the National Institute for Clinical Excellence, but the opinions in this review are his own and will not necessarily reflect those in the forthcoming guideline. MRC has received research support for clinical trials and honoraria for advisory boards, lectures, and attendance at scientific meetings related to several treatments mentioned in this review.

- Cowie MR, Mosterd A, Wood DA, Deckers JW, Poole-Wilson PA, Sutton
- GC, et al. The epidemiology of heart failure. Eur Heart J 1997;18:208-15. Petersen S, Rayner M. Coronary heart disease statistics: heart failure supplement. London, British Heart Foundation, 2002.
- Task Force for the Diagnosis and Treatment of Chronic Heart Failure, European Society of Cardiology. Guidelines for the diagnosis and treatment of chronic heart failure. *Eur Heart J* 2001;22:1527-60. Fox KF, Cowie MR, Wood DA, Coats AJS, Thompson SG, Underwood SR,
- et al. Coronary artery disease as the cause of incident heart failure in the population. Eur Heart J 2001;22:228-36.
- Davie AP, Francis CM, Love MP, Caruana L, Starkey IR, Shaw TRD, et al. Value of the electrocardiogram in identifying heart failure due to left ventricular systolic dysfunction. BMJ 1996;312:222.
- Cowie MR, Struthers AD, Wood DA, Coats A, Thompson SG, Poole-Wilson PA, et al. Value of natriuretic peptides in assessment of patients with possible new heart failure in primary care. Lancet 1997:350:1349-51.
- Vasan RS, Benjamin EJ, Levy D. Prevalence, clinical features and prognosis of diastolic heart failure: an epidemiologic perspective. J Am Coll Cardiol 1995;26:1565-74.
- Coats AJS. Exercise training in heart failure. Curr Control Trials Cardiovasc Med 2000;1:155-60.
- Faris R, Flather M, Purcell H, Henein M, Poole-Wilson P, Coats A. Current evidence supporting the role of diuretics in heart failure: a meta analysis of randomised controlled trials. *Int J Cardiol* 2002;82:149-58.
- 10 McMurray J, Cohen-Solal A, Dietz R, Eichhorn E, Erhardt L, Hobbs R, et al. Practical recommendations for the use of ACE inhibitors, beta-blockers and spironolactone in heart failure: putting guidelines into practice. Eur J Heart Fail 2001;3:495-502.
- 11 Goldstein S, Gottlieb SS. The impact of beta-blockade on mortality rates in patients with congestive heart failure. J Card Fail 2002;6(suppl 1):15-24.
- 12 Cowie MR, McIntyre H, Panahloo Z. Delivering evidence-based care to patients with heart failure: results of a structured programme. Br J Cardiol 2002-9-171-80
- 13 Cohn JN, Tognoni G. A randomized trial of the angiotensin receptor blocker valsartan in chronic heart failure. N Engl J Med 2001;345: 1667-75.
- 14 Pitt B, Zannad F, Remme WJ, Cody R, Castaigne A, Perez A, et al. The effect of spironolactone on morbidity and mortality in patients with evere heart failure. N Engl J Med 1999;341:709-17.
- 15 The Digitalis Investigation Group. The effect of digoxin on mortality and morbidity in patients with heart failure. N Engl J Med 1997;336:525-33.
- 16 Kasirajan V, McCarthy PM, Hoercher KJ, Starling RC, Young JB, Banbury MK, et al. Clinical experience with long-term use of implantable left ventricular assist devices: indications, implantation, and outcomes. Semin Thorac Cardiovasc Surg 2000;12:229-37.
- 17 Pitt M, Lewis ME, Bonser RS. Coronary artery surgery for ischemic heart failure: risks, benefits, and the importance of assessment of myocardial viability. *Prog Cardiovasc Dis* 2001;43:373-86.
- Abraham WT, Fisher WG, Smith AL, Delurgio DB, Leon AR, Loh E, et al. Cardiac resynchronization in chronic heart failure. N Engl J Med 2002;346:1845-53.
- 19 Linde C, Leclercq C, Rex S, Garrigue S, Lavergne T, Cazeau S, et al. Long-term benefits of biventricular pacing in congestive heart failure: results from the multisite stimulation in cardiomyopathy (MUSTIC) study. J Am Coll Cardiol 2002;40:111-8.
- 20 Kusumoto FM, Goldschlanger N. Device therapy for cardiac arrhythmias. IAMA 2001:287:1848-52.
- Troughton RW, Frampton CM, Yandle TG, Espiner EA, Nicholls MG, Richards AM. Treatment of heart failure guided by plasma aminoterminal brain natriuretic 2000;355:1126-30. peptide (N-BNP) concentrations.
- 22 McAlister FA, Lawson FME, Teo KK, Armstrong PW. A systematic review of randomized trials of disease management programs in heart failure. Am J Med 2001;110: 378-84.
- 23 Wood DA, De Backer G, Faergeman O, Graham I, Mancia G, Pyörälä K. Prevention of coronary heart disease in clinical practice: recommendations of the second joint task force of European and other societies on coronary prevention. *Atherosclerosis* 1998;140:199-270.
- 24 Dargie HJ on behalf of the CAPRICORN Investigators. Effect of carvedilol on outcome after myocardial infarction in patients with left-ventricular dysfunction: the CAPRICORN randomised trial. Lancet 2001:357:1385-90.