Acute heart failure and cardiogenic shock

Acute heart failure and cardiogenic shock are medical emergencies requiring urgent medical intervention. This article defines each syndrome and reviews the latest evidence regarding their clinical presentation, management and prognosis.

Acute heart failure and cardiogenic shock are both manifestations of cardiac pump failure but the two syndromes differ in their aetiology, clinical features, management and prognosis. Patients with cardiogenic shock should be treated in a 'heart attack' centre with facilities for coronary intervention. Younger patients with either condition may benefit from the additional treatments that are available from a tertiary heart failure service in a heart transplant centre.

Acute heart failure

Heart failure is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood (Hunt et al, 2005). Acute heart failure is defined as the gradual or rapid increase in heart failure signs and symptoms resulting in a need for urgent therapy (Gheorghiade et al, 2005).

Over 1 million hospitalizations for acute heart failure occur in the USA each year (Gheorghiade et al, 2005). Management of heart failure uses 1–2% of health-care expenditure in European countries and more than 75% of this goes on hospital care (Nieminen et al, 2005). Forty-five per cent of patients hospitalized for acute heart failure will need readmission and the 12-month mortality is 30–40%.

In most patients, the predominant symptoms are those caused by pulmonary or systemic congestion. Blood pressure is usually normal or elevated. Hypotension and low cardiac output are present in a small minority of cases. The acute heart failure syndrome differs from chronic heart failure although 65–87% of patients have history of chronic heart failure (Cleland et al, 2003; Fonarow and Corday, 2004; Adams et al, 2005).

In community hospitals, acute heart failure is a disease of the elderly (Adams et al, 2005); about half the cases of acute heart failure are associated with preserved systolic function. Common aetiologies are ischaemic heart disease, hypertensive heart disease and cardiomyopathy.

In contrast to chronic heart failure, the evidence base for treatment of acute heart failure is limited and many commonly used treatments appear deleterious. The standard treatments for congestion include diuretics and nitrate vasodilators; these are effective in relieving symptoms in most patients (Nieminen et al, 2005). However, therapy with high-dose loop diuretic is associated with increase mortality in acute heart failure (Neuberg et al, 2002). Although nitrate vasodilators are effective in the acute situation, tachyphylaxis can rapidly develop. Nesiritide (Scios inc. California, USA), a recombinant form of human B-type naturetic peptide (rhBNP), is an another vasodilator that is used for the treatment of acute heart failure in the United States (currently not available in UK); although its vasodilator effect is better sustained than glyceryl trinitrate, its use has been associated with a worsening of renal function (Sackner-Bernstein et al, 2005). Studies with type 2 vasopressin receptor antagonists have demonstrated that these agents can potentiate the effect of loop diuretics without exacerbating hyponatraemia, hypokalaemia or renal dysfunction (Gheorghiade et al, 2004). It remains to be seen whether vasopressin antagonists can reduce the readmission rate of patients with acute heart failure.

An alternative approach is the physical removal of fluid using ultrafiltration and a simplified filtration system has been developed for use in acute heart failure. Ultrafiltration can provide more rapid fluid removal than diuretic therapy without causing deterioration in renal function or neurohormonal activation, and sodium removal is greater than that achieved by diuretic therapy. In a recent study, ultrafiltration was associated with a lower readmission rate after treatment of acute heart failure compared with diuretic therapy (Costanzo et al, 2007).

Pulmonary oedema resulting in hypoxaemia should be treated by oxygen therapy. Dyspnoea can be reduced by low-dose morphine which also has a venodilator effect. Patients with severe respiratory failure can often be tided over by continuous positive airways pressure while diuretics and vasodilators have time to act. Continuous

Dr PR Moore *is Specialist Registrar in Cardiology,* **Dr R Kharbanda** *is Consultant Cardiologist and* **Dr NR Banner** *is Consultant Cardiologist at the Royal Brompton and Harefield NHS Trust, Harefield Hospital, Middlesex UB9 6JH*

Correspondence to: Dr NR Banner

positive airways pressure has been shown to reduce the need for intubation and mechanical ventilation in acute heart failure (Winck et al, 2006).

A minority of acute heart failure patients present with hypotension and/or a low cardiac output and poor tissue perfusion. When the arterial blood pressure will allow, such cases should be treated with vasodilators. Vasodilators can increase cardiac output and tissue perfusion by improving the impedance-match between the left ventricle and the arterial system as well as reducing functional mitral regurgitation (Nieminen et al, 2005). Treatment with inotropic agents should be reserved for those with a low arterial pressure. Inotropes are associated with a number of problems including the risk of arrhythmia and myocardial ischaemia (*Table 1*).

Haemodynamic monitoring of patients with acute heart failure has been a subject of considerable controversy. The ESCAPE trial established that there was no benefit or detriment to patients from the routine use of a pulmonary artery catheter during an episode of acute heart failure. However, cases where clinicians felt there was a definite indication for a pulmonary artery catheter were excluded from the study. It appears that while pulmonary artery catheters can produce useful functional and diagnostic information, routine use does not translate into improved outcomes because manipulation of haemodynamics with vasodilators and inotropes does not, in itself, lead to improved outcomes in acute heart failure (Binanay et al, 2005).

Once the acute episode has come under control, consideration should be given to possible treatable causes of the acute heart failure, including ischaemic or valvular heart disease, and appropriate investigations should be arranged. Occasionally the episode of acute heart failure may have been precipitated by an episode of arrhythmia leading to a worsening of ventricular function (tachycardia-associated cardiomyopathy). Other possible precipitants should also be considered; the most common is non-adherence to drug therapy or salt and water restriction in a patient with chronic heart failure. Drug interactions and adverse effects (e.g. use of non-steroidal anti-inflammatory agents, thiazolidinediones or glitazones); the presence of infection, anaemia or thromboembolism (all common complications in heart failure) should also be considered.

Before discharge the patient's left ventricular ejection fraction should be measured and a plan for further investigations made. Evidence-based therapy for chronic heart failure should be established including the use of beta-adrenergic receptor antagonists and angiotensin-converting enzyme (ACE) inhibitors (or angiotensin receptor blockers) and an aldosterone antagonist. Arrangements should be made for long-term care including uptitration of drug therapy to target doses and monitoring in the community. Patients should be encouraged to weigh themselves every day at home to provide early warning of increased fluid retention. In patients with a broad QRS complex, or other evidence of left ventricular dyssynchrony, cardiac resynchronization therapy and an implantable cardioverter-defibrillator should be considered (Swedberg et al, 2005).

Younger patients with severe underlying left ventricular systolic dysfunction may become candidates for heart transplantation if their response to other treatment for heart failure is inadequate.

Cardiogenic shock

Cardiogenic shock is defined as decreased cardiac output and tissue perfusion or hypoxia from a cardiac cause in the presence of an adequate intravascular volume (Hollenberg et al, 1999). Standard haemodynamic criteria include a persistently low systolic blood pressure (less than 90 mmHg for at least 30 minutes), a low cardiac index (less than 2.2 litres/min/m^2) and a pulmonary occlusion (wedge) pressure of greater than 15 mmHg (Hollenberg et al, 1999). Important clinical features include oliguria, impaired consciousness or confusion and cold mottled extremities.

In community hospitals, acute myocardial infarction is the commonest cause of cardiogenic shock. However, in a tertiary referral centre, a significant proportion of cases have an alternative aetiology such as fulminant myocarditis or an acute presentation of cardiomyopathy. The differential diagnosis is shown in *Table 2*. This article will focus on cardiogenic shock after acute myocardial infarction.

Table 1. Some problems with inotropic therapy

Promotes arrhythmia, including loss of rate control in atrial fibrillation (atrial fibrillation present in 30% of acute heart failure cases)
Increases myocardial oxygen consumption and exacerbates active ischaemia
Likely to promote adverse ventricular remodelling
Evidence of increased mortality related to their use
Lack of sustained 'haemodynamic benefit'
Practical issues – vascular access – patient mobility – line sepsis

Table 2. Causes of cardiogenic shock

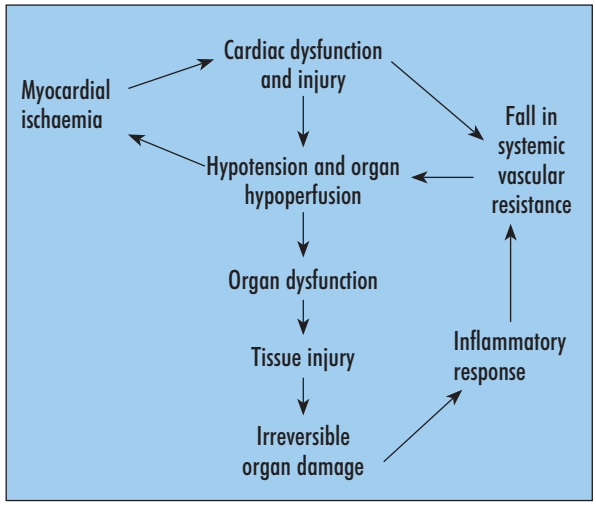
Acute ST segment elevation myocardial infarction	Left ventricular infarction
	Mechanical complications of acute myocardial infarction (papillary muscle rupture and mitral regurgitation, ventricular septal rupture, free wall rupture and tamponade)
	Right ventricular infarction
Fulminant myocarditis	
Acute presentation of cardiomyopathy	
Acute mitral regurgitation (infective endocarditis, chordal rupture)	
Acute aortic regurgitation (infective endocarditis, aortic dissection)	

Cardiogenic shock occurs in 7% of cases of acute ST segment elevation myocardial infarction (STEMI) and is the commonest cause of in-hospital death in this condition. Patients who present with cardiogenic shock frequently have multi-vessel coronary disease (left main stem in 29% and three-vessel in 58%); 75% have predominant left ventricular failure with a loss of 40% or more of the left ventricular myocardium. The clinical presentation, haemodynamics and management of right ventricular infarction differ from predominant left ventricular dysfunction (Jacobs et al, 2003). Shock occurs a median of 6 hours after the onset of symptoms, i.e. usually after the patient has been admitted to hospital and treatment has commenced. However, 25% of cases occur late (more than 24 hours after symptom onset) (Hollenberg et al, 1999; Webb et al, 2000; Hochman, 2003).

Cardiogenic shock is a progressive condition and both haemodynamic and inflammatory factors drive a vicious spiral of deterioration (*Figure 1*). Haemodynamically, hypotension and impaired cardiac output lead to impaired coronary perfusion, further myocardial ischaemia and infarction thereby worsening the hypotension and low cardiac output state. Another adverse mechanism is the development of a systemic inflammatory response whereby myocardial injury, as well as injury to other organs as a result of hypoperfusion, elicits the release of cytokines and nitric oxide causing a fall in systemic vascular resistance and worsening the hypotension (Hochman, 2003).

The implications of this model of progressive cardiogenic shock are that early coronary intervention and prompt haemodynamic support is more likely to be successful than intervention at a late stage when shock may have become irreversible as a result of tissue injury and vasomotor collapse. In principle, manipulation of the systemic inflammatory response could improve the recovery rate in cardiogenic shock although no specific intervention has yet been found to be effective (Landry and Oliver, 2001; Hochman, 2003).

Figure 1. Mechanisms of progressive cardiogenic shock.



The main treatment for cardiogenic shock in acute myocardial infarction is prompt revascularization. The benefits of revascularization in cardiogenic shock were first shown in a substudy of GUSTO 1 (a trial of thrombolytic therapies in myocardial infarction). In the subgroup of patients who developed shock, those who underwent early angiography and revascularization had a better survival than the patients who had either no angiography or only late coronary angiography (Berger et al, 1997). However, these conclusions came from a post-hoc subgroup analysis. Subsequently the SHOCK trial studied the benefits of myocardial revascularization (either by percutaneous coronary intervention or coronary artery surgery) in patients with cardiogenic shock resulting from myocardial infarction. The primary end-point of this trial (survival at 30 days) just failed to reach statistical significance, but with extended follow up it became clear that survival was better in the patients who had undergone early revascularization than in those treated with medical therapy alone (1-year survival 47% *vs* 34% respectively) (Hochman et al, 1999, 2001). To date, this is the only randomized trial that has been performed in the setting of cardiogenic shock complicating acute myocardial infarction.

Effective revascularization is an essential component of treatment and patients who achieve normal (Thrombolysis in Myocardial Infarction (TIMI) trial grade 3) coronary blood flow early after coronary intervention have a better prognosis than those in whom revascularization fails or coronary flow is persistently reduced (Gibson et al, 2002).

Therapy with an intra-aortic balloon pump is generally recommended for coronary interventions in patients with cardiogenic shock and as supportive treatment. The intra-aortic balloon pump can be placed rapidly using a percutaneous technique and it functions in series with the left ventricle providing partial circulatory support. Furthermore, balloon inflation during diastole augments coronary perfusion and balloon collapse during systole reduces left ventricular stroke work. Therefore, the intra-aortic balloon pump has a favourable effect on the myocardial oxygen supply: demand ratio and it may lead to some increase in cardiac output and organ perfusion. However, while it is a useful method to stabilize patients before or during revascularization, there is no evidence that the intra-aortic balloon pump improves overall survival in cardiogenic shock.

Mechanical complications of STEMI can also present as cardiogenic shock (*Table 2*). These arise as a result of rupture of infarcted myocardium and the clinical presentation usually occurs several days after the infarction. The diagnosis is made by echocardiography (*Figure 2*). The patient usually experiences an acute deterioration in his/her haemodynamic state and is acutely ill. The treatment is surgical, although the

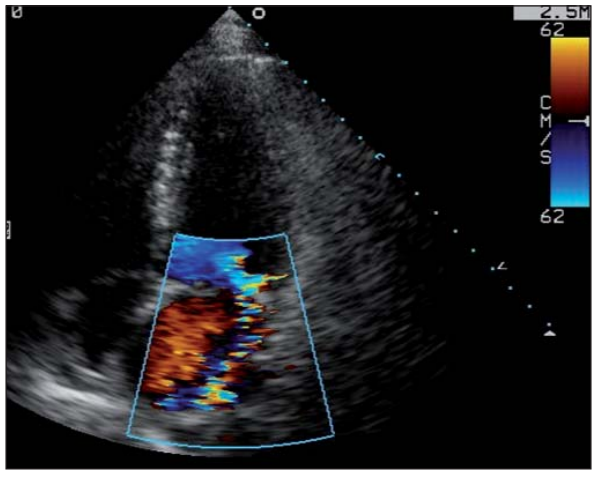


Figure 2. Transthoracic echocardiogram, apical four-chamber colour-flow image, demonstrating severe mitral regurgitation in a patient who had sustained a papillary muscle rupture following an acute ST elevation myocardial infarction.

mortality in such cases is high. Stabilization with an intra-aortic balloon pump can be valuable as a preparation for surgery.

The standard of care for cardiogenic shock complicating acute myocardial infarction includes early diagnostic evaluation by echocardiography to rule out mechanical complications, stabilization using an intra-aortic balloon pump and early revascularization usually by percutaneous coronary intervention. In patients with a left-main or three-vessel disease, immediate coronary bypass surgery is an alternative approach although, in the UK, cardiac surgeons usually recommend an interventional approach in the setting of acute myocardial infarction (Hochman, 2003). The development of primary angioplasty services in the UK means that most cardiogenic shock patients should have direct access to revascularization therapy. When a patient has been admitted to a centre without surgical facilities, the development of a mechanical complication of infarction necessitates transfer to a surgical centre as soon as the patient's condition has been stabilized.

In recent years the technology for temporary mechanical circulatory support has developed to the point where such therapy can be used as an adjunct to other interventions in cardiogenic shock. In pre-clinical studies, mechanical circulatory support is more effective than the intra-aortic balloon pump for unloading and protecting the left ventricle as well as being able to provide a better 'cardiac' output. Clinically successful 'bridge' and 'double bridge' to transplantation strategies have been reported. However, the overall results of mechanical circulatory support appear similar to those reported in other cardiogenic shock series with survival rates between 29% and 58% (Garatti et al, 2007). Possible detrimental effects of mechanical circulatory support in cardiogenic shock may include decreased coronary blood flow during support and exacerbation of the systemic inflammatory response. Further studies are required to clarify these issues.

Patients who recover following the treatment of cardiogenic shock will need appropriate post-myocardial infarction assessment and care including measurement of left ventricular ejection fraction and drug therapy that should include aspirin, a beta-adrenergic receptor antagonist and an ACE inhibitor. Those with chronic heart failure will need specific heart failure therapy; those with refractory heart failure could be candidates for long-term mechanical circulatory support (currently not funded by the NHS in the UK) or heart transplantation. Long-term circulatory support has been shown to extend life for patients with severe heart failure who are not eligible for heart transplantation (Rose et al, 2001) although late mortality remains a problem related to device malfunction, infection and thromboembolic complications. Newer types of circulatory assist device are becoming available which are smaller and easier to implant. Technological improvements may make such long-term 'destination' therapy a realistic clinical approach in the foreseeable future (Deng et al, 2005).

Currently heart transplantation remains the best long-term solution for patients with advanced heart failure. The International Society for Heart and Lung Transplantation (ISHLT) Registry reports a survival rate of 51% at 10 years after heart transplantation which is better than the results achieved with any other treatment for advanced heart failure (Taylor et al, 2006). Furthermore, the outcome after heart transplantation is independent of the severity of the original heart failure. Unfortunately, heart transplant activity is limited by the scarcity of hearts that are suitable for transplantation and currently less than 150 heart transplants are performed in the UK each year. Therefore, in practical terms, transplantation is restricted to younger patients who are free of serious co-morbidity and it will only be available to a small proportion of the survivors of cardiogenic shock who subsequently develop chronic heart failure.

Conclusions

Acute heart failure is a common cause of hospital admission. Congestion is the predominant problem in most cases. Many commonly used therapies lack efficacy and some appear detrimental. Newer approaches such as the use of ultrafiltration to remove salt and water rapidly and safely may have clinical advantages. For selected patients with advanced chronic heart failure, heart transplantation is likely to be the best long-term solution.

In community hospitals most cases of cardiogenic shock are caused by acute STEMI. Shock is the commonest cause of in-hospital death early after acute myocardial infarction. Effective early revascularization, usually by percutaneous coronary intervention, is the mainstay of prevention and therapy for cardiogenic shock. Mechanical complications of myocardial infarc-

tion must be identified and treated surgically. The intra-aortic balloon pump is a useful device for short-term stabilization of patients but probably does not affect overall outcome. Mechanical circulatory support may be used in selective cases where myocardial recovery seems likely or definitive treatment such as transplantation appears to be possible subsequently. BJHM

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KEY POINTS

- Acute heart failure syndrome is defined as the gradual or rapid increase in heart failure signs and symptoms resulting in the need for urgent therapy.
- Unlike chronic heart failure management, the evidence base for treatment of acute heart failure is limited. Trials involving newer therapies are ongoing. Diuretics and vasodilators are the mainstay of therapy.
- Cardiogenic shock exists when there is inadequate tissue perfusion as a result of decreased cardiac output and hypotension caused by cardiac disease. This establishes a vicious cycle which, without prompt treatment, will result in irreversible organ damage and death.
- The commonest cause of acute cardiogenic shock is ST elevation myocardial infarction. Treatment requires prompt coronary reperfusion coupled with supportive measures.
- Patients with acute heart failure and cardiogenic shock should be managed in centres with multidisciplinary expertise in the management of both acute coronary syndromes and heart failure.