87

Shock

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Shock is a syndrome in which an acute deficiency of vital tissue perfusion due to hemodynamic dysfunction leads to progressive metabolic and functional deterioration that, if not reversed, will lead to death. The common feature of shock is that cardiac output is inadequate to perfuse all the organs with sufficient blood to maintain tissue integrity. This inadequacy of perfusion is usually but not always accompanied by hypotension and intense regional vasoconstriction. The perfusion deficit may result in a cascade of further complications, such as the release of vasodilator factors that increase capillary permeability and may further lower blood pressure, leading ultimately to cardiac dysrhythmias and death. Shock can result from both cardiovascular and noncardiovascular illnesses (Table 87.1). Cardiac causes are the focus of concern for the cardiologist, and it is critical to exclude noncardiac causes before launching into aggressive cardiovascular therapy.

Hypovolemic Shock

Absolute or functional hypovolemia is the most common and most easily treated form of shock, whether caused by hemorrhage, severe intravascular plasma volume depletion, or an increased capacitance of the vascular system. Inadequate cardiac filling and a fall in cardiac output are hallmarks of the syndrome. Recognition of the problem and prompt restoration of volume are generally curative unless the perfusion deficit has persisted long enough to activate tissue-damaging local and circulating toxins.

Recognition of volume depletion as the cause of shock generally is simple when the patient has sustained hemorrhage or trauma. More subtle inadequacies of venous return may occur with dehydration, infections, malnutrition, and some edematous states.[1] A low blood pressure, a narrow pulse pressure, and a low jugular venous pressure are hallmarks of hypovolemia. A challenge with intravenous infusion of fluids is the most effective way to diagnose and treat the syndrome. When pulmonary symptoms cloud the picture and there is concern about volume loading in an individual who may have pulmonary edema, a bedside right heart catheterization may be necessary to clarify the hemodynamic abnormality.

Septic Shock

The mechanisms responsible for septic shock continue to be an area of considerable research. Unlike hypovolemic and cardiogenic shock, patients early after the onset of septic shock often have a normal or increased cardiac output and low systemic vascular resistance, suggesting a problem with the distribution of blood flow. Myocardial depression due to the direct effects of toxic substances or from prolonged hypotension and inadequate coronary perfusion, however, may also contribute to the clinical picture. The role of factors such as nitric oxide from the endothelium and the monokines and eicosanoids from macrophages continues to be pursued, and the use of arginine analogues and monoclonal antibodies in endotoxic shock has been a potential therapeutic advance. A role for endogenous opioids has been proposed, and the ability in some situations of the opioid antagonist naloxone to reverse endotoxic shock has been partly supportive.

Double-blind, randomized controlled trials have included a monoclonal antibody to tumor necrosis factor-α,[2] antithrombin III replacement,[3] low-dose corticosteroids,[4] pentoxifylline,[5] antioxidants,[6] human interleukin-1 receptor antagonist,[7] and p55 tumor necrosis factor receptor fusion protein.[8] Although the results of some of these trials have been encouraging, there is at present no established regimen for the treatment of septic shock beyond the prompt and effective eradication of infection coupled with appropriate supportive measures such as fluid administration along with dopamine, norepinephrine, or vasopressin as indicated by accurate and frequent physiologic and clinical assessment.

TABLE 87.1. Causes of shock

Hypovolemic shock	Hemorrhage Trauma Dehydration Diuresis Plasma volume loss
Vasodilation shock	Drugs Pyrexia Endogenous vasodilation
Cardiogenic shock	Acute myocardial infarction Myocarditis Arrhythmias Impaired filling Pericardial, valvular Pulmonary, vascular Obstructed emptying Aortic valve
Septic shock	Gram-negative and gram-positive infections

The role of high-dose corticosteroids is still unclear and continues to be investigated.[9]

Cardiogenic Shock

Cardiogenic shock can be defined as clinical shock due to a reduction of cardiac output in the presence of an adequate intravascular volume. In most circumstances the low cardiac output is due to myocardial infarction (MI) or ischemia, resulting in a deficit of regional or global myocardial contraction; however, on occasion shock may be the result of mechanical factors that interfere with left ventricular filling or emptying. These conditions require prompt and specific treatment and should always be considered and ruled out in patients with cardiogenic shock. *Pericardial tamponade* is suggested whenever a paradoxical pulse is detected or in patients with malignancy, renal failure, chest trauma, anticoagulant therapy, aortic dissection, or postinfarction free wall rupture. Bedside echocardiography can be used to confirm the diagnosis and is a useful guide during emergency pericardiocentesis. *Massive pulmonary embolization* must be considered in postoperative patients or in patients with other known risk factors. Emergency cardiopulmonary bypass followed by embolectomy or, in less critical patients, the administration of thrombolytic agents is indicated. *Tension pneumothorax* can impair ventricular filling, resulting in shock, and thus should be excluded particularly when shock develops in patients undergoing mechanical ventilation. In patients with mechanical heart valves, shock may develop as the result of *acute thrombi* that are occluding the valve orifice or preventing the valve from opening adequately. The treatment of this condition requires prompt surgical intervention or, for nonsurgical candidates, the administration of thrombolytic agents. Rarely *myxoma* or other *cardiac mass* can obstruct ventricular filling or emptying and cause cardiogenic shock. Echocardiography will usually quickly identify this problem.

When shock develops in a patient soon after an acute MI it is usually due to marked impairment of left ventricular contractile function. In a minority of patients, however, there is a mechanical abnormality that contributes to the development or persistence of shock and that may be amenable to surgical correction. *Rupture of the intraventricular septum* with a resultant left-to-right shunt places an excessive volume load on the already damaged left ventricle and has a nearly 100% mortality rate if not surgically corrected. Similarly, severe *acute mitral insufficiency* from necrosis and rupture of a papillary muscle or its head may lead to pulmonary edema and shock even in patients with relatively small infarctions. Finally, partial free wall rupture with a progressively enlarging left ventricular *pseudoaneurysm* can, in addition to suddenly rupturing, severely compromise cardiac function and lead to cardiogenic shock. Although these mechanical complications might be suspected in the presence of typical physical findings and hemodynamic abnormalities, the availability of high-resolution two-dimensional and Doppler echocardiography that is performed at the bedside has made it relatively easy to identify patients who may require immediate surgery to repair these mechanical complications. The decision as to whether to perform coronary angiography and, on occasion, angioplasty before taking such patients to the operating room will depend on the patient's stability, the availability of a catheterization laboratory, and the preferences of the surgeon and cardiologist.

The first physiologic studies on acute MI by Gilbert and associates[10] in 1951 were followed by studies in which more sophisticated equipment was used to define the hemodynamics of shock.[11] Procedures to obtain hemodynamic data in the acutely ill patient that were once difficult are now routine with the use of flotation catheters, intraarterial pressure measurements, and bedside thermodilution cardiac output measurements. Initial studies demonstrated that cardiac output was markedly reduced in the face of high ventricular filling pressures.[10,11] Systemic vascular resistance, however, was not increased in proportion to the fall in cardiac output. This was unexpected because the patients appeared to be markedly vasoconstricted. Animal shock models, usually as the result of hemorrhage, indicated marked vasoconstriction of the systemic vasculature, and it was expected that similar responses would pertain to shock in acute MI. As various receptors were isolated in the experimental models, it became apparent that vascular resistance in acute MI was being determined by conflicting afferent signals.[12–14] The aortic and carotid baroreceptors signaled systemic vasoconstriction. Chemoreceptors in the carotid arteries activated by hypoxemia and low pH produced differential vasoconstriction, with a shift of flow away from skeletal muscles and the splanchnic bed to the coronary and cerebral circulation. On the other hand, left ventricular chemoreceptors or stretch receptors were activated by ischemia or stretch and presented afferent signals that called for a decrease in vascular resistance. The integration of these afferent signals in the medullary centers is responsible for the level of efferent sympathetic outflow and differential vasoconstriction to various vascular beds.[13] Thus, patients with shock in MI are not maximally vasoconstricted, and α-adrenergic receptor agonists can be administered to elevate central arterial pressure by increasing systemic vascular resistance.

Although systemic hypotension is usually considered necessary to establish a diagnosis of cardiogenic shock, impaired peripheral perfusion with many of the clinical manifestations of shock but without severe hypotension may

be present. Menon et al.[15] studied 49 such patients whose systolic pressures were above 90 mm Hg without vasopressor support and compared them to 943 patients with hypotensive cardiogenic shock and with 76 patients who presented with hypotension but without clinical signs of shock. Mortality was highest in patients with hypotensive shock (66%), intermediate in patients with signs of shock but without hypotension (46%), and lowest in patients with hypotension but without signs of shock (26%). It seems clear, therefore, that clinical manifestations of impaired peripheral perfusion are equally or more important than blood pressure in predicting outcome following acute MI.

In shock after an acute MI, there usually is severe left ventricular dysfunction, and two autopsy studies established the association with loss of 40% or more of left ventricular myocardium.[16,17] These investigations also noted the high incidence of recent coronary thrombosis in 18 of 20[16] and 16 of 22[17] patients, with almost universal evidence of fresh marginal extension and focal areas of necrosis scattered throughout the remaining myocardium. The syndrome of *right ventricular infarction* as a cause of shock has also been recognized.[18] This is usually associated with right coronary occlusion and extensive right ventricular free wall and septal infarction that impair left ventricular filling and systemic blood flow. The hemodynamic hallmark of this syndrome is a right atrial pressure that equals or surpasses the pulmonary capillary wedge pressure or left ventricular end-diastolic pressure.[18] The elevated right atrial pressure may lead to a right-to-left shunt through a patent foramen ovale that may contribute to hypoxemia in this syndrome.[19]

Predictors, Incidence, and Mortality

The Multicenter Investigation of the Limitation of Infarct Size (MILIS) study group[19] attempted to define the predictors of in-hospital development of cardiogenic shock after MI to identify likely patients and improve therapy. Of their 845 patients who presented with acute MI, 60 (7.1%) developed cardiogenic shock. One half developed shock within 24 hours of hospital admission. Multivariate analysis indicated that the independent predictors of in-hospital development of cardiogenic shock were age above 65 years, left ventricular ejection fraction on admission below 0.35, large infarcts as estimated from enzyme determinations, a history of diabetes mellitus, and a previous MI. Webb and coworkers[20] reviewed the timing of shock onset in 815 patients. The median time from onset of symptoms was 6.2 hours but seemed to be related to the culprit artery with the earliest onset with the left main (1.7 hours), right coronary, or circumflex (3.5 and 3.9 hours respectively), and the latest being with the left anterior descending (LAD) or saphenous vein graft (11 hours). Late shock (more than 24 hours following infarct onset) occurred in 26% of the patients and was associated with recurrent ischemia, Q waves in two or more leads, and involvement of the LAD as the culprit vessel. Mortality was somewhat higher with early shock (62.6%) than with late shock (53.6%).

Shock has generally been considered a complication associated with ST-elevation myocardial infarction (STEMI). Holmes and others[21] examined the electrocardiograms (ECGs) in 12,084 patients in the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO-IIb) study who did not have shock on presentation. Of 4092 patients with STEMI 4.2% developed shock, whereas 2.5% of the 7991 with non–ST-elevation myocardial infarction (NSTEMI) developed shock. The patients with NSTEMI tended to develop shock later, were older, and were more likely to have diabetes and three-vessel coronary disease than patients with shock after STEMI. Mortality was similar in the two groups. Jacobs and coworkers[22] identified NSTEMI in 17% of 881 patients with cardiogenic shock from left ventricular dysfunction who were entered into the SHOCK trial registry. The patients with NSTEMI were older and were more likely to have had a prior MI, heart failure, azotemia, peripheral vascular disease, and prior coronary artery bypass graft (CABG) than did patients with STEMI. Among patients undergoing angiography, the circumflex coronary artery was the culprit vessel in 35% of patients with NSTEMI vs. 13% in patients with STEMI.

Goldberg and colleagues[23] reviewed the experience of a community hospital to define the incidence of and mortality rates for shock after acute MI. Those who developed shock were more likely to have very proximal occlusion of the left anterior descending coronary artery and to lack adequate collateral vessels. They were likely to have had one or more previous myocardial infarcts and severe multivessel coronary disease and to develop a left bundle branch block during the course of the acute infarction. The incidence of cardiogenic shock of 7.5% was consistent with that of several studies.[19,23] Patients who developed cardiogenic shock often had a faster heart rate, lower arterial pressure, neck vein distention, and pulmonary rales. Evidence of infarct extension occurred in 23%, and in two thirds of the patients this occurred before or at the time of onset of cardiogenic shock. Patients also had more frequent conduction defects, cardiac arrhythmias, and episodes of cardiac arrest before the development of cardiogenic shock. Hasdai et al.[24] found four clinical variables—age, reduced blood pressure, increased heart rate and Killip class II or III—to be highly predictive for the development of shock after thrombolytic treatment in the GUSTO I trial.

The Shock Study Trial[25] was a study conducted from 1993 to 1997 in which patients with cardiogenic shock following acute MI were randomized to emergency revascularization vs. initial medical stabilization. In addition to randomized patients, 1190 similar patients were entered into a registry. In 78.5% of patients in this study shock was associated with severe left ventricular failure. In the remaining patients, isolated right ventricular failure (2.8%), severe mitral regurgitation (6.9%), ventricular septal rupture (3.9%), or tamponade (1.4%) was present.

Some patients develop cardiogenic shock later, in the 7 to 10 days after an acute MI. They develop a low output state, arrhythmias, and then cardiogenic shock. The pathology is characterized by the softening of a large infarct that becomes aneurysmal and absorbs the energy of the remaining myocardium. It also absorbs the volume necessary to lengthen the normal myocardial fibers in diastole, so the normal myocardium functions less effectively on the Frank-Starling curve.[26] Because of the aneurysmal infarct, ventricular arrhythmias are more frequent and difficult to reverse. It is often difficult

to distinguish the relative contribution to the hemodynamic abnormality of pump failure and arrhythmias.

Patients with cardiogenic shock often have multivessel disease, and thus noninfarcted areas of the myocardium become ischemic at central aortic pressures that are adequate if the coronary vasculature were normal. Vessels leading to noninfarcted areas may be sufficiently narrow that the pressure drop across the partial obstruction leaves the myocardium supplied by these vessels pressure dependent and unable to autoregulate to improve myocardial blood flow. Therefore, in addition to the large area of infarction that is noncontractile, remaining segments of the myocardium may be hypocontractile on the basis of ischemia secondary to the low arterial pressure.

Clinical Recognition

Shock is defined clinically as inadequate perfusion of the vital organs manifested by obtundation, cyanosis, cold extremities, thready pulse, and oliguria. It should be distinguished from the low-blood-pressure, normal-output states sometimes seen in acute MI associated with increased vagal tone. These latter patients are not obtunded, they continue to excrete urine adequately, and they have warm extremities, even though their systolic blood pressure may be less than 100 mm Hg. They usually require no treatment—only observation.

Patients in cardiogenic shock frequently have a slightly elevated venous pressure. With right ventricular infarction, however, the neck veins may be quite distended. There is clinical evidence of pulmonary edema ranging from a few rales to pulmonary edema. The heart is quiet, and the heart tones are distant. The first sound is soft, the second sound may be single or paradoxically split, and the third and fourth sounds are usually present, but at the heart rates associated with cardiogenic shock they frequently fuse to form a summation gallop. There may be a subtle parasternal systolic lift, particularly in the presence of an anteroseptal infarct. A new systolic murmur from mitral insufficiency may arise. At the time of presentation in cardiogenic shock, there usually is no evidence of peripheral edema or hepatic congestion.

Monitoring

Before discussing specific treatment, other problems that may occur following acute MI and contribute to cardiogenic shock must be considered. Electrocardiograph monitoring is vital. Prompt treatment of severe bradycardia with temporary pacing or of tachyarrhythmias with antiarrhythmic drugs or cardioversion should be instituted if needed. Pulmonary congestion or edema may cause severe arterial hypoxemia, and inadequate ventilation may lead to respiratory acidosis superimposed on the metabolic (lactic) acidosis of poor tissue perfusion. Measurement of arterial blood gases helps determine if endotracheal intubation and assisted ventilation is necessary.

In the presence of marked vasoconstriction, blood pressure measurement obtained by cuff may be significantly lower than the true, directly measured central aortic pressure. Large discrepancies of arterial pressure between cuff pressures and central aorta have been described in patients in shock with acute MI.[27,28] There may even be a significant gradient from brachial to radial arteries because of arterial vasoconstriction. It is therefore essential that the arterial pressure be accurately measured and continuously monitored. Insertion of a central arterial line connected to a transducer permits continuous display of the arterial pressure and facilitates sampling of arterial blood for measurement of blood gases and pH.

When possible, left ventricular filling pressures and cardiac outputs should be monitored by a pulmonary artery flotation catheter. Also essential to overall patient management is the close monitoring of urine output and serum electrolytes and the use of high-dose loop diuretics or, on occasion, dialysis if required.

Hypovolemia may occur in patients with acute MI, leading to hypotension and clinical shock. This hypovolemia may be induced by overdosing of diuretics, third space redistribution of intravascular volume after cardiac arrest, the prolonged use of pressor agents, unrecognized sepsis or bleeding, and vomiting or profuse diaphoresis, which can occur early in the course of a MI.[29]

Patients with shock due to hypovolemia look clinically similar to patients with true cardiogenic shock, except for absent neck vein distention and third heart sounds. Recognition of hypovolemia is important because, unlike shock from severe left ventricular dysfunction, volume administration often leads to improved hemodynamics and resolution of shock. Hypovolemia should be considered whenever a patient with shock following acute MI has a left ventricular filling pressure under 15 mm Hg. Such patients should receive rapid fluid repletion to bring left ventricular filling pressure to 18 mm Hg before redefining the patient as having cardiogenic shock from pump failure.

Circulatory Support

The goal of interventions to correct the hemodynamic abnormality is to restore adequate peripheral perfusion while improving or at least not adversely affecting the myocardial metabolic balance of oxygen supply and oxygen utilization. Oxygen supply can be enhanced by correcting a low aortic diastolic coronary perfusion pressure and reducing left ventricular diastolic pressure that impedes subendocardial flow. Myocardial oxygen consumption is increased by peripheral constriction that raises systolic pressure and by a positive inotropic effect. The net effect of interventions that alter these determinants varies depending on the overall hemodynamic and metabolic state at the time. Thus pathophysiology should drive management, but therapy may need to be altered as the physiology changes with time.[30] Circulatory support can be pharmacologic or mechanical.

Pharmacologic Support

When aortic diastolic pressure is low, coronary perfusion may be critically impaired, especially in areas subserved by stenotic coronary arteries or collaterals. This then may lead to ischemia of noninfarcted myocardium and progressive infarction of myocardium in the infarct border zone, which

may be dependent on collaterals. A vicious cycle may be initiated, characterized by worsening myocardial function and progressively more severe hypotension with death as the end result. The goal of pharmacologic treatment in these circumstances is to raise arterial pressure to a level compatible with an adequate coronary perfusion pressure. Increasing afterload may increase myocardial oxygen consumption but might also augment coronary blood flow and at least temporarily improve left ventricular function.

Vasoconstrictor drugs augment arterial pressure, but often at the cost of a reduction in cardiac output and a rise in myocardial oxygen consumption.[11] In the presence of severe hypotension (i.e., arterial systolic pressure <80 mm Hg), a trial of such therapy may be warranted to determine if improved coronary perfusion may restore myocardial function. Norepinephrine[27,31,32] and dopamine[33,34] are the drugs of choice since they combine vasoconstriction with positive inotropism to support left ventricular function and cardiac output.

When severe hypotension is present (i.e., arterial systolic pressure under 80 mm Hg or mean arterial pressure under 70 mm Hg), agents with some vasoconstrictor activity are likely to be needed to raise the blood pressure. Among the earliest drugs used was methoxamine (a pure α-adrenergic agonist with no inotropic activity) since it was felt that drugs that increased myocardial contractility might be detrimental because they would also increase myocardial oxygen requirements. Methoxamine, however, was not effective.[11]

Dopamine is thought to combine a positive inotropic effect with a selective increase in renal and mesenteric blood flow through activation of dopaminergic receptors; however, the clinical importance of this effect in cardiogenic shock is unclear. At low doses dopamine tends to vasodilate, but as the infusion rate is raised, the α-vasoconstrictor activity increases. When infused at higher doses the hemodynamic effects of dopamine and norepinephrine are similar,[34] but dopamine exhibits more variability in its response than norepinephrine, its onset of action is slower, and it has the undesirable effects of increasing heart rate and causing arrhythmias.

Although norepinephrine may be the most reliable agent to raise a very low perfusion pressure in the setting of pump failure after MI, its use is rarely associated with long-term recovery and it therefore should be viewed only as temporary support before more definitive therapy (e.g., mechanical support or reperfusion) can be accomplished.

An alternative approach to managing pump failure is the use of vasodilator drugs that reduce aortic impedance, improve left ventricular emptying, and reduce myocardial oxygen consumption.[35,36] These drugs are particularly appropriate when cardiogenic shock is not accompanied by severe hypotension.[15] Even in the presence of low arterial pressure, however, infusion of nitroprusside may be accompanied by a large enough increase in cardiac output to raise arterial pressure.[36] This approach to management of pump failure has become standard practice in the treatment of chronic heart failure.[38,39] It might be theorized that vasodilation and inotropic support combined would produce the greatest circulatory benefit in shock. However, early studies with isoproterenol were often accompanied by severe hypotension and rapid clinical deterioration.[31,32]

The choice of vasodilator drug for optimal management of pump failure depends on the clinical circumstances. When cardiac output is critically depressed nitroprusside may be the preferred choice because it lowers elevated left ventricular filling pressure and strikingly augments output. In the first 12 hours after an MI, however, nitroprusside may aggravate periinfarction ischemia and worsen prognosis.[37] Nitroglycerin therefore may be a preferable choice. After this early post-MI phase, nitroprusside is the preferred agent.[37] The use of newer vasodilators in this clinical situation has not been carefully evaluated.

When hypotension limits the use of a pure vasodilator agent, the addition of an inotropic drug to further increase cardiac output and blood pressure may be useful. To develop an agent with pure inotropic activity, Tuttle and Mills[38] investigated a large number of synthetic catecholamines and selected dobutamine because it had potent inotropic activity with less chronotropic, arrhythmogenic, and peripheral vascular effects when compared to other agents. Dobutamine, through its β-adrenergic receptor effects, increases myocardial contractility and cardiac output,[39–41] and at doses that do not significantly increase heart rate the effects of increased contractility on myocardial oxygen demand may be offset by a reduction in ventricular volume and a withdrawal of compensatory vasoconstriction. In acute MI with hypotensive shock, however, dobutamine has not been shown to be an effective agent for increasing arterial pressure. The use of phosphodiesterase inhibitors such as milrinone in the setting of cardiogenic shock is more unpredictable because the balance of inotropic and vasodilator effects cannot be individually titrated as is possible with, for example, the infusion of dobutamine or low-dose dopamine and nitroprusside.

Recommendations for pharmacologic support:

1. To raise a critically low aortic pressure that threatens coronary and cerebral perfusion:
   a. Norepinephrine in a gradually titrated infusion rate to increase systolic blood pressure no higher than 110 mm Hg.
   b. Dopamine similarly employed is an alternative.
2. To increase a critically reduced cardiac output that threatens tissue perfusion:
   a. Nitroprusside titrated to optimal cardiac filling pressure and tolerable blood pressure.
   b. Nitroglycerin similarly employed is an alternative.
   c. Dobutamine titrated to an adequate cardiac output without induction of ventricular arrhythmias.
3. To reduce an elevated left ventricular filling pressure that threatens pulmonary gas exchange and may aggravate myocardial ischemia:
   a. Intravenous loop diuretics (e.g., furosemide) are capable of inducing increased urine flow.
   b. Nitroprusside and nitroglycerin can be used in titrated doses to lower filling pressure.

Mechanical Support

Intraaortic Balloon Counterpulsation

If the shock syndrome is not quickly corrected or the arterial pressure is profoundly reduced, intraaortic balloon counterpulsation should be instituted as quickly as possible [American College of Cardiology (ACC)/American Heart Association

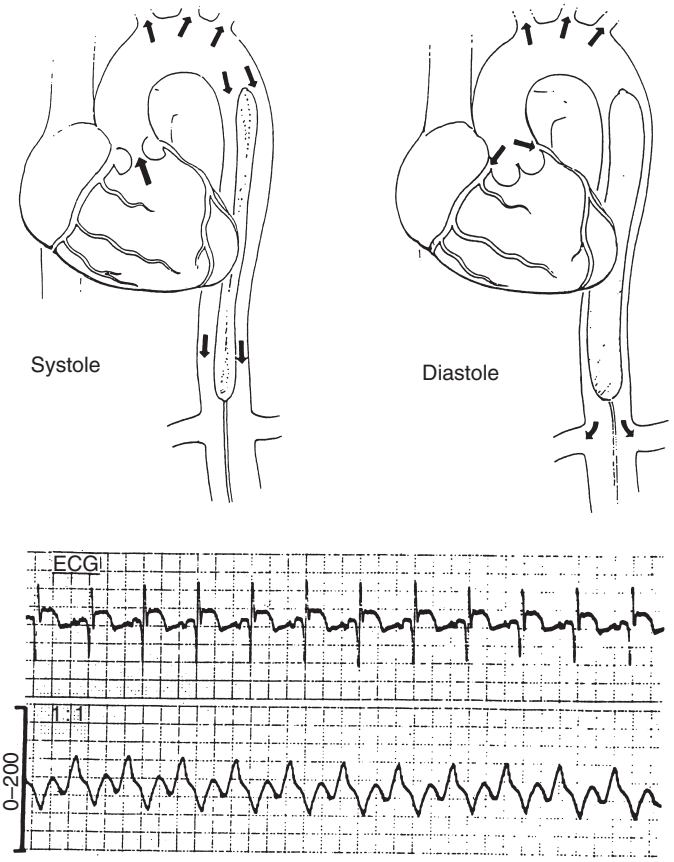

FIGURE 87.1. Top: Diagram of collapsed aortic balloon in systole and distended balloon in diastole augmenting perfusion to coronary arteries and aortic branches. Bottom: Electrocardiogram (ECG) is accompanied by a pressure recording showing proper timing of balloon inflation to produce prominent diastolic augmentation and low end-diastolic pressure to facilitate left ventricular systolic ejection.

(AHA) class I]. Proper timing of this counterpulsation should result in adequate diastolic pressure to maintain perfusion of the heart and brain and often will augment renal and peripheral perfusion as well (Fig. 87.1). The net effect on ischemia depends on the change in aortic diastolic pressure and its effect on myocardial perfusion. These considerations make clear the physiologic rationale for counterpulsation, which reduces aortic systolic pressure and augments aortic diastolic pressure. In most centers where emergency angiography is performed, balloon counterpulsation is used as soon as possible even when the initial response to pharmacologic treatment is favorable. Patients treated in centers not having facilities for emergency angiography can be supported with intraaortic balloon counterpulsation during transfer to an institution where angiography and revascularization can be performed.

Mechanical Circulatory Assistance

In addition to intraaortic balloon counterpulsation a variety of mechanical circulatory support systems have been used, mostly for temporary support or as a bridge to cardiac surgery or cardiac transplant. With cardiopulmonary bypass (CPB) systemic venous blood is withdrawn, passed through an oxygenator, and returned to the systemic arterial system. By cannulation of a femoral vein and artery, CPB can be instituted without thoracotomy, and portable systems have been designed for use in emergency rooms, intensive care units, and cardiac catheterization laboratories. This device has the advantage (unlike intraaortic balloon counterpulsation) of sustaining the circulation and arterial oxygenation even when left ventricular ejection is absent such as during cardiac arrest or electromechanical dissociation or when pulmonary function is severely compromised. The use of emergency CPB was investigated by Overlie and associates[42] in 109 patients with cardiogenic shock, and they reported a 50% 1-year survival rate in 52 patients who subsequently underwent surgery versus 37% in 57 patients who were treated medically. A major limitation to CPB is the damage done to blood cells by the oxygenator, which limits its use to hours rather than days.

To permit extended circulatory support, a variety of devices that do not require the use of an oxygenator have been developed and investigated.[43] Although techniques for percutaneous application have been tried, most clinical experience has required a thoracotomy. With a right ventricular assist device (RVAD), systemic venous blood is withdrawn and pumped back into the pulmonary artery, while with a left ventricular assist device (LVAD) blood returning from the lungs is removed and pumped back into the systemic circulation. Copeland and coworkers[44] reported results of implanting a total artificial heart in 81 patients who were awaiting cardiac transplantation. When compared with patients not receiving the artificial heart, the patients with the artificial heart were significantly more likely to survive to transplantation and had significantly improved 5-year survival. Unlike a total artificial heart during which the native heart is often removed, these devices have the potential of being discontinued and removed if cardiac function improves over time. Initially these devices were used primarily when patients undergoing cardiac surgery could not be weaned from CPB. In some patients cardiac function improved and the device could be removed, while in others it served as a bridge to cardiac transplantation.

Currently an LVAD is often used to support patients with acute or chronic left ventricular failure who are not surgical candidates but for whom cardiac transplantation is an option (Fig. 87.2). Improved pump design has permitted such patients to be discharged from the hospital and resume fairly normal activities. There is growing evidence that LVAD support prior to transplantation not only increases the chances of the patient surviving long enough to receive a heart but also improves the outcome following transplantation.[43] Additionally some patients destined for cardiac transplantation who were supported with an LVAD have shown improved cardiac function and remodeling to the point where the device could be removed and transplant avoided.

Because of the success of LVAD support as a bridge to cardiac transplant, the Randomized Evaluation of the Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) study was initiated to investigate the potential value of LVAD support in patients who had

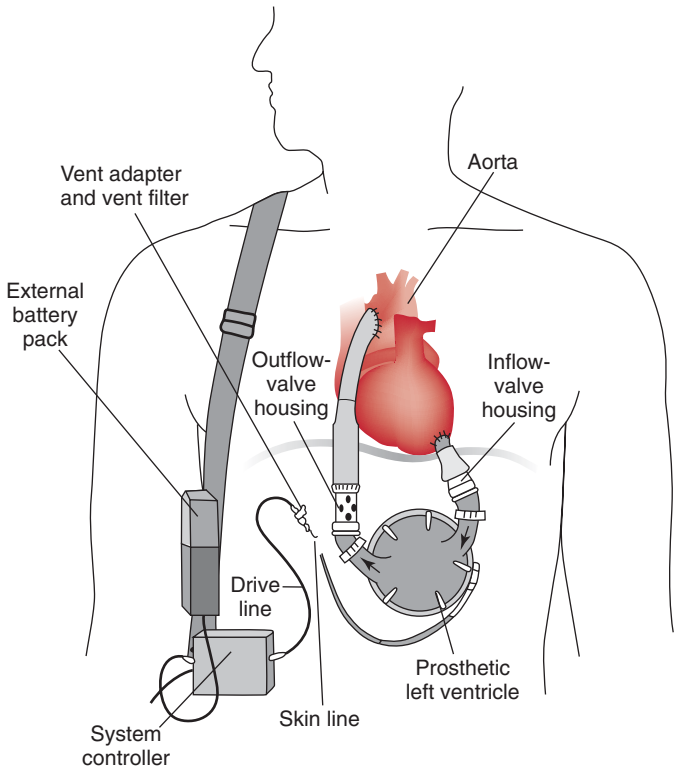

FIGURE 87.2. Components of the left ventricular assist device. The inflow cannula is inserted into the apex of the left ventricle, and the outflow cannula is anastomosed to the ascending aorta. Blood returns from the lungs to the left side of the heart and exits through the left ventricular apex and across an inflow valve into the prosthetic pumping chamber. Blood is then actively pumped through an outflow valve into the ascending aorta. The pumping chamber is placed within the abdominal wall or peritoneal cavity. A percutaneous drive line carries the electrical cable and air vent to the battery packs (only the pack on the right side is shown), and electronic controls, which are worn on a shoulder holster and belt, respectively.

advanced left ventricular failure [New York Heart Association (NYHA) class IV] but who were not eligible for cardiac transplantation, primarily because of advanced age.[45] Survival among the 68 patients randomized to LVAD was found to be significantly better than for the 61 patients randomized to optimal medical therapy. Although LVAD support is not without complications, which include stroke and infection, overall quality-of-life assessments tended to favor the LVAD over medical treatment. The results with mechanical circulatory support, particularly the LVAD, suggest that it may in the future play an important role for the management of patients with shock following acute MI who either are not candidates or fail to respond adequately to reperfusion therapy.

It must be stressed that unlike intraaortic balloon counterpulsation, which can be rapidly applied in the cardiac catheterization laboratory or even at the bedside and is usually managed by physicians and nursing personal trained in cardiac care, other types of mechanical circulatory assistance require a much greater commitment of hospital resources. In addition to major surgery required to apply an LVAD, the personnel monitoring its function need specialized training, which may not be available in many institutions. Likewise the commitment by the patient and family for extended or indefinite support is considerable. Clearly not all patients with end-stage heart failure or cardiogenic shock are suitable candidates for this aggressive therapy. The wishes and expectations of the patient and family must be considered with a realistic discussion of the likely outcome and potential problems. In high-risk patients these discussions should take place as early as possible since decisions made during a crisis, attendant with the emotions of imminent demise such as when a surgical patient fails to wean from CPB, may not reflect the true desires of the patient or family.

Recommendations for mechanical support:

1. For acute support to improve function and metabolism of the heart:
   a. Intraaortic balloon counterpulsation
   b. Other potential devices currently undergoing investigation
2. To replace the heart's function to place it at rest:
   a. Left ventricular assist device
   b. Biventricular assist devices

Reperfusion Treatment

The treatment for shock in acute MI often must include a mechanism to improve coronary blood flow to the ischemic area. Such patients have a high frequency of infarct extension and spotty myocardial necrosis even in areas not supplied by the infarct-related artery.[16] Pharmacologic therapy alone does not improve a dismal long-term outlook, except in patients with associated hypovolemia or predominant right ventricular infarction.[46]

Pifarre and colleagues[47] demonstrated that surgical reperfusion can be lifesaving with a good outcome in patients with acute MI, especially if the coronary anatomy was known and the infarct occurred in the hospital. The Spokane group showed the efficacy of such therapy in a larger group of patients in a community that organized for rapid identification of, catheterization of, and surgery in patients with chest pain. DeWood and associates[48] reviewed the Spokane data and demonstrated the importance of reducing the time from onset of pain to reperfusion. The advent of angioplasty has enabled coronary reperfusion without thoracotomy.

Prompt reperfusion therapy is currently recommended for patients presenting within 12 hours of acute STEMI.[49] If there are no contraindications, intravenous thrombolytics should be administered in centers where primary angioplasty [percutaneous coronary intervention (PCI)] cannot be performed within 90 minutes of patient arrival; however, whenever PCI can be done by experienced personnel within the 90-minute time frame, thrombolytics are currently not recommended. Recent data, however, suggest when given very early after symptom onset (often prior to hospital arrival) thrombolytics might be superior to PCI. In the CAPTIM study,[50] patients randomized to prehospital thrombolysis within 2 hours of symptom onset had a lower 30-day mortality (2.2%) than did patients randomized to PCI (5.7%). In this study very early thrombolytic therapy was also associated with a reduced incidence of shock (1.3% vs. 5.3%). Thus it

seems that the incidence of shock following acute MI can be significantly reduced by early reperfusion therapy.

For patients with established shock as well as for patients with mechanical complications that may require cardiac surgery, the value of thrombolytics is less well established. Reperfusion rates with thrombolytics are lower in patients with shock than in patients without shock,[51] and the outcome with thrombolytic therapy alone appears to be worse than with emergency reperfusion by PCI or CABG. Therefore, whenever possible coronary angiography and primary angioplasty or CABG should be done. In the Shock Study Trial patients randomized to initial medical stabilization, which included intraaortic balloon counterpulsation in the majority, who also received thrombolytics had an improved survival at 1 year compared to patients not receiving thrombolytics[52]; however, selection bias may have influenced the outcome in these patients. Although the value of thrombolytic therapy for patients with shock who refuse invasive therapy or for whom it is not available is less well established, it remains an ACC/AHA class I indication. If angioplasty is immediately unavailable, there may be a role for thrombolytic therapy in conjunction with intraaortic balloon support while transfer is being made to a center for invasive treatment.[53–55] O'Neill and colleagues[53] compared the use of thrombolysis with that of angioplasty and showed similar rates of reperfusion. However, in the patients who underwent angioplasty, there was significant improvement in wall motion, unlike in those who received thrombolytic therapy alone. The residual stenosis was much greater in the thrombolytic than in the angioplasty group.

Early studies of primary angioplasty for the treatment of acute MI complicated by cardiogenic shock supported this approach.[56–63] O'Neill and colleagues[56] proposed the use of angioplasty for the treatment of shock in acute MI, and their reported experience demonstrated improved survival rates in this group of patients. Using historical controls, they showed a 50% survival rate at 30 days in patients treated with angioplasty and a 17% survival rate at 30 days in those treated with conventional therapy without angioplasty. In patients with successful reperfusion, there was a 77% survival rate at 30 days.

In a multicenter registry arising out of experience in Michigan and reported by Lee and colleagues,[58] 69 patients were treated with attempted angioplasty for shock in acute MI. The procedure was unsuccessful in 20 patients who were, in all respects, similar to the 49 patients who had successful angioplasty. These two groups were then compared. The immediate survival rate in the two groups was 69% for those with successful angioplasty and 20% for those with unsuccessful angioplasty. The survival rate at 24 months was 54% for the successful angioplasty group and 11% for the unsuccessful group. A more recent report from Henry Ford Hospital confirms the efficacy of revascularization with either angioplasty or bypass surgery, with a 56% survival rate in the revascularized group and an 8% survival rate in the nonrevascularized group (Fig. 87.3).

Consistent with these results is a report on experience with primary angioplasty. Thirty-three patients with more than one diseased vessel had shock and 36 patients with one diseased vessel had shock. The survival rates were 55% in the multivessel group and 59% in the one-vessel group. The treatment consisted of placement of an intraaortic balloon pump, movement of the patient to the catheterization laboratory for angiography, and angioplasty where indicated. The long-term survival rate was excellent compared with pharmacologic therapy. Overall, the patients were treated within less than 6 hours of the onset of their chest pain. Rothbaum and colleagues[62] also reported the use of primary angioplasty for acute MI; shock was present in 18 of their patients. There were seven deaths, resulting in a survival rate of 61%.

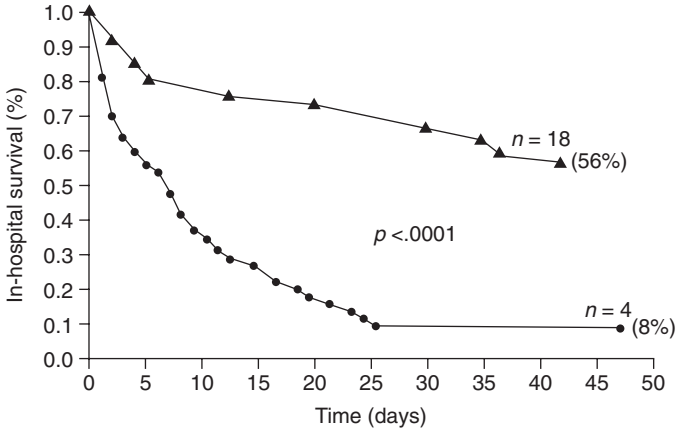

FIGURE 87.3. Comparison of in-hospital cumulative survival rates for 32 patients with (triangles) and 49 patients without (circles) revascularization. At 42 days, there were 18 surviving patients (56%) in the group with revascularization and four (8%) in the group without revascularization.

Berger and colleagues[63] reported the effects of early angiography and revascularization strategy in 2200 patients with cardiogenic shock who were entered into the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries trial. The 30-day survival rate was 62% among 406 patients who underwent early angiography (within 24 hours) versus a 30-day survival rate of only 38% in the 1794 patients who did not undergo early angiography. When these two groups were compared, however, it was found that patients undergoing early angiography tended to be younger, to have less prior infarction, and to have received thrombolytic therapy earlier. Among the 406 patients who underwent early angiography, 233 patients underwent early revascularization with angioplasty, bypass surgery, or both; the 30-day survival rate in these patients was 60%. In 173 of these patients, early revascularization was not performed after angiography, and the 30-day survival rate was 65%. Although these data suggest a favorable effect of early angiography in patients with cardiogenic shock after acute MI, it is unclear how much of this benefit is due to selection bias versus early revascularization for patients found at angiography to be suitable candidates.

Menon and Fincke[64] reviewed the Shock Study Trial in which 302 patients with cardiogenic shock following acute MI were randomized either to emergency revascularization to be done within 6 hours or initial medical stabilization with the provision for late (after 54 hours) revascularization. The majority of patents in both groups were supported with intraaortic balloon counterpulsation. Thrombolytics were given to 49% of patients randomized to emergency revascularization and to 63% of patients randomized to initial

medical stabilization. The primary end point of the study, which was survival at 30 days, failed to show a significant benefit for patients randomized to emergency revascularization vs. initial medical stabilization (53% vs. 44%, $p = .11$). However, at 6 months (50% vs. 37%, $p = .27$) and at 1 year (47% vs. 34%, $p = .25$) survival was significantly better in patients randomized to emergency revascularization. In the patients randomized to emergency revascularization who underwent PCI,[65] a major factor influencing survival status was post-PCI flow in the infarct related artery with a 1-year survival of 62% when flow was normal [Thrombolysis in Myocardial Infarction class 3 (TIMI 3)], 45% with TIMI 2 flow, and 0% when the artery remained occluded or had minimal flow (TIMI 0 or 1). Additional factors having a negative effect on survival in these patients was increased age, lower systolic blood pressure, increasing time from randomization to PCI, and multivessel PCI. Overall for randomized patents the survival benefit with emergency revascularization was limited to those under 75 years of age. Nonrandomized registry patients who were 75 years or older were less likely than younger patients to receive early invasive therapy; however, those elderly registry patients who did receive early revascularization had a significantly lower in-hospital mortality than those who received late or no revascularization therapy.[66]

Largely based on the results from the Shock Study Trial along with other recent studies, the current ACC/AHA guidelines consider primary PCI as a class I indication for patients younger than 75 years with STEMI or left bundle branch block who develop shock within 36 hours of infarction and are suitable candidates for revascularization when it can be performed within 18 hours of shock, unless further support is considered futile or against the patient's wishes. For patients who are 75 years or older but with good prior functional status, primary PCI is considered a class IIa indication. Similar ACC/AHA guidelines deal with the use of emergency surgical revascularization (assuming favorable coronary anatomy) for the management of cardiogenic shock following acute MI when PCI has failed or is not feasible due to coronary anatomy, or when surgery is required for correction of associated mechanical complications.

Experience with primary angioplasty in patients with acute MI, including those with cardiogenic shock,[67] has demonstrated the feasibility of coronary stenting coupled with antiplatelet therapy, including blockers of the platelet IIa/IIIb receptor, to achieve an optimal angiographic result. When primary PCI is performed in stable patients with STEMI it is usual practice to intervene only on the "culprit" artery, leaving other lesions to be treated later if necessary. However, in patients with cardiogenic shock in whom ischemia in regions not supplied by the infarct vessel may be contributing to the shock syndrome, complete revascularization should be attempted if at all possible. It seems very likely that revascularization with improved techniques will continue to have a favorable impact on the outcome of patients who develop cardiogenic shock after acute MI.

Recommendations for reperfusion:

1. In acute STEMI with shock:
   a. Immediate thrombolysis
   b. Immediate angiography and angioplasty if available
2. In other cases of cardiogenic shock:
   a. Angiography if warranted by clinical circumstances
   b. Angioplasty or surgical reperfusion if feasible

Right Ventricular Infarction

All patients with acute inferior infarction should have right precordial leads recorded to detect ST-segment elevation, which would indicate the presence of right ventricular infarction (ACC/AHA class I), which is associated with an increased risk of death, shock, ventricular fibrillation or tachycardia, and atrioventricular (AV) block independent of left ventricular infarct size.[68] Right ventricular infarction presents a therapeutic dilemma different from that presented by pump failure due to left ventricular damage. Right atrial and right ventricular diastolic pressures are elevated, whereas the cardiac index and arterial pressure are low. Left ventricular filling pressures can be elevated or normal. Unless left ventricular filling pressure is also elevated, the primary therapy is to increase right ventricular output by elevating right ventricular filling pressure while monitoring left ventricular filling pressure so the wedge pressure does not exceed 20 mmHg. Venodilators, particularly nitroglycerin, are contraindicated, and diuretics should not be administered unless there is pulmonary congestion.[69,70]

Because patients with right ventricular infarction usually have occlusion of the right (or a dominant left circumflex) coronary artery, bradyarrhythmias or atrioventricular conduction abnormalities are common and may cause an inadequate cardiac output and hypotension. Under these circumstances, temporary pacing should be instituted promptly.

Fluid infusion should be administered as a challenge because even slow infusion may not exceed loss from intravascular space and leads to diffuse edema, including pulmonary edema, without effectively raising the filling pressure. Furthermore, left ventricular damage may be masked by the right heart failure[70] and only manifest after right ventricular filling pressures have been increased. The pressor agent of choice is dobutamine because dopamine and norepinephrine increase pulmonary vascular resistance.[40] There is a good response to intraaortic balloon counterpulsation in these patients, and many improve remarkably after several days of counterpulsation and more aggressive intervention.[71,72] Although the above measures may result in hemodynamic improvement, mortality remains high and emergency revascularization should be undertaken as soon as possible[46] (ACC/AHA class I).

Summary

The goal of treatment of patients in shock with MI for which the cause is pump failure is to stabilize the patient with pharmacologic therapy according to a regimen based on the hemodynamic disorder. Patients with shock syndrome should have an intraaortic balloon pump placed and should be taken to the cardiac catheterization laboratory as quickly as possible, the anatomy should be defined, and revascularization with either angioplasty or surgery should be undertaken. The

attempt should be made to have this completed within the first 6 hours from the onset of the chest pain. The earlier such revascularization is established, the better the outcome, although patients presenting within 24 hours of the onset of MI have been treated in this manner with results improved over pharmacologic therapy. The value of intravenous thrombolytic therapy given prior to cardiac catheterization is questionable but may be considered if it can be given prior to hospital arrival and within 2 hours of the onset of symptoms or when a prolonged delay is anticipated before invasive therapy can be performed.

In patients for whom PCI or CABG is not an option, intravenous thrombolytic therapy in conjunction with intraaortic balloon counterpulsation is probably indicated if there are no contraindications. In patients with serious mechanical problems such as free wall rupture, ventricular septal rupture, or severe mitral regurgitation emergency, surgical repair offers the only realistic chance for survival. For patients who remain in shock following the above measures, prolonged mechanical circulatory assistance (primarily an LVAD) may be considered.

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