Cardiogenic shock

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Cardiogenic shock is the most common cause of death in patients hospitalized with acute myocardial infarction and is associated with a poor prognosis. More than 75% of cases are due to extensive left ventricular infarction and ventricular failure. Other causes include right ventricular infarction and papillary muscle rupture with acute severe mitral regurgitation. Activation of neurohormonal systems and the systemic inflammatory response worsens shock. To improve outcomes, cardiogenic shock needs to be recognized early in its course and its cause needs to be diagnosed rapidly. Treatment strategies using intra-aortic bal-

loon counterpulsation and emergency revascularization by percutaneous coronary interventions or coronary bypass surgery have been shown to improve outcomes. To decrease the incidence of cardiogenic shock, public education regarding early presentation to hospital in the course of acute chest pain is important. Emergency medical transport systems may need to take patients with complicated acute myocardial infarction to hospitals with the capability to perform urgent revascularization. (Crit Care Med 2008; 36[Suppl.]:S66–S74)

Cardiogenic shock is a life-threatening emergency and the most common cause of death in patients hospitalized with acute myocardial infarction. Studies of this condition over the past 10 yrs have changed the approach to cardiogenic shock patients so that there is now an opportunity to improve on the high mortality rate of this condition.

Definition

Cardiogenic shock (CS) is defined as persistent hypotension and tissue hypoperfusion due to cardiac dysfunction in the presence of adequate intravascular volume and left ventricular filling pressure. Clinical signs include hypotension, tachycardia, oliguria, cool extremities, and altered mental status. Hemodynamic findings are sustained hypotension with systolic blood pressure <90 mm Hg for ≥30 mins, low cardiac index <2.2 L/min/m^2, and elevated pulmonary artery occlusion pressure >15 mm Hg (1).

Incidence and Epidemiology

CS is a major complication of myocardial infarction. The incidence of CS has remained stable over the past 3 decades despite advances in diagnostic and therapeutic modalities. In an early trial of thrombolytic therapy for acute myocardial infarction, the incidence of CS complicating acute myocardial infarction was 7.2% (2). In an observational community-wide study, the incidence of CS averaged 7.1% over a 23-yr period from 1975 through 1997 (3). In a more recent analysis of the National Registry of Myocardial Infarction (NRMI) covering the period from June 1995 through May 2004, CS developed in 8.6% of patients with acute myocardial infarction (ST-segment elevation or left bundle branch block) hospitalized in 775 U.S. hospitals with revascularization capability (4) (Fig. 1).

The prognosis of CS is extremely poor. Mortality rates were reported at 50% to 80% in older series (1). In-hospital mortality in the SHould we emergently revascularize Occluded Coronaries for cardiogenic shocK (SHOCK) Trial Registry was 60% (5). In the NRMI data, the overall in-hospital mortality decreased from 60.3% in 1995 to 47.9% in 2004 (4).

In the NRMI database, 29% of patients with CS were in shock as they presented to hospital, and 71% developed CS after admission (4) (Fig. 1). Patients >75 yrs old were slightly more likely to present with CS. CS patients were more likely to have a history of hypertension, dyslipidemia, and prior coronary angioplasty. In

the SHOCK Trial Registry, the median time from onset of myocardial infarction to shock was 7 hrs (5). Rates of recurrent myocardial infarction or ischemia precipitating CS were 9.3% and 19.7%, respectively. Infarction location was anterior in 55% of cases and in multiple locations in 50% (5).

CS can occur in the setting of ST-elevation myocardial infarction (STEMI) as well as non-ST-elevation myocardial infarction (NSTEMI). In the Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO)-IIb trial, CS developed in 4.2% of STEMI and 2.5% of NSTEMI patients. In the latter group, CS tended to occur later after presentation (76.3 hrs vs. 9.6 hrs). NSTEMI patients with CS were older and had higher rates of diabetes mellitus, prior myocardial infarction, heart failure, azotemia, bypass surgery, peripheral vascular disease, and three-vessel coronary disease. In-hospital and 30-day mortality rates in STEMI and NSTEMI patients were similar (6, 7).

Patients with CS have extensive coronary artery disease. Angiographic data from the SHOCK Trial Registry revealed that 53.4% of patients had three-vessel disease and 15.5% had significant left main stenosis (8).

Etiology

Many conditions may lead to CS (Table 1). However, left ventricular failure due to extensive acute myocardial infarction remains the most common cause. In
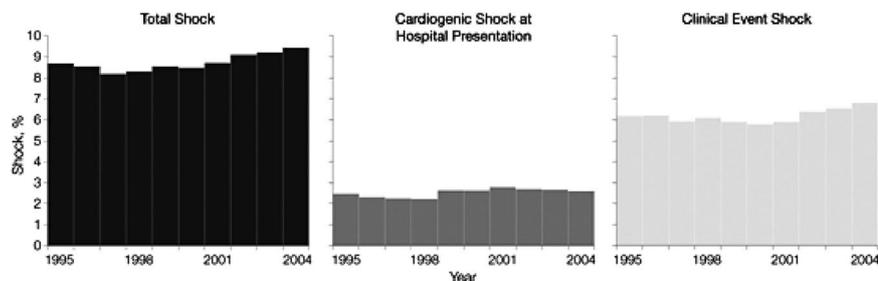
Figure 1. Frequency of cardiogenic shock among patients in the National Registry of Myocardial Infarction. Includes total shock at hospital presentation and shock that develops after hospital presentation as a clinical event. For hospitals with open-heart surgery and percutaneous coronary intervention capability, the ST-elevation myocardial infarction population was 293,633. Data are through May 2004. Reproduced with permission from Babaev A, Frederick PD, Paste DJ, et al: Trends in management and outcomes of patients with acute myocardial infarction complicated by cardiogenic shock. *JAMA* 2005; 294:448–454.

Table 1. Causes of cardiogenic shock

Acute myocardial infarction
  Pump failure
    Large infarction
    Smaller infarction with preexisting left
      ventricular dysfunction
    Infarction extension
    Severe recurrent ischemia
    Infarction expansion
  Mechanical complications
    Acute mitral regurgitation caused by
      papillary muscle rupture
    Ventricular septal defect
    Free-wall rupture
    Pericardial tamponade
  Right ventricular infarction
Other conditions
  End-stage cardiomyopathy
  Myocarditis
  Myocardial contusion
  Prolonged cardiopulmonary bypass
  Septic shock with severe myocardial
    depression
  Left ventricular outflow tract obstruction
    Aortic stenosis
    Hypertropic obstructive cardiomyopathy
  Obstruction to left ventricular filling
    Mitral stenosis
    Left atrial myxoma
  Acute mitral regurgitation (chordal rupture)
  Acute aortic insufficiency
  Acute massive pulmonary embolism
  Acute stress cardiomyopathy
  Pheochromocytoma

the SHOCK Trial Registry, left ventricular failure accounted for 78.5% of cases of CS complicating acute myocardial infarction. Acute severe mitral regurgitation accounted for 6.9%, ventricular septal rupture 3.9%, isolated right ventricular infarction 2.8%, and tamponade or cardiac rupture 1.4% (5). Other causes, such as coexistent severe valvular heart disease, excess β-blocker or calcium channel blocker therapy, severe dilated cardiomyopathy, recent hemorrhage, or cardiac catheterization laboratory complication, accounted for 6.7%.

Pathophysiology

Most commonly, CS occurs after a massive and extensive myocardial infarction or severe myocardial ischemia leading to impaired left ventricular function, reduced systolic contractility, and decreased cardiac output and arterial blood pressure. Coronary perfusion will decrease and further compromise coronary reserve. Compensatory neurohormonal responses take place, which include activation of the sympathetic and renin-angiotensin systems, leading to systemic vasoconstriction, tachycardia, and fluid retention. These mechanisms are maladaptive and worsen myocardial ischemia. Thus, "ischemia begets ischemia," leading to a progressive downward spiral of worsening ischemia, progressive deterioration of myocardial function, and worsening shock (1) (Fig. 2).

At the cellular level, inadequate oxygen delivery to myocytes affects cellular adenosine triphosphate production. Immediately, energy metabolism shifts from aerobic to anaerobic glycolysis with resultant lactic acid production. Intracellular ionic calcium rises and intracellular sodium competes to expel calcium (9). If hypoperfusion and ischemia are severe, as occurs in CS, myonecrosis ensues with mitochondrial swelling and subsequent plasma membrane disruption.

This ischemic cascade results in metabolic and biochemical alterations, which lead to left ventricular diastolic dysfunction from impaired myocardial relaxation and decreased compliance. This leads to increased left ventricular filling pressures, manifesting as pulmonary congestion and edema. This in turn increases wall stress

and further compromises coronary perfusion. Echocardiographic data from the SHOCK Trial showed that restrictive left ventricular filling, as assessed by Doppler mitral inflow deceleration time, was present in most patients (60.9%) (10). This restrictive pattern predicted pulmonary artery occlusion pressures >20 mm Hg.

New evidence has emerged that has led to expansion of the CS paradigm (11). Wide variations in left ventricular ejection fraction, left ventricular size, and systemic vascular resistance in patients with CS suggest that pathophysiologic mechanisms of CS may vary among patients. About one fifth of patients with CS complicating myocardial infarction in the SHOCK Trial had clinical evidence of a systemic inflammatory response syndrome, marked by fever, leukocytosis, and low systemic vascular resistance (12). Attempts to inhibit this inflammatory response focused on nitric oxide (NO), an endogenous vasodilator, which is produced by nitric oxide synthase (NOS). Inducible NOS (iNOS) is expressed at pathologic levels in many cells, especially myocytes, and has many deleterious effects (11). High levels of iNOS are associated with left ventricular dysfunction (13). Early work with a nonisoform-specific NOS inhibitor, N-monomethyl-L-arginine (L-NMMA), had promising effects on the hemodynamics of patients with CS, including significantly increasing urine output and mean arterial blood pressure (14). A mortality benefit was seen in a small group of CS patients treated with this NOS inhibitor (15) and led to larger randomized studies. However, the Tilarginine Acetate Injection Randomized International Study in Unstable AMI Patients/Cardiogenic Shock (TRIUMPH) Trial, a phase III randomized trial to study the benefit of the NOS inhibitor L-NMMA in patients with cardiogenic shock complicating AMI, did not show any benefit (16).

Approach to the Patient With Cardiogenic Shock

The most important aspects of the initial care of the patient with cardiogenic shock are recognizing the condition early in its course and understanding its cause. Rapid assessment of the history, physical examination, and chest radiograph is mandatory, recognizing the signs of heart failure, pulmonary edema (sometimes with clear lung fields on examina-
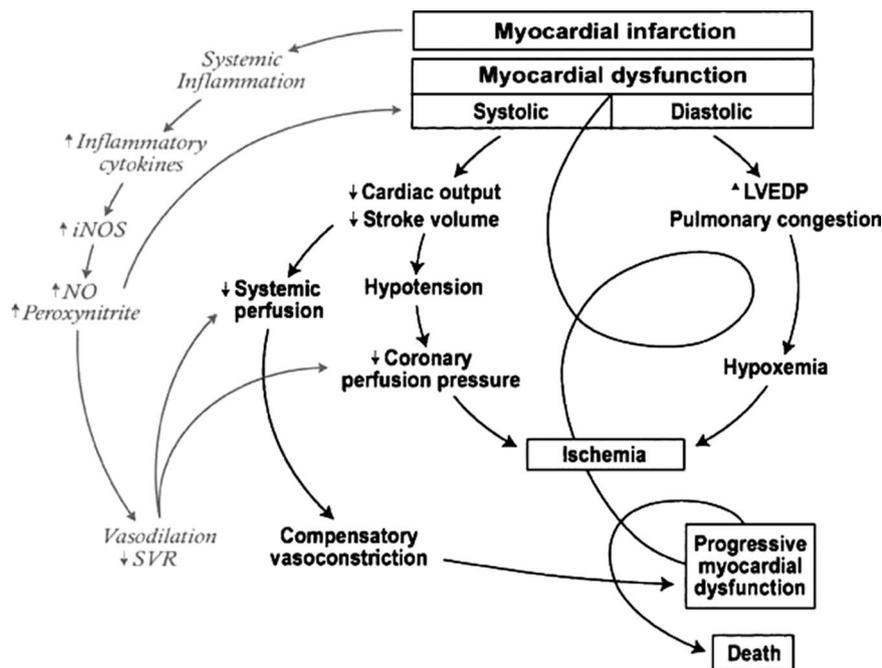
Figure 2. Classic shock paradigm, as illustrated by S. Hollenberg, is shown in black. The influence of the inflammatory response syndrome initiated by a large myocardial infarction is illustrated in gray. *LVEDP*, left ventricular end-diastolic pressure; *NO*, nitric oxide; *iNOS*, inducible NO synthase; *SVR*, systemic vascular resistance. Reproduced with permission from Hochman JS: Cardiogenic shock complicating acute myocardial infarction: Expanding the paradigm. *Circulation* 2003; 107:2998–3002.

Table 2. Hemodynamic profiles

Left ventricular shock	High PAOP, low CO, high SVR
Right ventricular shock	High RA, RA/PAOP >0.8, exaggerated RA y descent, RV square root sign
Mitral regurgitation	Large PAOP V wave
Ventricular septal defect	Large PAOP V wave, oxygen saturation step-up (>5%) from RA to RV
Pericardial tamponade	Equalization of diastolic pressures −20 mm Hg

PAOP, pulmonary artery occlusion pressure; CO, cardiac output; SVR, systemic vascular resistance; RA, right atrial; RV, right ventricular.

tion), and tissue hypoperfusion, manifesting as low blood pressure, rapid heart rate, agitation, confusion, oliguria, cyanosis, and cool and clammy skin. Appreciating the electrocardiographic signs of acute myocardial ischemia, myocardial infarction, new left bundle branch block, and arrhythmias is critical. Rapid echocardiographic assessment is key. The echo-Doppler study will assess regional and global left ventricular function, right ventricular size and function, the presence of mitral regurgitation and other valve abnormalities, pericardial effusion, and possible septal rupture. Echocardiographic assessment of left ventricular ejection fraction was found to be similar to ejection fraction as assessed by left ventriculography and can be used as the sole initial evaluation of systolic left ventricular function in patients with CS (17). Differential diagnoses to consider in pa-

tients with CS include hemorrhage, sepsis, aortic dissection, and massive pulmonary embolism.

Patients must be assessed regarding the need for sedation, intubation, and mechanical ventilation in order to correct hypoxemia and reduce the work of breathing (1, 18, 19). Initial medical therapy includes intravenous fluid challenge for patients with significant hypotension, if there is no evidence for pulmonary edema or significant elevation of jugular venous pressure. If CS is due to acute myocardial infarction or ischemia, emergency cardiac catheterization and revascularization need to take place in patients believed suitable for this approach (discussed subsequently).

The use of an intra-arterial catheter is helpful in managing patients in shock (20). Pulmonary artery catheterization

can assist in the precise measurement of volume status, left and right ventricular filling pressures, and cardiac output. It is also valuable in diagnosing right ventricular infarction and the mechanical complications of acute myocardial infarction (Table 2). Hemodynamic measurements can help guide fluid management and the use of inotropic agents and vasopressors. The American College of Cardiology/American Heart Association (ACC/AHA) guidelines list pulmonary artery catheterization as a class I recommendation in patients with hypotension not responding to fluid administration or when mechanical complications of myocardial infarction are suspected and echocardiography is not available. Pulmonary artery catheterization is a class IIa recommendation for patients in CS who have persistent signs of hypoperfusion and in patients receiving inotropic and vasopressor drugs (20, 21).

The goal of the initial medical therapy of CS is to maintain arterial pressure adequate for tissue perfusion. Initially, dopamine is the drug of choice because it acts as an inotrope as well as a vasopressor. Intravenous norepinephrine is a more potent vasoconstrictor, with somewhat less effect on heart rate, and should be used in patients with more severe hypotension. These drugs increase heart rate and systemic vascular resistance and thus increase myocardial oxygen demand, and they may aggravate ischemia and lead to cardiac arrhythmias. Doses should be adjusted to the lowest levels that improve tissue perfusion (1, 18, 20).

Dobutamine, an inotrope with arterial dilator properties, can be used in patients with less severe hypotension or can be combined with vasopressors to improve cardiac output (18). There also have been reports of the effective use of vasopressin in patients with CS (22). Intravenous diuretics are used in patients with pulmonary edema and elevated pulmonary artery occlusion pressure. Aspirin should be given to patients with acute myocardial infarction. Intravenous amiodarone can be given for patients with severe arrhythmia. The use of β-blockers and nitrates should be avoided in the acute phase (20).

Some patients will demonstrate signs of tissue hypoperfusion with systolic blood pressure >90 mm Hg. This has been termed *nonhypotensive cardiogenic shock* or *preshock*. In the

SHOCK Trial Registry, these patients demonstrated the hemodynamic profile of elevated pulmonary artery occlusion pressure with low cardiac index and high systemic vascular resistance. The hospital mortality rate in this group of patients was 43%, very high but lower than in patients diagnosed with full-blown cardiogenic shock. The mortality in patients with preshock compares with a mortality rate of 26% in patients with hypotension without signs of hypoperfusion. This preshock state needs to be recognized early so that appropriate, urgent diagnostic and therapeutic measures can be prescribed (23) (Fig. 3).

Intra-Aortic Balloon Counterpulsation (IABP)

IABP is very useful to support patients with CS. This device will increase coronary blood flow, decrease left ventricular afterload, and decrease left ventricular end-diastolic pressure without increasing oxygen demand (1, 19, 24). Cardiac output is increased only modestly, and this device does not provide total circulatory support (24).

The efficacy of IABP in acute myocardial infarction complicated by CS has not been evaluated in a randomized controlled trial. In nonrandomized trials, the use of IABP is associated with decreased mortality, but the use of this device is consistently associated with more frequent use of revascularization therapies and other aggressive supportive measures (25). Its use was not associated with improved survival in patients undergoing primary percutaneous coronary intervention (PCI) in the NRMI database.

Complications of IABP include bleeding, thrombocytopenia, hemolysis, leg ischemia, aortic dissection, femoral artery injury, thromboembolism, and sepsis. The complication rate has been reduced with percutaneous insertion and with smaller pumps (26). Complication rates have been reported at 10% to 30%, with major complication rates of 2.5% to
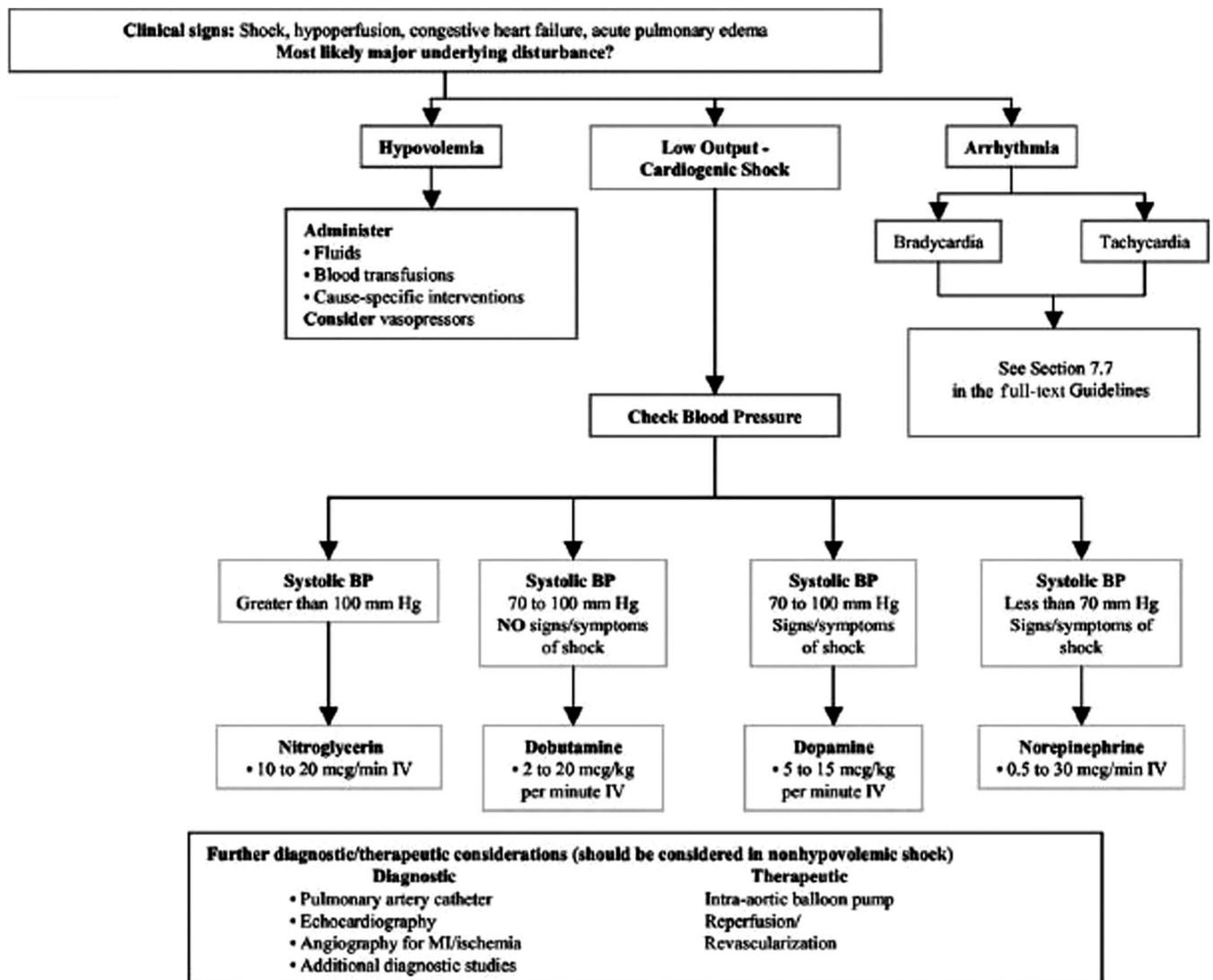

Figure 3. Emergency management of complicated ST-segment elevation myocardial infarction. American College of Cardiology/American Heart Association Practice Guidelines 2004. *BP*, blood pressure; *IV*, intravenous; *MI*, myocardial. Adapted with permission from Anbe DT, Armstrong PW, Bates ER, et al: ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of Patients With Acute Myocardial Infarction). ACC/AHA Practice Guidelines 2004. http://www.acc.org/clinical/guidelines/stemi/index.pdf. Accessed January 2007.

3.0% (25, 26). Patients usually must be anticoagulated during IABP use. Contraindications to the use of IABP include severe aortic insufficiency, severe peripheral vascular disease, and aortic aneurysm (18).

Current ACC/AHA guidelines list IABP as a class I recommendation for patients with low cardiac output states, hypotension, and CS not responding quickly to other measures (20). In the NRMI database, IABP was used in 39% of cases with CS, and the frequency of IABP use did not change over the 10-yr period 1995–2004 (4). In the Benchmark Counterpulsation Outcomes Registry, CS accounted for 27% of the use of IABP and was associated with a mortality rate of 38.7% (26). IABP is also recommended for use in patients with acute myocardial infarction complicated by severe mitral regurgitation or ventricular septal rupture, before urgent cardiac surgery, as well as in patients with right ventricular infarction not responding to fluid challenge and inotropic therapy.

In summary, the use of IABP in CS improves the short-term hemodynamic profile and may allow for improvement in function of ischemic myocardium. It likely does not improve outcomes unless it is combined with definitive coronary revascularization (25).

Emergency Revascularization

Many observations and nonrandomized studies have shown that the majority of patients with acute myocardial infarction who develop CS do so hours after onset of infarction, often after hospital presentation (2, 4, 5, 27). Shock that has a delayed onset results from infarction extension, reocclusion of a previously patent coronary artery, recurrent ischemia, or decompensation of left ventricular function in the noninfarcted zone because of metabolic derangements (1). The most successful strategy to successfully treat acute myocardial infarction is rapid restoration of flow in the infarct-related artery (28), and primary coronary angioplasty results in better outcomes than fibrinolytic therapy (29). Many reports have suggested that early mechanical revascularization with either PCI or coronary artery bypass graft surgery (CABG) is associated with survival benefit. The landmark SHOCK trial prospectively randomized 302 patients with CS due to acute myocardial infarction and left ventricular failure to emergency early revascularization (ERV) with PCI or CABG vs. initial medical stabilization (IMS) with drug therapy and IABP. PCI accounted for 64% of revascularization and CABG was performed in 36%. The 30-day mortality rate, the primary outcome measured, was lower in the early revascularization group (47% vs. 56%), which was not statistically significant. However, late mortality rates were significantly improved in patients who received ERV (30). At 6 months, 1 yr, and 6 yrs, a statistically significant absolute survival difference of 13% was seen in patients who received ERV (31, 32). At 6 yrs, overall survival was 32.8% in the ERV group and 19.6% in the IMS group. In patients who survived hospitalization, the 6-yr survival rate in patients with ERV was 62.4% vs. 44.4% in IMS patients. (Fig. 4) There was no significant difference in long-term survival between patients treated with PCI or CABG. Quality of life measures were also better in patients who had received ERV (33).

Unfortunately, invasive procedures continue to be underused in patients with CS (4, 5) In the NRMI, primary PCI use increased from 27.4% in 1995 to only 54.4% in 2004 (4 yrs after the SHOCK trial was published). CABG was used in only 3.2% of patients. This increased use of PCI for CS was likely translated into a mortality benefit (60.3% mortality in 1995, declining to 47.9% in 2004) (4). Patients who were transferred to hospitals with revascularization capability also had better outcome with ERV (34). This benefit from early mechanical revascularization was incorporated in the ACC/AHA practice guidelines. Both PCI and CABG are class I recommendations for patients <75 yrs old with STEMI or acute myocardial infarction with left bundle branch block, who develop shock within 36 hrs of onset of myocardial infarction (20, 35).

Patients >75 yrs old had worse outcomes with ERV in the SHOCK trial compared with IMS. However, the number of patients treated with ERV in this age group was relatively small (30–32). Analysis from the SHOCK registry showed that elderly patients were treated less aggressively, and their in-hospital mortality was higher compared with younger patients (76% vs. 55%). However, outcomes in elderly patients in the registry who were treated with ERV were better than in patients who were not revascularized (36). Clearly, patient selection plays a key role. Elderly patients with good functional status, shorter duration of shock,
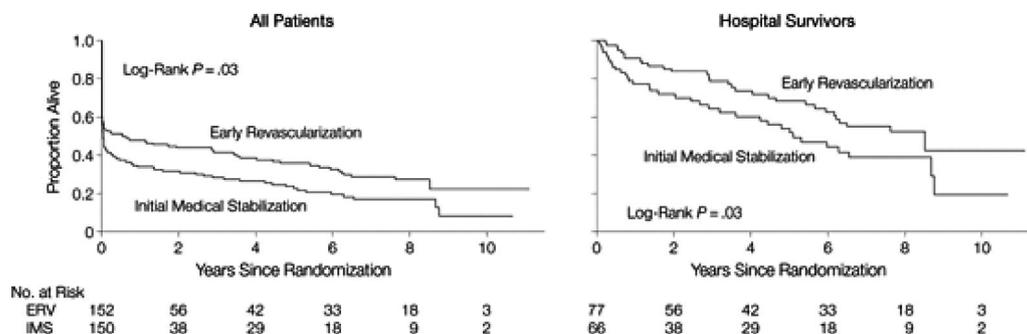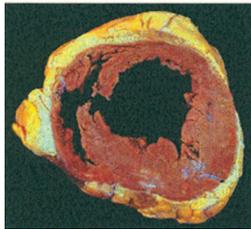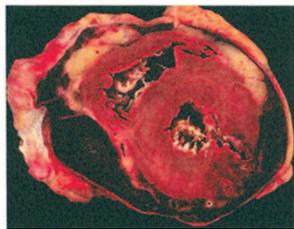

Figure 4. Among all patients, the survival rates in the early revascularization (*ERV*) and initial medical stabilization (*IMS*) groups, respectively, were 41.4% vs. 28.3% at 3 yrs and 32.8% vs. 19.6% at 6 yrs. With exclusion of eight patients with aortic dissection, tamponade, or severe mitral regurgitation identified shortly after randomization, the survival curves remained significantly different (*p* = .02), with a 14.0% absolute difference at 6 yrs. Among hospital survivors, the survival rates in the ERV and IMS groups, respectively, were 78.8% vs. 64.3% at 3 yrs and 62.4% vs. 44.4% at 6 yrs. Reproduced with permission from Hochman JS, Sleeper LA, Webb JG, et al: Early revascularization and long-term survival in cardiogenic shock complicating acute myocardial infarction. *JAMA* 2006: 295:2511–2515.
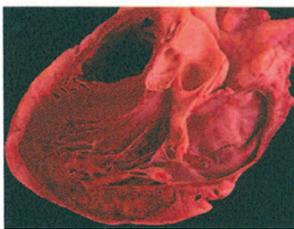
Ventricular Septal Rupture   **Free Wall Rupture**   **Mitral Regurgitation (Papillary muscle rupture)**

Figure 5. Mechanical complications of ST-elevation myocardial infarction. *Phy Exam*, physical examination; *PA*, pulmonary artery; *MI*, myocardial infarction; *JVD*, jugular venous distention; *EMD*, electromechanical dissociation; *Peric.*, pericardial; *Diast Press Equal.*, diastolic pressure equalization; *Regurg.*, regurgitation; *PCW*, pulmonary artery occlusion pressure. Reproduced with permission from Anbe DT, Armstrong PW, Bates ER, et al: ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of Patients With Acute Myocardial Infarction). ACC/AHA Practice Guidelines 2004. http://www.acc.org/clinical/guidelines/stemi/index.pdf. Accessed January 2007.

and absence of serious medical comorbidities should be carefully selected for aggressive therapies, including revascularization (21).

Fibrinolytic Therapy in Cardiogenic Shock

Urgent transfer to the cardiac catheterization laboratory for coronary angiography and emergency coronary intervention has largely supplanted thrombolytic therapy as first-line treatment for patients with acute myocardial infarction and CS. Fibrinolytics are not as effective as accomplishing reperfusion in STEMI with CS as in patients with STEMI without cardiogenic shock (1, 18). This is hypothesized to be due to decreased penetration of the coronary thrombus by fibrinolytics in hypotensive patients, a greater incidence of coronary artery reocclusion after thrombolysis, and longer times required to achieve coronary patency (1, 18, 19). In an overview of fibrinolytic trials, analysis of patients in CS showed nonsignificant reductions in mortality with fibrinolytic therapy. Subgroup analyses in individual trials have shown no effect on mortality (18). In the NRMI database, IABP combined with thrombolytic therapy was associated with a significantly lower mortality rate (49%) compared with thrombolytic therapy alone (67%) (25). In the SHOCK Trial Registry, the addition of IABP to thrombolytic therapy decreased mortality significantly from 63% with thrombolysis

alone to 47% with thrombolysis and IABP. Thrombolytic therapy was associated with a lower mortality than in patients who did not receive any reperfusion therapy (37). However, mortality in CS patients treated with fibrinolytic therapy combined with IABP was still higher than in patients who received revascularization with PCI or coronary bypass surgery.

The development of CS after fibrinolytic therapy is more likely to occur in older patients, patients with Killip class II–III heart failure on presentation, and patients with higher heart rate and lower blood pressure on admission (38). When thrombolytic therapy was given to patients with acute myocardial infarction before hospital arrival, during ambulance transport, the incidence of subsequent CS was lowered from 11.5% to 6.8% (39).

Current guidelines have relegated thrombolytic therapy for CS as a class I recommendation only in patients with STEMI who are unsuitable for invasive therapy with PCI or bypass surgery (20). In the NMRI observational database, the use of thrombolytic therapy for acute myocardial infarction and CS declined from 19.9% to 5.6% of cases in the years 1995–2004 (4). The strategy of administering fibrinolytics with or without IABP is recommended if patients present to a hospital that does not have a catheterization laboratory or when there will be unavoidable delays in transport to the catheterization laboratory (1).

Mechanical Complications of Acute Myocardial Infarction (Figure 5)

Right Ventricular Infarction. Right ventricular myocardial infarction (RVI) can accompany acute inferior wall myocardial infarction and lead to cardiogenic shock. It is estimated that 10% to 15% of inferior wall myocardial infarctions are complicated by hemodynamically significant RVI (1, 20). RVI accounted for 2.8% of cases of CS in the SHOCK Trial Registry (5). Acute right ventricular dysfunction and right ventricular failure lead to decreased left ventricular preload, decreased cardiac output, and cardiogenic shock. Right ventricular dilation and shift of the intraventricular septum toward the left ventricle can further compromise left ventricular function and worsen cardiogenic shock.

RVI results from occlusion of the right coronary artery proximal to the origin of the right ventricular branches. In the era before PCI for acute myocardial infarction, in-hospital mortality from RVI was around 7.1%, less than the mortality rate for anterior myocardial infarction but higher than that for inferior myocardial infarction without RVI (40). RVI was also an independent predictor of 6-month mortality and was associated with higher rates of CS and sustained ventricular arrhythmia.

The diagnosis of RVI should be strongly considered in patients who present with acute inferior wall myocardial infarction with hypotension, clear lung fields, and elevated jugular venous pressure or a positive Kussmaul's sign. Diagnostic findings on electrocardiogram include >1-mm ST-segment elevation in V_1 and in the right precordial lead V_4R, although these findings may be transient. Emergency transthoracic echocardiogram will show a dilated, hypocontractile right ventricle and may show bulging of the septum into the left ventricle. Right heart catheterization will demonstrate a mean right atrial pressure >10 mm Hg and right atrial pressure >80% of pulmonary artery occlusion pressure. Cardiac index will be low.

Initial therapy for hypotensive patients with RVI is a fluid challenge if jugular venous pressure is not elevated. Up to 1 L of intravenous saline should be infused, which may correct hypotension. Larger volumes may cause significant right ventricular dilation and impair left ventricular output. Inotropic medica-

tions and IABP are useful in patients who do not respond to fluid challenge (20). IABP helps to decrease wall stress and increase coronary perfusion pressure (1). Bradycardia and heart block should be corrected, and atrioventricular sequential pacing may be necessary to maintain atrioventricular synchrony and effective cardiac output.

Most patients with RVI will have spontaneous recovery of right ventricular function, but this may occur slowly and may be incomplete. Urgent revascularization with PCI is now the cornerstone of therapy. In a study of 53 patients with acute inferior wall myocardial infarction complicated by RVI, all 53 patients underwent emergency PCI (41). The right coronary artery was the culprit vessel in all cases. Seventy-seven percent of patients had successful intervention and reperfusion, and these patients demonstrated recovery of right ventricular function, decreased right heart pressures, and reduction in right ventricular size within 1 hr, with 95% recovery of normal right ventricular function in 3–5 days. In-hospital mortality was 2.4%. In the 12 patients with unsuccessful reperfusion, right ventricular dysfunction persisted at 24 hrs and only improved slowly during hospitalization. Ten of these 12 patients required support with inotropic drugs or IABP, and in-hospital mortality was 58.3%. Emergency revascularization efforts in these patients is now a class I recommendation in ACC/AHA guidelines for the treatment of acute myocardial infarction. If coronary bypass surgery is believed to be needed for multivessel disease and significant right ventricular dysfunction is present, then coronary bypass should be delayed for 4 wks, if possible, to allow for recovery of right ventricular function (20).

Acute Severe Mitral Regurgitation. Acute severe mitral regurgitation, due to infarction and rupture of the head of a papillary muscle, is an uncommon cause of cardiogenic shock. In the SHOCK Trial Registry, 6.9% of 1,190 patients with cardiogenic shock had acute severe mitral regurgitation (5, 42). Acute severe mitral regurgitation was more likely to complicate inferior and/or posterior myocardial infarction (87% of cases of acute mitral regurgitation) than anterior myocardial infarction (34%). Acute severe mitral regurgitation usually occurs within the first 24 hrs of acute myocardial infarction or may present at days 3–5. The diagnosis of acute severe mitral regurgi-

tation should be suspected in patients who present with acute pulmonary edema complicating acute myocardial infarction, especially inferior wall myocardial infarction. The murmur of mitral regurgitation may be loud but also may be relatively unimpressive due to high left atrial pressures and a lower left ventricular/left atrial systolic gradient. Diagnosis is made by urgent echocardiography.

Acute severe mitral regurgitation is associated with a high in-hospital mortality. In the SHOCK Trial Registry, patients who underwent urgent mitral valve surgery had a 40% mortality rate. Patients who did not receive surgery had a 71% mortality rate. The overall 55% hospital mortality rate was not different from the registry cohort with cardiogenic shock due to left ventricular failure (42).

In patients with acute severe mitral regurgitation, early diagnosis and aggressive support with inotropic drugs, IABP, and vasodilators (if blood pressure allows) are vital in appropriately selected patients. The ACC/AHA guidelines list urgent cardiac surgical repair as a class I recommendation (20).

Postinfarction Ventricular Septal Rupture. Rupture of the intraventricular septum (VSR) can complicate acute myocardial infarction and lead to CS. This often occurs in the first 24 hrs of infarction. This condition occurred in <1% of patients with STEMI in the GUSTO I study (20, 21) and accounted for 3.9% of the cases of CS in the SHOCK Trial Registry (15, 31). VSR may complicate either anterior or inferior wall STEMI. Patients will present with shock and pulmonary edema, and a loud holosystolic murmur is present on physical examination. Diagnosis is made by urgent Doppler echocardiography. A pattern of right ventricular volume overload is seen, with Doppler evidence of left-to-right shunting at ventricular level. The septal rupture may be visualized. Right heart catheterization will show higher oxygen saturations in the pulmonary artery than in the right atrium due to left-to-right shunting. However, when the diagnosis of VSR is made by echocardiography, performance of right heart catheterization should not delay surgical therapy.

Urgent surgical repair of VSR is a class I recommendation in the ACC/AHA guidelines. However, this condition is associated with a very high mortality rate with surgical or medical therapy. Waiting for several days before surgery in order to let healing occur is not recommended

because many patients will die during this waiting period. In the SHOCK Trial Registry, 31 of 55 patients with VSR underwent surgery, with a mortality of 81%. Only 4% of patients survived without surgery (43). In the GUSTO I trial, 30-day mortality was 73.8% (21). Another series of 76 patients with VSR who underwent surgery reported that 79% of patients presented with CS, and 30-day postoperative mortality was 49% for these patients (44).

Left Ventricular Free Wall Rupture and Cardiac Tamponade. Left ventricular free wall rupture is an uncommon, lethal complication of acute myocardial infarction. It is estimated to occur in 1% to 6% of patients with acute myocardial infarction (20), although the true incidence is difficult to ascertain as the majority of patients will die immediately after rupture from electromechanical dissociation. However, possibly 30% of free wall rupture may be spontaneously sealed off by elevated intrapericardial pressure from hemopericardium, and these patients may present with CS complicating acute myocardial infarction. The incidence of free wall rupture has decreased in the era of thrombolytic and primary angioplasty therapy for acute myocardial infarction. The diagnosis is made by emergency echocardiography, which shows a significant-sized pericardial effusion, either loculated or diffuse, and may show the area of rupture.

In the SHOCK Trial Registry, 1.4% of cases of CS were caused by free wall rupture and usually occurred in the first 24 hrs of infarction (2, 45). Twenty-one of 28 patients underwent surgery, with a 62% mortality rate. Six patients underwent pericardiocentesis only, and three survived. Another series listed operative mortality rates of 24% to 52% (46).

Ventricular Assist Devices (VADs)

VADs have been used in small series of highly selected patients with CS refractory to IABP and reperfusion strategies. The use of VADs should be considered in patients with very low cardiac output, <1.2 L/min/m^2 (19). Newer VADs can be inserted percutaneously. The Tandem-Heart percutaneous VAD, inserted in the catheterization laboratory, uses a catheter directed into the left atrium via a transseptal puncture, unloading the left atrium and left ventricle. Blood is then pumped into a 15- to 17-Fr catheter inserted in the femoral artery, producing

flows of 3.5–4.0 L/min. One report described 11 patients with acute myocardial infarction and CS refractory to inotropic and IABP therapy who received percutaneous VADs. These patients were supported for an average of 89 hrs, with mean cardiac index during VAD therapy of 2.6 L/min/m^2. It was concluded from this small series that percutaneous VADs could be effective as a bridge to implanted VADs or cardiac transplant therapy, with a low incidence of adverse effects. This device cannot be used in patients with right ventricular failure or severe peripheral vascular disease (24, 47).

Implanted VADs have also been used in patients with CS. In 49 patients treated with this device, 78% were successfully bridged to transplant. VADs were placed at an average of 6 days after myocardial infarction, and patients were supported for a mean time of 56 days until transplant. In-hospital mortality was only 33% in this group of patients (48). These patients had a 31% incidence in the need for dialysis and had a relatively high rate of infectious complications. Another series of 18 patients with CS received support with extracorporeal membrane oxygenation and/or VAD and cardiac transplant therapy. In these highly selected patients, hospital mortality was 33% and 5-yr survival was 30% (49).

Prevention of CS

Since most patients who develop CS after acute myocardial infarction do so at some time after presentation to hospital, there is an opportunity to prevent the occurrence of CS in individual patients, to reduce the overall incidence of CS, and to significantly improve outcomes in patients who develop this potentially lethal complication. The first step in prevention of CS involves educating the public, encouraging patients to present to hospital very early after the development of significant chest pain or other symptoms of acute myocardial infarction. Patients should be directed to call the emergency ambulance system, so that transport to an emergency department can occur quickly. In addition, hospital transport systems need to be developed to allow patients with STEMI to be transported directly to hospitals with PCI and coronary surgery capabilities, avoiding delays inherent when acute myocardial infarction patients are admitted to hospitals without these facilities and then emergently transferred to tertiary centers. If patients receive thrombolytic therapy for acute myocardial infarction in hospitals without revascularization capabilities, signs of failed thrombolysis should be recognized early, and these patients should be transferred quickly to tertiary centers with revascularization capabilities.

In patients hospitalized with acute myocardial infarction, prompt recognition of the preshock state or the early signs of CS is vital. Once the diagnosis of CS is made, rapid evaluation and institution of supportive medical therapy, insertion of the IABP, and emergency revascularization need to be performed. Admission of patients to hospitals with revascularization capabilities, or even directly to the catheterization laboratory, has led to the greater utilization of these lifesaving therapies with improved mortality rates in several nonrandomized studies (30, 31, 50). It is unlikely that further large randomized controlled trials in patients with CS will be carried out. It is now necessary to improve systems of care in order to translate the benefits of early revascularization to wide implementation.

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