A 58-year-old man has chest pain at 9:30 a.m.; 3 hours later, he calls for an ambulance. Paramedics arrive, provide standard treatment, and transport him to the nearest emergency department. On his arrival at a small hospital at 1 p.m., the findings are diagnostic of a myocardial infarction with ST-segment elevation. The emergency department physician recommends immediate transfer to a hospital 1 hour away for primary percutaneous coronary intervention (PCI).

THE CLINICAL PROBLEM

Coronary heart disease is the leading cause of death in the United States, with myocardial infarction a common manifestation of this disease. In 2006, approximately 1.2 million Americans sustained a myocardial infarction. Of these, one quarter to one third had a myocardial infarction with ST-segment elevation.

Of all patients having a myocardial infarction, 25 to 35% will die before receiving medical attention, most often from ventricular fibrillation. For those who reach a medical facility, the prognosis is considerably better and has improved over the years: in-hospital mortality rates fell from 11.2% in 1990 to 9.4% in 1999. Most of the decline is due to decreasing mortality rates among patients with myocardial infarction with ST-segment elevation, as a consequence of improvements in initial therapy, including fibrinolysis and PCI. In an analysis by the National Registry of Myocardial Infarction, the rate of in-hospital mortality was 5.7% among those receiving reperfusion therapy, as compared with 14.8% among those who were eligible for but did not receive such therapy.

PATHOPHYSIOLOGY AND EFFECT OF THERAPY

The pathogenesis of coronary atherosclerosis is multifactorial. Broadly, endothelial injury and dysfunction result in the adhesion and transmigration of leukocytes from the circulation into the arterial intima as well as the migration of smooth-muscle cells from the media into the intima, thus initiating the formation of an atheroma or atherosclerotic plaque.

Atherosclerotic plaques cause progressive narrowing of the coronary arteries and eventually can cause a coronary occlusion. However, myocardial infarctions with ST-segment elevation are more typically caused by the sudden thrombotic occlusion of a coronary artery that previously was not severely narrowed. When such an occlusion occurs, the abrupt rupture, erosion, or fissuring of a previously minimally...
obstructive plaque creates a potent stimulus for platelet aggregation and thrombus formation.\textsuperscript{6,8} If the stimulus for a thrombosis is robust, total arterial occlusion can result (Fig. 1).

On occlusion of the infarct-related artery, all the myocardium that is supplied by the artery becomes ischemic, resulting in chest pain and electrocardiographic evidence of transmural (full-thickness) ischemia (ST-segment elevation) in the leads reflective of that region of the heart. Subsequently, necrosis begins within minutes and progresses during several hours in a “wavefront” fashion from the endocardial surface to the epicardial surface. If ischemia persists for several hours, transmural infarction results.\textsuperscript{9} In contrast, if blood flow is restored during the period of progressive necrosis, the ischemic myocardium is salvaged and the size of the infarct is reduced. Since morbidity and mortality from a myocardial infarction correlate with the size of the infarct, prompt restoration of blood flow would also be expected to improve left ventricular function and survival.\textsuperscript{10}

Primary PCI consists of urgent balloon angioplasty (with or without stenting), without the pre-
vious administration of fibrinolytic therapy or platelet glycoprotein IIb/IIIa inhibitors, to open the infarct-related artery during an acute myocardial infarction with ST-segment elevation. After the identification on coronary angiography of the site of recent thrombotic occlusion, a metal wire is advanced past the thrombus over which a balloon catheter (with or without a stent) is positioned at the site of the occlusion and inflated, thereby mechanically restoring antegrade flow (Fig. 1). Primary PCI restores angiographically normal flow in the previously occluded artery in more than 90% of patients,"11,12 whereas fibrinolytic therapy does so in only 50 to 60% of such patients.

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**Clinical Evidence**

In comparison with conservative management (medical treatment without reperfusion therapy), fibrinolytic therapy leads to improved left ventricular systolic function and survival in patients with myocardial infarction associated with either ST-segment elevation or left bundle-branch block. In a pooled analysis of nine large trials, the rate of death at 35 days was 9.6% among patients receiving fibrinolytic therapy, as compared with 11.5% among control subjects.13

However, fibrinolytic therapy has several limitations. First, among those presenting with myocardial infarction with ST-segment elevation, some patients (27% in one report)14 have a contraindication to fibrinolysis. Second, in approximately 15% of patients given fibrinolytic therapy, thrombolysis does not occur.15,16 Third, about a quarter of those receiving fibrinolytic therapy have reocclusion of the infarct-related artery within 3 months after the myocardial infarction, with a resultant reinfarction.17 These limitations are minimized with the use of primary PCI.

In a meta-analysis of 23 randomized, controlled comparisons of primary PCI (involving 3872 patients) and fibrinolytic therapy (3867 patients), the rate of death at 4 to 6 weeks after treatment was significantly lower among those who underwent primary PCI (7% vs. 9%).18 Rates of nonfatal reinfarction and stroke were also significantly reduced. Most of these trials were performed in high-volume interventional centers by experienced operators with minimal delay after the patient’s arrival. If primary PCI is performed at low-volume venues by less-experienced operators with longer delays between arrival and treatment, such superior outcomes may not be seen.19

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**Clinical Use**

Reperfusion therapy (mechanical or pharmacologic) is indicated for patients with chest pain consistent with a myocardial infarction with a duration of 12 hours or less in association with ST-segment elevation greater than 0.1 mV in two or more contiguous electrocardiographic leads or a new (or presumed new) left bundle-branch block. Candidates for reperfusion therapy should be identified by an emergency department physician; the process can be initiated by emergency-medical-services personnel to minimize delay.

Primary PCI is preferred if a skilled interventional cardiologist and catheterization laboratory with surgical backup are available and if the procedure can be performed within 90 minutes after initial medical contact with the patient.20 For patients initially presenting to a hospital that does not have interventional capabilities, rapid transfer to such a facility is recommended.

Primary PCI is preferable for certain patients even if the interval between the first medical contact and the procedure (the “door-to-balloon” interval) exceeds 90 minutes. Such patients include those with a contraindication to fibrinolytic therapy20; those with a high risk of bleeding with fibrinolytic therapy, including patients 75 years of age or older (for whom the risk of intracranial hemorrhage with fibrinolytic therapy is increased)21; those with clinical findings (i.e., tachycardia, hypotension, or pulmonary congestion) suggesting a high risk of an infarct-related complicated medical course or death22; and those with cardiogenic shock.23

Fibrinolytic therapy is preferred for patients whose first medical contact occurs less than 3 hours after the onset of symptoms but for whom PCI is not immediately available, those who seek medical attention less than 1 hour after the onset of symptoms (in whom the therapy may abort the infarction),24 and those with a history of anaphylaxis due to radiographic contrast material.

As compared with patients who undergo balloon angioplasty, among those who undergo bare-metal stenting of the infarct-related artery, the rates of restenosis and the frequencies of recurrent angina and repeated revascularization pro-
As a result, stenting of the infarct-related artery is usually preferred. However, balloon angioplasty is preferred for patients in whom clopidogrel (Plavix, Bristol-Myers Squibb) is contraindicated (because of thrombocytopenia or the presence of left main or extensive multivessel coronary artery disease, who may require bypass surgery within days after successful primary PCI). Balloon angioplasty is also preferred when the size of the infarct-related artery is insufficient for the placement of a stent.

As compared with bare-metal stents, drug-eluting stents appear to reduce further the rates of restenosis within 12 months after primary PCI. If drug-eluting stents are used in this setting, it is imperative that dual antiplatelet therapy (aspirin and clopidogrel) be given for at least 12 months; otherwise, subacute thrombosis may occur. There are no good data on longer-term outcomes.

In addition to oral aspirin and intravenous unfractionated heparin, patients with a myocardial infarction with ST-segment elevation should receive oral clopidogrel after it has been determined that emergency bypass surgery is not required. Beta-adrenergic blockers should be initiated, provided that the patient has no contraindications and is stable hemodynamically. Platelet glycoprotein IIb/IIIa inhibitors or antibodies are often given to patients undergoing primary PCI. Treatment with a high dose of a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (statin) is recommended for all patients with acute myocardial infarction.

The monetary costs of fibrinolytic therapy and primary PCI are similar. Primary PCI is an expensive procedure, with professional fees ranging from approximately $4,000 to $5,000 and hospital charges ranging from approximately $20,000 to $25,000 in the United States. However, patients receiving fibrinolytic therapy have higher subsequent costs, because of higher rates of in-hospital morbidity and mortality and longer hospital stays.

In a report on 4366 primary PCIs performed at 40 sites in the United States between 1990 and 1994, the success rate (the proportion of patients with a patent infarct-related artery at the end of the procedure) was 91.5%. However, although antegrade flow in the epicardial coronary artery may appear normal after most of these procedures, perfusion of the tissue at the microvascular level is restored to normal in only a minority of patients. In some patients, embolization of microscopic debris with balloon inflation or stent deployment compromises tissue perfusion. In such patients, the magnitude of the ST-segment elevation does not diminish, even though antegrade flow in the epicardial artery is restored. Among these patients, survival is correspondingly reduced.

In about 15% of patients undergoing primary PCI, initial angiography shows a patent infarct-related artery. In these patients, it is presumed that spontaneous fibrinolysis occurred before angiography. In comparison with patients who have diminished or no antegrade flow, these patients are less likely to have hemodynamic instability or left ventricular systolic dysfunction with conges-tive heart failure or to die as a result of myocardial infarction.

**ADVERSE EFFECTS**

Complications occasionally occur as a result of primary PCI. Local vascular complications include bleeding, hematomas, pseudoaneurysms, and arteriovenous fistulae at the access site. These events occur in 2 to 3% of patients, about two thirds of whom require transfusion. Major bleeding (including bleeding at the access site) occurs in about 7% of patients undergoing the procedure. The incidence of bleeding has declined, probably because lower doses of heparin and smaller catheters are used now than in the past, as well as because of increasing experience among interventional cardiologists and ancillary personnel. The incidence of intracranial hemorrhage is lower with primary PCI than with fibrinolytic therapy (0.05% vs. 1%, P<0.001).

Severe nephropathy after PCI (caused, at least in part, by radiographic contrast material) occurs in up to 2% of patients. It occurs most often among those with cardiogenic shock or underlying renal insufficiency and those of advanced age. Anaphylactic reactions to radiographic contrast material are very rare.

Ventricular tachycardia or fibrillation is reported in 4.3% of patients undergoing primary PCI. Although these patients remain in the hospital longer than those who do not have ventricular tachyarrhythmias, the long-term prognosis for those with or without ventricular tachyarrhythmias is similar.
In patients undergoing elective balloon angioplasty, the abrupt closing of the infarct-related artery (during or within hours after the procedure) occurs in up to 3% of patients; it may occur even more frequently among those undergoing primary balloon angioplasty. Stenting of the infarct-related artery decreases the incidence of abrupt closing to about 1%, thereby diminishing the need for urgent bypass surgery and (in the opinion of some investigators) obviating the need for on-site surgical capability. Therefore, stenting is the preferred primary intervention if the coronary anatomy is suitable. As noted, stents also reduce the risk of restenosis, an effect shown to be even more marked with the use of drug-eluting stents. In most trials of stenting, stent thrombosis has occurred in less than 1.5% of patients receiving either a bare-metal stent or a drug-eluting stent within the first year.

Serious cardiovascular events occur in a small percentage of patients undergoing primary PCI. In the report of 4366 procedures described above, the rates of emergency cardiac surgery and in-hospital death were 4.3% and 2.5%, respectively. Such events occur much more frequently among patients in whom perfusion is not restored.

At centers where primary PCIs are performed, there is a direct relationship between procedural volume and outcomes. Among patients undergoing elective PCI at centers in which 200 or more such procedures are performed each year, the incidence of urgent bypass surgery and death is lower than among those whose procedure is performed at a center where fewer than 200 PCIs per year are performed.

**Areas of Uncertainty**

Although the use of primary PCI is widespread, some issues are unresolved. First, the administration of a fibrinolytic agent or platelet glycoprotein IIb/IIIa inhibitor or both before PCI — called a facilitated intervention — is based on the hypothesis that immediate pharmacologic therapy followed by prompt PCI will cause a faster and more complete restoration of flow in the infarct-related artery than PCI alone. A meta-analysis of trials comparing these two procedures concluded that patients with myocardial infarction with ST-segment elevation who received facilitated PCI were more likely to have a patent infarct-related artery at the time of initial coronary angiography than those receiving PCI alone. Despite this finding, patients receiving facilitated intervention had increased rates of nonfatal reinfarction, urgent target-vessel revascularization, stroke, and death, as compared with patients undergoing only PCI. The increased rate of adverse events with facilitated intervention was seen predominantly among patients receiving fibrinolytic therapy. At present, it is unknown whether facilitated PCI with the use of only platelet glycoprotein IIb/IIIa inhibitors is superior to primary PCI alone.

Second, the choice between the use of fibrinolytic therapy and the transfer of the patient to another facility for primary PCI depends on the patient’s clinical characteristics and the rapidity and efficiency of the transfer. Although several randomized studies comparing on-site fibrinolytic therapy with transfer for primary PCI showed better short-term outcomes in patients transferred to another hospital for PCI, these studies were conducted in highly efficient transfer networks. In the United States, such transfers often are inefficient, and unacceptable treatment delays occur. Since most Americans live near a facility proficient in the performance of primary PCI, they could receive this treatment if an organized and efficient system of triage and transfer were available.

Third, some patients with myocardial infarction with ST-segment elevation who undergo primary PCI are found to have severe multivessel coronary artery disease. After the urgent restoration of antegrade flow in the infarct-related artery, the management — medical, percutaneous, or surgical — of the care of these patients, including its timing, is uncertain.

**Guidelines**

According to the guidelines of the American College of Cardiology and American Heart Association, primary PCI is a class I indication in patients with myocardial infarction with ST-segment elevation who can undergo the procedure within 12 hours after the onset of symptoms, provided the procedure is performed in a timely manner (balloon inflation or stent placement or both within 90 minutes after the first medical contact) by experienced operators (those who perform more than 75 interventional procedures per year) in a facility in which more than 200 coronary interventional procedures are performed each year (at
least 36 of them being primary in nature) and which has a cardiac surgical capability, in case such surgery is required. Similarly, the European Society of Cardiology considers primary PCI the preferred reperfusion strategy for patients with myocardial infarction with ST-segment elevation (as a class I indication).

The patient in the vignette has an anterior myocardial infarction with ST-segment elevation. He was initially taken to a small community hospital that lacked interventional capabilities. Since he has no contraindication to fibrinolytic therapy, he could receive this therapy there or, alternatively, he could be transferred urgently for primary PCI. Because his symptoms have been present for more than 3 hours and he has high-risk features (i.e., tachycardia, rales, and anterior location of the infarction), we recommend his transfer for PCI, provided that the procedure can be performed in a timely fashion by an experienced operator in a high-volume catheterization laboratory. On the basis of the data available on facilitated PCI, we do not recommend administration of a fibrinolytic agent or glycoprotein IIb/IIIa inhibitor before the transfer.

No potential conflict of interest relevant to this article was reported.

**Recommendations**

The patient in the vignette has an anterior myocardial infarction with ST-segment elevation. He was initially taken to a small community hospital that lacked interventional capabilities. Since he has no contraindication to fibrinolytic therapy, he could receive this therapy there or, alternatively, he could be transferred urgently for primary PCI. Because his symptoms have been present for more than 3 hours and he has high-risk features (i.e., tachycardia, rales, and anterior location of the infarction), we recommend his transfer for PCI, provided that the procedure can be performed in a timely fashion by an experienced operator in a high-volume catheterization laboratory. On the basis of the data available on facilitated PCI, we do not recommend administration of a fibrinolytic agent or glycoprotein IIb/IIIa inhibitor before the transfer.

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