Primary Coronary Intervention for Acute Myocardial Infarction

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Despite dramatic improvements in the treatment of acute ST-segment elevation myocardial infarction (STEMI) during the past decade, approximately 1 in 10 patients still die of this disease. Three critical factors in the immediate management of patients with STEMI result in reduced mortality: prompt diagnosis, immediate treatment with aspirin, and rapid reestablishment of blood flow in the infarct-related artery. The latter aim may be achieved either pharmacologically, with administration of thrombolytic therapy, or mechanically, with percutaneous coronary intervention (PCI). Primary PCI refers to the strategy of emergent angiography followed by mechanical recanalization of the occluded artery with a balloon catheter, without prior administration of thrombolytic therapy. In its early years, the data regarding primary PCI were limited to observational studies from specialized centers. With the publication of randomized controlled trials (RCTs) comparing PCI with thrombolytic therapy, however, primary PCI has become accepted as part of the standard armamentarium in the treatment of STEMI. The most recent RCTs on this topic have begun to examine the role of primary PCI in specific subsets of patients with STEMI and the role of adjunctive therapies in patients undergoing primary PCI.

See also Patient Page.

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Pathophysiology of STEMI

ST-segment elevation myocardial infarction is the clinical correlate of full-thickness ischemia and infarction of myocardium and is the result of sudden thrombotic occlusion of its blood supply. The transition from a diseased but patent coronary artery to one that is occluded by thrombus begins with either rupture or erosion of a coronary atherosclerotic plaque. The cellular and molecular events within the plaque that lead to its disruption remain incompletely understood but are clearly unrelated to the severity of the preexisting luminal stenosis. In fact, the majority of STEMI evolve from mild to moderate stenoses. Plaque disruption results in exudation of its lipid-rich core into the lumen and adherence of platelets to the arterial subendothelium. The platelets become activated and develop high affinity for fibrinogen, causing their cross-linking and degradation. Simultaneously, the release of tissue factor from the lipid-rich core results in activation of the coagulation cascade and generation of thrombin. The result is a luminal thrombus consisting of aggregated platelets, cross-linked fibrin strands, and entrapped red blood cells (FIGURE 1). The enlarging thrombus can interrupt blood flow and lead to an imbalance between oxygen supply and demand that, if severe and persistent, causes transmural infarction of the myocardium.

Strengths of Thrombolytic Therapy and Primary PCI

Early studies of thrombolytic therapy, involving tens of thousands of patients with STEMI, consistently and unequivocally demonstrated that recipients of thrombolytic therapy had better left ventricular function and decreased mortality compared with patients receiving placebo. Despite its life-saving properties, ease of administration, and widespread availability, thrombolytic therapy has well-documented limitations compared with primary PCI: (1) Most patients who present with STEMI do not in practice receive thrombolytic therapy. Some of these patients are eligible for thrombolytic therapy, although many meet relative or absolute contraindications. Patients not treated with thrombolytic therapy are disproportionately women, elderly persons, and those with a history of prior MI, multivessel coronary disease, or depressed left ventricular systolic function. (2) Intracranial hemorrhage resulting in death or disabling stroke occurs in 0.6% to 1.4% of patients receiving thrombolytic therapy, disproportionately affecting elderly individuals. (3) Blood flow in the infarct-related artery is restored in only 85% of patients receiving thrombolytic therapy, only half of whom regain normal blood flow (the lack of normal blood flow in the infarct-related artery results in reduced myocardial salvage and worse short-term and long-term survival [FIGURE 2]). (4) 30% of patients receiving thrombolytic therapy receive thrombolytic therapy reoc-
clude the infarct-related artery and consequently experience reinfarction within the subsequent 3 months. In addition to avoiding these limitations of thrombolytic therapy, primary PCI results in better clinical outcomes compared with thrombolysis and provides immediate assessment of coronary anatomy and hemodynamic data, which facilitate patient care and allow earlier hospital discharge. Patients who should not undergo reperfusion therapy can be quickly identified; this group includes patients with spontaneous reperfusion of the infarct-related coronary artery and minimal residual stenosis, and those with coronary vasospasm, myocarditis, and aortic dissection involving the infarct-related artery.

**Figure 1.** Coronary Artery Erosion and Thrombosis

A. Platelet-rich occlusive thrombus on a noncritical (<75% luminal stenosis) plaque in the mid-right coronary artery following thrombolytic therapy. The thrombus is pale tan because it consists mainly of platelets and fibrin. Focal dark areas represent entrapped red blood cells; gross specimen. B. Low-power photomicrograph of a partially occlusive thrombus on an eroded, noncritical (<75% luminal stenosis) right coronary artery atherosclerotic plaque; hematoxylin-eosin stain; magnification 5×. Panels A and B printed with permission from William D. Edwards, MD, Mayo Clinic. C. Shallow erosion with thrombus on a right coronary artery fibrocalcific plaque (endarterectomy specimen); hematoxylin-eosin stain; magnification 62×. Printed with permission from Phillip J. Harrity, MD, William Beaumont Hospital.

**Figure 2.** Coronary Angiography of Infarct-Related Arteries

Patient 1, Angiograms from the same patient showing a totally occluded mid-left anterior descending coronary artery before and after primary angioplasty. Patient 2, Angiogram from a different patient showing a recanalized left circumflex coronary artery after administration of thrombolytic therapy. A significant residual filling defect, consistent with thrombus, is visible in the artery (arrowheads).
the coronary ostia. Patients ineligible for thrombosis have been shown to benefit from primary PCI.14

Primary PCI does have limitations. There is a 7% risk of major bleeding, usually from the femoral artery access site,12 and vascular complications requiring surgical repair occur in 0.4% to 2.0% of patients.13,16 There is a 0.5% to 1.3% risk of acute renal failure. The likelihood of this complication is associated with the patient’s age, volume status, preexisting renal function, and the volume of contrast material used during the procedure.15,17 Finally, the procedure is either unavailable or cannot be performed quickly in most centers.

**Randomized Trials Comparing Primary PCI and Thrombolytic Therapy**

To date, 23 published RCTs have compared primary PCI with thrombolytic therapy. These trials differ in many respects, including patient sample size, type of thrombolytic therapy, and whether stents, with or without platelet glycoprotein (GP) IIb/IIIa inhibitors, were used. In a recent meta-analysis of these trials, short-term and long-term outcomes of 3872 patients randomized to primary PCI were compared with outcomes for 3867 patients randomized to thrombolytic therapy.12 Subgroup analyses examined the effects of different thrombolytic therapies (fibrin-specific vs streptokinase), of cardiogenic shock, and of emergent transfer to another hospital for primary PCI. Primary PCI was found to be more effective than thrombolytic therapy in reducing short-term and long-term major adverse clinical events, including death. It was also associated with better clinical outcomes regardless of the type of thrombolytic agent used or whether the patient required emergent transfer to another hospital for primary PCI.

**Technical Aspects of Primary PCI**

Primary PCI is technically similar to elective PCI; however, it involves the added complexity of an actively symptomatic and sometimes hemodynamically unstable patient. Because primary PCI is often performed outside normal working hours, the cardiac catheterization laboratory must have a protocol in place for prompt activation of the team. The goals of the physician are to stabilize the patient and open the occluded coronary artery. Vascular access is obtained via the femoral artery but the brachial or radial arteries can also be used. All patients are anti-coagulated with heparin during the procedure. The patient is admitted to a monitored setting after the procedure and is usually discharged within several days.

**Primary PCI in Specific Patient Populations**

The most recent RCTs in this area have sought to define the role of primary PCI in specific subsets of patients with STEMI and to examine the role of adjunctive therapies in patients undergoing primary PCI.

An important subset of patients with STEMI are those in cardiogenic shock, who have mortality rates of more than 80% without reperfusion therapy. Early revascularization, percutaneous or surgical, is associated with improved 1-year survival when compared with delayed or no revascularization in all patients except those older than 75 years.18 Because of these proven benefits, the American College of Cardiology/American Heart Association (ACC/AHA) recommends that all patients in cardiogenic shock who are younger than 75 years undergo revascularization within 36 hours of STEMI.19

To our knowledge, there are no large RCTs comparing primary PCI with thrombolytic therapy in the elderly population. Although data from large observational studies have shown lower mortality rates with primary PCI compared with thrombolytic therapy,20,21 these results are confounded by selection bias, with healthier patients being disproportionately referred for invasive procedures. A large RCT of elderly patients with STEMI randomized to primary PCI vs thrombolytic therapy is currently being conducted and will provide additional data regarding optimal reperfusion therapy in this growing population.

In the past, primary PCI was performed only in hospitals with surgical backup because major dissection or abrupt closure of the coronary artery were feared complications of PCI that could result in devastating MIs if not managed with immediate bypass surgery. However, the incidence of emergency bypass surgery with primary PCI is now reported to be less than 0.5% in part because coronary artery dissection and closure can be effectively managed with stents.22,23 A recent RCT examined whether primary PCI could be performed safely at community hospitals with primary PCI programs in compliance with the standards set by the ACC/AHA but without access to on-site cardiac surgery.16 In this trial, short-term and long-term clinical outcomes were better in patients with STEMI treated with primary PCI compared with those receiving on-site thrombolytic therapy. The ACC/AHA guidelines require that the hospital perform 200 or more percutaneous interventions per year, that each physician perform 75 or more percutaneous interventions per year, and that door-to-balloon time be less than 120 minutes.19,24

The effectiveness of thrombolytic therapy decreases with increasing age of the occlusive coronary thrombus.25 In contrast, clinical outcomes after primary PCI appear to be less dependent on the time to treatment. Although primary PCI within 2 hours of presentation is associated with lower mortality compared with PCI performed 2 or more hours after presentation, both short-term and long-term mortality are independent of time to reperfusion in patients undergoing primary PCI after more than 2 hours.26,27 This observation led to the evaluation of safety and effectiveness of immediate transfer of patients with STEMI to hospitals capable of performing primary PCI compared with on-site administration of thrombolytics. A meta-analysis of 6 RCTs (3750 patients, with 1887 randomized to emergent transfer for primary PCI up to 12 hours after onset of symptoms, and 1863 to on-site thrombolytic therapy) showed that emergent transfer is technically fea-
sible and is associated with improved clinical outcomes.28

Adjunctive Therapies in Patients Undergoing Primary PCI
Randomized controlled trials have compared primary PCI alone with primary PCI with insertion of a stent in the infarct-related artery. Stent placement did not affect mortality but resulted in reduced restenosis and reocclusion rates during the ensuing 6 months.29,30 In another study, the platelet GP IIb/IIIa inhibitor abciximab was evaluated to determine whether its administration at the time of primary PCI improved clinical outcomes.31 Abciximab administration reduced subacute thrombosis, recurrent ischemia, and repeat revascularization procedures during the first month after primary PCI or stenting. However, it did not improve blood flow rates or reduce the rates of angiographic restenosis, late reocclusion of the infarct-related artery, or clinical outcomes at 6 months. Whether earlier administration of platelet GP IIb/IIIa inhibition leads to improved blood flow in the infarct-related artery at baseline is not known.

Facilitated PCI refers to treatment with low-dose thrombolytics, platelet GP IIb/IIIa inhibitors, or both prior to PCI. The rationale for this approach is to provide the earliest possible pharmacologic reperfusion before attempting definitive mechanical revascularization of the infarct-related artery. Four RCTs have compared facilitated PCI with primary PCI.12-15 These studies have shown no benefit and possible harm associated with the facilitated approach, primarily because of increased bleeding complications. Additional RCTs enrolling larger numbers of patients are ongoing and will evaluate the effectiveness and safety of this approach using various doses and combinations of thrombolytic therapy and platelet GP IIb/IIIa inhibition.

Conclusion
The primary treatment objective in patients with STEMI is to reestablish coronary blood flow in the infarct-related artery as quickly as possible. The available data suggest that when available and performed in experienced centers primary PCI is the method of choice to establish reperfusion.

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REFERENCES

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