Primary Angioplasty for Acute Myocardial Infarction — Is It Worth the Wait?

Alice K. Jacobs, M.D.

Nearly two decades after clinical trials established that fibrinolytic therapy for acute myocardial infarction preserves left ventricular function and reduces mortality, there is evidence that mechanical reperfusion therapy is superior in reducing the rates of death, reinfarction, intracranial bleeding, reocclusion of the infarct-related artery, and recurrent ischemia. Initially introduced as an alternative to fibrinolytic therapy (to circumvent contraindications to its use and the risk of intracranial bleeding), primary percutaneous coronary intervention is now increasingly recognized as the reperfusion therapy of choice. The ability to restore robust coronary flow promptly in more than 90 percent of patients and the nearly linear relation between patency of the infarct-related artery at 90 minutes after the initiation of reperfusion therapy and in-hospital mortality rates lend credibility to the momentum behind primary percutaneous coronary intervention for patients with myocardial infarction associated with ST-segment elevation. In fact, a quantitative review of 23 randomized trials in which primary percutaneous coronary intervention was compared with fibrinolytic therapy revealed that the former was superior in reducing the short-term rates of death (7 percent, vs. 9 percent with fibrinolytic therapy; P<0.001), nonfatal reinfarction (3 percent vs. 7 percent; P<0.001), stroke (1 percent vs. 2 percent; P=0.0004), and the combined end point of death, nonfatal reinfarction, and stroke (8 percent vs. 14 percent; P<0.001).

Nevertheless, fibrinolytic therapy remains the mainstay of reperfusion treatment around the globe because it is more widely available than coronary angioplasty. Even in the United States, the majority of hospitals do not have angioplasty capabilities, and in many that do, nearly 50 percent of the patients with myocardial infarction associated with ST-segment elevation are treated with fibrinolytic agents. The widespread unavailability of primary percutaneous coronary intervention appears to negate the superiority of this strategy as compared with fibrinolysis. It also raises the obvious question of whether primary percutaneous coronary intervention performed after a patient is transferred to a facility where it is available will still be superior to fibrinolytic therapy administered at the referral hospital. Given the inherent delay before transfer and the risks associated with transportation during acute myocardial infarction, the answer is not intuitive.

Five randomized trials have attempted to address this question. The Danish Multicenter Randomized Study on Fibrinolytic Therapy versus Acute Coronary Angioplasty in Acute Myocardial Infarction (DANAMI-2), reported in this issue of the Journal, is noteworthy for its randomized design, its practical approach to a critical question, and its careful consideration of the time between the onset of symptoms (in addition to arrival at the hospital) and reperfusion in its comparisons of strategies and treatment centers. Among patients at referral hospitals who were randomly assigned to be transferred to another center for primary angioplasty or to receive fibrinolytic therapy, the primary end point (a composite of death, reinfarction, or disabling stroke at 30 days) was reached in 8.5 percent of the patients in the former group, as compared with 14.2 percent of those in the fibrinolytic-therapy group (P=0.002), and the difference was driven by a reduction in the rate of reinfarction in the angio-
plasty group (1.6 percent, vs. 6.3 percent in the fibrinolytic-therapy group). Of note, 96 percent of the patients were transferred from the referral hospital to an angioplasty center within two hours after randomization. In fact, an analysis of all five trials that compared transfer for primary percutaneous coronary intervention with on-site fibrinolytic therapy revealed that despite the delay necessary for the transfer (43 minutes on average), primary percutaneous coronary intervention was associated with significant reductions in the rates of death, nonfatal reinfarction, and total stroke. Overall, untoward events during the transfer were infrequent (a mortality of 0.5 percent in one study and a rate of ventricular arrhythmias of 0.7 to 1.4 percent).

These provocative data raise the question of the importance of the time to reperfusion in patients undergoing primary angioplasty. Although the time dependency of catheter-based reperfusion may be less than that for fibrinolytic therapy, particularly in the case of patients presenting more than three hours after the onset of symptoms, several studies have shown that the interval between arrival at the hospital and inflation of the balloon catheter and restoration of flow to the infarct-related artery (the “door-to-balloon time”) is directly related to in-hospital mortality. Indeed, a door-to-balloon time of less than 90 to 120 minutes has been associated with improved in-hospital survival. It is noteworthy that in the DANAMI-2 study, conducted in Denmark, the median interhospital transfer time was 32 minutes, and the median interval between arrival at the first hospital and the initiation of the transfer was 50 minutes. Moreover, in the Czech Republic, where the Primary Angioplasty in Patients Transferred from General Community Hospitals to Specialized PTCA Units with or without Emergency Thrombolysis (PRAGUE-2) trial was undertaken, the time between randomization and balloon-catheter inflation was only 97 minutes.

In contrast, a U.S. report, from the National Registry of Myocardial Infarction 4,5 revealed a median door-to-balloon time of 185 minutes for patients transferred to centers capable of percutaneous coronary intervention and a door-to-balloon time of less than 90 minutes in only 3.0 percent of patients. Currently, in the United States, patients with acute myocardial infarction who are admitted to hospitals and who are in need of transfer to tertiary centers must wait for the next available emergency vehicle, whereas a prompt response can be triggered by public activation of emergency medical systems. Moreover, helicopter transportation is not completely reliable because weather conditions must be taken into account.

Given the practical and logistic issues currently associated with transport of patients during acute myocardial infarction in this country, an integrated approach to reperfusion therapy is critically important (Fig. 1). For patients with myocardial infarction associated with ST-segment elevation who present to hospitals without facilities for angioplasty within 2 to 3 hours after the onset of symptoms, fibrinolytic therapy should be considered and administered within 30 minutes after arrival ("door-to-needle time"). Transfer to a center capable of performing angioplasty should be strongly considered when fibrinolytic therapy is contraindicated or unsuccessful, when cardiogenic shock ensues, when the transfer delay will be less than 60 minutes, or

![Figure 1. Suggested Triage of Patients with Myocardial Infarction and ST-Segment Elevation.](https://www.nejm.org/doi/10.1056/NEJMe030724)
when more than 3 hours has elapsed since symptoms began. Data available to date reveal that the two reperfusion strategies become equivalent with respect to death as the difference between the door-to-needle time and the door-to-balloon time approaches 60 minutes and with respect to the composite end point of death, reinfarction, or stroke after a delay of 90 minutes. Furthermore, both the Comparison of Primary Angioplasty and Prehospital Thrombolysis in the Acute Phase of Myocardial Infarction (CAPTIM) trial and the PRAGUE-2 trial showed that primary percutaneous coronary intervention is superior to fibrinolysis when the duration of symptoms is two to three hours or more but not when the duration of symptoms is less than two hours.

Nevertheless, now is the time for evidence-based therapy to dictate optimal patient care. Now is the time to discard the practice of transporting patients with acute myocardial infarction to the nearest hospital and to transport them preferentially to centers of excellence for primary percutaneous coronary intervention (Fig. 1). This practice will foster the availability of highly experienced angioplasty teams that can perform primary percutaneous coronary intervention with minimal delay. The model for this type of care exists in the emergency system comprising regional centers of excellence for trauma victims. Moreover, now is the time for tertiary hospitals capable of performing primary angioplasty to offer it 24 hours a day, seven days a week.

Certainly, we need to continue to promote public education about the warning signs of myocardial infarction and to promote the immediate activation of emergency medical systems when symptoms do occur (50 percent of patients with acute myocardial infarction transport themselves to the hospital) in the effort to minimize the delay in the provision of treatment (with a goal of 30 minutes between the onset of symptoms and the start of reperfusion therapy). We also need to determine whether primary angioplasty performed immediately after arrival at angioplasty-treatment centers is superior to that performed after transfer from referral hospitals — a finding that might compel community hospitals that do not currently perform angioplasty procedures to begin to offer this reperfusion strategy. Clearly, we must continue to evaluate optimal pharmacologic and mechanical reperfusion strategies that may combine the advantages of both. Fibrinolysis before hospital arrival and facilitated percutaneous coronary intervention (combination therapy with reduced-dose fibrinolytic agents and glycoprotein IIb/IIIa platelet inhibitors before transfer for angioplasty) hold promise, although the latter strategy may be associated with an increased risk of bleeding.

When available and performed by experienced operators at high-volume centers, primary percutaneous coronary intervention saves 20 lives and results in 60 fewer events for every 1000 patients treated. This suggests that primary percutaneous coronary intervention is indeed worth the wait. However, as in Denmark and the Czech Republic, we must strive to minimize the wait by implementing systems that allow rapid transfer between hospitals and that ultimately will allow direct transport from the home or other off-site location to the nearest center of excellence for primary coronary angioplasty.

From the Cardiology Section, Department of Medicine, Boston University Medical Center, Boston.