

EDITORIALS



Timely PCI for STEMI — Still the Treatment of Choice

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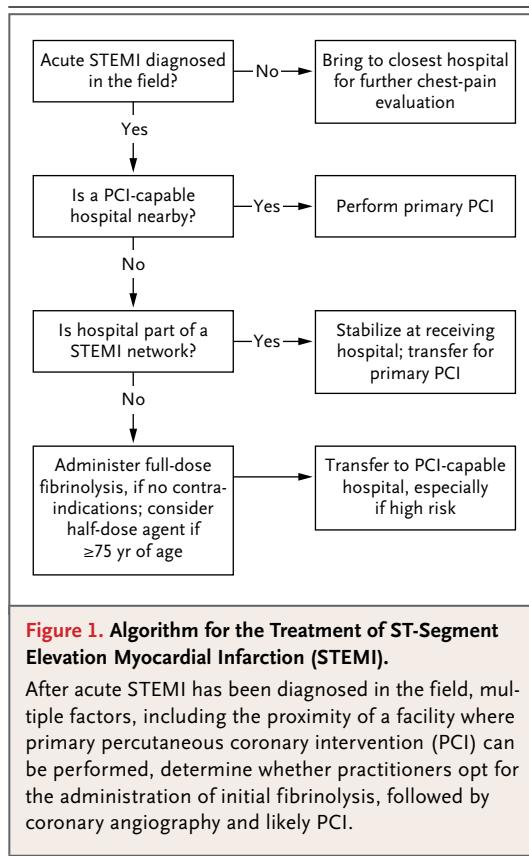
Timely primary percutaneous coronary intervention (PCI) is the preferred therapy for ST-segment elevation myocardial infarction (STEMI).¹ The challenge, however, lies in the definition of “timely.” In general, the shorter the time from symptom onset to PCI is, the higher the likelihood of myocardial salvage and lower associated mortality. Studies suggest that the tipping point for when primary PCI is no longer superior to fibrinolytic therapy is approximately 2 hours, though the exact time depends on the duration of ischemia, the amount of myocardium in jeopardy, and the bleeding risk of the patient, among other factors.^{2,3} In industrialized urban settings, there has been remarkable progress in reducing the so-called door-to-balloon time to less than 90 minutes and in many cases to less than 1 hour. In other settings, such as in geographically remote areas or in health care systems in which rapid PCI is not possible for economic or logistical reasons, prolonging the window for primary PCI with the use of fibrinolysis is theoretically attractive. To date, however, no study has clearly shown the optimal way to deliver this therapy.⁴

Armstrong et al.⁵ now report in the *Journal* the results of the Strategic Reperfusion Early after Myocardial Infarction (STREAM) trial. A total of 1892 patients with STEMI who had an onset of symptoms within 3 hours before medical contact and who could not undergo primary PCI within 1 hour were randomly assigned to receive either primary PCI or fibrinolysis and were then transported to a PCI-capable hospital. There was no significant between-group difference in the primary end point of death from any cause, shock, congestive heart failure, or reinfarction up to 30 days. However, the rate of intracranial hemorrhage in the fibrinolysis group was five times that in the primary PCI group (1.0% vs. 0.2%, $P=0.04$).

The authors concluded that prehospital fibrinolysis followed by angiography in 6 to 24 hours is a reasonable alternative to primary PCI when PCI would be delayed by more than 1 hour. This is an appealing interpretation of the data, since it would make the care of patients with STEMI much easier at sites that cannot perform prompt PCI. However, the lack of superiority of the fibrinolysis approach coupled with the increased rate of intracranial hemorrhage would seem to make this an inferior strategy, as compared with the alternative of striving to design systems that allow patients to receive rapid PCI uniformly.

In the STREAM trial, once it became apparent that there was an excess in intracranial hemorrhage, which appeared to be occurring predominantly in patients 75 years of age or older, the trial protocol was amended to allow use of half-dose fibrinolytic therapy among patients in that age group. The idea of dose modification in older patients makes intuitive and biologic sense. The investigators are to be commended for enrolling older patients in a STEMI trial and for changing course in the midst of the trial to enhance patient safety. As is the case with most trials, the study was not powered to examine this important subgroup of older patients, which makes determinations of efficacy difficult, even if safety is demonstrated. Thus, the logical approach to using half-dose fibrinolysis in older patients would need further prospective validation before such a strategy should be widely recommended.

In addition, since the start of the STREAM trial, several remarkable improvements have occurred in PCI. Advances in peri-procedural and post-procedural antiplatelet and anticoagulant therapy have further enhanced the results of PCI, especially in patients with STEMI.⁶ Manual thrombus aspiration before stenting appears to



reduce mortality in patients undergoing primary PCI.⁷ Second-generation drug-eluting stents have increased the durability of primary PCI and may even have lowered rates of stent thrombosis, as compared with first-generation drug-eluting stents or bare-metal stents.⁸ Thus, since the start of the STREAM trial, the results of primary PCI have gotten better and safer, creating an even higher bar for prehospital fibrinolysis.

The findings of this trial could have a major effect on clinical practice and further highlight the prominence of timely PCI as the treatment of choice for STEMI (Fig. 1). Health care systems can be reconfigured to provide such care, but there are a variety of practical barriers.⁹ When

primary PCI cannot be performed, prompt fibrinolysis should be administered, with transfer to a PCI-capable center in the next several hours, especially in high-risk patients.¹⁰ A pharmacoinvasive approach, including initial half-dose fibrinolysis in the elderly, may be an option in selected circumstances, though it does not represent optimal care as compared with timely primary PCI. The STREAM trial shows us that the best therapy for STEMI remains rapid mechanical restoration of coronary flow with a stent.

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Pain, Heat, and Emotion with Functional MRI

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Pain, in its various manifestations, is our most distressing human experience. A large volume of evidence extending from psychology to neuroimaging emphasizes the powerful influence of

both social and physical pain on mammalian well-being and survival.¹ Although pain is defined as an unpleasant sensation caused by nociceptive stimuli,² the concept encompasses social