Reperfusion Strategies in Acute ST-Segment Elevation Myocardial Infarction
Acute Angioplasty May Be Feasible for the Majority of U.S. Citizens

Recently, Boden et al. (1) published a comprehensive review on reperfusion strategies in acute ST-segment elevation myocardial infarction (STEMI). The review favors fibrinolysis in preference to primary percutaneous coronary intervention (PPCI) in the case of a percutaneous coronary intervention (PCI)-related delay (extra delay anticipated when considering PPCI instead of fibrinolysis) >60 min or symptom duration <3 h and state that “transport delays commonly limit the benefit of PPCI.” Furthermore, the authors recommend fibrinolysis particularly in the pre-hospital setting. There is, however, no evidence to support fibrinolysis in any of the aforementioned cases.

The idea of a 60-min maximal acceptable PCI-related delay is based on a previous meta-analysis by Nallamothu et al. (2), which included 23 randomized trials comparing fibrinolysis versus primary PCI. For each trial, they plotted the mortality benefit achieved by PPCI compared with fibrinolysis according to the observed PCI-related delay. Then, they performed a regression line and found that the intercept with the x-axis was approximately 60 min and concluded that fibrinolysis would be superior to PPCI if the extra delay used to perform PPCI exceeded 60 min.

However, Nallamothu et al. (2) plotted the PCI-related delay for the PRAGUE-1 (PRimary Angioplasty in patients transferred from General community hospitals to specialized PTCA Units with or without Emergency thrombolysis) study to be 10 min and for the PRAGUE-2 study to be 32 min (2). According to the original publications, the PCI-related delay was 70 and 85 min in the 2 trials, respectively (3,4) In addition, they plotted the PCI-related delay to be 7 min for a study by Ribicini et al. (5), 15 min for a study by Garcia et al. (6), 25 min for a study by Gibbons et al. (7), and 15 min for a study by Vermeer et al. (8). According to the original articles, the correct PCI-related delays were 16, 47, 45, and 90 min, respectively (5–8).

Finally, the PCI-related delay for the DANAMI-2 trial was plotted as 55 min. The PCI-related delay, however, varies considerably between nontransfer and transfer patients, and DANAMI-2 data should be split accordingly (e.g., into a nontransfer and transfer group) (9). If one repeats the regression analysis, including the original tabulated data and splitting the DANAMI-2 data into a transfer and a nontransfer group, then the x-axis intercept becomes 120 min. A more proper meta-analysis, however, has already been performed by Boersma et al. (10), who included data at center-level. Accordingly, 153 values instead of 23 values for the association between PCI-related delay and mortality were implemented in the Boersma et al. (10) meta-analysis, and they found that, even at a PCI-related delay of 80 to 120 min, there was a benefit of PPCI in preference to fibrinolysis.

Regarding the optimal reperfusion therapy in the early incomers, Boden et al. (1) refer to a previous subanalysis of the CAPTIM (Comparison of Angioplasty and Prehospital Thrombolysis in Acute Myocardial Infarction) trial that demonstrated a greater mortality in PCI-treated patients compared with fibrinolytic-treated patients who received reperfusion therapy within 3 h of symptom duration (11). The CAPTIM data, however, should be interpreted cautiously because: 1) the trial was stopped before scheduled because of a lack of funding, thus hampering the power of the study; 2) there was no significant difference between the primary end point in the main study and thus no reason to perform subgroup analysis; and 3) the authors might as well have compared mortality in PCI patients treated early versus late and then found that mortality was greatest in the group treated early.

Again, Boersma et al. (10) have provided us with the best-available evidence, performing the only meta-analysis so far based on individual data from patients included in 22 studies comparing PPCI with fibrinolysis. The Boersma et al. (10) meta-analysis documents that fibrinolysis is not superior to PPCI in the early presenters and that lower mortality was observed in PPCI-treated patients compared with fibrinolysis-treated patients.

Regarding the “limited benefit of PPCI due to transport delays” and recommendation of pre-hospital fibrinolysis, a feasible logistic may be to implement pre-hospital diagnostic strategies combined with rerouting of patients directly to catheterization laboratories. This strategy reduces the delay in initiation of PPCI by up to 90 min (12) and would considerably increase the catchment areas to interventional hospitals. Given that 80% of American citizens live within 60 min of transport to a PPCI hospital and that the estimated median transportation time to the invasive hospital is 11 min, this strategy would enable PPCI to be the preferred reperfusion therapy in the majority of STEMI patients (13).

In conclusion, the maximal acceptable PCI-related may be at least 80 to 120 min, there is no evidence to support fibrinolysis in the early incomers, and a pre-hospital diagnostic strategy combined with rerouting of STEMI patients directly to catheterization laboratories would ensure that the majority of American citizens could be treated with PPCI in the case of STEMI.

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doi:10.1016/j.jacc.2007.10.070
We appreciate the perspectives offered by Drs. Terkelsen and Nielsen regarding the optimal approach to achieving timely reperfusion for acute ST-segment elevation myocardial infarction (STEMI). In our review (1), we strongly favored the view that primary percutaneous coronary intervention (PCI) represents the best modality of reperfusion in STEMI patients and, in a perfect world with no resource limitations or cost restraints, would be the treatment of choice for all STEMI patients. However, we attempted to address the “real-world” challenges that exist within the U.S., where 1) fully one-third of all STEMI patients currently receive no reperfusion (fibrinolytic or mechanical) acutely; 2) the majority of STEMI patients (60% to 70%) present initially to non-PCI-capable hospitals, which creates inevitable transport delays to PCI-capable facilities that are frequently beyond the control of emergency medicine physicians and cardiologists; 3) the group of “transfer-in” STEMI patients to PCI-capable hospitals rarely achieve door-to-balloon (DTB) times of <90 min (only 8%, according to the Chakrabarti et al. [2] recent analysis of the National Registry of Myocardial Infarction); and 4) among STEMI patients who present within 3 h of initial STEMI symptom-onset, there is no clear advantage of a mechanical reperfusion strategy over a pharmacologic reperfusion strategy, which form the basis for the current American College of Cardiology/American Heart Association clinical practice guideline recommendations that, in such patients, either reperfusion approach is considered a Class IA recommendation (3).

Our goal in this review (1) was to address primarily the management issues confronting acute STEMI management in patients presenting to community hospitals without on-site PCI capability. In such settings, both emergency medicine physicians and cardiologists must quickly decide whether urgent transport to a PCI-capable hospital can likely achieve prompt reperfusion with a DTB <90 min or, alternatively, whether the use of a bolus fibrinolytic agent (in a patient without evident contraindications) would be a more appropriate reperfusion strategy. If, in fact, 92% of all such STEMI patients who require urgent transfer for primary PCI do not achieve DTB times <90 min, it seems reasonable to consider a pharmacologic reperfusion approach, because there is an almost a 40% relative increase in 30-day mortality among patients in whom reperfusion is delayed beyond 120 min.

Although both regional and national initiatives are presently underway within the U.S. to streamline and expedite STEMI management by using enhanced, field-based electrocardiogram diagnosis to bypass community hospitals without on-site PCI capability and instead direct such patients de novo to PCI-capable hospitals, these efforts are not yet widely developed in many communities and inherently conflict with existing Emergency Medical Service infrastructure nationwide, which continues to espouse the transport of myocardial infarction patients to the closest hospital. Accordingly, unlike most of European countries, where there is more highly coordinated and expedited STEMI transport to PCI-capable facilities, the logistical limitations that continue to exist within the U.S. regarding triage and transport of STEMI patients represent formidable barriers to expanding and achieving a more broad-based system of primary PCI for all STEMI patients.

Therefore, we believe our review highlights the need for both mechanical and pharmacologic reperfusion, as dictated by local resource availability, as the best overall approach to expediting timely reperfusion in patients who present with STEMI to either rural or urban hospitals where differential systems and processes of care may influence clinical decision-making.

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doi:10.1016/j.jacc.2008.06.010

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