Focused Perspective

Treatment Delayed Is Treatment Denied

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You may delay, but time will not.
—Benjamin Franklin

In 1977, Reimer and coworkers published in this journal the results of an experiment that established the basis of reperfusion therapy for patients with ST-elevation myocardial infarction (STEMI). These investigators identified a relationship between the duration of acute coronary occlusion and the magnitude of subsequent myocardial necrosis. In other words, the extent of infarct size that resulted from sustained occlusion could be reduced if the occlusion were interrupted and flow restored. Furthermore, reductions in the duration of occlusion were associated with incremental decreases in infarct size.


Such relationships were confirmed in early investigations of thrombolytic therapy for STEMI. Consequences of earlier treatment were improvements in indices of left ventricular systolic function and reductions in mortality rate. Although there was, in general, a linear relationship between time to treatment and outcome, the very best results were obtained when thrombolysis was initiated within the first hour.

To this point, such a tight relationship between time to treatment and outcome has been less apparent when primary angioplasty is selected as the method for achieving reperfusion. Reports on this subject describe conflicting findings. With these considerations in mind, De Luca and colleagues performed a single-center database analysis and reported their results in the March 16, 2004, issue of Circulation. They reviewed the baseline and angiographic characteristics and clinical outcomes of 1791 patients with STEMI who were treated by primary angioplasty. Time to treatment was defined as the elapsed time between symptom onset and the initial balloon inflation.

One key finding of their analysis was that time to treatment was influenced by several factors, including advanced age, female gender, and history of diabetes or prior revascularization. Presence of these factors prolonged time to treatment. An explanation for these relationships is not readily apparent. Another observation was that time to treatment was shorter among patients in whom primary angioplasty achieved successful, complete reperfusion than among those for whom treatment was not successful. This finding suggests that PCI is more likely to be successful when performed in the earlier hours of STEMI. Perhaps most importantly, a continuous mathematical relationship was identified between time to treatment and outcome. Longer time to treatment was associated with a greater likelihood of a predischarge left ventricular ejection fraction <0.30 and death at 1 year. Specifically, for every 30-minute delay in treatment, the risk of experiencing major left ventricular dysfunction at discharge was increased by 8.7% and risk of death at 1 year by 7.5%. In concluding, the authors emphasized the importance of shortening the time to treatment when performing primary angioplasty for patients with STEMI.

Certain points should be noted before addressing the implications of this report. First, De Luca et al. measured time to treatment beginning with the time of symptom onset. This approach differs from many prior investigations that have focused on elapsed time from hospital arrival to time of therapy. This latter time period is one that can be influenced readily by changes in hospital practice patterns.

A concern with using time of symptom onset as a metric relates to the ability to determine with accuracy and consistency when infarct symptoms really begin. Experienced clinicians are familiar with the erratic pattern of initial STEMI symptoms as well as marked differences in the quality or severity of these symptoms. Recognizing this concern, initial Thrombolysis in Myocardial Infarction (TIMI) trial investigators defined “symptom onset for STEMI” as the time when symptoms reached the point that a patient decided to seek medical attention. This approach, although arbitrary and perhaps imprecise in identifying the earliest infarct symptom, did ensure consistency. Unfortunately, in the report by De Luca et al. symptom onset is not defined. Also, we are not provided with a description of the range of times to treatment or the component of time to treatment that occurred before hospital arrival or between door and balloon.

Another subject for discussion is the magnitude of the effect that was observed as a consequence of delay. For each 30 minutes of delay, there was an increase in risk for death of 7.5% and for ejection fraction <30% of 8.7%. It is important to note that these are increases in relative and not absolute rates of risk. For example, if a patient who was treated promptly had a 1-year risk of death of 7% after STEMI, a 30-minute delay would increase his risk to 7.5%. When evaluated on an individual patient basis, such increases in risk may not appear to be that meaningful. When considering that in excess of 400 000 deaths per year result from myocardial infarction, however, the impact of these risk rates is substantial. Also, the benefit for reducing the proportion of patients...
with severe left ventricular dysfunction would have profound effects on quality of life, given the morbid consequences of advanced heart failure and the expense associated with new device-based therapies.

The principal implication of this investigation is to shorten the delay in primary angioplasty treatment for STEMI. In effecting such a change, it is appropriate to consider the components that comprise the interval from symptom onset to balloon inflation and their potential for contributing to delay of treatment. First, patients must become aware that they are experiencing a STEMI and seek appropriate medical attention. The Rapid Early Action for Coronary Treatment (REACT) study investigated this process and found that patients were often unaware of the characteristics of infarct symptoms, delayed requesting medical assistance, and rarely called 9-1-1.10 Efforts to correct these failings have been initiated.11,12 Second, when patients suspected of having a STEMI are transported by emergency medical services, they are often taken to the nearest healthcare facility rather than to the one that has primary angioplasty capability. Comparative analyses indicate such an approach is associated with the greatest magnitude of delay, averaging in excess of 3 hours, when there is a need to transfer a patient from one hospital lacking PCI capability to one that has this resource.13 Third, establishing the diagnosis of STEMI after hospital arrival often consumes more time than would be considered reasonable.14 Fourth, a catheterization laboratory and staff and an interventional cardiologist must be available to perform the primary angioplasty procedure. During routine working hours, a busy facility may not have a catheterization laboratory immediately available for an emergency. During off-hours, considerable time may be required for support staff to reach the hospital.

Optimally, a process aimed at minimizing time to treatment from STEMI onset to the performance of primary angioplasty should consider each of these components individually, as well as their interrelationships. An example of such an effort has recently been completed in Maryland under the guidance of the Maryland Health Care Commission.15 Developed through an advisory committee and Commission staff, a series of recommendations are now being implemented in that state. First, the Commission has recommended that the Maryland Institute for Emergency Medical Services develop and implement a protocol that will identify and triage STEMI patients to a designated primary angioplasty center. This approach is expected to include obtaining an ECG in the field, confirming the diagnosis of STEMI, and transporting patients not necessarily to the nearest hospital but rather to one with primary angioplasty capability. It is important to note the impact of the prehospital ECG on shortening time to treatment. The prehospital ECG eliminates the time required to establish the diagnosis of STEMI after hospital arrival and also permits the catheterization laboratory to be informed that a patient requiring primary angioplasty has been identified. This early warning allows catheterization laboratory staff to keep a catheterization laboratory available during routine working hours or to travel to the hospital during off-hours.

A second recommendation was to establish criteria for a primary angioplasty center. Such hospitals will need to demonstrate that their STEMI patient volume and door-to-balloon times meet established standards. The interventional cardiologists who will perform primary angioplasty must have appropriate training and experience.16 In this program, presence of on-site coronary artery bypass surgery programs is not a requirement for a hospital to become a primary angioplasty center. Hospitals without such programs, however, will need to have a formal agreement with a tertiary institution for immediate, supplemental patient care. Finally, the entire program will be formally monitored to determine compliance, safety, and effectiveness. A standardized dataset will be developed, collected, and analyzed for each aspect of the program. Continued participation will be based on acceptable performance.

A second issue with regard to the importance of time to treatment relates to the patient for whom, despite best effort, circumstances delay time to treatment by primary angioplasty. For many such patients, thrombolytic therapy remains a legitimate option. In fact, within the early hours of STEMI, recent studies suggest that there is no superiority of primary PCI over thrombolytic therapy in terms of mortality rate.17,18 Forthcoming American Heart Association/American College of Cardiology guidelines for treatment of STEMI will support this concept that circumstances do exist in which thrombolytic therapy is preferred as the initial reperfusion strategy. Furthermore, some have advocated the routine administration of full- or partial-dose thrombolytic therapy before performing primary angioplasty, particularly if a delay may be anticipated. Thrombolytic therapy in this setting would be considered as adjunctive therapy, facilitating reperfusion before definitive relief of coronary obstruction. To this point, such an approach has not been validated, although several clinical trials designed to evaluate this approach currently are being conducted.

The report by De Luca et al6 provides additional information that emphasizes the importance of reducing the elapsed time from infarct onset to reperfusion therapy. Although this relationship has been noted previously, a mandate to enhance the expediency of STEMI management across healthcare systems in the United States has not been forthcoming. On the other hand, the feasibility of such programs has been well demonstrated in other countries. More convincing evidence is not required to make the point. Coordinated efforts among community services, hospitals, and physicians will be necessary to achieve the goal of shortening time to treatment.

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References


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