EDITORIAL COMMENT

Is There a Role for Pre-Hospital Fibrinolysis in North America?*

Timothy D. Henry, MD†
Bernard J. Gersh, MB, CHB, DPHIL‡

Minneapolis and Rochester, Minnesota

The last 25 years of reperfusion therapy for STEMI has been a triumph. Well-designed clinical trials have provided answers and generated new questions leading to additional trials, and the end result is that we now have a wealth of information. Importantly, this systematically acquired body of knowledge has been translated into clinical practice leading to a significant improvement in the clinical outcomes of patients with STEMI (1).

Although it is well accepted that primary percutaneous coronary intervention (PCI) is the preferred reperfusion strategy in situations when this can be achieved within 90 min of first patient contact (2,3), the key to the successful implementation of reperfusion strategies is an awareness of geographic diversity among countries and within countries and an understanding that “one size does not fit all.” Key issues, as yet unresolved, are determining what degree of delay is acceptable in the transfer of patients from a community hospital without PCI facilities to a hospital that is PCI-capable and being able to determine which patients should be pre-treated with fibrinolytic drugs and in what setting should these be administered. One aspect of this issue is addressed by Huynh et al. (4) in this issue of JACC: Cardiovascular Interventions. They describe the results of a survey of programs worldwide that have successfully used pre-hospital fibrinolysis as a reperfusion strategy and comment on its underutilization in North America. What can we learn from these results?

Randomized clinical trials provide clear evidence that earlier treatment with pre-hospital fibrinolysis improves survival compared with in-hospital administration and can be safely administered in a wide variety of clinical settings (5–7). The results of the survey reinforce this fact, but overall use of in-hospital fibrinolysis has decreased in the United States with the growth of regional STEMI systems that have improved timely access to PCI. Pre-hospital fibrinolysis may also have advantages over PCI for patients who present early (<2 h after onset of symptoms) and for patients who are unable to receive PCI in a timely manner (>2 h door-to-balloon). Despite these potential advantages, pre-hospital fibrinolysis is seldom administered in the United States, unlike the situation in many European countries. Is this transatlantic divide the consequence of philosophical differences or is it a question of logistics?

The survey results do provide insights into the challenges inherent in a pre-hospital fibrinolytic strategy. Significant heterogeneity exists among the programs surveyed in regards to program design, the ultimate reperfusion strategy, and clinical outcomes. The design of a regional STEMI system is critically dependent on available emergency medical services (EMS) resources. For example, the majority of programs surveyed still require the reperfusion decision to be made by either emergency physicians or cardiologists. Therefore, a successful pre-hospital fibrinolysis program requires the presence of either physicians in the ambulance or advanced care paramedics who have ready access to an available physician. In France and Vienna, physicians are present in nearly 100% of ambulances, which is not (and likely never will be) the case in North America. Therefore, fundamental to any STEMI system using pre-hospital fibrinolysis is the availability of pre-hospital electrocardiography and transmission (8). Pre-hospital 12-lead electrocardiogram availability is improving in the United States, but still nearly one-half of STEMI systems lack this capability (9). Reliable transmission of the results to an available physician remains an even greater challenge in rural regions of the United States where pre-hospital fibrinolysis might be most needed (9).

The actual reperfusion strategy used varied significantly in the survey. Routine angiography following lytic ranged from 50% to 100%, and the timing of angiography varied as well. In fact, the reperfusion strategy used by several of the programs might be more accurately described as pharmacoinvasive. This heterogeneity likely contributes to the variability in outcomes. Although it is nearly impossible to compare outcomes in a survey of this type, it is interesting to note that the mortality was highest in Sweden where use of routine angiography was the lowest.

The survey has a number of important implications for care of the STEMI patient in North America today. It is
increasingly clear that regional STEMI systems significantly improve time to treatment, reperfusion use, and most likely mortality (10–13). These regional STEMI systems need to be designed with knowledge of both the availability of local resources and local challenges. This includes location and number of PCI centers, geography, weather, traffic, and perhaps the most critical factor, EMS resources. Carefully designed regional STEMI systems can meet these challenges with the use of standardized protocols and pre-designed transfer plans. Should pre-hospital fibrinolysis be considered as part of the reperfusion strategy?

The major challenge to successful implementation of a pre-hospital fibrinolytic strategy is the regional variations in EMS resources. The EMS system in the United States is particularly fractionated with a wide range of both funding and available services. For example, the Minneapolis Heart Institute’s regional STEMI system, which includes 33 hospitals and 10 clinics throughout Minnesota and Wisconsin, requires integration with nearly 50 different EMS agencies and a wide spectrum of resource availability. Theoretically, rural America with long distances and few PCI centers is the ideal location for a pre-hospital fibrinolytic strategy, yet paradoxically presents the greatest challenges due to scarce EMS resources. Many ambulances in rural America are staffed by volunteers with only basic life support training and pre-hospital electrocardiography capability is much less common than for urban EMS systems. Funding for both training and equipment is frequently the greatest challenge.

Perhaps the most important insight from the survey is that fibrinolytic and PCI reperfusion strategies should no longer be considered mutually exclusive. Many of the programs surveyed use a pharmacoinvasive approach with pre-hospital fibrinolysis followed by immediate transfer to a PCI center for early angiography and revascularization. The popularity of the pharmacoinvasive approach has been driven by the results of recent randomized clinical trials that have demonstrated superiority of this approach over fibrinolysis followed by standard care (revascularization only for failed reperfusion or recurrent ischemia) (14–16). A recent meta-analysis of 7 trials enrolling nearly 3,000 patients confirmed the benefits of the pharmacoinvasive strategy with a significant reduction in the combined endpoint of death/reinfarction at 30 days, without an increase in major bleeding or stroke (17). Current European Society of Cardiology guidelines now recommend routine transfer to a PCI center with early angiography and revascularization within 3 to 24 h (3). As illustrated by the survey, the specific pharmacologic regimen and the timing of early angiography remain unclear. Large regional STEMI systems in the United States frequently employ a combination of reperfusion strategies (10,11,13). The Minneapolis Heart Institute’s Level 1 MI program uses a pharmacoinvasive strategy for patients with an expected total door-to-balloon time >120 min (hospitals 60 to 120 miles from the PCI center [10]), whereas the Mayo Clinic STEMI system uses fibrinolysis for early presenters followed by transfer and early angiography (11). Results from 5 high-volume PCI centers indicate a reduced-dose fibrinolytic strategy with early PCI may have advantages over PCI alone (18).

The majority of patients with STEMI who present to PCI centers in the United States are currently being treated with door-to-balloon times <90 min. Therefore, remaining advances in the management of STEMI will likely come from non-PCI hospitals where total door-to-balloon times for patients transferred from non-PCI hospitals remain suboptimal. Well-designed regional STEMI systems require careful consideration of the optimal reperfusion strategy taking into account local resources and challenges. Whether pre-hospital fibrinolysis will become more common in North America is uncertain, but the lessons learned from this survey from successful programs around the world provide important insights for the development of regional STEMI systems. In the current era, it is not just the nature of the reperfusion therapy that is important but the speed and efficacy of delivery to all eligible patients, which will continue to improve the outcome of STEMI patients worldwide.

Reprint requests and correspondence: Dr. Timothy D. Henry, Minneapolis Heart Institute Foundation, 920 East 28th Street, Suite 100, Minneapolis, Minnesota 55407. E-mail: henry003@umn.edu.

REFERENCES


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