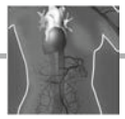
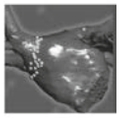


Delays in the treatment of STEMI: remarkable progress, room for improvement

"Dramatic improvement has been made in treatment times for STEMI in the past decade, but unique challenges remain."

KEYWORDS: delays ■ door-in to door-out ■ door-to-balloon ■ primary PCI ■ STEMI ■ treatment times

"*You may delay, but time will not, and lost time is never found again.*"

Benjamin Franklin

Plaque rupture, thrombosis and subsequent acute coronary occlusion leading to ST-elevation myocardial infarction (STEMI) remains one of the most catastrophic manifestations of coronary artery disease. Rapid reperfusion has become the hallmark of modern STEMI care. Dramatic improvement has been made in treatment times for STEMI in the past decade, but unique challenges remain.

Critical nature of time delays in STEMI care

The concept 'time is myocardium' arose from animal models in the late 1970s [1] and was confirmed by clinical trials using both fibrinolytic therapy and primary percutaneous coronary intervention (PCI) [2,3]. Treatment delays appear to be less critical for PCI compared with fibrinolytic therapy. For example, results from the Swedish RIKS-HIA registry indicate the benefit of fibrinolytic therapy declines after a 2-h delay, but not with PCI and, at every time point, PCI remains superior to fibrinolysis [4].

Time is especially critical in high-risk patients. In patients with Killip class 3 or 4, aged >70 years or with anterior myocardial infarction, a door-to-balloon (D2B) time of >2 h was associated with higher mortality rates (32.5% [≥2 h] vs 21.5% [<2 h]; hazard ratio: 1.53; 95% CI: 1.22–1.9; p = 0.0002). In contrast, time was less critical in lower-risk patients (10.8% [≥2 h] vs 9.2% [<2 h]; hazard ratio: 1.13; 95% CI 0.78–1.64; p = 0.53) [5].

PCI treatment delays have consistently correlated with increased mortality [6,7]. Cannon *et al.* demonstrated a linear association between mortality and D2B times, with a relative risk of mortality increasing from 1.0 (D2B time <60 min) to 1.15 (60–120 min) to 1.41 (120–150 min) and to >1.6 for >150 min [6]. De Luca *et al.* demonstrated similar results, showing a 7.5% increase per 30 min delay in time to treatment [7]. The benefit to mortality rate of PCI over prompt fibrinolysis diminishes as the D2B time increases and may be lost once the D2B time exceeds the door-to-needle time by 107 min [8]. Therefore, the primary goal in STEMI patients is timely access to PCI [9,10].

Treatment of STEMI at PCI-capable facilities: considerable progress

The American College of Cardiology (ACC) 'D2B Alliance' was designed to improve time-to-treatment in PCI hospitals and the American Heart Association (AHA) established 'Mission: Lifeline' to develop regional STEMI systems of care, in order to facilitate timely access to PCI. Using a cross-sectional survey of 362 primary PCI hospitals, six independent strategies were associated with faster treatment for STEMI patients:

- Activation of the cardiac catheterization laboratory by the emergency department (ED) physician;
- A single call to activate the laboratory;
- Catheterization laboratory activation while the patient is en route to the hospital;
- Catheterization laboratory availability within 20 min of being paged;
- Attending cardiologist on site;
- Real-time feedback from the ED and catheterization laboratory staff.

The median D2B time was inversely correlated with the number of strategies employed [9]. Another critical strategy to improve treatment times is prehospital identification of STEMI patients. The use of prehospital ECGs

Michael D Miedema

University of Minnesota Cardiovascular Disease Division, Minneapolis, MN, USA and Minneapolis Heart Institute Foundation at Abbott Northwestern Hospital, MN 55407, USA

Marc C Newell

Minneapolis Heart Institute Foundation at Abbott Northwestern Hospital, MN 55407, USA

Timothy D Henry

Minneapolis Heart Institute Foundation at Abbott Northwestern Hospital, 920 East 28th Street, Suite 100, Minneapolis, MN 55407, USA
Author for correspondence:
Tel.: +1 612 863 7372
Fax: +1 612 863 3801
henry003@umn.edu

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in 2712 consecutive patients, resulted in 86% of patients being treated with a D2B time of <90 min and is supported by an AHA consensus statement [11,12]. Prehospital identification allows triage of patients directly to PCI centers. Implementing prehospital ECG with activation of the catheterization laboratory directly from the field and direct triage to the PCI center resulted in a D2B time of <90 min in 80% of patients, compared with only 12% of patients taken to the nearest ED for evaluation prior to transferal to the PCI center [13]. A cross-sectional study examining the feasibility of prehospital triage demonstrated that 79% of the population of the USA are within 60 miles of a PCI-capable hospital [14]. The implementation of these strategies in the USA has been successful; D2B times in PCI hospitals improved dramatically from 2005 to 2010 (96 to 64 min) [15]. This is a remarkable accomplishment and is reflected by the declining mortality in STEMI.

Room for improvement

In contrast to the remarkable progress in PCI hospitals, there is room for improvement in patients transferred for primary PCI. Approximately 50% of patients with chest pain do not use emergency medical services and only 25–30% of hospitals in the USA are PCI-capable. Therefore, interhospital transfer of STEMI patients who present to non-PCI centers is a necessary part of STEMI care.

Randomized, controlled trials have demonstrated that transfer for primary PCI improves outcomes compared with fibrinolytic therapy [16]. In a recent metaregression analysis of 11 randomized trials, patients transferred for PCI had a significant reduction in 30-day mortality, reinfarction and stroke, compared with patients receiving fibrinolytics [16]. Therefore, both the European Society of Cardiology and ACC/AHA guidelines recommend transfer for PCI in STEMI patients, if the total D2B time is within 120 min [2,3].

> "*Rapid reperfusion is, and will remain, the hallmark of STEMI care.*"

Unfortunately, real life can be more challenging than clinical trials. Based on the 1999–2002 National Registry of Myocardial Infarction data, only 4% of transferred patients had a total D2B time of <90 min and only 16% were treated within 120 min. The median D2B time in the USA was 180 min and nearly 30% of patients had a total D2B time of >240 min [17]. More contemporary data from the National Cardiovascular Data Registry in 2005 and 2006 indicates that only modest improvement was made, with only 9% and 28% of transfered STEMI patients having a total D2B time of <90 and <120 min, respectively [18]. Clearly, this is a major challenge for ideal STEMI care.

The door-in to door-out (DIDO) time at referral hospitals appears to be the major problem. An analysis of over 14,000 STEMI patients transferred for primary PCI from 2007 to 2010 in the ACTION Registry-Get With the Guidelines, revealed that only 11% of patients had a DIDO time of 30 min or less, with a median of 68 min (Interquartile range: 43–120) and patients with a DIDO time of >30 min had increased mortality [19]. Similar results were seen in an analysis of 13,776 Medicare/Medicaid patients at 1034 hospitals which reported DIDO times <30 min in only 9.7% of patients and >90 min in 31% of patients [20].

We recently examined the frequency, magnitude and clinical impact of specific delays in 2034 STEMI patients transferred for primary PCI in the Minneapolis Heart Institute's regional STEMI system [21,22]. The good news is that regional STEMI systems are effective. The total D2B time was <120 min in 79% of patients transferred up to 60 miles and 47% in patients transferred 60–210 miles from the PCI centers. However, delays still occur even in a well-established regional STEMI system and all delays are not created equal. The most common source of delay was the referral hospital, where 64% of patients had DIDO times of >45 min. The most common reason for this delay was incured whilst awaiting transport (26.4%), followed by ED delays (14.3%). However, these delays were of relatively low duration and were not associated with an increased mortality (<4% in-hospital). In contrast, patients with delays due to cardiogenic shock or cardiac arrest had increased mortality (31% in-hospital). For the majority of these patients, the critical nature of the illness led to the delay and only rarely did the delay itself contribute to the mortality. Certain delays may be unavoidable, as noted in the recent ACC/AHA guidelines: "some patients have clinically relevant nonsystem-based delays that do not represent quality of care issues" [2].

Stepping up to meet the challenge

A recent editorial in *Archives of Internal Medicine*, advocated a return to fibrinolytic

therapy [23]. We disagree. We believe that going 'back to the past' would not solve the problem and the challenges we face are not insurmountable. In fact, the results from successful STEMI systems would suggest that these challenges have already been met in many regions [11,13,21,22]. These results led to the ACC/AHA guideline recommendation supporting regional STEMI systems [2] and the AHA 'Mission: Lifeline®' program that was created to stimulate the development of these systems [9]. Finally, recent evidence suggests a PCI-based pharmacoinvasive strategy may be preferred to fibrinolysis alone, which indicates progress is also being made for STEMI patients when timely access for PCI is just not feasible [24,25].

Conclusion

Rapid reperfusion is, and will remain, the hallmark of STEMI care. Remarkable progress has already been made in the quest for timely access to PCI for STEMI patients in PCI centers. Results from regional STEMI systems indicate that it is an achievable goal in the majority of patients. Innovative methods to improve prehospital identification, catheterization laboratory activation, appropriate triage to PCI centers. and effective state, regional and national STEMI systems will enable us to meet the challenge.

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