Selected Update: State of the Art in STEMI Care

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Appropriate STEMI Care Depends on Timing

It has been well established that primary percutaneous coronary intervention (PCI) is superior to fibrinolytic therapy for ST-segment elevation myocardial infarction (STEMI) but only if coronary reperfusion can be established in a timely manner (<90 minutes) by skilled operators. Achieving that goal has been a challenge, however, because of delays in diagnosis as well as in treatment. Two particular areas of concern are the effective use of prehospital electrocardiograms (PH-ECGs) and the appropriate treatment strategy for patients who must be transferred a long distance for PCI.

Prehospital ECGs

Ivan Rokos, MD, FACEP, FAHA, FACC, an emergency physician in Los Angeles, California, USA, emphasized that patients with STEMI identified on a PH-ECG consistently have the fastest door-to-balloon (D2B) times. For example, in a Canadian study of 344 STEMI patients, the median D2B time was much shorter for patients who were referred directly to a PCI center by emergency medical services (EMS) personnel who were trained in ECG interpretation than for patients who were referred via interhospital transfer (69 minutes vs 123 minutes) [Le May MR et al. *N Engl J Med* 2008]. The ACTION Registry – Get with the Guidelines (ARG) study of 7098 STEMI patients who were transported by paramedics to the hospital, showed that the use of a PH-ECG was also associated with a shorter D2B time (median of 61 minutes vs 75 minutes; p<0.001) [Diercks DB et al. *JACC* 2009]. In addition, a 2053-patient study that evaluated the integration of PH-ECGs across 10 independent STEMI receiving center networks demonstrated that 86% of patients had a D2B time of ≤90 minutes, 50% were treated with a D2B time of ≤60 minutes, and 25% were treated with a D2B time of ≤30 minutes [Rokos IC. *J Am Coll Card CV Interv* 2009]. The study also evaluated EMS providers by using the date/time that was autostamped on the PH-ECG as Time 0 (rather than the hospital's door time) and found that 68% of patients had a rate of EMS-to-balloon time of <90 minutes in these organized STEMI networks.

The greatest challenge with PH-ECGs is a higher rate of inappropriate activation of the cardiac catheterization laboratory. Various activation studies have shown rates of false-positive activation of the catheterization laboratory 5% to 10% for ECGs that are interpreted by emergency department (ED) physicians and of 10% to 25% for ECGs that are interpreted by EMS personnel. However, studies have also demonstrated that PH-ECG transmission systems can reduce the rate of false-positive activations, because another set of "critical eyes" can review the ECG (usually the on-duty ED physician) before the 4 to 5 member catheterization laboratory team is activated. Various proprietary PH-ECG transmission options currently exist, but their use is by no means universal, because of various technical, financial, and administrative issues.

Dr. Rokos cautioned that bringing patients with STEMI based on an ECG interpreted by paramedics directly from the field to the catheterization laboratory during the regular work day may be "great" for D2B times, but the cardiology team should also understand that significant potential exists for receiving a patient that did not have a STEMI. Thus, the role of the ED remains critical in filtering out inappropriate patients, especially if PH-ECG transmission is not available. The goal for efficient STEMI systems should be a <5% rate of inappropriate activation (red zone), as summarized in Table 1 [Rokos et al. *Am Heart J* 2010].

Table 1. Classification of Appropriate vs Inappropriate Cath Lab Activation.

Appropriate Cath Lab Activation → Ideal
Angiography and PPCI performed
Appropriate Cath Lab Activation → Reasonable

• Angiography without PPCI performed
  • Surgical revascularization indicated
  • Coronary anatomy is not amenable to PPCI intervention
  • 'Unavoidable angiogram' per index ECG and/or clinical scenario as documented by the real-time clinicians
  • No PPCI target-lesion identified but cardiac markers become elevated
• Before angiography, true STEMI per index ECG patient dies suddenly
• Angiography±PPCI for ROSC following witnessed OHCA from a shockable rhythm. Some ROSC patients may deteriorate and die before angiography

Appropriate Cath Lab Activation → Goal is <5% rate
• No angiography performed (Cath Lab activation cancelled by a physician) • Angiography without a PPCI target-lesion identified and normal cardiac markers: • Avoidable angiogram based upon erroneous ECG interpretation • Advanced co-morbidities: Patient is not a PPCI candidate

PPCI=primary percutaneous coronary intervention: ECG=electrocardiogram; ROSC=return of spontaneous recirculation; OHCA=out of hospital cardiac arrest; Classification based on retrospective and multidisciplinary peer-review of all index clinical data; Green zone represents the ideal scenario, yellow zone represents reasonable scenarios, and red zone occurrences should be minimized (<5%).

Lastly, Dr. Rokos stated that the ECG criteria that are used to identify patients who require primary PCI need updating. According to the 2004 American College of Cardiology/American Heart Association (ACC/AHA)

guidelines, STEMI is defined as ST elevation of ≥1 mm in 2 contiguous leads, new (or presumed new) left bundle branch block, or isolated posterior MI. He proposed that the criteria for STEMI should be broadened to include "semi-STEMI"—ST elevation <1 mm but with associated reciprocal changes—and "STEMI-equivalent"—any ECG pattern that lacks classic ST elevation but is associated with an acute coronary occlusion that requires primary PCI (eg, true posterior MI, diffuse inferolateral ST-depression with concomitant ST-elevation in lead aVR, de Winter T-waves [de Winter et al. *N Engl J Med* 2008], and certain cardiac arrest patients who have been resuscitated from a shockable rhythm). Importantly, Dr. Rokos emphasized that all frontline providers should be familiar with various ST-elevation mimics that cause inappropriate activations, including narrow QRS complex (eg, normal early repolarization, pericarditis) and wide/tall QRS complex (eg, ventricularly paced rhythms, left ventricular hypertrophy) rhythms.

Optimal Reperfusion Strategies with Expected Delays

According to the current standard of care for patients with STEMI, fibrinolysis is recommended when transferring the patient will mean a D2B time of >90 minutes (ACC/AHA guidelines) and >120 minutes (European Society of Cardiology guidelines). Even among the best-performing hospitals, the D2B time is not optimal in most cases, said Timothy D. Henry, MD, Minneapolis Heart Institute Foundation, Minneapolis, Minnesota, USA. According to data from the ARG Registry, the D2B time was <90 minutes for only 18% of patients. Overall in the United States, only an estimated 15% to 20% of patients with STEMI who are transferred for primary PCI have a D2B time of <2 hours.

The low rate of optimal time to PCI has a negative effect on outcomes, with the advantage of PCI over fibrinolysis decreasing as the PCI-related delay increases, said Duane S. Pinto, MD, MPH, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA. For every 10-minute delay to PCI, there is a significant reduction in the mortality difference between PCI and fibrinolysis [Nallamothu BK et al. *Am J Cardiol* 2004].

The standard of care for patients with STEMI is based on randomized trials, where D2B times are shorter than in real-world practice. Dr. Pinto and his colleagues reviewed data from the National Registry of Myocardial Infarctions and found that overall, the outcomes were better for patients who were transferred for PCI compared with patients who had onsite fibrinolytic therapy. The differences were not as pronounced when the outcomes for matched patients were compared. When the results were stratified according to time, the patients who benefited the most from transfer-PCI were those for whom the delay was shorter [Pinto DS et al. *Circulation* 2011].

Facilitated PCI was developed in an attempt to improve outcomes for STEMI patients with an expected delay to treatment. Giving fibrinolytic therapy before planned PCI was an excellent idea, said Dr. Henry, but based on data from initial randomized clinical trials, the authors of a key meta-analysis concluded that facilitated PCI provided no benefit [Keeley EC et al. *Lancet* 2006]. Dr. Henry suggested that the results of the meta-analysis need to be reconsidered, based on the newer practice patterns that include earlier and more frequent use of potent thienopyridines and more recent clinical trial data, especially for patients with an expected delay >120 minutes. There was wide variation in the fibrinolytics that were given across the trials in the meta-analysis; the patients were relatively low-risk, treated in a PCI hospital, or transferred only a short distance; and the studies that were done in the era prior to the introduction and use of potent thienopyridines. In addition, the majority of patients were from the ASSENT 4 trial, which used full-dose fibrinolytic, and "early generation antiplatelet and antithrombin regimens [Van de Werf F et al. *Lancet* 2006]. Furthermore, although 45% of patients were managed in a hospital with onsite PCI, none of us would give a fibrinolytic, without high potency thienopyridine, and go to the catheterization laboratory in a PCI hospital," said Dr. Henry. In addition, ASSENT 4 excluded patients with anticipated delays to PCI of >3 hours—"exactly the patients we're concerned about," he added.

More recently, pharmacoinvasive PCI has been studied as an option for patients with an expected delay to PCI. The difference between facilitated PCI and pharmacoinvasive PCI strategies is primarily timing, with facilitated PCI referring to PCI done immediately after fibrinolytic therapy and pharmacoinvasive PCI referring to PCI done within a few hours after fibrinolytic therapy. Recent data support the pharmacoinvasive approach, including both randomized trials that have demonstrated that fibrinolysis, followed by immediate transfer for PCI, has outcomes that are superior to fibrinolysis with standard of care, and registry data that have shown that a pharmacoinvasive approach in patients with delays >120 minutes has outcomes that are similar to patients who present to a PCI center [Di Mario C et al. *Lancet* 2008; Cantor WJ et al. *N Engl J Med* 2009; Bohmer E et al. *J Am Coll Card* 2009; Larson D et al. *Eur J Heart* 2011].

The use of pharmacoinvasive PCI in regional STEMI systems in the United States and Canada has shown that half-dose fibrinolysis, combined with immediate transfer for PCI, may be a safe and effective option for patients with STEMI who have expected delays due to transfer to a hospital with PCI facilities.