
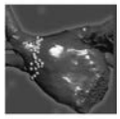
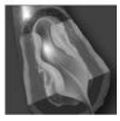

Optimizing primary percutaneous coronary intervention in ST-segment elevation myocardial infarction

"In an ideal world, all patients with [ST-segment elevation myocardial infarction] would be offered immediate primary [percutaneous coronary intervention] given its superiority to fibrinolytic therapy, but geographic and logistical challenges within existing healthcare systems have limited its universal delivery."

KEYWORDS: door-to-balloon time ■ primary percutaneous coronary intervention ■ regionalization ■ ST-segment elevation myocardial infarction

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Primary percutaneous coronary intervention (PCI) is superior to fibrinolytic therapy in ST-segment elevation myocardial infarction (STEMI), but geographic and logistical challenges within existing healthcare systems have limited its universal delivery. Three population-based strategies have emerged to optimize the use of primary PCI, primarily by broadening access to it:

- Standardized prehospital triage protocols, which identify STEMI patients and bypass non-PCI-capable hospitals when a PCI-capable hospital is close by;
- Systematic rapid transfer of STEMI patients from regional non-PCI-capable hospitals to PCI-capable hospitals when appropriate;
- Development of PCI-capable hospitals in areas of need.

In this article, we discuss these strategies and their impact on the construction of effective STEMI systems of care.

Primary percutaneous coronary intervention in ST-segment elevation myocardial infarction

Early reperfusion of an infarct-related artery in acute STEMI improves survival. Primary PCI is the preferred reperfusion strategy in STEMI if it can be performed rapidly and by experienced operators [1,2]. In an ideal world, all patients with STEMI would be offered immediate primary PCI given its superiority to fibrinolytic therapy, but geographic and logistical challenges within existing healthcare systems have limited its universal delivery [3]. The construction of effective STEMI systems of care, which optimize timely patient access to primary PCI without prohibitive delay in reperfusion time, is a complex and interdisciplinary process that raises several challenges and opportunities.

"Despite its overall superiority, the benefits of primary [percutaneous coronary intervention] are not equivalent for all patients."

Fibrinolysis improves survival in STEMI patients compared with placebo if given less than 12 h after symptom onset, but is limited by the risk of major hemorrhage (2–3%), individual patient contraindications (20%), inadequate Thrombolysis In Myocardial Infarction grade 3 (TIMI-3) flow in up to 30–40% of patients and poor efficacy in cardiogenic shock [4,5]. The Primary Angioplasty in Myocardial Infarction (PAMI) trial was among the first to demonstrate that primary angioplasty is more effective than fibrinolytic therapy – specifically, in reducing an overall combined end point of death, non-fatal reinfarction and stroke [6]. One of the largest trials, the Danish Multicenter Randomized Study on Fibrinolytic Therapy versus Acute Coronary Angioplasty in Acute Myocardial Infarction (DANAMI)-2 trial, was discontinued earlier than planned owing to a significant reduction in a similar combined end point in the primary PCI patients [7]. A meta-analysis of 23 randomized trials comparing primary PCI with fibrinolysis demonstrates that primary PCI improves TIMI-3 flow and reduces reinfarction, repeat revascularization, intracranial hemorrhage and, most importantly, death [1].

Despite its overall superiority, the benefits of primary PCI are not equivalent for all patients. In the DANAMI-2 trial, the mortality benefit of primary PCI was observed only in the

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25% of patients in the highest-risk subgroup (with a TIMI risk score of ≥5). Furthermore, patients who presented early with a symptom onset time of less than 3 h had similar outcomes with either primary PCI or fibrinolysis in the Primary Angioplasty in Patients Transferred from General Community Hospitals to Specialized Percutaneous Transluminal Coronary Angioplasty Units With or Without Emergency Thrombolysis (PRAGUE)-2 trial [8]. Understanding which patients are most likely to benefit from primary PCI is an important consideration when designing STEMI systems of care that focus on optimizing outcomes across populations of patients.

"Understanding which patients are most likely to benefit from primary [percutaneous coronary intervention] is an important consideration when designing [ST-segment elevation myocardial infarction] systems of care that focus on optimizing outcomes across populations of patients."

Another factor to consider is that results observed in clinical trials do not always reflect outcomes observed in real-world clinical practice. Some registries using a broader spectrum of patients, interventional cardiology teams and hospital systems have not consistently reproduced the mortality benefit of primary PCI over fibrinolysis [9,10]. This may reflect the more liberal use of rescue PCI, clopidogrel and enoxaparin in contemporary practice than that used in the randomized clinical trials [11,12]. This may also reflect longer times to reperfusion with primary PCI observed in actual practice that could diminish its overall benefits, especially in high-risk subgroups such as transfer patients. Door-to-balloon times of 3 h or more are not infrequently observed in patients who are transferred for primary PCI, and fewer than 10% of these transferred patients have a first door-to-balloon time of less than 90 min, as recommended by American College of Cardiology (ACC)/American Heart Association (AHA) STEMI guidelines [13,14].

Patient access to primary percutaneous coronary intervention

Limited resources also affect access to primary PCI for many patients. Only 25% of the nation's hospitals are capable of performing primary PCI, and more than 40 million adults in the USA do not live within 1 h of a PCI-capable hospital [15,16]. In addition, the lack of well-organized, regionalized prehospital systems in some communities limits expeditious paramedic triage of patients to PCI-capable hospitals, particularly in rural areas. Poorly integrated transfer systems of care have historically limited the number of patients who can be rapidly transported from non-PCI-capable hospitals for primary PCI within the recommended 90-min door-to-balloon window. Finally, even at PCI-capable hospitals, the use of primary PCI is not universal. More than a third of PCI-capable hospitals in the USA also report using fibrinolytic therapy, which may impact on their ability to optimally perform PCI [17,18].

Strategies to optimize the use of primary percutaneous coronary intervention

Three population-based strategies have emerged aiming to optimize the use of primary PCI, primarily by broadening access to it: first, standardized prehospital triage protocols, which identify STEMI patients and bypass non-PCI-capable hospitals when a PCI-capable hospital is close by; second, systematic rapid transfer of STEMI patients from regional non-PCI-capable hospitals to PCI-capable hospitals when appropriate; and third, development of PCI-capable hospitals in areas of need.

Prehospital transport protocols

Prehospital systems have been identified as a key component to improving the use of primary PCI. Prehospital ECGs, either interpreted by emergency medical services (EMS) or electronically transmitted to an emergency medicine physician, are a highly effective method of reducing the time from first medical contact to reperfusion [19]. Prehospital triage by EMS of patients with STEMI bypassing non-PCI-capable hospitals for PCI-capable hospitals reduces delays by nearly half of that achieved by interhospital transfers from the emergency department [20]. Each community has variable features that make implementation of effective prehospital systems uniquely challenging, and standardization and monitoring of EMS practice in dense urban areas or remote rural areas requires substantial oversight and cooperation by emergency medical personnel and hospital systems.

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Prehospital triage is only effective if patients use EMS. However, less than 50% of all STEMI patients use EMS, and community-based and patient-specific interventions to increase awareness of the symptoms of myocardial infarction have not improved delays in seeking medical care [21–23]. Given that the greatest opportunity for mortality reduction is in the first 3 h after symptom onset, and given that the average time from symptom onset to medical contact is 133 min, improving vulnerable patient awareness and utilization of EMS marks a key component to improving STEMI systems of care [24].

Regional interhospital transfer systems

Development of systematic emergency transfer systems from non-PCI-capable hospitals to PCI-capable hospitals has also been identified as a strategy to optimize access to timely primary PCI. Several 'hub-and-spoke' STEMI referral models have been developed to rapidly integrate care between non-PCI-capable and PCI-capable hospitals. Key components of such systems include simplified activation systems, standardized protocols, customized transfer plans for each referring hospital, in-depth training programs and feedback for the referring hospital and EMS providers and support systems for patients and families [25]. In one regional network, this has resulted in rapid transport of patients – even up to 240 miles away – with no differences in in-hospital (4.2%), 30-day (4.9%) and 1-year (7.2%) mortality between patients who presented to the non-PCI-capable or PCI-capable hospitals [26].

Given a potential risk of delays to primary PCI, many transfer systems have used combination approaches that include fibrinolytic therapy. For the most part, facilitated PCI – routine emergency PCI carried out immediately after pharmacologic reperfusion – does not improve outcomes compared with primary PCI, but instead increases major bleeding, nonfatal myocardial infarction, stroke and death [27]. On the other hand, routine but nonemergency PCI following fibrinolysis (i.e., the pharmacoinvasive approach) has shown improvement in reinfarction, recurrent ischemia and heart failure without increased major bleeding when compared with fibrinolytic therapy and routine care [28]. A pharmacoinvasive approach may prove to be a viable therapeutic option in many regions where primary PCI is simply not an option.

Expanding primary percutaneous coronary intervention-capable hospitals

Expanding the number of hospitals that perform primary PCI is another potential way to increase access to it. Early studies suggested that hospitals with lower volumes of primary PCI had higher in-hospital mortality [29]. Furthermore, the historical tie between requirements for on-site cardiac surgery and the development of PCI restricted its use to high-volume specialized centers. However, recent data have questioned whether there are significant differences in outcomes between low- and high-volume PCI hospitals [30]. In addition, a growing body of evidence suggests that expanding primary PCI to hospitals without on-site cardiac surgery may be safe and effective if carried out with adequate supervision and quality assurances [31]. With that said, challenges remain as to whether the allocation of community resources to develop new PCI-capable hospitals will really improve access for patients or simply lead to duplicative services [32].

Future persepctive

Introduction of STEMI systems of care continues to raise substantial challenges at the hospital, regional and national level. In addition to the practical limitations previously described, economic and political barriers exist. Although not insurmountable, these barriers contribute to the complexity of the process. Reimbursement for services provided by EMS, non-PCI-capable hospitals and PCI-capable hospitals need to be fairly allocated according to the resources invested. Regional transportation systems need to be developed and then maintained to optimize prehospital triage and to expedite interhospital transport. Standard expectations and accountability metrics for non-PCI-capable and PCI-capable hospitals will need to be clearly defined, monitored and made available to the public and to payers. Better methods for improving public and patient awareness are needed to reduce delays to medical contact.

> *"The ultimate goal for [ST-segment elevation myocardial infarction] systems of care is to improve patient outcomes across populations by using standardized, well-organized and rapidly implemented approaches to providing evidence-based care."*

Although daunting, many integrated models for regional STEMI systems of care are emerging. A statewide system in North Carolina, USA, the Reperfusion of Acute Myocardial Infarction in North Carolina Emergency Departments (RACE), is at the forefront of the AHA: Mission Lifeline program. Its experiences and approaches are being used to develop similar STEMI systems of care across the country. Additional data from newer regional pilot programs will provide even more insights. Each system will need to be adapted to that region's unique demographic, economic, geographic, political and professional challenges.

The ultimate goal for STEMI systems of care is to improve patient outcomes across populations by using standardized, well-organized and rapidly implemented approaches to providing evidence-based care. Implementation of these programs is a key step towards optimization of quality care delivery and will ultimately deliver on the great promise of optimizing primary PCI in STEMI.

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