

Reperfusion for all: reimagining STEMI care in low and middle income countries



Thomas Alexander^{1*}, MD, DM, FACC; Brahmajee K. Nallamothe², MD, MPH, FAHA, FACC

1. Kovai Medical Centre and Hospital, Coimbatore, India; 2. University of Michigan, Cardiovascular Center SPC, Ann Arbor, MI, USA

The development and use of reperfusion therapy in ST-elevation myocardial infarction (STEMI) has been one of the great achievements of modern medicine in the United States of America and Western Europe. In the 1960s, one-year mortality rates after STEMI approached 30% in these countries. However, their numbers are dramatically different today: under ideal circumstances, reperfusion therapy – in combination with cardiac care units and other evidence-based treatments – has now lowered one-year mortality rates after STEMI to well under 10% in clinical trials. The goal of the last two decades in these countries has been to translate these outcomes under “ideal circumstances” into “real-world” practice.

Article, see page 109

The article by Dharma et al¹ in this issue of AsiaIntervention turns the spotlight on STEMI systems of care in this process, focusing on the importance of delivering 24/7 reperfusion therapy. Most importantly, this retrospective analysis using the Jakarta Acute Coronary Syndrome (JAC) registry shows what is possible when adequate facilities and staffing exist within a regional STEMI network. Not only were outstanding outcomes achieved in STEMI patients at this large centre in Indonesia, with the one-year mortality rate of approximately 10% seen in the United States of America and Western Europe, but also the similarity of acute and one-year results between STEMI patients admitted during regular hours versus off-duty hours demonstrates that high performance is achievable even in challenging situations. However, as rightly emphasised by the authors, this has been achieved in an island of excellence where the catheterisation laboratory staff and “on-duty” cardiologists stay within the hospital during “off-duty” hours.

This is a luxury seldom available in most countries across Asia and perhaps the world. It is a testament to the dedication of this institution, these physicians and other healthcare providers.

What about the rest of the world which may practise in a more resource-constrained environment where PCI is not always readily available? How can the benefits of reperfusion therapy be extended to their STEMI patients, beyond the walls of these islands of excellence? These questions have implications not only for us but also for the National Cardiovascular Center in Jakarta and other large centres in Asia which have begun reporting outstanding outcomes. Of the 5,237 patients within the JAC registry during this period, for instance, only 1,126 patients were included in the analysis since the vast majority (78%) of the patients did not receive reperfusion due to late presentation. This raises the larger question facing STEMI systems of care today, particularly in low and middle income countries (LMIC): how do we extend reperfusion therapy when primary PCI is not an option. To tackle this issue requires considerable thought and urgent action.

While there are no accurate estimates of STEMI in LMIC, it is possible that there could be upwards of three to four million cases per year. The reduction of system delay in the developed countries has led to a significant drop in mortality in recent years; however, a further reduction below 60 minutes may have more limited mortality benefit². Detailed analysis of this has resulted in more effort being made to reduce the “non-system” delays associated with STEMI patients arriving too late for reperfusion therapy as being the way to improve outcomes further and reduce the total ischaemia time.

At first, it might seem that the challenge for most STEMI systems of care in LMIC in Asia and Africa is first to grasp the “low-hanging fruit” of addressing system delays within hospitals and then quickly to move on to developing pre-hospital systems. However, with the knowledge we have currently, it may make sense to take a different approach. We advocate that it may be prudent for these countries to address the issues of “non-system” and “system” delays

*Corresponding author: Kovai Medical Centre and Hospital, PB 3209, Avanashi Road, Coimbatore, 641014, India.

E-mail: tomalex41@gmail.com

simultaneously, while attempting to launch a STEMI system of care. Paradoxically, the lack of any system in many of these countries could help in developing a composite approach by preventing old biases and deeply seated special interests in the status quo. In addition, a deeper inspection of the available resources in many of these regions shows that most larger countries already have the building blocks of a system that could take into account their limited resources, both in terms of infrastructure and manpower.

To develop a STEMI system of care in LMIC, for example, it is important to understand first that primary PCI as the sole mode of reperfusion is not feasible. The CREATE registry from India³, a prospective registry study of 12,405 STEMI patients from 89 centres from 10 regions and 50 cities in India over a four-year period ending in 2005, showed that 58.5% received thrombolytic therapy and only 8% primary PCI. The China PEACE-Retrospective AMI Study⁴, which again was based on hospital data, analysed 13,815 patients treated for STEMI at 162 hospitals. Greater use of primary PCI in patients eligible for revascularisation was shown (from 10.2% in 2001 to 27.6% in 2011); however, the percentage of patients who underwent no reperfusion remained low and stagnant at around 55%. We feel the situation in other LMIC is likely to be similar and will remain unchanged if primary PCI becomes the ultimate goal.

In developing a STEMI system of care in LMIC, the STEMI INDIA Model⁵ stands as a stark alternative. STEMI INDIA utilised current evidence on the utility of the pharmacoinvasive strategy, including recent data from the STREAM (Strategic Reperfusion

Early After Myocardial infarction) trial⁶ and STEP-PAMI trial⁷ in India showing that the pharmacoinvasive strategy compared well with primary PCI when delays with primary PCI were anticipated. Based on this evidence and the success of the Kovai Erode Pilot STEMI Study⁸, STEMI INDIA proposes that STEMI management in India adopts the dual strategy of combining fibrinolysis with routine early PCI to develop a coherent framework for developing a STEMI system of care in LMIC.

The architecture of this system is based on a hub and spoke model, with each hub hospital connected to multiple spoke hospitals and the unit being called a STEMI cluster. Examples of this exist and, in fact, this appears to be what has already taken place in Jakarta through the National Cardiovascular Center. The other important component of these types of programme is the use of technology to link centres. For example, STEMI INDIA has developed a multifunctional STEMI device⁹ which not only records ECG, but also serves as a low-cost monitoring and data entry device. Thus, a 12-lead ECG can be done at the point of first contact – home, ambulance or hospital – and transmitted in real time from the device to a handheld device with the “on-call” cardiologist in the hub hospital for confirmation and early initiation of STEMI treatment. Addressing areas of delay before arrival into the system and within the system can be attempted simultaneously. Shown below are the various areas of non-system and system delays that we have identified in the STEMI INDIA system of care, and our attempts to address them (Figure 1).

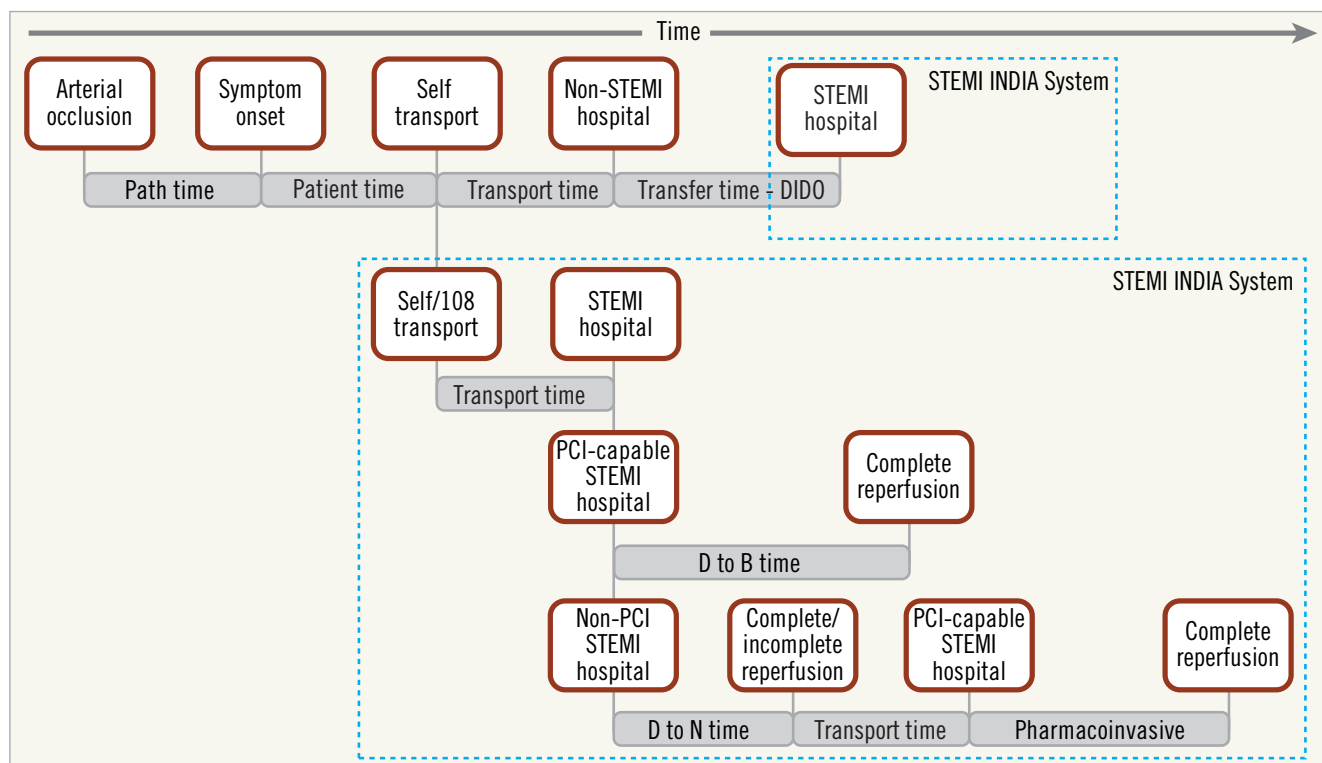


Figure 1. Non-system and system delays identified in the STEMI INDIA system of care. D to B: door to balloon; D to N: door to needle; DIDO: door in-door out

Some of the non-system delays can be overcome by public education, using pre-hospital ECG as in the STEMI INDIA project, and accrediting and publicising “STEMI hospitals”. This will ensure that patients do not lose time when they are admitted to “non-STEMI” hospitals and then have to be transferred to another hospital for STEMI management (beyond PCI services).

Pre-hospital fibrinolysis has been shown to be very effective and shows a significant increase in rates of aborted MI¹⁰. Traditionally, this term has been used to indicate fibrinolysis within the ambulance, as practised in many STEMI systems of care in Europe¹¹. STEMI INDIA has broadened the definition of “pre-hospital fibrinolysis” and coined a new phrase – pre-coronary care unit fibrinolysis (Pre-CCU Lysis). This will encompass any facility that does not have a coronary care unit and historically has not provided fibrinolysis in STEMI patients, such as primary or rural health centres, or, in certain locations, designated private clinics. These facilities would have trained doctors with third-generation fibrinolytics. They would also have “STEMI devices” capable of recording ECG and transmitting the ECG to “STEMI centres” for confirmation of the diagnosis before initiating fibrinolysis and monitoring patients until they are transported to a CCU.

Dharma et al are to be congratulated on showing the world what is possible within the walls of a modern Asian centre dedicated to providing high-quality performance in primary PCI. In an environment of resource constraints with a burgeoning population of patients in LMIC with coronary artery disease and STEMI, however, we need to move beyond these “islands of excellence” to ensure that, through innovation, we can deliver reperfusion for all.

Conflict of interest statement

The authors have no conflicts of interest to declare.

References

1. Dharma S, Sukmawan R, Siswanto BB, Andriantoro H, Dakota I, Sunil V, Rao S. One-year mortality of primary angioplasty for acute myocardial infarction during regular working hours versus off-hours. *AsiaIntervention*. 2015;1:109-15
2. Flynn A, Moscucci M, Share D, Smith D, LaLonde T, Changezi H, Riba A, Gurm HS. Trends in door-to-balloon time and mortality in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Arch Intern Med*. 2010;170:1842-9.
3. Xavier D, Pais P, Devereaux PJ, Xie C, Prabhakaran D, Reddy KS, Gupta R, Joshi P, Kerkar P, Thanikachalam S, Haridas KK, Jaison TM, Naik S, Maity AK, Yusuf S; CREATE registry investigators. Treatment and outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data. *Lancet*. 2008;371:1435-42.
4. Li J, Li X, Wang Q, Hu S, Wang Y, Masoudi FA, Spertus JA, Krumholz HM, Jiang L; China PEACE Collaborative Group. ST-segment elevation myocardial infarction in China from 2001 to 2011 (the China PEACE-Retrospective Acute Myocardial Infarction Study): a retrospective analysis of hospital data. *Lancet*. 2015;385:441-51.
5. Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC, Nanas J, Arntz HR, Halvorsen S, Huber K, Grajek S, Fresco C, Bluhmki E, Regelin A, Vandenberghe K, Bogaerts K, Van de Werf F; STREAM Investigative Team. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. *N Engl J Med*. 2013;368:1379-87.
6. Victor SM, Subban V, Alexander T, Bahuleyan CG, Srinivas A, Selvamani S, Mulasari AS. A prospective, observational, multicentre study comparing tenecteplase facilitated PCI versus primary PCI in Indian patients with STEMI (STEPP-AMI). *Open Heart*. 2014;1:e000133.
7. Alexander T, Mulasari A, Narula J. Developing a STEMI system of care for low- and middle-income countries: the STEMI-India model. *Glob Heart*. 2014;9:419-23.
8. Alexander T, Mehta S, Mulasari A, Nallamothu BK. Systems of care for ST-elevation myocardial infarction in India. *Heart*. 2012;98:15-7.
9. Alexander T, Victor SM, Mulasari AS, Veerasekar G, Subramaniam K, Nallamothu BK; TN-STEMI Programme Investigators. Protocol for a prospective, controlled study of assertive and timely reperfusion for patients with ST-segment elevation myocardial infarction in Tamil Nadu: the TN-STEMI programme. *BMJ Open*. 2013;3:e003850.
10. Lamfers EJ, Schut A, Hertzberger DP, Hooghoudt TE, Stolwijk PW, Boersma E, Simoons ML, Verheugt FW. Prehospital versus hospital fibrinolytic therapy using automated versus cardiologist electrocardiographic diagnosis of myocardial infarction: abortion of myocardial infarction and unjustified fibrinolytic therapy. *Am Heart J*. 2004;147:509-15.
11. Hanssen M, Cottin Y, Khalife K, Hammer L, Goldstein P, Puymirat E, Mulak G, Drouet E, Pace B, Schultz E, Bataille V, Ferrières J, Simon T, Danchin N; FAST-MI 2010 Investigators. French Registry on Acute ST-elevation and non ST-elevation Myocardial Infarction 2010. FAST-MI 2010. *Heart*. 2012;98:699-705.