Components and determinants of therapeutic delay in patients with acute ST-elevation myocardial infarction: A tertiary care hospital-based study

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Background: **Delayed reperfusion is associated with worse outcomes in ST-segment elevation myocardial infarction (STEMI). This study was conducted to assess the components and determinants of therapeutic delay in STEMI patients of our state.**

Methods: **This study included consecutive patients of STEMI admitted to the coronary care units of two tertiary care hospitals in Srinagar, between 2012 and 2015. Various components of treatment delay including the patient's decision to delay, referral delay, transportation delay, prehospital delay, and door-to-needle time were calculated. Factors associated with delayed treatment and clinico-demographic correlates of late presentation were identified.**

Results: **During a period of 3 years, 523 patients (mean age, 57.6 þ 10.5 years) were enrolled in this study. Thrombolysis was administered to 60.2% patients, while 39.8% of patients could not be thrombolysed because of late presentation. The median treatment delay was 250 minutes. Prehospital delay constituted about 83.8% of total treatment delay. Patient's decision to delay, referral delay, and transport delay constituted 59%, 16%, and 25% of prehospital delay, respectively. Median door-to-needle time was 40 minutes. Residence in rural areas [odds ratio (OR), 2.35; 95% confidence interval (CI), 1.60–3.46], absence of prior *coronary artery disease* (OR, 1.54; 95% CI, 1.00–2.39), and negative family history of *coronary artery disease* (OR; 2.76; 95% CI, 1.86–4.10), were identified as independent predictors of delayed presentation ($p < 0.001$). Interestingly, 44.7% of the patients presented late due to misdiagnosis by local healthcare providers.**

Conclusion: **The standard of STEMI management in our state is far from ideal, and calls for a lot of improvement. Major efforts to reduce prehospital and in-hospital treatment delays are urgently needed.**

Keywords: Coronary artery disease, Late presentation, Prehospital delay, ST-elevation myocardial infarction, Treatment delay

Disclosure: Authors have nothing to disclose with regard to commercial support.

Received 3 March 2016; revised 30 May 2016; accepted 3 June 2016. Available online 16 June 2016

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Peer review under responsibility of King Saud University.
URL: www.ksu.edu.sa
http://dx.doi.org/10.1016/j.jsha.2016.06.001

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Introduction

India has become the ''global capital'' of coronary artery disease (CAD) contributing to 60% of the global burden of CAD with about 64 million deaths attributable to CAD annually [1]. ST-elevation myocardial infarction (STEMI) is one of the most lethal presentations of CAD. Myocardial damage caused by acute STEMI is a time-dependent process. Timely reperfusion of ischemic myocardium using thrombolysis or primary percutaneous coronary intervention forms the cornerstone of acute management of STEMI; reducing infarct size, preserving left ventricular function, and improving short- and long-term outcomes [2].

Although primary percutaneous coronary intervention is currently the preferred modality of reperfusion in STEMI [3], thrombolysis still remains the most common reperfusion method used in our country due to logistic and financial constraints. Benefits from fibrinolytic therapy diminish on a minute-to-minute basis, with the greatest effect occurring in those patients who receive it within the 1st 2 hours of symptom onset [4–7]. It has been estimated that for every 30 minutes of delay in reperfusion therapy, the patient's life is shortened by ~1 year [8]. Despite significant efforts to improve the standard of care in STEMI patients over the past few decades, it is estimated that up to one-third of eligible patients with STEMI still do not receive timely reperfusion [2]. A number of factors determine the delay in starting thrombolytic therapy such as contacting emergency medical services (EMS), transporting the patient, admitting the patient in the emergency department, initial assessment of the patient including obtaining and interpreting the electrocardiogram, decision making, and delay in preparing the drug.

In scientific literature, there is very limited data about the different components and determinants of treatment delay, in developing countries like India. The present study was conducted with an aim of assessing various components of the delay to thrombolytic treatment for patients with acute STEMI, and to determine the demographic and clinical characteristics of the patients related to these delays. We also studied the reasons for late presentation in STEMI patients who had not received thrombolytic therapy.

Materials and methods

This observational study was conducted in two tertiary care hospitals of Srinagar, Jammu, and Kashmir, India, with Coronary Care Units (CCUs), namely Shri Maharaja Hari Singh Hospital and Sher-i-Kashmir Institute of Medical Sciences, between 2012 and 2015. All consecutive patients admitted in the CCUs of these hospitals during this period with a final diagnosis of acute STEMI who fulfilled the eligibility criteria (described below) were enrolled in this study.

Abbreviations

CAD	coronary artery disease
STEMI	ST-elevation myocardial infarction

Inclusion criteria

Inclusion criteria included patients who (1) had no contraindication to thrombolytic therapy except late presentation (>12 hours); (2) developed acute STEMI outside of the hospital; (3) had a known time of symptom onset; and (4) had not developed spontaneous thrombolysis (resolution of chest pain and ST-segment elevation without pharmacological thrombolysis).

In all the patients, a detailed medical history was taken, especially for cardiovascular disease (angina, transient ischemic attack, stroke, and peripheral vascular disease), hypertension, dyslipidemia, diabetes mellitus, smoking, prior CAD, and family history of CAD. We recorded the specific time of onset of symptoms, time of seeking first consultation from a pharmacist or healthcare professional (at district hospital, community health center, medical store, or private clinic), time of arrival at the tertiary care hospitals, and time of initiation of thrombolytic therapy (in patients who received thrombolysis). We reviewed all the clinical records of patients from the point of first medical contact, including discharge summaries and referral documents. The initial diagnostic evaluation, clinical impression made by the local healthcare providers, and the treatment that was provided to each patient before referral to our hospitals was recorded. We then calculated the various components of treatment delay including: (1) patient's decision delay (time of onset of symptoms to time of seeking 1st medical consultation); (2) referral delay (time of 1st medical consultation to time of referral to a tertiary care hospital); (3) transportation delay (time of referral to time of arrival at the tertiary care hospital); (4) total prehospital delay (time of onset of symptoms to time of arrival at the tertiary care hospital); (5) door-to-needle time (time of arrival at the tertiary care hospital to time of administration of thrombolysis); and (5) total treatment delay

(time of onset of symptoms to time of administration of thrombolysis).

Next, we determined the number and percentage of individuals who presented to the tertiary care hospitals in <6 hours, 6–12 hours, and >12 hours of symptom onset. We then attempted to identify factors associated with treatment delay in these three groups. Among late presenters (>12 hours), we determined the number and percentage of individuals who sought consultation from a healthcare professional in <6 hours, 6–12 hours, 12–24 hours, and >24 hours of symptom onset. Further, we assessed the reasons and their frequency resulting in late presentation of these patients.

Statistical analysis

Statistical analysis was performed using SPSS software package (version 20.0; SPSS Inc., Chicago, IL, USA). All continuous variables were expressed as mean ± standard deviation, and categorical variables were reported as frequency and percentages. Differences in the distribution of characteristics in the patients, classified according to the extent of prehospital delay, were examined using the Chi-square test for the categorical variables, while the *t* test was employed for continuous variables. A multivariate logistic regression analysis was performed to identify the sociodemographic and clinical characteristics of the patients contributing independently to a prehospital delay of >6 hours. Statistical significance was defined as a p value of <0.05.

Results

During a period of 3 years, 523 consecutive patients with acute STEMI admitted to CCUs of Shri Maharaja Hari Singh Hospital and Sher-i-Kashmir Institute of Medical Sciences Hospitals were enrolled in this study.

Patient characteristics

The mean age of our patient cohort was 57.6 ± 10.5 years with a range of 32–80 years. Of the total 523 patients, 80.3% (420) were men and only 19.7% (103) were women. Of the patients, 65.4% (342) belonged to a rural area and 34.6% (181) to an urban area. The most common risk factors in our patients were hypertension (67.3%) and smoking (64.1%), followed by diabetes mellitus (36.9%), family history of CAD (31.7%), dyslipidemia (28.3%), and prior CAD (22.4%). Thrombolysis was administered to 60.2% (315) of patients, while the remaining 39.8% did not receive any thrombolytic therapy because of late presentation to tertiary care centers.

Components of prehospital, in-hospital, and total treatment delays

The overall median time between the onset of symptoms and treatment was 250 minutes (range, 60–920 minutes). Prehospital delay (median, 210 minutes) constituted ~83.8% of the total treatment delay. Patient's decision delay (median, 100 minutes) constituted 59% of the prehospital delay, while referral delay (median, 40 minutes) constituted 16% and transport delay (median, 60 minutes) constituted 25% of the prehospital delay. Median door-to-needle time was 40 minutes and contributed to 16% of the total treatment delay (Fig. 1).

Frequency and characteristics of patients with acute STEMI according to prehospital delay

Among all 523 patients with STEMI, 50.3% presented to tertiary care centers within 6 hours,

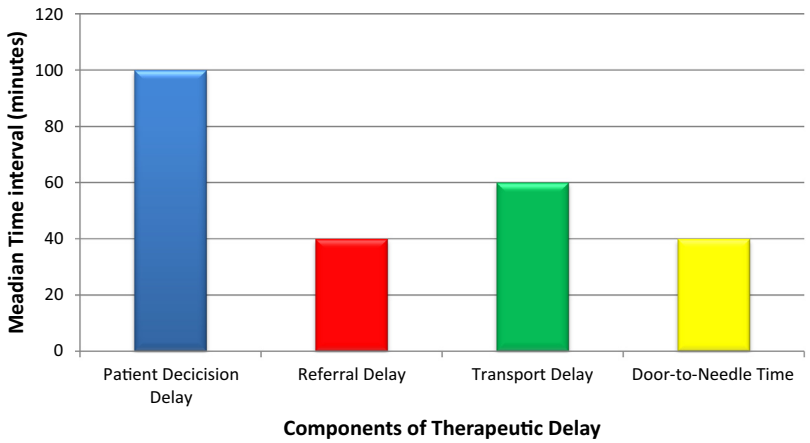

Figure 1. Components of prehospital, in-hospital, and total treatment delays.

9.9% between 6 hours and 12 hours, and the remaining 39.8% were late presenters (>12 hours). On univariate correlation analysis of patient characteristics of these three groups, we found that older age ($p = 0.001$), residence in rural areas ($p < 0.0001$), lack of prior history of CAD ($p = 0.022$), absence of dyslipidemia ($p = 0.010$), and no family history of CAD ($p = 0.0001$) were significantly associated with a prolonged prehospital delay (Table 1).

Predictors of prolonged prehospital delay in multivariate logistic regression analysis

Multivariate logistic regression analysis was performed to identify the sociodemographic and clinical characteristics of the patients that independently predicted prolonged prehospital delay (>6 hours). Variables that showed a significant correlation on univariate analysis, i.e., age, residence, dyslipidemia, past history of CAD, and family history of CAD, were kept as predictors. The results showed that the patients who lived in rural areas [odds ratio (OR), 2.35; 95% confidence interval (CI), 1.60–3.46], had no prior CAD (OR, 1.54; 95% CI, 1.00–2.39), and had a negative family history of CAD (OR, 2.76; 95% CI, 1.86–4.10), were significantly more likely to have a prolonged prehospital delay ($p < 0.001$).

Categorization of late presenters according to time of first medical contact and reasons of late presentation (>12 hours) to tertiary care hospital

Among late presenters admitted to our tertiary care centers only 44.7% of the patients sought first medical consultation within 12 hours and the remaining 55.3% after 12 hours of symptom onset

Table 1. Frequency and characteristics of patients with acute ST-elevation myocardial infarction according to prehospital delay.

Characteristics	Prehospital delay			
	<6 h *N* (%)	6–12 h *N* (%)	>12 h *N* (%)	*p*
Age, mean ± SD (y)	56.02 ± 10.32	57.98 ± 9.74	59.64 ± 10.62	0.001
Sex				
Male	218 (82.9)	40 (76.9)	162 (77.9)	0.323
Female	45 (17.1)	12 (23.1)	46 (22.1)	
Residence				
Rural	148 (56.3)	39 (75)	155 (74.5)	0.0001
Urban	115 (43.7)	13 (25)	53 (25.5)	
Hypertension	81 (68.8)	31 (59.6)	141 (67.8)	0.429
DM	95 (36.1)	22 (42.3)	76 (36.5)	0.693
Smoking	172 (65.4)	30 (57.7)	133 (63.9)	0.571
Dyslipidemia	67 (25.5)	24 (46.2)	57 (27.4)	0.010
Family history of CAD	111 (42.2)	14 (26.9)	41 (19.7)	0.0001
Prior CAD	48 (18.2)	18 (34.6)	51 (24.5)	0.022

CAD = coronary artery disease; DM = diabetes mellitus; SD = standard deviation.

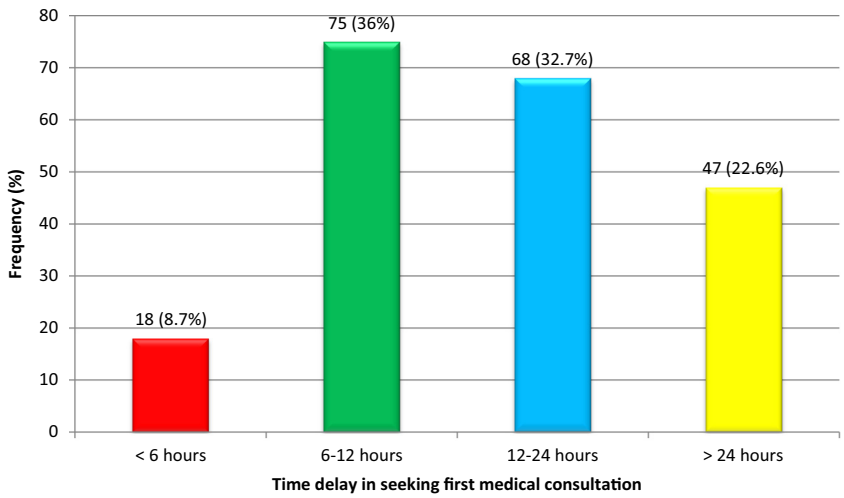

Figure 2. Distribution of patients according to time delay in seeking first medical consultation.

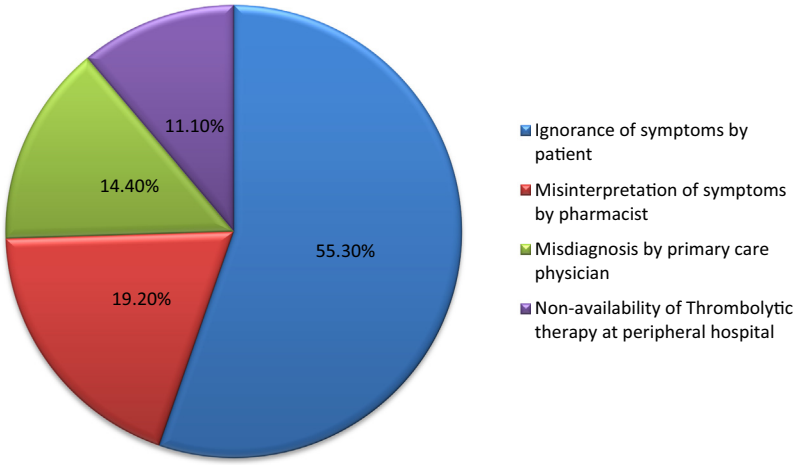

Figure 3. Categorization of reasons for late presentation beyond 12 hours of symptom onset.

(Fig. 2). Late medical attention seekers did so because of ignorance of symptoms by themselves and self-medication. The main reason of therapeutic delay among those who presented to a healthcare provider within 12 hours was misinterpretation of their symptoms by a pharmacist or misdiagnosis by primary care physician (Fig. 3).

Discussion

The main findings of our study were as follows. (1) Nearly 40% of our STEMI patients were ineligible for thrombolytic therapy due to late presentation to our hospitals. (2) Prehospital delay was the major contributor of delayed treatment, contributing to 83.8% of the total treatment delay. Patient's decision to delay constituted 59%, while transport and referral delays constituted 25% and 16% of the prehospital delay, respectively. (3) Residence in rural areas, absence of prior CAD, and negative family history of CAD were independent predictors of prolonged prehospital delay. (4) Nearly half (44.7%) of the patients presenting late to our hospitals had in fact sought a medical consultation within 12 hours of symptom onset. Misinterpretation of the symptoms by local pharmacists or physicians was the major reason of late presentation in these patients.

''Time is muscle'' is a well-established dictum in the management of STEMI. The risk of 1-year mortality is increased by 7.5% for each 30-minute delay in treatment [9]. Early patient presentation, rapid diagnosis, and early reperfusion constitute the pillars of success in STEMI management. Although the importance of prompt reperfusion in STEMI management cannot be over emphasized, it is appalling to know from global registries that up to one-third of eligible patients with STEMI do not receive timely reperfusion therapy [2]. As regards the mode of reperfusion, primary percutaneous coronary intervention (PCI) has established its unequivocal superiority over thrombolysis, both in terms of achieving rapid and sustained patency of the infarct-related artery in a lesser time-dependent fashion as well as minimizing bleeding complications [3,9]. However, recent data suggest that <10% of STEMI patients in India are reperfused with primary PCI [10]. Limited availability of regional centers of excellence, financial constraints, logistic and infrastructural difficulties, poor ambulance services, traffic congestion, and lack of public awareness and education are the major hurdles in routine implementation of this strategy in countries like India. Thus, thombolysis remains the most commonly used reperfusion modality for STEMI patients in our country. In contrast to relative time-independence of primary PCI, successful reperfusion with thrombolysis is highly time dependent. Trials on fibrinolytic therapy have documented benefits of 65 lives, 37 lives, 26 lives, and 29 lives saved per 1000 treated patients in the 0–1-, 1–2-, 2–3-, and 3–6-hour intervals, respectively [11]. The greatest benefit occurred in those patients treated within 1 hour of symptom onset, with a sharp drop off after 3 hours [12]. Studies on late presenters have shown that thrombolysis is of no benefit after 12 hours of symptom onset and may be potentially harmful in elderly patients, in whom it increases the risk of cardiac rupture [13,14]. Thus, timeliness of reperfusion assumes utmost importance in the efficient management of STEMI, especially when thrombolysis is chosen as the mode of reperfusion. The goal of reperfusing STEMI patients within the 1st 2–3 hours is, however, achieved in a minority of patients, even

in developed countries, and there is a considerable gap between recommended guidelines and real-world clinical practice. In recent years, considerable attention has been given to devise strategies that minimize pre- and in-hospital treatment delays in STEMI patients. Expansion of EMS services, quick EMS dispatch, on-site electrocardiogram, prehospital thrombolysis, rapid interhospital transfer, prehospital activation of a *catheterization laboratory* team, and shortening of door-to-device time are some of the strategies that have been shown to reduce treatment delays in Western countries. The situation is somewhat different in developing countries. As far as India is concerned, the most comprehensive data about contemporary trends in STEMI patients come from CREATE, a large clinical registry of acute coronary syndrome patients from 89 large hospitals in 10 regions and cities across India [10]. We shall discuss the findings of our study in the context of data from this registry as well as other data from various developed and developing countries.

The mean age of our patients was 57.6 ± 10.5 years. This is consistent with previous studies, suggesting that CAD occurs a decade or more earlier in Indians when compared with patients from developed countries [10,15]. The median prehospital delay in our study was 210 minutes. It was considerably lower than the delay found in the CREATE registry (300 minutes), but still significantly more than delays reported in Western registries (128–170 minutes) [10,16–19]. Furthermore, only 50.3% patients presented within 6 hours of symptom onset, while 49.7% of patients presented after 6 hours. In a study from Beijing, Song et al. [20] reported a delay of >6 hours in 20.3% patients, while Khan et al. [21] from Pakistan reported that 33.9% of STEMI patients arrived at the hospital beyond 6 hours of symptom onset. Additionally, 39.8% of our STEMI patients were ineligible for thrombolysis because of late presentation beyond 12 hours. This proportion of late presenters was considerably more than reported by Xavier et al. [10] in the CREATE registry (30.8%). Our study demonstrated that prehospital delay was the major contributor of delayed treatment, contributing to 83.8% of the total treatment delay and patient's decision to delay constituted 59% of the prehospital delay. This scenario is similar to what is seen in other developing countries, where patient's delay to seek medical care is very long [22,23]. The main reason for delay in seeking medical attention was patients thinking that symptoms would go away or that they were not serious. Given the high risk factor burden seen in the study population, this late attention seeking behavior looks particularly worrisome. Thus, there seems to be an urgent need of initiating public education programs to increase awareness about cardiovascular risks and improve the healthcare seeking attitude of our population. The median transportation delay in our study was ~60 minutes, which is longer than that reported in other countries [22–24]. Needless to say, the existence of congested urban traffic in large cities such as Srinagar, lack of EMS facilities, and the nonavailability of thrombolytic therapy in the peripheral healthcare centers contributed to this transportation delay. In particular, lack of EMS services appears to be the major hurdle in the process of delivering guideline-directed treatment to STEMI patients in our setting [25]. We would therefore stress on the establishment of state of art EMS services at the earliest, as an adapted response to this study. The median door-to-needle time in our study was 40 minutes. Although less than ideal (⩽30 minutes), it was shorter than reported in the CREATE registry (50 minutes) and comparable to the Western registry data (32–40 minutes) [10,17–19]. One probable reason for this longer door-to-needle time was the delay in shifting patients from the emergency department (ED) to the CCU, where thrombolysis was administered. In a study, Mclean et al. [26] demonstrated a 58-minute reduction in door-to-needle time when fibrinolysis was started in the ED rather than exclusively in the CCU. Hence, modification of hospital protocol to administer thrombolysis in the ED is likely to further shorten this delay. Another approach that has gained popularity in countries such as ours is to administer fibrinolysis at peripheral heath centers and then rapidly transfer the patients to PCI-capable hospitals for routine coronary angiography and PCI within 3–24 hours of thrombolysis (pharmacoinvasive approach). This approach combines the benefits of establishing flow in the infarct-related artery by early fibrinolysis and maintaining sustained patency of infarct-related artery by routine early PCI, and has been demonstrated to provide results equivalent to primary PCI [27].

Our study revealed that patients presenting late to tertiary care hospitals were more likely to be older and residing in rural areas. This finding is consistent with previous studies [22,28]. Elderly patients more often have atypical symptoms of CAD and are more likely to attribute their symptoms to other comorbidities, leading to a delay in seeking medical attention. Lack of awareness, nonavailability of standard treatment in remote

healthcare facilities, and transportation delay is responsible for late presentation among the rural population. Again, establishment of EMS services with widespread coverage of both rural and urban areas, ensuring access to quality and affordable healthcare seems to be the logical solution to this problem. Female sex has been identified as an independent predictor of treatment delay in previous studies [29]. This was not the case in our study and could be a reflection of different cultural views over health and life, held by Kashmiri men and women. Our study showed that history of CAD in the patient or a family member was associated with significantly shorter prehospital delay. As demonstrated in previous studies, a past history or family history of CAD could increase the awareness of patients on symptoms of CAD, making them more sensitive in noticing the seriousness of such symptoms early after onset [20,30,31]. Last, but not least, an important finding of our study was that 44.7% of the patients presenting late to our hospitals had in fact sought a medical consultation within 12 hours of symptom onset. Misinterpretation of the symptoms by local pharmacists or primary care physicians (assessed by reviewing the medical records of the initial diagnostic evaluation of the patients, and the treatment they received from peripheral healthcare providers) was the major reason of delayed presentation in these patients. In summary, public education aimed at increasing awareness about symptoms of CAD, modification of health seeking behavior of patients, improved training of paramedical staff, continued medical education of primary care physicians to reinforce the standard practice of care in *acute coronary syndrome* management, ensuring availability of thrombolytic therapy in peripheral hospitals and establishment of EMS services to provide state of the art ambulance services to the general population are some of the strategies to expedite treatment in STEMI patients in our present day healthcare system.

Limitations

Our study had certain important limitations. Firstly, this study was limited to only two tertiary care centers of a single city and the sample size was relatively small. Extrapolation of these results to a national level requires validation from larger multicenter studies. Secondly, because of a very limited number, we did not include patients who underwent primary PCI in this study. A larger study including a substantial proportion of primary PCI patients is therefore required to assess the profile of such patients, and to compare it with those included in the present study. Thirdly, although we meticulously reviewed all the clinical records of patients from the point of first medical contact, including discharge summaries and referral documents, our data is limited by the retrospective chart review nature of data collection. Lastly, we did not study the clinical outcomes of these patients. A dedicated study with an aim of assessing the in-hospital and long-term outcomes of different subgroups of such patients would provide further insights into the state of STEMI care in our healthcare setting.

Conclusion

Our study reiterates the fact that the standard of STEMI management in our country is far from ideal, and calls for a lot of improvement. Major efforts to reduce treatment delay are needed, including increased public awareness, improvement in peripheral healthcare infrastructure, training of paramedical staff, and establishment of EMS services for rapid triage, and expedited transfer of STEMI patients to the appropriate healthcare facilities.

References

[1] Alexander T, Mehta S, Mullasari A, Nallamothu BK. Systems of care for ST-elevation myocardial infarction in India. Heart 2012;98:15–7.
[2] Eagle KA, Goodman SG, Avezum A, Budaj A, Sullivan CM, Lopez-Sendon J. Practice variation and missed opportunities for reperfusion in ST-segment-elevation myocardial infarction: findings from the Global Registry of Acute Coronary Events (GRACE). Lancet 2002;359:373–7.
[3] Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomized trials. Lancet 2003;361:13–20.
[4] Morrison LJ, Verbeek PR, McDonald AC, Sawadsky BV, Cook DJ. Mortality and prehospital thrombolysis for acute myocardial infarction: a meta-analysis. JAMA 2000;283:2686–92.
[5] The Gruppo Italiano per lo Studio della Streptochi-nasi nell'Infarto Miocardico, (GISSI). Long term effects of intravenous thrombolysis in acute myocardial infarction: Final report of the GISSI study. Lancet 1987;2:871–4.
[6] Fu Y, Goodman S, Chang WC, Van de Werf F, Granger CB, Armstrong PW. Time to treatment influences the impact of ST-segment resolution on one-year prognosis. Insights from the assessment of the safety and efficacy of a new thrombolytic (ASSENT-2) Trial. Circulation 2001;104:2653–9.
[7] Simoons ML, Serruys PW, van den Brand M, Res J, Verheugt FWA, Krauss XH. Early thrombolysis in acute myocardial infarction: limitation of infarct size and improved survival. J Am Coll Cardiol 1986;7:717–28.
[8] Rawles JM. Quantification of the benefit of earlier thrombolytic therapy: Five-year results of the Grampian Region Early Anistreplase Trial (GRACE). J Am Coll Cardiol 1997;30:1181–6.

[9] De Luca G, Suryapranata H, Ottervanger JP, Antman EM. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction: every minute of delay counts. Circulation 2004;109:1223–5.
[10] Xavier D, Pais P, Devereaux PJ, Xie C, Prabhakaran D, Reddy KS, et al.. Treatment and outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data. Lancet 2008;371:1435–42.
[11] Boersma E, Maas ACP, Deckers JW, Simoons ML. Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. Lancet 1996;348:771–5.
[12] Taher T, Fu Y, Wagner GS, Goodman SG, Fresco C, Granger CB, et al.. Aborted myocardial infarction in patients with ST-segment elevation: Insights from the Assessment of the Safety and Efficacy of a New Thrombolytic Regimen-3 Trial Electrocardiographic Substudy. J Am Coll Cardiol 2004;44:38–43.
[13] LATE Study Group. Late Assessment of Thrombolytic Efficacy (LATE) study with alteplase 6–24 hours after onset of acute myocardial infarction. Lancet 1993;342:759–66.
[14] EMERAS Collaborative Group. Randomized trial of late thrombolysis in patients with suspected acute myocardial infarction. Lancet 1993;342:767–72.
[15] Sharma M, Ganguly NK. Premature coronary artery disease in Indians and its associated risk factors. Vasc Health Risk Manag 2005;1:217–25.
[16] Steg PG, Goldberg RJ, Gore JM, Fox KA, Eagle KA, Flather MD, et al.. Baseline characteristics, management practices, and in-hospital outcomes of patients hospitalized with acute coronary syndromes in the Global Registry of Acute Coronary Events (GRACE). Am J Cardiol 2002;90:358–63.
[17] Rogers WJ, Canto JG, Lambrew CT, Tiefenbrunn AJ, Kinkaid B, Shoultz DA, et al.. Through 1999: the National Registry of Myocardial Infarction 1, 2, and 3. J Am Coll Cardiol 1990;2000(36):2056–63.
[18] Hasdai D, Behar S, Wallentin L, Danchin N, Gitt A, Boersma E, et al.. A prospective survey of the characteristics, treatments and outcomes of patients with acute coronary syndromes in Europe and the Mediterranean basin; the Euro Heart Survey of Acute Coronary Syndromes (Euro Heart Survey ACS). Eur Heart J 2002;23:1190–201.
[19] Mandelzweig L, Battler A, Boyko V, Bueno H, Danchin N, Filippatos G, et al.. The second Euro Heart Survey on acute coronary syndromes: characteristics, treatment, and outcome of patients with ACS in Europe and the Mediterranean Basin in 2004. Eur Heart J 2006;27: 2285–93.
[20] Song L, Yan HB, Yang JG, Sun YH, Hu DY. Impact of patients' symptom interpretation on care-seeking behaviors of patients with acute myocardial infarction. Chin Med J 2010;123:1840–5.
[21] Khan MS, Jafary FH, Faruqui AM, Rasool SI, Hatcher J, Chaturvedi N, et al.. High prevalence of lack of knowledge of symptoms of acute myocardial infarction in Pakistan and its contribution to delayed presentation to the hospital. BMC Public Health 2007;7:284.
[22] Tabriz AA, Sohrabi MR, Kiapour N, Yazdani S. Factors associated with delay in thrombolytic therapy in patients with ST-elevation myocardial infarction. J Tehran Heart Cent 2012;7:65–71.
[23] Yusuf S, Rangarajan S, Teo K, Islam S, Li W, Liu L, et al.. Cardiovascular risk and events in 17 low-middle, and high-income countries. N Engl J Med 2014;371:818–27.
[24] Ortolani P, Marzocchi A, Marrozzini C, Palmerini T, Saia F, Serantoni C, et al.. Clinical impact of direct referral to primary percutaneous coronary intervention following pre-hospital diagnosis of ST-elevation myocardial infarction. Eur Heart J 2006;27:1550–7.
[25] Steg PG, James SK, Atar D, Badano LP, Lundqvist CB, Borger MA, et al.. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J 2012;33:2569–619.
[26] McLean S, O'Reilly M, Doyle M, Rathaille MO. Improving door-to-drug time and ST segment resolution in AMI by moving thrombolysis administration to the emergency department. Accid Emerg Nurs 2004;12:2–9.
[27] ElGuindy AM. STREAM and FAST-MI–Pharmacoinvasive therapy: a continued role for fibrinolysis in the primary PCI era. Glob Cardiol Sci Pract 2014;2014:56–60.
[28] Leizorovicz A, Haugh MC, Mercier C, Boissel JP. Prehospital and hospital time delays in thrombolytic treatment in patients with suspected acute myocardial infarction: analysis of data from the EMIP study. European Myocardial Infarction Project. Eur Heart J 1997;18:248–53.
[29] Leslie W, Urie A, Hooper J, Morrison CE. Delay in calling for help during myocardial infarction: reasons for the delay and subsequent pattern of accessing care. Heart 2000;84:137–41.
[30] Farshidi H, Rahimi S, Abdi A, Salehi S, Madani A. Factors associated with pre-hospital delay in patients with acute myocardial infarction. Iran Red Cres Med J 2013;15:312–6.
[31] Sari I, Acar Z, Ozer O, Erer B, Tekbas E, Ucer E, et al.. Factors associated with prolonged prehospital delay in patients with acute myocardial infarction. Türk Kardiyol Dern Arş 2008;36:156–62.