

## Door to Needle Time in Administering Thrombolytic Therapy for Acute Myocardial Infarction

Abdul Ameer Jaleel Awad

### ABSTRACT:

#### BACKGROUND:

Thrombolytic therapy is a standard treatment for patients presenting with acute myocardial infarction (MI). Early administration of these agents is crucial for the outcome of management.

#### OBJECTIVE:

This audit was conducted to evaluate the time between arrival to emergency department (ED) and the administration of thrombolysis (door to needle time).

#### METHODS:

Data was collected from patients admitted to the Coronary Care Unit of Al-Yarmook Teaching Hospital, with a diagnosis of acute MI and received thrombolytic therapy over a one-year period (April 2009 to April 2010). The time between arrival to the ED to the time of administration of thrombolytic therapy was obtained as well as the time of onset of chest pain up to presentation to the hospital, and the outcome (all cause mortality) post treatment.

#### RESULTS:

A total of 271 patients (256 males) admitted to the Coronary Care Unit of Al-Yarmook Teaching Hospital with a diagnosis of acute MI received thrombolytic therapy over a one-year duration. The median door to needle time was 95 minutes. The median time of onset of chest pain to arrival to ED was 5 hours (300 minutes). The outcome of these patients obtained either alive was 260 (96%) or dead was 11 (4%) ( $P < 0.00001$ ).

#### CONCLUSION:

The door to needle time was relatively similar to other centers. Delay in presentation to the hospital was more important and factors contributing to this delay should be looked for and corrected. Another audit is needed to evaluate the implementation of these recommendations.

**KEY WORDS:** door to needle, thrombolytic therapy, acute myocardial infarction, emergency department, coronary care unit, chest pain.

### INTRODUCTION:

The use of thrombolytic therapy in the treatment of acute myocardial infarction (MI) has been shown by several studies to improve survival<sup>(1,3)</sup>. Early administration is crucial in determining the outcome of patients in terms of survival, infarct size, and left ventricular function<sup>(4)</sup>. The maximum benefit of thrombolytic therapy to salvage the myocardium in a patient developing acute MI is when given within the first 60 minutes (one hour) of symptoms appearance<sup>(5,6)</sup>.

This study was carried out to determine whether this is the current practice in Al-Yarmook Teaching Hospital.

#### METHODS:

A total of 271 patients (256 males) (15 females), age 50-65 years old. Data was collected

from the charts of patients who were admitted to the coronary care unit in Al-Yarmook Teaching Hospital, with a diagnosis of acute MI over duration of one year from April 2009 to April 2010. Time of arrival, time of administration of thrombolysis, and time of onset of chest pain as well as outcome of patients was collected. Other data obtained was the electrocardiographic findings, cardiac enzyme elevation, risk factors for coronary artery disease, complications post MI, and discharge medications.

**Statistical analysis.** The analysis of collected data was performed using Stat Pack Gold. Student's T-test was used; testing whether mean differs from zero.

Baghdad Teaching Hospital, Department of Cardiology.

### RESULTS:

A total of 320 patients were admitted to the coronary care unit in Al- Yarmook Teaching Hospital, with a diagnosis of acute MI, 271 patients received thrombolytic therapy, 49 patients not received thrombolytic therapy. The median duration from time of arrival to emergency department (ED) to time of administration of thrombolytic therapy was 95 minutes. Twenty-six patients (9.6%) received thrombolysis within the first 60 minutes of arrival, while 113 patients (41.7%) were given thrombolysis between 60 and 120 minutes of arrival (Table 1). Other parameters observed in this audit are males 256 (94.5%), current smoking was reported by 165 patient (60.9%), whereas diabetes mellitus was identified risk factors among 80 (29.5%), hypertension among 63 (23.2%), and hypercholesterolemia among 9 patients (3.3%). The median duration from the onset of chest pain to arrival to the ED was 5 hours (300 minutes). Anterior MI was shown by electrocardiogram (ECG) in 113 (41.7%) patients, and 112 (41.3%) had inferior MI. Post MI complications were arrhythmia in 41 patients (15.1%), pericarditis in 9 patients (3.3%), cardiogenic shock in 21 patients (7.7%), ventricular septal defect in one patient (0.4%), and heart blocks in 9 patients (3.3%). Patients who were discharged alive were 260 (96%) and 11 patients (4%) died. Discharge medications were  $\beta$ -blocker in 201 (74.2%), angiotensin converting enzyme (ACE) inhibitors in 165 (60.9%), nitrates in 231 (85.2%), hypolipidemic agents in 13 patients (4.8%), and aspirin in all patients .

### DISCUSSION:

Our data shows that thrombolytic therapy was administered to the majority of patients presenting with acute MI within 2 hours of their hospital arrival. Another 5 hours were added to the delay in thrombolysis from the onset of symptoms until arrival to the hospital. Despite a comparable duration of the door to needle time with other centers; however, the delay in arrival to the ED was rather marked. Reduction in mortality by 1% occurs for each hour of time saved within the first 6 hours<sup>(7)</sup>. One should remember that the longer the delay in thrombolysis the less the myocardial salvage and functional benefit. This concept has to be emphasized not only to health care workers but also to the public to reduce the delay in presenting to the hospital after the onset of chest pain. Our data showed that many patients presented late to the hospital after the onset of their symptoms. One

study reported as many as 40% of patients had a delay of more than 6 hours before they presented to the hospital<sup>8</sup>. In another study from Finland, only 38% of patients received thrombolysis within 2 hours of onset of symptoms<sup>9</sup>. Factors associated with prolonged delay included advanced age and female sex, having symptoms during the evening and early morning hours (6:00 p.m. to 6:00 a.m.), and patients with a history of hypertension. Our patients were relatively of younger age group with a mean age of 49.1 years (range 25-90), and the majority were males, of lower educational and socioeconomic backgrounds, explaining the disparity in factors leading to delay in arrival to hospital. Moreover, the onset of symptoms was reported between 7:00 a.m. and 9:00 a.m. by most of our patients, nonetheless, there was a delay in arrival to the ED. Deficiencies in knowledge of symptoms may contribute to the delay and could be a target for intervention. Therefore, educational interventions that encourage the prompt use of emergency medical transport services and target specific patient populations, such as elderly persons, women, persons with cardiac risk factors, and persons with lower educational level may be most successful in reducing the length of delay and improving the outcomes of patients with acute MI<sup>(10)</sup>. Delay of thrombolysis may be due to time elapsed between evaluations of patients in the ED until referral to coronary care unit (CCU) where thrombolysis can be administered. In hospital factors accounted for 59% of the time delay from the onset of symptoms to thrombolytic treatment. After arrival in the emergency room, an average of 20 minutes was required to obtain an ECG and an additional 70 minutes delay before the administration of tissue plasminogen activator (TPA)<sup>(11)</sup>. One study evaluated the effectiveness of initiating thrombolysis in the ED; this resulted in reduction of door to needle time from 81 minutes in CCU to 25 minutes in ED<sup>(12)</sup>. Another study looked at employing an aggressive policy to reduce the door to needle time and investigated whether this approach is safe, it has reduced door to needle time from 70 to 20 minutes. However, greater pressure on medical staff to make rapid management decisions increased the proportion of patients being thrombolysed inappropriately<sup>(13)</sup>. The safety and efficacy of prehospital thrombolysis in order to reduce the time between the onset of symptoms and therapy with a thrombolytic agent has been evaluated. Treatment with thrombolysis

## THROMBOLYTIC THERAPY FOR ACUTE MYOCARDIAL INFARCTION

by a physician in a mobile CCU within 1.5 hours of symptom onset was associated with smaller infarcts, preservation of left ventricular function, and a lower 21-day mortality rate<sup>4</sup>. Prehospital thrombolysis has resulted in aborting an acute MI in some patients<sup>(14)</sup>. The results of Grampian Region Early Anistreplase Trial (GREAT trial) comparing prehospital to hospital thrombolysis showed that patients in the prehospital group received thrombolytic treatment more than 2 hours earlier (101 versus 240 minutes after the onset of symptoms), and it was correlated with a 50% risk reduction in mortality at one year<sup>(15)</sup>. The benefit of earlier treatment was maintained after a 5-year follow-up; the mortality in the prehospital treated group was 25% compared to 36% in the hospital treated patients<sup>(16)</sup>. Nonetheless, this concept was not consistent with the result of the MI triage and intervention (MITI trial). Despite significant reduction of total time to treatment from 110 to 77 minutes, there were no significant differences between the prehospital and hospital treatment groups in left ventricular ejection fraction, infarction size, or all-cause mortality<sup>(17)</sup>. A meta-

analysis of 6 randomized trials involving 6,434 patients found that prehospital thrombolysis significantly reduced all-cause hospital mortality compared to in-hospital thrombolysis<sup>(18)</sup>. Another approach to shorten the delay in thrombolysis is to provide a specialist cardiac nurse "thrombolysis nurse" for rapid assessment before thrombolysis. The effectiveness of this approach was evaluated and it was found that the presence of thrombolysis nurse produced a dramatic improvement in median door to needle and pain to needle times in patients presenting with definite MI<sup>(19)</sup>.

### CONCLUSION:

The delay taken by patients from onset of symptoms prior to arrival to ED can be dealt with by either education with emphasis on certain risk groups and promoting awareness of symptoms suggestive of MI, or providing prehospital thrombolysis. Studies have shown that prehospital thrombolytic therapy is possible and that, when treatment is given shortly after the onset of pain, there is a reduction of infarct size and an improvement in ejection fraction following acute MI.

Table 1: Door to needle time in minutes

Door to needle time (minutes)	Patients n (%)
<30	4 (1.5)
31-60	26 (9.6)
61-120	113 (41.7)
121-240	113 (41.7)
241-360	11 (4.1)
361-480	3 (1.1)
>480	1 (0.4)

### REFERENCES:

1. Wilcox RG, von der Lippe G, Olsson CG, Jensen G, Skene AM, Hampton JR. Trial of tissue plasminogen activator for mortality reduction in acute myocardial infarction. Anglo-Scandinavian Study of Early Thrombolysis (ASSET). *Lancet* 2003;8610:525-30.
2. Second International Study of Infarct Survival (ISIS-2) Collaborative Group. Randomized trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. *Lancet* 2003; 8607: 349-60.
3. AIMS Trial Study Group. Effect of intravenous APSAC on mortality after acute myocardial infarction: preliminary report of a placebo-controlled clinical trial. *Lancet* 2003; 8585: 545-49.
4. Linderer T, Schroder R, Arntz R, Heineking ML, Wunderlich W, Kohl K et al. Prehospital thrombolysis: beneficial effects of very early treatment on infarct size and left ventricular function. *J Am Coll Cardiol* 2003; 22:1304-10.
5. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. *Lancet* 2004;343:311.

## THROMBOLYTIC THERAPY FOR ACUTE MYOCARDIAL INFARCTION

---

6. Boersma E, Maas AC, Deckers JW, Simoons ML. Early thrombolytic treatment in acute myocardial infarction: Reappraisal of the golden hour. *Lancet* 2004; 9030: 771-75.
7. Timm TC, Ross R, Braunwald E. Left ventricular function and early cardiac events as a function of time to treatment with t-PA: A report from TIMI II. *Circulation* 2004; 84: II.
8. Gurwitz JH, McLaughlin TJ, Willison DJ, Guadagnoli E, Hauptman PT, Gao X et al. Delayed hospital presentation in patients who have had acute myocardial infarction. *Ann Intern Med* 2005;126: 593-99.
9. Hirvonen TP, Halinen MO, Kala RA, Olkinuora JT. Delays in thrombolytic therapy for acute myocardial infarction in Finland. Results of a national thrombolytic therapy delay study. Finnish Hospitals Thrombolysis Survey Group. *Eur Heart J* 2006;19: 885-92.
10. Goff DC Jr, Sellers DE, McGovern PG, Meischke H, Goldberg RJ, Bittner V et al for the REACT Study Group. Knowledge of heart attack symptoms in a population survey in the United States: The REACT trial (Rapid Early Action for Coronary Treatment). *Arch Intern Med* 2006; 158: 2329-38.
11. Sharkey SW, Bruneete DD, Ruiz E, Hession WT, Wysham DG, Goldenberg IF et al. An analysis of time delays preceding thrombolysis for acute myocardial infarction. *JAMA* 2007; 262: 3171-74.
12. Chan WK, Lam KN, Lau FL, Tang FM. Starting thrombolytic therapy for patients with acute myocardial infarction in Accident and Emergency Department: from implementation to evaluation. *Chin Med J (Engl)* 2007; 111: 291-94.
13. Kelion AD, Banning AP, Shahi M, Bell JA. The effect of reduction of door to needle times on the administration of thrombolytic therapy for acute myocardial infarction. *Postgrad Med J* 2007; 875: 533-36.
14. Lamfers EJ, Hooghoudt TE, Uppelschoten A, Stolwijk PW, Verheugt FW. Effect of prehospital thrombolysis on aborting acute myocardial infarction. *Am J Cardiol* 2008; 84: 928-30, A6-A7.
15. Rawles J, on behalf of the GREAT Group. Halving of mortality at 1 year by domiciliary thrombolysis in the Grampian Region Early Anistreplase Trial (GREAT). *J Am Coll Cardiol* 2008;23:1-5.
16. Rawles JM. Quantification of the benefit of earlier thrombolytic therapy: Five-year results of the Grampian Region Early Anistreplase Trial (GREAT). *J Am Coll Cardiol* 2008; 30: 1181 -86.
17. Weaver WD, Cerqueira M, Hallstrom AP, Litwin PE, Martin JS, Kudenchuk PJ et al. Pre-hospital initiated vs hospital-initiated thrombolytic therapy. The Myocardial Infarction Triage and Intervention Trial. *JAMA* 2009;270: 1211- 16.
18. Morrison LJ, Verbeek PR, McDonald AC, Saedsky BV, Cook DJ. Mortality and prehospital thrombolysis for acute myocardial infarction: A meta-analysis. *JAMA* 2009; 283: 2686-92.
19. Somauroo JD, McCarten P, Appleton B, Amadi A, Rodrigues E. Effectiveness of a thrombolysis nurse in shortening delay to thrombolysis in acute myocardial infarction. *J R Coll Physicians Lond* 2009;33:46-50.