Emergency physician versus cardiologist-initiated thrombolysis for acute myocardial infarction: a Singapore experience

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ABSTRACT

Introduction: To compare the door-to-needle time between thrombolysis administration for patients with ST elevation myocardial infarction (STEMI) in the emergency department (EMD) by emergency physicians and those administered in the coronary care unit (CCU) by cardiologists.

Methods: The data was collected prospectively for all patients with STEMI who received thrombolysis in the emergency department over a one-year period from January 2001 to December 2001. We recorded the time of arrival in the EMD as well as the time thrombolytic therapy was commenced. This data was compared to those from the previous year, obtained retrospectively, where the patients received thrombolysis in the CCU.

Results: 118 patients were thrombolysed in the CCU and 78 patients were thrombolysed in the EMD. The median door-to-needle time was significantly shorter in patients who are thrombolysed in the emergency department by emergency physicians than in the coronary care unit by cardiologists (29 minutes versus 60 minutes, p value is less than 0.001). There was no incident of inappropriate thrombolysis nor was there intracranial or gastrointestinal bleed in the patients who were thrombolysed in the EMD. There was one case of medication dose error but it was of no consequence to the patient.

Conclusion: Emergency physicians can administer thrombolytic treatment appropriately, quickly and safely in patients with STEMI.

Keywords: acute myocardial infarction, door-to-needle time, ST elevation, ST elevation myocardial infarction (STEMI), thrombolysis

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INTRODUCTION

Thrombolytic therapy is an established form of treatment for patients with ST elevation myocardial infarction (STEMI). Its benefits are, however, time dependent i.e. the earlier it is administered, the greater the benefits to the patient[1-9]. Traditionally, in our hospital, thrombolysis is administered in the coronary care unit (CCU) by the cardiologist. However, this process involves prior cardiologist review and transportation of patients to the CCU, resulting in significant time delay.

In order to shorten the time for administration of thrombolysis for patients with STEMI, the emergency department (EMD), along with the cardiology department in National University Hospital, jointly finalised a protocol for administering thrombolysis in the EMD instead of CCU. In the protocol, the emergency physician (of registrar grade and above), not the cardiologist, was responsible for assessing the patient and administering the thrombolysis in the EMD. This protocol was approved by the hospital administration and was started in January 2001. Our study compares the time interval between arrival in hospital and administration of thrombolytics between two groups of patients – those who were thrombolysed in the EMD in the year 2001 and those who were thrombolysed in the CCU in the year 2000.

METHODS

The study was conducted in the Emergency Department of a large teaching hospital with annual EMD census of about 75,000. Patients who had clinical and electrocardiographical (ECG) evidence of STEMI upon initial presentation in the EMD and who subsequently received thrombolysis for it were included in the study.

Patients with suspected STEMI (typical chest pain and ECG criteria) were nursed in a monitored bed and given sublingual glyceryl trinitrate, aspirin, as well as intravenous opiates (for pain relief) as appropriate. The criteria for use of thrombolytics were:

1. Typical chest pain of acute myocardial infarction.
2. ST segment elevation of at least 1mm in two limb leads and 2mm in at least two contiguous chest leads.
3. Less than 12 hours from onset of chest pain.
4. Less than 75 years of age.

Table I. Contraindications to thrombolysis.

- Suspected aortic dissection
- Previous stroke
- Known intracranial neoplasm
- Recent head trauma
- Other intracranial pathology
- Severe hypertension (BP>180/110mmHg)
- Acute peptic ulcer
- Acute internal bleeding
- Recent (less than 1 month) internal bleeding
- Recent (less than 1 month) major surgery
- Current use of anticoagulants
- Known bleeding diasthesis
- Prolonged cardiopulmonary resuscitation (>5 mins)
- Previous administration of thrombolytics (if yes, use rTPA)
- Pregnant

If the emergency physician was confident of the diagnosis of STEMI, the cardiologist would be called immediately to determine whether primary angioplasty was available. If this was not available, the emergency physician would then proceed to administer the thrombolytics if there were no contraindications to thrombolysis. The contraindications to thrombolytic therapy that we employed were largely similar to those of the American cardiac life support (ACLS) guidelines (Table I).

Thrombolysis was administered only after written consent had been obtained. The patient was then monitored in the EMD for a further 15-20 minutes after the thrombolytic was started, before being transferred to the CCU for further management. In the event where the diagnosis of STEMI was doubtful or there is a complicated infarction, e.g. cardiogenic shock, the cardiologist would be asked to review the patient urgently in the EMD prior to administration of thrombolysis. Streptokinase was generally used as a thrombolytic agent. However, recombinant tissue plasminogen activator (rTPA) was given if the patient is male, less than 60 years, and had anterior STEMI.

Data was collected prospectively for all patients with acute myocardial infarction (AMI) who received thrombolysis in the EMD over a one-year period from January 2001 to December 2001 (known as the EMD group). Using a specially-designed form, the time of arrival in the EMD as well as the time thrombolytic therapy was started in the EMD were recorded. The arrival time or "door time" was taken as the registration time or the time of the first ECG, whichever was earlier. The "needle time" was taken as the time the thrombolytic was started. We also examined the complications associated with administration of the thrombolytics in these patients.

This data was compared to those from the previous year – from January 2000 to December 2000,where the patients received thrombolysis in the CCU (known as the CCU group). Patients from this group were identified from the admitting log book in the CCU. In this group, the data was collected retrospectively. Similarly, the time of arrival in the EMD was represented by the registration time or the time of the first ECG. The time thrombolysis was started was the time recorded in the inpatient medication record (IMR). Statistical analysis was undertaken using the two sample t-test and Mann-Whitney U test. Statistical significance was ascribed at p-value of less than 0.05.

RESULTS

In the period from January 2000 to December 2000, there were 134 patients who were diagnosed with STEMI upon first presentation to the EMD and administered thrombolytics. Of these 134 patients, 118 were thrombolysed in the CCU. However, due to various reasons, such as lack of a CCU bed or individual preference of the cardiologist on duty that day, 16 patients were thrombolysed in the EMD (instead of CCU). These cases were excluded.

The median age in this CCU group was 55 +/- 11 (range 25-89) years, with 107 male and 11 female patients. There were 53 patients with hypertension, 37 patients with diabetes mellitus, 56 patients with dyslipedemia, 62 smokers, and three patients with previous myocardial infarction. Anterior AMI occurred in 55 patients and inferior AMI occurred in 63 patients. Equal numbers of patients received streptokinase and rTPA in this group (Table II). The mean door-to-needle time was 66 +/- 32 (range 12-230) minutes, median with a time of 60 minutes. The door-to-needle time refers to the time the patient arrived in the hospital to the time thrombolysis was started (Table III).

In the period from January 2001 to December 2001, 128 patients were diagnosed with STEMI upon first presentation to the EMD and were administered thrombolysis. Seventy-eight patients were thrombolysed in the EMD and 50 patients were thrombolysed in CCU. The reasons for not administering thrombolysis in the EMD include time delay in patients giving consent and non-compliance to the protocol. These cases were excluded.

The mean age of the EMD group patients was 56 +/- 12 (35-86) years, with 68 male and 10 female patients. There were 34 patients with hypertension, 26 patients with diabetes mellitus, 41 patients with dyslipedemia, 40 smokers, and four patients with previous myocardial infarction. Anterior AMI occurred in 34 patients and inferior AMI occurred in 44 patients.

Table II. Baseline characteristics of CCU and EMD groups.

	CCU group (n=118)	EMD group (n=78)	p-values
Demography			
Mean age	55 years	56 years	0.463
Male : female ratio	107 : 11	68 : 10	0.438
Anterior AMI	55 (45.6%)	34 (43.6%)	0.678
Inferior AMI	63 (53.4%)	44 (56.4%)	0.678
Comorbidities			
Hypertension	53	34	0.855
Diabetes mellitus	37	26	0.772
Dyslipedemia	56	41	0.484
Smoking	62	40	0.863
Previous myocardial infarction	3	4	0.439
Treatment characteristics			
Type of thrombolytic			
Streptokinase : rTPA ratio	59 : 59	57 : 21	0.001 (OR = 2.7, 95% CI 1.5-5.0)

Table III. Door-to-needle time for all patients.

	CCU group (n=118)	EMD group (n=78)	p-value
Mean	66 mins	32 mins	
Median	60 mins	29 mins	p<0.001
<30 mins	6 (5.1%)	43 (55.1%)	p<0.001
30 - 60 mins	54 (45.8%)	30 (38.5%)	p<0.312
>60 mins	58 (49.1%)	5 (6.4%)	p<0.001

Table IV. Door-to-needle time in EMD group (n=78).

	Without cardio review (n = 61)	With cardio review (n = 17)	p-value
Mean door-to-needle time	30 mins	41 mins	
Median door-to-needle time	27 mins	37 mins	p=0.012
Door-to-needle time <30 mins	39 (63.9%)	4 (23.5%)	p=0.003
Door-to-needle time 30-60 mins	19 (31.1%)	11 (64.7%)	p=0.012
Door-to-needle time >60 mins	3 (4.9%)	2 (11.7%)	p= 0.298

57 patients received streptokinase whereas 21 patients received rTPA (Table II). The mean door-to-needle time was 32 +/- 15 (range 13-85) minutes, with a median time of 29 minutes (Table III).

Out of these 78 patients, 61 patients were thrombolysed without prior cardiologist review. The mean door-to-needle time for these 61 patients was 30 +/- 14 (range 13- 85) minutes, with a median of 27 minutes. The remaining 17 patients received thrombolysis only after review by the cardiologist in the EMD. The mean door-to-needle time was 41 +/- 15 (range 23-80) minutes, with a median of 37 minutes. As far as choice of thrombolytics are concerned, CCU group were more likely to have rTPA given as thrombolytics compared to the EMD group (p=0.001, OR=2.7, 95% CI 1.5, 5.0).

EMD group patients were more likely to be thrombolysed in less than 30 minutes (p<0.001, OR 22.9, 95% CI 9.0, 58.4) (Tables III and IV). There were 35 patients (44.8%) who had door-to-needle time longer than 30 minutes in the EMD group. The reasons for delay in the EMD included: patients needed time to decide on thrombolysis, patients presented in the ambulatory area, time needed to evaluate possible contraindications e.g. head injury or aortic dissection, and time needed to resuscitate haemodynamically-unstable patients. Comparing the CCU group and the EMD group, for patients who were not reviewed by a cardiologist in the EMD, the decrease in the median door-to-needle time was statistically significant (p<0.001).

There were no cases of inappropriate thrombolysis in either group. We defined inappropriate thrombolysis as diagnosis other than AMI. In the CCU group, there was one case of intracranial haemorrhage which occurred four hours after completion of streptokinase. The patient was disabled at discharge. There were no cases of intracranial haemorrhage in the EMD group. Gastrointestinal tract bleeding did not occur in either group.

Minor complications that occurred in this study were transient dysrrhythmias and transient hypotension. There were 18 minor complications in the CCU group and 14 in the EMD group. One patient in each group who was given streptokinase developed allergy to the thrombolytic agent. One developed a rash and the other developed periorbital oedema, both after completion of the drug treatment. There was one isolated case of medication error in the EMD group. Initial bolus dose of rTPA 50mg was given instead of 15mg. The error was identified immediately and the remaining dose of rTPA needed by the patient was given over a longer period of time. This patient did not develop any complication.

The EMD group had four inpatient mortalities and the CCU group had one inpatient mortality. Three patients in the ED group died between 3 and 28 hours of presentation, all due to cardiogenic shock. The fourth patient died 21 days after thrombolysis due to thromboembolic stroke, renal failure and septicaemia. The one isolated death in the CCU group died of cardiogenic shock 16 hours after arrival (Table V).

Table V. Clinical details of all deaths.

Age / Sex / Type of AMI / Type thrombolysis	Complications / cause of death	CP-N time	D-N time	Arr-death time
CCU group (n=1) 72 yrs / F / Ant / Streptokinase	AMI	2 hrs	58 mins	16 hrs
EMD group (n=4) 39 yrs /M / Inf / Streptokinase	Acute pulmonary oedema Acute renal failure	4 hrs	57 mins	28 hrs
57 yrs / F / Inf / Streptokinase	Cardiogenic shock	8 hrs	18 mins	24 hrs
40 yrs / M / Ant / rTPA	Cardiogenic shock	3 hrs	26 mins	3 hrs
57 yrs / M / Inf / Streptokinase	Thromboembolic stroke 6 hrs after thrombolysis, septicaemia, renal failure	9 hrs	62 mins	21 days

AMI: Acute Myocardial Infarction; CP-N: Chest pain to needle; D-N: Door-to-needle; Arr-death: Arrival to death; Inf: Inferior; Ant: Anterior; M: Male; F: Female.

DISCUSSION

Administration of thrombolytics for patients with ST elevation myocardial infarction (STEMI) has been shown to improve survival. However, its benefits are strongly dependent on the door-to-needle time. Recent studies[10-12] have shown that primary angioplasty is the preferred reperfusion strategy for STEMI when appropriate facilities and skilled personnel are available. During our study, this facility is not available round-the-clock, hence thrombolytic therapy was generally the standard form of treatment for these patients.

For thrombolytic therapy to confer maximal benefit in AMI, it must be administered as soon as possible after the onset of chest pain. The American Heart Association (AHA) recommended the door-to-needle time to be within 30-60 minutes whereas the working group from the National Institutes of Health (National Heart, Lung and Blood Institute) advocated that emergency departments strive for the minimum door-to-needle time suggested by the AHA

The door-to-needle time was significantly shorter in the EMD group. Studies done in Australia and United Kingdom show similar findings when thrombolytic administration was changed from the CCU to the EMD[13,16]. In our study, there was still a substantial number of patients (50) who were not thrombolysed in the EMD after implementation of the protocol. The majority of these cases occurred in the first few months of protocol implementation, probably caused by non-compliance as well as non-familiarity of the protocols in both the emergency physicians as well as the cardiologist.

Cardiologist review of patients in the EMD prolonged the door-to-needle time. The reasons for consulting the cardiologist included: non-diagnostic ECG, possible contraindications for thrombolysis or unstable patients. However, this is a necessary step and reflected the safe practice of the emergency physicians. We anticipate that with greater confidence with thrombolytic usage, there will be lesser need to consult the cardiologist.

There has been concerns whenever non-cardiologists begin to use thrombolytic agents for AMI in their practice. Although there have been reports where errors of judgement had led to administration of thrombolysis in non-AMI patients leading to mortality[13], no such incident of inappropppriate thrombolysis occurred in our study. There was one incident of medication dosing error, and this occurred very early after the protocol implementation and could be explained by the learning curve of emergency physicians in thrombolytic administration. We defined adverse reactions attributed to thrombolytics as occurring during or just after thrombolytic infusion. There was no incident of major intracranial and gastrointestinal bleeds in our study. Other studies have quoted the incidence of these bleeds to be approximately 1%[14,15].

Despite significantly lower door-to-needle times in the EMD group, there was an apparent increase in the in-hospital mortality in this group. However, the mortality rate in EMD group was within the range of previously-reported mortality[13,14] for admitted patients with AMI, quoted to be around 8-10%. Four patients in our study group perished very early and the fifth died 21 days later. These deaths were unlikely to be thrombolysis-related. Several trials[2,5] have shown that benefits of thrombolytic therapy were not apparent in the immediate early period but rather at the 35-day period. In these studies, very early deaths were attributed largely due to cardiac causes such as electromechanical dissociation, cardiac rupture or cardiogenic shock. The CCU group had an unusually low in-hospital mortality rate. A Type 1 error is a possible explanation for the low mortality rate in this group.

We recognised several limitations of our study. The study occurred in different time frames with the data collection for the two groups differing, i.e. the CCU group's data was collected retrospectively whereas the EMD group's data was collected prospectively. Hence, there was a possibility that the two populations may be very different. However, this is unlikely since there were no significant difference in the baseline characteristics of the two groups. The criteria for recruitment of patients by the cardiologists as well by the emergency physicians were the same, according to the AHA Guidelines (1999). The EMD workflow for patients with chest pain did not change at any time during the period of study.

In our EMD, patients who present with chest pain will immediately have an ECG done. Hence, diagnosis was made very promptly, registration may be done concurrently or after the patient is attended to. In those very few cases who presented in the ambulatory area, however, registration will naturally be done before ECG. Hence, the rationale for using the registration time or time of the first ECG, whichever is earlier, to accurately record the "door time". We noted that the sample sizes of the two groups were not only small but different by a significant number. However, sample sizes are crucial if we had obtained non-significant results but in our case, we did show statistically-significant different results between groups.

In summary, this study demonstrated that thrombolysis can be administered quickly and safely by emergency physicians for patients with AMI.

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