Prevalence and causes of failure of receiving thrombolytic therapy in patients with acute ST-segment elevation myocardial infarction


Department of Cardiovascular Medicine, Suez Canal University Hospital, Ismailia, Egypt

Received 24 February 2012; accepted 26 May 2012
Available online 2 July 2012

Abstract Background: Missing thrombolytic therapy in patients with acute ST-elevation myocardial infarction (STEMI) can have dire consequences. We studied the prevalence and causes of failure of receiving thrombolytic therapy in patients with STEMI and its impact on the clinical outcome during hospitalization.

Patients and methods: This was an observational, analytic, cross sectional study carried out in the CCU and emergency departments of three public hospitals in Port Said, Egypt. We interrogated all patients admitted within 72 h of possible acute coronary syndrome and only patients proved to have STEMI as defined by the updated ACC criteria were analyzed for receiving thrombolytic therapy or not. All STEMI patients were subjected to: medical history taking, thorough clinical examination, 12-leads surface electrocardiography, cardiac biomarkers (troponin I), and predischarge trans-thoracic echocardiography.

Results: Of 6522 patients screened, only 288 patients had STEMI. The prevalence of missed thrombolysis in these patients was 45%. Delayed presentation after the onset of symptoms represented the most common cause for failure to receive thrombolysis (54% of the cases), while misdiagnosis at the emergency department represented 35% of the cases. Female gender, diabetes mellitus and inferior location of myocardial infarction were independent predictors of missed thrombolytic therapy. Cardiac death, clinical heart failure and significant cardiac dysrhythmias were higher in patients who missed thrombolysis than in those who received it.

Conclusion: In this study, up to 45% of patients with STEMI missed the opportunity to receive thrombolysis, most likely due to delayed presentation or misdiagnosis at the emergency department. Patients with missed thrombolysis were at higher risk of cardiac death, clinical heart failure, and hemodynamically significant cardiac dysrhythmias.

© 2012 Egyptian Society of Cardiology. Production and hosting by Elsevier B.V. All rights reserved.

1. Introduction

Acute myocardial infarction is a major cause of morbidity and mortality in our general population. It results from prolonged myocardial ischemia, precipitated in most cases by occlusive...
thrombus at the site of a pre-existing atheromatous plaque. Prompt reperfusion of an obstructed coronary artery by either thrombolytic therapy or primary angioplasty can limit myocardial necrosis, improve myocardial salvage, and reduce mortality.

Thrombolytic therapy in STEMI is generally safe and effective. It is most effective if given within the first 1.5 h after the onset of symptoms. In one study, the greatest relative difference in mortality was seen in a small number of the patients treated within the first hour after the symptom onset with a reduction in mortality and in almost 40% of the patients aborting infarction process, thus preventing irreversible myocardial damage and dysfunction. Collectively the large trials of thrombolytic therapy demonstrated a 25% reduction in 30-day mortality in patients received thrombolytic therapy within 6 h of the onset of symptoms.

Patients who are missing thrombolytic therapy are an unfortunate group of high risk patients at higher risk of subsequent cardiac events including death, heart failure and life-threatening arrhythmia. We undertook this study to determine the prevalence of missing thrombolytic therapy in patients with STEMI, to identify factors related to this failure, and to analyze the clinical outcome of these patients compared to those who received thrombolytic therapy.

2. Methods

This was an observational, cross sectional, analytic study targeting the emergency departments and cardiac care units (CCU) of three general public hospitals in Port-Said city during the period from September 2009 to March 2010. We screened all patients admitted within 72 h of possible acute coronary syndrome (ACS), while we included only patients with STEMI who had no contraindication to thrombolytic therapy at the time of presentation. Included patients were subjected to medical history taking, thorough physical examination, serial 12-lead surface ECG recordings, serial troponin I testing, and predischarge trans-thoracic echo-Doppler study. Patients with STEMI were divided into two groups: (1) who received thrombolytic treatment and (2) who did not receive this therapy.

2.1. Diagnosis of STEMI

We applied the criteria proposed by The Joint American College of Cardiology and European Society of Cardiology Committee for the definition of acute, evolving, or recent MI: typical rise and gradual fall (troponin) or more rapid rise and fall (Creatine kinase MB) of biochemical markers of myocardial necrosis with at least one of the following: ischemic symptoms, development of pathological Q wave on the ECG, electrocardiographic changes indicative of ischemia, coronary artery intervention, or pathologic finding of acute MI. Established MI was defined as any one criteria that satisfies the following: development of new pathologic Q waves on serial ECGs or pathologic finding of healed or healing MI.

2.1.1. Echocardiography

Two dimensional echo-Doppler study was performed in all patients before discharge. Images performed in the standard parasternal and apical views with the patient in the left lateral position. LV end-systolic and end-diastolic volumes were calculated and EF estimated by modified Simpson technique. Regional LV systolic function was assessed according to the 16-segment model of the American Society of Echocardiography and graded from 1 to 4 (1 – normal, 2 – hypokinesia, 3 – akinesia, 4 – dyskinesia). Wall motion score index (WMSI) was calculated by summing the score for each segment and divided by the number of segments analyzed. Mechanical complications (including mitral incompetence, ventricular septal defect and rupture myocardium) were also looked for and reported in all patients.

2.1.2. Clinical outcome

In-hospital death, clinical heart failure, and significant cardiac dysrhythmias (including sustained and hemodynamically compromising dysrhythmias) were compared between the two groups.

2.1.3. Statistical analysis

Data were analyzed on SPSS version 10.0. Rates of missed thrombolysis were compared among groups of patients with different demographic or clinical characteristics with the use of chi-square tests for dichotomous variables and Fisher’s exact tests for nominal variables. Logistic regression was used to explore multivariate associations between different variables and missing thrombolysis. A value of $P < 0.05$ was considered significant.

3. Results

We interrogated 6522 patients presented to the emergency room because of possible ACS, 4259 patients proved to have non-cardiac causes for chest pain and the remaining 2263 patients admitted as ACS patients. Of those who were admitted with ACS, only 288 had STEMI with no contraindication to thrombolytic therapy, of whom only 158 (55%) received thrombolytic therapy by intravenous streptokinase comprising group (1) while the remaining 130 (45%) patients missed this therapy (group 2). Baseline clinical characteristics of both groups are shown in Table 1.

Reasons for missing thrombolysis were: first, the delayed presentation to the emergency room (>24 h after the onset of symptoms) in 59% of the cases, most likely because the patient had similar attacks of chest pain in the prior few days, vague initial symptoms (e.g. dyspnea, nausea, and vomiting), refusal of hospital admission at first presentation, and living far away from the hospital. Second, misdiagnosis at the emer-

<table>
<thead>
<tr>
<th>Item</th>
<th>Missed thrombolysis</th>
<th>Received thrombolysis</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49.5 ± 28.6</td>
<td>45.7 ± 23.4</td>
<td>0.06</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>88/42</td>
<td>60/98</td>
<td>0.05</td>
</tr>
<tr>
<td>Smoking</td>
<td>73(56.2%)</td>
<td>120(64.8%)</td>
<td>0.07</td>
</tr>
<tr>
<td>DM</td>
<td>73(56.2%)</td>
<td>90(48.6%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Hypertension</td>
<td>68 (52.3%)</td>
<td>110(59.4%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>122(93.8%)</td>
<td>120(64.8%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Obesity</td>
<td>70(53.8%)</td>
<td>116(62.7%)</td>
<td>0.06</td>
</tr>
</tbody>
</table>
emergency department (35%), it was worth noting that 86% of patients missing thrombolysis were first seen by the emergency residents with only 14% seen by the cardiology specialists, while 78% of patients received thrombolysis were first seen by cardiology specialists. Third, lack of availability of beds in the CCU contributed to 6% of missed thrombolysis (Fig. 1).

Among patients with STEMI, only 85% had ECG recordings, and 12% had their cardiac enzymes checked at the time of presentation. Patients with missed thrombolysis were more likely to have inferior MI (42%) compared to patients who received thrombolysis (28%) \( (P < 0.05) \).

PredischARGE echocardiographic studies showed that patients who received thrombolysis had better systolic and diastolic functions (as measured by ejection fraction, and trans-mitral pulsed-wave Doppler recordings, respectively) than patients who missed thrombolysis, while WMSI was not different among the two groups (Tables 2 and 3).

Patients with missed thrombolysis had higher adverse in-hospital events including death, clinical heart failure and cardiac dysrhythmias than patients who received this therapy (Table 4). In addition, patients with missed thrombolysis had longer hospital stay (6 ± 3 days) than patients who received this therapy \( (4 ± 3 \text{ days}) \) \( (P < 0.05) \).

4. Discussion

There is overwhelming evidence of the beneficial effects provided by reperfusion strategies in patients with STEMI, however, thrombolytic therapy is still underused in the management of this condition.\(^9\) We designed this study to define the prevalence of missing thrombolytic therapy in STEMI, the causes of this failure and its impact on the in-hospital clinical outcome.

In this study the prevalence of missed thrombolytic therapy in patients with STEMI was 45%, this is higher than that reported by other investigators. In England the prevalence of missed thrombolysis in men aged below 64 was 6.3%\(^10\). In a report of Heart Disease prevalence in United States, the prevalence of missed thrombolysis in patients with STEMI ranged from 2.1% to 8.5%, and West Virginia had the highest prevalence.\(^11\) In Karachi (Pakistan) the prevalence of missed thrombolysis in STEMI was 32%, this relatively high prevalence was explained in the light of the longer pre-hospital delay (median 24 h) in non-thrombolysed patients, due to living far away from the health care providers and lack of fast transportation.\(^12\) More recently, Al-Mallah et al. found that 9.3% of patients with STEMI did not receive reperfusion therapy despite no contraindications; this study was carried out in six Arab countries in the Gulf area as a part of Quality of Care and Outcomes Assessment Program.\(^13\) This wide variation in

---

Table 2 | Comparison of left ventricular systolic function in patients who received thrombolysis versus those who missed this therapy.

<table>
<thead>
<tr>
<th>Ejection fraction</th>
<th>Missed thrombolysis</th>
<th>Received thrombolysis</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;55%</td>
<td>6(4.62%)</td>
<td>58(37%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>45-54%</td>
<td>7(5.38%)</td>
<td>48(31%)</td>
<td></td>
</tr>
<tr>
<td>30-44%</td>
<td>68(52.30%)</td>
<td>37(23%)</td>
<td></td>
</tr>
<tr>
<td>&lt;30%</td>
<td>49(37.69%)</td>
<td>15(9%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 3 | Comparison of diastolic function in patients who received thrombolysis versus those who missed this therapy.

<table>
<thead>
<tr>
<th></th>
<th>Missed thrombolysis</th>
<th>Received thrombolysis</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>32(24.62%)</td>
<td>65(41%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Mild dysfunction</td>
<td>64(49.23%)</td>
<td>42(26.8%)</td>
<td></td>
</tr>
<tr>
<td>Moderate dysfunction</td>
<td>25(19.23%)</td>
<td>48(31%)</td>
<td></td>
</tr>
<tr>
<td>Severe dysfunction</td>
<td>9(6.92%)</td>
<td>2(1.2%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 4 | Clinical outcome in patients received thrombolysis versus those who missed this therapy.

<table>
<thead>
<tr>
<th>Complications</th>
<th>Missed thrombolysis</th>
<th>Received thrombolysis</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency %</td>
<td>Frequency %</td>
<td>Frequency %</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>9</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Heart failure</td>
<td>46</td>
<td>37</td>
<td>15</td>
</tr>
<tr>
<td>Arrhythemias</td>
<td>30</td>
<td>23</td>
<td>11</td>
</tr>
</tbody>
</table>
the prevalence of missed thrombolytic therapy among our study and different studies represents the difference in socio-demographic and clinical characteristics of the studied populations.

Delayed presentation to the emergency department (> 24 h after the onset of symptoms) represented the most likely cause for missing thrombolytic opportunity (59% of the cases). Various causes for delayed presentation were encountered in this study including: similar attacks of chest pain in the prior few days, vague initial symptoms (e.g. dyspnea, nausea, and vomiting), refusal of hospital admission at first presentation, and living far away from the hospital. Consistent with this observation, Habib et al. reported delayed presentation to the emergency room as the most common reason for missing thrombolytic therapy.12

Misdiagnosis at the time of presentation to the emergency room was the second common cause for missing thrombolyis (35%). Previous studies had found that between 2% and 8% of patients with acute myocardial infarction who presented to the emergency department were misdiagnosed and sent home.14–17 In our study, 86% of patients missing thrombolyis were first seen by the emergency residents with only 14% seen by the cardiology specialists, while 78% of patients received thrombolyis were first seen by cardiology specialists. Failure by the emergency department clinician to detect ST-segment elevations of 1–2 mm in the electrocardiogram represented an important cause for missing the diagnosis in our study (44%). This incidence represents an important and potentially preventable contribution to missing thrombolytic therapy.

We found that female gender, diabetes mellitus and inferior location of myocardial infarction were all independent predictors of missing thrombolytic therapy. Hector et al. reported higher rates of misdiagnosis of myocardial infarction in women than in men; primarily related to atypical symptoms at presentations.18 Diabetics are more likely to have atypical symptoms of myocardial ischemia (dyspnea, fatigue, and vomiting) than non-diabetics, contributing to misdiagnosis of cardiac ischemia at the time of presentation in these patients.19 Similarly, compared with other locations of myocardial infarction, inferior location is more likely to present with upper abdominal rather than precordial discomfort.20

Pre-discharge trans-thoracic echocardiography showed lower global LV systolic functions (as measured by ejection fraction) in patients who missed thrombolytic therapy compared with patients who received it (P < 0.05). Similarly, patients with missed thrombolyis had higher grades of LV diastolic dysfunctions (as assessed by mitral inflow pulsed-wave Doppler) than patients who received this therapy (P < 0.05). This is easily understandable in the light of the beneficial effect of successful thrombolyis on myocardial salvage and preventing irreversible myocardial damage contributing to both systolic and diastolic dysfunctions.21

Compared with patients who received thrombolytic therapy, patients missing this therapy had higher in-hospital mortality (0.6% versus 6%, respectively, P < 0.05), clinical heart failure (9% versus 37%, respectively, P < 0.05), and significant cardiac dysrhythmias (6% versus 23%, respectively, P < 0.05).

This study had several limitations. First, the small number of patients with STEMI, limited the number of features that could be studied in our multivariable models of factors contributing to failure of receiving thrombolyis. Second, the study included only urban public hospitals and no rural hospitals without emergency physicians on site or private hospitals included, which could influence the rate of receiving thrombolyis. Third, patients who died outside the hospital, critically ill patients, and patients with silent myocardial infarction were not included in the study.

5. Conclusions

In this study, up to 45% of patients with STEMI and no contraindication to thrombolytic therapy missed the opportunity to receive thrombolyis, most likely due to late presentation or misdiagnosis at the emergency department. Patients with missed thrombolyis are at higher risk of in-hospital cardiac death, heart failure, and cardiac dysrhythmias. Urgent community and physician awareness programs are needed to increase the utilization of this life saving therapy.

References


