Outcome of Recombinant Tissue Plasminogen Activator in ST-Segment Elevation Myocardial Infarction in Buriram Hospital

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**Objective:** To study clinical outcomes of recombinant tissue plasminogen activator (alteplase) as primary fibrinolytic drug in patients with acute STEMI in Buriram Hospital.

**Material and Method:** Data on demographics, medications, in-hospital outcomes, and angiography were collected from a prospective registry of STEMI patients admitted by STEMI fast track from January 1, 2011 to December 31, 2013.

**Results:** During the 3-year period, 97 consecutive patients with STEMI who received alteplase were enrolled. The mean age was 64.3 year and 75.3% were male. There were high prevalence of dyslipidemia and current smoking. Median time from symptom onset to hospital presentation was 170 minutes. Median door to needle time was 30 minutes. Thrombolytic therapy was started in 30 minutes in 55.7% of cases. Overall bleeding was 19.6%. Intracranial hemorrhage was 1.0% of patients. ST-segment resolution was found in 79.4% of cases. In-hospital mortality was 11.3%. Angiographic data (n = 45) in patients with clinical reperfusion (n = 32), TIMI flow grade 2 and 3 combined was 90.6% and TIMI flow grade 3 was 56.3%. Revascularization was performed in 90.6%.

**Conclusion:** Alteplase in acute STEMI provided good clinical reperfusion with minimal major bleeding complication. Most of patients with clinical reperfusion required additional percutaneous coronary intervention to fix residual stenosis of infarct related artery.

**Keywords:** Acute coronary syndrome, ST-segment elevation myocardial infarction, Thrombolytic therapy, Tissue plasminogen activator
Material and Method

The present study was a prospective, observational study to characterize the clinical profile, management and in-hospital outcomes of STEMI patients who received alteplase as a fibrinolytic agent. Between January 2011 and December 2013, data from all consecutive patients presenting within 24 hours of acute STEMI who had received alteplase as a thrombolytic agent at the Buriram Hospital were collected prospectively. STEMI patients who had contraindications to thrombolytic drug, spontaneous reperfusion and not consent to treatment were excluded from the study. STEMI patients were defined as patients who had symptoms consistent with cardiac ischemia within 24 hours prior to hospital presentation, elevated biochemical markers of myocardial necrosis and electrocardiographic (ECG) changes consistent with STEMI. The ECG criteria were 1) ST-segment elevation at the J point >0.2 mV in men, or >0.15 mV in women, in the leads V2-V3 and/or >0.1mV in other leads at least two consecutive leads, or 2) new or presumed new left bundle branch block (LBBB). The decision regarding the administration of reperfusion therapy and ST-segment resolution was made by the attending cardiologist.

Data collection

Data collection was performed by well-trained critical care nurses and cardiologists. Data included; patient’s characteristics, coronary risk factors, clinical presentations, in-hospital treatments, complications and in-hospital outcomes of the STEMI patients. Diabetes was diagnosed when the patient’s fasting plasma glucose was 126 mg/dl or higher on at least two occasions or the presence of a history of diabetes treated with either dietary control or antidiabetic medication. Hypertension was defined as systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg or a previous diagnosis of hypertension. Dyslipidemia was diagnosed when total cholesterol was >200 mg/dl, LDL cholesterol >130 mg/ dl, HDL cholesterol <40 mg/dl or a previous diagnosis of dyslipidemia and/or currently being treated with a lipid lowering agent. Current smoking was defined by the habitual use of tobacco at index hospital admission. Typical angina chest pain was defined as chest pain typical of myocardial ischemia (chest, arm, or jaw pain/pressure aggravated by exertion or stress, and relieved by rest or nitroglycerin). Atypical angina chest pain was chest pain that could not be characterized as typical angina. Congestive heart failure was defined as present of bibasilar rales in lung fields or presence of an S3 gallop. Cardiogenic shock was defined as symptomatic hypoperfusion with systolic blood pressure <90 mmHg. In-hospital complications included bleeding, congestive heart failure, cardiogenic shock, serious arrhythmias, and death. Major bleeding was defined as overt clinical bleeding other than intracranial hemorrhage that resulted in requiring of blood transfusion. ST-segment resolution was evaluated by one cardiologists at 90 minutes after receiving thrombolytic agent and defined as more than 50% resolution in lead with previous maximum ST-segment elevation. Refer for routine coronary angiogram (CAG) after successful fibrinolysis was defined as referring cases for CAG in case of having ST-segment resolution. Refer for rescue PCI was defined as referring for CAG in cases of no ST-segment resolution.

All coronary angiograms were performed at Maharat Nakhon Ratchasima Hospital, the nearest cardiac catheterization laboratory center (Cath lab). Angiographic reports were obtained. Data about the extent of coronary vessels, degree of stenosis, Thrombolysis in Myocardial Infarction (TIMI) flow classification and choice of revascularization were compared between ST-segment resolution and non ST-segment resolution group.

Statistical analysis

Categorical variables are described as frequency and percentages. Continuous variables are presented as mean ± standard deviation or median (interquartile range) as appropriate. Differences between the two ST-segment resolution groups for frequencies of categorical variables were tested by Chi-square or Fisher’s exact test. Differences among continuous variables were tested by the unpaired t-test for mean values or Mann-Whitney U test as appropriate. All statistical tests are 2-tailed with p-value <0.05 considered statistically significant. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) for Windows version 20.

Results

During the 3-year period, 97 consecutive patients with STEMI who received alteplase as primary fibrinolytic agent were enrolled. Sixty-nine patients (71.1%) were referred to the author’s hospital. The baseline characteristics and risk factors for these patients are listed in Table 1. The mean age was 64.3±11.9 years and 73 patients (75.3%) were men.
Most common atherosclerosis risk factor was dyslipidemia (54.6%), followed by current smoking (48.5%). The majority of patients were under the universal health care program (76.3%). Most patients presented with typical chest pain (89.7%). Median time from symptom onset to hospital presentation was 170 minutes. The majority of infarct wall location was anterior wall (56.7%), followed by inferior wall (44.3%).

The pharmacologic treatment and in-hospital outcome of patients were listed in Table 2. Aspirin and clopidogrel were used in all of patients. Eighty-nine patients (91.8%) received low molecular weight heparin (LMWH). Twenty-seven patients (27.8%) received beta-blocker, whereas 23 patients (23.7%) received an angiotensin converting enzyme inhibitor (ACEI) or an angiotensin II receptor blocker (ARB). Median door to needle time was 30 minutes. The thrombolytic therapy was started within 30 minutes in 55.7% of the cases. Cardiogenic shock was a frequent in-hospital complication in 34% of the patients. Minor bleeding occurred in 15.5%; half of these (seven patients) had only gum bleeding from underlying periodontitis. One intracranial hemorrhage (1.0%) occurred in the 82 years old man with extensive anterior wall MI.

Overall in-hospital fatality rate was 11.3%. Excluding referral cases, the median length of stay (LOS) was 4.5 days. ST-segment resolution was observed in 79.4% of the patients. Forty-seven patients (48.5%) were referred to Maharat Nakhon Ratchasima Hospital. Thirty-four patients (35.1%) were transferred.
for early routine CAG after successful thrombolysis, whereas 13 patients (13.4%) for rescue PCI. Ninety percent of these were transferred within 24 hours after receiving thrombolysis. There was an increasing proportion of patients transferring to Cath lab when compared with previous years (Fig. 1).

Coronary angiographic reports were collected from Maharat Nakhon Ratchasima Hospital. Ninety-one percent of patients were performed coronary angiogram in one day after transferred. Angiographic data was missing in one case. One case was diagnosed as Takotsubo cardiomyopathy by normal coronary artery and apical ballooning on ventriculogram. Angiographic data (n = 45) were shown in Table 3. Median coronary stenosis in patients with ST-segment resolution was less than those without. TIMI flow III was observed in 56.3% of patients with ST-segment resolution and 23.1% of those without. TIMI flow II and III combined was seen in 90.6% of patients with ST-segment resolution and 61.5% of those without. Median stenosis of coronary artery was 90 and 99% in patients with and without ST-segment resolution respectively.

**Discussion**

The management of STEMI had been established by clinical trials and summarized in the guidelines(2,3). However, under limited resources in rural areas, the clinical outcome might be different. The present study was performed at Buriram Hospital, the government hospitals in rural areas, 120 kilometers far from Cath lab. Thrombolytic therapy is the only choice of reperfusion unless contraindicated. In Thailand, there are many reports from regional government hospitals or academic hospitals using thrombolytic treatment in STEMI. There were no published data of clinical reperfusion after thrombolytic therapy. The present study was the first to report of clinical

![Fig. 1](Discharge status in each year with proportion of each status.)

**Table 3.** Angiographic data of STEMI patients with ST-segment resolution and no ST-segment resolution (n = 45)

<table>
<thead>
<tr>
<th></th>
<th>ST-segment resolution (n = 32)</th>
<th>No ST-segment resolution (n = 13)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median stenosis, median (%, IQR)</td>
<td>90 (80, 95)</td>
<td>99 (87.5, 100)</td>
<td>0.026a</td>
</tr>
<tr>
<td>Open vessels, TIMI grades 2 and 3 combined, n (%)</td>
<td>29 (90.6)</td>
<td>8 (61.5)</td>
<td>0.034b</td>
</tr>
<tr>
<td>Complete reperfusion, TIMI grade 3, n (%)</td>
<td>18 (56.3)</td>
<td>3 (23.1)</td>
<td>0.043c</td>
</tr>
<tr>
<td>Infarct related artery, n (%)</td>
<td></td>
<td></td>
<td>0.588b</td>
</tr>
<tr>
<td>LAD</td>
<td>18 (56.3)</td>
<td>7 (53.8)</td>
<td></td>
</tr>
<tr>
<td>LCx</td>
<td>0 (0)</td>
<td>1 (7.7)</td>
<td></td>
</tr>
<tr>
<td>RCA</td>
<td>13 (40.6)</td>
<td>5 (38.5)</td>
<td></td>
</tr>
<tr>
<td>LM</td>
<td>1 (3.1)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Extent vessel, n (%)</td>
<td></td>
<td></td>
<td>0.147b</td>
</tr>
<tr>
<td>1 vessel</td>
<td>20 (62.5)</td>
<td>6 (46.1)</td>
<td></td>
</tr>
<tr>
<td>2 vessels</td>
<td>8 (25.0)</td>
<td>2 (15.4)</td>
<td></td>
</tr>
<tr>
<td>3 vessels</td>
<td>4 (12.5)</td>
<td>5 (38.5)</td>
<td></td>
</tr>
<tr>
<td>Revascularization, n (%)</td>
<td></td>
<td></td>
<td>0.999p</td>
</tr>
<tr>
<td>No intervention</td>
<td>3 (9.4)</td>
<td>1 (7.7)</td>
<td></td>
</tr>
<tr>
<td>PCI</td>
<td>28 (87.5)</td>
<td>12 (92.3)</td>
<td></td>
</tr>
<tr>
<td>Emergency CABG</td>
<td>1 (3.1)</td>
<td>0 (0)</td>
<td></td>
</tr>
</tbody>
</table>

TIMI = thrombolysis in myocardial infarction; LAD = left anterior descending; LCx = left circumflex; RCA = right coronary artery; LM = left main; PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft

a Mann-Whitney U test  
b Fisher’s exact test  
c Chi-square test
reperfusion after thrombolysis, and follow with the subsequent coronary angiographic data.

Reporting from TACSR 2007\textsuperscript{[10]}; median door to needle time was 85 minutes. After that, there were many studies\textsuperscript{[6-9]} from regional government hospital describing the effectiveness of the fast track system to improve door to needle time. The results were varied from 30-81 minutes. Median door to needle time in the present study was 30 minutes and thrombolytic treatment was initiated within 30 minutes in 55.7\% of the cases, closed to the current guideline recommendation. Even improve door to needle time, time to treatment still did not change. Median time to treatment in TACSR 2007 was 240 minutes and in subsequent studies were 226 to 250 minutes. Median time to treatment in the present study was 203 minutes, which longer than the best effective period of thrombolytic drug (180 minutes)\textsuperscript{[10]}. Delay onset to hospital presentation time is the principal cause of prolonged time to treatment in Thailand. No previous study in Thailand about patients delay, such as how patients recognize and react to angina pain, difficulty in transportation, utilizing an emergency medical service (EMS). These issues need further investigation.

Cardiogenic shock at the presentation was more than in TACSR 2007 (26.8\% vs. 16.3\%). This related to increased odd ratio of mortality in Thai STEMI\textsuperscript{[11]}. The explanations may be because 71.1\% of patients were referred from community hospitals, 15 to 80 kilometers far from the author’s hospital, resulting in prolonged time to treatment. Initiation of thrombolytic drug at community hospitals, the real first medical contact, is another way to improve time to treatment.

The present study used only ST-segment resolution to determine clinical reperfusion. There are many non-invasive markers used to evaluate clinical reperfusion. Chest discomfort was a typical feature of myocardial ischemia. However, chest pain perception is subjective and intensity of pain usually mask by using analgesic drug. Reperfusion arrhythmia was not specific for coronary reperfusion\textsuperscript{[12,13]}. The Early peak of cardiac biomarker is a useful indicator of clinical reperfusion. Peak value of serum CK and CK-MB beyond 12 hours from initiation of thrombolysis are an index of failing reperfusion\textsuperscript{[14]}. CK peak cannot be used in real life practice because physicians have to make a decision of successful reperfusion at 90-minute after thrombolysis. ST-segment resolution is a simple and most reliable noninvasive tool to determine clinical reperfusion. More complete and more rapid resolution of ST-segment results in better outcome\textsuperscript{[15]}. ST-segment resolution in the present study was 79.4\%. In setting of prolonged time to treatment in Thai population, the first-line thrombolytic regimen need to be reevaluated because the efficacy of streptokinase but not alteplase in restoring coronary patency is markedly lower when time to treatment is more than 180 minutes\textsuperscript{[16]}.

Overall bleeding complication was 19.6\%. Minor bleeding was more than the prior study\textsuperscript{[17]} (15.5\% vs. 11.0\%). Interestingly, half of minor bleeding came from cases with only bleeding per gum. These patients had underlying periodontitis. Intracranial hemorrhage was slightly less than the previous report (1.0\% vs. 1.43\%)\textsuperscript{[18]}.

During three years of investigation, there was a breaking strategy in STEMI standard of care. After the early routine PCI after thrombolysis strategy was announced in the current guideline\textsuperscript{[22]}. In the year 2012 as class IA recommendations. All patients after fibrinolysis were encouraged and transferred to Cath lab if they consented. This resulted in continuing and increasing percentage of patients transferred to perform coronary angiogram. At the year 2013, 65\% of patients who received thrombolysis were transferred.

In ST-segment resolution group, the overall patency of the infarct related artery (TIMI grades 2 and 3 combined) was 90.6\% and complete reperfusion (TIMI grade 3) was 56.3\%, but only TIMI grades 3 flow reported to associated with favorable outcome\textsuperscript{[19]}. The median residual stenosis of the infarct related artery was 90\%. Revascularization procedure in ST-segment resolution group was very close to previous study\textsuperscript{[20]}. These emphasize the need of early routine angioplasty after successful fibrinolysis\textsuperscript{[21]} to prevent reoclusion.

**Conclusion**

Use of recombinant tissue plasminogen activator (alteplase) as a fibrinolytic agent in patients with acute STEMI provided similar outcome to standard in literature. The majority of patients have ST-segment resolution, TIMI grades 2, 3 flow, and minimal major bleeding complication. Nevertheless, most of the patients with ST-segment resolution required additional percutaneous coronary intervention to fix residual stenosis of infarct related artery.

**Study limitation**

There were some limitations in the present study. First, all STEMI patients in Buriram Hospital may not receive thrombolytic agent, due to
contraindicate, do not consent, misdiagnosis, or death at emergency department. Second, decision of ST-segment resolution and angiographic result made by one attending cardiologists at the time of treatment. There was potential bias from physicians. Third, no available data of bleeding complication after cardiac catheterization. The bleeding complication in the present study counted only in the author’s hospital. This data reflect bleeding complications in non PCI-capable hospitals that use routine early angiogram after successful fibrinolysis strategy.

**What is already known on this topic?**

ST elevation myocardial infarction (STEMI) is serious medical condition associate with high mortality. Fibrinolytic therapy is recommended in patients without contraindications, if primary PCI cannot be performed within 120 minutes of first medical contact.

The current guideline recommend fibrin-specific over non-fibrin-specific drug.

In Thailand, data of fibrin specific drug in treatment of STEMI are limited. Most studies used streptokinase (non-fibrin-specific) as primary fibrinolytic agent.

**What this study adds?**

This report described use of recombinant tissue plasminogen activator (r-tPA; fibrin-specific fibrinolytic drug) in treatment of acute STEMI in Thailand. This is the first report about efficacy (ST segment resolution and subsequent angiographic data) and harm (bleeding complication) of r-tPA in treatment of acute STEMI Thailand.

**Acknowledgements**

The authors wish to acknowledge Warong Wasuchanong together with the STEMI team of Maharat Nakhon Ratchasima hospital who patiently and diligently assisted in angiographic data collections.

**Potential conflicts of interest**

None.

**Reference**

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ผลการรักษาโรคหลอดเลือดหัวใจตีบเฉียบพลันชนิด ST elevation ด้วยยา recombinant tissue plasminogen activator ในโรงพยาบาลบุรีรัมย์

ภัทรพงษ์ พีรวงศ์, บุหลัน เปลี่ยนไธสง

วัตถุประสงค์: เพื่อศึกษาผลการใช้ยา recombinant tissue plasminogen activator (alteplase) ในการรักษาโรคหลอดเลือดหัวใจตีบเฉียบพลันชนิด ST elevation (STEMI) ในโรงพยาบาลบุรีรัมย์

วัตถุประสงค์: เป็นโครงการศึกษาไปข้างหน้า โดยเก็บข้อมูลของผู้ป่วยโรคหลอดเลือดหัวใจตีบเฉียบพลันชนิด ST-segment และได้รับยา alteplase เป็นยาสลายลิ่มเลือดในระบบการรักษาแบบเร่งด่วนโรคหลอดเลือดหัวใจตีบเฉียบพลันชนิด ตั้งแต่วันที่ 1 มกราคม พ.ศ. 2554 ถึง 31 ธันวาคม พ.ศ. 2556 ข้อมูลที่เก็บได้แก่ ข้อมูลพื้นฐาน ยา การรักษาที่เกิดขึ้นในโรงพยาบาล และผลการเสียชีวิตที่เกิดขึ้น

ผลการศึกษา: ในระยะเวลา 3 ปี ผู้ป่วยที่ได้รับยาจำนวน 97 ราย อายุเฉลี่ย 64.3 ปี เป็นเพศชายร้อยละ 75.3 มีผู้ป่วยที่เป็นโรคไขมันในเลือดสูงและสูบบุหรี่ร้อยละ 37.3 ค่าสมดุลตามที่สิ้นสุดของผู้ป่วยในโรงพยาบาลเท่ากัน 170 นาที ค่าสมดุลตามเวลา door-to-needle เท่ากัน 30 นาที ผู้ป่วยได้รับยาภายใน 30 นาที ร้อยละ 55.7 มี ST-segment resolution เท่ากันร้อยละ 79.4 พบภาวะเลือดออกในผู้ป่วยร้อยละ 19.6 การเสียชีวิตในสมองร้อยละ 1.0 อัตราตายร้อยละ 11.3 ผลการสลายลิ่มหลอดเลือดหัวใจในผู้ป่วย (45 ราย) ที่มีการเสียชีวิตขึ้นการสลายลิ่มหลอดเลือด (32 ราย) พบ TIMI flow ระดับ 2 หรือ 3 ร้อยละ 90.6 TIMI flow ระดับ 3 ร้อยละ 56.3 ทำการเปิดหลอดเลือดหัวใจร้อยละ 90.6

สรุป: การใช้ยา alteplase มีประสิทธิภาพในการเปิดหลอดเลือดหัวใจได้ดีและเกิดภาวะเสียชีวิตกรุณาแจ้งได้ในยี่ แต่ยังไม่สามารถกำหนดได้ที่มีสมดุลตามที่แสดงถึงการเปิดหลอดเลือดที่ไม่ยังต้องการรักษาหรือทำการเปิดหลอดเลือดหัวใจต่อ