COMPARING MORTALITY AND COMPLICATIONS IN STEMI BETWEEN TWO TREATMENT GROUPS: PRIMARY PCI AND PHARMACO-INVASIVE GROUPS: MAHARAT NAKHON RATCHASIMA HOSPITAL

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Abstract

The current definitive treatment for STEMI is reperfusion therapy consisting of primary percutaneous coronary intervention (primary PCI) and thrombolysis following PCI within 3–24 h (pharmaco-invasive treatment). The aim of this study was to compare the mortality and complications between 2 groups of patients with STEMI, one undergoing undergoing primary PCI and the other undergoing pharmaco-invasive treatment. A total of 808 patients with STEMI were treated at Maharat Nakhon Ratchasima Hospital from 1st November, 2012 to 31st October, 2013. Among 483 patients who were included in the study, 345 were treated with primary PCI and 138 had pharmaco-invasive treatment. Patients in the primary PCI group are more likely to die and to have more frequent arrhythmic complications when compared with the pharmaco-invasive group (11.6% vs. 9.4%, p = 0.490 and 11.9% vs. 10.1%, p = 0.587, respectively. Patients in the primary PCI group had statistically significantly less TIMI minor bleeding complications than the pharmaco-invasive group (3.5% vs. 9.4%, CI 1.282-6.495; p = 0.008). Door-to-balloon time (from the first medical contact) was longer than door-to-needle time. In this study, the difference between door-to-balloon time and door-to-needle time, the PCI-related delay was 95.5 min. In summary, there was a time delay in treatment for STEMI in Nakhon Ratchasima province, with both the primary PCI and pharmaco-invasive treatment strategies. Due to the lack of a PCI center and the time delay in the transfer for primary PCI, pharmaco-invasive may be the treatment strategy of choice.

Keywords: STEMI, primary PCI, pharmaco-invasive treatment, Nakhon Ratchasima, Thailand

Introduction

STEMI is a clinical syndrome defined by characteristic symptoms of myocardial ischemia associated with persistent electrocardiographic (ECG) ST elevation and the subsequent release of biomarkers of myocardial necrosis. The most common triggering event is the disruption of an atherosclerotic plaque in an epicardial coronary artery, which leads to a clotting cascade, resulting in total occlusion of the artery. Patients with STEMI have a high incidence of death and complications. The current definitive treatment for STEMI is reperfusion therapy consisting

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of thrombolysis and percutaneous coronary intervention, as recommended by the American College of Cardiology Foundation/American Heart Association (O'Gara *et al*., 2013) and the European Society of Cardiology (Steg *et al*.,2012). Primary percutaneous intervention (PCI) is the recommended reperfusion therapy rather than fibrinolysis, if performed within 120 min from the first medical contact. If PCI cannot be performed within 90 to 120 min, then thrombolysis, preferably within 30 min of arrival at the hospital, is recommended. Fibrinolytic therapy is recommended in patients without contraindications.

Primary PCI must be performed by an experienced interventionist with access to a cardiac catheterization laboratory. In rural hospitals, a general practitioner can give thrombolytic drugs instead of primary PCI. Transfer to a PCI-capable center following fibrinolysis is indicated in all patients after fibrinolysis, referred to as pharmaco-invasive strategy. Angiography with a view to revascularization (of the infarct-related artery) is indicated after a successful fibrinolysis. The optimal timing of angiography for stable patients after successful fibrinolysis is from 3–24 h. Rescue PCI is indicated immediately when fibrinolysis has failed (<50% ST-segment resolution at 60 min). Emergency PCI is indicated in the case of recurrent ischemia or evidence of re-occlusion heart failure/shock after initial successful fibrinolysis.

Objective

The aim of this study was to compare the mortality and complications between 2 groups of patients, one with STEMI undergoing primary PCI and the other with STEMI receiving thrombolytic drugs and PCI after thrombolysis within 24 h (pharmaco-invasive strategy).

Methods

In this retrospective study, data were collected from patients with STEMI who were admitted to Maharat Nakhon Ratchasima Hospital from 1st November, 2012 to 31st October, 2013.

Patients

Inclusion Criteria

Patients aged 18–75 years old who had ischemic chest pain within 12 h after onset with the following ECG findings:

1. ST-segment elevation in at least 2 contiguous electrocardiographic leads;
2. New or presumed new left bundle branch block.

All patients had received 1 of 2 methods of treatment: primary PCI or PCI within 24 h after thrombolysis (pharmaco-invasive therapy).

Exclusion Criteria

1. Patients aged < 18 years old and those >75 years old;
2. Patients who had received thrombolytic drugs within 12 h from the onset of ischemic chest pain;
3. Pregnant patients.

Mortality and complications between the two treatment groups were compared; fatal ventricular arrhythmia which required cardioversion or defibrillation, bradyarrhythmia which required a temporary pacemaker, and bleeding complications (major and minor thrombosis in myocardial infarction (TIMI) bleeding).

Major Bleeding

1. Any intracranial bleeding (excluding microhemorrhages < 10 mm evident only on gradient-echo MRI);
2. Clinically overt signs of hemorrhage associated with a drop in hemoglobin of ≥ 5 g/dL or a ≥15% absolute decrease in hematocrit;
3. Fatal bleeding (bleeding that directly results in death within 7 days).

Minor Bleeding

1. Clinically overt (including imaging), resulting in a hemoglobin drop of 3 to < 5 g/dL or a ≥ 10% decrease in hematocrit;
2. No observed blood loss: ≥ 4 g/dL decrease in the hemoglobin concentration or ≥12% decrease in hematocrit;
3. Any overt sign of hemorrhage that meets one of the following criteria and does not

meet the criteria for a major or minor bleeding event, as defined above:

1. Requires intervention (medical practitioner-guided medical or surgical treatment to stop or treat bleeding, including temporarily or permanently discontinuing or changing the dose of a medication or study drug) ;
2. Leads to prolonged hospitalization;
3. Prompts evaluation (leading to an unscheduled visit to a healthcare professional and diagnostic testing, either laboratory or imaging).

Minimal Bleeding

1. Any overt bleeding event that does not meet the above criteria;
2. Any clinically overt sign of hemorrhage (including imaging) associated with a < 3 g/dL decrease in hemoglobin concentration or < 9% decrease in hematocrit.

Statistical Analysis

For the statistical analyses, the SPSS version 20.0.0 (SPSS Inc., Chicago, IL, USA) software was used. Continuous variables were delineated by their mean standard deviation or by the median and interquartile range, and frequencies were expressed as percentages, as appropriate. A chi-square test was used with $p < 0.05$ considered as clinically significant.

Results

A total of 808 patients with STEMI were treated at Maharat Nakhon Ratchasima Hospital from 1st November, 2012 to 31st October, 2013. Among 483 patients who were included in the study, 345 were treated with primary PCI and 138 had pharmaco-invasive treatment. The baseline characteristics of both study groups are shown in Table 1.

Table 1. Baseline characteristics

	Primary PCI group (n = 345)	Pharmaco-invasive group (n = 138)
Mean age – years	59.2+/-9.74	60.2+/-9.41
Male – persons (%)	265(76.8%)	100(72.5%)
Residence		
- Nakhon Ratchasima	306(88.7%)	39(28.2%)
- Outside NakhonRatchasima	39(11.3%)	99(71.8%)
Cerebro-vascular disease – person (%)	9(2.6%)	1(0.7%)
Diabetes mellitus – persons (%)	88(25.5%)	34(24.6%)
Mean HbA1C	6.71	6.45
Mean HDL (mg/dL) – (SD)	47.4 (12.3)	47.4 (13.6)
Mean LDL (mg/dL) – (SD)	123.7 (45.1)	113.9 (38.8)
Hypertension – persons (%)	147 (42.6%)	56 (40.6%)
Smoking – person (%)	179(51.9%)	74 (53.6%)
Area of infarction		
- Anterior wall	185 (53.6%)	84 (60.9%)
- Inferior wall	151 (43.8%)	50 (36.2%)
- Other wall	9 (2.6%)	4 (2.9%)
Killip class – persons (%)		
- Killip I	144 (41.7%)	49 (35.5%)
- Killip II	90(26.1%)	46 (33.3%)
- Killip III	15 (4.3%)	8 (5.8%)
- Killip IV	96 (27.8%)	35 (25.4%)
Time – minutes (mean +/- SD)		
Time from event-to-balloon	322 +/-158.4	
Door-to-balloon time	73.6+/-77.9	
Time from event-to-needle		237+/-128.1
Door-to-needle time		413.6+/-225.8
Time from FMC to reperfusion therapy	196.6+/-116.8	101.0+/-85.0

Patients in the primary PCI group had more frequent occurrences of cerebrovascular disease (2.6% vs. 0.7%), had more inferior wall STEMI (43.8% vs. 36.2%) but less anterior wall STEMI (53.6% vs. 60.9%). Both groups had equivalent diabetes mellitus, hypertension, and smoking status. Both groups also had equivalent Killip classes III and IV. Most patients in the primary PCI group came from Nakhon Ratchasima province while patients in the pharmaco-invasive group came from other provinces near Nakhon Ratchasima.

The event-to-balloon time was longer than event-to-needle time because patients in the primary PCI group had to transfer to the PCI center at Maharat Nakhon Ratchasima hospital but patients in the pharmaco-invasive group were able to receive thrombolytic drugs at the time of the first medical contact in the first hospital. The time from the first medical contact to fibrinolytic drugs was shorter than the time from the first medical contact to primary PCI (101+/-85.0 vs. 196+/-116.8 min) Patients in the primary PCI group had more intra-aortic balloon pump treatment than the pharmaco-invasive group.

Table 2 shows the outcome of the study by comparing the mortality and complications between the two treatment groups. Patients in the primary PCI group tend to be more likely to die and have arrhythmic complications when compared with the pharmaco-invasive group (11.6% vs. 9.4%, p = 0.490 and 11.9% vs. 10.1%, p = 0.587, respectively). However, these were not statistically significant. Patients in the primary PCI group had statistically significantly less TIMI minor bleeding complications than the pharmaco-invasive group (3.5% vs. 9.4%, CI 1.282-6.495; p = 0.008).

Discussion

In this study, comparison was made of the in-hospital mortality and complications in STEMI patients who received either of the two treatment strategies, primary PCI or pharmaco-invasive treatment. Patients in both groups had equivalent baseline characteristics except for more frequent cerebrovascular diseases in the primary PCI group. Patients residing outside Nakhon Ratchasima province had more of the pharmaco-invasive procedure because there was no PCI center in their areas of residence.

The two groups had equivalent areas of infarction and severity of disease, as defined by the Killip classification. Most patients in the pharmaco-invasive group were transferred for PCI due to residual chest pain after fibrinolysis.

In this study, there was found to be a delay in the door-to-balloon time in the primary PCI group (73.6 min) compared with the standard recommendations (within 60 min) of both the American College of Cardiology Foundation/ American Heart Association (O'Gara *et al*., 2013) and the European Society of Cardiology (Steg *et al*., 2013).

Table 2. Outcome between 2 strategy groups

Outcome	Primary PCI Group (n = 345)	Pharmaco invasive Group (n = 138)	Odds ratio (95% CI)	p-value
Total mortality	40(11.6%)	13(9.4%)	0.793 (0.410-1.533)	0.490
Bleeding complication				
- TIMI minor bleeding	12(3.5%)	13(9.4%)	2.886(1.282-6.495)	0.008
- TIMI major bleeding	2(0.6%)	1(0.7%)		
Arrhythmic complication*	41(11.9%)	14(10.1%)	0.837(0.441-1.590)	0.587

** Ventricular arrhythmia that required electrical cardioversion and defibrillation, and bradyarrhythmia that required a temporary pacemaker*

The door-to-balloon time (from the first medical contact) was longer than the door-to-needle time. In this study, the difference between the door-to-balloon time and the door-to-needle time, the PCI-related delay, was 95.5 min.

In the pharmaco-invasive group, it was also found that there was a delay in the time from the event to fibrinolysis and the time from fibrinolysis to the PCI (237+/-128.1 min and 413.6+/-225.8 min, respectively) when compared with most studies in western countries (Scheller *et al*., 2003; Di Mario *et al*., 2004; Le May *et al*., Armstrong, 2006; Cantor *et al*., 2009; Bøhmer *et al*., 2010), as shown in Figure 1.

The mortality rate in the pharmaco-invasive group was also higher when compared with most studies from western countries, as mentioned above, and) as shown in Figure 2.

Skilled interventionists prefer primary PCI when conducted in a timely manner. This recommendation was based on the results of multiple randomized trials comparing PCI with fibrinolytic therapy. In a meta-analysis of 23 clinical trials, the risk of immediate death was lower with primary PCI (Keeley *et al*., 2003). In this study when mortality between the two groups was compared, it was found that patients in the pharmaco-invasive group had a slightly

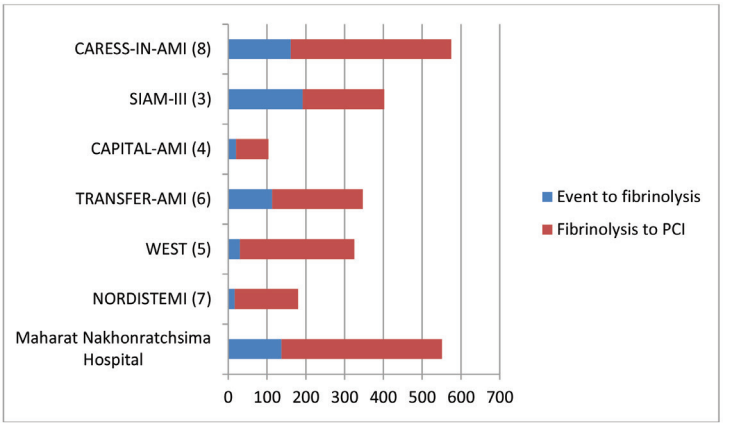

Figure 1. Time from event to fibrinolysis, and fibrinolysis to PCI – minutes

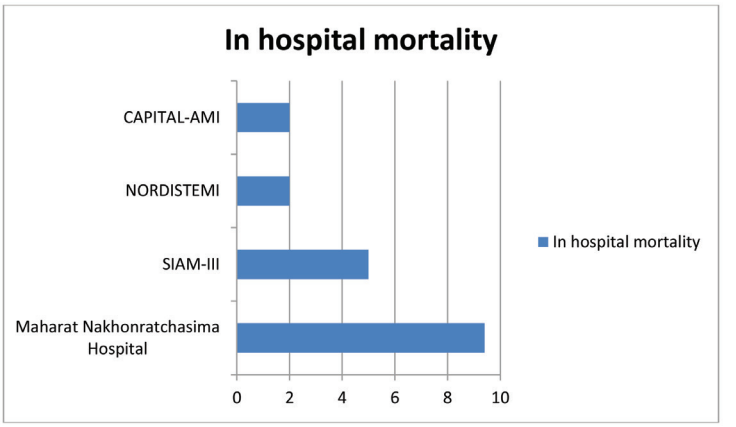

Figure 2. In hospital mortality in pharmaco-invasive strategy

less but not statistically significant likelihood of dying and arrhythmic complications than patients in the primary PCI group. Both groups had an equivalent severity of disease and baseline characteristics. When a comparison was made of the time from the event or first medical contact to the treatment strategy, it was found that the pharmaco-invasive group had a shorter time period and the difference in the time period between the two groups was 85.1 minutes and 95.5 min, respectively. Because fibrinolytic drugs can be given by a general practitioner, STEMI patients can have reperfusion treatment earlier with fibrinolytic therapy which results in a lower death rate.

Fibrinolytic therapy carries a greater risk of minor and major bleeding compared with primary PCI. Intracranial hemorrhage is the most serious of these risks and occurred in approximately 0.7 percent of patients treated with fibrinolytic therapy. In this study there were found to be more minor and major TIMI bleeding risks in the pharmaco-invasive group compared with the primary PCI group. However, there was no intracranial bleeding.

In Thailand, there are limited PCI centers that can perform primary PCI treatment. Most patients are transferred to PCI centers for the intervention. Delay in the transfer time may limit the benefit of primary PCI treatment. Pharmaco-invasive treatment may be appropriate in some cases in Thailand. When there is a delay in the transfer time, fibrinolytic therapy should be considered first before the patient is transferred later for primary PCI treatment. With the pharmaco-invasive treatment strategy, there is a high risk of minor bleeding. We found an equivalent major TIMI bleeding risk in both groups.

Conclusions

In this study, there was a time delay in treatment for STEMI in Nakhon Ratchasima province, both for primary PCI and pharmaco-invasive treatment strategies. Due to the lack of PCI centers and time delays in the transfer for primary PCI treatment, pharmaco-invasive may be the treatment strategy of choice. This strategy tends to have a lower risk of mortality, as shown in this study. In a situation when primary PCI cannot be performed in a timely manner, fibrinolytic therapy should be given first to the patient who should then be transferred for PCI. The clinicians should be aware of the bleeding complications in the pharmaco-invasive group.

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