Clinical research

Comparison of effects of thrombolytic therapy and primary percutaneous coronary intervention in elderly patients with acute ST-segment elevation myocardial infarction on in-hospital, six-month, and one-year mortality

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Abstract

Introduction: This study aims to evaluate the effect of primary percutaneous coronary intervention (PCI) and thrombolytic therapy (TT) on the in-hospital adverse events, in-hospital and long-term mortality in patients over 65 years of age with acute ST-segment elevation myocardial infarction (STEMI).
Material and methods: A total of 111 retrospectively screened patients (73 males, mean age: 73.4 ±5.9 years) over 65 years of age with STEMI, who underwent TT or primary PCI, were included in the study. Patients' characteristics, in-hospital outcomes, and 6-month and 1-year mortalities were recorded.
Results: Our study was conducted with 111 patients over 65 years of age with STEMI (73 males, 38 females). Of the patients, 66 (59.5%) were treated with thrombolytics, and 45 (40.5%) patients underwent primary PCI. Door-to-needle time was 25.9 ±7.8 min in the TT group, whereas door-to-balloon time was 84.4 ±20.0 min in the PCI group. Time from symptom onset to hospital admission was 213.6 ±158.4 min in the thrombolytic group, and 166.8 ±112.8 min in the PCI group. Rescue PCI was performed in 7 (10.6%) patients in the TT group due to lack of reperfusion. Recurrent infarction was observed in 5 (7.6%) patients in the TT group and in 2 (4.4%) patients in the PCI group. Non-haemorrhagic stroke was observed in 1 (1.5%) patient in the thrombolytic-administered group and in 4 (8.9%) patients in the PCI group. No intracranial haemorrhage was observed in any patient. Major haemorrhage was observed in 4 (6.1%) patients in the TT group and in 4 (8.9%) patients in the PCI group. Six-month and 1-year mortalities were present in 15 (22.7%) patients and 19 patients in thrombolytic group, and 8 (17.8%) and 8 (17.8%) patients in the PCI group, respectively. Binary logistic regression analysis indicated that the patient's age was the only predictor for 1-year mortality (odds ratio (OR) = 1.1, 95% confidence interval (CI): 1.019–1.188, p = 0.015).
Conclusions: Considering the in-hospital adverse outcomes, in-hospital mortality, and 6-month mortality rates, TT and primary PCI have similar effects in STEMI patients aged 65 years and over according to the results of our study. Although 1-year mortality was higher in the TT group, it was not statistically significant.

Key words: percutaneous coronary intervention, thrombolytic therapy, elderly patients, ST-segment elevation myocardial infarction.

Introduction

Acute myocardial infarction (AMI) is a common clinical syndrome with high morbidity and mortality throughout the world [1]. ST-segment elevation myocardial infarction (STEMI) is characterised by persistent ST elevation in electrocardiogram (ECG) or characteristic symptoms of myocardial ischaemia accompanied by newly developed left branch block and increased biomarkers associated with myocardial necrosis [1]. Today, 25% to 40% of patients presenting with myocardial infarction are known to have STEMI [2]. In recent years, about 5–6% in-hospital and 7–18% 1-year STEMI-related mortality rates are decreasing thanks to the interventions and drug treatment in accordance with current guidelines [3].

Early diagnosis and rapid reperfusion are essential in STEMI treatment. Delay in reperfusion has been found to be associated with increased mortality and morbidity [4]. Thrombolytic therapy (TT) or primary percutaneous coronary intervention (PCI) is used to restore patency and re-flow of blood in the coronary artery occluded by thrombus during STEMI. The main goal of the reperfusion is to reduce the time of total ischaemia by appropriate and timely treatment [5]. Some performance measures such as door-to-needle time and door-to-balloon time have been developed to assess the duration of total ischaemia. Today, the reperfusion period is prolonged due to the lack of primary PCI in many hospitals in developing countries, which negatively affects in-hospital and long-term mortality. In cases where primary PCI is not available, TT should be started without delay [1].

Acute myocardial infarction is more common in the elderly, in whom it has higher mortality and morbidity compared to that seen in the young population. Of the patients admitted to hospitals due to STEMI, 40–50% are composed of people aged 65 years and older [6]. More than 60% of myocardial infarction-related deaths occur in this age group [7]. In many studies, primary PCI has been found to be superior to TT in achieving successful reperfusion [8]. Primary PCI is superior to TT especially in elderly patients in terms of reperfusion success [9]. For this reason, there is a tendency to perform PCI in elderly patients with STEMI, but many of the elderly patients with STEMI are treated with TT because there is still no possibility of 24-hour primary PCI in many centres in developing countries.

Our aim is to compare the in-hospital major bleeding, stroke, and mortality rates and 6-month and 1-year mortality rates in elderly patients with STEMI and receiving TT and primary PCI treatment. We investigated the effect of TT on the in-hospital and long-term outcome, especially in elderly patients, compared to the primary PCI because many hospitals in developing countries do not have 24-hour primary PCI.

Material and methods

Our study was performed retrospectively by screening the files of the patients over 65 years of age who underwent TT or primary PCI between 2010 and 2013 with the diagnosis of acute STEMI and followed up at the Sakarya University Training and Research Hospital Department of Cardiology Coronary Intensive Care Unit. Approval of the Sakarya University Medical Faculty Ethics Committee was obtained for the study protocol. The inclusion criteria of the study were as follows: Patients with persistent chest discomfort or other symptoms suggestive of ischaemia and ST-segment elevation in at least two contiguous leads as STEMI, treated with TT or primary PCI, and over 65 years of age. The exclusion criteria were: Patients admitted at the subacute stage (symptom onset-to-admission > 12 h), patients who underwent cardiac arrest as a result of AMI and were followed up under mechanical ventilation, and patients admitted with cardiogenic shock manifestations.

The patients' records were accessed from the hospital records, and the patients' age, gender, hypertension, diabetes mellitus, smoking status, coronary artery disease history, door-to-balloon and door-to-needle times, lipid profile, urea, creatinine, haemogram, haematocrit, and blood glucose values were obtained. STEMI localisation was determined according to the ECG records taken at the time of admission.

Because there was no invasive catheter laboratory that was active 24 h a day in our hospital at that time, appropriate patients with STEMI admitted outside of working hours received TT. After administering acetylsalicylic acid and concomitant treatment with clopidogrel in the emergency department to the patients who would receive TT, they were taken into the coronary intensive care unit for thrombolytic therapy. After questioning about contraindications to thrombolytics, streptokinase or alteplase was administered intravenously to the appropriate patients. After thrombolysis, patients were evaluated for reperfusion. Non-reperfused patients were taken to the catheter laboratory for rescue PCI. Early coronary angiography was performed to the patients following TT. Only three of the 66 patients did not undergo coronary angiography because the patient and relatives did not accept the procedure. All the patients who were to undergo primary percutaneous intervention were taken to the catheter laboratory after administering acetylsalicylic acid and concomitant treatment with clopidogrel in the emergency department, and primary PCI (balloon angioplasty and/or stent implantation) was

performed on the infarcted coronary artery. After PCI, all patients were taken to a coronary intensive care unit. Antiplatelet, anticoagulant, ACEI/ARB, β-blocker, and statin therapy were administered according to the current guidelines.

The door-to-balloon time was defined as the time interval between admission to the hospital and coronary reperfusion after the application of the first device or balloon. The door-to-needle time, however, was defined as the time interval between the admission to the hospital and the administration of thrombolytic therapy. Re-infarction was defined as a 20% or more increase in new pathognomonic Q-wave development and troponin values or 0.1 mV ST elevation between two consecutive derivations in ECG in addition to ischaemic chest pain over 20 min. Oral hypoglycaemic agent at the time of admission or history of insulin therapy was considered as a diagnosis of diabetes mellitus. Hyperlipidaemia was defined as having an antihyperlipidaemic drug use history or having a total cholesterol level of 200 mg/dl. Hypertension was defined as high blood pressure requiring use of antihypertensive drugs. Positive family history for coronary artery disease was defined as the presence of coronary artery disease in siblings or parents under 60 years of age. Death from cardiovascular causes was defined as acute myocardial infarction, heart failure, arrhythmia, or unexplained sudden death.

Statistical analysis

SPSS 20.0 (SPSS Inc., Chicago, IL) software was used for statistical analysis of the study findings. Numerical data obtained from the study were presented as mean ± standard deviation, and the categorical data were expressed as percentages (%). The χ^2 test was used for categorical variables. Student's *t*-test was used for comparison of continuous variables with normal distribution. In all comparisons, $p < 0.05$ was considered statistically significant.

Binary logistic regression analysis was performed to indicate independent factors associated with 1-year mortality.

Results

Our study was conducted with 111 patients over 65 years of age with STEMI (73 males, 38 females). Of the patients, 66 (59.5%) were treated with thrombolytic therapy, and 45 (40.5%) patients underwent primary PCI. The ages of the patients ranged from 65 to 87 years. The mean age of patients in the TT group was 74.17 ±5.08 years, and the mean age of patients in the primary PCI group was 72.18 ±6.77 years; there was no significant difference between the groups ($p > 0.05$). Of the patients, 73 (65.8%) were male and 38 (34.2%) were female. There was no statistically significant difference between the primary PCI and TT group in terms of gender distribution ($p > 0.05$). There was no statistically significant difference between the two groups in terms of hypertension, diabetes mellitus, smoking, hyperlipidaemia, coronary artery disease history, and family history ($p > 0.05$). Door-to-needle time was 25.9 ±7.8 min in the TT group, whereas door-to-balloon time was 84.4 ±20.0 min in the PCI group. The time interval between the onset of ischaemic chest pain (the most significant symptom of acute myocardial infarction) to hospital admission was 213.6 ±158.4 min in the thrombolytic group and 166.8 ±112.8 min in the PCI group, and there was no statistically significant difference between the two groups ($p > 0.05$). Rescue PCI was performed in 7 (10.6%) patients in the TT group due to lack of reperfusion. In the TT group, 35 (53%) patients had anterior MI, whereas 21 (46.7%) patients in the primary PCI group had anterior MI (Table I). Table I shows the demographic and clinical characteristics of both groups.

Recurrent infarction was observed in 5 (7.6%) patients in the TT group and 2 (4.4%) patients in the PCI group. Non-haemorrhagic stroke was observed in 1 (1.5%) patient in the thrombolytic-administered group and in 4 (8.9%) patients in the PCI group. No intracranial haemorrhage was seen in any of the patients included in the study. Major haemorrhage was seen in 4 (6.1%) patients in the TT group and in 4 (8.9%) patients in the primary PCI group. The major haemorrhages in the TT group were of gastrointestinal system origin, whereas in the primary PCI group there were two gastrointestinal haemorrhage cases and two haemorrhage cases due to intervention location. There was no significant difference between the groups in terms of recurrent infarction, non-haemorrhagic stroke, major bleeding, and mortality in the inpatient follow-up after both applied reperfusion therapies ($p > 0.05$). When the 6-month mortality rates of the patients were taken into account, mortality was observed in 15 (22.7%) patients in the TT group and in 8 (17.8%) patients in the primary PCI group, and there was no statistically significant difference between the two groups ($p > 0.05$). Considering the 1-year mortality rates, mortality was observed in 19 (28.8%) patients in the TT group and in 8 (17.8%) patients in the primary PCI group. Although 1-year mortality was higher in the TT group, it was not statistically significant ($p > 0.05$). Patients' in-hospital outcomes, and 6-month and 1-year mortality are shown in Table II. Binary logistic regression analysis was performed to indicate independent factors associated with 1-year mortality. Age, gender,

Table I. Demographic and clinical characteristics of the patients

Parameter	All patients (*n* = 111)	Thrombolytic (*n* = 66)	Primary PCI (*n* = 45)	*P*-value
Age	73.4 ±5.9	74.2 ±5.1	72.2 ±6.8	0.080
Female gender, *n* (%)	38 (34.2)	22 (33.3)	16 (35.5)	0.809
Diabetes mellitus, *n* (%)	28 (25.2)	16 (24.2)	12 (26.7)	0.773
Hypertension, *n* (%)	62 (55.8)	33 (50.0)	29 (64.4)	0.132
Hyperlipidaemia, *n* (%)	43 (38.7)	27 (40.9)	16 (14.4)	0.570
Smoking, *n* (%)	19 (17.1)	11 (16.7)	8 (17.8)	0.879
Family history, *n* (%)	28 (25.2)	15 (22.7)	13 (28.9)	0.463
Time between symptom onset and admission [min]	194.4 ±142.8	213.6 ±158.4	166.8 ±112.8	0.089
Door-to-balloon time [min]	–	–	84.4 ±20.0	–
Door-to-needle time [min]	–	25.9 ±7.8	–	–
Anterior MI, *n* (%)	56 (50.4)	35 (53.0)	21 (46.7)	0.975

Table II. Patients' in-hospital outcomes, and 6-month and 1-year mortality

Parameter	All patients (*n* = 111)	Thrombolytic (*n* = 66)	Primary PCI (*n* = 45)	*P*-value
In-hospital mortality, *n* (%)	13 (11.7)	8 (12.1)	5 (11.1)	0.871
Recurrent infarction, *n* (%)	7 (6.3)	5 (7.6)	2 (4.4)	0.505
Non-haemorrhagic stroke, *n* (%)	5 (4.5)	1 (1.5)	4 (8.9)	0.066
Major bleeding, *n* (%)	8 (7.2)	4 (6.1)	4 (8.9)	0.572
6-Month mortality, *n* (%)	23 (20.7)	15 (22.7)	8 (17.8)	0.528
1-Year mortality, *n* (%)	27 (24.3)	19 (28.8)	8 (17.8)	0.184

presence of DM, localisation of MI, type of therapy (PCI vs. TT), and time from symptom onset to admission were entered into the equation. Age was found to be the only predictor for 1-year mortality (odds ratio (OR): 1.1, 95% confidence interval (CI): 1.019–1.188, $p = 0.015$).

Discussion

In this study, we investigated the effects of primary PCI and TT on in-hospital adverse events, and in-hospital and long-term mortality, in patients over 65 years of age with acute STEMI. According to the results of our study, TT and primary PCI have similar effects in STEMI patients aged 65 years and over, considering the in-hospital adverse outcomes, in-hospital mortality, and 6-month and 1-year mortality rates.

The elderly population is increasing worldwide. Elderly patients occupy account for a large proportion of patients admitted to Emergency Departments due to STEMI. The fact that the elderly population is excluded in most clinical trials suggests that it is necessary to investigate the efficacy and safety of TT and primary PCI practice for this age group. The treatment method to be chosen in this group is important because of the inadequate and contradictory studies performed in this age group, comorbid conditions increasing with age, and high mortality in the elderly [10].

Subgroup analysis of several studies has shown that TT reduces mortality rates in elderly patients compared with conservative treatment [11, 12]. Increased stroke incidence increasing with age and increased intracranial haemorrhage due to age-related amyloid angiopathy are the most feared adverse effects of thrombolytic therapy. In our study, no intracranial haemorrhage was observed in any of the 66 patients aged 65 years and over who received TT. In randomised controlled trials and in case-control studies, it has been shown that there is a greater risk of cerebral haemorrhage than t-PA and streptokinase in the elderly [13]. Despite all risks, thrombolytics increase the survival rate in elderly patients with STEMI [14]. The FTT (Fibrinolytic Therapy Trialists) study group

showed a greater reduction in absolute mortality rates in patients aged 75 years and older treated with thrombolytics compared to younger patients [11]. Again, the analysis showed a significant relative risk reduction of up to 15% in mortality in the fibrinolytic treatment group aged 75 years and older [12]. In patients older than 85 years, the risk of haemorrhagic stroke (1.7%) is significantly lower when compared with 30-day mortality (30%) [15]. The frequency of haemorrhagic events suggests the necessity of treatment when compared with the possible mortality reduction with fibrinolytic therapy. In a study carried out with patients aged 65 years and older, 30-day mortality rates were found to be 13.5% in the thrombolytic treatment group, 13% in the PCI treatment group, and 20.6% in the untreated group [16]. In our study, the in-hospital mortality rate was 12.1% in the TT group and 11.1% in the primary PCI group, and 6-month and 1-year mortality rates were 22.7% and 28.8 in the TT group, and 17.8% for both periods in the PCI group. When we look at the in-hospital and 6-month mortality rates, there was no significant difference between the two groups in our study. Although the 1-year mortality rate was higher in the TT group, it was not statistically significant.

In the elderly, primary PCI is recommended as a reperfusion strategy, which should be preferred for several reasons. First, primary PCI is a more effective and safer reperfusion therapy than TT. In studies, the rate of successful reperfusion has been found to be higher in patients with primary PCI than in those treated with thrombolytics [9, 14]. However, contradictions of thrombolytic therapy and its complications are more severe in the elderly. The most frightening complication of thrombolytic therapy is intracranial haemorrhage, which is more common in elderly patients, but is rare in primary PCI [17]. In our study, intracranial haemorrhage was not detected in either group. In addition, primary PCI is a complex process and requires complete personnel and catheter lab preparation, which causes a serious waste of time. TT, however, is a treatment option that can be applied at short notice, and the time between pain and treatment is reduced by rapid treatment. In our study, the door-to-needle time was approximately 26 min and the door-to-balloon time was approximately 84 min.

Considering the demographic characteristics of the 111 patients with STEMI included in our study, there was no statistically significant difference between primary PCI and TT groups in terms of gender and age distributions. In terms of clinical features, hypertension, diabetes mellitus, smoking, coronary artery disease history, and hyperlipidaemia were similar in both groups. Although the effect of thrombolytic therapy decreases with age, it is superior to conservative treatment. In elderly patients with increased risk due to comorbid conditions, TT provides significant improvement in mortality and morbidity, but due to the risk of haemorrhage, approximately half of these patients cannot be treated with thrombolytic therapy [18, 19].

Although there are many studies comparing primary PCI and thrombolytic therapy, there are no large-scale studies comparing these treatments in elderly patients. The available information is based on subgroup analysis of large-scale studies. In the NRMI-2 trial, primary PCI has been shown to be less risky for in-hospital mortality and non-fatal stroke in patients over 75 years of age [20]. Findings similar to the NRMI-2 study have also been observed in the PAMI study conducted with patients over 65 years of age. In the PAMI study, tPA infusion therapy and angioplasty had been compared in patients admitted with STEMI. There was no significant difference between the two groups (0.8% mortality was observed in both groups) when the end-points of death and myocardial infarction were examined in patients under 65 years of age. However, a significant decrease in the angioplasty group was found when the same end-points were observed in patients aged 65 years and over (8.6% in the angioplasty group and 20.0% in the thrombolytic group, $p = 0.048$) [21]. Similarly, in the SENIOR-PAMI study, it was reported that primary PCI administered in patients over 75 years of age causes a decrease in the rate of mortality and stroke and the combined end-point [22]. As a result of the GRACE and MITRA studies, it was shown that a significant proportion of elderly patients did not receive reperfusion therapy due to thrombolytic treatment contraindications and that PCI treatment provided a significant beneficial effect compared to conservative treatment [18, 19]. In the TRIANA study, which was conducted with patients aged 75 years and older, primary PCI was compared with new-generation thrombolytics tenecteplase, and the results are in favour of primary PCI [23]. In addition to these studies, in the STREAM study, primary PCI was compared with tenecteplase, from the new-generation thrombolytics, in patients in the first 3 h of the onset of symptoms, who could not undergo primary PCI within the first hour, and thrombolytic therapy was shown to be as effective as primary PCI. In the same study, after observing higher incidence of intracranial haemorrhage in patients over 75 years of age, the tenecteplase dose was halved in elderly patients, and then the incidence of intracranial haemorrhage in the thrombolytic group was found to be similar to that of primary PCI in this case [24]. The efficacy of the new-gen-

eration thrombolytic tenecteplase has been found to be superior regarding coronary revascularisation in these trials, but tenecteplase was not used widely in our country in the study period. In the GUSTO-IIB study, conducted with 1138 patients, the patients were randomised to angioplasty and thrombolytic therapy (tPA) groups, and although primary PCI was found to be superior at 30-day end-points (death, myocardial infarction, stroke), the difference between the two groups was not significant at the same outcome points in 6-month follow-up [10].

Due to the single-centred design of our study, the results cannot be generalised, and hence prospective, multi-centred studies are needed in this regard. The limited number of patients included in the study and its retrospective nature are other limitations of our study. Therefore, the study has all the disadvantages of retrospective research. The new-generation thrombolytics (such as tenecteplase) and novel advances in interventional therapy could affect the outcomes of this study. The study was performed in selected cases (patients with cardiac arrest and cardiogenic shock were excluded), so the outcomes cannot be generalised.

In conclusion, according to the results of our study, primary PCI and TT have similar effects on in-hospital, 6-month, and 1-year mortality rates in the treatment of patients with STEMI, who are over 65 years of age, in selected cases. In addition, non-haemorrhagic stroke, major haemorrhage and recurrent infarction rates were found to be similar. Due to increased morbidity and haemorrhage complications in elderly patients, physicians avoid TT. According to the study results, because they have similar reperfusion periods, thrombolytic treatment could be applied in elderly patients in centres without 24-hour service for primary PCI, which requires complex personnel and catheter laboratory preparation.

Conflict of interest

The authors declare no conflict of interest.

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