ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION FOR PHARMACOINVASIVE OR PRIMARY PERCUTANEOUS CORONARY INTERVENTION

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Abstract

Background

A primary percutaneous coronary intervention (P-PCI) still prefers the optimal reperfusion therapy among patients with ST segment elevation myocardial infarction (STEMI), however, in non-PCI capable hospitals, a pharmacoinvasive treatment (Ph-PCI) has can be done as alternative therapy to P-PCI. This study compares the efficacy between a Ph-PCI and P-PCI strategy among patients with STEMI.

Methods:

We randomized patients with STEMI who presenting within 12 hours of symptoms onset into two groups. Group 1 ;(N; 154 patients) P-PCI within 90 minutes after first medical contact. Group 2; (N;154 patients) Ph-PCI between 2-24 hours after finishing of thrombolytic treatment in emergency room at Alshifa hospital- Gaza- Palestine. The primary endpoint; a composite of heart failure and total death at 30 days. Secondary endpoint; the percent resolution of ST segment elevation 60 minutes after PCI.

Results:

Total 308 patients with acute STEMI and presentation (≤12 hours from symptom onset to first medical contact), mean age 58.05±11.3 years, 257 (83.5 %) patients were male. The primary endpoint in P-PCI was (16.2%) and in Ph-PCI (8.4%) P= 0.038. There was no difference in 30-day total death (5.2 % in P-PCI and 3.2 % in Ph-PCI) P=0.39, no difference in heart failure (11 % in P-PCI and 5.2 % in Ph-PCI) P=0.06. Secondary endpoint: after PCI Sum ST-elevation resolution more than 50%, was seen 65% in patients with P-PCI group and 76.2% in patients with Ph-PCI group. P;0.034.

Conclusions:

A Ph-PCI was associated with decreased composite end points of mortality and heart failure outcomes during 30 days after STEMI and improved ST-segment resolution within one hour after percutaneous coronary intervention.

Key words; Primary PCI, Pharmaco-invasive PCI, STEMI

Introduction

American College of Cardiology/American Heart Association guidelines is recommended primary percutaneous coronary intervention (P-PCI) for patients with ST segment elevation myocardial infarction (STEMI) who presenting ≤12 hours of symptom onset to first medical contact if P-PCI was done within time ≤ 90 minutes in PCI capable centers. The pharmacoinvasive strategy (Ph-PCI) is recommended between 2-24 hours after thrombolytics treatment for either rescue PCI in cases of failed thrombolytics or early routine coronary PCI in cases of successful thrombolytics treatment may be alternative treatment strategy to P-PCI in non-PCI capable centers or hospitals (1).
The STREAM study tested a dedicated Ph-PCI (with half-dose Tenecteplase) compared with P-PCI and found that similar clinical outcomes at 30-day and 1-year (2)
The aim of our study to comparison of efficacy and sum ST resolution more than 50% between P-PCI and Ph-PCI using double bolus of reteplase among patients with presentation of STEMI less than 12 hours of symptoms onset.

Methods

1. Study design

This prospective clinical randomized trial (Registration No; 139-2021. Istanbul Atlas University ethics committee) was conducted on 308 patients with acute coronary syndrome who had presentation to emergency room within 12 hrs. from symptoms onset of myocardial ischemia and have persistent ST segment elevation on electrocardiographic (ECG) additionally subsequent elevated biomarkers of myocardial necrosis.
The patients were randomly divided into 2 groups:
Group 1; Primary PCI (P-PCI) within 90 minutes after first medical contact.
Group 2; Pharmaco-invasive strategy (Ph-PCI); intravenous reteplase in emergency room followed by coronary angioplasty with 2-24 hrs.

2.Study populations

The study population was derived from Alshifa hospital- Gaza- Palestine between January 2021 and October 2023. We identified 308 patients (≥ 18 years) with STEMI with early presentation (<12 hours from myocardial ischemia symptom onset) eligible for either pharmaco-invasive strategy or Primary PCI.

All patients were received acetylsalicylic acid, clopidogrel, unfractionated heparin and high dose statin (Atorvastatin 80 mg) according to our guidelines.

Inclusion criteria

- Patients age ≥18 years and STEMI presentation <12 hours from symptoms onset
- No contraindications for thrombolytic treatment

Exclusion criteria

- Patients age was < 18 years
- No contraindications for thrombolytics treatments
- Late presentation more than 12 hours after symptoms onset.

- Multi-vessel coronary artery diseases not suitable for PCI
- If indications for urgent coronary artery bypass grafting.

3. Clinical definitions

STEMI definition.

STEMI defined as typical chest pain suggestive of myocardial ischemia for at least 30 minutes and elevated cardiac markers (troponin I/T) plus at least one of the following.

- ST-segment elevation > 1 mm, except V2-3 (female patients > 1.5 mm, male patients less than 40 years old > 2.5 mm, male patients more than 40 years old > 2 mm) in ≥2 contiguous leads.
- Left bundle branch block with positive Sgarbossa and/or Smith criteria,
- True dorsal STEMI, V7-9 > 0.5 mm

Primary PCI

was defined as PCI within 90 minutes in patients with symptom onset to emergency room presentation less than 12 hrs. and not receiving thrombolytics.

Pharmacoinvasive strategy

Defined as intravenous reteplase with total cumulative dose of 20 units (10 units intravenous bolus over 2 minutes, then the second dose given after 30 minutes from first dose) in emergency room followed by coronary angioplasty with 2-24 hrs., was divided into early routine PCI or Rescue PCI

Rescue PCI

Rescue PCI was defined as urgent PCI because of persisting symptoms or persisting ST-segment elevation (failure to achieve ≈ 50% ST resolution) within 90 minutes after the administration of thrombolytics treatment.

Early routine PCI

Defined as routine PCI (between 2-24 hours after successful thrombolytic treatment administration).

ECG Analysis

ECGs were collected at baseline, 90 minutes after thrombolytic therapy and 60 minutes post interventions (primary PCI, pharmaco-invasive PCI or rescue PCI)
ST-segment elevation was measured at the J point. The sum across all leads was used to calculate sums of ST-elevation at baseline, 90 minutes after thrombolytic therapy and 60 minutes post interventions. The percent resolution was calculated as the sum ST-elevation after thrombolytics or intervention to sum ST-elevation at baseline.

TIMI bleeding classification

Classified into two group, major and minor bleeding.

- TIMI major bleeding; Patients with intracranial hemorrhage or a > 5 g/dl decrease in hemoglobin concentration or a >15 % absolute decrease in hematocrit.

- TIMI minor bleeding; patients with blood loss >3 g/dl, decrease in hemoglobin concentration or >10 % decrease in hematocrit, or no observed blood loss with > 4 g/dl decrease in hemoglobin concentration or >12 % decrease in hematocrit (2)

4. End points

Primary endpoint: total death or heart failure at 30 days after STEMI.
Secondary end points; sum of ST elevation resolutions rate > 50% after PCI.

5. Statistical analysis

All data were analyzed by SPSS program version 26. Continuous variables were presented as mean± standard deviation (SD) and categorical variables as absolute numbers and percentages. Comparison of demographic and clinical data among the groups was performed using independent t-test for continuous variables and chi-square ($\chi 2$) for categorical variables. P values < 0.05 were considered significant.

Results

Baseline characteristics

Total 308 patients with STEMI and early presentation (≤12 hours from symptom onset to first medical contact), mean age 58.05±11.3 years, 257 (83.5 %) of patients was male. All patients with Ph-PCI group were used Reteplase (is administered as two boluses of 10 Units given 30 minutes apart and each bolus administered over 2 minutes) as thrombolytic therapy. Baseline characterizes of the patients in table 1.

Table 1: baseline characterizes of the patients.

	Primary PCI	**Pharmaco-invasive PCI**	**P value**
Age /years	58.3±11.72	57.8 ±10.87	0.82
Sex , male	126 (81.9%)	131 (85.1%)	0.53
Diabetes Mellitus	52 (33.1%)	43 (27.9%)	0.27
Hypertension	82 (53.2%)	91 (59.1%)	0.30
Smoker	79 (51.3%)	68(44.1%)	0.21
Hypercholesterolemia	61 (39.6%)	67 (43.5%)	0.48
Previous CABG	9 (5.8%)	5 (3.2%)	0.25
Previous PCI	35 (22.7%)	28 (18.2%)	0.32

COPD	14 (9.1%)	21 (13.6%)	0.20
Familial history of CAD	25 (16.2%)	16 (10.4%)	0.13

CABG; coronary artery bypass grafting, PCI; percutaneous coronary intervention, COPD; chronic obstructive pulmonary disease, CAD; coronary artery diseases

Localization of STEMI

One hundred Sixty-two patients (52.6%) of study population were presented with acute anterior STEMI, 123 patients (40 %) presented as acute inferior STEMI, 19 patients (6.2%) with acute lateral STEMI and only 4 patients (1.3 %) with acute posterior STEMI. There was no significant difference among the study groups as regards localization of STEMI.

Type of intervention

154 (50%) patients underwent P-PCI and 101 (65.6%) patients from Ph-PCI strategy group underwent early routine PCI and Rescue PCI was performed in 53 patients (34.4 %).

Culprit lesion

PCI was performed only to the culprit artery. The culprit artery was LAD in 161 patients, LCX in 28 patients, RCA in 94 patients, OM branch in 11 patients and diagonal branch in 8 patient diagonal branch

Door to needle and door to balloon time

In Ph-PCI strategy: Average time from first medical contact to thrombolytic administration was 32.16 ±15 minutes in patient with successful reteplase all Coronary angiography was performed with 24 hrs. with average time 14.8 ±2.3 hrs., but in patient with failed reteplase urgency angiography was required in 34.4% of the patients the median time 5.2 hours after randomization.

Endpoints

Primary endpoint: The primary endpoint in primary PCI (16.2%) and in pharmaco-invasive PCI (8.4%) p = 0.038. There was no difference in 30-day mortality (5.2 % in primary PCI and 3.2 % in pharmacoinvasive strategy (P=0.39) and was no difference in heart failure (11 % in primary PCI and 5.2 % in pharmacoinvasive strategy (P=0.06) Table2.

Table 2: endpoints of the study

	Primary PCI	**Pharmaco-invasive PCI**	**P value**
Primary end point: Total mortality or heart failure	**25 (16.2%)**	**13 (8.4%)**	**0.038**
Total mortality	**8 (5.2 %)**	**5 (3.3 %)**	**0.39**
heart failure	**17 (11 %)**	**8 (5.2%)**	**0.06**

Secondary endpoint.

ECG Analysis

ECGs were collected at baseline, 90 minutes after thrombolytic therapy and 60 minutes post interventions (primary PCI, pharmaco-invasive PCI or rescue PCI). The success rate of thrombolytic treatment was 65.6% after 90 minutes of thrombolytics and 53 patients need rescue PCI.
After PCI Sum ST-elevation resolution more than 50%, was seen 65% in patients with primary PCI group and 76.2% in patients with Pharmaco-invasive PCI group (P:0.034). Table 3

Table 3: ST elevation resolution rate

	Primary PCI	Pharmaco-invasive PCI	P value
Sum ST-elevation resolution (from baseline to 90 minutes after thrombolytics) ≥50%, N (%)	-	101 (65.6 %)	-
Sum ST-elevation resolution (from baseline to 60 minutes post-PCI ECG) ≥50%, N %	100 (65%)	117 (76.2 %)	0.034

TIMI flow after PCI

There were heavier thrombus burden and lower post-PCI TIMI flow (TIMI-III) in patients within primary PCI (69%) compared to Pharmacoinvasive PCI (83 %) (P value 0.003).

Major bleeding

Major bleeding was seen in 7 patients in primary PCI compared to 9 patients in Pharmacoinvasive PCI (P; 0.82).

Discussion

In our trial, we report that Ph-PCI compared with a P-PCI strategy among patients with early presentation of STEMI is more effective and the same risk of complications, we found that: First, patients enrolled in our trial had low risk 4.2% of 30-day mortality, second, the rate of composite end points (total mortality and heart failure) was less in pharmacoinvasive group. Third, a 34,4 % of patients in the thrombolysis arm required Rescue PCI.

The STREAM trial provided that in the patients who presented within 3 hours after symptom onset, similar rates of death, cardiogenic shock, heart failure or recurrent myocardial infarction occurred at 30 days and 1 year with Ph-PCI compared with P-PCI. (3) However, 59.4% of P-PCI patients within the registry had ischemic times >3 hours as compared with 32.2% with Ph-PCI. In this group superior results of Ph-PCI were reported.

The French registry on Acute STEMI have reported similar 1- and 5-year outcomes of STEMI patients with Ph-PCI who received fibrinolysis (about two-thirds prehospital) followed by coronary angiography versus P-PCI within 12 hours of symptoms. (5)
The Mayo Clinic STEMI network reported no difference in long-term mortality between two strategies in non-PCI capable hospitals (6)
The Korea Acute Myocardial Infarction Registry investigators reported similar rates of major adverse cardiac events (composite of death, target-vessel revascularization, recurrent myocardial infarction and coronary artery bypass graft surgery) among patients with Ph-PCI or P-PCI (7)

Another trial (Early Routine Catheterization After Alteplase Fibrinolysis Versus Primary PCI in Acute STEMI) where epicardial and myocardial perfusion (defined as thrombolysis in MI flow grade 3, thrombolysis in MI myocardial perfusion grade 3, and ST-segment resolution ≥70%) were improved using a half-dose alteplase pharmacoinvasive approach compared with primary PCI in STEMI patients presenting ≤6 hours after symptoms. (8)

In STEPP-PCI trial found that a strategy of fibrinolysis with streptokinase in emergency room and routine early angiography resulted in similar outcomes of primary PCI, but in that trial only streptokinase was used but in this trial all patients were received reteplase (9)

Our primary endpoints were similar with The STREAM trial. The failed of Tenecteplase was 36% in STREAM trial, in present trial the failure rate of reteplase was 34.4% and in STEPP-PCI trial the failed of streptokinase was 39.5% (9)

Our result is like result of the STEPP-AMI trial. In this study, Tenecteplase was given as the lytic agent followed by catheterization (pharmaco-invasive strategy) within 3–24 hours with timely coronary intervention as appropriate versus standard P-PCI in patients with acute myocardial infarction within 12 hours of symptom onset. The primary endpoint of 30-day incidence of death, cardiogenic shock, reinfarction, repeat revascularization, and congestive heart failure, was similar in both groups (10). Among high-risk patients who had a myocardial infarction with ST-segment elevation and who were treated with fibrinolysis, transfer for PCI within 6 hours after fibrinolysis was associated with significantly fewer ischemic complications than was standard treatment (11)

In recent large trial of ST-segment elevation myocardial infarction registry, a pharmacoinvasive strategy was associated with improved ST-segment resolution and enhanced outcomes within 1 year compared with primary PCI (12)

Limitations The limitations in this study were the small sample size and short term 30 days of follow-up

Conflict of interest: None

Funding the authors received no specific funding for this work

Author Contributions

Data curation Mohammed Habib (MH), Zeki Doğan (ZD), methodology MH, validation MH and ZD, formal analysis ZD, writing- original graft MH, writing review and editing ZD.

Conclusions

In this randomized trial, early presenting STEMI patients was randomized to primary PCI or a pharmaco-invasive strategy with reteplase followed by routine PCI. At 1 month follow-up, there was significant difference decreases in mortality and heart failure in patients underwent pharmaco-invasive strategy and more improved ST-segment resolution after 60 minutes of PCI.

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