Clinical research

ST-segment elevation myocardial infarction for pharmacoinvasive strategy or primary percutaneous coronary intervention in Gaza (STEPP 2- PCI) trial

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Abstract

Introduction: Primary percutaneous coronary intervention (P-PCI) is still preferred as the optimal reperfusion therapy among patients with ST-segment elevation myocardial infarction (STEMI). However, in non-PCI capable hospitals, pharmacoinvasive treatment (Ph-PCI) can be performed as alternative therapy to P-PCI. This study compares the efficacy between a Ph-PCI and P-PCI strategies among patients with STEMI.

Material and methods: We conducted a retrospective analysis of patients with STEMI presenting within 12 h of symptoms onset assigned to two groups: Group 1 (N = 154 patients) – P-PCI within 90 min after first medical contact; Group 2 (N = 154 patients) – Ph-PCI 2–24 h after completion of thrombolytic treatment in the emergency room at Alshifa Hospital in Gaza. Primary endpoint: a composite of heart failure and total death at 30 days. Secondary endpoint: the percentage resolution of ST-segment elevation 60 min after PCI.

Results: In total, 308 patients presented with acute STEMI (≤ 12 h 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 observed in 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 in 65% in patients in P-PCI group and 76.2% in patients in Ph-PCI group; p = 0.034.

Conclusions: Ph-PCI was associated with decreased composite endpoints of mortality and heart failure outcomes during 30 days after STEMI and improved ST-segment resolution within 1 h after percutaneous coronary intervention.

Key words: primary percutaneous coronary intervention, pharmacoinvasive percutaneous coronary intervention, ST-segment elevation myocardial infarction.

Introduction

American College of Cardiology/American Heart Association guidelines recommend primary percutaneous coronary intervention (P-PCI) for patients with ST-segment elevation myocardial infarction (STEMI) presenting ≤ 12 h of symptom onset to first medical contact if P-PCI was done within 90 min in PCI capable centers. The pharmacoinvasive strategy (Ph-PCI) is recommended between 2 and 24 h after thrombolytic treatment for either rescue PCI in cases of failed thrombolytics, or early routine

coronary PCI in cases of successful thrombolytic 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 similar clinical outcomes at 30 days and 1 year [2].

The aim of our study was to compare the efficacy and sum ST resolution of more than 50% between P-PCI and Ph-PCI using a double bolus of reteplase among patients presenting with STEMI less than 12 h after symptoms onset.

Material and methods

Study design

This retrospective clinical trial (Registration No. 139-2021. Alshifa Hospital Ethics Committee) was conducted on 308 patients with acute coronary syndrome who presented to the emergency room within 12 h of symptoms onset of myocardial ischemia and have persistent ST-segment elevation on electrocardiography (ECG) and additionally subsequent elevated biomarkers of myocardial necrosis.

The patients were randomly divided into two groups: Group 1: Primary PCI (P-PCI) within 90 min after first medical contact, during Sun-Thu 7 am-10 pm (not holiday). Group 2: Pharmacoinvasive strategy (Ph-PCI); intravenous reteplase in emergency room followed by coronary angioplasty within 2–24 h at nights/weekends/holidays.

Study populations

The study population was derived from Alshifa Hospital in Gaza between January 2021 and October 2023. We identified 308 patients (≥ 18 years) with STEMI with early presentation (< 12 h from myocardial ischemia symptom onset) eligible for either the pharmacoinvasive strategy nights/weekends/holidays or primary PCI during Sun-Thu 7 am-10 pm (excluding holidays).

All patients 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 h from symptoms onset.
- No contraindications for thrombolytic treatment.

Exclusion criteria

- Patient's age < 18 years.
- No contraindications for thrombolytic treatments.
- Late presentation more than 12 h after symptoms onset.
- Multi-vessel coronary artery diseases not suitable for PCI.
- Indications for urgent coronary artery bypass grafting.

Clinical definitions

STEMI definition

STEMI was defined as typical chest pain suggestive of myocardial ischemia for at least 30 min 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

Primary PCI was defined as PCI within 90 min in patients with symptom onset to emergency room presentation less than 12 h and not receiving thrombolytics, during Sun-Thu 7 am-10 pm (excluding holidays).

Pharmacoinvasive strategy

Defined as intravenous reteplase with a total cumulative dose of 20 units (10 units intravenous bolus over 2 min, then the second dose given after 30 min from first dose) in emergency room followed by coronary angioplasty with 2–24 h, at nights/weekends/holidays were 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 min after the administration of thrombolytic treatment.

Early routine PCI

Defined as routine PCI (2–24 h after successful thrombolytic treatment administration).

ECG analysis

ECGs were collected at baseline, 90 min after thrombolytic therapy and 60 min after interventions (primary PCI, pharmacoinvasive 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 min after thrombolytic therapy and 60 min after inter-

ventions. 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].

Endpoints

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

Statistical analysis

All data were analyzed using the program SPSS Statistics 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 (χ^2) for categorical variables. *P*-values < 0.05 were considered significant.

Results

Baseline characteristics

In total there were 308 patients with STEMI and early presentation (≤ 12 h from symptom onset to first medical contact), mean age: 58.05 ±11.3 years, and 257 (83.5%) patients were male. All patients in the Ph-PCI group used reteplase (administered as two boluses of 10 units given 30 min apart and each bolus administered over 2 min) as thrombolytic therapy. Baseline characteristics of the patients are shown in Table I.

Localization of STEMI

One hundred sixty-two (52.6%) patients of the study population presented with acute anterior STEMI, 123 (40%) patients presented with acute inferior STEMI, 19 (6.2%) patients with acute lateral STEMI and only 4 (1.3%) patients 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 (34.4%) patients.

Culprit lesion

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

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 min in patients with successful reteplase. All coronary angiography procedures were performed within 24 h with average time 14.8 ±2.3 h, but in patients with failed reteplase urgent angi-

Table I. Baseline characteristics of the patients

Parameter	Primary PCI	Pharmacoinvasive 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.

ography was required in 34.4% of the patients; the median time was 5.2 h after randomization.

Endpoints

Primary endpoint

The primary endpoint was reached in primary PCI in 16.2% and in pharmacoinvasive PCI in 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 no difference in heart failure (11% in primary PCI and 5.2% in pharmacoinvasive strategy; $p = 0.06$) (Table II).

Secondary endpoint

ECG analysis

ECGs were collected at baseline, 90 min after thrombolytic therapy and 60 min after interventions (primary PCI, pharmaco-invasive PCI or rescue PCI). The success rate of thrombolytic treatment was 65.6% after 90 min of thrombolytics and 53 patients needed rescue PCI.

After PCI sum ST-elevation resolution more than 50% was seen in 65% of patients in primary PCI group and 76.2% of patients in pharmacoinvasive PCI group ($p = 0.034$) (Table III).

TIMI flow after PCI

There were a heavier thrombus burden and lower post-PCI TIMI flow (TIMI-III) in patients within primary PCI (69%) compared to pharmacoinvasive PCI (83%) ($p = 0.003$).

Major bleeding

Major bleeding was seen in 7 patients in primary PCI compared to 9 patients in pharmacoinvasive PCI ($p = 0.82$).

Discussion

Based on our trial, we report that Ph-PCI compared with a P-PCI strategy among patients with early presentation of STEMI is more effective, with 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 endpoints (total mortality and heart failure) was lower in the pharmacoinvasive group; and third, 34.4% of patients in the thrombolysis arm required rescue PCI.

In the STREAM trial, patients who presented within 3 h 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 h as compared with 32.2% with Ph-PCI. In this group superior results of Ph-PCI were reported [4].

The French registry on acute STEMI 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 h of symptoms onset [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].

In another trial (Early Routine Catheterization After Alteplase Fibrinolysis Versus Primary PCI in Acute STEMI), 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 h after symptoms onset [8].

In the STEPP-PCI trial it was found that a strategy of fibrinolysis with streptokinase in the emergency room and routine early angiography resulted in similar outcomes of primary PCI. In that trial only streptokinase was used, whereas in this trial all patients received reteplase [9].

Table II. Study endpoints

Primary endpoint	Primary PCI	Pharmaco-invasive PCI	*P*-value
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

Table III. ST-elevation resolution rate

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

Our primary endpoints were similar to those of the STREAM trial. The failure rate of tenecteplase was 36% in the STREAM trial, in the present trial the failure rate of reteplase was 34.4%, and in the STEPP-PCI trial the failure rate of streptokinase was 39.5% [9].

Our results are comparable to the results of the STEPP-AMI trial. In this study, tenecteplase was given as the lytic agent followed by catheterization (pharmacoinvasive strategy) within 3–24 h with timely coronary intervention as appropriate versus standard P-PCI in patients with acute myocardial infarction within 12 h 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 h after fibrinolysis was associated with significantly fewer ischemic complications than was standard treatment [11].

In a recent large trial of an 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].

The limitations in this study were the small sample size and short-term (30 days) follow-up.

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

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Ethical approval

Not applicable.

Conflict of interest

The authors declare no conflict of interest.

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