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Research Article

Comparison between PCI in Anterior ST-Elevation Myocardial Infarction and Equivalents in Gaza (PCI-STEMI) -

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ABSTRACT

Background: A Primary Percutaneous Coronary (PCI) intervention and pharmaco-invasive Primary Percutaneous Coronary (PCI) continues to be the optimal reperfusion therapy in patients with anterior ST Elevation Myocardial Infarction (STEMI) however, the optimal treatment in patients with anterior STEMI equivalents (wellness and De Winter syndromes) is unknown.

Methods: Patients presenting within 2 hours of symptom onset, divided according to Electrocardiography (ECG) into two groups, the first group: acute anterior STEMI treated by primary PCI < 2 hours or pharmaco-invasive PCI 2-24 hours after streptokinase, and second group: acute anterior STEMI equivalents (wellness and De Winter syndromes) treated with early PCI < 24 hours. The primary (efficacy) endpoint a composite of death, shock and congestive heart failure at 30 days after hospitalization.

Results: Total 173 patients (134 patients: anterior STEMI, 39 patients: Anterior STEMI Equivalents) with mean age 56.2 ± 9.4 years, the mean age was 55.1 ± 9.2 years for the Anterior STEMI group, and 59.7 ± 9.1 years in Anterior STEMI equivalents group. ($p = 0.007$). The female gender was higher in Anterior STEMI Equivalents compared with anterior STEMI ($p = 0.036$). Efficacy (primary) endpoint: total death, shock or heart failure at 30 days after hospitalization was seen in myocardial infarction was significantly higher in patient with anterior STEMI group compared with anterior STEMI equivalent group ($p = 0.011$). The total death, shock and heart failure were significant in anterior STEMI group ($p = 0.047$, 0.024 and 0.028) respectively.

Conclusion: A strategy of early PCI less than 24 hours in patients with Anterior STEMI Equivalents has safe and less adverse events than anterior STEMI with primary PCI < 2 hours and/or pharmaco-invasive PCI 2-24 hours after streptokinase administration.

INTRODUCTION

American College of Cardiology/American Heart Association guidelines recommend primary Percutaneous Coronary Intervention (PCI) for patients with ST-segment-elevation myocardial infarction presenting ≤ 12 hours of symptom onset with a first medical contact-to-device time goal of ≤ 120 minutes. Pharmacoinvasive strategy where fibrinolysis is followed by immediate transfer to a PCI-capable hospital for either rescue PCI in case of failed fibrinolysis or routine coronary angiography and PCI in case of successful fibrinolysis may be a valid alternative to primary PCI and part of the primary reperfusion in patients with ST-segment-elevation myocardial infarction in whom long PCI-related delay is anticipated [1].

Wallen's syndrome or "Widow Maker", is referred to an Electrocardiogram (ECG) pattern (There are two ECG patterns with difference incidence: Pattern A with biphasic T wave in V2-V3n and pattern B with deep T wave in V2-V3) for proximal Left Anterior Descending (LAD) artery lesion). ECG abnormalities present at the Emergency Department (ED) in patients admitted with angina during pain free periods. Cardiac biomarkers are usually normal or slightly elevated, this syndrome requires urgent coronary angiography and PCI to avoid the development of extensive anterior Myocardial Infarction (MI) [2].

The De Winter syndrome was reported as an indicator of acute Left Anterior Descending (LAD) coronary artery occlusion. The ECG pattern typically include ST-depression and peaked T-waves in precordial leads, and it can be seen in around 2% of patients with anterior myocardial infarction [3].

Wellness and De Winter syndrome are considered an anterior ST-Elevation Myocardial Infarction (STEMI) equivalents [4,5].

The aim of our trial to evaluate the efficacy of the patients presenting within 2 hours of symptom onset of acute anterior ST elevation myocardial infarction to primary PCI < 2 hours or pharmaco-invasive PCI 2-24 hours after streptokinase, compared with acute anterior ST elevation myocardial infarction equivalents to early PCI < 24 hours The primary (efficacy) endpoint a composite of death, shock and congestive heart failure at 30 days after hospitalization.

METHODS

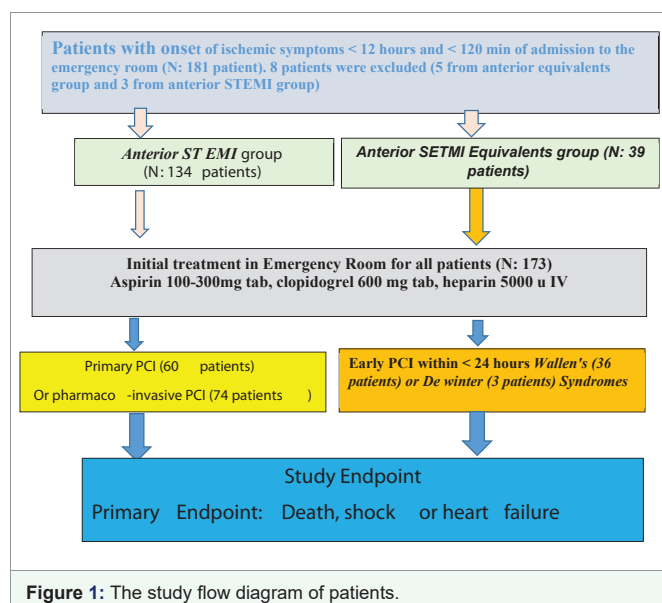
Study design

This prospective, cohort study was conducted on 173 patients who had symptoms onset of myocardial ischemia within 12 hours divided according to ECG into two groups:

Group 1: (Anterior STEMI): ST elevation in anterior precordial leads.

Group 2: (Anterior STEMI Equivalents): Biphasic T wave in V2-V3 or deep T wave in V2-V3 (Wallen's syndrome) and upsloping ST depression with peaked T-waves in precordial leads (De winter syndromes) (Figure 1).

The aim of the our study is to comparison of the efficacy of Primary PCI (< 2 hours) and/or pharmaco-invasive PCI (< 24 hours) in patient with anterior STEMI group compared to early PCI (< 24 hours) in anterior STEMI equivalents group in patients presents with onset of myocardial ischemia within 12 hours and less than 2 hours of admission to emergency room in Gaza.



Study population

The study population was single Center trial derived from al shifa hospital between March 2018 and October 2019. We identified 173 patients (≥ 18 years) with anterior STEMI (< 12 hours) and < 2 hours of presentation eligible for either pharmaco-invasive strategy or Primary PCI or early PCI < 24 hours in patients with anterior STEMI Equivalents.

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

Patients were excluded from the study if their age was < 18 years or if they have contraindications of fibrinolytic therapy or coronary artery disease not suitable for revascularization by PCI or patients who didn't underwent coronary angiogram and PCI within 24 hours.

Clinical definitions:

Anterior STEMI was defined as chest pain suggestive of myocardial ischemia for ≈ 30 minutes, ST-segment elevation > 0.1 mV in ≥ 2 contiguous leads in VI-6 and elevated cardiac markers (creatin kinase-MB or troponin I/T).

PPCI was defined as PCI within 12 hours of symptom onset in a patient not receiving streptokinase. Time to start of reperfusion therapy was defined as time to intravenous injection of fibrinolytics and time to balloon inflation in patients treated with fibrinolysis and PPCI, respectively.

Pharmacoinvasive strategy was defined as fibrinolysis followed by rescue or by routine elective PCI (beyond 2 hours of fibrinolytic administration).

The Wallen's' syndrome is presentation of anterior ischaemia and it is characterised by deeply inverted or biphasic T waves in multiple precordial lead

The De Winter ECG pattern typically displays tall T-waves with Upsloping ST depression in multiple precordial lead.

End points

Efficacy (primary) endpoint: total death, shock or heart failure at 30 days after myocardial hospitalization.

Statistical analysis

Data was analyzed by SPSS version 19. Continuous variables were presented as Mean \pm 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. Pearson's correlation coefficients were calculated to illustrate certain relationships. $P = < 0.05$ were considered significant.

RESULTS

Baseline characteristics

Total 173 patients (134 patients: anterior STEMI, 39 patients: Anterior STEMI Equivalents) with mean age 56.2 ± 9.4 years, the mean age was 55.1 ± 9.2 years for the Anterior STEMI group, and 59.7 ± 9.1 years in Anterior STEMI equivalents group. ($p = 0.007$). The female gender was higher in Anterior STEMI Equivalents compared with anterior STEMI ($p = 0.036$), the history of PCI was higher in

anterior STEMI group compared with STEMI equivalents group ($p = 0.025$), no significant difference between two groups in risk factors diabetes mellitus, hypertension, smoking, history of CABG, history of stroke, presence of COPD and family history of coronary artery disease (Table 1).

Efficacy (primary) endpoint

Total death, shock or heart failure at 30 days after hospitalization was seen in myocardial infarction was significantly higher in patient with anterior STEMI group compared with anterior STEMI equivalent group ($p = 0.011$). The total death, shock and heart failure were significant in anterior STEMI group ($p = 0.047$, 0.024 and 0.028) respectively (Table 2).

No difference between two groups in the number of significant coronary artery stenosis ($p = 0.72$), but the effected LCX was higher in anterior STEMI group ($p = 0.024$) (Table 3).

Type of intervention

In acute anterior STEMI, 60 (44.8%) patients underwent standard primary PCI and 75 (55.2%) patient underwent pharmacoinvasive strategy but in this group 28 patients (37.8%) had failed streptokinase and need emergency angiography and PCI. In acute anterior STEMI equivalents: 3 patients with De Winter syndrome underwent standard primary PCI within 2 hours and 36 patients with wellens syndrome underwent standard primary PCI within 24 hours.

Door to needle and door to balloon time

Table 1:

	Total (n = 173)	Anterior STEMI (n = 134)	Anterior STEMI equivalents (n = 39)	p value
Age, years	56.2 \pm 9.4	55.1 \pm 9.2 years	59.7 \pm 9.1 years	0.007
Female gender	26 (15%)	16 (11.9%)	10 (25.6%)	0.036
Diabetes mellitus	62 (34.8%)	49 (36.6%)	13 (33%)	0.71
Hypertension	103 (57.9%)	78 (58.2%)	25 (64.1%)	0.51
Smoking	75 (42.1%)	62 (46.3%)	13 (56.4%)	0.15
Previous PCI	23 (12.9%)	22 (16.4%)	1 (2.6%)	0.025
Previous CABG	2 (1.1%)	0 (0%)	2 (5.1%)	0.44
Previous Stroke/ TIA	2 (1.1%)	1 (0.07%)	1 (2.6%)	0.93
COPD	14 (7.9%)	12 (8.9%)	2 (5.1%)	0.44
Family history of CAD	29 (16.3%)	22 (16.4%)	7 (18%)	0.82

PCI: Percutaneous Coronary Intervention; CABG: Coronary Artery By-Pass Grafting; TIA: Transient Ischemic Attack; COPD: Chronic Obstructive Pulmonary Disease; CAD: Coronary Artery Disease

Table 2: Primary outcome between two groups.

	Anterior STEMI (n = 134)	Anterior STEMI equivalents (n = 39)	p value
Primary endpoint	31 (23%)	2 (5.1%)	0.011
Death	8 (5%)	0 (0%)	0.047
Shock	16 (12%)	0 (0%)	0.024
Heart failure	27 (20.1%)	2 (5.1%)	0.028

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Shock	16 (12%)	0 (0%)	0.024
Heart failure	27 (20.1%)	2 (5.1%)	0.028

In anterior STEMI: Average time from medical contact to streptokinase administration was 33.17 ± 15 min. in patient with successful streptokinase all Coronary angiography was performed with 24 hours with average time 16 ± 3.4 hrs., but in patient with failed streptokinase emergency angiography was required in 28 patients (37.8%) of the patients the median time 6 ± 1.3 hours after randomization. In primary PCI: The Door to balloon time was 75.25 ± 20 min. and the Door to balloon was performed in 81% in the time < 90 min.

In anterior STEMI equivalents: The Door to balloon time was (8 ± 1.2) hours.

SUBGROUP ANALYSIS

In the anterior STEMI equivalent group

The LAD totally occlusion was present in all 3 patients with De winter Syndrome and severe stenosis in all patients with Wallen's syndrome except one patient with wellens syndrome have aneurysmal dilatation and slow flow in LAD without significant stenosis was treated medically. Only one patient underwent PCI after 48 hours because anterior STEMI due to subacute stent thrombosis, primary PCI was done and the patient discharged from hospital with mild impaired left ventricle dysfunction and symptoms of heart failure, and 4 patients were died:

- One patient died within 24 h of presentation before coronary angiography.
- One patient had cardiac arrest just before reaching to the catheterization laboratory and *cardiopulmonary resuscitation* was done but patient died.
- One patient underwent diagnostic coronary angiography but PCI not done at that time because of the size of stent was not available in our center and the patient was transferred elective to another center to make PCI but the patient was died within 48 hours before PCI.
- One patient was missed diagnosed and discharged with medical treatment, 2 weeks after discharge, acute massive anterior MI and cardiogenic shock was developed the patient was admitted to coronary care unit, norepinephrine infusion was started, the patient intubated and primary PCI was done to LAD but patient died within 12 hours of admission.

Totally five patients were excluded from our analysis in this group because of 4 patients died before coronary angiography and PCI and one patient who had aneurysmal dilatation and slow flow in LAD without significant stenosis. Our analysis including only patients who underwent coronary angiogram and PCI within 24 hours. All three patients with De winter syndrome underwent coronary angiogram and PCI less than 2 hours.

In the anterior STEMI group

Three patients died within 2 hours of presentation, one patient during streptokinase infusion, and 2 patients just after reaching to emergency room. These patients were excluded from our analysis because of our analysis including only patients who underwent coronary angiogram and PCI within 24 hours.

DISCUSSION

In our trial, we report on the efficacy PCI (primary or pharmacoinvasive) strategy in patients with anterior STEMI compared with early PCI < 24 hours in patients with anterior STEMI equivalents (Wallen's and De winter syndromes) strategy in Gaza, we found that:

- First, the efficacy end point : composite of total death, shock or heart failure at 30 days after hospitalization was significantly higher in patient with anterior STEMI group compared with anterior STEMI equivalent group ($p = 0.011$).
- Second, actually, it has to be considered that patients enrolled in our trial were at low risk with a 30-day mortality of 5% in patient with anterior STEMI group compared with no death in anterior STEMI equivalent group who underwent early coronary angiography and PCI (two patients were died before coronary angiography).
- Third, the rate of heart failure and shock was higher in anterior STEMI group
- Forth, a 37.8% of patients in the acute anterior myocardial infarction with thrombolysis group required urgent coronary angiography.

Despite advancements in percutaneous coronary interventions, acute ST elevation myocardial infarction is still one of the global leading causes of death [6]. And its incidence is increasing [7]. One of the most important factors in treating STEMI patients is to achieve early reperfusion. Primary Percutaneous Coronary Intervention (PCI) is superior to fibrinolytic therapy but difference in mortality between primary PCI or pharmaco-invasive strategy [8].

In our trial we treated only 3 patients with early PCI with an ECG pattern "up-sloping ST depression and symmetrical long and distinct T waves starting from J-point in precordial leads" and in coronary angiography we found totally occluded in proximal LAD and successfully treated by PCI without any complications de Winter, et al. [9]. Reported this ECG pattern that is found in about 2% of patients with proximal left anterior descending artery occlusion Although de Winter T-wave ECG pattern was suggested to be managed as STEMI equivalent [10].

Wellens' syndrome was first described by De Zwann, et al. [2] in a study group of 145 patients with unstable angina, and 26 patients had the ECG pattern of Wellens' syndrome. Twelve patients out of this group did not undergo coronary revascularization and subsequently developed anterior myocardial infarction within a few weeks' time. Later on, a larger sample was used (1,260 patients, 180 patients with Wellens ECG findings) and all of the patients who showed these ECG changes were found to have stenosis in the proximal LAD ranging from 50% to 100% [11]. Rhinehardt, et al. [12] described the following diagnostic criteria for Wellens' syndrome:

- Deeply inverted or biphasic T waves in V2-3 (may extend to V1-6);

- Isoelectric or minimally elevated ST-segment (< 1 mm);
- No precordial Q waves;
- Preserved precordial R wave progression;
- A recent history of angina;
- ECG pattern present in the pain-free state;
- Normal or slightly elevated serum cardiac markers.

In our trial 36 patient with Wellens syndrome were treated by early PCI (in Wellens' syndrome: one patient was treated medically due to aneurysmal dilatation and slow flow in LAD was excepted from analysis, and only one patient have anterior STEMI after 48 hours of PCI related to subacute stent thrombosis).

The STREAM (Strategic Reperfusion Early after Myocardial Infarction) trial compared fibrinolysis followed by PCI within 6 to 24 h to primary PCI. The investigators found that there was no difference in the composite endpoint of death, shock, congestive heart failure, or reinfarction at 30 days between the 2 treatments. In this study, tenecteplase was given as the lytic agent followed by catheterization and failure rate of tenecteplase was 36%, in our trial we use the streptokinase in emergency Room and the failure rate was 37.8% [8].

So that we recommended ideally, the presence of Wellens or de Winter as urgent as STEMI with catheter laboratory activation for coronary angiography and PCI.

However, despite these findings, Wallen's syndrome and de Winter patterns are yet to be included in the ESC guidelines for management of acute coronary syndromes in both persistent (2017) or without persistent ST-elevation (2015) and ACC/AHA guidelines regarding STEMI (2013) and NSTEMI (2014) [13,14].

CONCLUSIONS

The LAD occlusion was present in all 3 patients with De winter Syndrome and severe stenosis in 36 patients with Wallen's syndrome and only one patient have aneurysmal dilatation and slow flow in LAD without significant stenosis. The purpose of this trial was to emphasize the importance of this ECG pattern because it is as important as STEMI and these patients need to undergo immediate or early percutaneous coronary intervention in the optimal time to reduce morbidity and mortality.

Wallen's and de Winter are not mentioned in any guidelines regarding acute coronary syndromes and until now there are no clear recommendations. We recommended that in patients with De winter syndrome with onset of myocardial ischemic symptoms less than 12 hours, PCI < 2 hours or fibrinolysis may be considered and in patients with Wellens syndrome the early PCI < 24 or immediately PCI < 2 hours after presentation is recommended.

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