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Comparison Between the Effects of Primary Angioplasty and Pharmaco-Invasive Strategy on Left Ventricular Functions in ST- Elevation Myocardial Infarction Patients

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ABSTRACT

Background: The preferred therapy for people with ST-elevation myocardial infarction (STEMI) is primary percutaneous coronary intervention (PPCI). Pharmaco-invasive therapy, which can be described as the combination of fibrinolytic therapy followed by angiography with or without PCI, either immediately when there is failed fibrinolysis or within 24 hours in case of successful fibrinolysis, is another technique for treating STEMI patients.

Objective: The aim of this study was to compare the effects of pharmaco-invasive strategy on infarct-related artery (IRA) patency and on left ventricular systolic and diastolic functions with those of primary angioplasty in STEMI patients assessed in-hospital before patient discharge.

Subjects and methods: This prospective cohort cross-sectional nonrandomized study included a total of 100 patients with 1st attack of acute STEMI who had symptom onset within 12 h, attending at Department of Cardiology, Zagazig University Hospital, Zagazig, Egypt. The patients were randomized into 2 groups (50 patients each), First group underwent PPCI, and the second group underwent pharmaco-invasive PCI. Assessment of myocardial blush grade, global longitudinal strain, and E/e` ratio was done for both groups.

Results: The mean age of the study population was 52.95 ± 8.41 with 54 % of the whole population being males. There was a statistically significant difference between the two groups regarding pain to ECG time with a P value of 0.03. The Myocardial blush grade was significantly higher in the Pharmaco-invasive arm with a statistically significant difference between the two groups with P value 0.03. After revascularization there was a better improvement in the diastolic function in the PHINV arm as assessed by E/e` with a P value of 0.004.

Conclusion: It could be concluded that pharmaco-invasive strategy could offer a superior outcome regarding the recovery of the diastolic function and a higher myocardial blush grade (which indicates a better microvascular circulation) in STEMI patients compared to those who underwent PPCI.

Keywords: Primary PCI, Pharmaco-invasive PCI, diastolic function.

INTRODUCTION

The preferred therapy for people with STEMI is PPCI. Benefits of PPCI are attributable to the rapid restoration of infarct-related artery (IRA) blood flow patency [(1)]. An important factor in determining clinical outcomes is the interval between the start of symptoms and myocardial reperfusion [(2)].

Pharmaco-invasive therapy, which can be described as the combination of fibrinolytic therapy followed by angiography with or without PCI, either immediately when fibrinolysis fails or within 24 hours in case of successful fibrinolysis, is another technique for treating STEMI patients [(3)]. Better outcomes and increased survival have been linked to infarct related arterial patency at first angiography (measured as TIMI 3 coronary blood flow grade) [(4)].

In the event of acute myocardial infarction microvascular blockage may occur due to disintegration of thrombus with subsequent distal embolization. This might occur during performing primary angioplasty due to pushing the thrombus by wires, balloons or stents. Blockage of microcirculation might impair left ventricular functions [(5)]. We hypothesized that using thrombolytic therapy before angioplasty (pharmaco-invasive strategy) might lyse the thrombus and prevent distal embolization.

The aim of this study was to compare the effects of pharmaco-invasive strategy on IRA patency and on left ventricular systolic and diastolic functions with those of primary angioplasty in STEMI patients assessed in-hospital before patient discharge.

PATIENTS AND METHODS

This prospective cohort cross-sectional nonrandomized study included a total of 100 patients with 1st attack of acute STEMI who had symptom onset within 12 h, attending at Department of Cardiology, Zagazig University Hospital, Zagazig, Egypt. This study was conducted between June 2020 to June 2022.

Inclusion criteria:

1. Patients having acute STEMI.
2. Patients who came within two hours of the start of chest discomfort and a Left Bundle Branch block (LBBB) pattern of new onset [(1)].

Exclusion criteria:

1. Those who had pain or non-ischemic chest discomfort.
2. Patients with established Q–wave acute myocardial infarction on presentation.

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3. Patients known to had previous ischemic heart disease, cardiomyopathy, severe valvular dysfunction, any type of congenital heart disease, AF or any type of chronic arrhythmia.

The included subjects were randomly divided into two groups (50 patients each); **Group 1 (Primary PCI: PPCI)** patients transferred directly to undergo primary angioplasty, and **Group 2 (Pahrmacoinvasive group: PI)** patients received thrombolytic therapy then were transferred for coronary angiogram within 24 hours when primary angioplasty couldn't be performed in a timely fashion. If any of these patients showed signs and symptoms of unsuccessful reperfusion after 90 minutes from receiving the thrombolytic therapy, they were transferred directly to PPCI capable center for mechanical reperfusion.

Baseline evaluation:

1) Review of medical history: Age, sex, risk factors for coronary artery disease (CAD) (smoking, diabetes, hypertension, dyslipidemia, and a family history of ischemic heart disease), a history of previous ischemic attacks or coronary revascularization (PCI or CABG), a history of comorbidities, and the time of chest pain onset were among the demographic information included.

2) Physical examination: Vital signs (pulse-BP-Temperature-RR), general examination, and cardiac examination: full examination, additional sounds, heart murmurs and basal pulmonary crepitations.

3) 12 Lead ECG: At the first hospital presentation and 90 minutes following PPCI, a typical 12-lead ECG was recorded. It took 20ms after the J-point to measure the ST-segment elevation. Infarcted leads had their sum of ST-segment elevations (sum STE) assessed. The percentage of total ST-segment decrease between baseline and after reperfusion was used to indicate STR. On the 90-minute post reperfusion ECG, the sum of residual ST-segment elevation (residual STE) across all infarct-related leads was also assessed.

4) Laboratory investigation: cardiac markers (CK-MB & Troponin), CBC, liver and kidney function tests and lipid profile.

5) Echocardiography: using General Electric System Vivid-9 machine with (2.5-5) MHZ probe. A transthoracic echocardiographic evaluation was performed to all patients upon admission, after the PCI during the hospital stay with special emphasis on evaluating on the left ventricular ejection fraction, diastolic function and resting wall abnormalities. The following measures were obtained:

LV end diastolic volume (LVEDV, E/e' PW tissue Doppler imaging (TDI), Resting segmental wall motion abnormalities (RSWMA) and Global longitudinal Strain (GLS) was estimated by 2D speckle tracking using QLAB software (Philips CX 50, USA).

6) - Coronary angiography and emergency PCI:

For determining the location, severity, number of afflicted vessels, and intensity of myocardial blush, which can be described as follows:

0: Absence of contrast density or myocardial blush.

1: Little contrast density or myocardial blush.

2: Moderate myocardial blush or contrast density, but not as much as what is seen during angiography of a non-infarct-related coronary artery on the ipsilateral or contralateral side.

3: A normal myocardial blush or contrast density that is equivalent to the results of an angiography of a non-infarct-related coronary artery on the opposite or ipsilateral side [(6)].

***Ethical Consideration*:**

This study was ethically approved by Zagazig University local ethics committee. Written informed consent of all the participants was obtained. The study protocol conformed to the Helsinki Declaration, the ethical norm of the World Medical Association for human testing.

Statistical Analysis

Microsoft Excel has been used historically to code, enter, and analyze data for routine clinical examinations, laboratory investigations, and outcome measurements. SPSS version 20.0 program was then used to import and analyze the data. The following tests were conducted to see if there were any statistically significant differences between the types of data, with quantitative data represented by means and standard deviation and qualitative data represented by numbers and percentages: Two qualitative variables were compared and their associations were examined using the Chi-square Test (X^2) and Fisher exact. To compare more than two groups with quantitative variables that had a normal distribution, the ANOVA (F) test was utilized (for parametric data). We were able to find independent predictors of improvement in LV systolic and diastolic function using univariate and multivariate analyses. P values <0.05 were regarded as significant.

RESULTS

Table (1) shows that there were no statistically significant differences between the two groups regarding the demographic characteristics (Age and Sex). There was a statistically significant difference between the two groups regarding DM (P value = <0.001) while there were no statistically significant differences regarding the other risk factors (Hypertension and Smoking).

Table (1): Demographic characteristics of the studied groups.

Demographic characteristics	All population (n=50)	Primary PCI (n=50)	Pharmaco-invasive (n=50)	P-value
Age (years)	52.95 ± 8.41	54.44 ± 9.94	51.46 ± 6.29	0.08
Male sex, No. (%)	54 (54%)	24 (48%)	30 (60%)	0.39
Cardiovascular risk factors				
Diabetes Mellitus	46 (46%)	26 (52%)	20(40%)	< 0.001**
Hypertension	54 (54%)	34 (68%)	20 (40%)	0.39
Smoking	48 (48 %)	26 (54%)	22 (48%)	0.27

PCI: percutaneous coronary intervention.
* Statistically significant difference between two groups ($p < 0.05$).
**Highly statistically significant difference between two groups ($p<0.001$).

Table (2) shows that there was a statistically significant difference between the two groups regarding pain to ECG time with a P value of 0.03. That time was significantly shorter in the pharmaco-invasive group with a mean of 107.4 ± 43.93 minutes compared to the PPCI group which was 136.6 ± 48.6 minutes. The table shows also that the mean door to balloon time was 68.4 ± 14.05 minutes while the mean door to needle time was only 26.35 ± 5.16 minutes. The mean door to PCI in the pharmaco-invasive group was 21.04 ± 7.44 hours. Regarding the ECG findings (The Type of MI). Most of the population of our study had AWMI 40 %, followed by Anteroseptal MI 20 %, IWMI and Inferolateral MI each of them 18% and finally high lateral MI only 4%. There was no statistically significant difference between the two groups. Regarding the sum of ST segment elevation. It was slightly higher in the PPCI group with a significant difference between the two groups with a P value = 0.03. The percentage of ST segment elevation resolution was also higher in the PPCI arm showing a statistically significant difference between the two groups with a P value = 0.03. The percentage of the worst lead ST segment elevation resolution was better in the PPCI arm with a statistically significant difference between the two groups of P value=0.02.

Table (2): Clinical characteristics of the studied groups.

	All population (n=100)	Primary PCI (n=50)	Pharmaco-invasive (n=50)	P-value
Clinical characteristics				
Pain to ECG (minutes)	122.0 ± 48.16	136.6 ± 48.6	107.4 ± 43.93	0.03*
Door to balloon (minutes)	68.4 ± 14.05	68.4 ± 14.05		-
Door to Needle(thrombolysis)(minutes)	26.35 ± 5.16	-	26.35 ± 5.16	-
Door to PCI (hours)	16.04 ± 7.44	16.04 ± 7.44	-	-
ECG				
Anterior wall MI	40 (40%)	24 (48%)	16 (32%)	0.84
Anteroseptal wall MI	20 (20%)	8 (16%)	12 (24%)	
Inferior wall MI	18 (18%)	8 (16%)	10 (20%)	
Inferolateral wall MI	18 (18%)	8 (16%)	10 (20%)	
High lateral wall MI	4 (4%)	2 (4%)	2 (4%)	
Sum STE, mm	9.9 ± 2.49	10.75 ± 2.27	9.05 ± 2.48	0.03
Sum STE resolution, %	71.25 ± 6.77	73.5 ± 5.16	69. ± 7.54	0.03
Worst lead STE resolution , %	61.5 ± 6.99	64 ± 5.53	59 ± 7.54	0.02

ECG: electrocardiogram; PCI: percutaneous coronary intervention; STE: ST segment elevation

Regarding the Myocardial blush grade only a few patients in both groups had MBG 1 (4 in the PPCI arm and 2 in the PHinv arm). The majority of the whole population had MBG 3.The number of those patients was slightly higher on the PHinv arm (84%) while on the PPCI arm only 62% of the patients had MBG 3. There was a statistically significant difference between the two groups regarding the myocardial blush grade (MBG) with P value < 0.03 (Table 3).

Table (3): Angiographic characteristics of the studied groups.

	All population (n=100)	Primary PCI (n=50)	Pharmaco-invasive (n=50)	P-value
Angiographic characteristics				
Culprit artery				
LMCA	2 (2%)	2 (4%)	0 (0%)	0.22
LAD	56 (56%)	28 (56%)	28 (56%)	
LCX	22 (22%)	8 (16%)	14 (28%)	
RCA	20 (20%)	12 (24%)	8 (16%)	
MBG (Post -PCI)				
1	4 (4%)	2 (4%)	2 (4%)	0.03
2	23 (23%)	17 (34%)	6 (12%)	
3	73 (73%)	31 (62%)	42 (84%)	

LAD: left anterior descending artery; LCX: left circumflex artery; LMCA: left main coronary artery; MBG: myocardial blush grade; PCI: percutaneous coronary intervention; RCA: right coronary artery.

Table (4) shows that before revascularization the three echo parameters measured in the current study (EF, GLS, and E/e`) were almost equal between the two groups. There were no statistically significant differences between the two groups regarding those echocardiographic findings (Ejection Fraction, Global longitudinal strain and E/e`). After revascularization there was a modest improvement in all parameters. There were no statistically significant differences found between the two groups regarding the Ejection Fraction and GLS, but there was a statistically significant difference between the two groups regarding E/e` with a P value of 0.004.

Table (4): Echocardiographic characteristics of the studied groups.

Echocardio-graphic characteristics	All population (n=50)	Primary PCI (n=25)	Pharmaco-invasive (n=25)	P-value
Before revascularization				
EF (%)	41.78 ± 5.84	41.36 ± 5.91	42.2 ± 5.82	0.62
GLS (%)	-12.35 ± 1.96	-12.2 ± 2.07	-12.5 ± 1.88	0.59
E/e`	18.67 ± 3.98	18.5 ± 3.72	18.84 ± 4.29	0.77
After revascularization				
EF (%)	46.06 ± 5.29	44.92 ± 5.42	47.2 ± 5.0	0.13
GLS (%)	-14.62 ± 4.65	-13.58 ± 5.95	-15.66 ± 2.52	0.11
E/e`	16.4 ± 3.51	17.78 ± 3.29	15.02 ± 3.22	0.004*

EF: ejection fraction; GLS: global longitudinal strain; PCI: percutaneous coronary intervention.

DISCUSSION

The present study's cohort had a mean age of 50.9 years, ranging from 42 to 64. This data is consistent with the observation that the prevalence of CVD, including atherosclerosis, stroke, and myocardial infarction, rises with age in both men and women [(7)]. There was a minor male predominance in terms of sex, with 54% of the population being male. This result confirms that, in most age groups, males had greater age-specific incidence of CVD than women [(8)].

Regarding the major cardiovascular risk factors, they were equally distributed among the two groups except for DM which varied significantly between the two groups with a P value of <0.001. Smoking, being overweight, diabetes, and dyslipidemia are all established cardiovascular risk factors that can cause early atherosclerosis and myocardial infarction in young people [(9)]**.** The mean pain to ECG time in the whole population was 122.0 ± 48.16. It was shorter in the pharmaco-invasive group that could be attributed to the fact that some patients sought medical help in another facility and presented to our center already diagnosed with an ECG.

The mean door to elective PCI in the PHINV group was 16.04 ± 7.44 which still complies with the ESC 2017 STEMI guidelines which states that PCI in PHINV strategy should be done within 24 hours post fibrinolysis [(1)]**.**

In current study, we found that ST segment resolution was better on the PPCI arm. This contradicts with what **Bainey *et al.*** [(10)] found who reported that when compared with pPCI, after cardiac catheterization, pharmaco-invasive method was linked to an improvement in cumulative ST-segment deviation resolution of 50% or more. This could be attributed to the fact that we measured ST segment resolution after the initial reperfusion strategy (thrombolytic therapy). Regarding the worst lead ST segment resolution, in our study it was better also on the pPCI arm while they found that it was better on the pharmaco-invasive arm.

In our study we assessed the myocardial blush grade in all patients following PCI whether it was done as a part of the PPCI or the PHINV procedures. Most of the patients who on both arms had MBG 3 but the number of patients with MBG 3 was higher on the pharmaco-invasive arm with a significant statistical difference between the two groups (P value 0.03) in favour of the PHINV arm. In their study **Shaheen *et al.*** [(11)] found that there was a significant improvement of the MBG in the PHINV arm which supports our results.

Moreover, it has been demonstrated that 2D speckle tracking echocardiography-measured left ventricular GLS is a very accurate predictor of unfavorable LV remodeling and cardiac events in individuals with acute myocardial infarction. GLS has the benefit of having less inter-observer variability than LVEF [(12)]. The left atrium and left ventricle's end pressures serve as the foundation for the diastolic function measure known as the E/e' ratio [(13)].

In our study analysis of the baseline measurements did not show any statistically significant variations between the two groups. Post PCI the readings have improved in both groups regarding (EF and GLS). The improvement was slightly higher on the PHINV arm but with no statistically significant variations between the two groups. This is in contrast to **Paul *et al.*** [(14)] findings that the pharmaco-invasive group's LV systolic function was considerably lower than the group who received primary angioplasty as measured by LV ejection fraction (2D Simpsons biplane technique) and global longitudinal strain (2D speckle tracking).

Regarding the diastolic function as measured by E/e` immediately post PCI, there was an improvement on both arms of our study with a statistically significant variation between the two groups in favor of the PHINV arm with P value of 0.004 which supports our study hypothesis that pharmaco-invasive strategy has better outcome regarding diastolic function.

CONCLUSION

It could be concluded that pharmaco-invasive strategy could offer a superior outcome regarding the recovery of the diastolic function and a higher myocardial blush grade (which indicates a better microvascular circulation) in STEMI patients compared to those who underwent PPCI.

This study demonstrated that for patients presenting with ST elevation myocardial infarction when primary PCI was not practical or could not be completed in a timely manner in accordance with the guideline's recommendations, early PCI after fibrinolysis within 24 hours constitutes a valid reperfusion strategy.

RECOMMENDATIONS

Using pharmaco-invasive strategies as a standard practise in healthcare would enhance outcomes for STEMI patients in Egypt who were unable to undertake primary PCI within 90 minutes of their initial medical encounter.

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