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ORIGINAL ARTICLE

Pharmaco-invasive versus Invasive-only Strategies in Therapy of ST-Elevation Myocardial Infarction: Comparative Study.

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ABSTRACT

Background: Primary percutaneous coronary intervention (PCI) for ST- elevation myocardial infarction (STEMI) remains the default strategy. However, when primary PCI cannot be performed expeditiously, a pharmaco-invasive strategy of fibrinolysis followed by PCI may be a reasonable alternative. This study is conducted to determine whether pharmaco-invasive strategy using fibrinolysis followed by routine early PCI represents a reasonable alternative to primary PCI when it is not readily available especially in patients with STEMI presenting early after symptom onset.

Methods: This is an observational prospective comparative single-center study that was conducted on acute STEMI patients who were presented within 12 hours from onset of symptoms at cardiovascular medicine department, Mansoura University Hospital; in the period from 1st February 2017 till 28th February 2019. The study includes two groups of STEMI patients; pharmaco-invasive group: involving 43 patients and primary PCI group: involving 51 patients; with a one month follow up comparing the safety and efficacy.

Results: Thrombolysis in Myocardial Infarction (TIMI) grade was better in pharmaco-invasive group (p=0.017), while there was no statistically significant difference in post PCI TIMI grade. Post-PCI myocardial perfusion grade was better in pharmaco-invasive group (P = 0.045). There was no statistically significant difference between the two groups regarding in-hospital complications (p=0.136) or complications at 1 month follow up (P > 0.05).

Conclusion: A pharmaco-invasive strategy is non-inferior to primary PCI in terms of reperfusion and complications.

Key words: STEMI, PCI, pharmaco-invasive.

INTRODUCTION

STEMI remains a major public health problem in developed and developing countries. Primary PCI is the most effective method to reestablish coronary perfusion in patients presenting with STEMI, and is associated with low rates of death, re-infarction and stroke [1].

Most of the studies that showed the superiority of primary PCI over fibrinolysis were performed before the widespread use of outcome-modifying adjunctive pharmacological therapies, and in those studies, primary PCI was compared to fibrinolysis alone rather than the pharmaco-invasive approach [2].

Primary PCI remains the default strategy recommended by major guidelines when revascularization is possible soon after the first medical contact [3]. However, when mechanical reperfusion with primary PCI cannot be performed expeditiously, a pharmaco-invasive strategy of fibrinolysis followed by coronary angiography and PCI may be superior to delayed primary PCI; especially in patients presenting very early after symptom onset [4,5].

The aim of our study is to determine whether pharmaco-invasive strategy using fibrinolysis followed by routine early PCI represents a reasonable alternative to primary PCI when it is not

readily available; especially in patients with STEMI presenting early after symptom onset.

METHODS

Our study is an observational prospective comparative single-center study that was conducted on convenient sample of STEMI patients who were presented within 12 h from onset of symptoms at cardiovascular medicine department, Mansoura University Hospital; in the period from 1st February 2017 till 28th February 2019. This study includes two groups of STEMI patients; pharmaco-invasive group involving 43 patients and primary PCI group involving 51 patients with a one month follow up comparing the safety and efficacy of a pharmaco-invasive strategy using a full dose streptokinase versus primary PCI. Written informed consent was obtained from all participants, the study was approved by the research ethical committee of Faculty of Medicine, Mansoura University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

This study included all patients who presented to the emergency department at Mansoura University Hospital with typical chest pain and who were diagnosed as STEMI defined according to ACC/AHA guidelines by evidence of myocardial injury (elevation of cardiac troponin values with at least one value above the 99th percentile upper reference limit) with necrosis in a clinical setting consistent with myocardial ischaemia; and STEMI patients with ongoing ischemia 12 -24 hours after the onset of chest pain [6].

In this study we excluded patients with contraindications to antiplatelets or anticoagulants or fibrinolytic therapy and patients presenting more than 24 hours from the onset of chest pain.

All participants were subjected to full history taking with emphasis on age, gender, chest pain, door to-needle time and time elapsed between thrombolytic therapy and early routine PCI in pharmaco-invasive group, door-to balloon time in primary PCI group, total ischemic time from onset of chest pain till reperfusion , coronary artery disease(CAD) risk factors as hypertension, diabetes, dyslipidemia, cigarette smoking and drug addiction, full clinical evaluation (pulse, blood pressure, heart failure signs), biochemical assessment, electrocardiography (ECG), and echocardiography.

An oral loading dose of clopidogrel 300-600 mg or 180 mg ticagrelor (ticagrelor was not given to patients who took fibrinolytic therapy) and 300 mg chewable aspirin were given before the intervention.

Primary PCI without a previous thrombolytic therapy was performed in patients who presented to our hospital within 24 hours after the onset of chest pain with ongoing ischemia (primary PCI group).

Patients in pharmaco-invasive group, who were referred from regional hospitals or when local primary PCI logistics are not fulfilled, received full dose intravenous streptokinase followed by PCI either elective PCI (if successful fibrinolysis) or rescue PCI (if failed fibrinolysis) within 3- 24 hours after thrombolysis.

Coronary angiography ± PCI was performed for patients in both groups at our center using Siemens Angiocore Machine (Germany) via femoral artery approach by experienced interventional cardiologists.

A thrombus aspiration catheter ± glycoprotein IIb/IIIa inhibitors (Eptifibatide with a loading dose of 180 mg/kg twice (10 minutes apart) and continuous infusion at 2 mg/kg/min (glomerular filtration rate (GFR) >50 ml/min) or 1 mg/kg/min (GFR<50 ml/min) was utilized as indicated in case of the presence of a heavy thrombus burden or absence of flow after the passage of the guiding wire

Pre and post PCI epicardial and myocardial perfusion (by TIMI grade and myocardial blush grade) and in hospital complications were assessed after coronary angiography.

After a duration of one month, follow up was carried out involving clinical assessment of major adverse cardiovascular events (MACE), including chest pain, recurrent infarction, sudden cardiac death (SCD), stroke, other cause mortality and heart failure (HF).

STATISTICAL ANALYSIS

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc). Qualitative data were expressed as number (percentage) within group and comparison between two groups of categorical data was conducted by using chi-square test or Fischer Exact test (FET) when it is expected to have less than 5 subjects in any group. Quantitative data was tested for normality by Kolmogorov-Smirnov test and expressed as mean± SD or median (range). Parametric data between two groups were compared using independent samples t-test (expressed as t). Non-parametric data between two groups was compared using Mann-Whitney U test (expressed as z). Comparison between parametric quantitative data at two different time points in the same group was conducted using Paired samples t-test (t). Comparison between non-parametric quantitative data at two different time points in the

same group was conducted using Wilcoxon Signed rank test (z). For all tests, $P < 0.05$ was statistically significant.

RESULTS

Our study is a comparative study included two groups of STEMI patients, 51 patients underwent primary PCI (invasive-only strategy), and 43 patients were eligible for pharmaco-invasive strategy (streptokinase followed by early routine PCI within 24 hours).

As regard all demographic data, both study groups were comparable except primary PCI group were more hypertensive (43.1% in primary PCI group and 20.9% in pharmaco-invasive group) with statistically significant difference between the two groups (p=0.013) (**Table 1)**.

As regard physical signs and ECG presentation, both study groups were comparable to each other **(Table s1)**.

The mean pain to door time in both groups was comparable to each other (P= 0.365). In the primary PCI group, the mean door to balloon time was 157.64 ± 98.92 minutes with range between 30 and 540 minutes In the pharmaco-invasive group, the mean door to needle time was 74.29 ± 39.21 minutes with range between 10 min and 180 minutes, In the same group, the mean onset of PCI after thrombolytic therapy was 9.76 ± 6.39 hours with range between 1 hour and 24 hours, total ischemic time from start of pain to start of reperfusion was 521.32 min. in primary PCI and 397.87 min. in pharmaco-invasive group with significant difference between two groups ($P < 0.001$) **(Table 2)**.

As regards the mean ejection fraction (EF) by echocardiography in both groups was comparable to each other. However, there was a statistically significant difference in the mean EF post-perfusion, as compared with the pre-perfusion value in the two groups **(Table s2)**.

Both study groups were comparable as regards the cardiac enzymes (P=0.789) and serum creatinine level (P=0.272) **(Table s3)**.

Regarding the culprit vessel, there was no statistically significant difference between the two groups. The most affected artery was left anterior descending artery (LAD) in 66.7% in primary PCI group vs 62.8% in pharmaco-invasive group **(Table s4)**.

The use of thrombus aspiration and I.V antiplatelet was lower in the pharmaco-invasive group (37.2% and 6.9% respectively) as compared with primary PCI group (41.2% and 15.7% respectively), however there was no statistically significant difference between the two groups **(Table s5)**.

As regards the TIMI grade between the two study groups, there was a statistically significant difference in the pre-PCI TIMI grade (p=0.017) while there was no statistically significant difference in post PCI TIMI grade ($P > 0.05$) **(Table 3 and Figure 1)**.

As regards the myocardial perfusion grade there was a statistically significant difference between two groups ($P = 0.045$) **(Table 4 and Figure s2)**.

Regarding the in-hospital complications, there was no statistically significant difference between the two groups (p=0.136). Death was experienced in 4 cases in the first group and 2 cases in the second group **(Table 5).**

Within the same context, the previously mentioned complications didn't reveal statistically significant difference between the two groups at 1 month after treatment, with mortality reported in 2 cases within each of the two groups **(Table 6).**

The causes of mortality in the primary PCI group were no reflow, failed PTCA and arrhythmia (ventricular fibrillation (VF)) during hospital stay while after 1 month the causes were complicated CABG and stroke. In the other group, the causes of mortality were no reflow and arrhythmia (VF) during hospital stay while after 1 month the causes were HF and reinfarction **(Table s6).**

In the cases who underwent primary PCI, diabetes mellitus (DM), hypertension (HTN), delayed time for intervention, higher serum creatinine, lower EF at admission and at 1 month, increased number of affected vessels and decreased post-PCI TIMI grade were all associated with MACE **(Table s7).**

In the cases who underwent pharmaco-invasive strategy, smoking, HPN, higher serum creatinine, lower EF at 1 month, increased number of affected vessels and decreased post-PCI TIMI grade; all were associated with MACE **(Table s8)**.

Table (1) Analysis of demographic data in the two study groups

		Groups					**Test of significance**
		Primary PCI (N=51)		Pharmaco-invasive (N=43)		Total (N=94)	
Age (years)		54.7 ± 9.94		52.3 ± 11.2		53.41 ± 10.09	P > 0.05
Gender	Male	43	84.3%	39	90.7%	82 (87.2%)	P > 0.05
	Female	8	15.7%	4	9.3%	12 (12.8%)	

		Groups					Test of significance
		Primary PCI (N=51)		Pharmaco-invasive (N=43)		Total (N=94)	
Special habits	No	18	35.3%	19	44.2%	37(39.4%)	P > 0.05
	Smoking	30	58.8%	24	55.8%	54(57.4%)	
	Ex-smoker	3	5.9%	0	0%	3(3.2%)	
	Tramadol abuse	1	1.9%	3	6.9%	4(4.3%)	
DM		19	37.3%	13	30.2%	32(34.1%)	P > 0.05
HTN		22	43.1%	9	20.9%	31 (32.9%)	P= 0.013*
Positive family history		3	5.9%	1	2.3%	4(4.3%)	P > 0.05
Dyslipidemia		9	17.6%	4	9.3%	13(13.8%)	P > 0.05

P: probability, continuous data expressed as mean±SD, categorical data expressed as Number (%)

Table 2. Analysis of time intervals.

	Groups		Test of significance
	Primary PCI (N=51)	Pharmaco-invasive (N=43)	
Pain to door time(hours)	6.64 ± 2.75	5.32 ± 1.98	P > 0.05
Door to needle time(min)		74.29 ± 39.21	
Time to PCI after lytic therapy (hours)		9.76 ± 6.39	
Door to balloon time(min)	157.64 ± 98.92		
Total ischemic time(min)	521.32± 215.82	397.87 ± 76.54	P < 0.001*

P: probability, continuous data expressed as mean±SD, *: statistically significant (p< 0.05)

Table 3 Pre and post PCI TIMI grade

	Groups				Test of significance
	Primary PCI (N=51)		Pharmaco-invasive (N=43)		
Pre PCI TIMI grade					
0	40	78.4%	14	32.6%	P= 0.017*
I	0	0%	2	4.7%	
I-II	1	1.9%	7	16.3%	
II-III	0	0%	2	4.7%	
III	10	19.6%	18	41.8%	
Post PCI TIMI grade					
0	6	11.7%	5	11.6%	P > 0.05
I-II	1	1.9%	0	0%	
II	1	1.9%	1	2.3%	
III	43	84.3%	37	86.1%	

P: probability, categorical data expressed as Number (%), *: statistically significant (p< 0.05), TIMI (Thrombolysis In Myocardial Infarction).

Table 4 Myocardial perfusion grade post PCI

	Groups				Test of significance
	Primary PCI (N=51)		Pharmaco-invasive (N=43)		
Myocardial perfusion grade					
0	0	0%	5	11.6%	P= 0.045*
I	2	3.9%	1	2.3%	
II	1	1.9%	1	2.3%	
III	40	78.4%	36	83.7%	

P: probability, categorical data expressed as Number (%), *: statistically significant (p< 0.05).

Table 5 Complications during hospital stay in the two study groups

	Groups				Test of significance
	Primary PCI (N=51)		Pharmaco-invasive (N=43)		
Complications during hospital stay					
Death	4	7.8%	2	4.7%	P > 0.05
Cardiogenic shock	4	7.8%	2	4.7%	
Pulmonary edema	2	3.9%	3	6.9%	
Arrhythmia	1	1.9%	1	2.3%	
Chest pain	1	1.9%	1	2.3%	
Block	1	1.9%	0	0%	
Bleeding (minor)	2	3.9%	2	4.7%	
Intracerebral bleeding	0	0%	1	2.3%	

P: probability, categorical data expressed as Number (%)

Table 6 Complications at 1 month in the two study groups

	Groups				Test of significance
	Primary PCI (N=51)		Pharmaco-invasive (N=43)		
Complications at 1 month					
Death	2	3.9%	2	4.7%	P > 0.05
Heart failure	4	7.8%	5	11.6%	
Arrest	1	1.9%	0	0%	
Arrhythmia	0	0%	0	0%	
Block	0	0%	0	0%	
Pericarditis	1	1.9%	0	0%	
Chest pain	2	3.9%	0	0%	

P: probability, categorical data expressed as Number (%)

SUPPLEMENTARY FILES

Table s1 Analysis of physical signs and ECG

	Groups				Test of significance
	Primary PCI (N=51)		Pharmaco-invasive (N=43)		
Mean ABP=(SBP +2DBP)/3	86.73 ± 16.558		83.93 ± 15.912		P > 0.05
HR	77.96 ± 14.03		80.19 ± 15.39		P > 0.05
Basal Lung rales	2	2.6%	2	4.7%	P > 0.05
Shock	1	1.9%	1	2.3%	P > 0.05
Heart block	1	1.9%	1	2.3%	P > 0.05
AF	0	0%	1	2.3%	P > 0.05
Arrest (VF) on presentation	0	0%	3	6.9%	P > 0.05
Anterior STEMI	34	66.7%	27	62.8%	P > 0.05
Inferior STEMI	14	27.4%	15	34.8%	P > 0.05
Lateral STEMI	2	2.6%	1	2.3%	P > 0.05
Posterior STEMI	1	1.9%	0	0%	P > 0.05

P: probability, continuous data expressed as mean±SD, categorical data expressed as Number(%)

Table s2 Follow up of the ejection fraction (EF) as detected by ECHO in the two study groups

Time	Primary PCI (N=51)	Pharmaco-invasive (N=43)	Test of significance
Preperfusion	55.13 ± 8.34	53.59 ± 6.34	P > 0.05
Post perfusion	56 ± 8.4	54 ± 6.37	P > 0.05
P1	0.008*	< 0.001*	

Time	Primary PCI (N=51)	Pharmaco-invasive (N=43)	Test of significance
1 month	59.17 ± 8.17	58.17 ± 7.71	P > 0.05
P1	< 0.001*	< 0.001*	

P: probability. (Significance between the two groups)**,** P1: significance in relation to the Preperfusion value, continuous data expressed as mean±SD, *: statistically significant (p< 0.05)

Table s3 Comparing of CPK and creatinine in the two study groups

Time		Primary PCI (N=51)	Pharmaco-invasive (N=43)	Test of significance
CPK	Mean ± SD	2909.41 ± 2087.63	2635.95 ± 1484.86	P > 0.05
Creatinine		1.07± 0.25	1.14 ± 0.35	P > 0.05

P: probability. (Significance between the two groups)**,** continuous data expressed as mean±SD,
*: statistically significant (p< 0.05).

Table s4 Culprit vessel in the two study groups

	Groups				Test of significance
	Primary PCI (N=51)		Pharmaco-invasive (N=43)		
Culprit vessels					
LAD	34	66.7%	27	62.8%	P > 0.05
LCX	3	5.9%	4	9.3%	
LM	0	0%	1	2.3%	
OM1	1	1.9%	0	0%	
OM3	1	1.9%	0	0%	
RCA	12	23.5%	11	25.6%	

P: probability, categorical data expressed as Number (%)

Table s5 Thrombus aspiration and use of I.V. antiplatelet in the two study groups

	Groups				Test of significance
	Primary PCI (N=51)		Pharmaco-invasive (N=43)		
Thrombus aspiration	21	41.2%	16	37.2%	P= 0.352
I.V antiplatelet	8	15.7%	3	6.9%	P= 0.086

P: probability, categorical data expressed as Number (%)

Table s6 Analysis of the cause of death the two study groups

Death during hospital stay					
	Primary PCI (N=4)		Pharmaco-invasive (N=2)		
No reflow	1	25%	1	50%	FET= 1.635 P > 0.05
Failed PTCA	1	25%	0	0%	
Arrhythmia (VF)	2	50%	1	50%	
Death during 1 month					
	Primary PCI (N=2)		Pharmaco-invasive (N=2)		
CABG	1	50%	0	0%	FET= 0.936 P > 0.05
Heart failure	0	0%	1	50%	
Stroke	1	50%	0	0%	
Reinfarction	0	0%	1	50%	

P: probability, categorical data expressed as Number (%)**,** FET= Fischer exact test.

Table s7 Relation between different variables and MACE in primary PCI group (n=51)

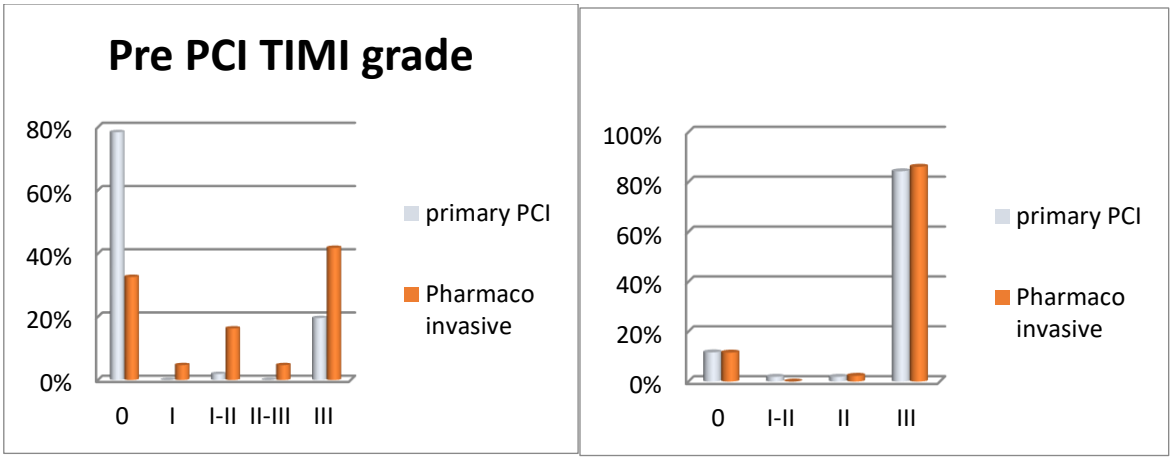
		Groups				Test of significance
		No MACE (N=38)		MACE (N=13)		
Age		53.47±9.50		58.31±10.69		t= -1.372 p= 0.131
Sex	Male	31 (81.6%)		11(84.6%)		FET= 0.874 P= 0.528
	Female	7 (18.4%)		2 (15.4%)		
Smoking		17 (36.8%)		4 (30.8%)		FET= 0.717 P= 0.605
DM		10 (26.3%)		9 (69.2%)		FET= 7.632 P= 0.006*
HTN		13 (34.2%)		9 (69.2%)		FET= 4.843 P= 0.028*
Dyslipidemia		6 (15.8%)		3 (23.1%)		FET= 1.325 P= 0.262
Time for intervention		122.31± 60.57		169.74±106.99		z= -3.846 P = 0.001*
Serum creatinine		1.02± 0.21		1.25± 0.31		t= -3.030 P = 0.004*
EF on admission		56.63± 8.19		50.77± 9.53		t= 2.137 P = 0.038*
EF at 1 month		60.50± 7.72		55.31± 8.53		t= 2.039 P = 0.047*
Number of affected vessels		1 (1-1)		2 (1-2)		z= -2.936 P = 0.009*
Post-PCI TIMI grade						
0 (no reflow)		0	0%	6	46.2%	FET= 23.817 P< 0.001*
I-II		0	0%	1	7.8%	
II		1	2.6%	0	0%	
III		37	97.4%	6	46.2%	

P: probability.
Continuous data expressed as mean±SD or median (range)
Categorical data expressed as Number(%)
FET= Fischer Exact test

Table s8: Relation between different variables and MACE in Pharmaco-invasive group (n=43)

		Groups		Test of significance
		No MACE (N=33)	MACE (N=10)	
Age		51.64±10.68	55.44±13.81	p= 0.379
Sex	Male	30 (90.9%)	9 (90%)	FET= 0.881 P= 0.348
	Female	3(9.1%)	1(10%)	
Smoking		17 (51.5%)	8 (80%)	FET= 4.864 P= 0.001*
DM		9 (27.3%)	4 (40%)	FET= 1.738 P= 0.182
HTN		4 (12.1%)	5 (50%)	FET= 6.271 P< 0.001*
Dyslipidemia		0 (0%)	1 (10%)	FET= 1.427 P= 0.236
Time for intervention		70± 33.54	75.45± 41.01	z=-1.964 P = 0.128
Serum creatinine		1.08± 0.19	1.40± 0.67	z= -2.423 P = 0.021*

	Groups				Test of significance
	No MACE (N=33)		MACE (N=10)		
EF on admission	54 ± 6.75		52.11± 4.86		t= 0.782 P = 0.439
EF at 1 month	59.85± 5.96		50.29± 10.42		t= 3.349 P = 0.002*
Number of affected vessels	1 (1-1)		2 (1-2)		z= -3.036 P = 0.005*
Post-PCI TIMI grade					
0 (no reflow)	1	3%	4	40%	FET= 19.365 P< 0.001*
II	0	0%	1	10%	
III	32	97%	5	50%	



P: probability, continuous data expressed as mean±SD or median (range), categorical data expressed as Number (%), FET= Fischer Exact test.

Figure 1 Pre and post PCI TIMI grade

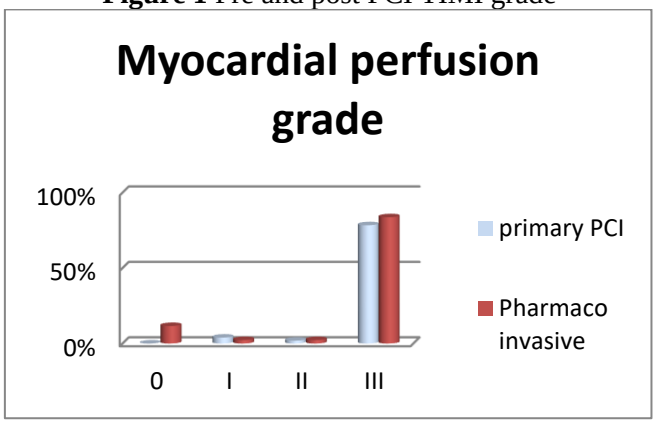


Figure s2 Myocardial perfusion grade

DISCUSSION

Our study is an observational study comparing the safety and efficacy of a pharmaco-invasive strategy with a full dose streptokinase versus invasive only strategy by primary PCI that was conducted on 94 STEMI patients including 51 were allocated to primary PCI and 43 to a pharmaco-invasive strategy at Mansoura University cathlab, after excluding those failed to contact for follow up.

The main finding in our study is that early reperfusion regardless the type of strategy was associated with improved outcomes in patients with acute STEMI, the pharmaco-invasive strategy was non inferior to primary PCI as regards the all outcomes and even superior in terms of incidence of myocardial and epicardial perfusion.

Baseline demographic characteristics: the mean age of our study population was 53 years with no significant difference between the two groups. Regarding EARLY-MYO the Chinese Trial, the mean age of their study was 58 years [7]. Our study found that the incidence of MACE was related to increased age. In old studies there was a correlation

between increase adverse outcomes in patients with myocardial infarction with increased age [8].
Most of our study patients were men (87.2%). In our study male gender had higher MACE than female. However, some studies have found higher mortality rates in females than in males [9].The decreased risk among our female participants assures the benefits of early reperfusion by either strategies; primary PCI or pharmaco-invasive in female patients.
As regards DM, 69.2 % of patients that developed MACE in primary PCI group were diabetic and 40 % in pharmaco-invasive group were diabetic, which is considered a statistically significant correlation between DM and occurrence of MACE meaning that DM is a strong risk factor for MACE after STEMI. We explain that by poor dietary habits, sedentary lifestyle among Egyptian people which may increase the overall prevalence of DM. Also Sadrnia et al showed that DM increased the risk of MACE in patients who received primary PCI for STEMI [10]. Numerous studies have also exhibited the short-term and long-term influences of diabetes on the MACE [11]**.**
Smoking is a well-established risk factor for CAD. The significance of smoking in the incidence of MACE after PCI is highly considerable. In this study, smoking was evident in 57.4% of all our study population; with 30.8% of patients who underwent primary PCI and 80% of pharmaco-invasive group who developed MACE being smokers. Thus, smoking in our study has significant correlation on MACE. The higher percentage of smokers among our study patients is explained by the low socioeconomic standard and bad social habits among the Egyptian population.
High arterial blood pressure (ABP) is a risk factor for CAD and enhances the complications after acute coronary syndrome [12]**.** In this study, HTN represented 32.9% of all our study population; 69.2% of primary PCI patients and 50% of pharmaco-invasive group who developed MACE were hypertensive, Thus HTN in our study has significant relation on MACE which is matching with EARLY-MYO Trial, however the percentage of HTN in their study was 51.1% [7]**.** The higher percentage of hypertensive patients among our study patients is explained by the low socioeconomic standard, and bad social and dietary habits, among the Egyptian population.
Despite the fact that hyperlipidemia is a risk factor for CAD, it had no significant effects on the incidence of MACE in our study as it represented 17.3% of patient that developed MACE. Thus, hyperlipidemia in our study didn't have any negative effects on MACE. This may be due to under diagnosis of hyperlipidemia in our patients and non-routine laboratory tests for diagnosis of hyperlipidemia. Our study results as regard hyperlipidemia is matching with Sadrnia et al [10]. Multiple trials have detected high serum levels of lipoprotein (a) to be linked to worse outcome in STEMI patients [13].
Baseline clinical characteristics and ECG: the two groups had a similar hemodynamic status, as regard HR, ABP, pulmonary congestion as well as the ECG of presentation.
Timing Intervals: in our registry the mean pain to door time was 5.9 hour, while in EARLY-MYO Trial, the mean pain to door time was 4.1 hour [7]**.** In our results we explained time delay by decreased patient awareness of the importance of seeking medical advice in the proper time after onset of chest pain, a matter which raises concerns for launching widespread national patient education programs. The mean time of door to needle in our registry was 74.29 ± 39.21 minutes with range between 10 min and 180 minutes while door to balloon in primary PCI group was 157.64 ± 98.92 minutes with range between 30 and 540 minutes. The mean time of allocation to PCI was longer in the thrombolytic group than in the primary PCI group, with about 9.76 hours delay from thrombolytic therapy to routine early PCI.
While in EARLY-MYO Trial, the mean time of door to needle and door to balloon (alteplase injection or arterial sheath insertion) was 57 minutes and 110 minutes, respectively. The mean time from allocation to PCI was longer in the fibrinolysis group than in the primary PCI group, with a delay of 10.2 hours, which is similar to our results [7]. We concluded that the duration from the onset of chest pain and first medical contact (FMC) was too long. Similarly, the time from FMC to reperfusion was much longer than the guidelines recommended time (90 minutes from door to PCI and 30 minutes to thrombolytic therapy). Such long delays increase patients' mortality and risk of MACE, so we need to study the reasons of such delays widely.
Laboratory findings: the most significant laboratory finding that correlate with MACE in our study was serum creatinine on admission. As regard the level of serum creatinine in our study; the mean level was 1.1 mg/dl with the minimum level 0.6 mg/dl and the maximum level 1.8 mg/dl. MACE appeared in a range of serum creatinine of 1.25±0.31 mg/dl in primary PCI group and 1.40±0.67 mg/dl in pharmaco-invasive group while patients without MACE serum creatinine range1.02±0.21, 1.08±0.19 mg/dl with P value 0.004 and 0.021 respectively, which is considered a statistically significant finding. This finding is found to be similar to a study done by ***Marenzi et***

al in Italy demonstrated that inpatients hospitalized with ACS, daily serum creatinine value and its change pattern are stronger predictors of in-hospital mortality than the initial serum creatinine value [14]**.** Their combined evaluation seems to provide a more accurate and dynamic stratification of short-term mortality risk.

Other laboratory findings like troponin had no significant correlation with MACE.

Echocardiography: a great facility to detect patients' survival and the incidence of MACE after primary PCI is assessment of left ventricular (LV) function. Better LV function is associated with improved outcomes and vice versa [15]**.** In our study, the mean EF by echocardiography within the two groups didn't reveal any significant difference at preperfusion, immediately post-perfusion, at 1 month after perfusion and at 6 months after perfusion. However, there was a statistically significant difference in the mean EF immediately post-perfusion, at 1 month after perfusion and at 6 months after perfusion as compared with the preoperative value in the two groups**.**

In our study, low LVEF had statistically significant impact on outcomes. MACE appeared in a range of LVEF 50.77±9.53%, while patients without MACE LVEF 56.63±8.19% in primary PCI group, with P value 0.038, which is considered a statistically significant finding in primary PCI group, while MACE appeared in a range of LV EF 52.11±4.86% in pharmaco-invasive group. Using echocardiography, the GRACIA-2 trial revealed that 6-week LVEF was comparable between primary PCI and pharmaco-invasive groups (p=0.11) [16]. While by left ventriculograms, the FAST-MI (French Registry on Acute ST-Elevation Myocardial Infarction) exhibited that in-hospital LVEF was significantly higher in the pharmaco-invasive group than in the primary PCI group (p=0.003) [17].

Angiographic data: A great determinant of the outcome of PCI in patients with STEMI is TIMI flow. Patients with TIMI 3 flow are expected to have higher survival rates and fewer complications after primary PCI [18].

In our study, there is a statistically significant correlation between angiographic success (TIMI 3) and occurrence of MACE with p value = 0.001; thus as long as the grade of TIMI flow decreased the occurrence of MACE increased.

Comparing the TIMI grade between the two study groups showed significant difference between the two groups, there was a statistically significant difference in the Pre PCI TIMI grade (p=0.017) while there was no significant difference between the two groups in Post PCI TIMI grade.

There were 3.9% cases with grade I myocardial perfusion grade, 1.9% of the cases with grade II and 78.4% with grade III in the cases who underwent primary PCI; while there were 2.3% cases with grade I myocardial perfusion grade, 2.3% of the cases with grade II and 83.7% with grade III in the cases who underwent pharmaco-invasive strategy with significant difference between the two groups in favor of pharmaco-invasive group.

In our study population, we found that LAD was the most revascularized target vessel as it represented about 66.7% in the cases who underwent primary PCI vs 62.8% in the cases who underwent pharmaco-invasive treatment with no significant difference between the two groups**,** In EARLY-MYO Trial They found that LAD represented about 52.1% of revascularized vessels in primary PCI and 47.8 in pharmaco-invasive group [7].

Moreover in our study, there was positive correlation between the number of involved vessels and occurrence of MACE.

Thrombus aspiration and use of glycoprotein IIb/IIIa inhibitors were more frequent in the primary PCI group, meaning that the thrombus burden in primary PCI group was significantly higher than in the pharmaco-invasive group which is similar to results in EARLY-MYO Trial**.** However, in our study, there was no statistically significant difference between the two groups, and we explained that by the relatively increased number of failed thrombolysis and rescue PCI.

In-hospital outcome: regarding the different complications of the cases included in the study including death, cardiogenic shock, pulmonary edema, arrhythmia, chest pain, block, bleeding and hemorrhagic stroke, there was no significant difference between the two groups (p=0.136). Death was experienced in 4 cases in the first group and 2 cases in the second group.

One-month follow up outcome: within the same context, the previously mentioned complications were not significantly different between the two groups at 1 month after treatment. With mortality reported in 2 cases within each of the two groups

The causes of mortality in the group who underwent primary PCI were no reflow, failed PTCA and malignant arrhythmia (VF) during hospital stay; while after 1 month the causes were complicated CABG and ischemic stroke. In the other group, the causes of mortality were no reflow and arrhythmia (VF) during hospital stay while after 1 month the causes were HF and reinfarction.

Regarding the safety issue, EARLY-MYO Trial somewhat unexpectedly showed that no intracranial hemorrhages were observed in both the

pharmaco-invasive and primary PCI groups at the 30-day follow-up supposing that a half-dose fibrinolytic regimen in the elderly might reduce bleeding risk in the pharmaco-invasive therapy setting [7].

On the other hand, the STREAM trial showed that the overall rate of intracerebral hemorrhage was significantly higher in the pharmaco-invasive versus primary PCI group (0.96% versus 0.21%, respectively; p=0.04) [19]. In our study we reported only one case with intracerebral hemorrhage in pharmaco-invasive group.

CONCLUSION

Pharmaco-invasive strategy is an effective non inferior alternative for patients with STEMI who cannot receive timely primary PCI.

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