EFFECT OF PRIMARY PERCUTANEOUS CORONARY INTERVENTION ON THE INCIDENCE AND SEVERITY OF ISCHEMIC MITRAL REGURGITATION IN PATIENTS WITH ACUTE ST-ELEVATION MYOCARDIAL INFARCTION.

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ABSTRACT

Background: Ischemic mitral regurgitation (IMR) is mitral incompetence resulting from coronary artery disease in the absence of intrinsic valve lesions. This common complication of acute myocardial infarction (AMI) (1) occurs in 15–64% of patients after this event, (2) and is an independent predictor of future cardiovascular mortality(3). The pathophysiology of ischemic MR is complex, and its presence may be related to several underlying processes that are often difficult to separate in a given patient(4). It may result from altered ventricular geometry(5,6,7), incomplete mitral leaflet coaptation, papillary muscle dysfunction and regional wall motion abnormalities (8). IMR severity is positively associated with development of heart failure after AMI.(9).Because of its complex pathophysiology and heterogeneous clinical presentation, the proper treatment of ischemic MR is often debated, and the relative utility of revascularization with and without concomitant mitral valve surgery is uncertain(4). Although primary percutaneous coronary intervention (PCI) for AMI is known to improve outcome(10,11,12), and that IMR after myocardial infarction (MI) worsens outcome, (13) the effect of primary PCI on IMR incidence has not been specifically studied.

Aim of the work: To detect the impact of Primary PCI on the development and severity of ischemic mitral valve regurgitation in patients presenting with acute ST segment elevation myocardial infarction.

Patients and methods: This study included 60 patients presenting for the first time with Acute ST segment elevation myocardial infarction The patients were divided into two groups group A: Included 30 patients who were treated with primary PCI group B included 30 patients who were treated by thrombolytic therapy..All patients had echocardiography after reperfusion , during the hospital stay then reevaluation after one month period.

Results:. During hospital stay the mean LV EF in the PCI group was 46.17± 7.51 % while in the SK group the mean EF was 41.67±6.06 %.In the PCI group the mean wall motion score index during the hospital stay was 1.25± 0.15 while in the SK group it was 1.39 ±0.14 with P value less than 0.001.At one month follow up. In the PCI group there were 6 patients with mitral regurgitation the mean jet area was (1.33±0.63) cm^2, while in the SK group there were 25 patients with mitral regurgitation the mean jet area was(4.45 ±2.17) cm^2 with P value <0.0001In the PCI group the severity of mitral regurge was positively correlated with the age of the patient P value less than 0.01,door to needle P value less than 0.01 and pain to hospital times P value 0.04.In the streptokinase group, the severity of mitral regurgitation was positively correlated with door to needle time delay with P value of 0.03.

Conclusion: Primary PCI decreased the incidence and severity of chronic ischemic mitral regurgitation when compared with medical reperfusion in patients with acute ST segment elevation myocardial infarction.

Key words : Ischemic mitral regurgitation, Acute ST elevation myocardial infarction, Primary PCI.

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INTRODUCTION

The mortality of STEMI is influenced by many factors, among them: age, Killip class, time delay to treatment, mode of treatment, history of prior myocardial infarction, diabetes mellitus, renal failure, number of diseased coronary arteries, ejection fraction, and treatment. (14).Several recent studies have highlighted a fall in acute and long term mortality following STEMI, in parallel with greater use of reperfusion therapy, primary percutaneous coronary intervention (primary PCI), modern antithrombotic therapy and secondary prevention treatments. (15) Randomized clinical trials comparing timely primary PCI with in-hospital fibrinolytic therapy in high-volume, experienced centers have repeatedly shown that primary PCI is superior to hospital fibrinolysis. (16)It was the Belgian anatomist and physician Andreas Vesalius, while working in Padua, Italy, who likened the bifoliate left atrioventricular valve to a bishop's mitre, hence the term ''mitral valve'' (17). The physiology of the working components of the valve, its two leaflets, can be understood only when note is taken of their crucial relationships to the adjacent anatomical structures, namely, the left atrium (LA), the left ventricle (LV), the aortic valve, the papillary muscles, the tendinous cords, and the cardiac central fibrous body.

In 1972, Perloff and Roberts(18) put forward the concept of a mitral valvular complex to underscore this essential and harmonious structural relationship. From a clinical perspective, the French surgeon Alain Carpentier introduced the paradigm of the pathophysiologic triad to better define regurgitation across the valve, pointing out that the underlying disease, the first leg of the triad, creates structural or geometric changes in the valvular apparatus, this being the second leg, which may lead to valvular dysfunction as the third leg.(19,20) Ischemic mitral regurgitation (IMR) is a common complication of coronary artery disease (CAD) and may develop in the acute or chronic phase. In chronic IMR, mitral valve (MV) leaks but the leaflets and subvalvular apparatus appear normal. Chronic MR is therefore not a disease of the valve per se, but rather a disease of the left ventricle.(21)

After the appearance of IMR, the aim of medical and/or surgical therapy is to ameliorate heart failure symptoms, and improve LV remodeling, ejection fraction and the intermediate/long-term outcome.(22)

Aim of the work To detect the impact of Primary PCI on the development and severity of ischemic mitral valve regurgitation in patients presenting with acute ST segment elevation myocardial infarction.

PATIENTS AND METHODS

This study included 60 patients presenting to the national heart institute for the first time with Acute ST segment elevation myocardial infarction according to the third universal definition of myocardial infarction which requires the presence of:

1-Symptoms of ischemia. 2-New or presumed new significant ST-segment–T wave (ST–T) changes (new ST elevation at the J point in two contiguous leads with the cut-points: ≥ 0.1 mV in all leads other than leads V2–V3 where the

following cut points apply:≥ 0.2 mV in men ≥ 40 years;≥ 0.25 mV in men

<40 years, or ≥ 0.15 mV in women.) 3- new left bundle branch block (LBBB). (23)

The patients were divided into two groups

Group A: Included 30 patients who were treated with primary PCI**.**

Group B Included 30 patients who were treated with thrombolysis

Inclusion criteria:

1-Patients presenting with acute myocardial infarction for the first time.

Exclusion criteria:

Failure of reperfusion either by PCI or thrombolysis,Patients with past history of ischemic heart disease,Patients known to have rheumatic valvular heart disease. Patients with previous myocardial infarction.Patients with dilated

cardiomyopathy. Patients With previous PCI or CABG.

All patients were subjected to:

1-Full history taking.

that includes the demographic data as age and gender,risk factors and the time between onset of symptoms to the first medical contact

2- Full clinical examination and risk assesment.

3-Twelve lead surface ECG.

With right ventricular leads (V3R,V4R) and posterior leads (V7,V8) when right ventricular and or posterior myocardial infarction were suspected.

4-Blood samples for

a- Cardiac enzymes b-Renal function tests

c-Random blood glucose

d- Complete blood picture

5-Reperfusion therapy was done using Primary PCI for group A or streptokinase 1.500.000 international unit intravenous infusion along one hour for group B.

Definition of successful reperfusion

Successful reperfusion is defined as

GroupA:

Reduction to residual stenosis of <30% by balloon angioplasty or successful stent deployment at the desired position with a residual stenosis <10%, followed by Thrombolysis In Myocardial Infarction (TIMI) grade 3 flow in the infarct-related artery when using primary PCI.

Group B:

ST-segment resolution of 50% at 60–90 min, typical reperfusion arrhythmia, disappearance of chest pain when using fibrinolytic therapy.(24)

6-Echocardiograpy was done to all patients during the hospital stay.

7- Follow up echocardiography: The follow up echo was done to all patients of both group A and group B at least Thirty days after hospital discharge to detect left ventricular ejection fraction, wall motion abnormalities,wall motion score index and the development of ischemic mitral regurgitation.

The echo machines that were used are Philips Envisor, Philips HD7,General electric Vivid 3 and General electric Vivid S5.

Assessment of Mitral Regurgitation :

Mitral regurgitation severity was evaluated during echocardiographic examination using colour Doppler flow mapping criteria according to the guidelines of the American college of cardiology and American heart association (maximal MR jet area-to-left atrial area ratio). MR severity was quantified using a 4-point scale: 0, if the percentage of maximal MR colour jet area-to-maximal left atrial area was 0%; 1 (trace MR), if the ratio was $\leq 10\%$; 2 (mild MR), if

10–19%; 3 (moderate MR), if 20–39 %; and 4 (severe MR) if the ratio was 40%. (25)

Statistical Analysis
Data were expressed as the mean (± standard deviation) or median (interquartile range) for continuous variables, and number (%) for categorical variables. Patient characteristics between the 2 treatment groups (PCI and non-PCI) and associations between risk factors and IMR grades will be compared using a Student's t-test for normal continuous data, a Wilcoxon rank sum test for skewed continuous data, and a chi-squared test for categorical

data. Data were analyzed using Statistical Program for Social Science (SPSS) version 18.0.
The following tests were done:
- Independent-samples t-test of significance was used when comparing between two means.
- Chi-square (X^2) test of significance was used in order to compare proportions between two qualitative parameters.
- Pearson's correlation coefficient (r) test was used for correlating data.
- Probability (P-value)
  - P-value <0.05 was considered significant.
  - P-value <0.01 was considered as highly significant.
  - P-value >0.05 was considered insignificant.

A. Demographic data and risk factors

Table (1) The demographic data and risk factors

	PCI group	SK group
Mean Age	62.2years	59.23years
Gender	23 Males	24 Males
	7 Females	6 Females
Mean Weight	79.67 kg	79.83 kg
Mean Creatinine	1.34mg/dl	1.39mg/dl
Diabetes no.	14	19
Hypertension no	25	26
Dyslipidemia	7	14
Smoking	21	20
Family history	5	6

B. Clinical and echocardiographic data during the hospital stay.
1. Myocardial area at risk
In PCI group there were 12 patients who had anterior MI, 5 patients with extensive anterior MI,11 patients with Inferior MI and 2 patients with inferoposterior MI. In SK group there were 17 patients with anterior MI,6 patients with inferior MI, 7 patients with inferoposterior MI and there were no patients with extensive anterior MI.
2- Time between first medical contact and treatment.
In the PCI group, the mean door to balloon time was (97.33±38) minutes, while in the SK group the mean door to needle time was (39.38±11.02) minutes.
3. Left ventricular Ejection Fraction during hospital stay

During hospital stay the mean LV EF in the PCI group was 46.17± 7.51 % while in the SK group the mean EF was 41.67±6.06 %
4. Wall motion score index during hospital stay
In the PCI group the mean wall motion score index during the hospital stay was 1.25± 0.15 while in the SK group it was 1.39 ±0.14
5. Presence of ischemic mitral valve regurgitation during hospital stay
During hospital stay there was only one patient who had mild ischemic mitral regurgitation in the PCI group, while in the SK group there were 5 patients who had ischemic mitral regurgitation, there was no statistical significance between the two groups regarding number of patients with mitral regurgitation during hospital stay.
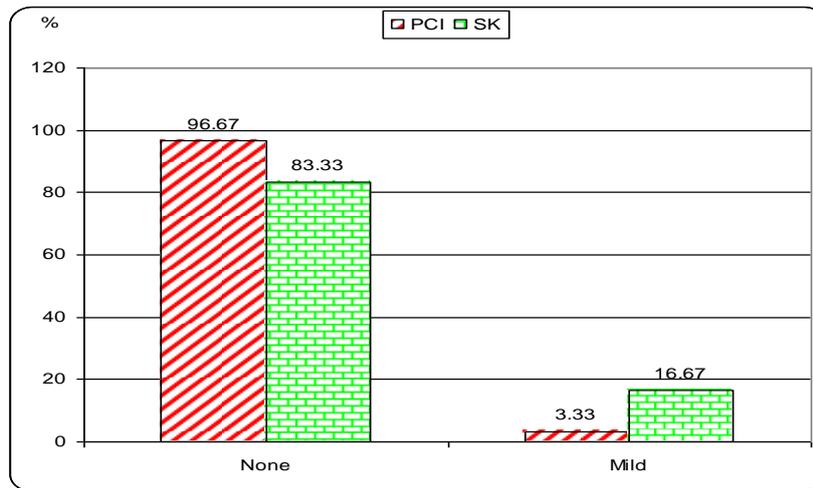
Figure (1): Relation between PCI and SK as regard presence of mitral regurgitation during hospital stay.

6.Mitral regurgitant jet area in patients who developed mitral regurgitation during hospital stay.

In the PCI group there was just one patient who had mild mitral regurgitation during hospital stay so the mean jet area was (0.37 ± 0.17) cm^2, while in the SK group there were five patients who developed mitral regurgitation while they were still at the hospital with mean jet area of (1.19 ± 0.057) cm^2 p value < 0.00001.

Table (2): Comparison between PCI and SK groups as regard mitral regurgitant jet area (cm^2) during hospital stay.

Groups	Jet area (cm2)		t-test	
	Mean	**±SD**	**t**	**p-value**
PCI	0.37	0.17	7.551	**< 0.00001**
SK	1.19	0.57		

C.Comparison between the two groups in the follow up echo one month after discharge..

1.Ejection fraction

In the PCI group the mean ejection fraction was (53.5 ± 5.75) % while in the SK group the mean ejection fraction was (48.83 ± 5.83) %. There was highly statistically significant difference between groups, with p-value <0.0001 HS.

Table (3): Comparison between PCI and SK groups as regarding follow up ejection fraction.

Groups	Follow up echo ejection fraction		t-test	
	Mean	**±SD**	**t**	**p-value**
PCI	53.50	5.75	3.124	**<0.0001**
SK	48.83	5.83		

2. Wall motion abnormalities in the follow up echo

In the follow up echocardiography, 13 patients had no segmental wall motion abnormalities in PCI group versus 4 patients in SK group, there was a significant difference between the two groups ($\chi^2 = 6.648$, p = 0.01), 2 patients had akinetic anterior septum in PCI group versus 2 patients in SK group, there was no significant difference between the two groups ($\chi^2 = 0$, p = 1), 7 patients had hypokinetic anterior septum in PCI group versus 13 patients in SK group, there was no significant difference between the two groups ($\chi^2 = 2.7$, p = 0.1), 3 patients had akinetic inferior wall in PCI group versus 2 patients in SK group, there was no significant difference between the two groups ($\chi^2 = 0.218$, p = 0.64), 3 patients had hypokinetic inferior wall in PCI group versus 2 patients in SK group, there was no significant difference between the two groups ($\chi^2 = 0.218$, p = 0.64), no patient had inferoposterior akinesia in PCI group versus 2 patients in SK group, there

was no significant difference between the two groups (χ^2 = 2.069, p = 0.15), 2 patients had inferoposterior hypokinesia in PCI group versus 5 patients in SK group, there was no significant difference between the two groups (χ^2 = 1.455, p = 0.228),

3.Wall motion score index at the follow up
In the PCI group the mean wall motion score index was 1.12±0.13 while in the SK group the mean wall motion score was 1.22±0.12, there was highly statistically significant difference between groups, with p-value <0.001 HS.

Table (4): Comparison between PCI and SK as regard wall motion score at follow up.

Groups	Follow up echo wall motion score		t-test	
	Mean	±SD	t	p-value
PCI	1.12	0.13	3.092	<0.001
SK	1.22	0.12		

4.Presence and severity of ischemic mitral regurgitation at the follow up
Table (5): Relation between PCI and SK as regards presence of mitral regurgitation at the follow up echo.

Presence and degree of mitral regurgitation in the follow up	Groups				Total	
	PCI		SK			
	No.	%	No.	%	No.	%
None	24	80.00	5	16.67	29	48.33
Mild	6	20.00	12	40.00	18	30.00
Moderate	0	0.00	11	36.67	11	18.33
Severe	0	0.00	2	6.67	2	3.33
Total	30	100.00	30	100.00	60	100.00
x2	27.448					
p-value	<0.01					

5.Mitral regurgitant severity (jet area) at the follow up echo
In the PCI group there were 6 patients with mitral regurgitation the mean jet area was (1.33±0.63) cm^2, while in the SK group there were 25 patients with mitral regurgitation the mean jet area was(4.45 ±2.17) cm^2 with P value <0.0001

Table (6): Comparison between PCI and SK groups as regards to mitral regurgitant jet area (cm^2) at follow up echo.

Groups	Jet area (cm2)		t-test	
	Mean	±SD	T	p-value
PCI	1.13	0.63	7.563	**<0.0001**
SK	4.45	2.17		

This table shows the difference between groups as regard jet area (cm^2) there was mean (1.33±0.63 & 4.45±2.17) respectively, there was highly statistically significant difference between groups, with p-value <0.0001 HS.
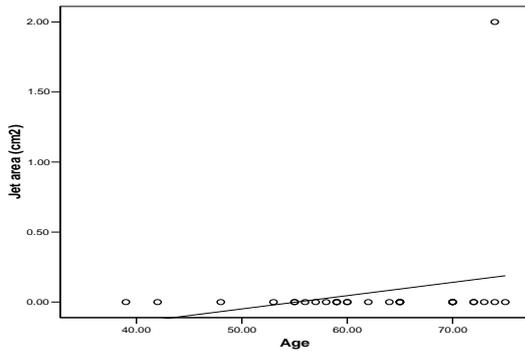
6. Correlation between jet area in patients who had mitral regurgitation in the PCI group and

**Age, Diabetes, Door to balloon time and Pain to hospital admission time.**

There was highly statistically significance between jet area (cm^2) and age, door to balloon time (minutes) and statistical significant pain to door time (minutes), with positive correlation, the rest of parameters are insignificant.

Table (7): Correlation study between Jet area (cm^2) during follow up and the age, diabetes mellitus, door to balloon (min) and pain to door parameters in PCI group Using Pearson Correlation Coefficient test.
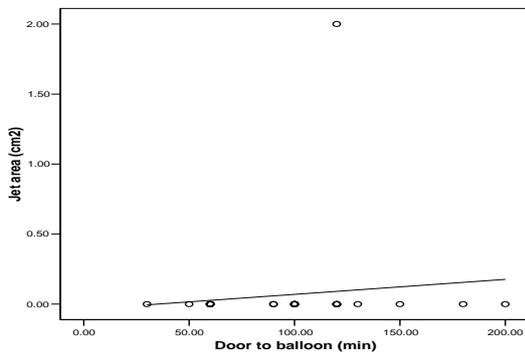
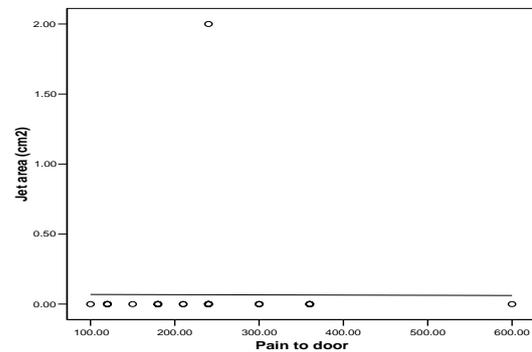|	Jet area (cm2)	
	r	p-value
Age	0.514	**<0.01**
Diabetes mellitus	-0.263	0.160
Door to balloon (min)	0.470	**<0.01**
Pain to hospital	0.377	**0.040**

Fig. (4): Correlation between jet area (in cm^2) at the follow up echo and age in the PCI group
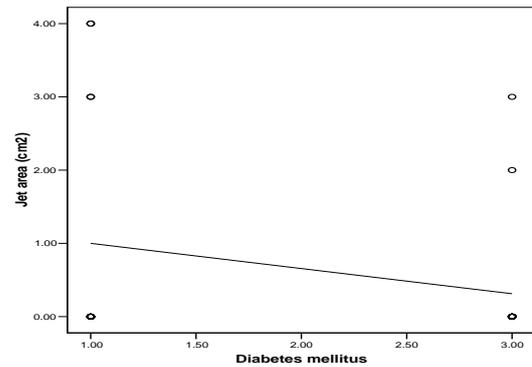
Fig. (5): Correlation between jet area(in cm2) at the follow up echo and diabetes mellitus in the PCI group.

Fig. (6): Correlation between jet area(in cm2) at the follow up echo and door to balloon time(in minutes) in the PCI group.
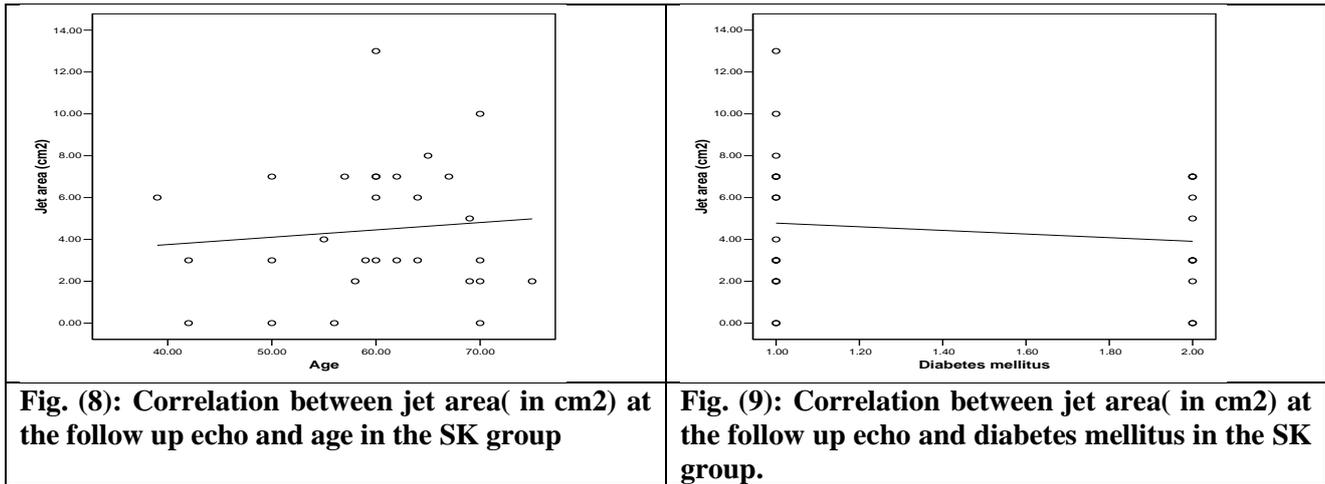

Fig. (7): Correlation between jet area(in cm2) at the follow up echo and pain to door time(in minutes) in the PCI group.

Table (8): Correlation study between Jet area (cm^2) and the age, diabetes mellitus, door to needle and pain to door parameters in SK group Using Pearson Correlation Coefficient test.
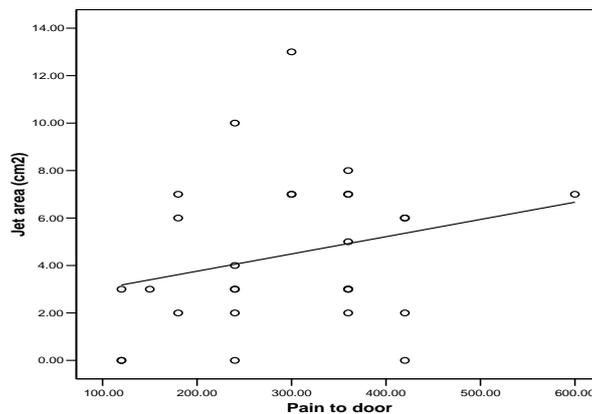
	Jet area (cm2)	
	r	p-value
Age	0.101	0.601
Diabetes mellitus	-0.135	0.484
Door to needle	0.399	**0.032**
Pain to hospital	0.260	0.173

Correlation is significant at the 0.05

Fig. (8): Correlation between jet area(in cm2) at the follow up echo and age in the SK group

Fig. (9): Correlation between jet area(in cm2) at the follow up echo and diabetes mellitus in the SK group.

Fig. (10): Correlation between jet area(in cm2) at the follow up echo and pain to door time(in minutes) in the SK group.

DISCUSSION

It is well known that MR alone is an independent factor of poor prognosis (26) and when associated with a myocardial infarction prognosis is even worse (27)**.**Chronic IMR following MI also entails a negative impact on long-term survival (13)

In a recent registry by **López-Pérez et al., (2014)**, they found that moderate or severe MR detected early with echocardiography was independently associated with a worse long-term prognosis in patients with STEMI treated with primary PCI.(28)

So, it appears an important issue to search for treatments or therapeutic issues that may prevent or minimize the incidence and/or severity of IMR in acute STEMI aiming to improve their prognosis. Generally, it was proved that primary PCI is more successful in preserving myocardium and decreasing complications of STEMI than thrombolysis (29).

Primary PCI of the infarct artery is preferred to fibrinolytic therapy when time-to-treatment delays are short and the patient presents to a high-volume, well-equipped center with experienced interventional cardiologists and skilled support staff (24)

Compared with fibrinolytic therapy, primary PCI produces higher rates of infarct artery patency, TIMI 3 flow, and access site bleeding and lower rates of recurrent ischemia, reinfarction, emergency repeat revascularization procedures, intracranial hemorrhage (ICH), and death (30).

In our study, initial echocardiographic results showed that patients in the thrombolysis group had a higher MR jet area by color-Doppler flow mapping.. These differences were still noteable in the follow-up echocardiography after one month. According to the follow-up echocardiographic results, there were significantly more patients with moderate or severe mitral regurgitation and significantly fewer patients without mitral regurgitation in the streptokinase group than in the PCI group.

Our results were in concordance with the study done by.**Chua et al.,(2010)** They found that PCI for first acute STEMI was associated with a decreased incidence of IMR compared to a medically managed group. Early, rapid coronary revascularization with PCI was strongly associated with a significant risk reduction for having moderate or severe IMR by 14.6%.(31)

Also, similar results were found by **Poh et al., (2012)**, as they found that both thrombolytic therapy and primary PCI were associated with decreased incidences of IMR following inferoposterior STEMI, with less incidnece of moderate and severe mitral regurgitation in patients treated by primary PCI than those treated with thtombolysis, and in those treated with thrombolysis early in the frist hour after the onset of symptoms than in those treated with thrombolysis late after the first hour has been passed.(32)

Resic et al., (2013) have compared the reperfusion effect of streptokinase versus alteplase in STEMI patients by analyzing the echocardiographic parameters including the presence and the severity of IMR. They have found that patients in the alteplase group had significantly less incidence of moderate or severe MR than those in the streptokinase group. When they took into consideration time from occurrence of chest pain to admission at clinic, the best outcomes were shown in patients who were treated with alteplase within 1.5 hour from occurrence of chest pain.(33)

In our study, and in the PCI group, we have found significant positive correlations between the jet area of mitral regurgitation by color-Doppler flow mapping and both age (r = 0.514, p < 0.01), and door to balloon time (r = 0.47, p < 0.01), and pain to hospital time (r = 0.377, p = 0.04).

While in the streptokinase group, we have found only significant positive correlations between the jet area of mitral regurgitation by color-Doppler flow mapping and door to needle time (r = 0.399, p = 0.032). (

Chua et al., (2010) have found that factors associated with a significantly higher risk of positive IMR included: advanced age, Killip class ≥ 3, increased left atrial diameter, increased LV end diastolic volume, and isolated inferior MI. When MI type (isolated inferior over isolated anterior) was used as a covariate, patients with an isolated inferior MI were 2.37 times more likely to have moderate or severe IMR than those with an anterior MI. Patients with PCI had a significantly lower incidence of positive IMR than non-PCI patients in both isolated pure anterior and inferior MI (31)

Constituents to the development of heart failure after AMI included the loss of functioning myocytes, development of myocardial fibrosis, and subsequent LV remodeling. The ensuing chamber dilatation and neurohormonal activation lead to progressive LV dysfunction **(9)**. The presence of IMR further inflicts the hemodynamic load during a period of active LV remodeling **(13)**.

Aronson et al., (2006) reported that there is a graded independent association between the severity of

ischemic MR and the development of heart failure after MI(9).

Ishikawa et al., (2009) reported ischemic MR to be a common cause of congestive heart failure, caused by the process of MI remodeling(34).

As early as 1989, coronary angioplasty was found to be useful for treating IMR in 5 patients and was associated with a favourable long-term outcome (35). Emergent PCI has been shown to improve the outcome in IMR in follow-up studies (2,28)

The physiopathological mechanism of ischemic MR is still under discussion, although the current preference is to explain it by a myocardial abnormality rather than by a valvular abnormality in itself, (36), which fits with the fact that STEMI patients with moderate or severe mitral regurgitation were older and had more diseased vessels, greater anterior descending artery disease, decreased LVEF, and more wall motion abnormalities (37).The benefits in mortality and cardiovascular events achieved by early invasive strategy over conservative strategy in NSTEMI patients are partly because of the reduction of incidence and severity of IMR occurring with early invasive strategy (36).Our study has shown that STEMI patients who were treated with primary PCI have less incidence and severity of IMR than those treated with streptokinase, which was found to be associated with better prognosis **(Grigioni et al., 2001; Bursi et al., 2006; Levine and Schwammenthal, 2006; López-Pérez et al., 2014).**So, finally we conclude that STEMI patients treated with primary PCI have less WMSI, have better EF, and have less incidence and severity of MR.(26,28,36)

CONCLUSION

We conclude that primary PCI may decrease the incidence and the severity of chronic ischemic mitral incompetence if it is done as soon as possible and in a large volume PCI center.

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