CULPRIT VERSUS CULPRIT AND NON- CULPRIT PRIMARY CORONARY REVASCULARIZATION

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ABSTRACT

Background: Primary percuteneous coronary intervention (PPCI) is the prefered strategy for acute ST segment elevation myocardial inferction (STEMI). CAD is a diffuse process and patients presenting with a coronary syndrome in 20- 40% of cases have multiple significant coronary lesions, which confer a substantially increased risk of cardiovascular morbidity and mortality. Recent studies suggest that acute coronary syndromes, including AMI, may result from a systemic inflammatory process, causing multiple unstable lesions. Thus, a strategy of multivessel PCI in the peri-infarct period may be important in improving the outcomes of primary angioplasty. Such an attempt of complete revascularization may prevent recurrent ischemia from 'non-infarct-related' lesions, obviating the need for repeat angiography and intervention, and also possibly improves the late outcome by reducing the ischemic burden following myocardial damage. Contemporary guidelines recommend dilating only the infarcted related artery (IRA) during the urgent procedure, leaving the other stenosed vessels untreated "culprit-only revascularisation" (COR) or to dilate during a second elective procedure (staged revascularisation). Simultaneous treatment of IRA and non-IRA is recommended only in patients with cardiogenic shock. However, these guidelines are based on the results of earlier studies. With advancing technology and newer antiplatelet drugs, outcomes have improved even in patients undergoing multivessel and higher-risk elective procedures. Therefore, the optimal management of patients with multivessel disease in this setting still unclear.

Aim of the Work: to compare between primary PCI for culprit lesion only and that for both culprit and non culprit lesion in ST segment elevation MI patients with multi-vessel disease.

Patients and methods: this study concluded 50 patients with acute ST segment elevation myocardial infarction (STEMI) eligible for primary PCI and the patients were devided into two groups: 1st group: 25 patients were managed by primary percutaneous coronary intervention for infarct related artery only "culprit only revascularization" (COR). 2nd group: 25 patients were managed by primary percutaneous coronary intervention for infarct related artery and non infart related artery "total revascularization" (TR). All patients had done transthorthic echocardiography during admission and after six months to assess ejection fraction.

Results: During follow up period 52% of patients in COR group had recurrent angina and chest pain while in TR group 36% of the patients had recurrent angina and chest pain with p-value 0.039. In culprit only revascularization group contrast induced nephropathy occur in 12% of patients while in total revascularization group 36% had contrast induced nephropathy with p-value 0.047. In culprit only revascularization group the mean LVEF was 50.40± 3.18 while in total revascularization group the mean left ventricular ejection fraction (LVEF) was 51.36±4.37 with p-value 0.155.

Conclusios: Total revascularization can be done in primary PCI in selected cases (simple lesion, low thrombus burden), which is safe and less expensive than culprit only revasvularization by reducing the possibelity of further unplaned procedures.

Key words: Acute myocardial inferction, Multivessel diseases, primary PCI, Multivessel angioplasty.

INTRODUCTION

Coronary artery disease (CAD) is a major cause of mortality and morbidity in developed countries. Before developing the technique of PCI coronary artery bypass graft (CABG) had been the only standard revascularization procedure .Fortunately, there is an alternative treatment for CAD, the PCI which is effectives, safe less disabling and less expensive revascularization procedure compared with CABG.[1]

Early restoration of normal coronary perfusion after myocardial infarction limits infract size, preserve left ventricular function and reduce mortality.

Although primary percutaneous coronary intervention (PPCI) is the most effective method of reperfusion for acute MI, Significant LV contractile dysfunction is still evident months after the index event in significant number of patient,[2,3] while convalescent LV function is the strongest determinant of late survival after MI, the predictor of myocardial recovery in patient who are treated by contemporary PCI techniques have been incompletely characterized.[4,5]

Primary percutanous coronary intervention in acute myocardial infarction result in greater patency of infarct related artery and lower rates of death reinfarction and stroke when compared with fibrinolysis done.

Clinical evidence demonstrates that around 40-65% of patients with St-segment elevation myocardial infarction (STEMI) have angiographic documented multi vessel disease for these patients early revascularization of the culprit lesion by primary percutanous coronary intervention (PCI) is

recommended according to recent guidelines. But strategy for treatment of non culprit lesion in this setting remain unclear.[6]

It seem reasonable to investigate an alternative strategy based on rapid relief of all significant lesions when dealing with multi vessel disease patient as an effort to promote collateral circulation & further limit the infracted size.

AIM OF THE WORK

To compare between primary PCI for culprit lesion only and that for both culprit and non culprit lesion in ST segment elevation MI patients with multi-vessel disease.

PATIENTS AND METHODS

This study included 50 patients presented to cardiology department Zagazig Unviersity and national heart institute with acute ST segment elevation myocardial infarction (STEMI) eligible for primary PCI.

Acute ST segment elevation myocardial infarction is detected by rise and /or fall in cardiac biomarkers (preferred troponin) with at least one value above 99th percentile of the upper reference limit with at least one of the following:

a) Symptoms of ischemia.

b) ECG changes of new ischemia (ST elevation or LBBB).

c) Development of pathological Q waves.

d) Imaging evidence of new loss of viable myocardium.

Criteria of AMI Adapted from (Thygesen et al., 2007)[7].

The patients were divided into two groups

- **1st group:** 25 patients were managed by primary percutaneous coronary intervention for infarct related artery only (culprit revascularization)**.**
- **2nd group:** 25 patients were managed by primary percutaneous coronary intervention for infarct related artery and non infart related artery (total revascularization).

Inclusion criteria:

All our patients:

A) Present with Acute ST-Segment elevation myocardial infarction (STEMI).

B) Have multi vessel coronary artery disease on angiography suitable for percutaneous coronary intervention.

Multi vessel disease

Defined as the presence of at least one lesion > 70% in major epicardial vessel, or one of its branches other than the infarct related artery (IRA).

Exclusion criteria:

1- Any contraindication for antiplatelet therapy.

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. Echo Cardiography

Transthorthic echocardiography was done during admission and after Six months to assess ejection fraction

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

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 (culprit and total re-vascularization) and associations between risk factors 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 (X2) test of significance was used in order to compare proportions between two qualitative parameters.
- 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.

RESULTS

A. Demographic data and risk factors

Table (1): Comparison between both studied groups as regard demographic data and comorbidities.

	Groups					
	Group I		Group II			
	No.	%	No.	%	t*/x^2	p-value
Age (years)						
Mean(±SD)	54.72 (±10.76)		54.60 (±12.08)		0.037*	0.971
Sex						
Male	19	76.00	19	76.00		
Female	6	24.00	6	24.00	0.000	1.000
DM						
Yes	15	60.00	18	72.00		
No	10	40.00	7	28.00	0.357	0.550
HTN						
Yes	14	56.00	21	84.00		
No	11	44.00	4	16.00	4.667	0.031 (S)
Smoking						
Yes	15	60.00	17	68.00		
No	10	40.00	8	32.00	0.347	0.556
Dyslipedemia						
Yes	17	68.00	19	76.00		
No	8	32.00	6	24.00	0.099	0.752
Post menopause						
Yes	6	100.00	5	83.33	1.091	0.296
No	0	0.00	1	16.67		
Family history						
Yes	16	64.00	17	68.00		
No	9	36.00	8	32.00	0.183	0.862
Prior CAD						
Yes	16	64.00	15	60.00		
No	9	36.00	10	40.00	0.162	0.862
Prior PCI						
Yes	1	4.00	0	0.00		
No	24	96.00	25	100.00	1.020	0.312
Prior CABG						
No	25	100	25	100	--	--

*** independent sample t-test**

This table shows that there was no statistically significant difference between both studied groups as regard age, sex, dibaites, smoking, post menopose, family history, dyslipidemia, prior CAD, prior PCI, prior CABG and there was statistically significant increase in hypertension in group (II) as compared to group (I) with p-value (0.031).

B. Clinical and echocardiographic data and PCI procedures.

1. Site of myocardial infarction according to ECG findings.

In group (I) (36%) of the patients had inferior MI and (64%) had anterior MI while in group (II) (56%) of the patients had inferior MI and (44%) had anterior MI.

2. Time from onset of symptoms to hospital admission

In group (I) the mean time was 6.84±3.09 and group (II) the mean time was (5.92±2.78).

3. Time from door to balloon

In group (I) the mean time from door to ballon was (64.40±30.83min.) while in group (II) mean time of door to ballon was (78.80±44.47min.).

4. In hospital complications

In group (I) recurrent chest pain and angina occur in 13 patients (52%), Arrhythmia, occuar in 3 patients (12%), minor bleeding occur in 6 patients (24%) contrast

induced nephropathy (CIN) occur in 3 patients (12%) and the following MACE (major bleeding, stent thrombosis, cardiogenic shock strock, reinfraction, further revascularization were no't observed in this patients, while in group (II) recurrent chest pain and angina occur in 5 patients (20%), Arrhythmia, occuar in 3 patients (12%), minor bleeding occur in 3 patients (12%), CIN occur in 9 patients (36%), stent thrombosis, occur in 2 patients (8%) and further revascularization occur 2 patients (8%) and the following MACE (major bleeding, , cardiogenic shock, strock) were not observed in this patients, there was statistically significant increase in CIN in group II as compared to group I ($p<0.05$) and show the statistically significant increase in recurrent angina in group I ascompared to group II ($p= 0.039$).

Table (2): Comparison between both studied groups as regard in hospital complications

Complications		Groups				Total		Chi-square	
		Group I		Group II					
		No.	%	No.	%	No.	%	x2	p-value
Stroke	No	25	100	25	100	50	100	0	1.000
Further revascularization	Yes	0	0.00	2	8.00	2	4.00	2.083	0.149
	No	25	100.00	23	92.00	48	96.00		
Contrast induced nephropathy (CIN)	Yes	3	12.00	9	36.00	12	24	3.947	**0.047 (S)**
	No	22	88.00	16	64.00	38	76		
Minor bleeding	Yes	6	24.00	3	12.00	9	18	1.220	0.269
	No	19	76.00	22	88.00	41	82		
Major bleeding	No	25	100	25	100	50	100	0	1.000
Arrhythmia	Yes	3	12.00	3	12.00	6	12	0	1.000
	No	22	88.00	22	88.00	44	88		
Recurrent angina	Yes	13	52.00	5	20.00	18	36	4.253	**0.039 (S)**
	No	12	48.00	20	80.00	32	64		
Cardio genic shock	No	25	100.000	25	100.000	50	100	0	1.000
Stent thromosis	Yes	0	0.00	2	8.00	2	4.00	2.083	0.149
	No	25	100.00	23	92.00	48	96.00		
Re infarct	Yes	0	0.00	2	8.00	1	2	1.020	0.312
	No	25	100.00	23	92.00	49	98		
Nothing	Yes	11	44.00	15	60.00	26	52	1.282	0.258
	No	14	56.00	10	40.00	24	48		
Renal failure	No	25	100.00	25	100.00	50	100.0	0	1.000

This table shows that there was statistically significant increase in CIN in group II as compared to group I ($p<0.05$) and show the statistically significant increase in recurrent angina in group I ascompared to group II ($p= 0.039$).

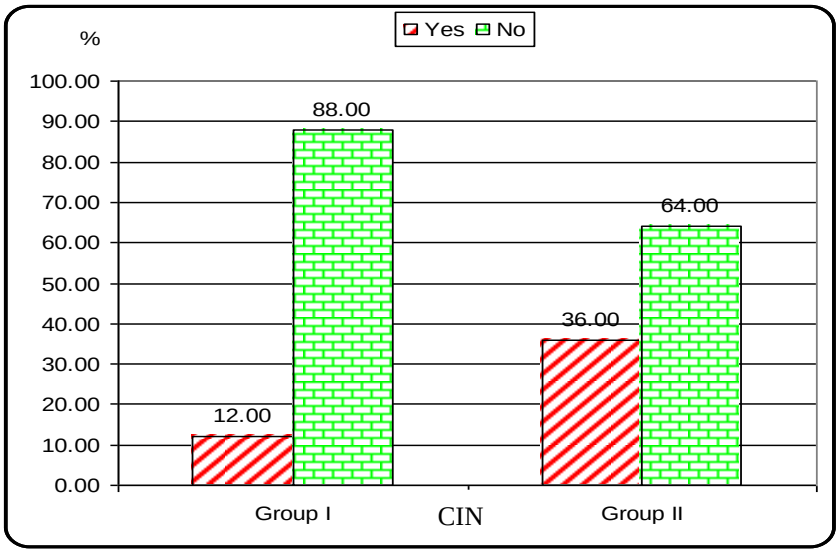

Fig. (1): Comparison between both studied groups as regard CIN.

This Fig. shows that there was statistically significant increase in CIN in group II as compared to group I ($p<0.05$)

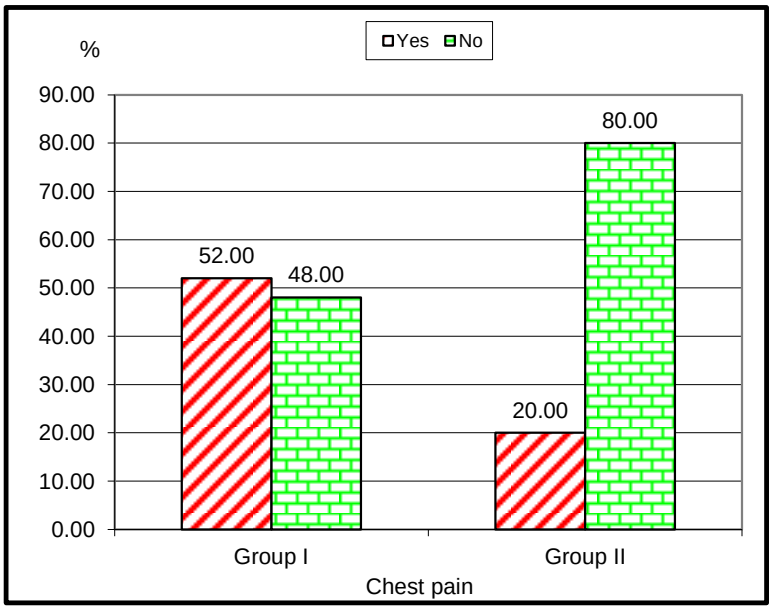

Fig. (2): Comparison between both studied groups as regard chest pain.

This fig. shows that there was statistically significant increase in recurrent angina in group I ascompared to group II ($p= 0.039$).

5. Left ventricular ejection fraction (LVEF) before and 6 months after PPCI.

In group (I) the mean EF before primary PCI was 38.88± 3.78 and in group (II) the mean EF was (39.04±5.07), while in group (I) the mean EF 6 months after primary PCI was (50.04±3.18) and in group (II) the mean EF was (51.96±4.37).

6. PCI time

In group (I) the mean PCI time was (40.80±8.38min.) and in group (II) the mean PCI time was(50.80±11.15min), there was highly statistically significant decrease in PCI time in group I as compaired to group II ($P<0.001$).

Table (3): Comparison between both studied groups as regard PCI time.

	PCI time (minute)			t-test	
Groups	**Mean**	**±SD**	**Mean Difference**	**t**	**p-value**
Group I	40.80	8.38			
Group II	50.80	11.15	-10.00	-3.585	**<0.001 HS**

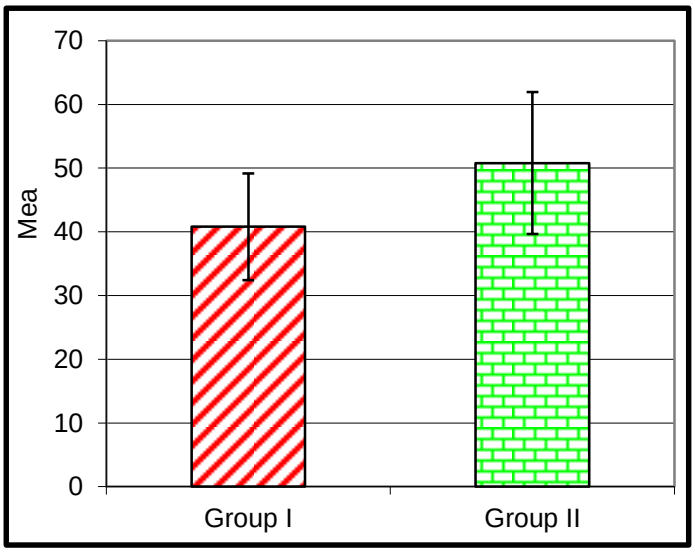

Fig. (3): Comparison between both studied groups as regard PCI time.

This table and fig. shows that there was highly statistically significant decrease in PCI time in group I as compaired to group II (P<0.001).

7. PCI contrast

In group (I) the mean PCI contrast (mL) was (166±68.8) and in group (II) the mean PCI contrast (mL) (266± 55.38), there was higly statistically significant decrease in PCI contrast used in group I as compaired to group II (P<0.001).

Table (4): Comparison between both studied groups as regard PCI contrast (mL).

	PCI contrast (mL)			t-test	
Groups	**Mean**	**±SD**	**Mean Difference**	**t**	**p-value**
Group I	166.00	68.80			
Group II	266.00	55.38	-100.00	-5.661	**<0.001 HS**

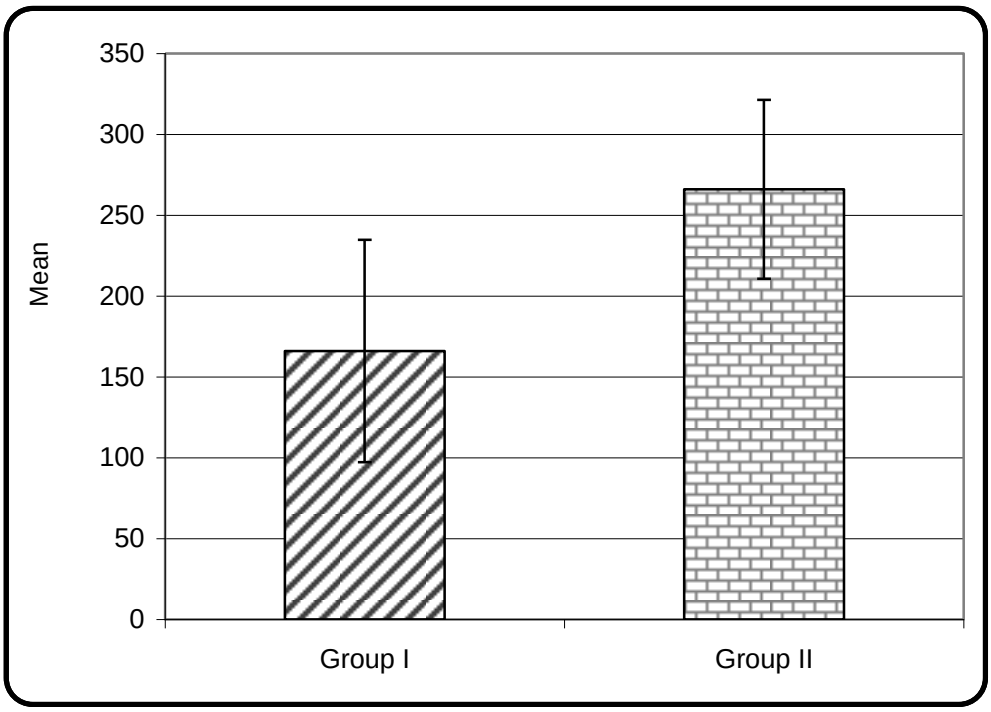

Fig. (4): Comparison between both studied groups as regard PCI contrast (mL).

This table and fig. shows that there was higly statistically significant decrease in PCI contrast used in group I as compaired to group II (P<0.001).

8. PTCA using ballon dilatation

In group (I) (44%) of the patients had done ballon dilatation while in group II (68%) of the patient had done ballon dilatation.

DISCUSSION

PCI is currently the treatment of choice in patients with STEMI. CAD is a diffuse process and patients presenting with a coronary syndrome in 20-40% of cases have multiple significant coronary lesions, which confer a substantially increased risk of cardiovascular morbidity and mortality.[6]

Recent studies, suggest that acute coronary syndromes, including AMI, may result from a systemic inflammatory process, causing multiple unstable lesions. Thus, a strategy of multivessel PCI in the peri-infarct period may be important in improving the outcomes of primary angioplasty.[8]

Such an attempt of complete revascularization may prevent recurrent ischemia from 'non-infarct-related' lesions, obviating the need for repeat angiography and intervention, and also possibly improves the late outcome by reducing the ischemic burden following myocardial damage.[9] Contemporary guidelines recommend dilating only the IRA during the urgent procedure, leaving the other stenosed vessels untreated (culprit-only revascularisation) or to dilate during a second elective procedure (staged revascularisation). Simultaneous treatment of IRA and non-IRA is recommended only in patients with cardiogenic shock.[10] However, these guidelines are based on the results of earlier studies. With advancing technology and newer antiplatelet drugs, outcomes have improved even in patients undergoing multivessel and higher-risk elective procedures.[11] Yet, few reports have described outcomes of multivessel compared with IRA-only revascularisation in patients undergoing urgent mechanical reperfusion for STEMI.[12] Therefore, the optimal management of patients with multivessel disease in this setting still unclear.

The aim of this study was to compare between primary PCI in patients with STEMI and multivessel CAD: culprit only revascularization (group I) and simultaneous treatment of IRA and non IRA (total revascularization) (group II).

The risk factors of patients in our study were higher than the risk factors of patients in other studies as ***Toma et al.***[6] in which COR group had 20% diabetes mellitus, 55% had hypertension. While in TR group 19% had diabetes mellitus, 54% had hypertension. So as regarding comorbidities the risk of patients in our study was higher than other trials and this may have affected the out come.

We found that there was statistically significant increase in hypertension in total revascularization group (p-value 0.031) which may be a predesposing factor to increase contrast induced nephrotpathy in total revascularization group.

There was no staitstically significant difference between both studied groups as regard time from onset of symptoms to admission where the time was 6.84±3.09 hours in COR group, while in TR group was5.92±2.78 hours.

This was discordant with ***Di Mario et al.***[13] in which time from onset of symptoms till hospital arrival was 167±180 min in COR and 122±97 min in TR group,This difference can be explained by delayed diagnosis, delayed contact with the operator and lack of facilities.

There is increased incidence of inferior MI in TR group than COR group as inferior wall MI represent 56% in TR group while 36% in COR group, however this did not reach statistical significance. This is discordant with other studies as ***Rigattieri et al.***[14] in which TR group that included 46patients anterior wall MI represent 56%. While COR group that included 64 patients anterior wall MI represents 39%, however this was concordant with ***Varani et al.***[15] that included 346 patients in COR group in which anterior wall MI represents 49% while in TR group that included 399 anterior wall MI represents 42%.

In COR group culprit vessel is LAD in 64%, RCA in 28% and LCX in 8 % while in TR group culprit vessel is LAD 44%, RCA in 48% and LCX in 8 %.**Other studies** as ***Varani et al.***[15] COR group that included 346 patients, LAD represent 52%, RCA 37%, LCX 11%, while TR group that included 399 patients LAD represent 40%, RCA 39% and LCX 18%.

The number of non infarct related artery was single vessel in 68%, two vessel in 32% of both group, this was disconcordant with other studies as ***Chen et al.***[16] in which non IRA were single vessel in 52 % of COR group and 42% of TR group while two vessel disease occurred in 48 % of COR group and in 58% of TR group.

There was statistically significant diference between the two group as regard mean PCI time/ min as the mean PCI time/min in group II was 50.8+11.5 versus 40.8+8.3 in group I (p value <0.001). Also there was statistically significant diference between the two group as regard the mean PCI contrast/ml as the mean PCI contrast in group II was 266+55.38 ml versus 166+68.8 ml in group I .This was concordant with other studies As ***Di mario et al.***[13] in which in TR group the mean PCI time/min was 69+38 min and mean PCI contrast was 341+163 ml while in COR group the mean PCI time/min was 53+24 min and mean PCI contrast was 242+106 ml.

As regard stent thrombosis it was occurred in 2 cases in TR group while it didn't occur in COR group and this didn't reach a statistically significant

difference, while there was increased incidence of recurrent chest pain in COR group (recurrent chest pain occurred in 52% of COR group versus 20% of TR group and this difference was statistically significant (P value =0.039),and this decrease in recurrent angina and chest pain in TR group improve the quality of life and reduce the need for further revascularization.

There was statistically significant increased in contrast induced nephropathy in TR group (CIN occurred in 36% of TR group versus 12% of COR group), this is because of using large amount of contrast medium which mostly was ionic contrast. This was concordant with ***Marenzi et al.***[17] that reported a higher rate of CIN (19%) in 208 patients with STEMI undergoing total revascularization during PPCI.

Contrast induced nephropathy had occurred more in patients that had done PCI to more than one vessel other than the culprit vessel than in patients which had done PCI to only one vessel other than the culprit vessel ,and this may be explained by the usage of larger amount of contrast medium which mostly was ionic contrast. Also contrast indused nephropathy had occurred in patients that had more risk factors like diabetis and hypertension ,and in patients that had more complex lesions in the non infarcted related artries which prolong the duration of the procedure and increase the amount of dye used during the procedure,and in our study no one of the patients who had contrast indused nephropathy needs dialysis on further follow up, the incidence of contrast indused nephropathy can be redused by adequete hydration of the patient,administration of low osmolar contrast media,limitation of contrast dose and a combination prophylaxis of N-acetyle cystiene and NaHco3 adminestration according to the ejection fraction and killip class.

These results were concordant with the studies comparing both groups as:

Ijsselmuiden et al.[11] who found that multivessel approach had better outcome by decreasing the need for further revascularization.

Also ***Kong et al.***[18] found that multivessel angioplasty during acute myocardial infarction may be safe compared with PCI to infarcted related artery. ***Qarawani et al.***[19] observed that patients underwent total revascularization during PPCI had lower incidence of further revascularization. Also ***Politi et al.***[8] suggested that the multivessel approach is safe and possibly less expensive than an incomplete approach by reducing the probability of further unplanned procedures and without affecting the length of hospitalization.

Also ***Chen et al.***[16] found that short term, long term survival and cardiac events rates in patients undergoing multivessel PCI are similar to those in patients undergoing single vessel intervention (IRA).

However this was discordant with other trials, as ***Corpus et al.***[20] revealed that 30 days follow up of patients underwent TR had more fatal re-infarction and more MACEs than patients undergoing COR strategies. Also ***Moreno et al.***[21] found that patients with MVD undergoing TR during primary angioplasty for STEMI, had higher rate of in hospital &30 days mortality than those undergoing COR strategy.

Also ***Hannan et al.***[22] found that patients with multivessel disease STEMI undergoing multivessel primary PCI at the time of the index procedure had mortality rates that were higher than rates for patients with culprit vessel PCI alone.

As regard the previous data we found that old trials suggest that COR strategy is the best, while many new trials suggest that TR strategy can be done safely with less need to further revascularization, this may be explained by improvement in PCI techniques, aspiration devices, medication as glycoprotein IIb/IIIa inhibitors and newer generation of stents.

CONCLUSIOS

Total revascularization can be done in primary PCI in selected cases (simple lesion, low thrombus burden), which is safe and less expensive than culprit only revasvularization by reducing the possibelity of further unplaned procedures.

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