

Comparison Between Primary Percutaneous Coronary Intervention To The Culprit Only Versus Culprit And Non-Culprit Vessels In ST Elevation Myocardial Infarction

Mahmoud Abdelghafar¹, Waleed Yousof¹, Ahmed El – Tayeb¹

¹Lecturer of Cardiology Faculty of MedicineAl-Azhar University, Cardiology Departments, Assiut, Egypt.

Abstract:

Background and aim: Primary percutaneous coronary intervention (p-PCI) has become the treatment of choice for patients presenting with ST-segment elevation myocardial infarction (STEMI) when it can be performed expeditiously by an experienced team. This strategy has been found to be superior to thrombolytic therapy in improving morbidity and mortality. The presence of multi-vessel disease (MVD) has been found to be associated with worse prognosis in patients with STEMI.Treatment strategies vary widely from an aggressive approach which treats all significant lesions in the acute phase of p-PCI to a conservative approach with p-PCI of only the infarct-related artery (IRA) and subsequent medical therapy unless recurrent ischemia occurs. **Aim**This study aimed to compare the safety and efficacy of PCI for culprit vessel only (culprit PCI) and multi-vessel PCI (MVD-PCI) during p-PCI procedure in patients with STEMI and MVD.

Patients and methods: this study included 100 patients with acute STEMI who were amenable to p-PCI were admitted to CCU department at AI Hussin university Hospital and EI Marwa Cardiac Center. 100 Patients were divided in 2 groups; <u>group A</u> 50 Patients: complete coronary revascularisation during primary PCI. <u>Group B</u> 50 Patients: culprit-only revascularisation during primary PCI. The following done for all patients: An I-written informed consent was obtained from every patient before the procedure II-Detailed history taking: III. Complete clinical and general examination. IV. Standard ECG: using Fukuda 3channels (Japan). V. Routine Laboratory investigations: VI. Echocardiography: Using Philips IE33 USA. II. PCI procedure.

Results: LV EF improved significantly after 6 month in group A EF increased from 50.3 ± 4.1 to 55.4 ± 6.2 (P value 0.003). While in group B, it increase non-significant from 49.9 ± 3.2 to 50.7 ± 4.2 (P value 0.50). The improvement of EF was more observed in patients with anterior MI Incidence of MACCE in both groups was comparable during hospital stay, one month and 6month follow up .Three cases of MACE in group B while no MACE in group A. (P

value 0.11) Safety of aggressive strategy for complete revascularization is comparable for culprit –only strategy as regard risk. CIN was observed in five patients of group A and three patients of group B (P value 0.52). Vascular complication .no cases in group B while only one case in group B P value 0.34. Door to balloon time less than 90m is associated with better EF in comparison to more than 90m.

Conclusionsa.Complete coronary revascularization during primary PCI in patients with multi-vessel disease is safe. b.Complete coronary revascularization during primary PCI is associated with better improvement of EF at 6 months espacially in patients with anterior wall myocardial infarction in comparison to culprit-only revascularization. c.Door to baloon time less than 90 minutes is associated with better EF in comparison to more than 90 minutes. d. No difference in incidence of MACE between complete and culprit-only revascularizations.

Key words: Primary percutaneous coronary intervention, ST-segment elevation myocardial infarction, Culprit and non-Culprit lesions, Mul-tivesseles diseases

Introduction: Coronary reperfusion with pPCI or fibrinolytic therapy improves outcomes in patients with acute STEMI, if performed in a timely fashion; pPCI is the reperfusion therapy of choice because randomized trials have shown superior outcomes compared to fibrinolytic therapy [1]. The goal is restoration of flow within 90 min of presentation to a PCI-equipped center. [2] An important piece of information gained at the time of angiography and p-PCI is information not only about the culprit lesion but also about the extent and severity of the underlying CAD. In patients presenting with STEMI, multi-vessel CAD is found to be present from 40 to 65% of patients depending upon the baseline characteristics (especially age) of the specific population studied [3] however, in one study only 10% of STEMI patients initially treated by p-PCI had a clinical indication for non-culprit PCI during the subsequent follow-up of up to 3 years. [4]. Identification of optimal strategies for treating these patients is the subject of considerable interest and controversy. Treatment strategies vary widely from an aggressive approach which treats all significant lesions in the acute phase of p-PCI to a conservative approach with p-PCI of only the infarct-related artery (IRA) and subsequent medical therapy unless recurrent ischemia occurs. Between these two extremes are other alternatives; mainly that of staged procedures with the IRA treated acutely and other lesions treated later during the hospital stay or within the first month following discharge. There is no randomized data to definitely answer the issues about the specific scientific merits of any of these approaches. However, there are increasing data from observational series. Each approach has advantages and disadvantages [5]. Advances in device technology, pharmacological therapy and non-ionic contrast media made an aggressive approach more feasible, with simultaneous or staged treatment of all suitable, angiographically significant lesions. This could lead to a reduced incidence of prolonged in

hospital stay and adverse events at follow-up and could be cost-effective, reducing the need for further hospitalization and interventions. **[6]**. On the other side, multi-vessel PCI in the early phase could be associated with increased risk—because of higher amount of contrast medium, ischemia in non-infarcted myocardial regions, longer procedural time and with overtreatment of clinically silent lesions relying only on their angiographic severity **[7]**

<u>Aim of the study</u>: This study aimed to compare the safety and efficacy of PCI for culprit vessel only (culprit PCI) and multi-vessel PCI (MVD-PCI) during p-PCI procedure in patients with STEMI and MVD.

<u>Patients and methods</u>: this study included 100 patients with acute STEMI who were amenable to p-PCI were admitted to CCU department at AI Hussin university Hospital and El Marwa Cardiac Center . 100 Patients were divided in 2 groups;

<u>Group A</u>50 Patients : complete coronary revascularisation during primary PCI. <u>**Group B**</u> 50 Patients : culprit-only revascularisation during primary PCI.

Inclusion criteria: 1-Acute STEMI defined as a. ongoing chest pain, b. \geq 1mm ST elevation in \geq 2 contiguous leads or new left bundle branch block, c. Presentation \leq 12 hours from symptom onset. 2-Multivessel CAD is defined as \geq 70% diameter stenosis of \geq 2 epicardial coronary arteries or their major branches.

Exclusion Criteria a. Patients with cardiogenic shock, b. Single vessel disease, c. Left main disease (≥50% diameter stenosis), d. Previous bypass surgery (CABG), e. severe valvular heart disease, f. In-stent restenosis, g. Any contraindication to primary angioplasty like patients with mechanical complication. The following done for all patients :An written informed consent was obtained from every patient before the following: 1-Detailed history: 1-Personal history, 2-Time of admission, 3-Present history: stressing on chest pain & dyspnea; time of onset, frequency, duration, severity, causative & relieving factors, drugs taken and important associated symptoms, 4-Past history: History of hypertension, DM, hyper-lipidemia, 5-Tobacco history (current, former or never), 6-Drug history, and 7-Family history of CAD. II. Clinical evaluation: All patients were submitted to full clinical evaluation on admission (level of consciousness, pulse, and blood pressure and Killip class). III. Timing variable: Were computed as follows: chest pain-to-emergency room (ER) which was defined as the time difference between the time of chest pain onset, as obtained from the history, and the time of presentation to the ER and was given in minutes; door-to-balloon or medical contact-to-balloon time which is defined as the time from arrival to the hospital to first balloon inflation and was also given in minutes. IV. Standard ECG: using Fukuda

3channels (made in Japan) All patients obtained standard 12 leads ECG ,2 right precordial leads[V3r, V4r] and 3 posterior leads [V7, V8, V9] if need within 10 minutes of presentation to hospital, after PCI and whenever indicated during hospital course . All ECGs were viewed for evidence of ischemia, infarction or any abnormalities. V. Laboratory investigations: Viral Marker (Hepatitis C,B & HIV), Random blood sugar, Kidney function tests on admission and 48h after PCI to exclude CIN (BUN and creatinine), Liver function tests (PT, PC, INR,SGOT, SGPT), Cardiac enzyme Troponin and CK-MB, Complete blood count on admission and 24 hours after the procedure. VI. Echocardiography: Using Philips IE33 USA : M-mode, 2-D, Doppler and tissue Doppler transthoracic echocardiography(TTE) were performed in all patients who were examined according to the American society of echo after PCI, one Month and 6 months for: Detection of signs of LV&RV infarction including, Ventricular dilatation, Abnormal ventricular wall motion, Paradoxical motion of the inter-ventricular septum, Mitral or tricuspid regurgitation (MR&TR), Assessment of LV dimensions :Longitudinal dimension, Transverse mid-cavity, Assessment of ventricular wall motion abnormalities including hypokinesis, akinesis&dyskinesis, Assessment of ventricular systolic function, Assessment of ventricular diastolic function VII. PCI procedure:a-Pre- procedural preparation:Informed consent: A detailed discussion with the patient & family outlined indications, benefits, potential complications; possibility to need emergency CABG as well as alternative options then an informed consent was taken. Medications: Aspirin 300 mg PO, in the form of chewable tablets, was given before the procedure. Clopidogrel 75 mg, a loading dose of 600 mg PO was given prior to the procedure. b. PCI procedure: i-Access site: Trans-femoral standard technique was used in all patients ii-Intra-procedural medications: As soon as the arterial sheath is in place, a dose of 10.000 units of heparin is injected, If the procedure continues for more than 1 hour, another 5000 units of heparin was given after 1 hour, Tirofiban was used : Dosage: weight-based bolus of 12 μ g/kg and infusion of 0.1 μ g/ kg/ min, with adjustment in infusion for renal function (if CrCl< 30 mL/min) to bolus of 6 μ g/kg and infusion to 0.05µg/kg/min. iii- Coronary angiography was performed assessing:Culprit lesion as regards: a. Site of the occlusion, b.Severity of the occlusion, c. TIMI flow grade, d. Side branch involvement, e. Presence of thrombus & assessment of thrombus burden. Other lesions, if present, were assessed with same criteria in addition to: Degree of stenosis: The degree of stenosis was estimated from the percent reduction in luminal diameter compared to a non-affected proximal segment of the vessel by visual assessment. Several projections were performed in order to better visualize the coronary arteries and overcome the problem of foreshortening and superimposition of the vessels. 1-PCI: Guiding catheter & guide wire selection: Utilization of 6 Fr. guiding catheters in most of cases and several types of guide-wires used including floppy, intermediate and hydrophilic wires. Although the guiding catheter and guide-wire selection is influenced by criteria related to the vessel anatomy, the lesion morphology and the devices to be used, in real life scenario the selection is based upon operator's experience and preference. 2- After guide wire successfully crossed the culprit lesion, subsequent balloon angioplasty if needed and stent implantation were performed with appropriate-sized devices. DES was selected according to the lesion needed, 3-Criteria used for assessing success: a. Technical success: defined as restoration of TIMI flow grade 2 or 3 & MBG 2 or 3 with a residual stenosis of \leq 20%, b. Procedural success: defined as technical success without in-hospital major adverse cardiac events (MACE) c. MACE: defined as as the composite of death, recurrent MI or ischemia, emergent coronary artery bypass grafting (CABG), or repeat target vessel revascularization (TVR). 5. Angiographic complications assessment: a) Distal Embolization: Migration of a filling defect to cause a new abrupt cut-off or circumscribed filling defect distally in the target vessel or one of its branches. b) No Reflow: TIMI flow grade <1 that cannot be explained by severe dissection or abrupt closure of target lesion. c) Abrupt vessel closure: Obstruction of contrast flow (TIMI 0 or 1) in a dilated segment with previously documented antegrade flow. d) Dissection: A radiolucent defect within the lumen of the vessel. e) Perforation: Extravasation of contrast from the artery. It may be localized or not localized to the pericardial space potentially associated with clinical tamponade.c. Post-PCI management: Access site care a. Detection access site complication and Management A-V fistula, pseudo-aneurysm, major hematoma (hematoma+15% decrease in hematocrite ratio) or the need for surgical repair, b. Monitoring for myocardial ischemia: A 12 lead ECG is obtained after PCI. The patient is monitored in a coronary care unit that has continuous ECG monitoring with routine post-PCI care, d. Bleeding complications : Classified into major and minor bleeding according to the criteria of the Thrombolysis in Myocardial Infarction trials: Major bleeding: Hemoglobin drop of >5 gm/dl with or without an identified site retroprotenial hemorrhage, intracranial hemorrhage or cardiac tamponade.Minor bleeding: Hemoglobin drop of >3 gm/dl with bleeding from a known site, spontaneous gross hematuria, hematemesis, or hemoptysis.

e. Medications after PCI:Aspirin forever 100 mg/d for all patients without allergy.Clopidogrel 150 mg/d for 7days then 75 mg/d for all patients for at least 12 months.UFH or LMWH for all patients during the hospital stay.Beta-blockers in all patients who tolerate these medications and without contraindications.ACE-I or ARBs and Spironolactone when indicated & no contraindications. Statins in all patients without contraindications irrespective of cholesterol levels to achieve LDLc< 70 mg/dl.

VIII. Follow up: Follow-up information was obtained by clinical visits and telephone interviews.

Clinical end points were the occurrence of: 1) Cardiac death (Defined as death caused by acute myocardial infarction, ventricular arrhythmias, or refractory heart failure). 2) Nonfatal myocardial infarction (Defined based on criteria of typical chest pain, elevated cardiac enzyme levels, and typical changes on the electrocardiogram). 3) Need for repeated percutaneous intervention for the target lesion or CABG. 4) Unstable angina requiring hospitalization. 5) Stroke

Statistical analysis: Data were collected and coded prior to analysis using the professional statistical Package for Social Science (SPSS 12). All data were expressed as mean and standard deviation (SD). Frequency tables for all categorical data. Student t-test (unpaired) after checking normality for all continuous data. Mann Whitney test was used when the value of standard deviation was violated. Chi-square test for all categorical data to test for the presence of an association. For small sample size fisher exact test was calculated. A P value < 0.05 was considered significant

Results: 100 patients with acute STEMI were admitted for primary PCI at the CCU department, Al Hussinuniversity&Al Marwa Cardiac Center from October 2015 to July 2017. 100 patients with acute STEMI with MVD were meeting our inclusion and exclusion criteria. The study included 69 males (69%) and 31 females (31%) with a mean age of 56.2 ± 7.1years.

The patients were divided into 2 groups:

<u>Group A: (complete revascularisation (CR):</u> included 50 patients, 40 males (80%) and 10 females (20%) with a mean age of 55.1+9.26.

<u>Group B: (culprit-only revascularisation(COR))</u>: included 50 patients, 29 males (58%) and 21(42%) with a mean age 54.25<u>+</u>9.1. (I) Demographic and clinical data Baseline clinical characteristics were comparable in both groups regarding age, sex and risk factors for CAD (hypertension, diabetes mellitus, smoking, dyslipidemia, family history of IHD) and previous history of IHD. (table 1 & figure 1).

 Tab. (1): Demographic and clinical data of the two groups.

	Group A	Group B	P value
Males	40 (80%)	29 (58%)	0.21

Females	10 (20%)	21(42%)	
Age	55.1 <u>+</u> 9.26	54.25 <u>+</u> 9.1	0.46
Diabetes	30 (60%)	28 (56%)	0.75
Hypertension	28 (56%)	30 (60%)	1
Dyslipidemia	40 (80%)	25(50%)	0.75
Smoking	46(92%)	40 (80%)	0.7
Family history	22(44%)	20 (40%)	0.46
previous history of IHD	10(20%)	12 (24%)	0.3
MAP (mmHg)	89 ± 12	86 ± 11	0.64
HR (ppm)	80 ± 14	84 ± 16	0.41
Site of MI by ECG		I	
Anterior Inferior	36(72%)	23 (46%)	
Lateral	10 (20%)	25 (50%)	0.32
	4(8%)	2 (4%)	

Killip class.				
Class I	37(74%)	43 (86%)		
Class II	7(15%)	6(12%)	0.34	
Class III Class IV			_	
	6(12%)	1 (2%)		
	0 (0%)	0 (0%)		
D to B time(mins)	96 ±7.6	95 ±6.4	0.86	
Hospital stay(days)	2.4 ± 0.76	2.5 ± 1.19	0.75	
	Laboratory data			
Hb1(gm/dL)	13 ± 1.8	14.6 ± 1.3	0.43	
Hb2	12.6 ± 1.6	13.8 ± 1.4	0.82	
CREAT.1 (mg/dl)	$1.0 \pm .4$	1.13 ± .39	0.75	
CREAT.2	1.2 ± .39	1.33 ± .30	0.9	
INR	1.07 ± .16	1.10 ± .15	0.22	
Medications data				

ACEI	44 (89%)	49 (98%)	0.63
BB	44 (89%)	49 (98%)	0.63
Copidogrel	50 (100%)	40 (100%)	
Statins	50 (100%)	50 (100%)	
Inotropes	2(4%)	0 (0%)	0.54
GPIIb/IIIa	50(100%)	50 (100%)	

Tab. (2): Angiographic and PCI data.

	Group A	Group B	P value
Angiographic data			
Infarct related artery			
LAD	36 (72%)	25(50%)	
Lt CX	4(8%)	10 (20%)	0.37
RCA	10 (20%)	15 (30%)	
Diseased vessels			
2 vessels	44 (88%)	45 (90%)	0.13
3 vessels	6 (12%)	5 (10%)	

PCI data			
Total stents	106	50	< .0001
BMS	0	0	
DES	106	50	
Cotrast dose	290 ± 82.5	200 ± 58.9	0.08
Procedural duration	70.2 ± 10.1	42 ± 11.3	< ,0001
Procedural success	50 (100%)	48 (96%)	
Angiographic complications	5(10%)	3(6%)	0.5

LAD=left anterior descending, Lt CX=left circumflex, RCA=right coronary artery, BMS=bare metal stent, DES=drug eluting stent

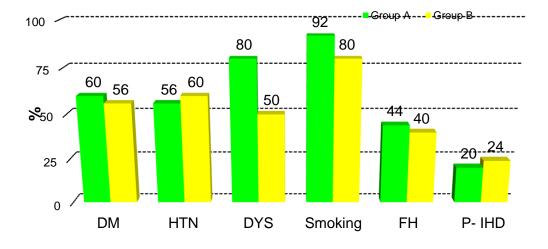


Fig (1): Risk factors in both groups

Admission data: The admission data, including: mean BP, ECG, HR and Killip classification, were analyzed and tabulated for both groups. Mean blood pressure and HR were comparable in both groups. In group A:Killip classification; 37patients (74%) had class I, 7 patients (15%) had class II and 6 patients (12%) had class III. while In group B: Killip classification; 43 patients (86%) had class I, 6 patients (12%) had class II and one patients (2%) had class III. Site of MI; 36 patients (72%) had anterior wall MI, 10 patients (20%) had inferior wall MI and 4 patient (8%) had Lateral MI.while In group B; 23 patients (46%) had anterior wall MI, 25patients (50%) had inferior wall MI while 2 patient (4%) had Lateral MI.

Figure (2): Site of MI as detected by 12 lead ECG in both groups P value = 0.11

(II) Laboratory data: The following laboratory data were analyzed and tabulated for both groups; CKMB & Troponin at admission. Hemoglobin at admission (1) and at 24 hours after PCI (2).Creatinine level at admission (1) and after 48 hours (2).The mean values of hemoglobin in both groups on admission (13 \pm 1.8 versus 14.6 \pm 1.3) and after 24 hours (12.6 \pm 1.6 versus13.8 \pm 1.4) were comparable.Creatinine level on admission (1.0 \pm 0.4 versus 1.13 \pm 0.39) was comparable in both groups. Also after 48 hour post PCI (1.2 \pm 0.39 versus 1.33 \pm 0.30), there was no statistical significant difference. (III)Angiographic data: The results of pre-PCI angio for both groups were analyzed and compared. In group A: The IRA was LAD in 36 patients (72%), RCA in 10 patients (20%), LCx and its branches in 4 patients (8%). two-vessel disease was seen in 44 patients (88%), while three-vessel disease in 6 patients (12%).

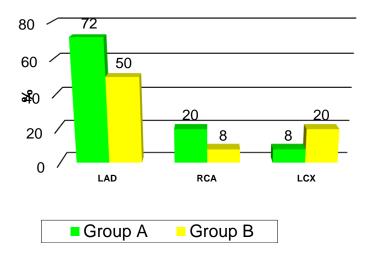
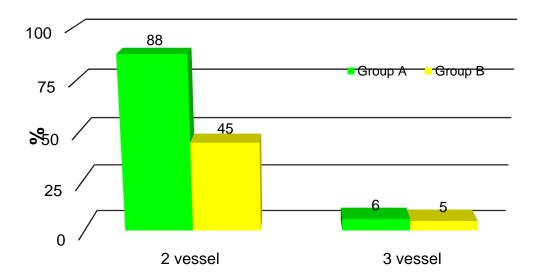


Figure (3): IRA distribution in both groups.

In group B: The IRA was LAD in 25 patients (50%), RCA in 10 patients (20%), and LCX in 15 patients (30%). 2-vessel disease was seen in 45 patients (90%), while 3-vessel disease in 5 patients (10%).



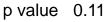
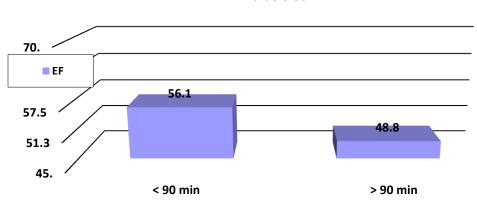


Fig. (4): Diseased vessels distribution in both groups.

<u>PCI data</u>: the results of PCI for patients of both groups were analyzed. **Door to balloon time**: Mean door to balloon time was comparable between two groups (in group A, 96 min ±7.6 while in group B 95min ±

6.4 with P value 0.86). But it was more than 90 minutes which exceed the recommended time in the guidelines of primary PCI. Patients with door to balloon time less than 90 minutes had better EF than patients with door to balloon time more than 90 minutes (56.1 ± 5.3 versus 84.8 ± 8.3 P value 0.004)



P value 0.004

Fig. (5): EF in relation to D to B time.

Stents: The number of DES used in group A is significantly more than that used in group B (106 versus 50 stents, P value < .0001) and this is due to complete revascularisation in group A and culprit- only revascularisation in group B during primary intervention.

Contrast dose: The contrast dose used during primary intervention was higher in group A, but it was not statistically significant (290 ml \pm 82.5 versus 200ml \pm 58.9, P value 0.09). **Procedure duration:** Duration of intervention was significantly higher in group A in relation to group B (70.2 mins \pm 10.1 versus 42 \pm 11.3 P value < 0.0001).

Procedure success and complications: The intervention was successful in all patients of group A and group B and the incidence of complications was not significant between both groups (in group A, 1 patient distal embolization, 2 patients serious arrhythmia and 2 hypotension necessitating inotropic support. While in group B, 2 distal embolization and 1 serious arrhythmia).

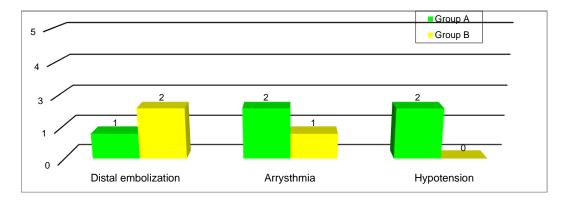


Figure (6): Procedure complications in both groups.

(IV) Hospital course In-Hospital MACE: No MACE was observed in group A, while two cases of MACE (death) was observed in group B (P value 0.31). As patients had TIMI II flow after PCI and the cause death was VF.

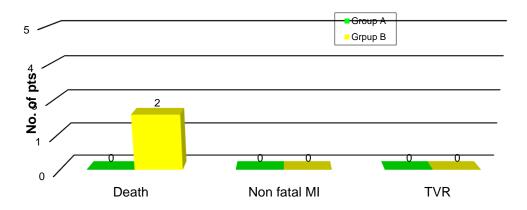


Fig. (7): In-hospital MACE in both groups.

Hospital stay: Mean hospital stay (days) was 3.4 ± 0.76 in group A and 2.5 ± 1.19 in group B (P value 0.75). So hospital stay was comparable between both groups and no need for more stay in case of complete revascularisation. **Vascular complications:** There were no incidence of major bleeding nor site access complications in both groups while only one patient with minor bleeding in A group. P value 0.34

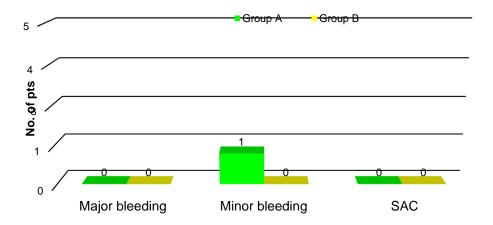


Fig (8): Bleeding complications & SAC in both groups.

Contrast induced nephropathy (CIN): CIN was observed in 5 patients of group A and 3 patients of group B (P value 0.52). So the incidence of CIN was comparable between both groups indicating no added risk to the patient with aggressive strategy of complete revascularisation. The incidence of CIN was statistically significant in patients with anterior MI (11.5 % in patients with anterior MI while 1 % in patients with inferior MI, P value 0.03)

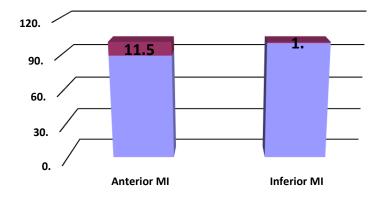


Fig. (9): incidence of CIN according to the ECG.

Ejection fraction (EF): There was no significant difference between both groups (50.3 ± 4.1 in group A versus 49.9 ± 3.2 in group B, P value 0.81). There is a negative correlation between EF and Door to Balloon (D to B) time (r equal -.63, P value < 0.001). **(V) 30 days follow up: 30 days MACE** (including inhospital MACE): In group A, there was no incidence of MACE. While in group B, there were three cases, two hospital deaths and the other non-fatal MI requiring re-intervention in Non-culprit vessel as the patient developed NSTEMI. (P value = 0.11).

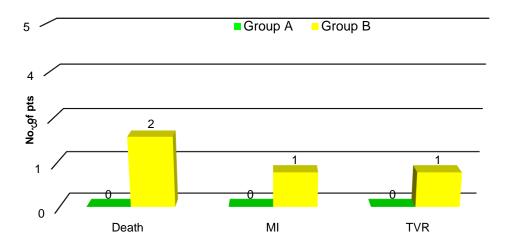
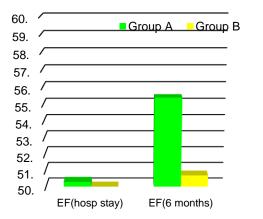


Fig. (10): 30 days MACE in both groups.

30 days re-hospitalization: Was comparable between both groups (no patient in group A and one patient in group B, P value 0.31) **(VI) 6 months follow up: 6 months MACE and re-hospitalization:** the incidence of MACE and re-hospitalization at 6 months were the same as at one month follow up between both groups .only one patient in group A developed UA as subtotal in-stent stenosis at non culprit vessel required re-intervention **6 months PCI:** Only one patient in group A need re-intervention . While all patients in group B received intervention in the non- culprit vessels after 3 month from primary PCI at Governmental hospital all stents are DES not known by the patinets**6 months EF:** <u>At 6 months follow up</u>: EF in group A increased significantly to 55.4 ± 6.2 (P value 0.003). While in group B, it increases non-significant to 50.7 ± 4.2 (P value 0.50)



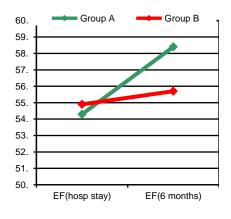


Fig. (11): Ejection fractions(EF) in both groups.

The increase of EF after 6 months was significant in patients with anterior MI (50.89 \pm 4.5 » 54.16 \pm 5.8, P value 0.004). While it was not significant in patients with inferior MI (53.20 \pm 4.7 » 54.7 \pm 3.6, P value 0.36).

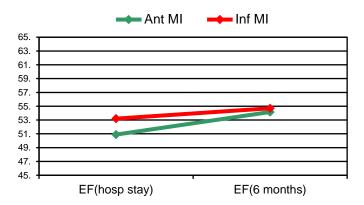


Fig. (12): The increase of EF in Anterior and Inferior MI

Discussion This study was intended to compare in-hospital and long-term outcomes (6 months) between complete re-vascularization and culprit - only revascularization (followed by staged PCI of secondary lesions) in STEMI patients with MVD CAD undergoing primary angioplasty. The patients were divided into 2 groups matching in their baseline clinical and angiographic characteristics. Group A (50 patients, mean age 55.1+9.26). Was subjected to complete revascularization during primary PCI; while group B (50 patients, mean age 54.25+9.1). Was subjected to culprit-only revascularization followed by staged re-intervention of secondary lesions. p-PCI has become the treatment of choice for patients presenting with STEMI when it can be performed expeditiously by an experienced team. [8]. The goal is restoration of flow within 90 min of presentation to a PCI-equipped center. This strategy has been found to be superior to thrombolytic therapy in improving morbidity and mortality.[2]. An important piece of information gained at the time of angiography and p-PCl is information not only about the culprit lesion but also about the extent and severity of the underlying CAD. In patients presenting with STEMI, MVD of CAD is found to be present from 40 to 65% of patients depending upon the baseline characteristics (especially age) of the specific population studied; [9].however, in one study only 10% of STEMI patients initially treated by p-PCI had a clinical indication for non-culprit PCI during the subsequent follow-up of up to 3 years. [10]. The presence of MVD has been found to be associated with worse prognosis in patients with STEMI. [11]. Identification of optimal strategies for treating these patients is the subject of considerable interest and controversy. During pPCI most invasive cardiologists follow these guidelines

and leave treatment of the other stenotic vessels for future intervention. The one caveat in the guideline recommendations is for patients in cardiogenic shock [12]. This policy intends to avoid the procedural complications that may compromise patient's condition during an acute MI. Currently, use of stents and platelet glycoprotein IIb/IIIa inhibitors has markedly improved outcomes of elective MVD PCI [13]. Thus, only a few reports describe the results of non-culprit vessel PCI for patients undergoing mechanical reperfusion for STEMI. A small prior study of primary PCI for patients with MVD demonstrated favorable results with a strategy of staged PCI revascularization after immediate recanalization of the culprit artery [14]. More reports suggest that this may be a suitable strategy for patients with AMI found to have MVD during pPCI as well [15]. Actually only a few small reports describe the results of simultaneous non-culprit vessel PCI and have contradictory results and it remains unclear whether treatment of coronary lesions of non-IRA is required, and if so, then when this should be performed The prevalence of MVD in the present trial was 42%, comparable to previous reports that observed prevalence ranging from 40to 65%. Our study has shown a number of interesting findings: 1-Assessment of LV function during hospital stay ,6 months showed that Lt ventricle EF improved significantly after 6 months in group A [EF increased significantly from 50.3 ± 4.1 to 55.4 ± 6.2 (P value 0.002)] compared to group B [it increased non-significantly from 49.9 ±3.2to 50.7 ± 4.2 (P value 0.53)]. 2-Incidence of MACE in both groups was not significant during hospital stay and at 1 & 6 months follow up. Three cases of MACE in group B at 1month and no MACE at 6, while no MACE in group A at 1 month and only one patient at 6 months follow up (P value 0.11). 3-Safety of aggressive strategy for complete revascularization is comparable for culprit- only strategy as regard incidence of -Contrast induced nephropathy; 5 cases in group A, while 3 case in group B (P value 0.52). -Vascular complications; one case with minor bleeding in group A, while No case in group B (P value 0. 34). -The restoration of normal systolic function of the LV is known to be a predictor of better long-term results after AMI. Prolonged myocardial ischemia due to significant stenosis in non–IRA vessels may compromise the hemodynamic stability in the course of AMI, and may be associated with ischemia-induced myocardial hibernation. Furthermore, hibernated myocardium degenerates, so the sooner the blood-flow is restored, the greater the chance to prevent fibrosis and scar formation. [16]. The influence of MVD on the recovery of LV function was assessed by Ottervanger et al.2001 in 600 patients with AMI treated with pPCI. They showed that despite the regained flow in the IRA, the presence of MVD was correlated with lack of a significant improvement of LVEF. [17]. The recovery of LV function after complete MVD one-stage PCI in patients with acute STEMI was assessed by [18]. in 48 patients (group A) and 2-stage PCI in 44 patients (group B). In group A, the absolute LVEF increase after 30 days was significantly higher in comparison to group B (p < 0.01). A similar

trend was observed after 180-day follow-up and the difference was borderline significant (p = 0.052). Significantly higher % of patients in group A reached the primary endpoint (increase in LVEF > 5%) compared to group B (44.7% versus 32.4%, p = 0.028). In our study, the one-stage complete revascularization was associated with significant improvement of the LVEF throughout the 6-month follow-up. The 2stageS approaches are also effective in terms of LVEF improvement, but observed increase of LVEF was significant only after the complete revascularization. Italian studycompared three different revascularization strategies in 214 consecutive patients with STEMI and MVD CAD undergoing pPCI: culprit vessel angioplasty-only (COR group); staged revascularization (SR group), and simultaneous treatment of non-IRA (CR group). During a mean follow-up of 2.5 years, at least one major adverse cardiac event occurred in 50% patients of the COR group, 20% of the SR group, and 23% of the CR group (P, 0.001). [6]. Another single-center registry [19] found among 745 p-PCI patients MVD PCI in STEMI to be feasible and safe. This registry realistically described the relative proportions of single- (46%) vs. MVD (54%) and the 3 most frequently used strategies for MVD: p-PCI of the IRA only (39%), staged PCI (24%), and acute MVD (37%) PCI. Kong et al 2006. Analyzed patients undergoing PCI for STEMI (MVD angioplasty, n = 632 and infarct-related vessel angioplasty, n = 1350) from the New York State Angioplasty Registry database. The highest risk patients (previous MI, angioplasty, CABG, or cardiogenic shock) were excluded. In-hospital mortality was lower (0.8 vs. 2.3%, P = 0.018) in the MVD angioplasty group. No differences were observed in other ischemic complications, renal failure, or length of stay. After multivariate analysis, MVD angioplasty remained a significant predictor of lower in-hospital death [P = 0.03]. The previous mentioned studies support the aggressive approach of complete revascularization. While there are many other trials with better r neutral outcome with culprit-only revascularization [20]. The study of (Hannan et al 2010), found no mortality benefit from acute MVD PCI[21]. Roe et al 2001. Described even increased mortality with acute MVD PCI strategy and also an increased risk of major adverse cardiac events with this strategy. One study allocated 214 STEMI patients with MVD to three arms: IRA PCI simultaneous treatment of non-IRA lesions, and staged revascularization of the non-IRA. At a mean followup of 2.5 years, patients allocated to IRA angioplasty-only had more major adverse cardiac events (MACE) (i.e. death, re-infarction, re-hospitalization for ACS, and repeat coronary revascularization) than the patients treated with other strategies. [22]. The meta-analysis of Sethi et al 2010. revealed nine nonrandomized studies (with a total of 4530 patients treated by acute complete revascularization and 2723 patients treated by the IRA PCI in the acute phase) and two small randomized studies. MACE (OR = 0.95, 95% CI 0.47– 1.90) and long-term mortality (OR = 1.10, 95% CI 0.76–1.59) were similar for both strategies [23]. Published secondary analysis of the APEX-acute MI trialfound non-IRA PCI to be performed

only in 9.9% of patients with STEMI and MVD. Ninety-day death and death/congestive HF/shock were higher in this non-IRA group compared with the IRA-only PCI group (12.5 vs. 5.6%, P = 0.001 and 17.4 vs. 12.0%, P = 0.020, respectively). After adjusting for patient and procedural characteristics as well as propensity for performing non-IRA PCI, this procedure remained independently associated with an increased hazard of 90-day mortality [adjusted hazard ratio 2.44, 95% CI (1.55-3.83), P=0.001] [24].PRAMI (Preventive Angioplasty in Acute MI) trial is the first randomized multicenter comparison of the 2 invasive therapeutic approaches: 1-stage versus 2-stage PCI in patients with STEMI and MVD in relationship to the recovery of LV systolic function. The principle finding of the study is that in patients randomly assigned to 1-stage PCI, the LVEF recovers more rapidly and more significantly in comparison to the standard 2-stage procedure .The 1-stage complete PCI led to a significant improvement of LVEF in AMI patients with MVD after 30 days, with a trend towards further improvement at 6-month follow-up as compared to the 2-stage approach. This may be particularly significant in patients with anterior AMI with low LVEF (< 40%), since these parameters were independent predictors of primary endpoint. [25]. Manari A, et al. reported that in culprit only primary PCI; 10.6 % of patient were Killip 2-3, the mean heart rate was 77.0± 16.7 bpm and the mean systolic BP was 130.7±16.7 mmHg, anterior MI represented in 43.5% of patients and 11.2% of patient had LVEF < 35%. in staged MVD pPCI 3.6% of patient were Killip 2-3, the mean heart rate was 73.5± 16.1bpm and the mean systolic BP was 128.0±25.5 mmHg, anterior MI represented in 35.4% of patients and 8% of patient had LVEF < 35% . culprit only PPCI the median of the door to balloon= 83min and symptoms to balloon=210 min and in staged MVD pPCI the median of door to balloon =70 min and the median of the symptom to balloon= 180 min reported that 87.4% of patients in culprit only PPCI had two vessel disease, LAD represented the culprit lesion in 44.5% of patients, LCX represented in 12.4% and RCA represented in 43.1% of patients, 85.3% of patients in staged MVD pPCI had 2 vessel disease, LAD represented the culprit lesion in 35.2% of patients, LCX represented in 13.1% and RCA represented in 51.7% of patients. reported that at least one BMS implanted in 77.7 % and at least one DES implanted in 13.6 in culprit only PPCI group, in staged MVD PPCI group at least one BMS implanted in 56.5 % and at least one DES implanted in 41.6%. Glycoprotein (GP) Ilb/Illa inhibitor was used at the discretion of the operators in 75.7% of patients in culprit only PPCI and in 85.5% in staged MVD PPCI.TIMI 3 flow post PCI was 90.2% in culprit only PPCI vs.95.9% in staged MVD PPCI .reported that culprit-only PPCI was associated with higher rate of short- or long- term mortality or MACE as compared to a staged MVD PCI [hazard ratio (HR): 2.81, 95%; confidence interval (CI): 1.34-5.89, p=0.006 for 30-day mortality and HR: 1.93, 95% CI 1.35-2.74, p=0.0002 for 2-year mortality , respectively] [26].After This STUDY there are three randomized clinical trials have compared. The Complete Versus Lesion-Only Primary PCI Trial (CvLPRIT) (n = 296, 12months follow-up), [27]. The Complete revascularization versus treatment of the culprit lesion only in patients with STEMI and MVD (DANAMI-3-PRIMULTI) trial (n = 627, 27months follow-up) [28] . The Comparison Between FFR Guided Revascularization Versus Conventional Strategy in Acute STEMI Patients With MVD (Compare-Acute, n = 885, 12 months follow-up) trial. [29]. PCI of non-IRA was done either during the index procedure (Compare-Acute), staged during hospital admission (DANAMI- 3-PRIMULTI), or any time before discharge (immediate or staged) (CVLPRIT). Indication for PCI in non-IRA was angiography-guided in lesions with >70% stenosis (CVLPRIT), or fractional flow reserve (FFR)-guided (DANAMI-3-PRIMULTI and Compare-Acute). Primary outcome (composite of different endpoints) was significantly reduced in the complete revascularization group in all trials. Total mortality was not statistically different in any of the trials. Repeat revascularization was significantly reduced in the complete revascularization arm in the DANAMI- 3-PRIMULTI, and Compare-Acute trials. The lack of significant treatment effect of non-IRA lesion intervention on death or MI was confirmed by three meta-analyses [30]. Based on these data, revascularization of non-IRA lesions should be considered in STEMI patients with MVD before hospital discharge. As the optimal timing of revascularization. Our study was not powered to determine the incidence of clinical endpoints, however no significant differences in MACE was observed between the group undergoing 1stage PCI and the group treated with the 2-stage procedure. The contrast dose used during primary intervention was higher in group A, but it was not statistically significant (290 ml ± 82.5 versus200ml ± 58.9, P value .09). The higher dose in group A is due to complete revascularization of all vessels while its insignificance may result from using most of the dose during culprit intervention and little was used during non-culprit intervention. This may reflect that there is no added risk to the patient with complete revascularization from contrast material. One-stage revascularization is associated with higher contrast medium load and longer procedure time in the setting of the acute phase of STEMI, But no increased incidence of adverse events and complications were noted in long-term follow-up. Two-stage PCI is associated with additional vascular access, stress to the patient, and prolonged hospitalization which increases costs. The mean hospital stay was comparable in patients treated with 1-stage PCI, thus no increased costs. In our study, Patients with door to balloon time less than 90 minutes had better EF than patients with door to balloon time more than 90 minutes (56.1 \pm 5.3 versus 49.5 \pm 8.3 P value 0.005). This matched with the international guidelines for the door to balloon to be less than 90 minutes. One of the limitations of 1-step MVD PCI in the setting of AMI is an overestimation of non-IRA stenosis severity on angiography which can affect clinical decision making. The primary cause of such an exaggeration is vasospasm, which is frequently found on coronary angiograms of AMI patients. The coronary angio-

grams in our study were recorded post-nitroglycerine injection and re-evaluated by an independent interventionist blinded to the treatment assignment to prevent the described exaggeration.

<u>**Conclusions</u>**: 1-Complete coronary revascularization during primary PCI in patients with multi-vessel disease is safe 2-Complete coronary revascularization during primary PCI is associated with better improvement of EF at 6 months especially in patients with anterior wall myocardial infarction in comparison to culprit-only revascularization. 3-Door to balloon time less than 90 minutes is associated with better ter EF in comparison to more than 90 minutes. 4-No difference in incidence of MACE between complete and culprit-only revascularizations.</u>

Summary: Primary percutaneous coronary intervention (PCI) has become the preferred reperfusion strategy in ST-elevation myocardial infarction (STEMI) when performed in a timely manner. The current American College of Cardiology/American Heart Association (AHA) and European Society of Cardiology (ESC) guidelines suggest that primary PCI should be the favored approach compared with fibrinolysis in STEMI if the first medical contact to reperfusion/device time of <90 minutes (<60 minutes in early presenters [ESC guidelines]) can be achieved. Primary PCI has been shown to be superior to fibrinolysis in reducing morbidity and mortality in STEMI. Approximately 40% to 70% of patients undergoing primary PCI will have MVD with at least 1 additional severe lesion in an artery other than the culprit vessel. These patients have worse outcomes with over a 2-fold increase in death at 1 year compared with patients who have single-vessel disease. Various treatment strategies for non-culprit vessels have generated considerable interest and controversy. These include medical therapy, MVD revascularization at the time of primary PCI, and staged PCI. Current guidelines recommend against performing PCI for the nonculprit vessels at the time of primary PCI unless there is hemodynamic instability. The aim of this study is to determine MACE (cardiacdeath, re-infarction, and stroke, the need forrevascularization, major bleeding) & Lt ventricular EF in STEMI patients with angiographic patterns of MVD with clinical indication to undergo PCI (culprit lesion only)versus complete revascularization. This study included 100 patients, 69 males (69%) and 31 females (31%) with a mean age of 56.2 ± 7.1 years & divided into two groups.

<u>Group A(complete revascularisation, CR)</u>: included fifty patients, 40 males (80%) and 10 females (20%) with a mean age of 55.1<u>+</u>9.26.

<u>Group B(culprit-only revascularisation, COR)</u>: included fifty patients, 29 males (58%) and 21(42%) with a mean age 54.25<u>+</u>9.1. Study was started from October 2015 to June 2017 at Al Hussin University Hospital Al Marwa Cardiac center. All patients were subjected to detailed history taking, clinical evaluation, ECG

analysis and laboratory investigations assessing at admission & at discharge. Chest pain-to-ER & door-toballoon times were computed and given in minutes. Diagnostic coronary angiography was performed and angiographic measurement and determination of coronary TIMI flow before and after any procedure were done. p PCI was performed according to current guidelines and described including materials used and the intra-procedure complications were also documented. Patients were put under observation to detect the occurrence of any in-hospital MACE or other hemodynamic complications. All patients were followed up for 6 month for incidence of any complications MACE, rehospitalisation and PCI and EF.

Results: -LV EF improved significantly after 6 month in group A EF increased from 50.3 ± 4.1 to 55.4 ± 6.2 (P value 0.003). While in group B, it increase non-significantly from 49.9 ± 3.2 to 50.7 ± 4.2 (P value 0.50):The improvement of EF was more observed in patients with anterior Wall STEMI. -Incidence of MACCE in both groups was comparable during hospital stay,1 month and 6month follow up .3 cases of MACE in group B, while no MACE in group A. (P value 0.11). -Safety of aggressive strategy for complete revascularization is comparable for culprit –only strategy as regard risk -CIN was observed in five patients of group A and three patients of group B (P value 0.52) .-Vascular complication .no cases in group B while only 1 case in group B P value 0.34. -Door to balloon time less than 90m is associated with better EF in comparison to more than 90m.

Recommendations :

1-Complete coronary revascularization during primary PCI in patients with MVD is safe and possible technique. It is associated with better LV function at 6 months follow up especially in patients with anterior wall MI.

2-In our study there was time delay between patient's symptoms and first medical contact ranged from 40m to 12h which is considered higher than that published in the literature in many developed countries, So insisting that our patients have to be better educated to minimize this delay,

3 -It is recommended to follow the ninety minutes of the door to balloon time during primary PCI for its better outcome on LV function.

4 -To make further study with greater number of patients to see effect on MACE in primary PCI of MVD patients between complete and culprit-only revascularizations.

Study limitations: 1) the sample size is relatively small, and larger studies are needed to validate these results. 2) They do not represent all-comers who presented with acute STEMI because there are still many patients treated with fibrinolysis only without further PCI because of availability of tools, prepared places and financial aspect. 3) There is a proportion of the delay to PCI comprises the time taken by patients to decide whether they can proceed with the procedure, based on financial constraints especially in private hospital. 4) Data represent a high expert centres where the operators are experienced and the hospital has good medical and paramedical team and good ambulance system. Whether these results can be less than our results when less expert and less facilities in some hospitals in our country. 5) Cases of cardiac death were not investigated, for example by autopsy, to define well and help to further prevent the causes of in hospital cardiac death post PPCI.

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