IFR - Guided Complete Revascularization Versus Culprit Lesion Only Revascularization In Patients With STEMI Undergoing Primary PCI

Ahmed Zayed*, Bassem Zarif*, Gamal Abdelhady*, Tamer El Banna**

*Cardiology department, National Heart Institute
**Cardiothoracic surgery department, National Heart Institute

Abstract

Back ground: In patients with STEMI and multi vessel disease, it is uncertain whether it is safe or even desirable to also Treat the non culprit vessel during the primary PCI procedure.
***Objectives*:** The purpose of this study was to compare 1 year outcome of IFR guided complete revascularization versus culprit lesion only revascularization in patient with STEMI and multivessel disease undergoing primary percutaneous coronary intervention.
Methods: This is prospective controlled study included 75 patients with STEMI who were presented within 12 hour from onset of symptoms undergoing primary PCI with at least one non-culprit intermediate lesion during coronary angiography. 6 patients were referred to coronary artery by pass graft surgery (CABG) due to left main and multivessel disease. In 9 patients, the IFR of non-culprit lesion was performed and showed insignificant stenosis (IFR $\geq$ 0.89) , 30 patients underwent PCI for the culprit lesion only (group A) and 30 patients underwent PCI for the culprit lesion and IFR significant non-culprit lesion (group B) at National Heart Institute from May 2017 to May 2019 . 1 year outcome for major adverse cardiovascular events (MACE) including mortality, reinfarction, heart failure, need for repeat revascularization were reported.
Results: After 1 year of follow up , there was insignificant difference between both groups as regard MACE, death, MI, repeated revascularization or heart failure. *MACE was reported in 10 patients (33.3%) in group A versus 6 patients (20%) in group B (P>0.05). Death was reported in 2 patient (6.6%) in group A versus 1 patient (3.3%) in group B (P>0.05). Myocardial infarction was present in 3 patients (10%) in group A versus 2 patients (6.6%) in group B (P>0.05). Repeated revascularization was reported in 3 patients (10%) in group A versus 1 patient (3.3%) in group B (p>0.05). Heart failure was reported in 2 patients (6.6%) in each group .No reported cases of cerebrovascular stroke in both groups.*
Conclusion: There is no significant difference between two strategies at 1 year follow up as regard major adverse cardiovascular events including death , recurrent myocardial infarction, heart failure and repeat revascularization.

Keywords: ST-segment elevation myocardial infarction, multivessel disease, primary PCI, the instantaneous wave-free ratio (IFR).

{**Citation**: Ahmed Zayed, Bassem Zarif, Gamal Abdelhady, Tamer El Banna. IFR - Guided complete revascularization versus culprit lesion only revascularization in patients with STEMI undergoing primary PCI. American Journal of Research Communication, 2020, Vol8(11): 1-8} www.usa-journals.com, ISSN: 2325-4076.

*Cardiology department, National heart institute

Introduction

Assessment of non-culprit lesions in patients with acute coronary syndrome (ACS) after percutaneous coronary intervention { PCI) of the culprit vessel is an important issue . Also, the treatment of non-culprit vessels in patients with multivessel and intermediate.
stenosis is always debatable (1-2). the use of intracoronary pressure indices would allow rapid assessment of significant non-culprit stenosis that cause ischemia while the patients still in the catheterization laboratory allowing the patients to avoid second procedure . However ,multiple hemodynamic and physiological variations that occur during ACS ,as variations in the adrenergic state and myocardial blood flow , may affect intracoronary pressure. The instantaneous wave-free ratio { IFR }, a pressure-only index, has some characteristic features that make it useful in physiological assessment of coronary stenosis during ACS. IFR is calculated from the mean distal to aortic pressure ratio during a period of diastole. During this period , the resistance is at its lowest point during the cardiac cycle allowing optimal physiological measurements to be made. IFR has been evaluated in several studies and showing good agreement with functional flow reserve {FFR) in detection of ischaemia (3,4). IFR was recently used in patients with stable coronary artery disease to evaluate the severity of stenosis (5) . Despite Ntalianis and colleagues showed reliability of FFR measurements in non- culprit lesions during acute myocardial infarction (6), no available data on reliability and feasibility of IFR in such clinical setting.

Objectives

The aim of this study was to compare culprit lesion only revascularization versus IFR guided multivessel PCI in patients with ST- segment elevation myocardial infarction (STEMI) and multivessel disease undergoing primary PCI.

Methods

This is prospective study included 75 patients with STEMI presented within 12 hour of onset of symptoms undergoing primary PCI with at least one non-culprit intermediate lesion, visually judged as an angiographic stenosis ≥ 50% and ≤ 70% of major non-culprit epicardial coronary artery, during coronary angiography.
6 patients were referred to coronary artery by pass graft surgery (CABG) due to left main and multivessel disease. In 9 patients, the IFR of non-culprit lesion was performed and showed insignificant stenosis (IFR ≥ 0.89). 30 patients underwent PCI for the culprit lesion only (group A) and 30 patients underwent PCI for the culprit lesion and IFR significant non-culprit lesion (group B) at National Heart Institute from May 2017 to May 2019 . Exclusion criteria included prior administration of fibrinoltytic therapy, history of bleeding diathesis, cardiogenic shock, severe renal impairment, platelet count < 100.000 cells/mm^3. All patients were subjected to 1) clinical examination including: age, sex, history of chest pain, risk factors for ischemic heart disease, blood pressure and cardiac examination. 2) 12 leads ECG was performed on admission and during follow up. 3) Routine laboratory investigation including CK. MB, troponin I, s. creatinine, lipid profile and random blood sugar. 4) Coronary angiography and primary PCI, oral anti platelets were administrated (aspirin 300mg plus clopidogrel 600 mg loading dose followed by 75 mg maintenance). local ethics committee approved the study, and informed consent was obtained for each patient . Coronary angiography was performed by percutaneous femoral approach. After diagnostic coronary angiography , 6F guiding catheter was introduced and primary PCI for the culprit lesion was done after intravenous injection of 10.000 units of unfractionated heparin. After PCI of the culprit lesion was performed , 100 ug of intracoronary bolus of nitroglycerine was administered and a pressure wire was calibrated and introduced into the guiding catheter . The wire was advanced to the tip of the guiding catheter and the pressure was equalized against that measured through the guiding catheter . The wire is then advanced through the target lesion. After base-line trans-stenotic pressure measurement had been performed , IFR was calculated as the ratio of mean distal coronary pressure measured by the pressure

wire to mean aortic pressure measured by the guiding catheter. PCI was performed for the non-culprit lesion if IFR ≤ 0.89. When IFR exceeded this threshold , PCI was deferred. Primary PCI was performed according to current guideline recommendations and could include aspiration thrombectomy or glycoprotein IIb/IIIa inhibitor if indicated. Drug-eluting stents were used in all patients in both groups to reduce risk of in-stent restenosis. Patients were treated after the procedure with contemporary optimal medical therapy. The primary end points was major adverse cardiovascular events (MACE) defined as the composite of death, nonfatal myocardial infarction (MI) , repeated revascularization or heart failure (HF) at 1 year .

Statistical analysis

for statistical analysis, statistical package for social science (SPSS) software version 17 was used. Continuous variables were presented as mean ± standard deviation. The categorized variables were given as percentages. To compare variables ,the paired t-test (for parametric variables), Wilcoxon test (for the nonparametric variables), and McNemar test (for categorized variables) were used and P. value < 0.05 was considered to be significant.

Results

60 patients presented with STEMI underwent primary PCI were screened and divided into two groups: 30 patients were subjected to culprit lesion only revascularization (group A) and 30 patients were subjected to culprit lesion and IFR significant non-culprit lesion revascularization (group B). There was no significant difference between both groups as regard demographic and clinical data. All patients in both groups were male. The mean age was 58 ± 5.6 in group A versus 61 ± 3.4 in group B (P> 0.05). Typical chest pain was the main symptom on admission in all patients in both groups. Smoking was present in 22 patients (73.3%) in group A versus 20 patients (66.6%) in group B (P > 0.05). Diabetes mellitus was present in 15 patients (50%) in group A versus 20 patients (66.6%) in group B (P> 0.05). Hypertension was present in 17 patients (56.6%) in group A versus 19 patients (63.3%) in group B (P > 0.05). Dyslipidemia was present is 18 patients (60%) is group A versus 14 patients (46.6%) in group B (P>0.05). No history of previous PCI or CABC in all patients in both groups. In group A, the mean HR was 99 ± 6.5 beat/ minute versus 95 ± 5.8 beat/minute in group B (P>0.05). Normal sinus rhythm was present in all patients in both groups. Anterior myocardial infarction (MI) was present in 20 patients (66.6%) in group A versus 16 patients (53.3%) in group B (P>0.05). Inferior myocardial infarction was presents in 10 patients (33.3%) in group A versus 14 patients (46.6%) in group B (P > 0.05). (table1).

Table 1: Demographic and clinical data in both groups

	Group A n=30	Group B n=30	P value
Age (in years)	58 ± 5.6	61 ± 3.4	>0.05
Smoking	22 (73.3%)	20 (66.6%)	>0.05
Diabetes mellitus	15 (50%)	20 (66.6%)	>0.05
Hypertension	17 (56.6%)	19 (63.3%)	>0.05
Dyslipidemia	18 (60%)	14 (46.6%)	> 0.05
Heart rate	99 ± 6.5 b/m	95 ± 5.8 b/m	> 0.05
Anterior MI	20 (66.6%)	16 (53.3%)	> 0.05
Inferior MI	10 (33.3%)	14 (46.6%)	> 0.05

The culprit artery was left anterior descending artery (LAD) in 18 Patients (60%) in group A versus 14 patients (46.6%) in group B (P. > 0.05). The left circumflex artery (LCX) was the culprit artery in 6 patients (20%) in group A versus 8 patients (26.6%) in group B (P.> 0.05) .While the right coronary artery (RCA) was the culprit artery in 6 patients (20%) in group A versus 8 patients (26.6%) in group B (P.> 0.05) . Non infarct related artery was LAD in 6 patients (20%) in group A versus 7 patients (23.3%) in group B (p> 0.05), while RCA was non infarct related artery in 8 patients (26.6%) in group A versus 6 patients (20%) in group B (P>0.05). The LCX was non infarct related artery in 4 patients (13.3%) in group A versus 7 patients (23.3%) in group B (P. >0.05). The LAD and LCX were non culprit arteries in 6 patients (20%) in group A versus 5 patients (16.6%) in group B (P> 0.05). The LAD and RCA were non culprit arteries in 6 patients (20%) in group A versus 5 patients (16.6%) in group B. (table 2).

Table (2): Coronary angiography data in both group

	Group A	Group B	P. value
Culprit artery			
LAD	18 (60%)	14 (46.6%)	>0.05
LCX	6 (20%)	8 (26.6%)	>0.05
RCA	6 (20%)	8 (26.6%)	>0.05
Non infarct related artery			
LAD	6 (20%)	7 (23.3%)	>0.05
RCA	8 (26.6%)	6 (20%)	>0.05
LCX	4 (13.3%)	7 (23.3%)	>0.05
LAD, LCX	6 (20%)	5 (16.6%)	>0.05
LAD, RCA	6 (20%)	5 (16.6%)	>0.05

After 1 year of follow up , there was insignificant difference between both groups as regard MACE, death, MI, repeated revascularization or heart failure. MACE was reported in 10 patients (33.3%) in group A versus 6 patients (20%) in group B (P>0.05). Death was reported in 2 patient (6.6%) in group A versus 1 patient (3.3%) in group B (P>0.05). Myocardial infarction was present in 3 patients (10%) in group A versus 2 patients (6.6%) in group B (P>0.05). Repeated revascularization was reported in 3 patients (10%) in group A versus 1 patient (3.3%) in group B (p>0.05). Heart failure was reported in 2 patients (6.6%) in each group . No reported cases of cerebrovascular stroke in both groups.) .
(table 3).

Table 3: 1-year outcome in both groups

	Group A	Group B	P. value
MACE	10 (33.3%)	6 (20%)	>0.05
Death	2 (6.6%)	1 (3.3%)	>0.05
MI	3 (10%)	2 (6.6%)	>0.05
Repeat revascularization	3 (10%)	1 (3.3%)	>0.05
HF	2 (6.6%)	2 (6.6%)	>0.05

Discussion

Multivessel disease experienced during primary PCI in patients with STEMI creates therapeutic dilemma (7). Although, Some studies have shown that multivessel PCI was associated with increased mortality and reinfarction (8,9) , recent advances in PCI procedures make some operators to perform multivessel PCI in patients with STEMI (10). The assessment of non-culprit lesion in patients with STEMI an important issue as intermediate stenosis rate of non-culprit vessel in STEMI patients accounts for about 70% (7). In these patients, a coronary vasoconstriction due to alpha-adrenergic hyperactivity may induce vasoconstriction (11). Therefore, how and when to deal with a non-culprit intermediate lesion is still unknown.

On the other hand, IFR is calculated by measuring the resting pressure gradient (Pd/Pa) across a coronary lesion during a certain period of diastole at which minimal resistance and maximal flow occur (12). A cut off value ≤ 0.89 has been settled to detect ischemia (13).

In addition IFR, a non-hyperdynamic index, is promising technique for assessment of non- culprit intermediate lesions in patients with acute coronary syndrome, and matching it with FFR in this clinical setting is non-inferior compared to stable coronary artery disease (14).

In this study, we evaluated 1 year–outcome of culprit lesion only revascularization compared to total revascularization of the culprit and IFR –significant non-culprit lesion in patients with STEMI and multivessel disease undergoing primary PCI .

There was no significant difference between the two groups at 1- year follow up in major adverse cardiovascular events including mortality, recurrent myocardial infarction, heart failure and repeat revascularization.

Our results are in agreement with the American College of Cardiology /American Heart Association guidelines, which recommended that PCI should be limited to the culprit vessel only with exception of cardiogenic shock (15).

Similarly , the European Cardiology Society guidelines stated that primary PCI should be directed only at the infarct-related artery and PCI of non-culprit lesions should be guided by objective evidence of residual ischemia at later follow up (16).

Furthermore , analysis from the HORIZONS-AMI trial (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) stated that deferred PCI of non-culprit lesion should be the standard approach during primary PCI in patients with STEMI as multivessel intervention may be associated with increased risk of mortality and stent thrombosis (17). In addition, the results from CULPRIT- SHOCK trial showed that preventive PCI in patients with STEMI and multivessel disease was associated with increased relative risk of death (18)

Protagonists of culprit vessel only revascularization assume that multivessel PCI may be associated with prolonged time , increased amount of contrast, renal impairment and heart failure . Also, non-culprit

lesion severity may be overestimated by circulating vasoconstricting catecholamine, and accurate assessment for need of revascularization may be obstructed. Furthermore, multivessel intervention might lead to increased rates of periprocedural MI , and increased revascularization rate secondary to restenosis (19-20) .

In the other hand, our results showed insignificant lower incidence in MACE, death, recurrent MI and repeat revascularization in patients with PCI of culprit and IFR significant non-culprit lesion (group B) than in patients with PCI of only culprit lesion (group A) and although this difference is statistically insignificant, may be due to limited number of patients, it may be physically significant.

In contrast to these results, the results of CVLPRIT trial demonstrated that complete revascularization during primary PCI in patients with STEMI resulted in significant lower rate of MACE at 12 months with no significant difference in MI and death (21). Also, the result of PRAMI trial reported that preventive PCI strategy was associated with lower rate of MACE than PCI of the culprit vessel only (22).

Protagonists of multivessel PCI assume that STEMI patients have multiple plaque disruptions and lack of therapy of other lesions may be associated with adverse outcome. Furthermore, severe disease in non-culprit vessels may worsen the compensatory contractility of remote myocardial segments . Finally, early discharge may be anticipated is patients undergoing complete revascularization (23-24).

Conclusion

In patients with STEMI and multivessel disease undergoing primary PCI, There is no significant difference between IFR –guided complete revascularization and culprit lesion only revascularization at 1 year follow for MACE ,mortality, recurrent MI, heart failure and repeat revascularization.

Limitation of the steady

The study was not powered to show differences in the components of the primary end point may be due to limited number of patients or short follow up period so, larger trials powered for death, and MI and HF with long follow up period are needed.

References

1) P.J. Vlaar, K.D. Mahmoud, D.R. Holmes Jr., et al., Culprit vessel only versus multivessel and staged percutaneous coronary intervention for multivessel disease in patients presenting with ST-segment elevation myocardial infarction: a pairwise and network meta-analysis, J. Am. Coll. Cardiol. 58 (2011) 692–703.

2) D. Carrick, M. Behan, F. Foo, et al., Usefulness of fractional flow reserve to improve diagnostic efficiency in patients with non-ST elevation myocardial infarction, Am.J. Cardiol. 111 (2013) 45–50.

3) S. Sen, J. Escaned, I.S. Malik, et al., Development and validation of a new adenosine independent index of stenosis severity from coronary wave-intensity analysis results of the ADVISE (Adenosine Vasodilator Independent Stenosis Evaluation) study, J. Am. Coll. Cardiol. 59 (2012) 1392–1402.

4) Nijjer SS, Sen S , Petraco R , et al. *Advances in coronary physiology. Circ J 2015; 79: 1172–84.*

5) R. Petraco, J.J. Park, S. Sen, et al., Hybrid iFR–FFR decision-making strategy: implications for enhancing universal adoption of physiology-guided coronary revascularization, Euro Intervention 8(2013) 1157-1165.

6) A. Ntalianis, J.W. Sels, G. Davidavicius, et al., Fractional flow reserve for the assessment of nonculprit coronary artery stenoses in patients with acute myocardial infarction, JACC Cardiovasc. Interv. 3 (2010) 1274–1281.

7) Qarawani D, Nahir M, Abboud m, Hazanov Y, Hasin Y. Culprit only versus complete coronary revascularization during primary PCI. Int J cardiol 2008; 123: 288-92.

8) Roe MT, Cura FA, Joski PS, et al. Initial experience with multivessel Percutaneous coronary intervention during mechanical reperfusion for acute myocardial infarction. Am J Cardiol 2001; 88:170-3.

9) Corpus RA, house JA, Marso SP, et al. Multivessel percutaneous coronary intervention in patients with multivessel disease and acute myocardial Infarction. Am Heart J 2004; 148: 493-500.

10) Varani E, Balducelli M, Aquiline M, et al. Single or multivessel Percutaneous coronary intervention in ST elevation myocardial infarction patients. Cathet Cardiovasc Interv 2008; 72: 927-33.

11) Indolfi C , Piscione F , Ceravolo R , et al. *Limb vasoconstriction after successful angioplasty of the left anterior descending coronary artery. Circulation 1995 ;92: 2109–12.*

12) F. Díez-Delhoyo, E. Gutiérrez-Ibañes, G. Loughlin, R. Sanz-Ruiz, M.E. Vázquez-Álvarez, F. Sarnago-Cebada, *et al.*Coronary physiology assessment in the catheterization laboratory. World J Cardiol, 2015; 7 :525-538.

13) Gotberg M. , E.H. Christiansen, I.J. Gudmundsdottir, L. Sandhall, M. Danielewicz, L. Jakobsen, *et al.* Instantaneous wave-free ratio versus fractional flow reserve to guide pci N Engl J Meditor, 376 (2017), pp. 1813-1823.

14) Indolfi C , Mongiardo A , Spaccarotella C , et al. *The instantaneous wave-free ratio (iFR) for evaluation of non-culprit lesions in patients with acute coronary syndrome and multivessel disease. Int J Cardiol 2015;178:46–54.*

15) Kushner FG, hand M, smith SC jr., et al. 2009 focused updates: ACC / AHA guidelines for the management of patients with ST elevation. Myocardial infarction (updating the 2004 guideline and 2007 focused update) and ACC/ AHA / SCAI guidelines on Percutaneous coronary intervention (updating the 2005 guideline and 2007 focused update). A report of the American College of Cardiology Foundation / American Heart Association task force on Practice Guidelines. J Am Coll Cardiol 2009; 54: 2205-41.

16) Van de Werf F, Bax J, Betriu A, et al., for the ESC committee for Practice Guidelines. Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation: the task Force on the management of ST-segment elevation acute myocardial Infarction of the European Society of Cardiology. Eur Heart J 2008; 29: 2909-45

17) Ran Kornowski, Roxana Mehran, George Dangas,et al. Prognostic Impact of staged versus one- time multivessel percutaneous intervention in acute myocardial infarction. J am Coll Cardiol 2011; 58:704-11.

18) Thiele H, I. Akin, M. Sandri, S. de Waha-Thiele, R. Meyer-Saraei, G. Fuernau, *et al.* One-year outcomes after PCI strategies in cardiogenic shock N Engl J Meditor, 379 (November (18)) (2018), pp. 1699-1710.

19) O' Gara pt, Kushner FG, Ascheim DD, et al. 2013 ACCF / AHA guideline for the management of ST- elevation myocardial infarction: a report of the American College of Cardiology foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013; 61: e78-140.

20) Steg PG, James SK, Atar D, et al. ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur heart J 2012; 33: 2569-619.

21) Anthony H. Gershlick, Jamal Nasir Khan, Damion J. Kelly, etal. Randomized trail of Complete Versus lesion- only revascularization In patients undergoing Primary Percutaneous Coronary Intervention for STEMI and multivessel disease. J of American College of Cardiology 2015; 65:963-72.

22) Wald DS, Morris JK, Wald NJ, et al., for the PRAMI investigators. Randomized trial of preventive angioplasty in myocardial infarction. N Engl J med 2013; 369: 1115-23.

23) Sorajja P, Gersh BJ , Cox DA, et al. impact of multivessel disease on reperfusion success and clinical outcomes in patients undergoing primary Percutaneous coronary interventions for acute myocardial infarction . Eur Heart j2007, 28:1709-16.

24) Cavender MA, Milford- Beland S, Roe MT, Peterson ED, Weintraub WS, Rao SV. Prevalence, predictors and in-hospital outcomes of non-infarct artery intervention during primary percutaneous intervention for ST – segment elevation myocardial infarction (from the national Cardiovascular data registry). Am J Cardiol 2009; 104: 507-13.