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Primary Percutaneous Coronary Intervention of Infarct Related Artery Only Versus Complete Revascularization in ST – Segment Myocardial Infarction: Meta-Analysis of 926 Patients

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ABSTRACT

Background: Primary percutaneous coronary intervention (PCI) is the treatment of choice for acute ST-segment elevation myocardial infarction (STEMI). The objective of our study was to determine the outcome differences that may exist between Culprit only PCI versus Complete PCI during primary PCI for STEMI patients. **Methods:** A systematic literature search was performed using PubMed, Embase and MELDINE to identify trials evaluating Culprit only PCI versus Complete PCI in STEMI patients. Primary outcome of interest was major adverse cardiac events (MACE), which is a composite of all cause mortality, new myocardial infarction, and repeat revascularization between the two groups namely Culprit only PCI and Complete PCI. Secondary outcome studied was repeat revascularization. **Results:** We included a total of 926 participants enrolled in 4 randomized controlled trials. Major adverse cardiovascular events were reduced in the Complete PCI group compared to Culprit only PCI group (OR 0.30, 95% CI 0.21-0.42, p<0.001). Complete PCI group had significantly reduced revascularization rates (OR 0.29, 95% CI 0.19-0.45, p<0.001). **Conclusion:** This meta-analysis demonstrates the efficacy of multi vessel PCI in Complete PCI group as compared to Culprit only PCI group, with a statistical significant reduction of MACE and revascularization rates.

Keywords: Primary percutaneous coronary intervention, Infarction.

INTRODUCTION

Primary percutaneous coronary intervention (PCI) of the culprit coronary artery is the treatment of choice in patients presenting with acute ST-segment elevation myocardial infarction (STEMI). Current guidelines from American College of Cardiology/American Heart Association (ACC/AHA) recommend revascularization of infarct related artery (IRA) only leaving other stenosed vessel medically treated or to dilate noninfarct related stenosed artery at a later time especially in patients with intermediate or high-risk findings on noninvasive testing (staged revascularization).[1]

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Simultaneous treatment of IRA and non-IRA artery is only recommended in a setting of cardiogenic shock. However, Complete PCI may be superior compared to Culprit only PCI, as plaque instability may be not only limited to IRA and may involve other vessels in the coronary tree.[2] Importantly, Complete PCI has also demonstrated improved long-term clinical outcomes in patients with stable coronary artery disease.[3,4] In a recent randomized controlled trial (RCT) (CvLPRIT investigators),[5] patients who underwent complete revascularization demonstrated statistical significant better outcomes in terms of major adverse cardiovascular events including all-cause mortality. The findings of this study reinforce the results of a similar study published last year.[6] However, other RCT and observations studies have demonstrated conflicting results.

The most recent systemic review did not include a large RCT that was presented in European Society of Cardiology.[5] The aim of this updated meta-analysis

is to assess whether performing complete revascularization as a part of initial intervention in patients with STEMI is associated with reduction in major cardiovascular events (MACE), and revascularization rates.

MATERIALS AND METHODS

Search Strategy

A search of PubMed, EMBASE, the Cochrane Controlled Trial registry, US Clinical Trials databases was performed until August 2019 using these key terms: ST-elevation myocardial infarction, coronary revascularization and multivessel disease, complete revascularization, culprit only revascularization and preventive angioplasty. No language limitations were imposed in the search strategy. Reference lists of included articles were also examined for additional studies. To identify studies reported only in scientific meetings, we performed electronic search of the annual scientific sessions of the American College of Cardiology, the American Heart Association, and the European Society of Cardiology. The search strategy, study selection and analysis were carried out in accordance with the PRISMA statement for systematic reviews.[7]

Study Selection.

All selected abstracts and titles were independently scanned, and data extraction was then performed independently by the co-primary authors (HG and RG). Studies included in this analysis were required to have - a) randomized controlled study design; b) a clearly defined intervention (complete revascularization) group and control groups (Culprit only PCI); c) outcome data available such as all cause mortality, new myocardial infarction, and repeat revascularization. This review incorporates only those randomized controlled trials for analysis, which reported baseline and follow up data for both intervention and control groups. Observational studies and case reports were not included for the analysis.

Data extraction and risk of bias assessment.

Clinical, interventional, and outcome data were extracted from individual studies by 2 independent abstractors (HG and RG) and entered into a data extraction form. This included information about study design, patient characteristics (age, gender, intervention strategy (Complete PCI versus Culprit only PCI), cardiac death, non-cardiac deaths, nonfatal MI, refractory angina and revascularization (PCI or coronary artery bypass grafting).

Statistical Analysis.

Statistical Analysis was performed using STATA version 11.0 [StataCorp. 2009. Stata Statistical Software: Release 11. College Station, TX: StataCorp LP] and using Cochrane Collaborative software, RevMan 5.3. All p-values were two-tailed with statistical significance specified at < 0.05 and confidence intervals (CI) computed at 95% level. Measure of heterogeneity between the studies was assessed using the chi square test and was considered significant if p values < 0.10 or I2 > 50%.

Outcome Variables.

Primary outcome of interest was major adverse cardiac events (MACE), which is a composite of all cause mortality, new myocardial infarction, and repeat revascularization between the two groups namely Complete PCI and Culprit only PCI. Other clinical outcome studied was repeat revascularization rates between the two groups. Studies comparing Complete PCI versus staged PCI or staged PCI versus Culprit only PCI were excluded from the analysis. Odds Ratio (OR) and their respective 95% confidence intervals (CI) were estimated for each study and for the analysis of primary and individual clinical outcomes. We assessed the heterogeneity using the Higgins I2 test.[8] I2 >50% was considered to show significant heterogeneity in this meta-analysis.[8] Random effects model described by Der-Simonian and Laird was used for our main analysis.[9]

RESULTS

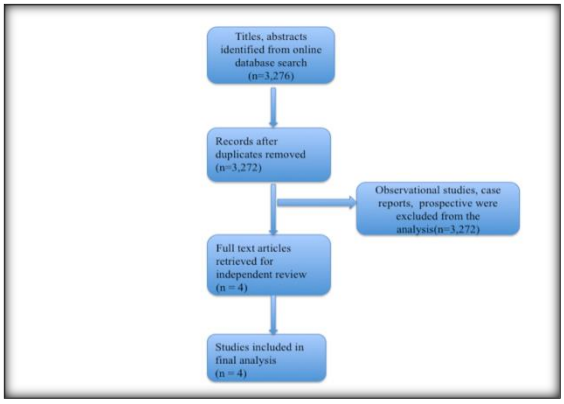

Figure 1: Search strategy according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist (PRISMA).

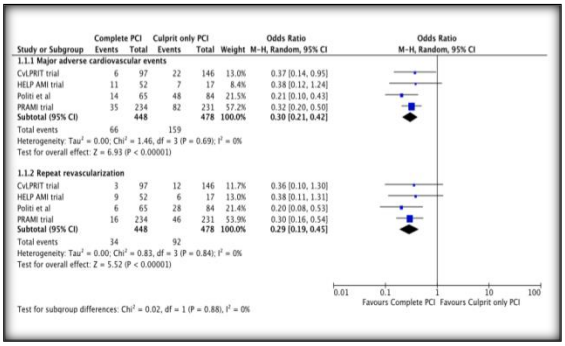

Figure 2: Forest plots comparing the outcomes with Complete PCI and Culprit only PCI OR= Odds Ratio; CI = confidence interval.

Table 1: Baseline characteristics of studies included in our analysis.

Characteristics	Wald et al (PRAMI Trial) [6]	Politi et al [10]	Gershlick et al (CvLPRIT Trial) [5]	Di Mario Carlo et al (HELP AMI) [11]
Total number of patients included in our study	465	149	243	69
Patients with complete revascularization (CR)	234	65	97	52
Patients with infarct related revascularization (IRA)	231	84	146	17
Study outcomes (including primary and secondary end points)	Primary outcome was composite of death from cardiac causes, nonfatal myocardial infarction, or refractory angina. Individual outcomes studied were death from non cardiac causes, repeat revascularization (PCI or CABG)	Primary outcome was composite of cardiac or non-cardiac death, in-hospital death, re-infarction, re-hospitalization for acute coronary syndrome and repeat coronary revascularization. Individual outcome studies were repeat revascularization (PCI or CABG)	Primary outcome was composite of all-cause mortality, recurrent myocardial infarction (MI), heart failure hospital admission, and repeat revascularization. Individual outcomes studied were all cause mortality, recurrent MI, repeat revascularization.	Repeat revascularization over a period of 12 month (any revascularization, infarct-related artery as well as non-infarct related artery)
Major adverse cardiovascular events (MACE) CR IRA	 35 82	 14 48	 6 22	 11 7
Repeat Revascularization CR IRA	 16 46	 6 28	 3 12	 9 6
Inclusion criteria	STEMI patients with successful PCI of infarct related artery and stenosis of 50% or more in one or more coronary arteries other than infarct artery	STEMI patients with >70% stenosis of two or more epicardial arteries or major branches	STEMI patients with multivessel disease; with infarct related artery plus at least one non-infarct related epicardial artery with at least one lesion deemed angiographically significant (>70% diameter stenosis in one plane or > 50% in 2 planes).	STEMI patients with multivessel disease and one or more with a maximum of 3 lesions in non-culprit artery technically amenable to revascularization
Exclusion criteria	Patients with cardiogenic shock, previous CABG, non infarct related artery stenosis of 50% or more in left main stem or the ostia of both left anterior descending or circumflex artery, chronic total occlusion of non-infarct related artery	Cardiogenic shock, left main disease > 50%, previous CABG, severe valvular heart disease or unsuccessful procedure. All patients who underwent stage PCI were excluded in our study.	Cardiogenic shock, previous CABG, ventricular septal defect, moderate/severe mitral regurgitation, chronic kidney disease, chronic total occlusion of non infarct related artery, suspected/confirmed thrombosis of previously stented artery. All patients who underwent stage PCI were excluded in our study.	Significant disease in vein grafts or arterial conduits or in segments previously treated with angioplasty or stent implantation, recent thrombolysis, cardiogenic shock, left main disease > 50%), or unsuccessful procedure or intention to treat more than one totally occluded major epicardial vessel

PCI: percutaneous coronary intervention, CABG: coronary artery bypass grafting, STEMI: ST-segment myocardial infarction
MACE: Major adverse cardiovascular events defined as composite of all cause mortality, new myocardial infarction, and repeat revascularization between the two groups namely CR and IRA revascularization

A total of 3276 abstracts were identified by our electronic database search. After removing, duplicates, non-relevant publications, we accessed 4 full text articles for eligibility and independent review [Figure 1]. Additional online search engine records from scientific meetings were also identified. Finally, 4 randomized control trials involving 926 patients were included in the present analysis (5, 6, 10, 11) [Table 1]. Of 926 patients, 448 patients were randomized to Complete PCI and 478 patients to Culprit only PCI groups.

Major adverse cardiovascular events

Major adverse cardiovascular events occurred in 66 of 448 (14.7%) patients in Complete PCI group as compared with 159 of 478 (33.2%) patients in Culprit only PCI revascularization group. There was a statistically significant reduction in MACE in the Complete PCI group compared to Culprit only PCI group (OR 0.30; 95% CI 0.21-0.42, p<0.001). There was no evidence of heterogeneity (I2 = 0%, p=0.69) [Figure 2].

Repeat revascularization

Repeat revascularization events occurred in 34 of 448 (7.5%) patients in Complete PCI group as compared with 92 of 478 (19.2%) patients in Culprit only PCI group. Complete PCI group demonstrated a significantly reduced revascularization rates (OR 0.29; 95% CI 0.19-0.45, p<0.001) as compared to Culprit only PCI group. There was no evidence of heterogeneity (I2 = 0%, p=0.84).

DISCUSSION

The prevalence of multivessel disease in STEMI patients has been reported to be as high as 60-80%.[12-14] Although the advent of emergent PCI has revolutionized the management of patients with STEMI, it has been unclear if a complete revascularization approach is inferior, equivalent or superior to Culprit only PCI. Current ACC/AHA guidelines recommend revascularization of infarct related artery (IRA) only; and revascularization of noninfarct related stenosed artery at a later time especially in patients with intermediate or high-risk findings on noninvasive testing (staged revascularization).[1] However, the exact time frame for staged revascularization has not been well defined. Complete revascularization can be performed during index PCI or before discharge or even later depending on the other comorbidities and logistics. ACC/AHA gives Class III recommendation (Level of Evidence: B) for primary PCI of non-infarct related artery in hemodynamically stable STEMI patients,[1] however ESC/EACTS classify it as Class IIa (level of evidence B).[15] Evidence against complete revascularization approach has mostly come from retrospective studies and it has been suggested that lesion in non IRA tend to appear more severe in setting of acute MI due to relatively reduced flow.[16,17] Angiographic reevaluation of non-IRA has been reported significantly lesser degree of obstruction when evaluated after resolution of acute MI.

Our results show that there is a statistically significant reduction in rate of major adverse cardiovascular events in patients undergoing Complete PCI compared to those who undergo primary Culprit only PCI. This reduction in MACE is driven primarily by a significant reduction in repeat revascularization rates. Although previous analyses included large number of patients from prospective and RCT's, the lack of homogeneity between the studies was an important limitation of those meta-analyses. Cohort studies are susceptible to confounding effects as they often fail to adjust for unmeasured variables. Thus, meta-analysis of cohort studies might be inaccurate and could be significantly different from those of RCTs.

In this study we only included data only from randomized controlled trials and excluded all observational trials to maintain homogeneity between study groups. In a recent meta-analysis by Pandit et al similar to our study, but including only 3 RCT,[18] demonstrated a statistical significant reduction in cardiovascular deaths, repeat revascularization, and non-fatal MI in patient undergoing complete revascularization as compared to Culprit only PCI. In another recent meta-analysis by Sardar et al (which is similar to ours), there was a statistical significant reduction in MACE, repeat revascularization, cardiovascular mortality and recurrent MI.[19] One of the major limitations of their study was having incomparable groups as they included entire Complete PCI arm from CvLPRIT trial into account (however, according to the study, Complete PCI arm consisted of both complete PCI in single sitting and staged PCI during index hospitalization).[5] In our study, we only included Complete PCI performed in single sitting from all 4 randomized controlled trial and excluded all staged PCI in order to maintain homogeneity between study groups.

There are several limitations in this study. First, a relatively small number of studies were included in our meta-analysis, as we have only included randomized control trials. Another important limitation in our study was inclusion of trials with different study designs and indication to perform revascularization in non-infarct arteries (for example, Politi et al and CvLPRIT trial performed revascularization of non IR artery if greater than 70% stenosis while patients with non IR artery greater than 50% were vascularized in PRAMI trial). Also, our study did not demonstrate any heterogeneity between the studies.

CONCLUSION

Taken together, findings from our study suggest that complete revascularization in patients with acute STEMI is associated with decreased MACE, and repeat revascularization rates as compared to Culprit only PCI. However, further studies with long term follow up looking at clinical endpoints are needed to determine if these findings can translate into significant clinical improvement in these patients.

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