# Preliminary Report on the Safety and Efficacy of Staged versus Complete Revascularization in Patients with Multivessel Disease at the Time of Primary Percutaneous Coronary Intervention

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## Abstract

This study aims to determine the safety and efficacy of complete versus staged-percutaneous coronary intervention (PCI) of nonculprit lesions at the time of primary PCI in patients with multivessel disease. Recent trials had suggested that revascularization of nonculprit lesions at the time of primary PCI is associated with better outcomes, however; the optimum timing and overall safety of this approach is not well known. An observational prospective study was conducted, including 50 patients who presented with ST-segment elevation myocardial infarction and found to have at least an additional nonculprit significant ($>$ 70%) type A or B lesion. According to the operator's discretion, patients either underwent complete revascularization of nonculprit significant lesions during primary PCI procedure or within 60 days of primary PCI (staged-PCI). Safety outcomes evaluated were contrast-induced nephropathy (CIN), the amount of contrast used, and fluoroscopy time. Efficacy outcome assessed was major adverse events (MACE) at 1 year. The fluoroscopy time and amount of contrast used were increased in complete revascularization group (35.3 $\pm$ 9.6 vs. 26.3 $\pm$ 6.7 minutes, $p < 0.001$, and 219.5 $\pm$ 35.1 vs. 187.5 $\pm$ 45.5 mL, $p = 0.01$, respectively); while incidence of CIN remained similar ($p = 0.73$). The incidence of MACE at 1 year was similar in both groups (23% in the complete revascularization group vs. 25% in the staged-PCI group, $p = 0.43$). Complete revascularization and staged-PCI of nonculprit type A or B lesions at the time of primary PCI were associated with similar long-term outcomes and safety profile. Larger studies are needed to further validate these results.

**Keywords**

- ST elevation myocardial infarction
- revascularization
- primary percutaneous coronary intervention

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Primary percutaneous coronary intervention (PCI) is currently the treatment of choice in patients with ST elevation myocardial infarction (STEMI).[1] Approximately, 30 to 40% of patients presenting with STEMI are found to have concomitant significant lesions (nonculprit lesions) and have been known to have worse outcomes.[2–4] The best approach for revascularization of the nonculprit lesions has remained an area of debate.[5] The American College of Cardiology (ACC) and the American Heart Association (AHA) guidelines recommended culprit vessel PCI for STEMI patients with multivessel disease at the time of the index PCI unless the patients are hemodynamically compromised.[6] These recommendations were based on retrospective and nonrandomized studies.[7–10]

Recent trials and meta-analyses had shown that complete revascularization was associated with lower incidence of major adverse cardiac events (MACE) driven mainly by a future reduction in the risk of revascularization.[11–14] However, in these recent studies the safety of this approach was not addressed. Furthermore, the optimum timing for performing revascularization of the nonculprit lesions (i.e., at the index procedure vs. staged procedure) remains unknown. In this study, we sought to compare the safety along with the long-term outcomes of staged-PCI versus complete revascularization in patients with multivessel coronary artery disease undergoing primary PCI.

## Methods

### Study Population

We enrolled 50 patients who presented to our tertiary medical center with acute STEMI with the onset of symptoms $< 12$ hours, and found to have multivessel disease demonstrated by coronary angiography, that is, one or more significant ($> 70\%$) nonculprit lesions—type "A" or "B" lesions—besides the culprit lesion in the infarct-related artery. Lesion classification was done according to the ACC/AHA PCI guidelines. Type A lesions were lesions that were nonostial, discrete, concentric, smooth, and readily accessible, located in a nonangulated segment ($< 45$ degrees) with minimal or no calcification, and absence of total occlusion, thrombus, or involvement of a major branch. Type C lesions were either diffuse ($> 2$ cm), located after a severely tortious proximal segment or in a markedly angulated segment ($> 90$ degrees), degenerated vein grafts with friable lesions, involvement of major branch that cannot be protected or demonstrating a total occlusion $> 3$ months. Type B lesions were non-A, non-C lesions.[15] Institutional review board approved the study and this study was confirmed according to the Declaration of Helsinki.

Patients were excluded from this study if they: (1) were hemodynamically unstable, (2) exhibited nonculprit lesions of type "C,"[15] (3) had left main coronary artery disease, and (4) had a history of old MI. According to the operator's discretion, the patients were divided into two groups. In the first group, patients underwent PCI to the culprit lesion during the index procedure followed by PCI to the other significant lesions in a later session within 60 days (staged-PCI group). In the second group, patients underwent multivessel PCI during the index procedure (complete revascularization group). All patient received aspirin, clopidogrel, and high-dose statins before the index procedure. Angiographic success of PCI was defined as in-stent residual stenosis of $\leq 20\%$ with thrombolysis in myocardial infarction flow of 3.

### Outcomes and Definitions

Clinical outcomes were the safety and efficacy of complete revascularization compared with staged PCI. For the safety outcomes, we assessed the amount of contrast administered; contrast-induced nephropathy (CIN), and fluoroscopy time. CIN was defined as absolute ($\geq 0.5$ mg/dL) or relative ($\geq 25\%$) increase in serum creatinine at 48 to 72 hours after exposure to a contrast agent compared with baseline serum creatinine values, when alternative explanations for renal impairment have been excluded.[16] Efficacy outcomes included the composite of cardiac death, nonfatal MI, and target vessel revascularization.

All patients were prospectively followed through a 12-month period for adverse cardiovascular events through hospital record review, outpatient visits, and telephone contact.

### Statistical Analysis

Continuous variables were presented as mean $\pm$ standard deviation. Categorical variables were presented as counts and percentages. Differences in baseline and angiographic characteristics were compared using the Wilcoxon rank sum test for continuous variables and the chi-square test for categorical variables.

## Results

Among the 50 patients initially included, 4 patients (3 in complete revascularization group and 1 in staged-PCI group) lost follow-up and were excluded from the study. The baseline characteristics and risk factors were similar in both groups. A total of 55% patients had anterior wall MI. The left anterior descending artery was the commonest culprit vessel among both the groups. In ►**Table 1**, we report the baseline characteristics, infarct wall, and the culprit vessel in both the groups. Six patients developed arrhythmia (five in the staged-PCI group and one in the complete revascularization group) before the PCI procedure.

### Procedural Data

The mean door-to-balloon time was $55.2 \pm 20.6$ minutes in the staged-PCI group versus $56.8 \pm 16.7$ minutes in the complete revascularization group ($p = 0.77$). In ►**Table 2**, we summarize the procedure characteristics in both groups.

In the staged-PCI group, one patient had a distal edge dissection in the culprit vessel, which was treated with an overlapping distal stent. In the complete revascularization group, one patient developed "no reflow" that improved after intracoronary nitrates and verapamil. No bleeding complications were reported in both groups. Three patients in the staged-PCI group developed subcutaneous hematomas at the vascular entry site, two occurred after the staged (second) procedure; one of these cases required surgical intervention. In the complete revascularization group, one patient developed a subcutaneous hematoma that was managed conservatively.

**Table 1** Baseline clinical and angiographic characteristics

| | Staged-PCI group | Complete revascularization group | *p* value |
|---|---|---|---|
| Age, y | 58 ± 12 | 53 ± 11 | 0.15 |
| Male, % | 79 | 77 | 0.88 |
| DM, % | 42 | 32 | 0.49 |
| HTN, % | 46 | 55 | 0.56 |
| Smoker, % | 63 | 59 | 0.81 |
| Dyslipidemia, % | 88 | 82 | 0.59 |
| Positive FH of CAD, % | 21 | 14 | 0.52 |
| Serum creatinine, mg/dL | 1.0 ± 0.31 | 0.94 ± 0.18 | 0.41 |
| **Infarction location** | | | |
| Anterior wall, % | 63 | 50 | |
| Inferior wall, % | 21 | 3 | |
| Lateral wall, % | 0 | 5 | |
| Other, % | 16 | 42 | |
| **Culprit vessel** | | | |
| LAD, % | 63 | 50 | |
| LCX, % | 13 | 5 | |
| RCA, % | 21 | 32 | |
| Other, % | 6 | 13 | |

Abbreviations: CAD, coronary artery disease; DM, diabetes mellitus; FH, family history; HTN, hypertension; LAD, left anterior descending; LCX, left circumflex; PCI, percutaneous coronary intervention; RCA, right coronary artery.

**Table 2** Procedural characteristics

| | Staged-PCI group | Complete revascularization group | *p* value |
|---|---|---|---|
| Number of lesions treated | 2.13 ± 0.34 | 2.09 ± 0.29 | 0.72 |
| Number of stents used | 2.3 ± 0.6 | 2.3 ± 0.4 | 0.91 |
| DES, % | 15 | 28 | 0.29 |
| QCA of nonculprit lesions, mm | 15.3 ± 2.1 | 14.2 ± 2.43 | 0.09 |
| Glycoprotein IIb/IIIa inhibitors, % | 46 | 64 | 0.23 |

Abbreviations: DES, drug-eluting stent; PCI, percutaneous coronary intervention; QCA, quantitative coronary angiography; TIMI, thrombolysis in myocardial infarction.

### Safety Outcomes

The mean fluoroscopy time in the index procedure was higher in complete revascularization group compared with the staged-PCI group (35.3 ± 9.6 and 26.3 ± 6.7 minutes, respectively, $p < 0.001$). The mean amount of contrast used in the index procedure was higher in the complete revascularization group versus the staged-PCI group (219.5 ± 35.1 and 187.5 ± 45.5 mL, respectively, $p = 0.01$). The mean rise in the serum creatinine level in 72 hours was 19.2 ± 30.43% in complete revascularization group versus 16.1 ± 29.6% in staged-PCI group ($p = 0.73$).

### Efficacy Outcomes

The incidence of MACE at 1 year was 23% in the complete revascularization group versus 25% in the staged-PCI group, $p = 0.43$. In the complete revascularization group, one patient expired 2 days after the procedure due to cardiogenic shock while two patients in the staged-PCI group expired, one from cardiogenic shock, and the other from sudden bradyasystole. One patient in the staged-PCI encountered a nonfatal MI due to subacute stent thrombosis 27 days after the procedure and was treated with balloon angioplasty. During the follow-up period, one patient underwent balloon angioplasty for stent restenosis. Two patients (one in each group) underwent coronary artery bypass surgery due to recurrence of ischemia. In ►**Table 3**, we report the MACE outcomes in both the groups.

## Discussion

In this prospective observational study of 50 patients with STEMI who were found to have multivessel disease at the time of primary PCI, we demonstrated that a strategy of complete

**Table 3** Efficacy outcomes at 1 year in both the groups

| Outcome | Staged-PCI group | Complete revascularization group | *p* value |
|---|---|---|---|
| MACE, % | 25 | 23 | 0.43 |
| Cardiac death, % | 8 | 5 | 0.60 |
| Myocardial infarction, % | 1 | 0 | 0.25 |
| TVR, % | 8 | 9 | 0.93 |

Abbreviations: MACE, major adverse cardiac events; PCI, percutaneous coronary intervention; TVR, target vessel revascularization.

revascularization of nonculprit lesions at the time of the index procedure was associated with similar outcomes at 1 year to undergoing a staged-PCI approach. Although the amount of contrast used with the complete revascularization approach was higher, yet the rise in the serum creatinine level or CIN risk was similar. The mean fluoroscopy time was higher with the complete revascularization approach. The total number of stents used per patient was similar with both approaches. We included the patients with type A and B lesions only since these lesions are known to have a high rate of success (> 85 and 60–85%, respectively) with lower incidence of complications.[15,17]

The topic of revascularization of nonculprit lesions at the time of primary PCI has been an area of debate with the more recent meta-analyses demonstrating benefit compared with the older ones.[8,18] Furthermore, two large randomized trials had further supported revascularization of the nonculprit lesions.[11,12] However, these two trials did not address the proper timing to perform the revascularization of the nonculprit lesions. In the complete versus lesion-only primary PCI trial, 21% of the patients underwent staged-PCI within 1.5 days, however; the investigators did not compare the outcomes of the patients who underwent complete revascularization versus a staged-PCI.[12] The results from our study demonstrate that both approaches are similar in terms in safety and long-term efficacy, however; the sample size of our study was small which might have precluded to detect any statistical difference between both the approaches. An ongoing trial, complete versus culprit-only revascularization to treat multivessel disease after primary PCI for STEMI, has been designed to address the safety and efficacy with both the approaches on a larger population.[19]

## Limitations

This study was conducted in a single center with a small sample size. The patients in this study were not randomized and the decision of complete revascularization during the index procedure, versus staged PCI, was according to physician discretion. However; both the groups were similar in regards to the baseline and the procedural characteristics. Furthermore, we did not have information about the second PCI procedure in the staged-PCI group since a big proportion of these patients underwent the second procedure at a different facility. Finally, the significance of nonculprit lesions was not determined hemodynamically by fractional flow reserve (FFR), however; the usage of FFR to guide revascularization of nonculprit lesions at the time of STEMI remains a debatable topic.[20,21]

## Conclusion

Both complete revascularization and staged-PCI of nonculprit type A or B lesions at the time of primary PCI were associated with similar long-term outcomes. The fluoroscopy time and contrast usage were higher with the complete revascularization approach. Larger studies are needed to further validate these results.

Disclosure
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