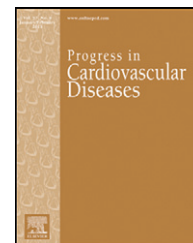


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# Culprit-Only vs. Complete Revascularization During ST-Segment Elevation Myocardial Infarction



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## ABSTRACT

Primary percutaneous intervention (PCI) is the treatment of choice for ST-segment elevation myocardial infarction (STEMI). Patients with STEMI frequently have obstructive non-culprit lesions. In addition, STEMI patients with multivessel disease are at increased risk of major adverse cardiac events. However, current guidelines do not recommend revascularization of non-culprit lesions unless complicated by cardiogenic shock. Prior observational and small randomized controlled trials (RCTs) have demonstrated conflicting results pertaining to the optimal revascularization strategy in STEMI patients with multivessel disease undergoing primary PCI. Recent randomized studies, PRAMI, CvLPRIT, and DANAMI-3-PRIMULTI, provide encouraging data that suggest potential benefit with complete revascularization in STEMI patients with obstructive non-culprit lesions. However, further data from large RCTs are needed to investigate the impact of this strategy on recurrent myocardial infarction/death and to determine the best timing of staged procedures for complete revascularization. Until then, a personalized approach should be taken to optimize the revascularization strategy in STEMI patients with obstructive non-culprit lesions.

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Timely primary percutaneous coronary intervention (PCI) is the treatment of choice for ST-segment elevation myocardial infarction (STEMI).<sup>1</sup> Despite timely and successful restoration of coronary blood flow by PCI, a significant proportion of patients with STEMI remain at substantial risk of recurrent events. Patients with acute coronary syndrome (ACS) with STEMI frequently demonstrate multivessel coronary artery disease (CAD). An analysis of pooled data from multicenter randomized controlled trials (RCTs) showed that roughly 50% of patients undergoing primary PCI for STEMI have obstructive disease ( $\geq 50\%$  stenosis) in a non-culprit artery during index coronary angiography.<sup>2</sup> In addition, that study also demonstrated approximately 50% higher 30-day mortality in patients with obstructive disease in a non-culprit artery.<sup>2</sup>

Furthermore, patients with extensive CAD in a non-culprit artery have reduced reperfusion success, increased major adverse cardiac events (MACE) and higher early and late mortality following PCI compared with patients who have single vessel CAD.<sup>3,4</sup>

The American College of Cardiology/American Heart Association guidelines do not currently recommend revascularization of non-culprit lesions in the setting of STEMI unless complicated by cardiogenic shock.<sup>5</sup> Similarly, the European Society of Cardiology guidelines encourage primary PCI of the culprit-lesion only, unless there is evidence of cardiogenic shock or persistent ischemia after PCI of the culprit-lesion.<sup>6</sup> These recommendations were based on observational studies due to a lack of large RCTs to guide the nature of revascular-

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**Abbreviations and acronyms**

ACS = Acute coronary syndrome

CAD = Coronary artery disease

CV = Cardiovascular

FFR = Fractional flow reserve

HF = Heart failure

LV = Left ventricular

MACE = Major adverse cardiac events

MI = Myocardial infarction

NSTEMI = Non ST-segment elevation myocardial infarction

OMT = Optimal medical therapy

PCI = Percutaneous coronary intervention

RCT = Randomized controlled trial

STEMI = ST-segment elevation myocardial infarction

ization in STEMI patients with multivessel CAD. Treatment options for STEMI patients with multivessel CAD include intervention of the culprit-lesion only, multivessel PCI during the index procedure, or staged PCI either during the index hospitalization or after discharge.

Frequently, patients with STEMI receiving primary PCI undergo treatment of the culprit-lesion only rather than treatment of obstructive non-culprit lesions. The best approach for management of STEMI patients with multivessel CAD who underwent primary PCI of the culprit-lesion with remaining obstructive

non-culprit lesions is not well established. This uncertainty has led to wide variation in practice; some clinicians routinely practice an approach involving optimal medical therapy (OMT) after primary PCI and treatment of non-culprit lesions only if there are symptoms of angina or evidence of ischemia on functional tests. Some routinely perform staged revascularization using PCI or coronary bypass surgery of obstructive non-culprit arteries.

Prior studies investigating the safety and benefit of a complete revascularization strategy versus a culprit-lesion only revascularization strategy in STEMI patients with obstructive non-culprit lesions have shown conflicting results. Many observational and a few small RCTs have shown that treating all obstructive lesions would provide clinical benefit.<sup>7–11</sup> Conversely, some studies have shown that risk of treating obstructive non-culprit lesions outweighs the benefits.<sup>12–14</sup> It was also unclear if immediate complete revascularization is safe and more effective than delayed complete revascularization. Non-randomized data have generally suggested no benefit and possible harm with treatment of obstructive non-culprit lesions during index cardiac catheterization.<sup>12,13,15,16</sup>

In a robust meta-analysis of 46,324 patients with STEMI without hemodynamic compromise, Baine and colleagues explored the efficacy and safety of culprit-lesion only or complete revascularization in patients with STEMI and multivessel CAD undergoing primary PCI.<sup>17</sup> Study participants were recruited from three RCTs and twenty-three non-RCTs; culprit-lesion only and complete revascularization were performed in 83% and 17% of study participants, respectively. The authors reported an in-hospital and long term survival benefit with complete revascularization if a staged procedure was performed during index hospitalization

or after initial hospitalization. Furthermore, the investigators found treatment of obstructive non-culprit lesions to be associated with reduced need for repeat revascularization with a mean follow up duration of 14.5 months. However, if complete revascularization was performed during the index cardiac catheterization, excess in-hospital mortality was seen.

Recently, three randomized trials have tried to resolve the clinical dilemma pertaining to optimal management of STEMI patients with significant multivessel disease.<sup>18–20</sup>

**PRAMI**

In the Preventive Angioplasty in Acute Myocardial Infarction (PRAMI) trial, 465 patients with STEMI and multivessel CAD were randomly assigned to undergo treatment of the culprit-lesion alone or revascularization of all obstructive ( $\geq 50\%$  stenosis) non-culprit lesions as well during index procedure (preventive PCI).<sup>18</sup> The investigators found a 65% reduction in the primary endpoint composite of CV death, myocardial infarction (MI), or refractory angina within 23 months with complete revascularization during the index procedure. Furthermore, a complete revascularization strategy was associated with a 65% reduction in the need for repeat revascularization and a trend towards a lower incidence of CV death. This study suggests that pronounced changes in systemic inflammation, coagulation, and endothelial function in ACS could make non-culprit lesions vulnerable and preventive PCI in the PRAMI trial might have stabilized these lesions and aborted a clinical event. However, it was unknown from this study if the benefit would be similar if the preventive PCI were performed later during the index hospitalization rather than during the index procedure.<sup>21</sup>

**CvLPRIT**

In the Complete versus Lesion-only Primary PCI Trial (CvLPRIT), Gershlick and colleagues randomized 296 patients with STEMI to either in-hospital complete revascularization or culprit-lesion only revascularization.<sup>19</sup> Complete revascularization was performed either at the time of the index procedure or before hospital discharge. The investigators found a significant 53% reduction in the primary endpoint composite of all-cause mortality, recurrent MI, heart failure (HF), or ischemia driven repeat revascularization within 12 months with complete versus culprit-lesion only revascularization. The study was not powered for individual end points; the investigators observed individual components of the primary end point and CV death to be lower in patients randomized to complete revascularization, however these findings were not statistically significant. There was a trend towards greater benefit in two-thirds of the patients who underwent complete revascularization during the index procedure compared with later during the index hospitalization. There was no increase in stroke, major bleeding, or contrast-induced nephropathy with complete versus culprit-lesion only revascularization. Taken together, in a

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