Do We Really Know the CvLPRIT in Myocardial Infarction? Or Just Stent All Lesions?*

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Primary percutaneous coronary intervention (PCI), where available, is the clear treatment of choice for ST-segment myocardial infarction (STEMI) (1). A major controversy is whether to only treat the culprit lesion or to also treat obstructive nonculprit lesions—and when. Many interventionalists believe that treating all significant lesions would provide clinical benefit, but recent guidelines and reimbursement patterns have discouraged this (2). The PRAMI (Preventive Angioplasty in Acute Myocardial Infarction) trial addressed this question in 465 patients and found an ~65% reduction in ischemic events with complete revascularization during the index procedure (3). Questions persisted after this well-done but modestly sized trial, such as whether it was necessary to complete the revascularization during the index procedure or whether it could be staged during the index hospitalization.

In this issue of the Journal, Gershlick et al. (4) have published the primary results of CvLPRIT (Complete versus Lesion-only Primary PCI Trial), which randomized 296 patients with STEMI to complete versus culprit lesion-only revascularization. They found a significant reduction in the primary endpoint of mortality, recurrent myocardial infarction (MI), heart failure, or ischemia-driven revascularization within 12 months with complete versus culprit-only revascularization (10.0% vs. 21.2%; hazard ratio: 0.45; p = 0.009). The reduction in the primary endpoint was evident early, within the first 30 days (p = 0.055). There was a trend toward greater benefit in the approximately two-thirds of patients in whom revascularization was completed during the index procedure versus later during the index hospitalization. The study was not powered for individual endpoints, although all were consistently lower in the complete revascularization group.

Pooled data from international randomized clinical trials show that approximately 50% of patients with STEMI have obstructive disease (>50% stenosis) in a nonculprit artery (5). Furthermore, there was an approximately 50% excess in 30-day mortality associated with the presence of obstructive nonculprit stenoses in this pooled analysis, which remained on adjusted analyses, which implies that “fixing” these nonculprit stenoses very early should decrease 30-day mortality. The early benefits noted in CvLPRIT lend support to this concept. Perhaps, these seemingly stable nonculprit plaques are trouble waiting to happen.

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In patients with STEMI in cardiogenic shock, data from the SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial provided a strong basis for complete revascularization (6). Many interventionalists extrapolated those results to patients with STEMI and multivessel disease but without shock. In contrast, observational data suggested that this approach was not beneficial and might be harmful (7), although with the possibility of differential effects depending on the exact timing of the nonculprit PCI (8). However, despite sophisticated statistical adjustment, nonrandomized analyses can never fully account for unmeasured confounders that may have caused the operator to perform the multivessel PCI, such as the “eyeball test,” in which the patient appears ill in ways that are difficult to capture on a case report form.

Therefore, in contradistinction to the nonrandomized data, we have 2 rigorously performed, albeit modestly sized, contemporary randomized clinical trials, PRAMI and now CvLPRIT, which find substantial benefit from complete revascularization in STEMI patients. Formal patient-level meta-analyses will surely be performed and will likely corroborate the beneficial findings seen in the individual trials (Figure 1). Nevertheless, because the overall sample size will remain modest, the observed degree of benefit may be an overestimation. Still, given the findings of these 2 trials, even if the experiment were repeated, it is unlikely that the complete revascularization approach would be found harmful.

The debate over whether to stent nonculprit lesions in STEMI has occurred in a larger context. After the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial, there has been a swing to treat nonacute lesions more conservatively (9). Using fractional flow reserve guidance in stable lesions, FAME 2 (Fractional Flow Reserve versus Angiography for Multivessel Evaluation 2) showed a reduction in death or MI in landmark analyses after discounting periprocedural events during the first week (10). Although the number of events was low, the FAME 2 data support the concept that stenting severe ischemia-causing lesions in stable patients not only reduces the need for future urgent revascularization but may also reduce death or MI. The ongoing ISCHEMIA (International Study of Comparative Health Effectiveness With Medical and Invasive Approaches) trial (11) should provide further insight into the impact of stenting stable lesions.

The older SWISSI II trial (Swiss Interventional Study on Silent Ischemia Type II) found that in 201 patients with recent MI and silent ischemia, those randomized to full percutaneous revascularization had a lower major adverse cardiac event rate than those treated medically (12). Thus, the question of whether to treat “stable” lesions in STEMI patients might be quite different from whether to treat “stable” lesions in stable patients. Patients with STEMI have already demonstrated the ability to rupture plaque and form occlusive thrombus once and may be more likely to do it again, potentially in the short term. Thus, they may represent a different phenotype from those with severe stable plaque but no prior ischemic events.

The large, ongoing COMPLETE (Complete vs. Culprit-only Revascularization to Treat Multi-vessel Disease After Primary PCI for STEMI) trial (13), powered for cardiovascular death or MI, will provide a more detailed evaluation of the question of complete versus culprit revascularization, although differences in study design may limit direct comparisons. The role of fractional flow reserve in potentially refining the treatment of the nonculprit lesions merits further study, although lesion stability, as well as lesion severity, may need assessment. How the results of PRAMI and CvLPRIT should be interpreted in non-STEMI remains an open question (14). Second-generation and third-generation drug-eluting stents may further favorably affect the balance toward more aggressive revascularization (15). Many interventionalists will find the CvLPRIT data consistent with their preexisting beliefs and the data compelling.

**Figure 1** Pooled Analysis of CvLPRIT and PRAMI Trial-Level Data for Cardiac Death, MI, and Revascularization

Boxes represent hazard ratios (HR); lines represent 95% confidence intervals. CvLPRIT = Complete versus Lesion-only Primary PCI Trial; MI = myocardial infarction; PRAMI = Preventive Angioplasty in Acute Myocardial Infarction.
enough to change practice. In contrast, trialists and guideline writing committees will probably demand further randomized data to provide more robust estimates of benefit, more definitively evaluate effects on “hard” outcomes (Figure 1), and resolve issues regarding the exact timing and nature of the complete revascularization.

For now, a very reasonable approach would incorporate clinical judgment. In a patient with STEMI undergoing primary PCI who is in borderline cardiogenic shock—in whom the numbers do not really meet the definition, but the blood pressure is low, for example—complete revascularization during the initial procedure may make good sense. In a hemodynamically stable patient with relief of chest pain after stenting the culprit right coronary artery lesion, it may be prudent to defer treatment of a complex left-sided bifurcation lesion until later in the hospitalization. Factoring in hemodynamic status, renal function, lesion severity/complexity, left ventricular function, vascular access/bleeding risk, and time of day/night may be the most appropriate way to determine whether to treat the nonculprit lesion(s) during the initial procedure or later during the hospitalization, or to defer treatment decisions to the outpatient setting, while awaiting the accrual of additional trial data.

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REFERENCES


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