INTERVENTIONAL STRATEGIES FOR ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION AND MULTIVESSEL CORONARY ARTERY DISEASE*

John A. Bittl, MD
Ocala, Florida

Many patients with ST-segment elevation myocardial infarction (STEMI) have multivessel coronary artery disease (CAD) (1, 2), yet interventional cardiologists can almost always identify a single lesion responsible for the infarction. After successful percutaneous coronary intervention of the infarct-related lesion (culprit PCI), there are 2 competing strategies available for STEMI patients with multivessel CAD. Additional lesions in noninfarct vessels can be treated immediately at the same sitting (multivessel PCI) or they can undergo delayed evaluation and treatment during another session (staged PCI).

Practice guidelines concerning multivessel PCI during STEMI written by the major cardiac societies are similar in intent but different in tone and classification. The writing group for the American College of Cardiology Foundation and American Heart Association makes a restrictive “thou shalt not” recommendation by stating, “PCI should not be performed in a noninfarct artery at the time of primary PCI in patients without hemodynamic compromise. (Class III Harm, Level of Evidence: B)” (3). The writing group for the European Society of Cardiology and the European Association for Cardio-Thoracic Surgery makes a more permissive “thou shalt” recommendation by stating, “With the exception of cardiogenic shock, PCI for STEMI should be limited to the culprit stenosis (Class IIa, Level of Evidence: B)” (4). Although the language differences seem trivial, the classification differences (Class III Harm vs. Class IIa) between the American and the European guidelines have significant implications for practice appropriateness.

Most evidence against performing multivessel PCI during STEMI has been indirect or retrospective. Mechanistic studies suggest a cautious approach, because lesions in noninfarct arteries appear to be more severe (5) and flow in noninfarct vessels to be more reduced (6) during an acute MI than in the absence of an MI. Hanratty et al. (5) reported that in 21% of patients, lesions initially assessed as >50% during infarct angiography became <50% during noninfarct angiography (5).

Retrospective analyses also support a cautious approach to multivessel PCI during STEMI. In a cohort analysis published in this issue of the Journal, Kornowski et al. (7) report that multivessel PCI performed in the HORIZONS-AMI (Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction) trial was associated with a higher 1-year mortality (9.2% vs. 2.3%) and stent thrombosis rate (5.7% vs. 2.3%) than staged PCI. And in a meta-analysis published in this issue of the Journal, Vlaar et al. (8) report that multivessel PCI was associated with a 60% higher risk of long-term mortality than culprit PCI (odds ratio [OR]: 1.6, 95% confidence interval [CI]: 1.3 to 2.0). Multivessel PCI was also associated with a higher long-term mortality than staged PCI (OR: 5.3, 95% CI: 2.3 to 122).

Multivessel PCI in practice. Whereas retrospective studies report unfavorable outcomes and guidelines discourage multivessel PCI during nonshock STEMI, the practice remains relatively common. In the HORIZONS-AMI study, 18.5% of patients underwent multivessel PCI but only 1.5% had cardiogenic shock (7). In the APEX AMI (Assessment of Pexelizumab in Acute Myocardial Infarction) trial, 9.9% of patients underwent multivessel PCI (1) but only 1.0% was in Killip class IV (9). In the New York State Registry, 12.5% underwent multivessel PCI, but only 4.4% met the definitions of hemodynamic compromise (10).

Reasons for the use of multivessel PCI in 10% to 20% of STEMI cases cannot be explained by financial incentives, which would favor the strategy of staged PCI, but may be explained by the presence multiple complex lesions that appear to be pathogenic (2). Patients who die of MI often have >1 culprit lesion. In an autopsy series of 100 patients, Davies and Thomas (11) observed 115 separate thrombi in 74 patients and concluded that the majority of patients who die within 6 h of MI have “one or more rapidly developing arterial lesions.” In some cases, identifying a single culprit lesion in the presence of multivessel CAD may be hampered by the variable ability of the electrocardiogram to localize infarctions (12). While ST-segment elevation in 2 or more of leads I, aVL, or V1 to V4 may be predictive of disease in the left anterior descending artery (LAD), ST-segment elevation in 2 or more of leads II, III, or aVF may not distinguish between disease in the right coronary, the distal LAD, or the left circumflex coronary artery (12). Lateral MIs with ST-segment elevation in leads I and aVL may be

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From the Ocala Heart Institute, Munroe Regional Medical Center, Ocala, Florida. Dr. Bittl has reported that he has no relationships to disclose.
more likely caused by diagonal occlusion than by left circumflex disease (12).

**Limited evidence.** Patients undergoing culprit PCI, multivessel PCI, or staged PCI are inherently different from each other. The STEMI patients with multivessel CAD have higher mortality rates than patients with single-vessel CAD (13). Patients undergoing multivessel PCI have lower ejection fractions than patients undergoing staged PCI (50% vs. 55%) (7).

Cohort studies, based on the analysis of records, cannot identify the reasons for the selection of 1 PCI strategy over another. In the HORIZONS-AMI trial analysis (7), “the specific reasons why operators chose a single procedure vs. a staged approach were not prospectively collected.” Although many demographic features may have been similar between the treatment groups (8), other variables such as multiple complex lesions, left ventricular dysfunction, or persistent hemodynamic instability are more common in patients undergoing multivessel PCI. By failing to consider such covariates, cohort studies are susceptible to confounding.

Meta-analyses accrete the confounding effects and overstate the strength and precision of individual-trial results (14). Statistical adjustments cannot eliminate confounding when treatment decisions are based on unmeasured variables, and propensity analyses cannot produce accurate models if few patients have overlapping risks. When confounding occurs, as in the classic case of hormonal replacement therapy for cardiac prevention in postmenopausal women, cohort studies may yield different results than controlled trials.

In the current meta-analysis (8), the results of the large cohort studies seem to disagree with the results of smaller prospective studies. The pooled results of 9 cohort studies of 5,128 patients (8) suggested higher long-term mortality after multivessel PCI than after culprit PCI (OR: 1.8, 95% CI: 1.4 to 2.2), whereas pooled results of 3 prospective studies of 288 patients suggested no difference (OR: 0.7, 95% CI: 0.3 to 1.6). No prospective trial was large enough to show a significant mortality difference, but a randomized trial (15) reported nominally lower mortality rates after multivessel PCI than after culprit PCI (9.2% vs. 15.5%).

The results of the current meta-analysis (8) also appear to contradict the conclusions of other contemporary meta-analyses (16,17), which suggest no difference in long-term mortality rates after multivessel PCI or culprit PCI (OR: 1.1, 95% CI: 0.8 to 1.6). Because of methodological differences, “it is not uncommon to find that 2 or more meta-analyses done at about the same time by investigators with the same access to the literature reach incompatible or even contradictory conclusions” (14). Interpreting conflicting trial results remains challenging, but framing the problem within the clinical context may provide perspective.

**Practical considerations.** Practice guidelines define a standard, but they are not commandments. No single approach is applicable to the myriad presentations of STEMI. However, a reasonable first step (despite the pressure to shorten door-to-balloon times) involves both right and left coronary angiography with diagnostic catheters to assess the entire coronary anatomy before a lesion is targeted for PCI. After culprit PCI, almost all patients show improvement. Patients with severe multivessel CAD may require follow-up angiography. Fractional flow reserve can be considered during the acute phase (18), but the results should be used whenever possible to support a decision for staged PCI.

Practice guidelines do not support the practice of multivessel PCI during noshock STEMI (3,4). However, no set of recommendations governs the treatment of every patient in every clinical situation. Multivessel PCI may be necessary in some STEMI patients who have multiple complex lesions and do not improve after culprit PCI.

Reprint requests and correspondence: Dr. John A. Bittl, Ocala Heart Institute, 1221 SE 5th Street, Ocala, Florida 34471. E-mail: jabittl@mac.com.

**REFERENCES**


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