In patients with acute coronary syndrome (ACS), the pathophysiological process is not limited to a single coronary lesion but involves the entire coronary tree, with 30% to 60% patients presenting with multiple significant coronary lesions, with significant increase in cardiovascular morbidity and mortality in patients with multivessel coronary artery disease.1,2 In the Predictors of Events in the Coronary Tree trial, patients with ACS who underwent percutaneous coronary intervention (PCI), major adverse cardiovascular events occurring during follow-up were equally attributable to recurrence at the site of culprit lesions and to nonculprit lesions, which were frequently angiographically mild.3 In contrast, in the COURAGE trial in patients with stable coronary artery disease (CAD) on optimal medical therapy, the only angiographic predictor of future ACS was the number of lesions originally ≥50% that had not been revascularized.4 The above studies attest to the importance of both angiographically significant lesions as well as angiographically mild lesions on future events. These studies highlight the importance of a multipronged approach with the use of evidence-based aggressive medical management (to prevent progression of angiographically mild and also significant CAD), as well as judicious use of optimal revascularization strategies. Several surgical studies have shown that incomplete revascularization in patients undergoing coronary artery bypass graft surgery has worse prognosis with higher mortality, myocardial infarction (MI), and more angina.5–7 As a result, complete anatomic revascularization has become the standard of treatment for coronary artery bypass graft surgery. The concept has been adapted by interventionalist to patients undergoing PCI with several studies (nonrandomized), including an analysis from the Bypass Angioplasty Revascularization Investigation 2 Diabetes trial8 showing substantial increase in cardiovascular events with incomplete revascularization. Similarly, in the Acute Catheterization and Urgent Intervention Triage Strategy trial of patients with nonST-segment elevation ACS, incomplete revascularization was associated with increased risk of major adverse cardiac events, MI, and numerically higher mortality when compared with patients with complete revascularization.9 In many of the above observational studies, patients who underwent incomplete revascularization were in a higher-risk group with lesions less amenable to PCI, and it is difficult to rule out the effect of baseline confounding on worse outcomes in this cohort. Moreover, recent data from surgical registries seem to suggest that a strategy of reasonably incomplete revascularization may be acceptable.10 Similarly, in the DEFER trial, patients with intermediate stenosis without functionally significant lesion (as measured by fractional flow reserve [FFR]), randomized to deferral of PCI had similar outcomes at 5 years, when compared with the patients randomized to the performance of PCI.11 These and other results therefore seem to suggest that complete anatomic revascularization may not be a necessity.

In this issue of Circulation: Cardiovascular Interventions, Hannan et al12 evaluate the outcomes of staged versus one-time complete revascularization with PCI in patients with multivessel CAD without ST-segment elevation myocardial infarction. The topic is timely and relevant for several reasons: First, although there is a recent increase in interest in strategies for how best to treat nonculprit lesion in patients with ST-segment elevation myocardial infarction, this is less so for ACS patients without ST-segment elevation myocardial infarction and for patients with stable CAD. Second, there is no clear guideline recommendation on staging in patients without ST-segment elevation myocardial infarction, which has led to variability in practice patterns. Third, the safety of deferring/staging PCI of a significant lesion is not well defined, especially in patients with ACS. Fourth, given the decreasing volume of coronary interventions in the United States, staging creates incentive for interventionalist to meet the PCI volume requirements artificially and for the hospital, given the additional reimbursement for a staged procedure. Finally and most the Centers for Medicare and Medicaid Services is experimenting with bundled payment initiatives, whereby hospitals and physicians would not receive additional payment for staged readmissions.

The results of the present study from a highly select group of patients without an overarching clinical indication for staging (such as presence of chronic total occlusions, major complications at first procedure, higher volume of contrast used) suggests that the 3-year mortality were similar for staged versus one-time complete revascularization either for patients with ACS or CAD patients, leading the authors to conclude that there is no mortality benefit to justify the extra cost of a staged procedure. There are several advantages of a one-time complete revascularization. First, it avoids the risk of procedural complications arising out of a second procedure, especially access site-related complication; Second, it is convenient and preferable to patients as it avoids a second hospital visit and a second post procedural care (bed rest, restriction on physical activity, and others); Third,
it is more cost effective and likely will result in enormous cost savings and at the same time is associated with similar long outcome when compared with a staged procedure. Finally, data from this study suggests that ≈1900 patients scheduled for staging did not undergo a staged PCI and is consistent with data suggesting that the majority of patients with multivessel CAD undergoing PCI receive incomplete revascularization. A one-time staging thus avoids this risk of incomplete revascularization. The premise of a Centers for Medicare and Medicaid Services bundled payment initiative is to improve health, improve the quality of care, and lower costs. A one-time complete revascularization fits this bill, as it can potentially lower cost but not necessarily result in major improvement in health or quality of care. However, it is unlikely that a one-size fits all strategy will be applicable to all patients and in a subgroup of patients a staged procedure may be preferred and even necessary due to patient- or physician-related factors and other factors not captured in the current database (frailty, patient preference, high-radiation dose, complex anatomy, or even laboratory throughput and physician fatigue). The results of this study suggest that staging is performed only in a minority of patients (20%–30%) and that this strategy of deferring PCI was safe without increased risk of death. The study has obvious limitations of a registry-based analysis, including lack of information for reason for staging and evaluating anatomic completeness, rather than the current gold standard of complete functional revascularization.

The Fractional Flow Reserve Versus Angiography for Multivessel Evaluation (FAME) trial13 changed the paradigm of complete revascularization for PCI from an anatomic one to that of a complete functional revascularization. In FAME, of all patients with angiographically defined multivessel disease, only 46% had functional (as measured by FFR) multivessel disease.13,14 A strategy of stenting based on fractional flow reserve (FFR) value <0.80 resulted in a 28% reduction in the risk of composite outcome of death, MI, and repeat revascularization compared with a strategy of stenting based on angiography alone. In addition, there were other advantages of an FFR-based functional strategy, including a significant reduction in the mean number of stents implanted (1.9 versus 2.7 stents; P<0.001), reduction in volume of contrast used (mean, 272 versus 302 mL; P<0.001),13 and was cost effective.15 Moreover, a functional strategy incorporating information about hemodynamic significance of a lesion leads to a recategorization of complexity of coronary anatomy with 32% shift toward a lower-risk group.16 In addition, data in patients undergoing coronary artery bypass graft surgery suggest that the patency rates of bypass grafts were significantly higher in functionally significant lesions (determined by FFR) than the patency rates in nonsignificant lesions.17 It therefore seems that a strategy of complete functional revascularization leads to better health, improves quality of care, and reduces cost, and thus satisfies all of the 3 premises of the Affordable Care Act and the Centers for Medicare and Medicaid Services bundled payment initiative. In addition, this strategy reduces the prevalence of functional multivessel disease, decreases the number of lesions that need to be treated, thereby potentially reducing the need for a staged procedure.

The current body of evidence with data derived from contemporary randomized clinical trials suggests that in patients with ACS, revascularization improves long-term survival, reduces MI and rehospitalization for unstable angina compared with medical management alone.18 In patients with stable ischemic heart disease, data from randomized trials suggest no difference in death or MI between PCI and medical therapy, with a suggestion of greater/faster freedom from angina.19 It is therefore prudent that in contemporary practice, revascularization is the preferred approach for all high-risk patients with ACS and selectively for stable patients with CAD who fail medical therapy. Just like the pundits for an optimal medical therapy approach would strongly advocate the use of the right medication at the right dose before qualifying as optimal, it behooves that once a patient is referred for revascularization, a strategy of optimal revascularization which in this day and age translates to a heart team approach for complex coronary artery disease, appropriate referral to coronary artery bypass graft surgery where needed, and complete functional revascularization using the best available stents,20 adjunctive pharmacotherapy, with meticulous attention to optimize stent deployment and minimize complications, should be used.

Disclosures
None.

References


Key Words: Editorials ■ complete revascularization ■ functional complete revascularization