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EDITORIAL COMMENT

Incomplete Revascularization in Patients Treated With Percutaneous Coronary Intervention

When Enough Is Enough*

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The optimal degree of revascularization for patients with multivessel coronary artery disease is not well established. Although there is growing evidence to support early and more complete revascularization of significant noninfarct artery stenoses among selected patients with ST-segment elevation myocardial infarction (STEMI) (1,2), there are few prospective studies evaluating patients with acute coronary syndromes or stable coronary disease to support a similar approach (3,4). Therefore, the decision whether to pursue multivessel or more limited percutaneous coronary intervention (PCI) continues to remain discretionary, and dependent on multiple factors including the patient's clinical status, severity and distribution of the coronary artery disease, characteristics of the stenoses, degree and location of ischemic and/or viable myocardium, left ventricular function, and other comorbidities.

However, the advantage of a strategy of complete revascularization to decrease subsequent cardiovascular events seems intuitive. This concept was supported by early studies in patients undergoing coronary artery bypass graft (CABG) surgery where the benefit of complete revascularization was demonstrated (5). Furthermore, subsequent randomized clinical trials comparing CABG with PCI in patients with multivessel disease showed CABG was associated with improved outcomes (particularly in patients with diabetes and with complex coronary anatomy) (6,7), mostly due to less repeat revascularization (6,8,9). Yet, since its introduction into clinical practice, single vessel ("culprit lesion") PCI has been performed in the majority of patients with multivessel disease, fueled by the concept of correct identification of the "culprit lesion" and by favorable outcomes associated with this approach (10). Indeed, in the 1977 to 1981 initial National Heart, Lung and Blood Institute (NHLBI) Percutaneous Transluminal Coronary Angioplasty (PTCA) registry, 25% of patients had multivessel disease, and 14% of procedures involved attempts to dilate lesions in more than 1 vessel (11). In more contemporary experience, nearly 72% of patients undergoing PCI within the National Cardiovascular Data Registry in 2010 to 2011 had multivessel disease although 86% underwent single-vessel PCI (12). Moreover, in the SYNTAX (SYNergy between PCI with TAXus and Cardiac Surgery) trial comparing PCI and CABG for triple-vessel or left main disease, complete revascularization was performed in only 56.7% of patients in the PCI group (9).

SEE PAGE 207

In this issue of *JACC: Cardiovascular Interventions*, Hambraeus et al. (13) describe the practice of incomplete revascularization and its association with a pre-defined composite endpoint of all-cause death, myocardial infarction, and repeat revascularization at 1 year. Patients with multivessel coronary disease treated with PCI between 2006 and 2010 within an observational study of prospectively collected data from SCAAR (Swedish Coronary Angiography and Angioplasty Registry) merged with official Swedish

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health data registries were evaluated. Of 23,342 patients, 15,165 (65%) were classified as incomplete revascularization at the end of the index procedure. Incomplete revascularization was defined as any untreated significant stenosis (more than 60% of the vessel diameter) in a coronary artery supplying more than 10% of the myocardium. Incomplete revascularization patients were older with more comorbidities and higher prevalence of female sex, more often presented with STEMI, received more emergency procedures during the afterhours, had more extensive coronary disease, received fewer stents and more drug-eluting stents, and were more likely to be discharged with long-acting nitroglycerin. All-cause mortality (7.1% vs. 3.8%), myocardial infarction (10.4% vs. 6.0%), and repeat revascularization (20.5% vs. 8.5%) were higher in the incomplete compared with the complete revascularization group. Propensity score matching (39% of the incomplete revascularization group) revealed a significantly higher adjusted hazard ratio (HR) for the composite of death, myocardial infarction, or repeat revascularization at 1 year in the incomplete revascularization group (HR: 2.12; 95% confidence interval [CI]: 1.98 to 2.28; $p < 0.0001$). Adjusted HR for death (1.29, 95% CI: 1.12 to 1.49; $p = 0.0005$) and death/myocardial infarction (1.42, 95% CI: 1.30 to 1.56; $p < 0.0001$) was also higher, suggesting that incomplete revascularization at the time of hospital discharge was associated with an increased risk of adverse outcomes within 1 year.

This study adds to growing evidence suggesting that complete revascularization should be the preferred strategy in patients with multivessel coronary disease and that it is related to favorable outcomes. Notwithstanding the absence of data that would influence the revascularization approach including clinical (recurrent ischemia, ongoing angina symptoms), functional (left ventricular ejection fraction, resting or stress echocardiography, myocardial perfusion studies, or other imaging modalities), specific anatomic (presence of chronic total occlusions), and hemodynamic (fractional flow reserve) variables, or procedural restrictions and challenges (volume of contrast, radiation dose, operator fatigue), the present study is fortified by experienced investigators and a robust database that has contributed to numerous clinical studies. Moreover, thoughtful analyses were performed to account for baseline differences between groups, potential staged PCI procedures, duration of dual antiplatelet therapy, and change in revascularization group following subsequent PCI. However, perhaps most important, is the absence of the intent of revascularization, that is, whether incomplete revascularization was intended or the result of a procedural complication or an uncomplicated technical failure.

Observational studies comparing complete with incomplete revascularization have been limited by the bias to perform incomplete revascularization in sicker, more complex patients and by the lack of a universal and consistent definition of the terms. Revascularization decisions are often based upon the integration of factors not routinely collected in registries (or in those excluded from participation in randomized trials) such as frailty, bleeding risk, ability to comply with dual antiplatelet therapy, patient preference and quality of life. Revascularization approaches are also based upon the potential to achieve completeness defined on an anatomic basis as well as on a functional basis. Whereas complete anatomic revascularization is most often defined as treatment of all stenoses greater than or equal to either 50% or 70% of vessel diameter in vessels with distal size >1.5 or 2.0 mm in diameter, complete functional revascularization is defined as treatment of all anatomically significant stenoses (or with fractional flow reserve ≤0.8) serving ischemic, viable, or noninfarcted myocardium. This supports the concept of incomplete anatomic, but complete functional, revascularization that is both adequate and may be intended. It follows that incomplete revascularization that is unintended would occur when all lesions serving viable myocardium are not adequately treated.

Prior smaller studies and subset analyses have shown that planned or intended incomplete revascularization in patients with multivessel coronary disease is unrelated to risk of cardiac death or death/myocardial infarction, but independently associated with subsequent CABG at 5 years (10,14). Moving forward, it will be helpful to adequately evaluate a strategy of intended, incomplete, but functionally adequate PCI, particularly in patients deemed to be at high risk for complete revascularization (that may be unnecessary). Careful consideration of the spectrum of incomplete revascularization employing catheter-based tools to measure fractional flow reserve and assess physiological and functional significance of coronary stenoses and newer imaging modalities to evaluate ischemia and viability may improve outcomes for patients across the continuum of stable ischemic heart disease, acute coronary syndromes, and STEMI.

When advances in technology essentially eliminate stent thrombosis and decrease in-stent restenosis to a few percent, or allow us to identify and

prophylactically treat vulnerable plaque so as to preserve myocardium against future events (similar to CABG), complete revascularization may become the norm. Until then, the ideal degree of revascularization in patients with multivessel disease may remain unclear. Although the totality of data suggests that complete, in comparison to generally defined incomplete, revascularization is associated with more favorable outcomes, yet to be determined is whether performing complete revascularization will improve outcomes in the presumably more complex, incomplete revascularization patient group in whom jeopardized myocardium remains. Absent robust evidence to inform our clinical practice guidelines and management decisions, it is the individual physician and patient who will continue to synthesize the clinical, angiographic, and procedural variables supported by anatomic, hemodynamic, and functional studies in addition to quality-of-life preferences and to determine together, how much revascularization is enough revascularization.

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