Reasonable Incomplete Revascularization

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Incomplete coronary artery revascularization could increase the risk of death, myocardial infarction, repeat revascularization, and lifestyle-limiting angina. Data to support this hypothesis extend back to the early 1980s, when patients with incomplete surgical revascularization had an absolute 15% reduction in 5-year survival in comparison with patients with complete revascularization.1,2 This hypothesis should extend to percutaneous coronary intervention (PCI). Two New York State registry analyses demonstrated an increased risk of death associated with incomplete stent-based revascularization, and the Arterial Revascularization Therapies Study (ARTS) trial described a greater need for subsequent bypass surgery after incomplete stent revascularization.3–5 One study has linked incomplete stent-based revascularization with impaired improvement in left ventricular function, and thus suggests a mechanism for increased mortality risk.6

Incomplete Revascularization: Definition and Characteristics

The standard definition used in previous trials and registries may be overly punitive, and does not clearly apply to the more common clinical discussions of stentable and graftable vessels; namely, incomplete revascularization is commonly defined as any nonrevascularized vessel with >1.5-mm diameter and 50% to 100% stenosis.5,8 Other registry studies have used a more stringent stenosis requirement of >70% severity.4 The current registry analyzed the frequency of incomplete revascularization in multiple ways, including using the 1.5-mm diameter/50% to 100% definition (overall incidence, 52%) and a 2.5-mm diameter/50% to 100% stenosis definition (overall incidence, 41%). Other registry definitions provide estimates of stent-based incomplete revascularization as high as 69% of patients with multivessel disease.4

Incomplete revascularization occurs more frequently in PCI patients, but it is not rare in CABG populations—in the current study, incomplete revascularization occurred in 33% of CABG patients in comparison with 59% of PCI patients (P<0.001). Although the practice of incomplete revascularization by traditional definition is common, it is also variable. In the New York State registry study, incomplete revascularization with drug-eluting stents ranged from 45% to 89% of multivessel coronary artery disease procedures across 39 different hospitals.4 Explanations for this wide variation in practice are speculative, but could range from individual practice preferences to hospital-dictated economic factors regarding utilization of multiple drug-eluting stents.

Patients with incomplete revascularization are different than those with complete revascularization. The differences in baseline characteristics vary according to study design, but may include the extent of coronary disease, the presence of diabetes mellitus, older age, and renal insufficiency.3,4,8–10 Thus, the comparison of absolute event rates according to nonrandomized treatment strategy (incomplete versus complete revascularization) is meaningless, and comparing adjusted outcomes within registry populations may be challenging.11 It is noteworthy that incomplete revascularization does not mean that the interventionalist or surgeon was in a hurry. In a Leipzig registry of coronary artery bypass patients notable for coining the term “reasonable incomplete revascularization,” patients with incomplete revascularization had longer total operative and bypass times than patients with complete revascularization, consistent with a potentially sicker, more anatomically challenging group.9

The Incomplete Revascularization Spectrum of Risk

There have been hints for many years in the surgical and PCI literature that the general hypothesis regarding completeness of revascularization may be flawed. For example, in the Bypass Angioplasty Revascularization Investigation (BARI) trial, completeness of revascularization had no impact on 7-year outcome among surgical patients.12 On the other hand, the ARTS trial5,13 and New York State registry studies3,4...
suggest that incomplete revascularization with stenting may limit the potential benefit of revascularization and thus conflict with the results of the Asan registry.

Further scrutiny of the previous negative data is warranted. First, other large, multicenter prospective registry studies have failed to demonstrate a measurable disadvantage from incomplete stent-based revascularization. Second, the New York State registry points to a cumulative risk that is maximal at 18-month follow-up; on the other hand, the ARTS trial shows an increased risk of multivessel stent-based incomplete revascularization that is already apparent at the time of discharge from the index procedure. Third, one might hypothesize that patients at highest risk of cardiovascular events (ie, patients with diabetes mellitus, older age, or decreased left ventricular function) would benefit most from complete revascularization, but this relationship is not seen in the registry studies. Clinical trial data challenge the black-and-white notion that anatomic incomplete revascularization is uniformly bad. In the Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) trial, no difference in death or myocardial infarction was apparent at 1-year follow-up between the CABG and multivessel drug-eluting stent groups. Furthermore, functional status at 1 year was similar between the 2 groups. These encouraging results were obtained despite significantly less complete revascularization in the PCI group (56.7% versus 63.2%, P=0.005). SYNTAX has shades of gray that are worth considering in light of the Asan registry results. Clinical trial data challenge the black-and-white notion that anatomic incomplete revascularization is uniformly bad. In the Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) trial, no difference in death or myocardial infarction was apparent at 1-year follow-up between the CABG and multivessel drug-eluting stent groups. Furthermore, functional status at 1 year was similar between the 2 groups. These encouraging results were obtained despite significantly less complete revascularization in the PCI group (56.7% versus 63.2%, P=0.005). SYNTAX has shades of gray that are worth considering in light of the Asan registry results. First, angina was slightly but significantly greater in PCI patients than in CABG patients at 12-month follow-up, a finding that was more pronounced in the ARTS trial. Previous data have linked degree of incomplete revascularization to recurrence of angina, suggesting that the Asan findings regarding extensive incomplete revascularization may be important for both cardiovascular events and symptomatic status. Furthermore, in patients with extensive coronary artery disease and severe anatomic risk (SYNTAX score ≥33), the penalty for PCI-based revascularization may extend beyond the realm of angina and repeat revascularization. On the basis of registry studies, we know that patients with complete revascularization are more likely to have 2-vessel disease than more extensive 3-vessel disease. Thus, it is plausible to assume that PCI in high SYNTAX score groups may lead to a phenomenon similar to that seen in the Asan registry—namely, multiple incomplete revascularization targets correlating with an increased risk of death/myocardial infarction.

At the opposite extreme of incomplete revascularization risk, it is hard to demonstrate the value in routine stenting of side branch arteries during bifurcation lesion PCI. In recent trials of complex versus simple stent strategies for bifurcation lesions, patients were randomly assigned to complete revascularization (definite stenting of both the main vessel and side branch) versus incomplete revascularization (a main-vessel–stenting approach). Despite achieving better revascularization of the ≥2.0-mm side branches with a complete revascularization approach, no benefit of complete bifurcation revascularization could be found, and the potential harm of oculostentotic stenting was demonstrated. Similarly, the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial may represent the ultimate trial of incomplete revascularization in the setting of optimal medical therapy and stable, lower-risk coronary artery disease. This trial failed to show a benefit for routine revascularization in patients with stable angina compared with optimal medical therapy. Like the Park registry, COURAGE points to an important spectrum of incomplete revascularization risk. Functional testing in COURAGE identified 2 factors linked to subsequent rates of death and myocardial infarction: (1) patients with at least moderate to severe ischemia at baseline testing and (2) significant residual ischemia (≥5% ischemic myocardium) 18 months after randomization. Anatomy (SYNTAX score) and functional testing (nuclear measurement of ischemic burden) are not the only methods to estimate the incomplete revascularization risk profile (Figure). The Fractional Flow Reserve Versus Angiography for Multivessel Evaluation (FAME) trial randomly assigned 1005 patients with multivessel coronary artery disease to anatomic complete revascularization (PCI of 50% to 100%
lesions in adequately sized vessels) versus reasonable incomplete revascularization. In this case, reasonable incomplete revascularization was not based on anatomic guidance (vessel size, jailed side branches, intravascular ultrasound defined anatomic risk) or functional guidance (completely infarcted territories, degree of ischemic burden). Rather, the guiding principle of reasonable incomplete revascularization was physiological and based upon fractional flow reserve of <0.80. Incomplete anatomic revascularization, albeit complete ischemic revascularization, resulted in 37% of lesions in the fractional flow reserve–guided group. This practice was not harmful; in fact, it was beneficial, with a 34% less relative risk of death or myocardial infarction at 1 year.

**What Do We Do Now?**

The extreme examples are easy to identify in current clinical practice—it is not reasonable to perform right coronary artery PCI and leave the patient with a high-risk left main lesion conferring severe ischemic burden. It is equally unreasonable to perform 3-vessel PCI treating all small side branches and nonischemic, chronically infarcted territories. In addition, regardless of our patient’s place on the spectrum of risk, we know that optimal medical therapy plays a critical role in the management of patients with multivessel coronary artery disease. The Asan registry extends the findings of the Leipzig cardiac surgery study that, within limits (ie, left internal mammary artery to the left anterior descending artery is mandatory, non-PCI of multiple large diseased vessels may be risky), a strategy of reasonable incomplete revascularization can be identified.

For interventional cardiologists, the gold standard for choosing the right vessels to leave anatomically incomplete is determination of fractional flow reserve. Other anatomic or functional tools may be identified or used to similarly guide target lesion choices for reasonable incomplete revascularization. Notably, the Asan interventional cardiologists did not use fractional flow reserve guidance to choose which vessels to revascularize, and they presumably relied on anatomic/functional parameters to guide clinical, interventional, and surgical judgment.

The current results support the concept of reasonable incomplete revascularization for both stent and surgical approaches. On the other hand, extensive incomplete revascularization is likely to be hazardous and associated with significant residual angina burden, myocardium at risk, and adverse cardiovascular events; each patient’s place on the ischemic spectrum of risk needs to be identified before embarking on a revascularization strategy. The administration of optimal medical therapy (including dual antiplatelet therapy) may be critical to the choice and efficacy of different revascularization strategies. In the post-COURAGE, SYNTAX, FAME era, we should not be shocked by the current findings—the old hypothesis regarding the black-and-white importance of anatomic complete revascularization has been refined and replaced by a graded spectrum of anatomic, functional, and physiology-guided reasonable incomplete revascularization.

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