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EDITORIAL COMMENT

Impact of Drug-Eluting Stent Length on Outcomes

Less Is More . . . More or Less*

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"Complete revascularization" traditionally has been defined as alleviating all angiographically apparent coronary artery stenoses. For many years the dogma in interventional cardiology has been to achieve complete revascularization when performing percutaneous coronary intervention (PCI). The impetus behind this teaching stems from early reports demonstrating improved outcomes after achieving complete revascularization with coronary artery bypass grafting (1). Improvements in interventional equipment and technique and, in particular, the advent of drug-eluting stents have all made it more attractive and easier to achieve complete revascularization with PCI, further solidifying it as one of our primary goals. This has occurred despite early reports suggesting that complete anatomic revascularization was important only when there was a large ischemic burden (2,3).

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The importance of ischemia in predicting adverse cardiac outcomes has been known for some time (4). Relief of ischemia results in improved outcomes, whereas PCI of non–ischemia-producing lesions provides no additional benefit over medical therapy and might actually increase adverse events (5,6). Recent data are now leading to a paradigm shift away from our obsession with complete anatomic revascularization toward the realization that equivalent if not improved outcomes can be achieved with a functionally complete revascularization (i.e., stenting of ischemia-producing lesions and medical treatment of non–ischemia-producing ones). For example, the FAME (Fractional Flow Reserve versus Angiography for Multivessel Evaluation) Study showed that fractional flow reserve (FFR)-guided PCI results in fewer stents being placed, yet outcomes are significantly improved (7). At 1 year, the rate of major adverse cardiac events was significantly reduced, and each individual component (death, myocardial infarction and the need for repeat revascularization) was reduced by 30% to 40% in patients randomized to FFR-guided PCI of their multivessel coronary disease, compared with those randomized to standard angiographic guidance.

Measuring FFR allows the interventionalist to identify stenoses that are responsible for ischemia and are likely to benefit most from PCI. Likewise, it identifies lesions that might appear significant angiographically but are not causing ischemia and therefore can be safely treated medically. In this way, the benefits of PCI are maximized, and its risks are minimized. In the FAME study, the patients randomized to angiography guidance had PCI performed on a significantly greater number of lesions, resulting in greater stent number and length. This difference not only exposed patients in this arm to greater risk at the time of the procedure but also to greater risk for restenosis and stent thrombosis manifesting as a higher rate of death, myocardial infarction, and the need for repeat revascularization at 1 year.

This potential downside to indiscriminate stenting is also highlighted in the current report by Shirai et al. (8) in this issue of *JACC: Cardiovascular Interventions*. In this evaluation of over 10,000 patients treated with sirolimus-eluting stents as part of the j-Cypher registry, the investigators found a significant correlation between stent length and the rates of target lesion revascularization, thrombosis, and death or myocardial infarction at 3-year follow-up. After adjusting for differences in baseline characteristics, the quartile of patients with the greatest total stent length continued to have increased rates of target lesion revascularization and thrombosis, although the rate of death and myocardial infarction was no longer significantly different. Interestingly, total stent length/lesion (as opposed to total stent length/patient) correlated only with increased target lesion revascularization and not with thrombosis, suggesting that deploying a slightly longer stent to make sure one covers the entire lesion is not as hazardous as placing another stent in a second lesion. This is different from other studies, which have found increasing rates of stent thrombosis with each additional millimeter of stent length, and it might be because stent thrombosis rates were very low in the present study in all groups, when evaluated on a per-lesion basis (9).

The strengths of this study include its size, the fact that patients were consecutively enrolled from a number of Japanese centers, and the relatively long-term follow-up. Some weaknesses include that, although patients were consecutively enrolled, a large number were excluded from this analysis because they were treated with bare-metal stents, other drug-eluting stents, or angioplasty in conjunction with a sirolimus-eluting stent. The study included only Japanese patients, and there was a large variability in the number of patients included from each of the participating centers, both of which might limit the applicability of these findings. We are never told the number of patients lost to follow-up in each group. Another main

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limitation of this study is inherent in its design as a registry; there were significant differences in baseline patient and lesion characteristics in those who had the greatest stent length, which might have contributed to the increased rate of adverse outcomes in this group, despite attempts to adjust for these variables. Finally, there seems to be an inflection point in the rates of target lesion revascularization at 6 months depicted in Figure 2A of Shirai et al. (8), which might be due to routine angiographic follow-up and which might exaggerate the differences in target lesion revascularization rates between the different stent lengths.

Another aspect of this study worth discussing is the rate of stent thrombosis reported in this cohort. It is not clear why the authors only reported rates of definite stent thrombosis, instead of including probable and possible stent thrombosis like they had in previous reports from this registry (10). At 3 years, the rate of definite stent thrombosis was approximately 1%. This is similar or somewhat lower than rates reported in other registries, and as the authors mention, it is significantly lower than the rate seen in the SYNTAX (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) study. The differences in rates of stent thrombosis might be explained not only by ethnic differences, as hypothesized by the authors, but also by use of different drug-eluting stents, differing definitions of stent thrombosis, and procedural differences (e.g., more routine use of intravascular ultrasound) in the current study (11–14). It is impressive that, even with this low overall rate of stent thrombosis, significant differences were seen in the rate of stent thrombosis, depending on the length of stent deployed.

The authors should be congratulated for compiling long-term follow-up in such a large number of patients after PCI with sirolimus-eluting stents. Their report adds to the published data demonstrating that event rates increase significantly with increasing stent length. As they suggest, a more judicious approach to PCI with the aim of achieving functionally complete revascularization and not necessarily complete anatomic revascularization could result in improved outcomes. Clearly, in some patients multiple and long stents are necessary, but this decision should be guided by relieving ischemia and not by the coronary angiogram alone. In other words, in the case of drug-eluting stent length, less is more . . . more or less.

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