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EDITORIAL COMMENT

Current Treatment of Bifurcation Lesions

Re-Examining the 1- Versus 2-Stent Argument*

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The study by Lee et al. (1) in this issue of *JACC: Cardiovascular Interventions* provides important insights into the evolving treatment of coronary bifurcation lesions, as well as the utility of well-designed clinical registries. Before the introduction of stents, "plain old balloon angioplasty" was limited by procedural unpredictability (abrupt closure) and poor durability (restenosis). The introduction of bare-metal stents was transformative, providing procedure reliability with virtual elimination of emergent coronary artery bypass surgery.

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The introduction of drug-eluting stents brought durability to the procedure, reducing clinical restenosis to acceptable rates (2,3). Technological advances, along with refinement of technique, have led to the uniform adoption of a stenting strategy for almost all lesions (4). The only major lesion subset in which a stent-all strategy has not become the standard is the treatment of side branches involved in bifurcation lesions. The currently accepted strategy for "true" bifurcation lesions is, in fact, to avoid the use of a second stent. Lee et al. (1) provide data that challenge the current dogma.

Coronary bifurcation lesions continue to challenge the interventional cardiologist. The wide pathoanatomic variation makes these lesions difficult to treat and study. Currently available stents have been designed for treatment of straight (nonbifurcation) lesions. Using these stents to treat bifurcation lesions forces the interventionist to adopt creative solutions, e.g., the crush, mini-crush, culotte, double barrel, "V," "T," and so on, all of which are complex and fail to provide the same predictability and durability we now have with the treatment of straight lesions (5). This has led many, including myself, to develop stents designed specifically for bifurcation lesions.

The current 1-stent strategy zeitgeist is based on a series of randomized controlled trials (RCTs), most notably the BBC ONE (British Bifurcation Coronary Study) and NORDIC ONE (Nordic Bifurcation Study), which failed to show benefit of a 2-stent strategy (6,7). Although the role of randomized trials is central to the formation of our treatment strategies, there are many factors that may limit the generalizability of a specific RCT to current practice. These include the highly selected study population, the technology being used, and the technique used. The markedly variable nature of bifurcation anatomy and distribution of angiographically apparent disease, as well as evolving stent technology and techniques, have made the published data particularly difficult to generalize to "real world" usage and underlines the importance of registries in placing RCTs into appropriate context.

The NORDIC ONE (September 2004 to May 2005) and BBC ONE (December 2004 to December 2007) studies were performed early in the drug-eluting stent era and capture the technology and technique of that time. These studies used first-generation stent technology (NORDIC ONE: Cypher Select sirolimus-eluting stent [Cordis Corporation, Bridgewater, New Jersey]; and BBC ONE: Taxus paclitaxel-eluting stent [Boston Scientific, Natick, Massachusetts]). Contemporary stent technology has improved strut and polymer drug delivery systems. A measure of this change is the reduction in strut diameter: for example, the first-generation Cypher strut had an overall thickness of 153 μM (metal 140 μM, polymer 12.6 μM), whereas the second-generation Xience V/Promus (Abbott Vascular, Santa Clara, California)

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has an overall strut thickness of 88.6 μM (81 μM metal, 7.6 μM polymer) (8). The 2-stent techniques utilized in these studies favored the crush technique (NORDIC ONE: crush 50%, culotte 21% and other [primarily 'T"] 29%; BBC ONE: crush 68.1%, culotte 30.2%, other 1.6%) differ from current 2-stent practice, which favors the "T" stent technique. Furthermore, current technique emphasizes final kissing inflations with "noncompliant" balloons as well as post-optimization technique (1).

Lee et al. (1) present a patient-level pooled analysis from 3 Korean Registries: the COBIS (Coronary Bifurcation Stenting Registry) dedicated bifurcation registry, which is combined with appropriate patients enrolled in the EXCELLENT (Efficacy of Xience/Promus Versus Cypher to Reduce Late Loss After Stenting) (everolimus-eluting stents: Xience V/Promus) and Resolute-Korea, "all comers" registries. These 3 registries together provide a well-characterized large study population (n = 3,162). Utilizing sophisticated statistical tools, the authors compared outcomes of patients with bifurcation lesions treated with 1 or 2 stents utilizing first-generation stents (Cypher and Taxus) versus those treated with second-generation stents (Xience V/Promus, Endeavor-Resolute [Medtronic, Minneapolis, Minnesota]) stents. Significant outcome differences were observed between the first- and second-generation groups. In the first-generation group, the 2-stent group had a greater target lesion failure rate with increased cardiac death, spontaneous myocardial infarction, target vessel revascularization, and stent thrombosis (definite and probable). In the second-generation group, these differences were not observed.

The Korean Group reports interesting changes in procedural technique in the 2-stent strategy including a decrease in crush stenting (from 48.0% in first-generation to 35.2% in second-generation cases) and an increase in T-stenting (from 36.4% in first-generation to 52.9% in second-generation cases). There was an overall increase in the use of noncompliant balloons during the final inflation in both the main branch (23.0% to 49.5%) and side branch (10.0% to 37.1%). Also of interest was the frequency with which a second stent was used in the provisional arm (increased from 10.8% to 18.5%, rates derived from the provisional 2-stent rates [see Table 2 of Lee et al. (1)]). Both rates are higher than reported in the NORDIC ONE (4.3%) or BBC ONE (2.8%) trial. This difference likely reflects the protocol recommendation as well as differences between the BBC ONE and Nordic ONE study populations and "real world" lesions encountered in the unselected population studied by the Korean investigators. It is important to note that despite changes in technique, intraprocedural side branch closure remained high in both the first- (6.2%) and second-generation (7.3%) cohorts.

Lee et al. (1), show how interventional technique is continuing to evolve and suggest that our ability to treat bifurcation lesions is improving. The emphasis of RCTs in the published data pushes the interventionist to adopt 1 approach (e.g., 1- vs. 2-stent strategy) for *all* lesions and not just those matching the highly focused lesion subset studied in a single study. This forces a false choice, which ignores the wide pathoanatomic variation observed among bifurcation lesions. It seems more appropriate to individualize one's approach focused on anatomic variables that make a lesion appropriate for 1 of a number of 1- or 2-stent strategies. Data from Lee et al. (1) should give us further comfort that utilization of a 2-stent strategy with current technology and technique does not carry long-term penalties.

Bifurcation lesions, with their wide pathoanatomic variation, are particularly difficult to study in RCTs, which by their nature, examine only a narrow portion of the lesion spectrum (e.g., limiting recruitment to patients with discrete side branch disease), where there is perceived equipoise between strategies among investigators. The difficulty and expense associated with RCTs will severely limit the number of future studies, requiring us to rely increasingly on registry data like those presented by Lee et al. (1) to guide our treatment decisions.

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