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EDITORIAL COMMENT

IIb or Not IIb? Toward a Rational Application of Left Main Stenting*

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For over 30 years, the elective treatment of significant left main (LM) coronary disease has been the province of coronary artery bypass surgery (CABG). Recently, several large registries using either bare-metal stents (BMS) or drug-eluting stents (DES) and 1 large clinical trial, the SYNTAX (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) trial, have provided insights into stenting as an acceptable alternative to CABG (1–4). These studies have demonstrated the relative safety and efficacy of stenting, similar mortality and myocardial infarction (MI) outcomes with BMS and DES, and decreased target vessel revascularization (TVR) with DES compared with BMS (4,5).

See page 2544

In this issue of the *Journal,* Kim et al. (6) address the question from a large "real-world" registry (2) as to whether the extent of coronary disease as characterized by the number of coronary vessels outside the LM with a significant (>50%) diameter stenosis affects long-term outcomes (4 years) with percutaneous coronary intervention (PCI) versus CABG. There was no significant difference in the combined end point of death, MI, or stroke in any coronary artery disease subgroup, including patients with the greatest disease burden. These "real-world" results are similar to those reported in the SYNTAX randomized trial (1). TVR was more frequent with PCI in the entire group and in both the DES and BMS subgroups. Incidence of TVR was similar in magnitude to that reported in SYNTAX. However, unlike SYNTAX, where there was a somewhat lower rate of major adverse cardiac or cerebrovascular events (death, MI, cerebrovascular accident, TVR) with DES in relatively less extensive disease (isolated LM or LM plus 1-vessel disease) and a somewhat higher rate of major adverse cardiac or cerebrovascular events in more extensive disease, the rate of major adverse cardiac or cerebrovascular events was higher with PCI in all subgroups in this registry. As noted by Kim et al. (6), this finding may have been related in part to the policy of surveillance follow-up angiography (performed in 73% of PCI patients vs. 15% of CABG patients). Routine follow-up angiography has been previously shown to increase TVR rates in asymptomatic post-PCI patients (7).

The inherent limitation of this study, as in all registry studies, relates to selection and other hidden biases. That being said, the size of the study, the thoroughness of the data analysis, and similarity of results with other data including the SYNTAX trial provide a measure of confidence in the reliability of the findings.

This study, in combination with other reports, particularly SYNTAX, allows for certain conclusions regarding outcomes for stenting compared with CABG:

- Major adverse outcomes—death, MI, and stroke—at intermediate follow-up are similar for both therapies. Follow-up has been presented through 2 years for SYNTAX (8), through 4 years in the current study (6), and as long as 10 years for BMS (9).

  In ARTS (Arterial Revascularization Therapies Study), comparing BMS in multivessel disease (excluding LM) to CABG, 5-year follow-up showed that the majority of the adverse events and separation of curves occurred within the first year, with the curves flattening out for both therapies through 5 years (10). Multiple registries of LM stenting of 3 years or longer including the present one have shown similar results (2,3,6,9,11). Thus, it seems unlikely that there will be a major shift in the SYNTAX trial in the relative safety of these 2 therapies as follow-up time increases.
- Stroke risk may be higher with CABG than PCI, although the absolute incidence and difference between therapies are small (1). In the SYNTAX trial, the stroke rate for LM patients was 2.7% with CABG and 0.3% for DES ($p = 0.01$). In the present study, the difference was less impressive both in the entire cohort (CABG: 1.7%, PCI: 1.1%) as well as in both the BMS and DES (CABG: 1.8%, DES: 1.5%) subgroups.
- Repeat TVR risk with DES is higher with PCI (2 times in SYNTAX, almost 5 times in the current study).

These conclusions do not sustain a New York Heart Association functional class III recommendation that LM stenting demonstrates a risk greater than benefit ratio (12,13). The American Heart Association/American College of Cardiology PCI guideline has recently been updated to reflect this fact (14). Left main stenting in patients eligible for CABG has been changed to a class IIb recom-

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mendation. Class IIb has been defined as an intervention in which the benefit is greater than the risk and "may be considered" in an individual patient but the efficacy and safety are far from certain and that "additional studies with broad objectives are needed" and "additional registry data may be considered." The update emphasizes caution in the use of LM stenting because of the severe downside risk should complications occur and presents the need to clarify some of the unknown aspects to optimize results such as the use of intravascular ultrasound. It is likely that further discussion will ensue as to whether the current knowledge base for LM stenting justifies an IIa rather than an IIb recommendation. Selection of which patient "may be considered" for LM stenting will certainly be an actively debated topic.

To make the best decision for an individual patient, Alfonso (15) has recommended "balanced counseling" among physicians and the patient. In this context, it seems reasonable that physicians in a given center should (to use a legal term) "stipulate" that the preceding 3 conclusions are true and need not be argued in deciding how to best treat the individual patient. The discussion will then focus on the approximated surgical versus PCI mortality risk for that patient; the anticipated completeness of revascularization with each technique; patient compliance (particularly for PCI with the need for prolonged dual antiplatelet therapy); the potential for CABG complications such as stroke, atrial fibrillation, wound infection, and such versus the estimated risk of repeat revascularization with PCI; and other patient-specific issues. To illustrate, we might ask what the best treatment would be for a frail octogenarian with severe life-limiting angina and multiple comorbidities. Existing data, albeit with their own limitations, suggest that PCI may be particularly valuable in this setting (16). On the other hand, a 50-year-old otherwise healthy individual with no comorbidities at low surgical risk may be better served in terms of minimizing health care utilization by undergoing CABG. Further clarification of which clinical characteristics may best recommend a patient for either PCI or CABG will aid in decision making (15).

As a procedure in evolution, there are many unresolved questions related to optimizing outcome. For example, as noted in the updated guidelines, should intravascular ultrasound be routinely used in evaluating results (17)? Should stenting be confined to ostial and shaft lesions, as suggested by the guidelines update, or should bifurcation lesions as in the current study be included? Is increased TVR at bifurcations versus shaft/ostial lesions due to anatomical or technical factors or both? Should fractional flow reserve be used to select appropriate candidates and to optimize results (18)? Should an anatomic score such as the SYNTAX score be used as a guide to the type of treatment (19)? Should 1 stent or 2 be used routinely for bifurcation lesions? When 2 stents are needed, which technique should be preferred? How long should dual antiplatelet therapy be given? These and other questions will certainly be addressed in future studies. Kim et al. (6) have provided, in their large patient cohort analysis, reassurance that long-term major adverse outcomes after LM stenting, both with BMS and DES, compare favorably with bypass surgery, thus providing increased confidence to the treating physician who must evaluate which therapy is preferred for the individual patient.

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