

EDITORIAL COMMENT

What Is the Standard of Care for Patients With Left Main Stenosis?*

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Invasive treatment strategies for coronary artery disease (CAD) are highly scrutinized and constantly evolving. Coronary artery bypass graft (CABG) surgery has long been the gold standard for revascularization in patients with complex CAD; however, advances in the safety and efficacy of percutaneous coronary intervention (PCI) have allowed interventional cardiologists to challenge the status quo and possibly expand the indications for coronary stenting. We read with interest the meta-analysis by Athappan et al. (1)

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reviewing the available published reports comparing unprotected left main stenting (UPLMS) in the drug-eluting stent (DES) era with CABG surgery. The analysis included 3 randomized, controlled trials and 21 observational studies that were published between 2006 and 2012. The authors selected appropriate primary (all-cause mortality, target vessel revascularization, stroke, and myocardial infarction) and secondary (major adverse cardiac and cerebrovascular events) endpoints and performed a thorough and statistically sound analysis. The result is a valuable contribution to the published reports that succinctly summarizes much of the available data comparing CABG surgery with PCI for UPLMS and gives clinicians a snapshot of the data, although the authors' conclusions are slightly overstated. The report also serves to highlight the limited availability of high-quality short- and long-term efficacy and safety data on UPLMS. Unfortunately, as the authors themselves point out, including a majority of observational studies in this meta-analysis entails accepting

a certain degree of heterogeneity and uncontrollable bias within the results.

In the most recent 2012 American College of Cardiology/American Heart Association guidelines (2), CABG surgery is the only Class I recommendation for revascularization to improve survival in left main disease. This is based on many studies performed over the past 2 decades that compared CABG surgery with optimal medical therapy (3,4). PCI has now been upgraded to a Class IIa indication only in patients with very favorable anatomy (SYNTAX score <22, ostial or trunk lesion) and who are at increased risk with CABG surgery (Society of Thoracic Surgeons predicted risk of mortality >5%). PCI is a class IIb indication if left main anatomy is less favorable. These recommendations are strongly driven by results from the SYNTAX (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) trial, which randomized patients with left main or multivessel coronary artery disease to undergo CABG surgery or PCI (5). The SYNTAX trial, which was underpowered to evaluate left main disease, was also the only randomized trial included in this meta-analysis that offered long-term (5-year) follow-up data. This is a fundamental flaw of the present meta-analysis, and readers should interpret these results with this important limitation in mind. The short-term data, which come largely from non-randomized, observational studies, suggest that UPLMS is safe and effective early on. However, because the benefits of CABG surgery should become more evident over the long term, a reasonable comparison with CABG surgery must include longer follow-up of at least 3 to 5 years or more. When the authors combined the randomized SYNTAX data with nonrandomized, observational studies, they found no difference in all-cause mortality, nonfatal myocardial infarction, and cardiac mortality. In addition, whereas CABG was found to be advantageous regarding target vessel revascularization, stroke favored PCI, and there was no difference in major adverse cardiac and cerebrovascular events. These data are important and can certainly be considered hypothesis generating; however, the effective percutaneous treatment of left main disease is highly nuanced and is dependent on the skills and experience of the operator. Moreover, nonrandomized studies of PCI versus CABG surgery are notoriously biased in numerous ways that cannot be statistically adjusted with confidence. For these reasons, we believe that it is dangerous to draw concrete conclusions from this very heterogeneous dataset.

When considering UPLMS, the anatomic location of the lesion is of the utmost importance. The authors appropriately focus part of the discussion on the significance of location of disease in left main lesions; however, this key concept was not stressed in the paper's conclusion. We suspect, as the data suggest, that UPLMS is equal to or better than CABG surgery in a select group of patients with noncomplex ostial or mid-shaft left main lesions. Regarding

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distal left main lesions that may be heavily calcified and encroaching on the ostial left anterior descending and/or circumflex arteries, we remain skeptical as to how long-term results with PCI will compare with those with CABG surgery. For diabetic patients, it is possible that even noncomplex lesions are better treated with CABG surgery. The FREEDOM (Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease) trial, a large prospective, randomized trial comparing PCI and CABG surgery among diabetic patients with multivessel disease demonstrated that CABG surgery was superior during 5 years of follow-up, with respect to death, myocardial infarction, target vessel revascularization, and major adverse cardiac events (6). Although this trial excluded patients with left main disease, it clearly demonstrated that diabetic patients can have a response to revascularization therapy that differs from that of nondiabetic patients. Further objective randomized data are necessary to test the equivalence of outcomes after PCI for simple versus more complex left main stenosis in both diabetic and nondiabetic patients. The need for a large, randomized, controlled trial evaluating UPLMS is clear, and enrollment has already begun in such a trial. The EXCEL (Evaluation of XIENCE PRIME or XIENCE V vs. Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) trial will randomize 2,600 patients to receive either PCI with a second-generation DES, or CABG surgery (7). When 3-year follow-up is completed, the results of this trial should provide some much-needed answers regarding the optimal treatment strategy for this group of patients with CAD.

The authors conclude that PCI with DES is comparable to CABG surgery for left main disease patients with low and intermediate SYNTAX scores. We would caution that this statement may be premature and not fully substantiated. In addition to the SYNTAX score, the decision to proceed with UPLMS should also take into consideration the location of the lesion and the experience of the operator. The large series and randomized studies that have been published originated in high-volume centers with very experienced operators. It is not known whether similar results can be achieved in smaller centers. Injudicious broad adoption

of UPLMS may put patients at unnecessary risk. As mentioned earlier, the EXCEL trial should answer many important questions about which patients may benefit from UPLMS, and we, along with the authors of this meta-analysis, await the results of EXCEL with keen anticipation.

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