Unprotected Left Main Intervention
The Light at the End of the Tunnel?

Gregg W. Stone, MD; Gary S. Mintz, MD

Despite impressive advances in stent technology, unprotected left main coronary artery (LMCA) disease requiring revascularization remains the province of the surgeon at most institutions. In a 2007 editorial, we summarized the evolution of percutaneous coronary intervention (PCI) for LMCA disease, concluding that given the available evidence at that time, coronary artery bypass graft surgery (CABG) should remain the procedure of choice for most good surgical candidates with significant LMCA disease. Moreover, just a few months ago in 2009, a consensus document from 6 cardiac societies was published describing “Appropriateness Criteria for Coronary Revascularization,” in which PCI was considered to be “inappropriate” for significant LMCA disease, regardless of the extent of concomitant coronary artery disease, presence or absence of diabetes, and left ventricular function. Since these publications, important new evidence has emerged that has challenged the surgical gold standard. In the large-scale multicenter MAIN-COMPARE registry, stent implantation and CABG had comparable 3-year rates of mortality and composite death, Q-wave myocardial infarction, or stroke in patients with LMCA disease, although target vessel revascularization was more common with bare metal stents or drug-eluting stents (DES) than with surgery. Of even greater significance, among 1800 patients with LMCA or triple vessel disease randomized to paclitaxel-eluting stents versus surgery in the SYNTAX trial, paclitaxel-eluting stents compared with CABG resulted in nonsignificantly different 1-year rates of death and myocardial infarction, with 76 more revascularization procedures but with 16 fewer strokes per 1000 patients treated, both significant differences. The results with paclitaxel-eluting stents were even more favorable in the 705 randomized patient LMCA disease cohort especially among the two thirds of patients with lesser anatomic complexity. Nonetheless, because of the greater revascularization rate with PCI, SYNTAX failed its primary goal of demonstrating noninferiority of paclitaxel-eluting stents compared with CABG for composite major adverse cardiovascular events.

The results of PCI may be further improved by procedural guidance with intravascular ultrasound (IVUS), an intracoronary tomographic imaging modality that is significantly more accurate than angiography in defining the nature and extent of atherosclerosis, delineating the true vessel wall and lumen boundaries (facilitating precise dimensional measurements with resolution of 100 to 200 μm), determining the significance of borderline lesions, and characterizing the results of stent implantation. Although many IVUS investigations have been underpowered or otherwise limited by selection bias or suboptimal technique, the collective results from numerous randomized and registry bare metal stent studies have demonstrated that IVUS guidance compared with angiographic guidance alone likely results in improved freedom from target vessel revascularization and major adverse cardiovascular events. Although randomized IVUS trials have not been completed in the DES era, emerging data suggests that by optimizing stent expansion and ensuring full lesion coverage, IVUS guidance may decrease both DES thrombosis and restenosis. Moreover, IVUS interrogation of the left main stem will not infrequently reveal the presence of a severe lesion despite a benign angiographic appearance, or that an angiographically “severe” LMCA lesion has minimal plaque burden (thereby not requiring intervention).

In this issue of Circulation: Cardiovascular Interventions, Park et al report the findings from a post hoc analysis from the MAIN-COMPARE registry in which the nonrandomized outcomes of IVUS guidance and angiography guidance for LMCA stenting were evaluated in 975 patients. As numerous baseline differences were present between the 2 groups (which is typical of observational studies), a sophisticated propensity-score matching technique was used to identify 201 pairs of patients for whom the baseline clinical and angiographic characteristics were comparable. Among 145 matched pairs of patients receiving DES, the 3-year incidence of mortality was 61% lower with IVUS guidance as compared with angiography guidance, though after multivariable adjustment this difference just missed statistical significance (P=0.055).

Is this evidence strong enough to conclude with a high degree of confidence that the use of IVUS during LMCA intervention might reduce mortality? In a nonrandomized study, no amount of statistical adjustment can correct for major imbalances in unmeasured confounders. In this regard the angiography-guided group had a significantly greater burden of atherosclerosis with more triple vessel involvement and less isolated LMCA disease, important predictors of a
poor prognosis among PCI patients in the SYNTAX trial. Although we are not told how many lesions were treated, or how many stents were implanted per patient, it is likely that the angiography-guided group required more extensive revascularization (one example of an unmeasured, unadjusted for variable). Other examples include that IVUS may not have been used in clinically or hemodynamically tenuous patients or in heavily calcified or tortuous vessels that may have had worse outcomes. The use of debulking devices and chronic compliance with life-preserving medications (such as thienopyridines and statins) are not reported and may have significantly varied between the groups. The angiography-guided group was also at significantly higher risk for mortality with reduced baseline left ventricular function and a higher Euroscore. The total sample size of the matched pair analysis (402 total patients) is greatly underpowered to reliably estimate an effect on mortality, equally raising concerns for alpha error (false-positives) as well as beta error (false-negatives). Finally and importantly, no plausible mechanism has been offered as to why IVUS may have reduced mortality. No data are provided to evaluate how often and in what manner IVUS guidance impacted the procedure or whether IVUS led to improved acute results. The putative benefit of IVUS in reducing stent thrombosis\textsuperscript{15–18} was neither realized in this study, and the rates of myocardial infarction were not different between the groups. Nor was IVUS guidance in this registry associated with reduced target vessel revascularization, a potential advantage\textsuperscript{15–18} that might result in improved survival with DES.\textsuperscript{5} Thus, the borderline trend toward lower mortality in the LMCA DES group treated with IVUS guidance likely represents at least in part the influence of unmeasured confounders, although a modest favorable effect of IVUS cannot be excluded.

Nevertheless, Park et al\textsuperscript{20} are to be congratulated for once again bringing to the forefront the issue of IVUS guidance of interventional procedures, now in patients undergoing unprotected LMCA stenting, a high-risk cohort, which is increasingly being managed by the interventional cardiologist. Absent a definitive randomized trial of LMCA PCI versus CABG to guide revascularization decisions, if PCI of the left main stem is performed, it is essential that optimal clinical judgment and technique are used. Does this standard mandate the use of IVUS during LMCA PCI? Unfortunately, 1 or more adequately powered positive randomized trials would be necessary to establish a class I guideline for the use of IVUS guidance during complex PCI. As no such trial has been funded in the more than 2 decades in which intracoronary ultrasound has been available, such a study should not be expected in the near future, especially given the current economic climate. Nonetheless, the existing weight of evidence from (underpowered) randomized trials and registry data, coupled with clinical experience supports the belief that IVUS guidance (with appropriate lesion preparation) to ensure maximal stent expansion and coverage of residual disease will in aggregate result in superior outcomes (ie, enhanced safety from stent thrombosis and ischemia-driven target lesion revascularization) in patients with complex ischemic heart disease treated with DES. As such, in agreement with the study authors, we strongly recommend the routine use of IVUS during LMCA interventions, first to ensure the lesion is “real” and truly requires angioplasty, and second to optimize short-term and late clinical results. Our patients deserve no less.

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References


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