Change We Can Believe In: The Hyper-Evolution of Percutaneous Coronary Intervention for Unprotected Left Main Disease With Drug-Eluting Stents

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The initial adoption of percutaneous coronary intervention (PCI) for unprotected left main coronary artery (LMCA) obstruction was tempered by poor acute outcomes after balloon angioplasty and the potential lethality of restenosis in the left main trunk suggested by bare-metal stent registries.1 The marked antirestenotic efficacy of drug-eluting stents (DES) ushered in a new wave of enthusiasm for unprotected LMCA intervention. However, the accumulation of robust data to guide and support clinical practice has been challenged by the relatively low prevalence of this lesion subset combined with its historical characterization as a “forbidden zone” for PCI. The DES left main database has grown from initial, small, single-center experiences2–4 to larger multi-center registries,5 prospective, risk-adjusted comparisons with coronary artery bypass grafting,6 and most recently to small randomized clinical trials and prespecified subgroups of larger clinical trials.7,8 Catalyzed by an ethos in interventional cardiology that embraces (1) investigation, (2) dissemination of new information through journals, conferences, and a tradition of live-case demonstration; and (3) rapid adaptation of new techniques, there has been a marked evolution and improvement of the technical approach to unprotected LMCA intervention in a remarkably short period of time. The study reported by Palmerini et al9 in this issue of the Circulation Cardiovascular Intervention provides further pressure on interventional cardiologists to follow a straightforward maxim: simpler is usually better.

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The interpretation of the studies of left main PCI with DES has been complicated by heterogeneity within study populations related to both the disease location (ostial, shaft, or distal bifurcation) and the technical approach used (single stent, dedicated 2-stent technique, or provisional stenting of the left main with “bail-out” stenting of the branch vessel). The early, single-center observational studies of DES for the unprotected LMCA demonstrated the dependence of clinical outcome on the anatomic location of the obstruction within the left main: higher major adverse cardiac event (MACE) rates were observed in cohorts with a heavy burden of distal disease10 and subsequent meta-regression confirmed that distal disease predicted MACE and target vessel revascularization.11 Centers that frequently used dedicated 2-stent techniques (ie, “crush” or simultaneous kissing stents)1,3,4,12 also reported higher target lesion revascularization (TLR) and MACE rates compared with those using a single stent or provisional approach.13,14 Determining the optimal approach is difficult because stent technique is driven by a combination of clinical and angiographic characteristics and a strong dose of operator preference for which an analysis cannot be easily adjusted. Indeed, the relative predilection to use a single versus 2-stent technique was initially geographic in nature, with a 2-stent approach favored in the United States and parts of Europe, whereas the single stent or provisional approach was championed by interventionalists in Asia and France. Although clinical practice remains balkanized in other fields of medicine—for example, adoption of coronary artery bypass grafting with full arterial revascularization or bilateral internal mammary conduits is relatively limited and varies greatly by geography despite its proven benefit15,16—interventional cardiology is remarkably globalized and has established unique mechanisms for the exchange of information to continually improve patient outcomes. Using the left main as an example, a yearly international left main summit is held, and the Transcatheter Cardiovascular Therapeutics (TCT) conference has entire daily sessions focused on the evidence-base underlying left main intervention. Live-case demonstrations and internet case-based learning from Asia, Europe, and the Americas have eradicated regional barriers and enabled high-volume operators, in combination with a panel of experts in the field who provide commentary, to disseminate the practical aspects of evolving techniques to help them be adopted safely and effectively within the global interventional community. The body of published data regarding left main intervention has also exploded: a PubMed search with the keywords “left main” and “drug-eluting stent” revealed 88 studies and 12 reviews of the subject, with more than half of publications listed within the past 2 years.

The approach to left main intervention has shifted broadly in a short time period as a result of this unique interplay of evidence-based medicine and global information exchange. At the most recent TCT conference, during which this topic was thoroughly addressed, an international consensus appeared to emerge: for distal left main intervention, less is more. In this issue of Circulation Cardiovascular Intervention, Palmerini et al9 present data to further support this
simple approach. The authors examined the safety and efficacy of a 1- versus 2-stent strategy for distal left main disease using a risk-adjusted analysis of a retrospective, observational, multicenter registry of patients who underwent distal left main intervention in 19 high-volume centers in Italy. Perhaps somewhat counterintuitively, patients treated with a single stent were at generally higher risk, with a greater prevalence of diabetes mellitus, more frequent presentation with acute coronary syndrome, higher EuroScore, and older age. The techniques in the 2 stent group used by the investigators reflect current, dedicated, 2-stent approaches to the left main bifurcation, with T-stenting used in 41% of patients, crush stenting in 38%, and simultaneous kissing stents in 14%. Despite higher baseline clinical risk, the single stent cohort had a lower unadjusted incidence of 2-year MACE, driven entirely by TLR. Freedom from TLR at 2 years was quite acceptable in the single-stent cohort (87%), compared with 73% in the 2-stent cohort. The propensity-adjusted hazard ratio for 2-year cardiac mortality and MI was significantly lower for the single stent cohort (hazard ratio = 0.38; 95% CI = 0.17 to 0.85; \( P = 0.02 \)). Irrespective of the stenting approach, lack of kissing balloon postdilation was an independent predictor of MACE, a finding also consistent with nonleft main bifurcation studies.\(^{17} \) Therefore, this study supports the contention that a single stent with final kissing balloon inflation for distal left main disease decreases TLR compared with a 2-stent strategy, and according to risk-adjusted and propensity score analysis, seems to be safer.

The findings of the unadjusted analysis of Palmerini et al and consistent with that of smaller single-center studies,\(^{13,18} \) other LMCA registries,\(^{19} \) and randomized studies of PCI with DES for bifurcation lesions outside of the LMCA.\(^{20} \) The conclusions are strengthened by the relatively large number of patients studied and the duration of follow-up. However, the results of the adjusted analysis are less firm because the propensity score analysis used by the investigators to overcome the lack of randomization is based on clinical, not angiographic criteria, even though in practice the operator decision to use a 2-stent strategy is often driven by angiographic findings. For example, a 2-stent strategy may be more commonly used in the presence of severe obstruction involving ostia of both the left anterior descending artery and a large, dominant left circumflex artery, especially in the setting of an narrowly angled distal bifurcation. A greater disease burden in the 2-stent group may have led to an increased risk for restenosis, TLR, and, potentially, long-term mortality. Indeed, in the SYnergy between PCI with TAXus and cardiac surgery (SYNTAX) study, patients with left main disease and concomitant 2- or 3-vessel disease had worse outcomes than patients with isolated left main or left main with 1-vessel disease.\(^{21} \) A detailed comparison of the atherosclerotic burden of the 2 groups would therefore be helpful. Furthermore, intravascular ultrasound, possibly by ensuring more complete disease coverage with a stent and/or appropriate stent expansion, has been associated with a reduced rate of stent thrombosis and decreased mortality after unprotected LMCA stenting.\(^{22} \) Inclusion of this variable into the regression analysis might have provided important information regarding the relationship between intravascular ultrasound findings, stenting strategy, and clinical outcomes. Finally, the duration of and compliance with dual antiplatelet therapy is not provided and could have also influenced outcome.

Despite these limitations, the study by Palmerini et al adds to the preponderance of data supporting the use of a simple rather than complex approach to left main disease whenever possible. Yet, several questions remain unresolved: which patients with left main disease are still best be served by a dedicated 2-stent strategy? And in such patients, which 2-stent approach is optimal? Or will specially designed bifurcation stents address the limitations of the 2-stent approach? Randomized clinical trials are unlikely to fully provide the answers. Yet these questions will no doubt be asked, and the proposed answers tested, reexamined, and retested within the crucible that defines academic interventional cardiology—and where we stand 3 years from now will undoubtedly surprise us all.

The rapid evolution of LMCA stenting technique also illustrates the importance many cardiologists place on practicing evidence-based medicine and the highly effective means we have created to communicate new evidence (eg, journals, internet, and live demonstration conferences) to our peers. Surprisingly, the “live demonstration case” has been subject to recent criticism. Our surgical colleagues have questioned its value and recent Society of Thoracic Surgery guidelines state “Cardiothoracic societies should consider prohibiting live surgery broadcasts to large audiences at their annual meetings.”\(^{23} \) We believe that the rapid advancement of LMCA stenting technique is an example of the positive impact live-case demonstrations can have on patient care. Experiencing global shifts in stenting technique first hand has a profound influence on physician education and goes far to quickly and efficiently promote best practices. Considering the recent, rapid changes in LMCA stenting as an example, cardiologists should be proud of their eagerness to investigate, readiness to teach, and willingness to change.

**Disclosures**

None.

**References**


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