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EDITORIAL COMMENT

Left Main Percutaneous Coronary Intervention

Growing in Maturity*

Fausto Feres, MD, PhD, Ricardo A. Costa, MD, PhD

Sao Paulo, Brazil

In the past, the presence of >50% stenosis in an unprotected left main (ULM) trunk had been classically considered a "surgical" indication for revascularization, and only nonsurgical candidates would be considered for percutaneous coronary intervention (PCI) (1). Optimized medical therapy alone for severe stenosis at this location has not been recommended as a standard procedure, regardless of the clinical condition. With the evolution of technique and material, PCI for ULM has now become an alternative, associated with quite predictable and favorable long-term outcomes, meriting an upgrade in guideline indications for myocardial revascularization (1–3). This has occurred due to more contemporary published data with drug-eluting stents (DES) derived from large registries and randomized trials with prespecified subgroup analyses, which provided convincing evidence of the feasibility and effectiveness of such a procedure. A meta-analysis involving 3 randomized trials and 9 observational studies with 5,079 patients compared the 1-year outcomes of patients with ULM disease treated by PCI with DES implantation versus coronary artery bypass graft (CABG) surgery. Results demonstrated trends toward a lower risk of death and the composite endpoint of death/myocardial infarction/stroke in the PCI DES group (odds ratio [OR]: 0.68; 95% confidence interval [CI]: 0.45 to 1.02); however, target vessel revascularization (TVR) was significantly higher in the PCI DES group versus the CABG surgery group (OR: 3.52; 95% CI: 2.72 to 4.56) (4). Such outcomes appear to remain consistent over time (5–9). In the multicenter DELTA registry, 2,775 patients with ULM disease were consecutively treated with DES PCI (n = 1,874) and CABG surgery (n = 901), and at a mean follow-up of ~3.5 years, there were comparable outcomes in terms of the occurrence of death/myocardial infarction/stroke (adjusted hazard ratio [HR]: 1.11; 95% CI: 0.85 to 1.42), mortality (adjusted HR: 1.16; 95% CI: 0.87 to 1.55) or death/myocardial infarction (adjusted HR: 1.25; 95% CI: 0.95 to 1.64), but a significant advantage of CABG was observed for the composite endpoint of death/myocardial infarction/stroke/TVR (major adverse cardiac and cerebrovascular events [MACCE]) driven exclusively by lower rates of TVR compared with PCI (adjusted HR: 1.64; 95% CI: 1.33 to 2.03) (9). Compared with CABG surgery, PCI has been associated with increased vessel revascularization. With DES implantation, this gap has decreased dramatically, but more complex lesion morphology remains an important predictor of recurrences. In the pre-specified left main cohort of the SYNTAX (SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery) trial, there were comparable 5-year outcomes for DES PCI versus CABG surgery in terms of death (12.8% vs. 14.6%, p = 0.53), cardiac death (8.6% vs. 7.2%, p = 0.46), myocardial infarction (8.2% vs. 4.8%, p = 0.10), and death/myocardial infarction/stroke (19.0% vs. 20.8%, p = 0.57) (10). However, PCI with DES implantation was associated with significantly lower rates of stroke (1.5% vs. 4.3%, p = 0.03), but significantly higher rates of TVR (26.7% vs. 15.5%, p < 0.01). When stratifying these outcomes according to lesion complexity as assessed by the SYNTAX score, there are comparable results in both low and intermediate scores, but at the high score (>32), the rates of TVR were significantly higher with PCI with DES implantation versus CABG surgery (34.1% vs. 11.6%, p < 0.001).

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Hence, what do we need to know when planning ULM PCI? First, the extent of the disease, whether restricted to the ostium and mid-shaft or involving the distal bifurcation; second, the angulation between distal branches, if involving the distal bifurcation; third, the degree of mismatch between proximal and distal segments; and fourth, lesion severity. In this issue of the *JACC: Cardiovascular Interventions*, 2 studies shed light on some of the issues and mechanisms associated with PCI failure after DES implantation for ULM. In a subanalysis of the DELTA registry reported by Naganuma et al. (11), distal ULM disease was a significant predictor of major adverse cardiac events (MACCE) (death/myocardial infarction/TVR) at follow-up. There were also trends toward higher rates of death and death/myocardial infarction with distal versus nondistal LM disease. In addition, double stenting was associated with higher MACCE and TVR rates compared with single stenting, regardless of the technique applied. Compared with nonbifurcation lesions, long-term follow-up of bifurcation lesions, in general, shows a relatively higher incidence of restenosis, especially at the side branch ostial location (12). This appears to be the case with ULM, because recurrences after PCI with DES

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implantation are frequently found at the left circumflex ostium (13). In the study by Naganuma et al. (11), increased MACE rates in ULM bifurcation lesions were mainly driven by TVR, but the anatomic location of the recurrences was not provided. A substudy of the SYNTAX trial reported by Girasis et al. (14) investigated the impact of a 3-dimensional bifurcation angle on late outcomes of patients with ULM undergoing PCI with DES implantation. A very interesting finding from this substudy was that a post-PCI systolic-diastolic angle $<10^{\circ}$ between the distal branches of the left main bifurcation, as measured by 3-dimensional dedicated quantitative coronary angiographic analysis, was associated with worse 5-year clinical outcomes. The findings of both studies illustrate the negative impact of distal bifurcation disease and the complex approach to bifurcation PCI in ULM. The use of the complex approach with double stenting for coronary bifurcation PCI is a direct marker of more complex disease (15). Thus, worse outcomes in this subset are not surprisingly observed. Incomplete lesion coverage, stent malaposition, and stent underexpansion are frequently encountered with complex techniques and explain, at least in part, the mechanisms of failure (12). Also, the overall geometry of the coronary tree and the natural dynamic of the bifurcation throughout the cardiac cycle may play a role. Coronary bifurcations are likely the arterial regions with the greatest movement, and those dynamic changes in the relationship between the different segments occur continuously (16). Thus, altering this geometry may lead to sustained and repetitive stresses, which may cause excessive injury to the vessel wall and stent fracture or recoil.

Ostial and mid-shaft lesions are relatively straightforward procedures with predictable results. However, to optimize the results in bifurcation ULM PCI, the issues pointed out here need to be adequately assessed. For lesions without significant involvement of the side branch, the cross-left circumflex artery technique with a single stent is the best approach (6). For true bifurcation lesions with extensive and severe disease involving both branches, a complex approach with elective double stenting may be required. In this situation, an intravascular ultrasound-guided procedure and proper determination of the angulation are critical for selecting the ideal technique (17). These aspects help continue the left main PCI journey toward maturity.

Reprint requests and correspondence: Dr. Fausto Feres, Instituto Dante Pazzanese de Cardiologia Av. Dante Pazzanense, 500 Ibirapuera, São Paulo, SP, Brazil 04012-180. E-mail: fferes@lee.dante.br.

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