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EDITORIAL COMMENT

Leaving Nothing Behind

Bioresorbable Vascular Scaffolds for Femoropopliteal Disease*

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Endovascular intervention is increasingly performed for symptomatic femoropopliteal (FP) occlusive disease. Stand-alone balloon angioplasty is limited by dissection, elastic recoil, and restenosis rates of up to 70% at 1 year (1). Nitinol stents, drug-eluting stents (DES), and drug-coated balloons have all been shown to be superior to stand-alone balloon angioplasty for relatively short (<100 mm) FP lesions (2–4). The long-term patency of bare nitinol stents is disappointing when used for more complex (longer, calcified, and occluded) disease. Permanent implants (either metal and/or polymer based in the case of DES) may remain a trigger for inflammation and smooth muscle proliferation long after implantation. Although better options are now available for the treatment of FP in-stent restenosis, diffuse in-stent restenosis and in-stent occlusion remain a challenging clinical problem (5,6). The limitations of FP stents have led many to advocate for a "leave nothing behind" strategy. In that light, clinical results of drug-coated balloons have been promising (3). When used for longer and more complex lesions, however, "bailout" stenting is required in up to 40% of drug-coated balloon cases.

The next evolution or revolution in the technological arms race for the treatment of FP disease is the bioresorbable vascular scaffold (BVS). The BVS offers several theoretical advantages. First, the dissipated scaffold may limit long-term inflammation and physical irritation to the vessel wall. Second, the BVS facilitates positive vascular remodeling by returning the vessel to its natural "uncaged" state and can preserve vessel biomechanics (i.e., vessel vasomotion). Third, when combined with an antiproliferative agent (such as everolimus), a BVS may improve patency compared with stand-alone balloon angioplasty and other modalities. Fourth, the presence of a BVS does not preclude or impair subsequent imaging with computed tomographic angiography or magnetic resonance angiography. Finally, the potential to "burn bridges" or hamper future endovascular or open surgical procedures is mitigated by this type of implant.

The current generation of BVS is composed primarily of poly-L-lactide (PLLA), a biodegradable polymer with resorption occurring after cleavage of an ester linkage, yielding smaller molecular weight particles (ultimately phagocytosed) along with carbon dioxide and water. The vast majority of clinical experience with PLLA-based scaffolds comes from the Absorb everolimus-eluting coronary BVS (Abbott Vascular, Santa Clara, California). Initial clinical experience demonstrated sustained efficacy of the Absorb BVS in a low-risk patient population with noncomplex coronary artery disease (7). In the past 18 months, several randomized trials have been published, demonstrating noninferiority of coronary BVS to the current generation of coronary DES (8–10).

BVS have been investigated for the treatment of FP disease with both PLLA-based and poly-lactide co-glycolide–based scaffolds. The first of the studies was the PERSEUS study, which evaluated the non-drug-eluting Igaki-Tamai PLLA stent (Kyoto Medical, Kyoto, Japan). This trial included 45 claudicants with lesions of <60 mm in length (11). Although the technical success rate for these noncomplex lesions was 100%, the 6-month restenosis rate was a disappointing 30%. In a separate study with similar lesion characteristics, the non-drug-eluting Igaki-Tamai BVS

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performed poorly, with 12-month restenosis and target lesion revascularization (TLR) rates of 68% and 57%, respectively (12). The Belgian REMEDY study (13) evaluated the next-generation Remedy non-drug-eluting BVS (Kyoto Medical) in 100 patients with short (<75 mm) superficial femoral artery lesions and demonstrated 100% technical success but a 6-month restenosis rate of 29.8%. The initial theoretical promise of BVS for FP disease fell short of expectations, likely because of the platform design and non-drug-eluting property of these particular scaffolds. There has been preliminary investigation with a paclitaxel eluting poly-lactide co-glycolide-based BVS (Stanza DRS; 480 Biomedical, Watertown, Massachusetts) and a novolimus-eluting PLLA-based BVS (DESolve SFA; Elixir Medical, Sunnyvale, California).

SEE PAGE 1178

In this issue of *JACC: Cardiovascular Interventions*, Lammer et al. (14) present 2-year clinical and imaging results from the ESPRIT I clinical trial. This was a prospective trial of 35 claudicants with focal (<50 mm) superficial femoral artery and external iliac lesions treated with an everolimus-eluting BVS (Abbott Vascular). Immediate technical success was 100%, suggesting relative ease of delivery of the scaffold for these straightforward lesions. The 2-year amputation rate was 0%, with only 1 unrelated death, suggesting safety of the therapy. The 2-year restenosis rate was 16.1%, with a clinically driven TLR rate of only 9%. Clinical benefit with regard to Rutherford category improvement was sustained out to 2 years. In a post hoc angiographic analysis, restenosis was less frequent in smaller diameter arteries, suggesting that adequate oversizing of the vascular scaffold is important. Failure to embed the scaffold into the artery wall (as a result of undersizing) may result in a higher risk for BVS thrombosis or restenosis.

The investigators are to be congratulated on successfully demonstrating the safety and efficacy of the everolimus-eluting BVS with impressive 2-year angiographic and clinical outcomes. These findings highlight the importance of the combination of the PLLA backbone with poly-D,L-lactide polymer and everolimus antiproliferative drug coating. One must be cautious in the interpretation of these results, however, given the small sample size and unusual inclusion criteria. Important limitations include the treatment of only short lesions (mean lesion length 36 mm), limited device diameter and length (6 × 58 mm), inclusion of lesions in the external iliac artery (11%), and exclusion of lesions in the popliteal artery. The narrow inclusion criteria limit the broad applicability of the findings from this study. Nonetheless, the data from ESPRIT I are intriguing, especially when comparing against 2-year TLR rates of 22% with bare-metal stents (2) and 17% with DES (4) in patients with similar lesion characteristics. The findings of this phase 1 study provide further evidence that strategies that "leave nothing behind" may yield acceptable restenosis and TLR rates for symptomatic FP disease.

In the current era, we have several good options for the endovascular treatment of FP disease. Unfortunately, randomized head-to-head comparisons between the technologies are lacking, and there are limited data demonstrating the effectiveness of these devices for more complex (calcified, longer than 150 mm, and occluded) lesions. Bioresorbable technologies hold promise for complex lesions for which a scaffold may be needed in the short term but avoidance of a long-term metallic implant is desirable. In ESPRIT I, we saw encouraging results with a first-generation everolimus-eluting BVS. Unfortunately, the pathway to U.S. Food and Drug Administration approval for this first-generation platform or subsequent iterations of this device will be long and arduous. Until approval, when a scaffold is needed during endovascular treatment of complex FP disease, we will be relegated to "leaving metal behind."

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