The DEFINITIVE LE
Atherectomy’s Ability to Leave No Trace or Need for More DEFINITIVE Data?*

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The conservation principle of “Leave No Trace” emerged as a way to preserve the environment for future generations. At the turn of this century in the vascular realm, there was the development of nonstent strategies for the endovascular treatment of infrainguinal peripheral arterial disease to similarly preserve the native vessel. This approach provides numerous advantages, including the preservation of future potential surgical targets and the natural conformability of the vessel while avoiding the placement of a restenosis nidus. The challenge that plagues nonstent technologies, such as directional atherectomy, is the dearth of randomized clinical trials and comparative effectiveness data to support their use. Indeed, many have noted the nonuniformity of the current endovascular literature (1), citing the relatively small patient numbers studied, the lack of core laboratory adjudication of residual stenosis and/or patency, and the limited long-term clinical follow-up. In this issue of JACC: Cardiovascular Interventions, the DEFINITIVE LE (DEtermination of EFFECTiveness of the SilverHawk® Peripheral Plaque Excision System (SilverHawk Device) for the Treatment of Intrainguinal Vessels in Lower Extremities) Investigators (2) present the 1-year results of a large, multicenter study of directional atherectomy and argue that indeed we can treat infrainguinal disease while “leaving no trace.”

The need for an effective yet minimally invasive treatment of infrainguinal disease is clear. With a current worldwide estimate of 202 million people living with peripheral arterial disease (3) and the obesity epidemic driving a rise in diabetes, the investigators appropriately highlight the predicted 552 million people who will be living with peripheral arterial disease by 2030 (4,5). Of this group, a large number will have symptoms refractory to medical and/or exercise therapy and that will require revascularization. For these patients, the vascular specialist must determine which revascularization strategy confers the lowest risk to the patient while ensuring the highest long-term patency. A barrier to this goal is the diffuse, calcific nature of infringuinal atherosclerosis along with its high propensity for progression to occlusive disease. These vessels are additionally subjected to well-documented complex 3-dimensional biophysical forces (6) that have been shown to limit the success of endovascular stenting (7). In response, some operators choose to use angioplasty alone as the primary strategy for infrainguinal revascularization, yet this technique is associated with high restenosis rates, particularly in the treatment of long lesions (8). Many operators choose to use stents based on data showing an enhanced patency over angioplasty in the femoropopliteal segment (9), the relative ease of the procedure, and the high procedural success rate. Stenting, however, leaves a permanent implant that can limit future therapies, can alter the conformity of the vessel, and carries the risk of stent fracture and its associated elevated restenosis rates (7). This restenosis is often diffuse (10) and represents a major limitation of stenting as it is both challenging to treat.

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as well as to preclude from reoccurring. All of these factors have contributed to interest in debulking strategies to treat obstructive infragingual disease. Directional atherectomy is such a strategy that physically removes the obstructing arterial atheroma, potentially obviating the need for a permanent implant.

Data for the use of directional atherectomy is from registries or is limited to single centers and subject to selection bias. These studies were plagued further by the errors associated with interobserver variability when reporting percentage of residual stenosis or restenosis. As such, patency rates have widely varied across these studies depending on patient and/or lesion characteristics and study methodology. DEFINITIVE-LE was designed to address some of these limitations by being a large prospective registry with core laboratory adjudication. The study was also designed to answer whether atherectomy is as effective in diabetic as well as nondiabetic claudicants given the decreased efficacy of endovascular therapies noted previously in this group. The primary endpoint was divided by presentation status, that is, primary patency for claudicants versus freedom from unplanned amputation in critical limb ischemia (CLI) patients at 12 months.

Several aspects of the study group should be noted. First, the patient population consisted of 45% women, and as women typically have smaller vessels than men, restenosis/reocclusion can occur more frequently in this patient subset. Although DEFINITIVE LE permitted inclusions up to 200 mm, the majority of the lesions were evenly divided among <50, 50 to 100, and >100 mm with a mean lesion length of 75 mm, which is comparable to contemporary stent trials. Operators familiar with directional atherectomy also will note a reported average procedural time of just over 1 h (71 min) with a mean fluoroscopy time of 20 min despite a mean stenosis of 74% and an average lesion length of 73 mm, which either reflects a highly experienced group of operators or suggests more focal disease.

Notably, in this large registry, there was a 5.3% arterial perforation rate that is alarmingly high and likely is a byproduct of the small vessels included (mean reference lumen diameter 4.2 ± 1.2 mm), use of atherectomy in the subintimal space, and atherectomy of infrapopliteal vessels, which are smaller and require a less aggressive technique. In contrast, there is a relatively low rate of distal embolization reported (mean 3.8%, n = 30), despite only a 20% use of embolic protection. This highlights the experience of the operators and less calcific disease, as embolization is both lesion- and technique-driven. Although the investigators report that there was no difference in distal embolization with or without a filter, the event rate is too small to have detected a difference, and operators should consider placement of embolic protection for these procedures to truly “leave no trace.”

Finally, the primary 1-year patency of treated vessels in claudicants (Duplex ultrasound peak systolic velocity ratio <2.4) was 78% overall, which is comparable to contemporary stent trials. Surprisingly, given the small caliber of these vessels, infrapopliteal vessels remained 90% patent at 1 year. Additionally, noninferiority of this revascularization strategy in diabetic versus nondiabetic claudicants was demonstrated, which is interesting and demands future study. Limb preservation was achieved in 95% of cases in the CLI group, which exceeds most surgical studies (12,13).

Although all nonstent technologies lack large randomized data to support their use, proponents of directional atherectomy underscore the ability of this approach to preclude stenting; in this large registry, the overall stent bailout rate was 3.2%. In Table 8 of their paper, McKinsey et al. (2) appropriately compare their results with those of contemporary nitinol stent trials. They found that for superficial femoral artery lesions <100 mm, directional atherectomy achieves similar patency rates at 1 year without the need to place a permanent intravascular device. Readers will also note the infrapopliteal lesion subgroup results where the patency rates (mean lesion length 55 mm in claudicants and 60 mm in CLI) surpassed that of the ACHILLES study (Comparing Angioplasty and DES in the Treatment of Subjects With Ischemic Infrapopliteal Arterial Disease Study) (14), wherein drug-eluting stents were placed (mean lesion length 27 mm).

The major weakness of DEFINITIVE LE, as in previous studies of directional atherectomy, lies in its lack of a randomization to a comparative arm. At the time of the study’s creation, there were no U.S. Food and Drug Administration–approved nitinol stents for the femoropopliteal segment, precluding a randomized clinical trial, and it was stated that comparison to balloon angioplasty would have been inadequate given the poor patency associated with balloon alone. Indeed, it is disappointing that to date there have been no large randomized head-to-head trials of atherectomy (any device) versus stenting in the periphery.

The strengths of this registry are its large size, use of core laboratory adjudication, and diversified patient population. DEFINITIVE LE demonstrates that it is possible to effectively treat atherosclerotic disease...
of the infrainguinal vessels with directional atherectomy. The investigators cite the exciting prospect of combination therapy of atherectomy with a drug-coated balloon and cite a small single-center study (n = 30) of heavily-calciﬁed femoropopliteal vessels treated with this approach that reported a 1-year primary patency rate of 90% (15). Perhaps directional atherectomy may not only preserve the vessel, but also prepare the vessel for adjunctive more deﬁnitive therapies such as drug-coated balloons. Overall, the DEFINITIVE LE trial suggests that directional atherectomy for the treatment of claudication and CLI is a promising “leave no trace” endovascular strategy, but we are still left with the need for randomized comparative data examining directional atherectomy versus stent therapy, that is, more deﬁnitive data, prior to fully embracing this technology in the periphery.

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REFERENCES

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