Informing Our Atherectomy Decisions

New data and specialized technologies are emerging, but where do we still need more information?

BY LAWRENCE A. GARCIA, MD

Endovascular treatment of lower limb atherosclerosis has become the default initial, and in many cases, repeat, therapy for patients with symptomatic lower limb claudication and critical limb ischemia (CLI).[1-3] There are many tools and options available to treat the superficial femoral artery (SFA), ranging from simple balloon angioplasty (PTA), to endovascular stenting with nitinol and drug-eluting stents and the more recent drug-coated balloon technologies.[3-7] Other alternative technologies include atheroablative approaches, such as laser and rotational or directional atherectomy approaches.

Figure 1. Spectranetics Excimer laser.

However, robust supporting data have not yet accompanied this increasing usage in some instances. Durability, long-term patency, and outcomes in longer lesion subsets appear to remain major challenges to the modalities for which concrete data are even available.[3,4] What has been critically missing for many of the "alternative" therapies, as is the case with more commonly used options, are data necessary to denote any one device as a default therapy, dictating whether an option should be considered for all, a majority, or only a carefully selected few patients with lower limb atherosclerotic disease.

Here we will provide an update of the current data pertaining to atherectomy devices in the setting of lower limb atherosclerotic disease.

LASER

The currently available atheroablative laser technology is the CVX-300 Excimer laser (Spectranetics Corporation, Colorado Springs, CO) (Figure 1). This device uses a flexible fiber optic catheter to produce photoablation of atherosclerotic disease using an ultraviolet light at 308 nm to penetrate atheroma, dissolve the molecules thereby producing thermal energy, and create kinetic energy that breaks chemical bonds at the molecular level and vaporizes intracellular water to disrupt atheroma and remove plaque. There have been several older studies,[8-11] but few new data have been offered using this device in the last 2 to 3 years.

One of the earliest trials was the PELA (Peripheral Excimer Laser Angioplasty) trial, in which 251 patients with claudication and total SFA occlusions were randomized to either PTA alone or laser-assisted PTA.[8] There was no difference in the primary outcomes between the two strategies. Another previous study on laser therapy was the LACI (Laser Angioplasty for CLI Phase 2) study.[11] In this trial, 145 patients were enrolled, and all were considered poor surgical candidates. Laser atherectomy and adjunctive PTA were performed in 96%, and stenting was performed in only 45% of the patients studied. The 6-month limb salvage rate was 92.5%, with an 8% major amputation rate and 10% mortality, primarily due to cardiac issues.

Many reports suggest that laser is useful in crossing chronic total occlusions[10] or long stenotic lesions, whereas other investigators have advocated its use in highly calcified or thrombus-laden arteries or for in-stent restenosis. Almost universally, laser requires adjunctive balloon therapy after its use, and the potential for using laser with a drug-coated balloon seems like an attractive option.

One important step in obtaining further data for this device is the recently started US EXCITE trial. This trial is attempting to define the unique role of laser for in-stent restenosis, with a safety endpoint at 30 days and a primary efficacy endpoint at 6 months. This trial is

currently enrolling and will have data on 353 patients. It will randomize patients with in-stent restenosis in a 2:1 fashion between laser with adjunctive PTA compared with PTA alone for patients with in-stent restenosis in the femoropopliteal location. This trial builds on the presented 6-month data of the PATENT trial, which evaluated 90 patients with in-stent restenosis. The 6-month data were presented at the LINC meeting in 2012 by Dr. van den Berg and showed a freedom from target lesion revascularization rate of 76%. These data, although early, suggest a meaningful early role for laser in the treatment of patients with significant in-stent restenosis, an indication that, to date, no device can claim. These trials, in addition to the PHOTOPAC study using laser with drug-coated balloon technology, may afford some signals regarding this intriguing combination therapy.

With these data, the current landscape suggests that there may be a role for laser with adjunctive PTA, with or without drug, in the treatment of long SFA lesions. The ability of this device to treat patients with tibial disease and CLI remains likely, although its amputation-free survival rate is similar to PTA alone. The final evaluation will depend on the 12-month outcomes of current trials that are underway.

ROTATIONAL AND ORBITAL ATHERECTOMY

There are currently two types of rotational or orbital atherectomy devices available in the United States: the Jetstream Navitus atherectomy system (Bayer Radiology & Interventional, Indianola, PA) (Figure 2) and the Diamondback atherectomy system (Cardiovascular Systems Inc., St. Paul, MN).

The Jetstream Navitus system uses a fluted, differential cutting tip with an expandable cutting surface on two models for active removal of both hard and softer plaque, as well as calcium and thrombus, from the peripheral arteries. The expandable cutting surface, which is deployed by counterclockwise rotations of the catheter, allows the system to treat several vessel sizes from the tibial to a larger common femoral artery, giving the device a variable-use design with one insertion. The device further flushes from distal ports and then actively aspirates from a proximal port, allowing the debris that is liberated to be withdrawn before distal embolization occurs.

The first trial for this device was the Multicenter Pathway PVD trial,[12] which was used to obtain CE Mark approval in Europe. This trial was a nonrandomized prospective study enrolling 172 patients (47% of which were diabetics) treating 210 lesions. The primary study endpoint was the 30-day major adverse event rate (1%). The mean lesion length treated was 27 mm, including

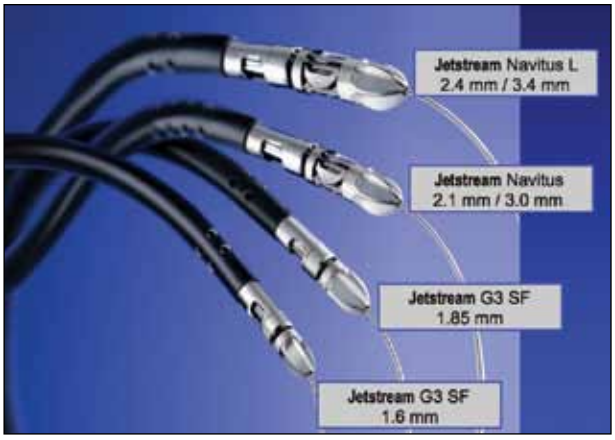

Figure 2. The Jetstream atherectomy device line.

total occlusions (31%). The lesions were considered moderate to severely calcified in 52%. Procedural success was achieved in 99% of the target lesions, and 33% of the interventions were standalone atherectomy procedures. All imaging data were adjudicated via independent angiographic and sonographic core labs.

Currently, the device is being evaluated in two post-approval studies. The first is the JET registry, which will enroll up to 500 patients in a nonrandomized study evaluating the Jetstream device in de novo lesions in the femoropopliteal location, with a primary outcome of binary restenosis at 12 months as defined by duplex ultrasound. There are currently 21 patients enrolled at 15 eligible sites.

The second study is a prospective, single-arm study to evaluate the effects of the Jetstream Navitus system on calcified peripheral vascular lesions. An independent IVUS core lab will adjudicate the treatment effects of the system in moderate to severely calcified peripheral artery disease in the common femoral, superficial femoral, or popliteal arteries. Current enrollment is 24 patients at five US sites.

Despite the overall lack of data, this device appears to be safe and effective in the treatment of calcified lesions of the femoropopliteal location; the durability seems less clear. The need for distal protection in heavily calcified lesions has not been evaluated or reported with any great vigor; its overall use as a primary therapy remains unclear.

The Stealth orbital atherectomy system (Cardiovascular Systems Inc.) (Figure 3) consists of an eccentric diamond grit–coated abrasive crown that, when activated at various speeds, creates an ablative surface proportional to the displaced radius of the crown.

The device's basis of operation presumes that elastic, healthy tissue flexes away from the crown, thereby not

Figure 3. Stealth orbital atherectomy device.

Figure 4. The TurboHawk plaque excision system.

being affected as it passes through. Use of the device in hardened, diseased tissue, however, results in resistance and the "sanding" away of plaque. The debris are embolized but relatively small (1–7 µm in 99.93%) (Data on file from Cardiovascular Systems, Inc.). The debris is embolized distally to pass through the distal capillary beds and is filtered from the circulation in the lungs or other filter organs, not unlike rotational atherectomy in the coronary circulation.

The first trial for this device was OASIS (Orbital Atherectomy System for the Treatment of Peripheral Vascular Stenosis).[13] This trial was a nonrandomized, prospective, investigational device exemption study that enrolled 124 patients with 202 lesions. The primary outcome was patient safety and acute procedural effectiveness. The average lesion length studied was 30.2 mm, treating mostly claudicants (55% of the subjects). Procedural success was achieved in 90.1% of the lesions and was used as a stand-alone therapy in 57.7%. The major adverse event rate at 30 days was 9.7%. There was no primary patency endpoint for this trial. A study of the orbital atherectomy system for the treatment of peripheral vascular disease (PAD II) evaluated 66 patients and 86 lesions, with an average lesion length of 35.1 mm. Standalone therapy was achieved in only 39.5% of the lesions, and there was 24.2% adverse event rate at 30 days.

Results from the CONFIRM 3,000-patient registry will be released in 2012. CONFIRM evaluated the Stealth system in more than 4,700 lesions in the femoropopliteal location. There were no exclusion criteria. The outcomes are purely clinical, without core lab–adjudicated outcomes either at 6 months or 1 year. In addition, the COMPLIANCE 360° and CALCIUM 360° studies revealed that the need for high-pressure balloon inflation was less likely in the atherectomy group compared with the balloon-only group. The acute results revealed that stenting was not required in the group with antecedent atherectomy compared with balloon alone.[14,15]

DIRECTIONAL ATHERECTOMY

The TurboHawk, the newest addition to the SilverHawk family of products (Covidien, Mansfield, MA), is a directional atherectomy device that debulks atheroma without a balloon for apposition using a hinged system (Figure 4). The device uses a tungsten carbide cutter with variable height and consistent rotation at speeds of 8,000 rpm, which allows it to appose atheroma for debulking. There have been no randomized trials to date using this device; however, several registries[16-18] have demonstrated its safety, but with limited long-term benefit with regard to durability in longer lesions. There have been some signals regarding its benefit in diabetic patients and in the infrapopliteal space.

Recently, DEFINITIVE LE (Determination of Effectiveness of Directional Atherectomy for the Treatment of Infrainguinal Vessels/Lower Extremities) evaluated the intermediate and long-term effectiveness of standalone atherectomy in the treatment of peripheral arterial disease in the lower limbs. In this largest study of its kind, 800 patients and just fewer than 1,100 lesions were treated with SilverHawk and TurboHawk devices in both claudicants and patients with CLI. This study enrolled patients with any lesion up to 20 cm in length, with the primary endpoint being primary patency at 12 months or freedom from major unplanned amputation through 12 months for those with CLI. The preliminary data (6 month) were presented in 2011 at VIVA.[19] At 6 months, the primary patency rate was 87.4% for claudicants and 89.7% for diabetics. Interestingly, short (< 4 cm), medium (4–9.9 cm), and long (> 10 cm) lesions all had a similar primary patency at this time frame; a 95.9% freedom from amputation rate was also observed. The final dataset will be presented this year at VIVA. The safety profile for this device has always been under scrutiny (primarily its distal embolic event rate); however, in the DEFINITIVE LE trial, adjudication is via independent angiographic and sonographic core labs. The overall embolic event rate presented at 6 months was 4.1%.

FUTURE DEVICES

The Phoenix catheter (AtheroMed, Inc., Menlo Park, CA) (Figure 5) is currently undergoing evaluation in an

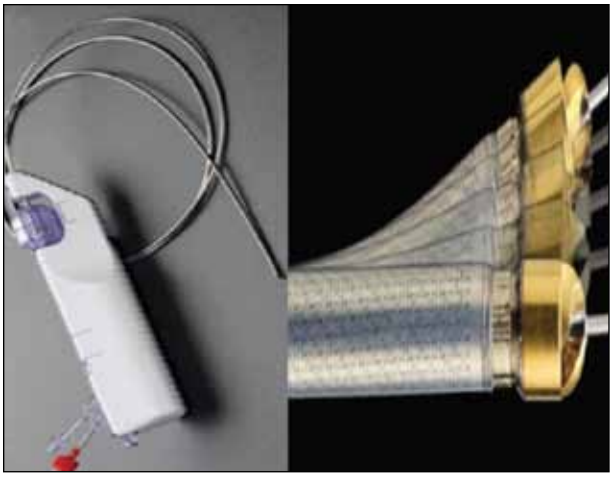

Figure 5. The Phoenix atherectomy catheter.

FDA-approved, investigational device exemption trial enrolling 90 patients to evaluate the procedural safety and effectiveness of this device in treating de novo and restenotic lesions. This device is already CE Marked and has a front-cutting mechanism with a deflectable tip that is engineered to treat several sizes of blood vessels with a single insertion device. The results of this trial are currently unavailable.

CONCLUSION

Durability and long-term patency remain a major challenge to all devices in the endovascular treatment of short, medium, and long SFA obstructive disease. The principal failure for all devices remains target lesion restenosis. Atherectomy remains a viable option for the treatment of lower limb symptomatic disease; however, current devices for the treatment of lower limb atherosclerosis remain limited, based on the data alone. The data set for stenting has become more robust, and this technology has set the standard that all other devices need to meet to become a "default" therapy in this region.

To date, single-device evaluative trials have shown that atherectomy, regardless of style, is a reasonable alternative to direct stenting in most patients studied in the lower limb. The recently completed directional atherectomy (DEFINITIVE LE) trial has undergone scrutiny with independent angiographic and sonographic core lab analyses on outcomes. This key trial will likely be the one to either support atherectomy's current use and growth or put the halt on its "workhorse" use for many patients we treat in the endovascular suites or our respective institutions.

For future device directions, one can envision that the marriage of debulking followed by the promise of drug-coated balloons will afford our patients the greatest primary patency without the need to leave an endoprosthesis behind. This alluring combination is currently under investigation in the DEFINITIVE AR trial that is enrolling in Europe. The benefits with the overt costs of such an approach compared with the current stenting environment and cost analysis are yet to be seen. If both long and short lesions can be effectively treated in this manner and the restenosis rates are low or occur more focally, then simple balloon angioplasty alone can be the intervention of choice in achieving assisted primary patency. If successful, a cost analysis of this combination treatment would likely be favorable when compared to repeat treatment strategies involving recurrent restenosis of indwelling endoprostheses. What remains elusive are the direct comparative trials that would allow operators to determine which device is superior to another without having to infer data from one trial to another. ■

Lawrence A. Garcia, MD, is Chief, Section Interventional Cardiology and Vascular Interventions, St. Elizabeth's Medical Center, Tufts University School of Medicine in Boston, Massachusetts. He has disclosed that he is on the advisory board for Boston Scientific, ev3/Covidien, Spectranetics, Pathway Medical/MedRad, AngioSculpt, and Idev Technologies; has research support from TriReme; is an equity shareholder in Scion Cardiovascular, Arsenal Medical, TissueGen Medical, Primacea, CVI Technologies; and was a global Principal Investigator for the DEFINITIVE LE trial. Dr. Garcia may be reached at lawrence.garcia@steward.org.

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