

# Treating Calcified Below-the-Knee Arteries

Orbital atherectomy and other techniques and considerations.

BY RAYMOND DATTILO, MD, FACC

An aging population along with an increasing prevalence of diabetes means that an escalating incidence of critical limb ischemia (CLI) can be anticipated. Growing recognition of the morbidity and cardiovascular mortality associated with CLI has spurred increased efforts aimed at earlier diagnosis and treatment to avoid amputation. Patients with diabetes and those undergoing dialysis in particular more frequently develop vessel calcification that complicates both diagnosis and therapy and is associated with a worse prognosis than patients without calcification. The ankle-brachial index measurement becomes falsely elevated with calcification, and even palpable pedal pulses cannot ensure vessel patency. An elevated ankle-brachial index has been shown by Silvestro et al<sup>1</sup> to be predictive of major amputations in CLI patients. It has been further demonstrated by Guzman and colleagues<sup>2</sup> that the greater the tibial artery calcification, the greater the likelihood of CLI and the risk of amputation. Therefore, like coronary calcium scoring, tibial artery calcification scoring correlates with the severity of disease and serves as a useful prognostic marker.

Revascularization therapy for CLI continues to prove challenging. Although surgical bypass for infrainguinal and infrapopliteal disease has a well-established track record for the treatment of CLI in patients who are acceptable surgical candidates, the BASIL (Bypass Versus Angioplasty in Severe Ischemia of the Leg) trial<sup>3</sup> showed similar clinical outcomes between surgery and balloon angioplasty (BA), the latter being associated with lower cost. Consequently, there has been a growing trend toward endovascular treatment for this disease, with BA remaining the cornerstone of this form of therapy.

Long total occlusions of the infrapopliteal vessels have become increasingly amenable to therapy with longer and lower profile balloons and innovative techniques such as retrograde pedal access. However, the diffuse nature of the disease, in addition to a high prevalence of calcification, has

highlighted the shortcomings of BA and encouraged efforts to develop more effective and durable therapies. Despite a plethora of such devices, none have proven to be superior to BA for treating below-the-knee (BTK) disease in CLI in a large, randomized trial. With that acknowledged, this article reviews some of these devices as they pertain to the treatment of calcified BTK disease, which often accompanies CLI.

## STENTING FOR CLI PATIENTS

The inadequacies associated with BA in calcific disease are well known but in essence involve vessel dissection and recoil acutely and negative remodeling and smooth muscle cell proliferation in the long-term. Stents have been used successfully in other vascular territories and can overcome some of these shortcomings but have not performed as well in BTK vessels. Interim data reported from the XCELL trial,<sup>4</sup> a single-arm, prospective trial that treated 120 patients with CLI using the Xpert nitinol self-expanding stent (Abbott Vascular, Santa Clara, CA) (87.5% were placed in the tibioperoneal trunk, tibial artery, or peroneal artery), showed a 6-month major amputation rate of 6.1%, total lesion revascularization (TLR) rate of



Figure 1. Nonhealing first and second toe amputations, gangrene of third toe, and lateral foot ulcer.

31.3%, and a complete wound healing rate of 53.5%. This method does not seem able to provide the desired results. Furthermore, the wound healing data highlight the fallacy of the conventional wisdom that patency must only be maintained for 6 months to heal the wound.

Additionally, the issue of durability does not take into consideration the problem of recurrent CLI after initial wound healing. The true recurrent CLI rate has not been well studied but is estimated to be approximately 15%. Therefore, one is forced to consider the notion that for a great many of these CLI patients, patency durability may be as important as it is for claudicants. In contrast to self-expanding bare-metal stents, drug-eluting coronary stents have shown more positive results. The PARADISE trial,<sup>5</sup> a single-arm trial in which investigators implanted 228 drug-eluting stents (83% Cypher [Cordis Corporation, Bridgewater, NJ] and 17% Taxus [Boston Scientific Corporation, Natick, MA]) in 118 limbs in 106 patients, showed a 3-year amputation rate of 6% and a TLR rate of 15%. However, these stents would seem to be impractical for treating the relatively long diseased segments that are often present in CLI patients.

### EXCIMER LASER

The Turbo Elite laser ablation catheter (Spectranetics Corporation, Colorado Springs, CO) has been used with some success in treating patients with CLI. The LACI 2 (Laser Angioplasty for Critical Limb Ischemia Phase 2 Trial) study treated 177 infrapopliteal lesions (a total of 432 lesions including femoropopliteal) with a limb salvage rate at 6 months of 93%, making it at least comparable to BA.<sup>6</sup> However, despite being able to traverse calcified segments and reduce dissection, the laser is not very effective in ablating calcium. Mintz et al<sup>7</sup> showed that in coronary lesions, lumen improvement as determined by intravascular ultrasound after excimer laser therapy was the result of both tissue ablation and vessel expansion (increase in the external elastic membrane area of the vessel), with no change in calcium and was in effect partially “dottering” its way through calcified segments. In addition, 84% of lesions with superficial calcium demonstrated dissections, and fibrocalcific lesions tended to present with a fragmented appearance after excimer laser treatment on intravascular ultrasound.

### CUTTING BALLOONS AND FOCAL FORCE BALLOONS

Cutting balloons (Boston Scientific Corporation) and focal force balloons, including the AngioSculpt (AngioScore, Inc., Fremont CA) and VascuTrak (Bard Peripheral Vascular, Inc., Tempe, AZ) devices, have been used to treat fibrocalcific lesions. With these devices, the blades or wires act to concentrate force and fracture plaque in a slow and controlled



**Figure 2.** There are no continuously patent tibial vessels to the foot (A, B). There is no significant flow to the forefoot (C).

manner, reducing the frequency of extensive dissection and decreasing vessel barotrauma as a result of the lower balloon inflation pressures that are required to expand the vessel. The Cutting balloon is relatively short and rigid and is most appropriate for ostial lesions and bifurcations. The AngioSculpt balloon incorporates spiral nitinol wires encircling the balloon and provides improved flexibility compared to the Cutting balloon. A multicenter registry using this balloon to treat 51 patients for infrapopliteal disease (90.2% with CLI) showed a 12.5% rate of dissection that required stenting.<sup>8</sup> Clinical follow-up was not reported for this study. The VascuTrak focal force balloon is available in longer lengths (up to 300 mm) and is also more trackable than the Cutting balloon due to its use of two flexible external wires (an intrinsic wire and a guidewire) that act as the force concentrators and therefore is more suitable for the diffuse disease that is generally encountered in CLI patients.

A retrospective, nonrandomized white paper report of 25 CLI patients<sup>9</sup> showed a 3-month limb salvage rate of 88% in these patients, with an adjunctive therapy rate of 16%. Although Cutting balloons and focal force balloons may be effective for treating lesions with mild to moderate superficial calcium, they more frequently result in tears with heavier or more circumferential calcium, which then requires adjunctive stenting.

### EXCISIONAL ATHERECTOMY

Excisional atherectomy using the SilverHawk device (ev3 Inc., Plymouth, MN) has shown proficiency in debulking lesions and has yielded excellent acute results in both infrainguinal and infrapopliteal lesions, with TLR and limb salvage rates that have historically been comparable to BA. Initial iterations were largely ineffective for heavily calcified lesions but later versions of the device (TurboHawk) have incorporated changes to the material and geometry of the

cutting blade, which allow it to more effectively excise calcified plaque for treating femoropopliteal disease. However, the demonstration of plaque macroembolization has often prompted the adjunctive use of embolic filter protection devices. Furthermore, at this time, a calcium-cutting SilverHawk device is unavailable for infrapopliteal vessels.

## ORBITAL ATHERECTOMY

The Diamondback 360° orbital atherectomy system (OAS) (Cardiovascular Systems Inc., St. Paul, MN) was developed for treating infrapopliteal calcific disease, although its efficacy has also been demonstrated in treating calcific femoropopliteal disease. This system has been previously well described<sup>10</sup> but, briefly, an eccentrically weighted, diamond-coated crown orbits as it rotates, preferentially sanding calcium and other relatively noncompliant components of the target lesion. The particulate has a mean diameter of 2 μm, and macroembolization has been distinctly uncommon.

The therapeutic benefit of the device is derived from its ability to differentiate noncompliant tissue (calcific and fibrocalcific plaque) from compliant tissue (normal elastic vessel wall). By removing the noncompliant elements of the plaque, it allows adjunctive BA when necessary to be effective at lower inflation pressures and minimizes dissection by creating uniform, circumferential vessel compliance. At the same time, decreased injury to the vessel wall resulting from the Diamondback 360°s compliance differentiation preserves medial integrity (shown on histologic sections from treated porcine and cadaver arteries),<sup>11</sup> which should lead to decreased restenosis rates. The consequent low stent bailout rates after OAS therapy for infrapopliteal and femoropopliteal disease, which has been demonstrated by

several small studies<sup>12-14</sup> and will hopefully be confirmed by the recently completed multicenter, randomized COMPLIANCE 360° trial,<sup>15</sup> may also favorably affect restenosis given the poor patency rates exhibited by bare-metal stenting in the tibial vessels.

OASIS (Orbital Atherectomy System for the Treatment of Peripheral Vascular Stenosis)<sup>10</sup> is a single-arm, prospective, multicenter trial using OAS to treat 124 claudicant and CLI patients; 85% of the lesions were infrapopliteal, 55% contained calcium, 39% were chronic total occlusions, and 32% of patients had CLI. Furthermore, 58.2% of the lesions achieved a residual stenosis of < 30% with OAS alone. There were no major dissections and there was a stent rate of only 2.5%, with no major amputations out to 6 months. The OASIS Long-Term study,<sup>16</sup> a retrospective analysis of just more than half of the OASIS patients who had similar demographics and lesion characteristics as the original total cohort, found a TLR rate at 12 and 24 months of 8.7% and 13.6%, respectively. This fares well compared to historical controls using BA in this difficult group of patients and speaks to the durability of this approach. Patola et al<sup>13</sup> reported on 150 patients with tibial vessel disease, 80 who received OAS therapy and 70 who received BA, and noted a stent bailout rate of 45% in the BA group and a 5% rate in the OAS group, which is consistent with the OASIS data for this outcome.

CONFIRM<sup>17</sup> is a real-world trial of unconditional OAS or adjunctive therapy use that prospectively studied 728 consecutive patients with peripheral arterial disease from 57 institutions treated with OAS; 53.5% of the patients were treated for popliteal and tibial disease. Bailout stenting for dissection occurred in 2.2% of the patients, and the total stent rate was 5.6%, which is also consistent with the other trials noted. Remarkably, distal embolization was reported in only 0.7%. The CALCIUM 360° trial is a 50-patient, multicenter, prospective, randomized pilot study comparing OAS to BA for treating CLI with calcified BTK disease and has completed enrollment. The primary endpoint is core lab adjudicated acute angiographic success (≤ 30% residual stenosis) without major dissection, although 6 and 12 month clinical and functional follow-up is planned.

Mustapha<sup>14</sup> reported retrospectively on 32 CLI patients who were treated in a similar manner to the patient in the subsequent case report with occlusion of all calf vessels and who were evaluated for major amputation.



**Figure 3.** The Crosser catheter (Bard Peripheral Vascular) in the anterior tibial (A) and dorsalis pedis (B); note the calcium shown.



**Figure 4.** The Diamondback catheter.



Figure 5. BA of dorsalis pedis (A) and anterior tibial (B) vessels.

Approximately one-third of these patients were reported to have no distal vessel reconstitution upon initial angiography. The presence and degree of calcium was not specifically reported. Successful entry into a distal foot vessel with the Crosser catheter was followed by OAS therapy and adjunctive low pressure BA. A 100% success rate was reported, as judged by one or more palpable or dopplerable foot pulses postprocedure and angiographic patency at 6 weeks without bailout stenting. Clinical follow-up was not reported.

### CASE STUDY OF OAS FOR CLI

A 67-year-old diabetic man with CLI and a history of cigarette smoking was treated with OAS by the author (Figure 1). Note that the first two toes have already been amputated and have not healed, the third toe has gangrene, and the lateral surface of the foot has developed an ulcer from an ill-fitted walking boot. The patient has been planned for a transtibial amputation. It is unclear whether the remaining toes can be salvaged, but converting this into a lesser transmetatarsal amputation would allow the patient greater mobility and a much better overall prognosis. Figure 2 shows the lack of a continuous tibial conduit and absent flow in the forefoot.

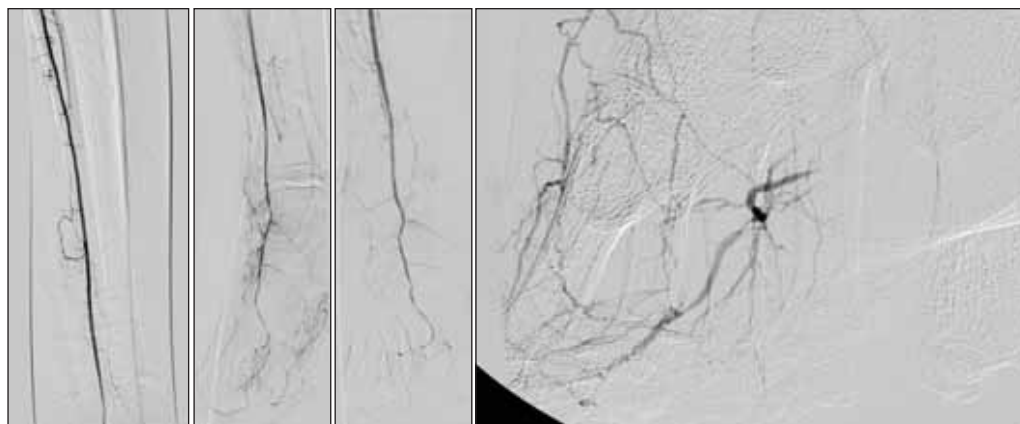


Figure 6. Final angiograms; note the improved flow to the forefoot.

It is important to note that although BA and stenting can be performed in a subintimal plane, atherectomy requires intraluminal passage of the guidewire. To this end, the Crosser device has proven to be effective in maintaining intraluminal status through chronic total occlusions and was used in this case to traverse the long occlusion of the anterior tibial artery into the dorsalis pedis in the foot (Figure 3).

Finally, Figures 4 through 6 show the remaining procedural steps, including OAS and adjunctive, low-pressure BA ( $\leq 4$  atm), and the resulting improved flow to the foot. Note the smooth lumen and distinct lack of any dissection despite the vessel calcification, features typical of OAS therapy in this vascular segment.

### CONCLUSION

Although definitive data in the form of large randomized trials are still lacking, treatment with OAS for calcified infrapopliteal disease appears to offer distinct advantages based on the growing data that are available for this therapy. The Diamondback device largely overcomes the acute mechanical problems that are often associated with treating calcific disease by improving lesion compliance, and thereby minimize major dissection and vessel recoil and the need for bailout stenting. In addition, decreased barotrauma and maintenance of medial integrity should translate to decreased late restenosis via neointimal hyperplasia. The smooth lumen that is usually created also contributes to more laminar (less turbulent) flow, which is known to favorably affect wall shear stress and restenosis.

As investigations into the use of antirestenotic drugs such as paclitaxel continue to be explored beyond its use with stents, the hope for additional reductions in recurrence rates may be anticipated with such combination therapies. In any case, as the population ages, diabetes continues to increase, and awareness of CLI grows,

*(Continued on page 95)*

(Continued from page 89)

endovascular specialists will be challenged to avoid limb loss in these patients. As the paradigm continues to shift from surgical to endovascular therapy and limb salvage, emphasis must be placed not only on conceiving better devices but also on patient and physician education, earlier diagnosis, and better coordination among the multiple specialties involved in the care of these patients. ■

*Raymond Dattilo, MD, FACC, is Director of Peripheral Vascular Interventions at the Kansas Heart and Vascular Center; Cardiology Consultants of Topeka, PA in Topeka, Kansas. He has disclosed that he receives research funding and speaking honoraria from Cardiovascular Systems, Inc., and consultative, speaking, and physician training fees from Bard Peripheral Vascular, Inc. Dr. Dattilo may be reached at (785) 233-9643; icardmd@aol.com.*

1. Silvestro A, Diehm N, Savolainen H, et al. Falsely high ankle-brachial index predicts major amputation in critical limb ischemia. *Vasc Med.* 2006;11:69-74.
2. Guzman RJ, Brinkley DM, Schumacher PM, et al. Tibial artery calcification as a marker of amputation risk in patients with peripheral arterial disease. *J Am Coll Cardiol.* 2008;51:1967-1974.
3. Adam DJ, Beard JD, Cleveland T, et al; BASIL trial participants. Bypass versus angioplasty in severe ischemia of the leg (BASIL): multicenter, randomized controlled trial. *Lancet.* 2005;366:1925-1934.
4. Interim results from the VIVA I: Xcell trial [news release]. *Endovascular Today*; October 22, 2009. [http://bmctoday.net/evtoday/2009/10/article.asp?f=eNews102909\\_06.htm](http://bmctoday.net/evtoday/2009/10/article.asp?f=eNews102909_06.htm). Accessed July 29, 2010.

5. Feiring AJ, Krahn M, Nelson L, et al. Preventing leg amputations in critical limb ischemia with below-the-knee drug-eluting stents: the PARADISE (Preventing Amputations Using Drug-Eluting Stents) trial. *J Am Coll Cardiol.* 2010;55:1580-1589.
6. Laird JR. Laser angioplasty for critical limb ischemia (LACI): results of the phase 2 clinical trial. Presented at: ISET 2003; January 19-23, 2003; Miami Beach, FL.
7. Mintz GS, Kovach JA, Javier SP, et al. Mechanisms of lumen enlargement after excimer laser coronary angioplasty. *Circulation.* 1995;92:3408-3414.
8. Scheinert D, Graziani L, Peeters P, et al. Results from the multicenter registry of the novel angioplasty scoring balloon catheter for the treatment of infrapopliteal disease. *Circulation.* 2006;114:11820.
9. Patlola R, Hebert C, Walker C, et al. VascoTrak 2 balloon angioplasty in infrapopliteal peripheral arterial disease: a review in limb salvage rates. [http://www.medpoint.co.il/news\\_reports/ymed/vascu-trak2\\_whitepaper.pdf](http://www.medpoint.co.il/news_reports/ymed/vascu-trak2_whitepaper.pdf). Accessed July 29, 2010.
10. Safian RD, Niazzi K, Runyon JP, et al. Orbital atherectomy for infrapopliteal disease: device concept and outcome data for the OASIS trial. *Cathet Cardiovasc Interv.* 2009;73:406-412.
11. Cardiovascular Systems, Inc. [unpublished data]. Animal studies, February 2004 and November 2004; cadaver study, November 2006.
12. Dattilo R. Compliance change using the Diamondback orbital atherectomy system for treatment of calcified femoropopliteal disease. Abstract presented at: New Cardiovascular Horizons; New Orleans, LA; July 9-11, 2009.
13. Patlola R, Hebert C, Allie D. Orbital atherectomy in treatment of peripheral arterial occlusive disease below the knee: a large single-center experience. Abstract presented at: Transcatheter Cardiovascular Therapeutics 2009; September 21-26, 2009; San Francisco, CA.
14. Mustapha JA. Limb salvage with novel endovascular devices in the absence of target vessel reconstitution. Presented at: International Symposium on Endovascular Therapy; January 18-22, 2009; Hollywood, Florida.
15. Dattilo R. The COMPLIANCE 360° trial: the principal investigator discusses its rationale, study design, and potential therapeutic implications. *Endovascular Today.* 2010;9:71-73.
16. Cardiovascular Systems, Inc. OASIS LT. <http://www.csi360.com/clinical-data.html#oasislt>. Accessed July 29, 2010.
17. Dattilo R, Aggarwala G, Nasser N. Real-world results CONFIRM application of orbital treatment in effectively modifying noncompliant lesion morphology and successfully restoring ample blood flow in patients with calcific peripheral arterial disease. In press. *JACC.*