Atherectomy in the Treatment of Lower-Extremity Peripheral Artery Disease: A Critical Review

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ABSTRACT: In the United States, peripheral artery disease (PAD) is on the rise due to an epidemic increase in metabolic diseases like diabetes, aging population, and tobacco use. Until recently, accepted management strategies for treatment of symptomatic lower extremity PAD were limited to balloon angioplasty and self-expanding nitinol stents (either open design or covered). The goal for endovascular PAD intervention is to maintain and improve the mobility of the patient. With ambulation there are specific movements to the superficial femoral artery and it is subjected to various and continuous stresses to include compression, torsion and bending which can ultimately result in stent fracture or in-stent restenosis for endovascular therapy. Treatment with atherectomy for symptoms of lower extremity disease has now been shown to be effective in re-establishing blood flow with minimal vessel trauma and may serve as an alternative to a stent-first approach. Additionally, the presence of plaque with modest to severe calcification remains common and a debulking approach initially with further adjunctive therapy remains appealing.

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Nearly 8 million Americans are affected by peripheral artery disease (PAD) involving the arteries of the lower limb (iliac, femoral, popliteal, and tibial). This number is expected to increase in the future as the population ages, leading to more symptomatic atherosclerotic plaque in various arterial systems including the coronary, carotid, and lower extremity. Additionally, risk factors such as diabetes, hypertension, smoking, morbid obesity, and renal disease are expected to further contribute to the worsening disease spectrum of PAD in the United States. Even though there has been an explosion in the treatment options for coronary artery disease in recent years, choice of therapy for PAD is still in its infancy.

Lower-extremity arteries such as the superficial femoral artery are exposed to a multitude of chronic conditions such as torsion, lengthening, and rotation during the activities when the patient is ambulatory. Along with other metabolic risk factors and physical strain of the vessel, the lower extremity arteries undergo pathophysiological stresses that are unique and different than other vascular beds, resulting in higher calcified atherosclerotic burden in the lower extremities. Most often PAD is undiagnosed or goes undiagnosed until the patient presents with severe lifestyle-limiting claudication, rest pain, critical limb ischemia, or tissue loss.

In the United States, treatment options for the management of PAD have increased in number but remain limited in scope. Also we are lacking substantial scientific data and large-scale studies to help define which if any therapy is best or the “gold standard” for most or all patients. The majority of interventionalists use balloon expansion as the principal therapy in treating lower-extremity PAD. This can be associated with vascular baro-trauma leading to an increased incidence of restenosis and the need for reintervention as lesions become longer (RESILIENT, ABSOLUTE, Zilver) or more heavily calcified. The use of stents in the lower extremity vascular tree has been shown in broad studies to reduce the restenosis rate and increase the patency of the vessel.
at 1 and 2 years compared with simple balloon angioplasty. However, this therapy has limited applicability in lesions beyond 10 cm or in those with heavily calcified territories and in lesions of considerable length (usually approaching 20 cm). From a scientific perspective, because of ongoing vessel extrinsic forces from ambulation, the effective use of stents can be limited especially near the joint spaces or in highly constrained locations, which may contribute stent fractures and contribute ultimately to stent failure. Changing arterial compliance through debulking, particularly with calcified target lesions, has been reported as beneficial. Recent data has suggested an increased benefit with atherectomy with or without adjunctive therapy compared to expanding the vessel by compressing and dissecting the plaque by balloon angioplasty, theoretically, debulking of the atheromatous plaque will give rise to the larger luminal diameter. In a study reported by Aboufakher et al, total plaque volume was decreased by 24%, which resulted in a lumen increase of 66% due to plaque excision with atherectomy without any significant increase in the overall vessel area by intravascular ultrasound (IVUS).

Principally, atherectomy devices remove plaque, including calcified plaque, by physically shaving, drilling, or pulverizing by sanding the plaque, resulting in modification of the vessel and its arterial compliance in the case of those vessels with calcium. Because this can be achieved through minimal vessel barotrauma, the incidence of acute complications including dissection and acute vessel occlusion may be reduced. It has also been reported that the final results are superior to balloon angioplasty alone in these vessels treated. Current directional atherectomy has been theorized to provide revascularization without adjunctive treatment including PTA, thereby decreasing resultant vessel injury through barotrauma, which may reduce the rate of restenosis. Atherectomy may also provide the ability to treat longer lesions without the need for a lengthy endoprosthesis and further can preserve side branches as compared to a balloon–stent approach. By preserving the native vessel anatomy and configuration with regard to compliance and inherent torsional forces, future interventions can also be performed including stenting or repeated atherectomy. Potential complications associated with atherectomy devices include hematoma, pseudoaneurysm, distal embolization, or vessel rupture.

Atherectomy devices were initially used in the management of coronary artery disease and were found to be ineffective compared to contemporary bare metal stents of the day. Ahn et al reported 82% to 100% success rate with directional Simpson AtheroCath (Flexi-Cut). However the intermediate-term patency rates were 35% to 84% with 6-month restenosis rates ranging from 11% to 55%. Another study reported a large amount of retained plaque with the Simpson device, which led to reduced use of atherectomy devices. Many small studies were performed using distal protection devices in the treatment of PAD to reduce the incidence and complications associated with embolizations during atherectomy.

Current available atherectomy devices function on several principles such as rotational, directional, orbital, or atheroablative in the management of PAD for both claudicants and patients with critical limb ischemia.

**LASER ATEROABLATIVE TECHNIQUES**

Laser therapy received FDA approval with the LACI (Laser Angioplasty for Critical Limb Ischemia) multicenter trial, which showed 92% limb salvage at 6-month follow-up of critical limb ischemia. A total of 145 patients were included in the study with 155 critical limbs. 71% patients had severity of the disease with Rutherford class IV or VI. The diseased segments were equally distributed involving superficial femoral artery and infrapopliteal segments (41%) and 15% were popliteal lesions. Seventy percent of the patients had combined occlusion and stenotic lesions. In this study, a 308-nm excimer laser was used to ablate the plaque and thrombus, restoring the flow in diseased segments. Laser was delivered through a flexible fiberoptic catheter using short bursts of ultraviolet energy, which vaporize the plaque into small particles with minimal thermal injury in the surrounding tissues. Hence there is less chance for distal embolizations. Similarly, Dave et al showed reduced TLR in 76.9% of the patients at 1-year follow-up with laser therapy.

There are currently three ongoing studies involving laser atheroablative strategies: PATENT (Photo-Ablation
Using the Turbo-Booster and Excimer Laser for In-Stent Restenosis Treatment), EXCITE-ISR (EXCImer Laser Randomized Controlled Study for Treatment of Femoropopliteal In-Stent Restenosis) and PHOTOPAC (Photoablation Followed by a Paclitaxel-Coated Balloon to Inhibit Restenosis in Instant Femoropopliteal Obstructions) evaluating the role of laser therapy in the treatment of peripheral artery in-stent restenosis. Recently the PATENT study reported 6-month interim results showing significant reduction in the percentage of diameter of the diseased vessel from 87.1% to 7.5% using a combination of laser atherectomy and balloon angioplasty. Major adverse events were reported to be 2.2% at 1-month follow-up. The final outcome report will be presented after 1-year follow-up.

EXCITE-ISR is a phase 3, 2:1 randomized trial, which is currently recruiting patients in the United States. There will be a total of 318 subjects enrolled in the study with Rutherford class I-IV with femoropopliteal artery in-stent restenosis. Similarly, the PHOTOPAC study is an ongoing pilot study in Europe that is evaluating the use of laser therapy and Paclitaxel-coated balloon therapy vs balloon therapy alone in the management of superficial femoral artery in-stent restenosis. Completion of this study is expected in 2013.

**ROTATIONAL DEVICES**

The Jetstream Navitus System (Bayer HealthCare) is a rotational atherectomy device that has differential and circumferential cutting blades to debulk both hard (calcified, fibrotic) and soft (thrombus, plaque) tissues with minimal damage to the vessel wall. The tissue debris are aspirated through the side port and disposed into the bag attached to the pathway console. The pathway device has the advantage of being able to adapt to different sizes with each clockwise (2.1 mm) and counterclock (3.0 mm) rotation. This device has two units, the main console and a single-use catheter electrically driven with a central pod. The main console is reusable and includes the main power supply as well as the infusion and aspiration chambers. The atherectomy catheter is advanced over the wire (0.14 in/135 cm) proximal to the diseased segment and cautiously driven back and forth maintaining the rotational speed rate (70 krpm) for better outcome.

The Pathway PVD Study for Percutaneous Peripheral Vascular Interventions was a multicenter prospective efficacy study including 172 patients with Rutherford class I to V lower-limb ischemia. All patients had more than 70% stenotic lesions up to 10 cm long for the above-knee or 3 cm for the below-knee segment. The reference vessel diameter was between 3 mm and 5 mm and the mean lesion length treated was 2.7 cm with 31% being total occlusions. Major adverse events at 30 days were 1% with device success rate being 99%. At 1-year follow-up, Duplex study showed primary patency of 61.8% and the Ankle Brachial Index (ABI) improved from 0.59 to 0.82.21

In 2011, the Jetstream G3 SF device (Bayer HealthCare) was approved by the FDA for treating vessel sizes 1.6 mm and smaller, especially in the below-knee segment involving tibial vessels. This device has a fixed cutter and is designed to navigate easily through small-caliber tortuous vessels, debulking heavily calcified segments and chronic total occlusions. The Jetstream G3 Calcium Study (NCT01273623) is an ongoing nonrandomized trial assessing the treatment effect of the G3 device on severely calcified lower-extremity disease using IVUS.

**ORBITAL ATERECTOMY**

The Diamondback 360 Orbital Atherectomy System (Cardiovascular Systems, Inc.) uses a rotational technique causing preferential sanding of the calcified plaque, resulting in a fixed luminal gain. The catheter tip has an eccentrically placed diamond-coated crown (30 micron) which is driven through a pneumatic powered console. This device requires a proprietary wire (ViperWire) to advance the catheter to the desired segment and lubricant (ViperSlide) to avoid thermal damage to the vessel wall. The rotational speed can range between 60 krpm and 200 krpm. Sanding the plaque results in microscopic particulate matter that is flushed by the bloodstream and hence large-size distal embolizations are minimal.

The OASIS trial was a nonrandomized multicenter registry involving 124 patients with severe infrapopliteal disease (201 stenoses). Of these, 45% had critical limb ischemia and 55% were claudicants. At 30 days, major adverse events were seen in 3.2% including death, myocardial infarction, amputation, and repeat revascularization. The procedural success rate was
defined as <30% stenosis and was achieved in 90.1% of the study subjects.23 Recently, the CALCIUM 360 randomized pilot trial showed significant benefit with orbital atherectomy and balloon angioplasty vs balloon angioplasty alone. This study included 50 patients with 1:1 randomization. Procedural success was noted for 93.1% of patients in the atherectomy and angioplasty arm compared to 82.4% in the angioplasty arm. After 1-year follow-up there were no amputations in the angioplasty arm. After 12-month follow-up the primary patency was 86.2%. 25

Final outcome data from CONFIRM 360 was recently reported at VIVA 2012, combining results from three consecutive prospective registries (CONFIRM-I, CONFIRM-II, and CONFIRM-III) involving 3,135 patients with 4,766 lesions. This is the largest real-world PAD study including all comers from over 200 hospitals in the United States between 2009 and 2011. Among these patients, 42% of the lesions were above the knee and 28% were below the knee and 21% of the total lesions were multivessel disease. One of the three orbital atherectomy devices (Diamondback 360, Predator 360, Stealth 360; Cardiovascular Systems, Inc.) were used with final residual stenosis of 10%±11%. Overall, the orbital atherectomy devices used resulted in lower incidence of perforation (0.7%), vessel closure (1.6%), distal embolization (2.2%), and use of bailout stents (4.9%). Comparing the final outcomes among the three registry studies, it was noted that the complication rates significantly reduced over time, suggesting the expertise with the use of devices is associated with improved clinical outcome. Also, during this period it was also observed that the use of crown size changed from 2.25 to 1.25 in CONFIRM-I and CONFIRM-III respectively.

Similarly, COMPLIANCE 360 study was a prospective multicenter study involving 50 patients randomized to orbital atherectomy and low-pressure balloon angioplasty vs angioplasty alone in the treatment of above-the-knee disease. After 12 months, the use of the atherectomy device resulted in lesser mean balloon pressure inflation, 3.97 vs 9.15 atm (P<.0001) as well as significantly reduced need for bailout stents 5.3% lesions vs 78.6% (P<.0001) respectively. CALCIUM 360 was also a similar study except that below-knee diseased segments were included in the study. Use of atherectomy devices resulted in reduced maximum average balloon inflation (5.9 atm vs 9.4 atm), dissections (3.3% vs 11.4%), perforation (0% vs 2.8%), embolization (0% vs 2.8%), and bailout stenting (6.9% vs 14.3%) compared to balloon angioplasty alone.

DIRECTIONAL AHERETECTOMY

The SilverHawk catheter (Covidien) is a directional cutting device that contains a rotating blade inside a tubular housing. This catheter is connected to a battery driven cutter driver and can be used to treat vessels of 2 mm to 4 mm in diameter. As the plaque is shaved using this device, there is minimal or no distal embolization.

Zeller et al reported a 2-year follow-up after using a directional atherectomy device in 36 patients (49 lesions) with Rutherford class IV to V ischemia and infrapopliteal disease. Of these, 67% of the lesions were treated with atherectomy. The primary patency was 67% at 12 months and 60% after 24-month follow-up. The secondary patency rate was 91% and 80% at 12- and 24-month follow-up respectively.23 McKinsey et al reviewed 275 patients (579 lesions) of whom 174 patients (63.3%) had critical limb ischemia and 101 patients (36.7%) were claudicants. Overall limb salvage was 92.4% with 100% among claudicants. At 18 months, primary patency was 52.7% and secondary patency was 75%.24 Keeling et al reported 61.7% primary patency and 76.4% secondary patency at 12-month follow-up of 60 patients (66 limbs) following directional atherectomy using the SilverHawk device. Restenosis of the vessel was noted in 16.7% of the patients at 3-month follow-up. Overall limb salvage was 86.2%.25

DEFINITIVE LE (determination of effectiveness of the SilverHawk peripheral plaque excision system [SilverHawk Device] for the treatment of infranigual vessels/lower extremities) is the largest prospective non-randomized PAD atherectomy device study assessing the effectiveness of directional atherectomy in the management of lower-extremity arterial disease. The final results were presented at the annual VIVA meeting in 2012. This study, using sonographic and angiographic independent core lab adjudicated events enrolled 800 subjects.
Among claudicants, 78% vessel patency was noted in lesion lengths of less than 4 cm (mean length was 2.3 cm) as compared to 82% in CLI patients. Similarly, 83% patency was seen among claudicants vs 60% in CLI patients with lesion lengths of 4 cm to 9.9 cm (mean length was 6.5 cm for claudicants and 6.9 cm in CLI patients). The SFA lesion length of more than 10 cm showed 65% vessel patency in claudicants (mean length 14.6 cm) as compared to 63% in CLI patients (mean length 15.5 cm). Future trials with DEFINITIVE AR, which is a prospective, randomized, multicenter pilot study involving debulking methods with drug-eluting (paclitaxel) balloon vs drug-eluting balloon alone is currently recruiting patients and the results are awaited.

The EASE (Endovascular Atherectomy Safety and Effectiveness) study is an ongoing study to assess for the safety and effectiveness of the Phoenix Atherectomy Catheter (AtheroMed, Inc.) aiming to recruit 90 patients among 20 centers. This device is proposed to be used in the treatment of chronic total occluded vessel and projected to have minimal distal embolization-related complication.

**CONCLUSION**

Atherectomy devices have evolved to become a major therapy in the management of PAD, specifically in the lower limbs. Because lower-extremity vessels are exposed to various physical and anatomic stresses, balloon angioplasty or stenting alone may not be appropriate for all patients and all scenarios of plaque burden or calcification. Appropriate use of atherectomy devices to debulk large plaque burdens or heavily calcified atherosclerotic plaque proves to be an important step in establishing circulation with minimal trauma to the vessel and a potential for little to no plaque left behind following therapy. Adjunctive therapy with balloon angioplasty and stenting has been shown to improve vessel patency in selected patients, however, with the data from DEFINITIVE LE it seems that directional atherectomy has an equal seat at the revascularization table with all other methods of lower-limb revascularization. With the advent of new technologies and devices, atherectomy has become a more feasible option in the management of PAD. An initial debulking strategy allows for the native vessel and intrinsic vessel characteristics to be maintained such that if further intervention is required in the future for restenosis, all intervention options are still available. Ongoing studies are expected to further strengthen the use of these devices and potentially allow more robust scientific head-to-head comparisons between devices, which is critically necessary to define any one technology’s role in the treatment of lower-limb PAD compared to another. Ultimately, these direct trials will afford us the critical level of evidence to determine our “gold standard” for treatment of our patients with symptomatic lower-limb PAD.

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