From Trial to Treatment: Transforming BTK Care With AMBITION

Advancing BTK standards through data-driven vascular intervention.

By Ehrin Armstrong, MD, and Anahita Dua, MD

Interventions for below-the-knee (BTK) lesions pose several challenges for endovascular surgery in chronic limb-threatening ischemia (CLTI), the end stage of peripheral artery disease (PAD). Although percutaneous transluminal angioplasty (PTA) is currently standard of care for endovascular treatment of these lesions, 12-month primary patency is as low as 50%, with high rates of repeat revascularization, major amputation, and all-cause mortality when PTA is used alone.[1,2] Proper vessel preparation prior to PTA with atherectomy or specialty balloons is often used in difficult lesions such as chronic total occlusions or severely calcified lesions, yet these technologies have come under fire in recent years for their potential overuse as well as limited clinical evidence for superiority over standard of care with PTA alone.

Although previous meta-analyses comparing atherectomy to PTA have focused on femoropopliteal disease and have revealed only minor improvements over PTA alone,[3,4] there have been even fewer investigations comparing these modalities among patients with CLTI. In fact, over a decade ago, only one preliminary randomized controlled trial (RCT) attempted to compare orbital atherectomy with PTA to PTA alone in CLTI patients.[5] The CALCIUM 360 randomized pilot study provided evidence for use of atherectomy prior to PTA to decrease the need for high inflation pressures for PTA acutely while also decreasing rates of all-cause mortality and major adverse events out to 1 year.[5] Yet, there have been no additional data built upon this preliminary investigation, especially among newer atherectomy technologies. In fact, recent failed trials such as SAVAL (NCT03551496) have limited the adoption of technologies that were effective above the knee (ATK) to the BTK space.

Recent advancements in laser atherectomy technology have proven safe and effective both ATK and BTK. The Auryon Laser Atherectomy System (AngioDynamics, Inc.) utilizes a neodymium-doped yttrium aluminum garnet (Nd-YAG), solid-state laser, producing 355-nm wavelength light ("B" laser) in 10 to 25 ns pulses, operating at 40 Hz with selectable fluency levels of 50 or 60 mJ/mm^2, and is designed to induce photomechanical ablation of thrombus and plaque[6,7] while also being able to crack calcium to improve subsequent angioplasty procedures.[8] An early feasibility study,[9] a pivotal investigational device exemption trial,[10] and a real-world registry[11] have provided consistent safety and effectiveness data across > 280 lesions for this new 355-nm laser atherectomy system. With zero reported perforations or flow-limiting dissections (> grade C) and very low rates of emboli or need for bailout stenting during these investigations, the Auryon Laser Atherectomy System is both very safe and highly effective across all forms of infrainguinal lesions, including BTK lesions.

AMBITION BTK RCT AND REGISTRY

The AMBITION BTK RCT and Registry is a multicenter, prospective, RCT comparing the clinical outcomes of Auryon Atherectomy System and PTA (treatment group) versus PTA alone (control group) to treat subjects with infrapopliteal PAD with Rutherford classification 4 or 5 disease. The trial will enroll up to 224 patients with CLTI across 30 sites in the United States. The primary endpoint will be analyzed based on a Finkelstein-Schoenfeld/win-ratio approach, comparing pairs of subjects on the components of the composite endpoint in a hierarchical fashion: (1) freedom from major amputation, (2) freedom from clinically driven target lesion revascularization, and (3) primary patency at 12 months. This unique test will allow for comparison of groups across multiple endpoints in order of clinical severity of relevancy to the intervention.

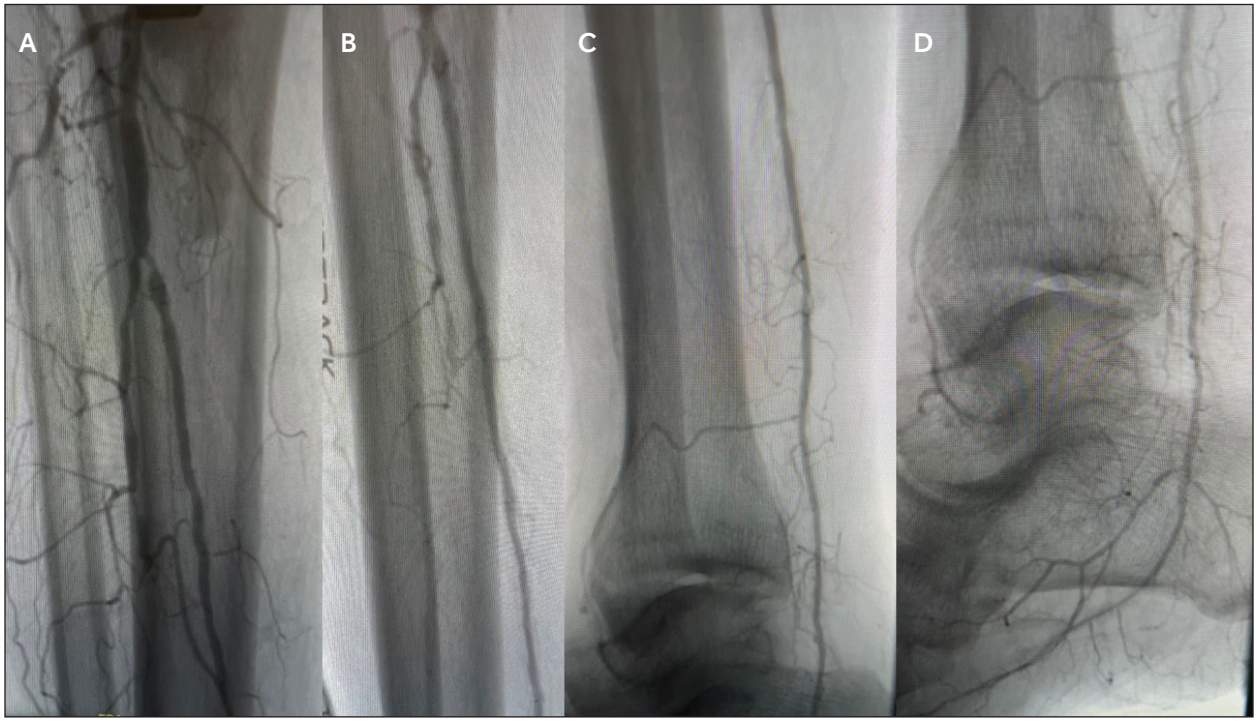

Figure 1. Angiogram showing 80% to 90% stenosis and mid-vessel occlusion in the right posterior tibial artery (A). Angiogram after atherectomy with the Auryon System showing excellent debulking of the proximal lesion and no dissection (B). Angiograms after PTA of the distal posterior tibial artery showing straight-line flow from the posterior tibial artery into the plantar arteries (C, D).

The Centers for Medicare & Medicaid Services, along with other government regulatory agencies, have encouraged clinician scientists and industry to adopt clinical endpoints that are relevant to the Medicare population.[12] In the AMBITION BTK RCT, the investigators seek to determine several relevant clinical endpoints through 24 months, including Rutherford classification, wound assessment, WIfI (Wound, Ischemia, and foot Infection) classification, ankle-brachial index or toe-brachial index, Walking Impairment Questionnaire, and the EQ-5D quality-of-life survey.

While the RCT component of the study highlights the potential for level 1 evidence for laser atherectomy for BTK lesions, the registry component of the study will also include up to 1,500 subjects with infrainguinal lesions and provide further real-world evidence for safety and effectiveness of the Auryon Laser Atherectomy System. This trial truly will stand alone in the BTK space and provide much-needed data for interventionalists.

The AMBITION BTK RCT/Registry is currently enrolling sites and looks forward to enrolling its first subject in the coming weeks. Sites for the trial are being specifically selected to encompass interventional cardiologists, vascular surgeons, and interventional radiologists from across the United States in academic and private hospitals.

CASE STUDY

Case Presentation

A male patient in his mid-70s with a past medical history of long-standing diabetes and coronary artery disease presented with a chronic nonhealing wound of the 3rd and 4th digits on his right foot. He had dry gangrene of these toes for 3 months and had been receiving regular wound care. He had a history of a contralateral BTK amputation. On physical examination, there was a brisk popliteal artery pulse but no distal pulses by palpation or Doppler interrogation. Based on these findings, an urgent lower extremity angiogram was performed.

Procedural Overview

Baseline angiography demonstrated no inflow disease to the level of the distal popliteal artery. The right anterior tibial and peroneal arteries BTK were chronically occluded. The right posterior tibial artery had 80% to 90% stenosis with mid-vessel occlusion (Figure 1A). There was reconstitution of the right posterior tibial artery at the ankle joint, with flow in the medial and lateral plantar arteries via collaterals. The right posterior tibial artery was crossed with a support catheter and a 0.014-inch Hi-Torque Command wire (Abbott), which was able to stay true lumen after looping the wire at the

site of the occlusion. Laser atherectomy was then performed with the Auryon System at a setting of 60 Hz proximally, with four passes performed in the proximal one-third of the vessel. Three additional passes were then performed at 50 Hz in the mid to distal vessel to the level of the ankle. Repeat angiography revealed excellent debulking of the proximal lesion with no dissection (Figure 1B). After PTA of the distal posterior tibial artery with a 2.5- X 150-mm balloon, there was excellent straight-line flow via the posterior tibial artery into the plantar arteries (Figure 1C and 1D).

The patient's wound subsequently healed in the next 3 weeks, and he was able to ambulate again once fitted with a prosthesis for his other leg.

CONCLUSION

The AMBITION BTK RCT and Registry is a much-needed advancement in clinical data generation for treating patients with CLTI. There are few proven strategies to treat BTK lesions, and this trial will certainly advance our understanding of atherectomy for this complex disease. ■

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