

New Technologies to Solve the Challenges of CLI

The unique features of this disease are finally being addressed with new devices.

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Over the last 30 years, revascularization specialists have used the same techniques over and over, expecting different outcomes but continuing to have the same results. In

some situations, worse results have been experienced. Infrapopliteal plain old balloon angioplasty (POBA) has failed to show sustainable results in patients with critical limb ischemia (CLI), with 1-year primary patency rates reported as low as 63% and major amputation rates as high as 15% in a recent meta-analysis.¹ Yet, in some instances, POBA continues to be considered the gold standard of endovascular therapy for infrapopliteal disease.

LIMITATIONS OF CURRENT TREATMENTS

In a recent study on infrapopliteal calcification patterns in CLI, the nature of atherosclerotic disease in popliteal and tibial vessels was examined. The results were surprising, as calcification involving tibial vessels extended through multiple layers across the vessel from the intima to the adventia.² Findings such as this could certainly contribute to the suboptimal results noted with balloon angioplasty and, in theory, limit the success of drug-coated balloons (DCBs).

Results from bare-metal self-expanding stent trials have been disappointing, such as the XCELL trial, which showed a high rate of

restenosis, a high rate of clinically driven target lesion revascularization, and a low rate of wound healing.³ We believe that the distal tibial vessels through the plantar circulation behave differently on multiple levels, including mechanically and pathologically (Figure 1). Most treatment modalities have failed in these segments, and in some trials, these segments were excluded.

Although DCB technology in the infrapopliteal regions was met with enthusiasm, current data evaluating DCB use in the tibial segments do not support its long-term benefit. Reasons behind the lack of efficacy are complex and poorly under-

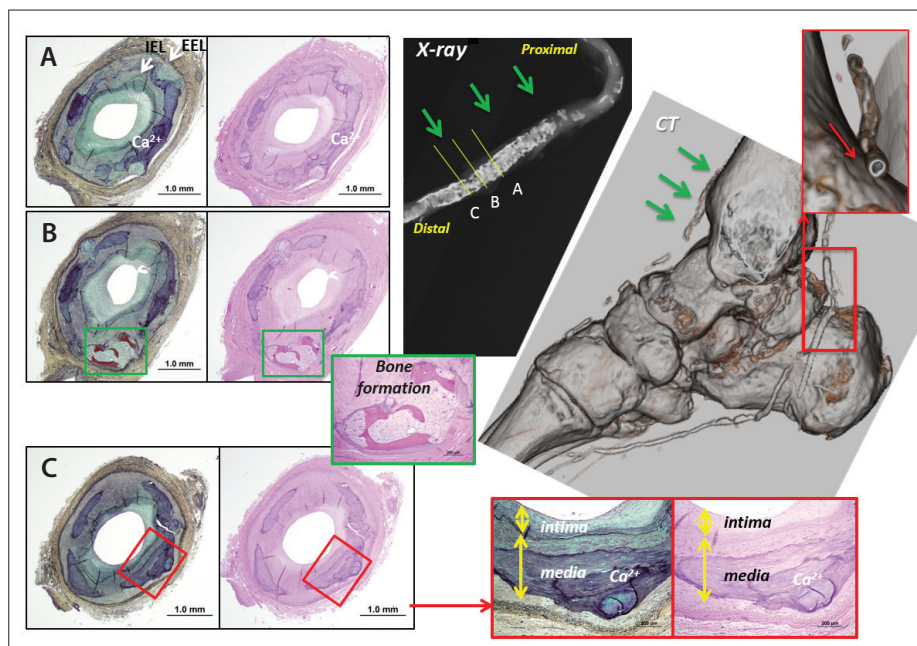


Figure 1. Monckeberg's calcification in the pedal arteries of a patient with end-stage renal disease. Calcium deposits are seen (Ca^{2+}), as well as the disruptions of the IEL and EEL (A); inset shows bone formation (osseous metaplasia) (B); inset shows a calcium deposit (C). High-resolution x-ray and high-resolution CT depicting medial arteriosclerosis. Abbreviations: EEL, external elastic lamina; IEL, internal elastic lamina. Reprinted with permission from Mustapha JA, Diaz-Sandoval LJ, Saab F. Infrapopliteal calcification patterns in critical limb ischemia: diagnostic, pathologic and therapeutic implications in the search for the endovascular holy grail. *J Cardiovasc Surg (Torino)*. 2017;58:383–401.

stood.⁴⁻⁶ Again, we believe that calcification and undersizing of tibial balloons most likely played a significant role in the suboptimal results.

In a substudy of 356 patients enrolled in the Peripheral Registry of Endovascular Clinical Outcomes (PRIME) registry,⁷ the rate of tibial vessel recoil and late lumen lost after angioplasty was examined via duplex ultrasound. The substudy found that patients who required reintervention had a recoil rate of 32% at 1-month postintervention.⁸ In our opinion, this is a reflection of the complexity of tibial calcification and occlusions.

Trials examining the benefit of balloon-expandable drug-eluting stents in the tibial vessels showed significant promise. However, the lesion length evaluated falls short of real-world tibial lesions and chronic total occlusions, with average treated lesion length of 4 to 6 cm. In the PRIME registry, the treated lesion length ranged from 200 to 260 mm.⁹⁻¹¹

ADDRESSING THE CHALLENGES OF CLI

Given the previously mentioned challenges in treating infrapopliteal disease, a scaffold-based drug-eluting technology may provide a better treatment solution. Boston Scientific Corporation is developing a new, purpose-built, below-the-knee drug-eluting stent designed to resolve two critical challenges to CLI pathophysiology: (1) poor uptake of the antiproliferative agent through calcified vessels, and (2) the elastic vessel recoil frequently seen following balloon dilatation in infrapopliteal arteries. This new technology (currently an investigational device) is designed to optimize drug delivery in calcified lesions through the use of a highly biocompatible polymer that maintains a reservoir of antiproliferative agent adjacent to the lesion for an extended period of time. This sustained drug release is intended to improve clinical outcomes by facilitating a more efficient drug uptake in the vessel. The technology is designed to address the challenge of elastic recoil in infrapopliteal lesions by providing a self-expanding scaffolding in long lengths with adequate radial force.

In recognition of the unmet clinical need for better solutions to treat infrapopliteal disease and the unique solution provided by this technology, the US Food and Drug Administration has granted Boston Scientific an Expedited Access Pathway designation for this product. This accelerated pathway allows the device to be clinically tested in the United States and in other sites around the world with a goal of speeding innovation to patients.

CONCLUSION

In conclusion, CLI involving tibial and plantar disease remains a very challenging space to treat. Balloon angioplasty as the main revascularization modality has not been shown to be effective in achieving adequate short- and long-term outcomes. The pathological and mechanical properties of tibial vessels are certainly different and will require new tech-

nology to address the stark differences from other vascular conduits. We remain cautiously optimistic as newer technologies designed specifically for this space evolve. ■

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