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Treatment of Anatomically Challenging Lesions in Patients With Advanced Critical Limb Ischemia: A Contemporary Approach to Popliteal and Tibial Disease

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Critical limb ischemia (CLI) represents the most advanced form of peripheral artery disease (PAD) and is characterized clinically by rest pain, non-healing wounds, and gangrene. In a retrospective analysis of Medicare and Medicaid data of patients aged ≥ 40 years, the reported annual prevalence of CLI was 11.1% of total PAD patients.[1] CLI patients often present with multilevel disease, and > 70% have some degree of infrapopliteal involvement.[2] Patients with CLI tend to suffer from multiple comorbidities and have an increased risk of major amputation, cardiovascular events, and death.[3] Major amputation rates in patients with CLI are as high as 40% at 6 months after presentation.[4] The risk of mortality is further compounded after major amputation. A recent study of 651 patients with CLI reported that the overall mortality rate was 44% in the year after a major amputation, which was further increased to 66% and 85% at 3 and 5 years, respectively.[5]

In recent years, endovascular procedures have been on the rise[6]; however, primary amputation continues to be performed. Of concern, the majority of these patients with a primary amputation received no diagnostic angiography or revascularization procedure prior to the amputation.[7,8] In our view, diagnostic imaging should be performed in all suspected CLI patients, and major amputation should be reserved for only if revascularization attempts have failed.

CLI treatment can be complex and multidisciplinary, reflecting the multifaceted pathophysiology of this disease. Current evidence supports the value of revascularization in patients with CLI.[3] The decision of whether lower extremity arterial revascularization should be performed via surgical bypass versus endovascular therapy is an ongoing debate. Hopefully, some of these questions will be addressed in the ongoing BEST-CLI trial.[9]

Of note, the presence of various underlying comorbidities and anatomic conditions precludes a significant number of CLI patients from surgery. At the Advanced Cardiac and Vascular Centers for Amputation Prevention, our primary limb-related therapy is arterial revascularization using endovascular techniques to augment distal flow, with the overall goal of reducing pain and preserving the limb. We primarily treat patients with advanced PAD; almost 80% of our patient population presents with an official diagnosis of CLI. Our patient population tends to have both popliteal and tibial disease, and we are starting to see more patients (10%) with end-stage plantar disease. The popliteal and tibial disease creates a unique challenge. In these types of challenging lesions, atherectomy with plaque reduction to reduce disease burden and the risk of mechanical complication and bailout stenting is extremely important.

One of the key considerations for an endovascular procedure is choosing an appropriate site for arterial access, which may be limited by the severity of disease in common femoral artery conduits, obesity, infection in the groin area, or previous surgery. The tibiopedal arterial access is becoming one of the cornerstones of endovascular interventions for CLI patients and is typically performed under ultrasound guidance. Based on the findings of the CTOP (chronic total occlusion crossing approach based on plaque cap morphology) classification, pedal access was required in up to 67% of cases.[10] This appears to be the case especially when the disease involves the popliteal and tibial vessels. We have recently published our experience with the tibiopedal arterial minimally invasive (TAMI)

retrograde revascularization technique in the PRIME registry.[11] The use of the TAMI technique allowed us to treat patients who could not be treated via traditional common femoral artery access. Via a pedal approach, the operator was able to cross lesions and deliver therapies, including atherectomy, balloon angioplasty, drug-coated balloon (DCB) angioplasty, and stenting.

For the diagnostic evaluation of PAD, especially when treating vessels below the knee, we go beyond digital angiography alone. Although it is considered the gold standard, there are certain limitations to angiography. Digital angiography only allows for evaluation of the lumen, without the ability to fully examine the vessel wall. In our center, intravascular ultrasound (IVUS)—a dynamic imaging modality—is often employed for the diagnosis of CLI cases. IVUS provides more information about the vessel wall, allowing identification of plaque morphology, the extent of disease, and plaque burden.

TREATMENT MODALITIES

Despite the availability of many different treatment modalities, there is no consensus on evidence-based treatment for CLI. Patients with CLI tend to have severely calcified arteries. This is a major challenge to endovascular revascularization techniques. Dilatation with balloon angioplasty performs poorly in these types of lesions, with frequent vessel recoil, potential spiral dissections, and perforations. The presence of calcium may also serve as a physical barrier against the antiproliferative drugs delivered by current DCBs and stents. Vessel preparation by debulking plaque and removing calcium burden have been proposed for these types of challenging lesions. Twelve-month results from the DEFINITIVE LE study have supported this notion and demonstrated the effective use of directional atherectomy, a modality designed to precisely remove the obstructing arterial atheroma. DEFINITIVE LE was a large, prospective, core lab–adjudicated study that evaluated the safety and effectiveness of directional atherectomy for the endovascular treatment of 800 patients (1,022 target lesions) with PAD, including CLI patients with infrapopliteal lesions.[12] Acute and follow-up results were encouraging. Of particular interest were the outcomes by lesion location in CLI patients: target lesion location patency at 12 months was 68% for the superficial femoral artery, 67% for the popliteal artery, and 78% for the infrapopliteal artery.[12] The freedom from major amputation rate at 1 year was 97.1% in the infrapopliteal CLI cohort, which is remarkable considering the severity of the disease.[13] A contemporary review analysis of 36,860 Medicare patients with CLI who underwent revascularization revealed that mortality and major amputation rates over 4 years were lower in atherectomy compared with other modalities, including surgical bypass.[14] Among endovascular modalities, plain balloon angioplasty alone tends to have the worst outcomes.[14] Taken together, these results support the use of atherectomy for endovascular therapy in CLI patients.

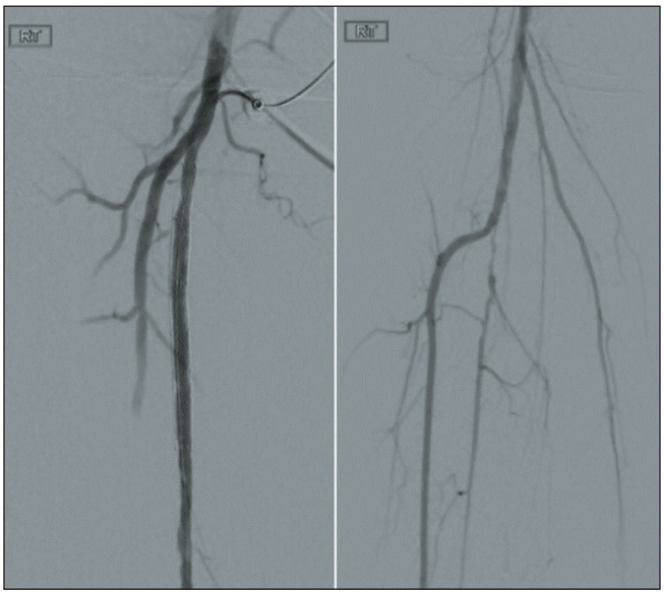

Figure 1. Diagnostic angiography of a patient with CLI, showing an occluded posterior tibial artery.

CASE PRESENTATION

A woman in her 40s presented with a medical history of CLI and comorbidities including type 1 diabetes mellitus, hyperlipidemia, and a smoking addiction. The patient had a previous wound with partial ray amputation. Despite wound healing, the patient presented after 9 months with complaints of rest pain. An arterial duplex ultrasound showed evidence of occluded tibial vessels with increased velocities in the popliteal artery. The patient's ankle-brachial index was in the normal range, most likely due to the presence of calcified vessels. The decision was made to proceed with revascularization. Because the disease was most likely going to involve the distal popliteal artery with tibial vessels, antegrade access was achieved using ultrasound guidance. Diagnostic images shown in Figure 1 illustrate the nature of the disease.

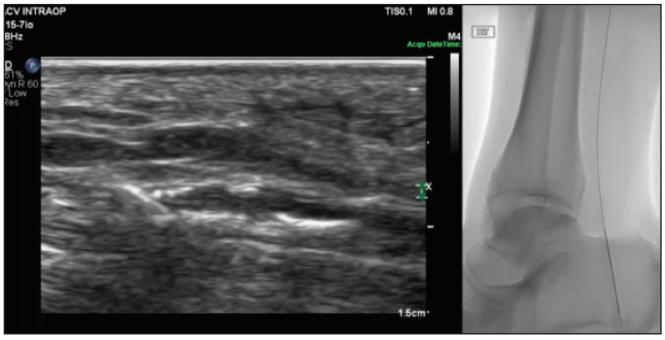

Figure 2. Pedal arterial access in a patient with CLI.

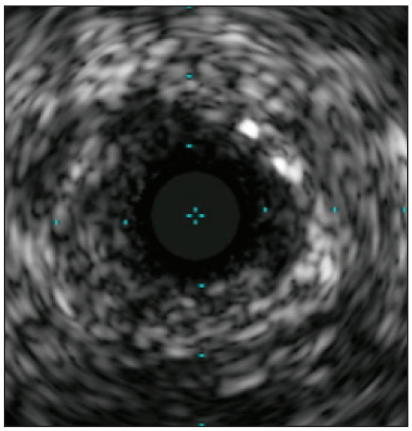

Figure 3. IVUS image showing plaque morphology observed in a patient with CLI.

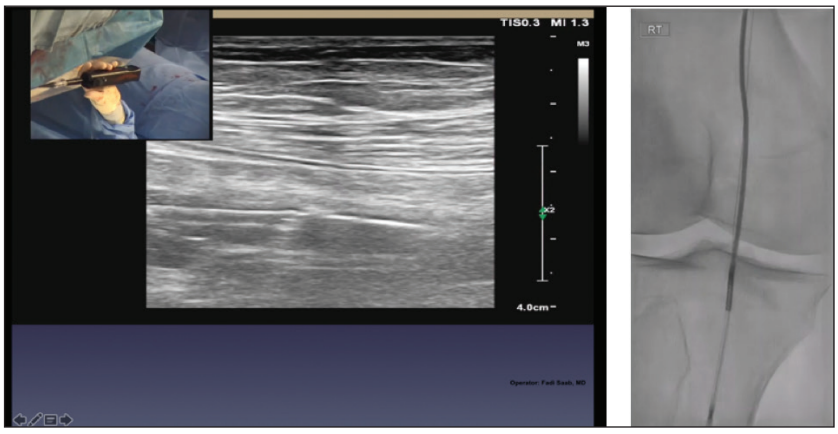

Figure 4. Fluoroscopic and extravascular ultrasound images of the SilverHawk DS directional atherectomy system in the tibial artery.

In patients with CLI, we have incorporated IVUS to better assess vessel size and plaque morphology. Digital subtraction angiography tends to underestimate the size of vessels, especially tibial vessels.[15]

Based on the CTOP analysis of the chronic total occlusion, the decision was made to proceed with pedal access (Figure 2). A 0.014-inch wire was flossed, followed by IVUS evaluation. The nature of plaque shown on IVUS suggested that there was significant plaque burden (Figure 3).

At this point, a SilverHawk™ DS plaque excision system (Medtronic) was used for directional atherectomy. Based on IVUS images, the device was activated in the popliteal artery into the proximal posterior tibial artery. After six passes, the plaque was significantly debulked. One of the unique features of directional atherectomy is that it allows the operator to choose how much tissue to remove. Using extravascular ultrasound, the device could be directed to appropriate high plaque burden plains, away from the adventitia (Figure 4).

After directional atherectomy, low-pressure balloon angioplasty was performed in the posterior tibial, tibioperoneal trunk, and popliteal arteries. A tapered 4- (4 mm proximally, 3.5 mm distally) X 210-mm NanoCross™ Elite 0.014-inch percutaneous transluminal angioplasty (PTA) balloon catheter (Medtronic) was used in the tibioperoneal trunk and posterior tibial artery, and a 5- X 120-mm NanoCross Elite 0.014-inch PTA balloon catheter was used to treat the popliteal artery. Then, a 6- X 120-mm IN.PACT™ Admiral™ drug-coated balloon (Medtronic) was used in the popliteal artery. Final angiographic results showed resolution of stenosis to < 20%, with no mechanical complications (Figure 5). The pedal access site was managed with manual compression, and the antegrade access site was closed with a Mynx™* vascular closure device (Cordis, a Cardinal Health company).

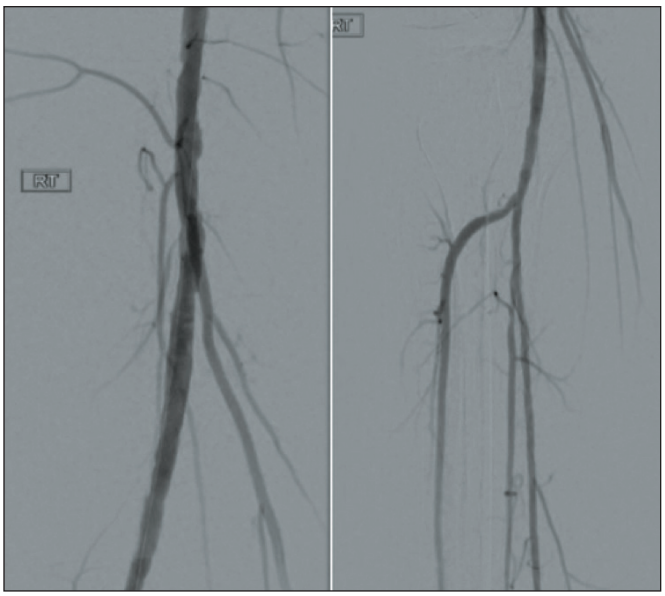

Figure 5. Final angiography of the tibial artery after directional atherectomy with a SilverHawk DS plaque excision system, followed by balloon angioplasty, showing stenosis of < 20% with no mechanical complications.

CONCLUSION

CLI is a deadly disease that carries significant challenges in terms of prognosis and treatment. The complexity of the arterial anatomy mandates the use of appropriate tools to treat these diseased vessels. The use of directional atherectomy in CLI patients is advantageous to reduce the rate of complications. This is more important in areas where stenting is less favorable. In addition, in our practice, the combination of directional atherectomy with DCB technology is superior to balloon angioplasty alone. ■

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SilverHawk™ peripheral plaque excision system Reference Statement
Important Information: Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.
Indications for Use: The SilverHawk peripheral plaque excision system is intended for use in atherectomy of the peripheral vasculature. The catheter is NOT intended for use in the coronary, carotid, iliac or renal vasculature.
CAUTION: Federal (USA) law restricts this product for sale by or on the order of a physician.

NanoCross™ Elite 0,014" OTW PTA balloon catheter Reference Statement
Important Information: Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.
Indications for Use: The NanoCross Elite 0.014" OTW PTA balloon dilatation catheter is intended to dilate stenoses in the iliac, femoral, ilio-femoral, popliteal, infra-popliteal, and renal arteries, and for the treatment of obstructive lesions of native or synthetic arteriovenous dialysis fistulae. This device is also indicated for stent post-dilatation in the peripheral vasculature.
CAUTION: Federal (USA) law restricts this product for sale by or on the order of a physician.

IN.PACT™ Admiral™ Paclitaxel-coated PTA balloon catheter Brief Statement
Indications for Use: The IN.PACT™ Admiral™ Paclitaxel-coated PTA Balloon Catheter is indicated for percutaneous transluminal angioplasty, after appropriate vessel preparation, of de novo, restenotic, or in-stent restenotic lesions with lengths up to 360 mm in superficial femoral or popliteal arteries with reference vessel diameters of 4-7 mm.
Contraindications
- The IN.PACT Admiral DCB is contraindicated for use in:
- Coronary arteries, renal arteries, and supra-aortic/cerebrovascular arteries
- Patients who cannot receive recommended antiplatelet and/or anticoagulant therapy
- Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the delivery system
- Patients with known allergies or sensitivities to paclitaxel
- Women who are breastfeeding, pregnant or are intending to become pregnant or men intending to father children. It is unknown whether paclitaxel will be excreted in human milk and whether there is a potential for adverse reaction in nursing infants from paclitaxel exposure.

Warnings
- **A signal for increased risk of late mortality has been identified following the use of paclitaxel-coated balloons and paclitaxel-eluting stents for femoropopliteal arterial disease beginning approximately 2-3 years post-treatment compared with the use of non-drug coated devices. There is uncertainty regarding the magnitude and mechanism for the increased late mortality risk, including the impact of repeat paclitaxel-coated device exposure. Physicians should discuss this late mortality signal and the benefits and risks of available treatment options with their patients.**
- Use the product prior to the Use-by Date specified on the package.
- Contents are supplied sterile. Do not use the product if the inner packaging is damaged or opened.
- Do not use air or any gaseous medium to inflate the balloon. Use only the recommended inflation medium (equal parts contrast medium and saline solution).
- Do not move the guidewire during inflation of the IN.PACT Admiral DCB.
- Do not exceed the rated burst pressure (RBP). The RBP is 14 atm (1419 kPa) for all balloons except the 200 and 250 mm balloons. For the 200 and 250 mm balloons the RBP is 11 atm (1115 kPa). The RBP is based on the results of in vitro testing. Use of pressures higher than RBP may result in a ruptured balloon with possible intimal damage and dissection.
- The safety and effectiveness of using multiple IN.PACT Admiral DCBs with a total drug dosage exceeding 34,854 µg of paclitaxel in a patient has not been clinically evaluated.

Precautions
- This product should only be used by physicians trained in percutaneous transluminal angioplasty (PTA).
- This product is designed for single patient use only. Do not reuse, reprocess, or resterilize this product. Reuse, reprocessing, or resterilization may compromise the structural integrity of the device and/or create a risk of contamination of the device, which could result in patient injury, illness, or death.
- Assess risks and benefits before treating patients with a history of severe reaction to contrast agents.
- The safety and effectiveness of the IN.PACT Admiral DCB used in conjunction with other drug-eluting stents or drug-coated balloons in the same procedure or following treatment failure has not been evaluated.
- The extent of the patient's exposure to the drug coating is directly related to the number of balloons used. Refer to the Instructions for Use (IFU) for details regarding the use of multiple balloons and paclitaxel content.
- The use of this product carries the risks associated with percutaneous transluminal angioplasty, including thrombosis, vascular complications, and/or bleeding events
- Vessel preparation using only pre-dilatation was studied in the clinical study. Other methods of vessel preparation, such as atherectomy, have not been studied clinically with IN.PACT Admiral DCB.
- This product is not intended for the expansion or delivery of a stent.

Potential Adverse Effects
- The potential adverse effects (e.g. complications) associated with the use of the device are: abrupt vessel closure; access site pain; allergic reaction to contrast medium, antiplatelet therapy, or catheter system components (materials, drugs, and excipients); amputation/loss of limb; arrhythmias; arterial aneurysm; arterial thrombosis; arteriovenous (AV) fistula; death; dissection; embolization; fever; hematoma; hemorrhage; hypotension/hypertension; inflammation; ischemia or infarction of tissue/organ; local infection at access site; local or distal embolic events; perforation or rupture of the artery; pseudoaneurysm; renal insufficiency or failure; restenosis of the dilated artery; sepsis or systemic infection; shock; stroke; systemic embolization; vessel spasms or recoil; vessel trauma which requires surgical repair.
- Potential complications of peripheral balloon catheterization include, but are not limited to the following: balloon rupture; detachment of a component of the balloon and/or catheter system; failure of the balloon to perform as intended; failure to cross the lesion.
- Although systemic effects are not anticipated, potential adverse events that may be unique to the paclitaxel drug coating include, but are not limited to: allergic/immunologic reaction; alopecia; anemia; gastrointestinal symptoms; hematologic dyscrasia (including leucopenia, neutropenia, thrombocytopenia); hepatic enzyme changes; histologic changes in vessel wall, including inflammation, cellular damage, or necrosis; myalgia/arthralgia; myelosuppression; peripheral neuropathy.
- Refer to the Physician's Desk Reference for more information on the potential adverse effects observed with paclitaxel. There may be other potential adverse effects that are unforeseen at this time.
- Please reference appropriate product Instructions for Use for a detailed list of indications, warnings, precautions and potential adverse effects. This content is available electronically at www.manuals.medtronic.com.

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