The Multilevel Nature of Complex Lesions in Critical Limb Ischemia

Assessing plaque morphology, optimal access, patency, and presence of chronic total occlusions to determine appropriate tools and techniques for treatment.

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Peripheral artery disease (PAD) has emerged as a major public health concern, currently affecting 8 million Americans.[1] Disease can range from asymptomatic stenosis to critical limb ischemia (CLI) resulting in rest pain and/or nonhealing arterial ulcers on the extremities. The complexity of the disease is dictated by the presence of risk factors, such as kidney disease, diabetes, and advanced age. The rising prevalence of diabetes and kidney disease in the United States, as well as the aging population, contributes to increasingly complex PAD cases.

PAD commonly exhibits a multilevel nature, extending both above (inflow) and below the knee (outflow). As the disease progresses, the patient may develop CLI, and if untreated, nonhealing ulcers may develop, which may subsequently lead to amputation. Patients with PAD who have undergone an amputation have a 5-year mortality rate of 50%,[2] which serves as motivation to prevent amputation by restoring both inflow and outflow patency to support wound healing. Focusing on the multilevel nature of PAD allows for proactive treatment and improved outcomes for patients. This article focuses on endovascular treatment techniques, taking into consideration plaque composition at different arterial levels and the tools available to treat these complex lesions.

TREATING MULTILEVEL DISEASE

Percutaneous endovascular revascularization is the preferred treatment for patients with PAD because of the high technical success rate, shorter recovery time, and reduced risk of complications as compared to open surgery. Successful treatment of CLI relies on restoring inline flow to both inflow and outflow lesions of the lower extremities, which alleviates rest pain and increases the likelihood of healing ulcers and wounds. Nearly 67% of patients with CLI have both femoropopliteal and infrapopliteal disease.[3] Treating both inflow and outflow is critical to effectively heal wounds and eliminate claudication. Davies et al examined the effect of distal runoff after interventions of femoropopliteal occlusions in the superficial femoral artery (SFA) and found that 5-year patency rates of the inflow vessel

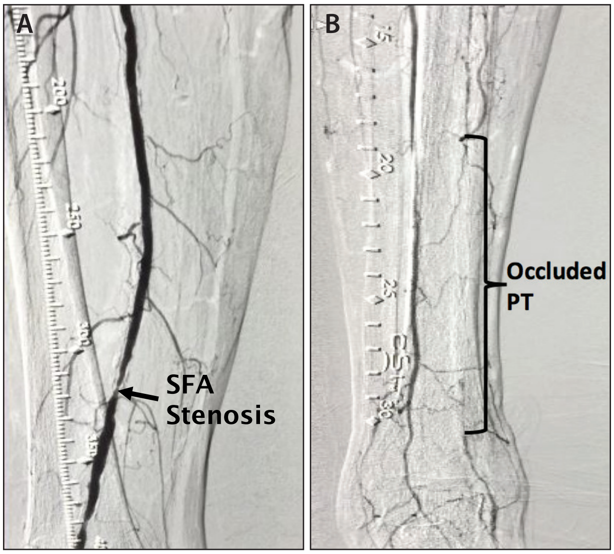

Figure 1. Preintervention angiogram showing stenosis of the superficial femoral artery (SFA) (A) and occlusion of the posterior tibial (PT) artery (B).

with good runoff were significantly better as compared with compromised or poor runoff (82% ± 9% vs 56% ± 4% and 52% ± 7%, respectively).[4] The same trend was found for patients experiencing recurring symptoms as well as for limb salvage rates.[4] This study illustrates the importance of treating CLI from a multilevel perspective and ensuring that interventions are targeted at restoring both inflow and outflow.[3,5]

CHALLENGES OF TREATING MULTILEVEL CLI LESIONS

Pathophysiology and Device Selection

Treating lesions that extend both above and below the knee pose a number of technical and clinical hurdles that increase the time, effort, and resources required. The size of peripheral arteries varies greatly, with the vessel diameter above the knee ranging from up to 10 mm at the level of the iliac artery to up to 5 mm at the level of the popliteal artery. Below the knee, the proximal tibial vessels are < 4 mm in diameter and decrease to 1 mm at the level of the foot.

The size of the vessel and distance from the access point should be taken into consideration to determine which device is utilized to treat the stenosis. For example, if a stenosis of the SFA was present and the access point was the contralateral femoral artery, the length of the device shaft would play little role in the device selected considering most shafts are > 100 cm. Additionally, considering the SFA is typically at least 5 mm in diameter, devices that produce larger lumen sizes are preferred. On the other hand, below-the-knee stenosis using a contralateral femoral approach would require a device with a longer shaft and lower profile considering the smaller vessel size and longer distance from the access point.

Plaque Morphology

Plaque morphology can range from a soft/homogenous to hard/calcific. Plaque morphology of the target lesion can be assessed by intravascular ultrasound, angiography, and to a lesser extent the feel of the wire as the stenosis is traversed. The plaque morphology varies greatly at different levels of the peripheral artery tree. Bishop et al found that calcium deposits within the plaque were nearly 3 times denser in tibial arteries as compared with popliteal arteries (33.8% ± 5.6% vs 10.6% ± 1.9%; $P < .001$). Popliteal arteries also had a higher mean plaque burden, whereas tibial vessels had less fibro-fatty and fibrous plaque as compared with popliteal arteries (fibro-fatty plaque, 7.7% ± 1.4% vs 13.1% ± 1.2% [$P < .005$]; fibrous plaque, 42.4% ± 4.7% vs 61.4% ± 2.2% [$P < .001$], respectively).[6]

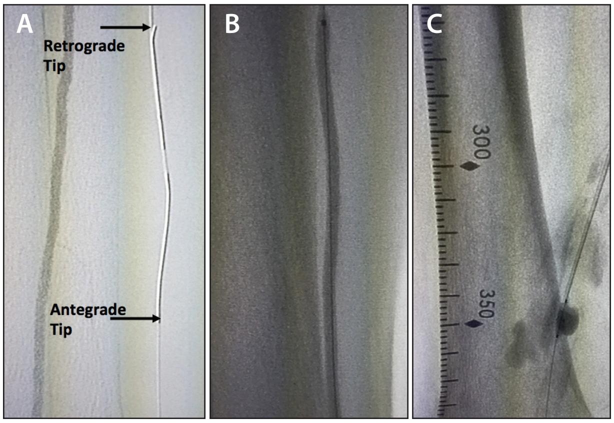

Figure 2. Re-entry of retrograde wire into true lumen after successful use of the double-balloon technique (A), plain old balloon angioplasty of the posterior tibial artery (B), and injection of dexamethasone to the adventitia of the superficial femoral artery to prevent restenosis (C).

Plaque morphology determines which device is selected to treat the stenotic lesion. For example, if a soft/homogenous plaque is present, photochemical ablation and/or thrombectomy with or without a filter may be the preferred treatment strategy to modify the plaque and prevent distal emboli. If the stenotic lesion is a hard/calcific plaque, orbital atherectomy, rotational atherectomy, directional atherectomy, and/or cutting or scoring balloon with or without a stent may be the preferred treatment strategy in order to modify the plaque and prevent dissection and recoil.

Patency

If the patient has a nonhealing wound, patency may become the utmost concern, since decreased patency in inflow can affect outflow and vice versa. Two recent trials evaluating superficial femoral artery drug-coated balloons (DCBs) showed improved patency rates compared with plain old balloon angioplasty (POBA).

The IN.PACT SFA was a multicenter, single-blinded, randomized trial that showed IN.PACT DCBs were more effective as compared with POBA in terms of primary patency rates (82.2% vs 52.4%; $P < .001$) and target lesion revascularization (2.4% vs 20.6%; $P < .001$).[7] The LEVANT 2 study compared the Lutonix DCB (Bard Peripheral Vascular) with POBA in limiting femoropopliteal restenosis. The multicenter study found that DCB was more effective in improving primary patency rates as compared with POBA at 1 year (65.2% vs 52.6%; $P = .015$).[8,9] Additionally, recent data evaluating drug-eluting stents (DES) showed improved patency rates over 4 years with DES as compared with POBA combined with bail-out bare-metal stents in the

SFA (66.4% vs 43.4%).[10] The 5-year data for Zilver PTX (Cook Medical) recently revealed a 5-year primary patency rate of 66.4% as compared to 43.4% for patients treated with POBA and bare-metal stents.[11]

Although these trials have shown promising data for the use of DCBs in treating above-the-knee lesions, the recent IN.PACT DEEP trial has shown that more work may be needed to optimize these devices for treating below-the-knee lesions. The IN.PACT DEEP trial was a prospective, multicenter, randomized controlled trial that evaluated the efficacy of DCBs as compared with POBA for reducing restenosis in below-the-knee lesions. The study found no significant difference in clinically driven target lesion revascularization and late lumen loss between the two groups (clinically driven target lesion revascularization, 9.2% vs 13.1%; $P = .291$ and late lumen loss, 0.61 ± 0.78 mm vs 0.62 ± 0.78 mm; $P = .950$). Additionally, the data indicate a trend toward a higher amputation rate in the DCB arm as compared with the POBA arm (8.8% vs 3.6%; $P = .080$).[12]

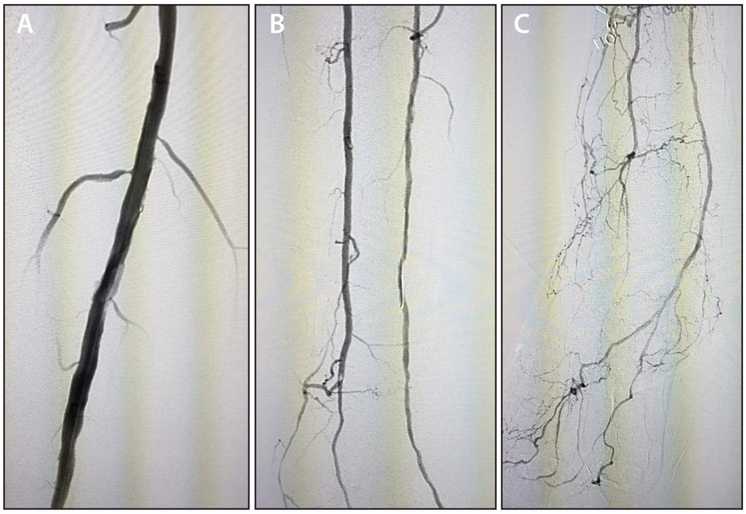

Figure 3. Postintervention angiogram showing successful recanalization of the superficial femoral artery (SFA; inflow) (A), recanalized posterior tibial artery (outflow) (B), and inline blood flow restored to the foot to promote wound healing (C).

Chronic Total Occlusions

Chronic total occlusions (CTOs) are prevalent in multilevel disease and are encountered in 40% of all cases.[13] The success of treating CTOs varies between 34% and 91% and is largely dependent on the skill of the operator.[13-15] Treatment of CTO below the knee requires specialized tools that are long, low profile, and have the stiffness and support to cross rigid lesions. Advanced techniques may also be required, such as obtaining retrograde access to cross a CTO distally, utilizing a transcollateral approach to navigate through collateral channels to cross the distal cap of the CTO, and sometimes obtaining brachial and/or antegrade access. Using these exotic access approaches increases the success rate of treating these tough lesions. Additionally, crossing techniques, such as the wrapping wire technique and/or double-balloon technique, as well as crossing/reentry devices may improve crossing success.[16] Once crossed, treatment typically starts with outflow first, followed by inflow. This allows any proximal microemboli to be cleared distally when the inflow is treated. The interventionist should take into account the location and length of the lesion, characteristics of the plaque, and patient comorbidities to determine the best tools to safely and effectively treat the patient.

CASE STUDY

A 74-year-old woman with a history of hypertension, end-stage renal disease, and diabetes mellitus presented with a nonhealing wound on the plantar side of her right foot. Computed tomographic angiography with bilateral lower extremity runoff showed approximately 90% stenosis of the right distal SFA. The right anterior tibial artery was occluded proximally with multiple CTOs of the posterior tibial artery as seen in Figure 1. The peroneal artery supplies blood flow to the distal posterior tibial artery through a posterior communicating branch. Because the patient presented with CLI and stenotic lesions in her right lower extremity extending both above and below the knee, a multilevel approach was taken to treat the disease.

An 18-g, 0.014-inch interventional wire was used to cross the first posterior tibial CTO, but it was unable to cross the distal posterior tibial CTO. Therefore, retrograde posterior tibial access was achieved with a 2.9-F sheath. An 18-g CTO wire was then advanced through the retrograde access but entered a subintimal plane in the attempt to cross the CTO in the distal posterior tibial artery. A double-balloon technique was successfully used to bring the retrograde wire into the proximal true lumen (Figure 2A). A 0.018-inch crossing catheter was placed through the retrograde access point to allow the antegrade wire to be externalized in a “flossing” fashion. This was followed by POBA through the common femoral access site of the distal CTO with a 2- X 80-mm balloon, resulting in 20% residual stenosis (Figure 2B).

After recanalizing the outflow, we focused on the calcified stenosis of the SFA and proximal posterior tibial artery. Intravascular ultrasound was used to assess the size of the lumen before the intervention, revealing an SFA with a 5-mm lumen and a posterior tibial artery with a 2.5-mm lumen. The morphology of the plaque was mostly heterogeneous/calcific. Orbital atherectomy was performed on the distal SFA and proximal posterior tibial artery to modify the plaque using the Diamondback orbital atherectomy device with a 1.5-mm classic crown (Cardiovascular Systems, Inc.) at medium to high revolutions, followed by POBA with a 5- X 100-mm balloon of the distal SFA, resulting in 30% residual stenosis. A 3- X 120-mm balloon was used at the level of the proximal anterior tibial artery leading to a 20% residual stenosis. Finally, a large Bullfrog Micro-Infusion Device (Mercator MedSystems) was used to inject dexamethasone into the adventitia of the SFA (Figure 2C). The goal of this intervention was to recanalize both inflow and outflow and restore inline flow to the foot to heal the wound. The results of the intervention are shown in Figure 3.

This case illustrates a real-world example of treating a complex multilevel lesion. These lesions present multiple challenges, and their treatment requires a skill in the use of interventional and diagnostic tools as well as sufficient training in exotic access and crossing techniques.

CONCLUSION

Treating multilevel lesions in patients with CLI can greatly improve their quality of life. Patients facing the prospect of amputation have a bleak outlook postamputation with high mortality and morbidity. Multilevel lesions present a number of challenges, including the time required to operate and the various interventional tools required to navigate and treat them. An operator must carefully assess plaque morphology and available vascular access points to determine the appropriate tools and techniques to successfully treat complex multilevel lesions. Treating lesions to improve both inflow and outflow can lead to improved patency rates and minimize symptom recurrence. Furthermore, improving patency of vessels allows previously nonhealing wounds to heal and can prevent amputation.

Success in treating multilevel lesions is largely dependent on the skill and commitment of the operator. An operator must take the time to be trained in using advanced techniques, such as retrograde access, transcollateral crossing techniques, and the use of a variety of wire and catheter maneuvers to successfully treat lesions at various levels of the peripheral arterial tree. These procedures are often long and require patience and commitment from the health care team. In addition to being well versed in exotic access and crossing techniques, the operator must be competent in the use of all available tools. The success of CLI programs at centers of excellence is driven by physician champions who are committed to serving this vast and growing patient population. A successful CLI program can only be established with a top-down approach, starting with administrative support of physicians to perform these high-risk procedures that place a large burden on scarce health care resources. The impact of these procedures is enormous and drives the need for a dedicated program that can address these critical needs in the community. ■

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