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A Tale of Two Legs: Putting Patients Ahead by Leaving Nothing Behind

By Gregory A. Stanley, MD

With the widespread use of various endovascular technologies for lower extremity revascularization, it is only appropriate that interventionists have a fundamental understanding of the efficacy, safety profile, and general limitations of the available options to guide treatment decisions. Pertinent to any (nonstandardized) interventional algorithm is the state of the patient (age, comorbidities), the existent lesion (length, stenosis/occlusion, calcium), and options for future revascularization (endovascular, surgical). These factors are particularly important to consider when a vessel-altering approach is selected, such as femoropopliteal stent placement.

The limitations of lower extremity stenting have thus far been inescapable. Beyond the obvious in-stent restenosis and the challenges of treatment therein,[1] recognition of the changes to surgical anastomotic sites and collateral circulation become increasingly significant with progression of the disease. Stent fracture remains a reality, especially in anatomic locations frequently subjected to flexion and torsional forces. Further, newer stents intended to decrease fracture rates by the use of an interwoven design are limited by a challenging deployment mechanism, which may lead to a permanently uneven stent distribution and subsequent loss of patency. As such, a movement toward vessel-preserving endovascular interventions (eg, atherectomy and drug-coated balloon [DCB] angioplasty) is well underway.

The following case is a unique example of a single-patient, leg-to-leg comparison illustrating not only the limitations of extended femoropopliteal stenting, but also the significant detriment that an imprudent intervention can have on the patient and possibly on the natural history of peripheral artery disease.

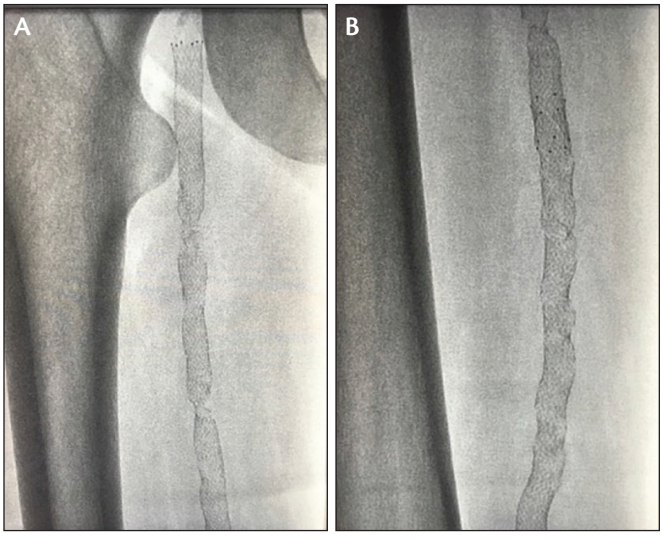

Figure 1. Right femoropopliteal bare-metal stents with multiple fractures, which were occluded on angiography (not pictured).

CASE REPORT

A 45-year-old African American diabetic woman with a complex history of both coronary and peripheral artery disease presented to our institution. She was status postcoronary artery bypass grafting, which was followed by multiple subsequent percutaneous coronary interventions to both the grafts and native vessels. In addition, she underwent multiple endovascular interventions of the right lower extremity at another institution, resulting in extended femoropopliteal stenting (full metal jacket).

Upon referral, the patient presented with ischemic rest pain of both lower extremities for several months, and noninvasive testing revealed severe hypoperfusion (ankle-brachial indices, 0.4 bilaterally). We proceeded with CTA and peripheral angiography to further assess her options for endovascular and surgical revascularization. Fluoroscopy of the right lower extremity confirmed that the stents in the femoropopliteal segment had multiple fractures (Figures 1A and 1B), including several areas of stent separation. Angiography confirmed the stents were occluded with reconstitution of the below-knee popliteal artery (P3), equating to an estimated 50-cm chronic total occlusion. Left lower extremity angiography demonstrated mid and distal superficial femoral artery (SFA) disease (total lesion length, 16 cm), including a

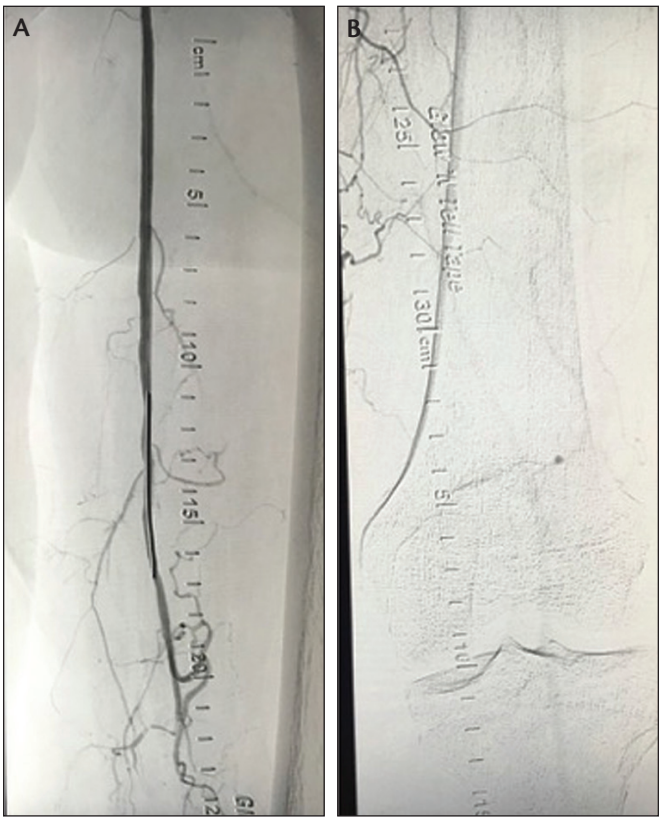

Figure 2. Initial angiogram of left femoropopliteal segment with diffuse adductor canal stenosis and 5-cm chronic total occlusion.

5-cm chronic total occlusion with reconstitution of the above-knee popliteal artery (Figures 2A and 2B).

We proceeded with left lower extremity endovascular revascularization. Standard wire and catheter techniques were used to successfully traverse the SFA occlusion. Reentry was confirmed via angiography, and a 7-mm SpiderFX™ distal embolic filter (Medtronic) was placed in the distal popliteal artery. The occlusion was then treated with directional atherectomy using a HawkOne™ 6-F atherectomy system (Medtronic), achieving luminal gain to < 20% residual stenosis in multiple views. Luminal gain was confirmed with a low-pressure balloon inflation technique.[2] Next, multiple 5-mm DCBs (IN.PACT™ Admiral™ DCB, Medtronic) were used, inflated for 3 minutes at each station. This produced an excellent angiographic result (Figures 3A and 3B) without dissection, perforation, or distal embolism.

In follow-up, the patient's left lower extremity rest pain resolved, and postprocedure testing demonstrated normalization of her left ankle-brachial index. Expectedly, bilateral lower extremity venous mapping demonstrated surgically absent saphenous veins (used for coronary bypass). She is currently undergoing further cardiac evaluation prior to surgical revascularization of the right lower extremity.

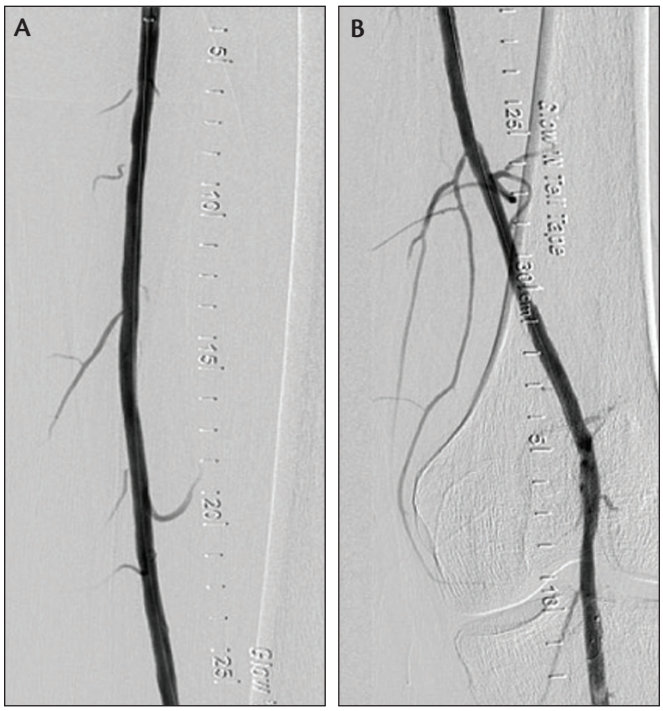

Figure 3. Completion angiogram of the left femoropopliteal segment after directional atherectomy with a HawkOne™ 6-F atherectomy system and angioplasty with IN.PACT™ Admiral™ DCBs.

The limitations of lower extremity stenting have thus far been inescapable. Beyond the obvious in-stent restenosis and the challenges of treatment therein, recognition of the changes to surgical anastomotic sites and collateral circulation become increasingly significant with progression of the disease.

DISCUSSION

The patient presented in this case had multiple coexisting patient- and lesion-related factors that placed her at significantly increased risk for endovascular failure, especially when stents are selected for revascularization. Lesion length > 8 cm, diabetes, and TASC C or D lesions carry in-stent restenosis hazard ratios of 2.6, 2.5, and 2.1, respectively[1]; our patient possessed all three risk factors. Additionally, stent fractures are more commonly observed in patients with increased exercise frequency, lesion length, number of overlapping stents, number of total stents, and degree of calcification.[3–5] When consideration is given to the patient's age, it is difficult to imagine a scenario in which bare-metal stents would not become problematic.

Alternative stent options, such as the Supera™* interwoven nitinol stent (Abbott Vascular) or the Viabahn™* stent graft (Gore & Associates) would be equally challenged to maintain patency in long-term follow-up in this patient. Although the Supera™* stent design has avoided stent fracture at 1 year in femoropopliteal lesions,[6] patency and freedom from target lesion revascularization (TLR) rates correlate directly with proper stent deployment, dropping dramatically when the stent is implanted in an elongated state. Likewise, the 3-year results of the VIBRANT trial were disappointing: 24.2% primary patency of the Viabahn™* stent graft with an average lesion length of 18 cm.[7] No stent fractures were observed. Drug-eluting stent placement may have also been considered in this case. The Zilver™* PTX™* drug-eluting stent (Cook Medical) randomized controlled trial[8] noted a 5-year primary patency of 66.4% with a mean lesion length of 6.6 cm. The stent fracture rate was reported as 1.9% in this trial.

Unfortunately, surgical revascularization options for this patient have been sabotaged by the extent of femoropopliteal stent placement. Coverage of the above-knee popliteal artery eliminates this segment as a distal target, leaving the below-knee popliteal artery as the next best choice. Importantly, both great saphenous veins have been harvested for coronary bypass, and thus the patient is facing a prosthetic lower extremity bypass (arm vein is being preserved for possible future dialysis access). This point is critical when consideration is given to the significant drop in patency of a prosthetic bypass with an above-knee versus below-knee popliteal artery distal anastomosis: 81% versus 53% at 2 years, respectively.[9]

With these limitations in mind, a desire to leave the vessel without a permanent scaffold has emerged and is gaining traction. Paclitaxel-based DCBs have been a welcomed technology to fill this space. Early positive outcomes were seen in both the IN.PACT SFA[10] and LEVANT 2 trials,[11] demonstrating significantly better primary patency at 12 months over standard angioplasty alone. However, the IN.PACT SFA trial showed significantly lower rates of TLR at the 1-year mark, which was not demonstrated in LEVANT 2. Further, a clear difference has borne out with increasing follow-up out to 24 and 36 months in favor of the IN.PACT™ Admiral™ DCB over the Lutonix™* DCB (Bard Peripheral Vascular).[12-15] Despite this success, it is worthwhile to note that the IN.PACT SFA trial was designed specifically to prove a drug effect; indeed, paclitaxel paired with urea effectively maintains patency over standard angioplasty out to 3 years in patients who had a successful balloon predilatation before DCB application.

Nonetheless, implementation of DCB as a primary treatment strategy also has limitations, which are demonstrated in review of the IN.PACT Global study data. At 12-month follow-up of nearly 150 patients with long lesions (> 15 cm), the bailout stent rate after DCB use for flow-limiting dissection or > 30% residual stenosis approached 40%.[16] We await further follow-up regarding patency and TLR rates for this patient cohort, but there is justifiable concern regarding the high rate of permanent implants required in this real-world data. In fact, the bailout stent rate in the IN.PACT SFA trial was 7.3% (in patients who were deemed to have a successful predilatation).[10]

Although the Supera™* stent design has avoided stent fracture at 1 year in femoropopliteal lesions, patency and freedom from TLR rates correlate directly with proper stent deployment, dropping dramatically when the stent is implanted in an elongated state.

With these data, we ask a simple question: "How can we overcome the limitations of angioplasty?" In other words, if we can universally achieve < 30% residual stenosis and minimize the risk of dissection *before* employing DCB technology, then it is reasonable to expect that the patient will have outcomes similar to IN.PACT SFA trial results *without* the need for bailout stenting. In our practice, we have found that this goal can be achieved with directional atherectomy.

In our experience of over 3,000 cases using directional atherectomy, we have observed results very similar to that published in the DEFINITIVE LE trial.[17] Using the first- and second-generation devices (SilverHawk™ atherectomy system and TurboHawk™ atherectomy system, Medtronic), operators were able to achieve < 30% residual stenosis with directional atherectomy alone in 74.9% of patients, and when coupled with postdirectional atherectomy angioplasty, procedural success improved to 89.1%, per core lab assessment. The bailout stenting rate was 1.3% for residual stenosis, and flow-limiting dissections were observed in 2.3%. Now with the use of the third-generation HawkOne™ atherectomy system, we routinely achieve < 20% residual stenosis with directional atherectomy alone and confirm adequate luminal gain with a low-pressure balloon inflation (1–2 atm).[2] As such, our bailout stenting rate is negligible.

In our practice, vessel preparation has only one definition: acute luminal gain with directional atherectomy alone to < 20% residual stenosis relative to the healthy vessel diameter. Once achieved, we proceed with IN.PACT™ Admiral™ DCB to deliver drug to the vessel wall. Thus, DCB has become a tool to maintain the luminal gain that was realized with directional atherectomy, leaving the native vessel without a permanent implant.

CONCLUSION

The limitations of currently available treatment options for lower extremity peripheral artery disease must always be considered, and this is especially important when utilizing modalities that permanently alter the vessel. A strategy that preserves the native vessel is very attractive, such as combination therapy employing directional atherectomy for luminal gain followed by DCB angioplasty for luminal maintenance, and early data suggest very promising results. This concept is currently being investigated by the REALITY trial (VIVA Physicians), which will further help determine if the gain/maintain concept is a durable solution for this challenging disease.

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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 180 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
- 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 (14 atm [1419 kPa]) 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 20,691 µg of paclitaxel in a patient has not been clinically evaluated in the IN.PACT SFA Trial.

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.
CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician.

Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.
Medtronic directional atherectomy products are contraindicated for use in patients with in-stent restenosis.
CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.