

## Treating Peripheral Artery Disease in the Popliteal Artery: DA + DCB Versus DCB Alone

By Konstantinos Stavroulakis, MD

The popliteal artery is a known area of high mechanical stress and dynamic force that has been associated with accelerated restenosis and high rates of stent fracture and occlusion. Although newer stents have improved outcomes in this territory, in-stent restenosis still represents a challenging complication in patients with peripheral artery disease.<sup>1-5</sup> Leave-nothing-behind modalities such as drug-coated balloons (DCBs) and directional atherectomy (DA)\* followed by DCB (DA + DCB) could potentially overcome the challenges posed by the mobility of the knee joint.

DCBs have shown to be superior to plain angioplasty in femoropopliteal lesions in randomized controlled trials.<sup>6</sup> The DEFINITIVE AR study suggested an added benefit of DA + DCB in long and calcified femoropopliteal lesions, and more recently, our single-center experience demonstrated promising results in the popliteal segment.<sup>7,8</sup> However, data on the efficacy of DCBs in the popliteal artery were lacking, as well as a comparison of DCB and DA + DCB in this challenging segment. In order to fill this gap, our group in Münster decided to conduct a comparative study evaluating the performance of DCB angioplasty alone compared to DA + DCB for isolated popliteal artery lesions.<sup>9</sup>

The investigation included 72 patients with isolated popliteal lesions treated at St. Franziskus-Hospital in Münster, Germany, between October 2009 and December 2015, with DCB angioplasty alone (n = 31) or with DA + DCB (n = 41). The selection of debulking device (DA) and paclitaxel-coated balloon was left to the discretion of the operator. DA was applied to reduce the plaque burden of the target lesion by at least 50%,

followed by DCB use. Follow-up examinations were scheduled at 6 and 12 months after the initial procedure and annually thereafter.

Primary patency was defined as freedom from significant restenosis or occlusion based on duplex ultrasound and no reintervention. Secondary endpoints were technical success, secondary patency, and freedom from clinically driven target lesion revascularization (TLR).

At baseline, the two groups presented similar Rutherford classifications, with most patients considered class 3. Patients undergoing DCB angioplasty alone were older (mean age, 72 vs 68 years;  $P = .03$ ), and men were more predominant in the DA + DCB group (71% vs 29% for DCB alone;  $P < .001$ ). The mean lesion length was similar for both groups ( $47 \pm 24$  mm vs  $42 \pm 24$  mm, DCB vs DA + DCB, respectively;  $P = .42$ ), as were vessel calcification ( $P = .984$ ) and calcification severity.

Technical success was comparable between the two groups. Mean contrast volume was higher in DA + DCB patients ( $160 \pm 62$  mL vs  $121 \pm 45$  mL;  $P = .009$ ); but there was no difference in terms of median radiation dose area ( $P = .16$ ). Despite a greater need for bailout stenting in the DCB-only group, the difference was not statistically significant (16% vs 5%;  $P = .13$ ).

Final angiography revealed a popliteal artery injury in one DA + DCB patient following atherectomy, and the problem was treated by prolonged dilation with an uncoated balloon followed by DCB. Distal embolization was comparable between the groups and was treated by endovascular means. Additionally, a female patient complained of painful edema of the popliteal fossa 24 hours after DA + DCB. CTA revealed a perforation of the popliteal artery, which was treated surgically.

The mean follow-up was 12 months in the DCB group and 10 months in the DA + DCB group. No amputations were performed. One DA + DCB patient died of unknown causes (overall mortality rate, 1.3%). At 12 months, the results showed a primary patency rate of 82% for the DA + DCB group and 65% for patients treated with a DCB alone ( $P = .021$ ). The 12-month freedom from TLR was comparable between the groups (94% for DA + DCB vs 82% for DCB alone, respectively;  $P = .07$ ). Secondary patency was 96% for both modalities. The majority of patients in both groups became and remained asymptomatic (Rutherford class 0-1) in follow-up.

Reinterventions (clinically driven TLR) were performed in eight patients who had restenosis, treated initially by DCB

\*Medtronic directional atherectomy products are contraindicated for use in patients with in-stent restenosis.

angioplasty; three patients were treated with DA + DCB, two with DCB angioplasty, two with a nitinol interwoven (NIW) stent, and one underwent surgical conversion. In the DA + DCB group, five reinterventions were performed; DA + DCB was the treatment of choice in three patients, a NIW stent was used to treat a popliteal reocclusion, and a stent graft was deployed to treat aneurysmal degeneration of the popliteal artery. Popliteal aneurysm formation was observed in three (7%) patients treated by DA + DCB versus none in the DCB group ( $P = .25$ ). The remaining two patients with aneurysmal degeneration of the popliteal artery remain under strict surveillance.

In summary, in this cohort of isolated popliteal artery lesions, DA + DCB achieved better primary patency compared with patients treated by DCB alone, but both modalities showed excellent 12-month secondary patency and no statistically significant differences in TLR, adjunctive stent therapy, or aneurysmal degeneration.

It is likely that vessel preparation (DA) prior to DCB angioplasty leads to better paclitaxel penetration into the arterial wall and improved drug uptake. Moreover, the antiproliferative treatment minimizes the inflammation caused by the rather aggressive mechanical plaque excision and, consequently, the risk of excessive neointimal development.<sup>10</sup>

The high risk of dissections with the consequently increased need for adjunctive stent therapy and the poorer outcomes of DCB in calcified lesions are the two main concerns about the use of DCBs in peripheral artery disease.<sup>6,11</sup> In regard to dissections and provisional stent therapy, the reported stent rates vary among studies.<sup>6</sup> Notably, the 7.3% bailout stent rate in the IN.PACT SFA trial was far lower than the 46.8% provisional stent use reported in the chronic occlusion subgroup of the IN.PACT Global registry.<sup>12,13</sup> In our cohort, 16% of the lesions treated with DCB alone required adjunctive stents.

In a subgroup analysis of the THUNDER trial, dissections following DCB angioplasty were not associated with poorer outcomes even without stent placement, suggesting that a less aggressive approach could be equally effective.<sup>14</sup> Nonetheless, the main aim of leave-nothing-behind therapies is to avoid stent implantation in an arterial segment exposed to mechanical stress. Concerning calcified lesions, Tepe et al observed higher rates of late lumen loss after DCB angioplasty among calcified lesions and suggested that vessel preparation with debulking devices could be beneficial prior to antiproliferative treatment.<sup>11,15</sup> On the other hand, aneurysmal degeneration of the popliteal artery limited the performance of DA + DCB in this cohort. Aneurysm formation has been reported after DA and DCB angioplasty in the femoropopliteal vessels.<sup>16,17</sup> However, the reported rates were lower than the 7% observed in our study.

New-generation devices with increased flexibility and radial force have been linked to improved patency and reduced need for reintervention. In our opinion,

stent therapy with dedicated devices remains a viable treatment option, especially in severely calcified lesions; in elderly, fragile patients; and in the settings of chronic kidney disease or long combined superficial femoropopliteal lesions.

In this nonrandomized, single-center study evaluating the performance of leave-nothing-behind therapies for isolated popliteal artery lesions, DA + DCB was associated with a higher primary patency rate than DCB angioplasty alone. Nonetheless, both modalities showed exceptional overall patency, offering an alternative endovascular approach in this region of high mechanical stress. ■

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## IN.PACT™ Admiral™ Paclitaxel-Coated PTA Balloon Catheter

### 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](http://www.manuals.medtronic.com).

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

### HawkOne™ Directional Atherectomy System

**Important Information:** Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.

**Indications for Use:** The HawkOne™ peripheral directional atherectomy system is intended for use in atherectomy of the peripheral vasculature. The HawkOne catheter is indicated for use in conjunction with the SpiderFX embolic protection device in the treatment of severely calcified lesions. The HawkOne 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.

### SilverHawk™ Plaque Excision System

**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.

### TurboHawk™ Plaque Excision System

**Important Information:** Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.

**Indications for Use:** The TurboHawk™ Peripheral Plaque Excision System is intended for use in the atherectomy of the peripheral vasculature. The TurboHawk catheter is NOT intended for use in the coronary, carotid, iliac, or renal vasculature.

The TurboHawk Catheter is indicated for use in conjunction with the SpiderFX™ Embolic Protection Device in the treatment of severely calcified lesions (LS-C and LX-C only).

**CAUTION:** Federal (USA) law restricts this product for sale by or on the order of a physician.