Endovascular Management of Drug-Eluting Balloons in the Lower Limbs

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ABSTRACT: Lower-extremity PAD limits quality of life as it often results in severe limb ischemia, possible limb loss, and is accompanied by serious cardiovascular morbidity and high mortality. Interventional approaches have come a long way, with angioplasty and stenting remaining at the forefront. But arterial restenosis continues to limit the benefits of these treatments. New DEB technologies offer the hope of significant reductions of such problems, enhancing the results of angioplasty while, at the same time, providing the opportunity for avoidance of a permanent metal stent implant. Results so far are most encouraging, and are illustrated with several case examples. More and better trials and long-term outcomes in larger series of patients are eagerly awaited to determine if the early promise becomes an established reality and a place of therapeutic prominence for DEB devices.

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Lower-extremity peripheral arterial disease (PAD) is a highly prevalent and morbid condition carrying tremendous potential to cause severe leg ischemia, and is accompanied by notorious risks of premature cardiovascular morbidity and mortality. Avoidance of limb loss and disability constitute the principal goals of treatment.

Complex and extensive PAD have steadily risen to become a serious challenge for vascular specialists, mainly because of the frequent occurrence of long lesions, multiple stenoses, heavily calcified lesions, restenosis (arterial or intrastent), and chronic total occlusions1 often requiring the performance of difficult and potentially risky leg bypass surgery.

Balloon angioplasty (PTA) alone has proven disappointing when used to treat such complex atherosclerotic lesions. Bare-metal stents have fared better, at least in the short and mid term, but the long-term results have been compromised by the high rate of in-stent restenosis caused by neointimal hyperplasia.2,3 The problem is compounded further in the femoropopliteal segment because of its mobility and exposure to external forces that can lead to stent fractures and increased risk of restenosis.4,5 Atherosclerotic lesions in the below-the-knee (BTK) arteries have similarly been observed to cause high rates of restenosis after angioplasty and stenting.4

One relatively new therapeutic option to prevent (and even treat) restenosis, and at the same time avoiding all potential problems related to the implantation of a permanent metal device, is through the use of drug-eluting balloons (DEB) that carry and release an antiproliferative drug (such as Paclitaxel) directly in and around the target area of the vessel wall at the time of balloon inflation. The drug achieves a high concentration in the wall at the site of the lesion thereby inhibiting the above-referenced hyperplastic response and leading to improved long-term patency.6,7

The purpose of this article is to provide an overview of percutaneous DEB angioplasty of the lower limbs, and a brief technical description through the report of several clinical cases.

CASE 1
A 51-year-old female former smoker with diabetes, hypertension, and dys-
A 52-year-old man with hyperlipidemia presented with intermittent claudication of the right calf and a non-healing right foot ulcer. Angiography showed several areas of long critical stenosis of the right superficial femoral artery (SFA) and total occlusion in its distal third – classified as a TASC II type C femoropopliteal lesion (Figure 1).

An initial attempt at antegrade crossing of the total occlusion with a Terumo hydrophilic guidewire (via retrograde puncture of the left common femoral artery) proved unsuccessful. Then, retrograde puncture of the posterior tibial artery (using a 21g micropuncture needle) was performed with subsequent placement of a 5 Fr sheath (Figure 2).

The SFA was crossed with a 0.014” guidewire sheath reaching to the left common femoral artery.

Angioplasty was performed using a 5 mm x 80 mm DEB catheter (Figure 3). Post-angioplasty angiography showed a residual stenosis in the SFA, treated with a 6 mm x 40 mm self-expanding stent was deployed (Figure 4 A-C). The final control angiogram
confirmed satisfactory patency of the SFA throughout (Figure 4D).

A follow-up diagnostic angiogram at 3 months confirmed the patency of the right SFA and by physical examination the patient had complete healing of the ulcer and no claudication. However, at 6 months after the initial intervention, the patient complained of recurrent claudication, and repeat angiography confirmed that the stent had become totally occluded and obvious fracture of the metal stent as well (Figure 5). Reintervention was undertaken in the attempt to reopen the vessel; transluminal recanalization was followed by DEB angioplasty using a 6 x 120 and 4 x 80 mm DEB catheters. The procedure proved successful (Figure 6), and patient re-evaluation and testing 6 months later revealed continued patency without evidence of further restenosis in the right SFA.

**CASE 2**

A 58-year-old man presented with a history of endovascular revascularization of the right lower extremity who required treatment of a nonhealing right foot ulcer. The procedure had consisted of PTA of the right popliteal, posterior tibial, and peroneal arteries. Additionally a left below-knee amputation had become necessary because of severe complications related to a diabetic foot. Reassessment and noninvasive Doppler and duplex ultrasound evaluation revealed evidence of significant post-PTA arterial restenosis at multiple levels. Reintervention via direct antegrade femoral puncture was performed, with repeat angioplasty involving the use of appropriately sized DEB balloon catheters for the various arterial segments with restenosis (Figures 7A-D). The patient did well, and right leg circulation remained intact and without evidence of restenosis 12 months later.

**CASE 3**

A 60-year-old female with diabetes, hypertension, and dyslipidemia complained of rapidly progressive left leg claudication of 10 months’ duration. She could only walk very short distances and was incapacitated. Doppler ultrasound showed confirmed the presence of multilevel severe disease, and angiography revealed critical stenosis of the distal superficial femoral artery plus a long occlusion of the...
Popliteal and tibioperoneal trunk lesion. The lesions were classified as TASC II type D (Figure 8 A-B). Via direct antegrade femoral puncture, femoropopliteal, and tibiopercanal trunk PTA with a 5 mm x 120 mm DEB balloon catheter was performed (Figure 8C). The patient was asymptomatic and doing well 6 months later.

CASE 4

A 66-year-old male heavy smoker presented with chronic progressive claudication and a non-healing toe ulcer that had been present for 4 months. Angiography showed long-segment occlusion of the SFA with heavy calcification (Figure 9A). PTA was performed using a 5 mm x 120 mm DEB balloon catheter with a good result (Figure 9 B-C). Follow-up after 6 months revealed a healed ulcer and no claudication.

DISCUSSION

The development and commercial availability of DEBs promise to enhance the long-term patency of lower-limb angioplasty. DEBs would appear to effectively reduce or inhibit neointimal proliferation and, potentially, widen the horizons for endovascular treatment of femoropopliteal lesions TASC II types C and D. It is rapidly emerging as a good therapeutic option particularly for 2 subgroups of PAD patients: those who may not be good candidates for surgical bypass operations, and in situation where placement of a stent is unappealing or outright contraindicated – the so-called “no-stent zones” such as the femoral bifurcation, Hunter’s canal, the popliteal artery, and BTK arteries.

The SFA is particularly difficult to treat because of exposure to powerful forces and stresses related to flexion, compression and torsion – as demonstrated in Case 1. Stent fracture, restenosis and occlusions can easily result from such influences. Beyond that, the overall restenosis rates after PTA alone range from 40% to 60% in the first year for short lesions and may reach up to 70% in long lesions.8

The BTK vasculature is another worthy and important therapeutic target for DEBs as these vessels are frequently involved – especially in the diabetic population – and PTA and stenting produce suboptimal results in arteries that tend to be small and calcified. The DEBATE-BTK trial showed that DEB angioplasty is more beneficial than conventional angioplasty, both in terms of a lower restenosis (27% for DEB vs 65% for PTA) and reocclusion (16% for DEB vs 56% for PTA).9,10
Traditional bypass surgery remains first-line treatment for femoropopliteal TASC II type D lesions, but this is changing rapidly at present, not only because of new and superior chronic total occlusion crossing devices but also because of better results from new endoplastry technologies – DEB in particular. Several trials have reported a good response in reducing late lumen loss and preventing neointimal hyperplasia, significantly lowering the restenosis rate at 6 months.6,7,8,10,11

**CONCLUSION**

DEB technology is an exciting new tool for the management of many difficult PAD patients, and results and studies so far would seem to confirm the concept works as hyperplastic restenosis can be prevented in the majority of instances. However, it is too soon to declare a total triumph. More and better studies as well a much larger pool of patients with long-term follow-up will eventually provide the final answers vascular specialists are awaiting. In the meantime, DEB angioplasty can be added to the armamentarium with caution and without fear as these devices do offer an exciting new option and renewed hope for avoidance of interventional complications and limb salvage.

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