

Complexity of SFA Disease Is Driving the Need for Dual Therapy

A discussion of potential differential indications for drug-eluting devices.

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The global prevalence of peripheral artery occlusive disease (PAOD), defined as an ankle-brachial index < 0.9, was estimated to affect 202 million people worldwide in 2010. Between 2000 and 2008, the incidence of PAOD increased by 28.7% in countries with low and moderate incomes and by 13.1% in those countries with high incomes.¹ This worldwide epidemic increase of PAOD demands effective treatment solutions with regard to durability and costs. The prevalence of endovascular treatment in superficial femoral artery (SFA) therapy in Germany is increasing steadily. In an analysis of all in-hospital patients with a diagnosis of PAOD based on the nationwide German diagnosis-related group system comparing the years 2005 and 2009, there was a 46% increase in endovascular treatment. In contrast, open surgical revascularization procedures are decreasing.²

In the claudicant patient population, which represents the majority of symptomatic patients with PAOD, the femoropopliteal artery is the most frequently diseased. This long vessel segment has been considered a "bad conduit" for years due to the unique mechanical challenges to which the vessel segment is exposed.³ Moreover, extensive vessel wall calcification requires either plaque preparation or the use of dedicated scaffolds. After disappointing experiences with first-generation nitinol bare-metal stents (BMSs), new stent designs and drug-eluting technologies are intended to improve outcomes following femoropopliteal artery treatment. With reported 1-year primary patency peaking at

around 80%, long-term patency after use of BMSs still leaves room for improvement. Likewise, target lesion revascularization (TLR) rates for BMSs show room for improvement, with 1-year rates averaging approximately 13% in recent clinical trials.⁴⁻⁶

DRUG-COATED BALLOONS VERSUS DRUG-ELUTING STENTS

As with coronary interventions 15 years ago, drug-eluting techniques are now considered the most appropriate endovascular treatment modalities for femoropopliteal artery disease. The current approach to prevent restenosis, and thereby reduce reintervention rates, includes applying an anti-restenotic agent such as paclitaxel to the vessel wall by means of a drug-coated balloon (DCB) or drug-eluting stent (DES). Paclitaxel, which arrests the cell cycle in the G2/M phase, interrupts arterial smooth muscle cell proliferation and migration, as well as extracellular matrix formation.⁷ In particular, DCBs

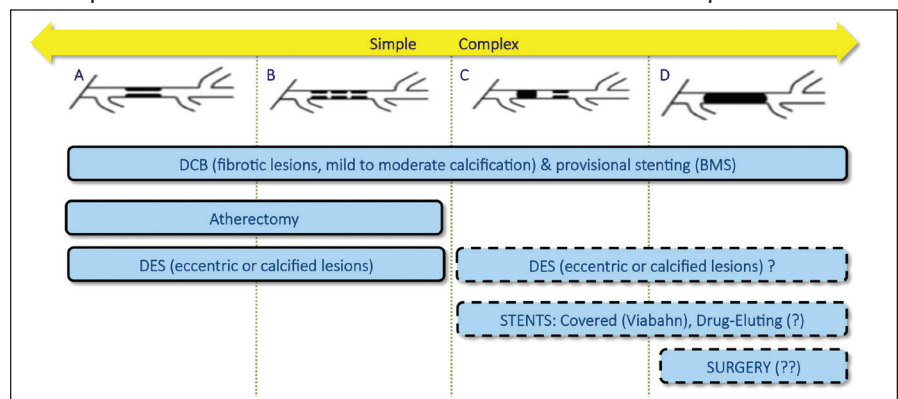


Figure 1. Potential treatment algorithm for femoropopliteal lesions based on published literature data (solid line frame represents level 1 evidence, spotted line frame represents level 2 or 3 evidence). Adapted from J Am Coll Cardiol, Vol 59, Tosaka A, Soga Y, Iida O, et al, Classification and clinical impact of restenosis after femoropopliteal stenting, pg 16-23, Copyright 2012, with permission from Elsevier.

provide an attractive method to locally deliver paclitaxel into the artery wall without the need of a chronically implanted delivery system. Even if those devices are indicated, they can be delivered focally (ie, spot stenting). Following the first positive pilot studies, two large pivotal trials have confirmed the superiority of DCBs over plain old balloon angioplasty in the treatment of TASC II A and B femoropopliteal lesions.^{8,9} Even for more complex femoropopliteal lesions (eg, long lesions and in-stent restenosis), single-center studies, global registries, and small randomized studies have shown promising midterm technical and clinical results.

For DESs, follow-up data up to 5 years for the first commercially available polymer-free device (Zilver PTX, Cook Medical) are now published, with excellent clinical outcomes regarding freedom from TLR and improved walking capacity.¹⁰ One limitation of DCBs and polymer-free DESs is that subsequent steps of the restenotic cascade might not be covered by paclitaxel beyond several weeks or months after an angioplasty or stenting procedure. Preclinical studies suggest that paclitaxel is present in the artery wall for only a few weeks at most after exposure to a balloon or stent with a polymer-free drug coating.¹¹ The Eluvia Drug-Eluting Vascular Stent System (Boston Scientific Corporation) was designed to elute paclitaxel over time. The Eluvia stent incorporates paclitaxel in a biocompatible fluoropolymer coating to provide sustained and controlled drug release. Just recently, the MAJESTIC single-arm study demonstrated promising 2-year technical and clinical outcomes with a freedom from TLR rate of 92.5%.¹²

Patients presenting with femoropopliteal disease have a relevant limitation of life expectancy when the indication for revascularization is made. Thus, the decision regarding which technology should be used for treatment is driven by independently controlled studies' durability data. DCBs and DESs seem to be almost equally effective in TASC II A and B lesions and superior to plain old balloon angioplasty and/or BMS placement.⁸⁻¹⁰ Therefore, the choice between both devices could be driven by the likelihood of provisional stenting. Eccentric and calcified lesions might represent a better indication for DESs, whereas fibrotic and concentric lesions (not necessarily excluding chronic total occlusions) might be better suited for DCBs, following the approach of avoiding unnecessary implants. Experience is still limited with regard to TASC II C and D lesions for both drug-eluting technologies.¹³ In such lesions, the full lesion coverage with DESs seems to be attractive due to the excellent initial lesion appearance after stenting. However, longer-term follow-up technical and clinical data beyond 1 year for this approach is lacking. Single-arm studies for DCB angioplasty with spot stenting on indication have shown promising 1-year outcomes.^{14,15} As a result, the decision between DESs and DCBs in this complex lesion subset is mostly driven by operator preference.

CONCLUSION

In summary, drug-eluting devices offer an attractive, minimally invasive treatment option for femoropopliteal lesions of all complexities—replacing bypass surgery as the first-line strategy even in TASC II D lesions. Head-to-head trials are mandatory to compare the safety and durability of interventional revascularization based on drug-eluting devices with bypass surgery. ■

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