

Zilver PTX in Long Lesions: Try the Jacket On

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Peripheral arterial disease (PAD) is estimated to affect over 200 million people worldwide, with increasing rates in patients in their 60s and 70s.¹ While the majority of these patients are asymptomatic, many require treatment to relieve the symptoms of claudication and limb ischemia. In the subset that have symptomatic femoropopliteal (FP) disease requiring treatment, the *endovascular-first* approach tends to be the preferred method, particularly in shorter lesion lengths. Due to high rates of restenosis, over the last several years endovascular treatment methods have shifted from percutaneous transluminal balloon angioplasty (PTA) with or without the use of bare-metal stents (BMS), to using a balloon or stent to administer antiproliferative agents to help reduce restenosis and retreatment rates.

More recently, drug-based technologies utilizing the antiproliferative agent paclitaxel have been developed to reduce restenosis rates and improve clinical durability.^{2,3} The first drug-coated PAD device approved for use in the United States was a nonpolymer-based, paclitaxel-coated drug-eluting stent (DES), the Zilver PTX (Cook Medical), which has demonstrated reduced rates of restenosis and re-intervention now at 5 years when compared with PTA and BMS.⁴ The second wave of devices have been drug-coated balloons (DCBs), which also have demonstrated improved outcomes compared with PTA.^{3,5}

Although it appears that the use of drug-elution has changed the endovascular treatment paradigm in the FP segment, there is still a paucity of real-world data for DES and DCB in complex TASC C and D lesions. For example, the only level-1 randomized trial that demonstrated the safety and effectiveness of the paclitaxel-coated DES for treating FP disease had a mean lesion length of 5.5 cm and a stented length of 6.6 cm.² A Registry from Germany supported the use of DES in slightly more complex lesions with a mean length of 10 cm.⁶ More recently, a 1-year postmarket surveillance study from Japan with mean lesion lengths of 14.7 cm also demonstrated the effectiveness of paclitaxel-coated DES.⁷

The question remains of what to do with the “real-world” lesions, particularly those that are long and often chronically occluded, with lengths sometimes >30 cm. Diffuse FP (>20 cm) arterial disease is a common entity and treatment of these lesions with DES warrants formal clinical evaluation in an effort to better understand their durability and clinical effectiveness in a real-world setting. Unfortunately, this population is typically excluded from device-approval study cohorts.

In a single-center registry, we evaluated our 1- and 2-year patency rates as well as the clinically driven reintervention rates in our patients with diffuse de novo and in-stent restenotic FP atherosclerotic lesions greater than 20 cm who received the Zilver PTX DES. The formal results were recently accepted for publication in *the Journal of Endovascular Therapy*. We did this with the hope of better understanding how the Zilver PTX stands up to this complex lesion cohort.

Eight-nine patients were included, with clinical presentation ranging from function-limiting claudication to critical limb ischemia (34% had CLI). Anatomic lesions included the superficial femoral artery (without exclusion of ostial disease) and popliteal artery segments I and II. Over 60% of the lesions were chronic total occlusions (CTO), and 27% had in-stent restenosis. The lesion lengths were broken up into 2 pre-specified subsets for comparison: a shorter lesion length group (SLG) ≤ 20 cm (41 patients) versus full metal DES jacket group (FDJ) of >20 cm (48 patients). The mean lesion length for all patients was 24.2 cm, with an average length of 13.9 cm in the shorter group and 33 cm in the long lesion. Technical success with a residual stenosis of <30% was achieved in all patients.

In general, we believe our results are encouraging, specifically in those treated with the “full drug jacket.” Before addressing the “full drug jacket” group, it is important to note that our short lesion cohort has patency and freedom from reintervention rates that compare to other Zilver data sets with similar lesion lengths. Our 12-month primary patency rate of 81.2% is similar to 4 other registries, including the “longer lesion” Zephyr study of 17 cm, Zilver PTX randomized trial (86.2%), the Zilver PTX European registry (84.8%), the Japanese postmarket single-arm surveillance study (84.4%), and the Zephyr study (83.3%). Our rates of freedom from reintervention both at 12 months (97.6%) and 24 months (87.8%) are comparable as well.^{2,4,7,8}

Perhaps the more provocative information from our analysis was that of the FDJ cohort. Despite having a 40.5% restenosis rate at 12 months, increasing to 53.6% at 24-months, the 12-month re-intervention rate was 20.8% and the 24-month rate was 33.3%, representing freedom from target lesion revascularization of approximately 80% and 67%, respectively. These data suggest that if the treated segment develops restenosis, regardless of lesion length, the restenosis perhaps is more likely to happen within the first year with less progression thereafter. This lowered need for

revascularization may also be in part due to a lower plaque burden pattern from the paclitaxel as recently suggested.

As one would expect, our short lesion cohort was similar to that of other trials. However, what do we glean from the full drug-jacket group? Does a single-center retrospective registry, that reports over 50% restenosis rate at 24 months, yet a 67% revascularization rate, provide enough evidence to support the use of Zilver PTX in lesions that average over 30 cm in length? While we had no delusions of grandeur when analyzing the data to assume patency rates of the randomized trial, a 50% restenosis rate at 24 months may call into question the efficacy of this treatment modality. However, we do feel that the reintervention rates both at 12 and 24 months are acceptable, particularly in a patient population that is underrepresented in trials and often left with limited treatment options. Certainly, more data are needed long term and in larger patient cohorts. Nonetheless, I feel the “full drug-jacket” deserves, at a bare minimum, to at least be tried on. ■

Disclosure: The author has completed and returned the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr. Phillips reports personal fees from Cook Medical, outside the submitted work.

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REFERENCES

1. Criqui MH, Aboyans V. Epidemiology of peripheral artery disease. *Circ Res.* 2015;116(9):1509-1526.
2. Dake MD, Ansel GM, Jaff MR, et al. Paclitaxel-eluting stents show superiority to balloon angioplasty and bare metal stents in femoropopliteal disease: twelve-month Zilver PTX randomized study results. *Circ Cardiovasc Interv.* 2011;4(5):495-504.
3. Laird JR, Schneider PA, Tepe G, et al. Durability of treatment effect using a drug-coated balloon for femoropopliteal lesions: 24-month results of IN.PACT SFA. *J Am Coll Cardiol.* 2015;66(21):2329-2338.
4. Dake MD, Ansel GM, Jaff MR, et al. Durable clinical effectiveness with paclitaxel-eluting stents in the femoropopliteal artery: 5-year results of the Zilver PTX randomized trial. *Circulation.* 2016;133(15):1472-1483; discussion 1483.
5. Rosenfield K, Jaff MR, White CJ, et al. Trial of a paclitaxel-coated balloon for femoropopliteal artery disease. *N Engl J Med.* 2015;373(2):145-153.
6. Dake MD, Scheinert D, Tepe G, et al. Nitinol stents with polymer-free paclitaxel coating for lesions in the superficial femoral and popliteal arteries above the knee: twelve-month safety and effectiveness results from the Zilver PTX single-arm clinical study. *J Endovasc Ther.* 2011;18(5):613-623.
7. Yokoi H, Ohki T, Kichikawa K, et al. Zilver PTX post-market surveillance study of paclitaxel-eluting stents for treating femoropopliteal artery disease in Japan: 12-month results. *JACC Cardiovasc Interv.* 2016;9(3):271-277.
8. Iida O, Takahara M, Soga Y, et al. 1-year results of the ZEPHYR Registry (Zilver PTX for the Femoral Artery and Proximal Popliteal Artery): predictors of restenosis. *JACC Cardiovasc Interv.* 2015;8(8):1105-1112.