DES Versus Bypass for Femoropopliteal Disease

Should the current data on drug-eluting devices cause surgeons to reconsider when to use bypass?

BY MARC BOSIERS, MD, AND KOEN DELOOSE, MD


Vascular surgeons have more options for treating femoropopliteal disease available today than ever before. Whereas other physician specialties only have to consider the appropriateness of medical, exercise, and endovascular therapies for treating their patients, the vascular surgeon also has to consider bypass surgery. Good-quality randomized data comparing different endovascular options have significantly increased over the past decade. Among the different endovascular options, percutaneous transluminal angioplasty (PTA) and stenting are the most common and would have been considered standard care not too long ago.

The emergence of drug-coated balloons and drug-eluting stents, however, are now showing superiority to their bare counterparts. In the IN.PACT SFA trial, the In.Pact Admiral drug-coated balloon (Medtronic, Inc.) demonstrated superiority to a standard, bare PTA balloon catheter.[1] In the Zilver PTX randomized controlled trial, the Zilver PTX stent (Cook Medical) demonstrated superiority to both PTA and bare-metal stents (BMS).[2] These trials have given physicians great confidence in using drug-eluting devices over their bare counterparts.

A largely unanswered question, however, is how drug-eluting devices compare to bypass. Data comparing percutaneous coronary intervention/drug-eluting stents to coronary artery bypass grafting in the coronary arteries suggest that target lesion revascularization (TLR) rates are higher with percutaneous coronary intervention/drug-eluting stents, but the risk of stroke is higher with coronary artery bypass grafting.[3,4] Unfortunately, substantial data comparing femoropopliteal bypass to superficial femoral artery (SFA) drug-eluting stents are lacking.

In the BASIL trial, bypass was compared to PTA. For the first 2 years of follow-up, there was no difference between PTA and bypass; but after 2 years, bypass showed more durable results.[5] Although the trial provided some insight into the performance of bypass compared to PTA, it is greatly limited for drawing conclusions about choosing modern SFA treatment options. The evidence comparing drug-eluting therapies to bypass is far from complete, but there is some evidence available to help surgeons re-examine their treatment philosophies and consider whether they should make any adjustments to how they approach treatment selection for SFA lesions. This article examines how drug-eluting SFA stents compare to three forms of bypass: "endovascular bypass" (polytetrafluoroethylene stent grafts), synthetic bypass, and vein bypass.

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ZILVER PTX VERSUS ENDOVASCULAR BYPASS

Although femoropopliteal stent grafts are not technically a mode of bypass, some vascular surgeons choose them based on their perceived similarities to synthetic bypass. The most widely used femoropopliteal stent graft is the Viabahn endoprosthesis (Gore & Associates). Currently, there are no head-to-head data comparing Zilver PTX to the Viabahn device, but there are some good randomized data for each device. From these data, we may be able to formulate hypotheses about which device to choose.

The Viabahn device was randomized against BMS in two different trials: the VIBRANT trial and, most recently, the VIASTAR trial. In the VIBRANT trial, the first-generation Viabahn device did not demonstrate a difference in patency when compared to BMS (24.2%

vs 25.9% at 3 years, respectively). However, the second-generation Viabahn fared better than the first-generation device. In the VIASTAR trial, Viabahn showed an improvement in patency to a BMS at 24 months (63.3% vs 41.4%).[6] That said, the primary patency results were somewhat dampened by the secondary patency rates and freedom from TLR rates. Viabahn showed no significant improvement over BMS for secondary patency (89.7% vs 88.8%) and no significant improvement in freedom from TLR at 24 months (76.1% vs 68.4%).[6] Regardless of which device generation is used, the benefit of Viabahn over BMS appears to be marginal.

In the Zilver PTX randomized trial, the Zilver PTX device showed significant improvement over both optimal PTA and BMS, cutting both restenosis and reinterventions by nearly half. At 2 years, Zilver PTX showed a 46% reduction in restenosis (83.4% vs 63.1%).[2] Further, Zilver PTX demonstrated a 53% reduction in reinterventions at the 2-year mark (89.1% vs 76.7%).

In addition to considerations of effectiveness, one must consider safety factors, as well. Thrombosis can be a challenge for permanently implanted devices. However, Zilver PTX showed a 2.3% thrombosis rate through 2 years compared to the BMS rate of 3.6%.[7] Further, a scan of the literature shows that a thrombosis rate of 2% to 5% is typical for bare-metal SFA stents and that Zilver PTX is within that range. Although Viabahn has shown modest acute thrombosis rates, it has not fared as well in terms of late stent thrombosis. In the Viabahn 25-cm study, Gore reports that the latest generation of Viabahn has a 12-month thrombosis rate of 15.5%.[8] In one physician-initiated study, thrombosis rates through 12 months were reported to be at 17%.[9] Further, that same study reports that 12% of patients undergoing Viabahn placement presented with acute limb ischemia.

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ZILVER PTX VERSUS SYNTHETIC BYPASS

Before assessing differences between an endovascular device trial to a surgical bypass trial, one must account for the historically different definitions of patency between the two. Importantly, one should take note that bypass patency is not the same as endovascular patency. In an endovascular trial, such as the Zilver PTX randomized trial, patency is often measured in a binary fashion and is determined by the patient's peak systolic velocity ratio (PSVR) relative to the PSVR threshold set in the trial design (usually 2.0 or 2.4). By contrast, bypass is assessed simply by observing the flow through the bypass: either it is open or closed.

In a recent prospective study, Deloose et al found that 11% of those considered to be patent by classic vascular definitions were restenosed when using an endovascular standard of binary restenosis at a PSVR of 2.4.[10] Therefore, comparing patency between surgical and endovascular trials handicaps any endovascular therapy (especially if a more conservative PSVR of 2.0 is used).

Although there are no completed trials directly comparing Zilver PTX to bypass, data from various randomized controlled trials can help formulate hypotheses about which one might perform better (Table 1). A selective scan from 2005 to 2010 of trials that include bypass primary patency showed a 12-month primary patency rate of between 70% and 80%.[11] For the Zilver PTX randomized trial, single-arm study, and Japanese postmarket surveillance study, the 12-month primary patency rates for Zilver PTX ranged from 80% to 90%. A comprehensive literature review of bypass trials from 1966 to 2002 shows that the 2-year patency rate for synthetic bypass was 67%.[12] Results from the Zilver PTX randomized trial show that the primary patency rate at 2 years was 83.4%. It will be interesting to see how the 5-year patency rate for Zilver PTX compares to the 5-year patency rates for synthetic bypass.

Obviously, the most reliable method of comparison would be to randomize patients to either bypass or Zilver PTX in the same trial. By conducting a head-to-head comparison of Zilver PTX to bypass in the same trial, the patency bias that was previously discussed will be eliminated. That is why this author has initiated the ZILVERPASS study. The study will include two arms with a 1:1 randomization to either Zilver PTX or synthetic

TABLE 1. COMPARISON OF PATENCY RATES BY PROCEDURAL MODALITY

Treatment Type	2-Year Patency	4-Year Patency	5-Year Patency
Synthetic bypass	67%	NA	49%
Vein bypass	80%	NA	69%
Zilver PTX	83%	75%	NA (data will be reported later this year)

Abbreviation: NA, not available.

bypass. Further, as previously noted, the definition of patency will be the same for both arms, giving us one of the best comparisons of Zilver PTX to synthetic bypass to date. The trial is currently in the process of enrolling, and we look forward to seeing these data, which will inform treatment options for vascular surgeons.

ZILVER PTX VERSUS VEIN BYPASS

For most vascular surgeons, vein bypass is the gold standard for treating the femoropopliteal segment. But given the aforementioned differences between how patency is measured for a surgical bypass trial and an endovascular trial, comparisons can be difficult to assess. Nonetheless, there are some data available to again help us formulate hypotheses about the relative effectiveness of femoropopliteal bypass compared to SFA drug-eluting stents.

The same comprehensive literature review of bypass trials from 1966 to 2002 (as previously mentioned) shows the 2-year patency rate for vein bypass at 80%.[12] Results from the Zilver PTX randomized trial demonstrated a 2-year primary patency rate of 83%. From the same literature review of multiple bypass trials, the aggregated 5-year patency rate for vein bypass was 69%. The 4-year primary patency rate for Zilver PTX was 75%. We look forward to the publication of the 5-year Zilver PTX RCT data.

The ZILVERPASS study, comparing head-to-head bypass versus Zilver PTX for above-the-knee long femoropopliteal lesions, will shed new light on how the next long overdue revision of the TASC classification should be handled. ■

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Neither Dr. Bosiers nor Dr. Deloose were paid for writing this article.

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