

Treating Femoropopliteal Occlusive Disease

What will be the workhorse therapy to address this disease over the next 3 to 5 years?

WITH GARY M. ANSEL, MD; WILLIAM A. GRAY, MD; AND DIERK SCHEINERT, MD

The treatment of superficial femoral and proximal popliteal artery (femoropopliteal) occlusive disease has recently started to mature. For years, we have seen various treatment modalities recommended based primarily on limited registry data. In the last few years, however, we have seen the development of comparative objective performance criteria.¹ More recently, large, higher-quality, core laboratory–controlled, multicenter, randomized trials, such as the Zilver PTX trial (Cook Medical, Bloomington, IN), have been completed. In the United States, there are multiple technologies currently being used in the femoropopliteal region, including balloon angioplasty, atherectomy, bare-metal stents (BMS), and stent grafts. The use of drug-eluting stents (DES) in this anatomy has only recently been approved in the United States. The first two drug-eluting balloon (DEB) trials, LEVANT 2 (Bard Peripheral Vascular, Inc., Tempe, AZ) and IN.PACT (Medtronic, Inc., Minneapolis, MN), have recently completed enrollment, and, if efficacy and safety are again demonstrated, we anticipate the technology to be available in the United States in the next 3 to 5 years.

Thus, physicians are being faced with an ever-changing decision process for treating the femoropopliteal region. Vessel characteristics that may influence the choice of technology include vessel size, disease length, extent of calcification, location in respect to the vessel ostium, the patient's ability to tolerate antiplatelet therapy, blockage relationship to important collaterals, renal function, vascular runoff status, etiology of the obstructive process, available vascular access sites, and the patency duration requirement. Other variables that may influence physician treatment strategies include ease of use, outcomes data, physician reimbursement, and procedural cost.

In this discussion, we will classify the various therapeutic options into three categories—yesterday's technology, niche use, or workhorse.

—Gary M. Ansel, MD

PARTICIPANTS



Gary M. Ansel, MD

Dr. Ansel is System Medical Chief, Vascular Services at Ohio Health/Riverside Methodist Hospital in Columbus, Ohio. He has disclosed that he is a paid consultant for Cook

Medical as well as a Co-Principal Investigator for the Zilver PTX trial, and serves on the advisory board for Gore & Associates, Boston Scientific Corporation, Cordis Endovascular, Abbott Vascular, Covidien, Bard Peripheral Vascular, and Idev. He has also disclosed stock ownership in Flexible Stenting Solutions.



William A. Gray, MD

Dr. Gray is Associate Professor of Medicine at Columbia University Medical Center in New York, New York. He has disclosed that he is a consultant for Abbott Vascular, Johnson &

Johnson, Medtronic, Inc., and Gore & Associates, and holds stock in Contego Medical.



Dierk Scheinert, MD

Dr. Scheinert is Director, Center of Vascular Medicine, Angiology & Vascular Surgery at Park Hospital in Leipzig, Germany. He has disclosed that he serves on the advisory board and

is a consultant to Abbott, Angioslide, Atheromed, Biotronik, Boston Scientific, Cook Medical, Cordis, Covidien, CR Bard, Gardia Medical, Medtronic, TriReme Medical, Trivascular, and Upstream Peripheral Technologies. He has also disclosed that he is a stockholder and consultant to Idev.

EXERCISE THERAPY AND CILOSTAZOL

Niche Use

Dr. Ansel: Certainly, with access to supervised vascular rehabilitation, this avenue has shown promise for the motivated claudicant patient and should be considered as a first-line treatment strategy.² However, due to the lack of reimbursement, the logistics of travel, and the time commitment involved, this treatment strategy has a limited application. Likewise, cilostazol and, to a lesser degree, statins have demonstrated efficacy in up to 50% of the patients who are able to tolerate these medications.³⁻⁵ Medication and exercise efficacy is typically limited to a doubling of the walking distance.

Niche Use

Dr. Gray: There is little question that superficial femoral artery (SFA) patients don't die from their SFA disease—they die from cardiovascular complications of myocardial infarction, stroke, and other related illnesses. Therefore, secondary prevention strategies are critical for these patients. The severity of the clinical presentation with peripheral arterial disease predicts patients' ultimate outcomes, and those outcomes may be modified by medical therapy.

Exercise is a component to any therapeutic plan for a peripheral arterial disease patient. But to be fair, even if you get a good effect from exercise, you may only double walking distance. For somebody who is already experiencing claudication after one block in New York City, that's not going to get you very far. For many people, that is significantly limiting.

If you're less limited in your initial presentation, you may be able to get adequate ambulation. I think the bottom line is that exercise and medical therapy are important components, but they may not replace a need for revascularization because of continued lifestyle limitation.

Niche Use

Dr. Scheinert: There's no question that, particularly for patients with claudication, exercise therapy is a first-line option. It is an option for patients in a good general medical condition. We certainly attempt treatment with structured exercise plans and/or the addition of cilostazol. For medical therapy, many patients actually suffer from unwanted side effects, which reduces compliance to take this medication. There are of course patients who benefit from taking these drugs. The problem with exercise is that many of these patients are not suitable candidates due to comorbidities. In real practice, in our patient cohort, exercise is only applicable to a small number of patients.

BALLOON ANGIOPLASTY

Yesterday's Technology

Dr. Ansel: Although balloon angioplasty has been the cornerstone of endovascular therapy for the femoropopliteal region, we are seeing it slowly vanish as newer technology demonstrates superior efficacy. Since the VIVA group's objective performance criteria were published utilizing both line-item data and literature comparisons showing a combined patency rate of 33% at 1 year for somewhat simple disease, this treatment modality has been increasingly replaced by more effective approaches.¹ Currently, only patients with very focal lesions would appear to routinely be potential candidates for stand-alone angioplasty, and even this appears to be in question with the results of the Zilver PTX trial.

Workhorse

Dr. Gray: I think for selected, short lesions, POBA is quite effective. Especially for traditional no-stent zones (popliteal artery, common femoral junctions, etc.), angioplasty may be adequate for short-segment occluded stenoses. After atherectomy, POBA is helpful and can provide a stent-like result, reducing the need for stent placement after atherectomy, as has recently been demonstrated with several atherectomy devices. As drug coating comes down the road, I think you are going to see angioplasty replaced by those antiproliferative balloon and stent therapies, possibly as adjuncts to other revascularization therapies.

Yesterday's Technology

Dr. Scheinert: Balloon angioplasty is no question the basic interventional treatment modality after wire crossing to open up a vessel. However, as a standalone therapy, it has only value for short focal lesions (shorter than 4 or 5 cm). For longer lesions, the restenosis rate is just too high to offer this as a standalone solution.

ATHERECTOMY

Niche Use

Dr. Ansel: The recently presented DEFINITIVE LE trial findings were certainly a step forward for data on the atherectomy front.⁶ Although we still need a randomized data set to help us compare patency with angioplasty, the ultrasound core lab patency rate of 78% for directional atherectomy gives us some insight as to what to expect for patency of the lesion types enrolled in this study. However, we will also need to continue to be selective, because there was a reported combined perforation and distal embolization rate of 9.1%. Also, recently presented data on orbital atherectomy (CONFIRM trial) have demonstrated high procedural

success with minimal dissection, leading to low bailout stenting.⁷ Until there are data on the combined use of DEB and atherectomy (trials have started in Europe), these devices appear to still be niche devices for certain challenging lesions or as debulking devices before stent placement in lesions that are expected to be resistant to balloon dilation.

Niche Use

Dr. Gray: Atherectomy can be useful for long diffuse disease and heavily calcified disease. Because there is a lot of that kind of disease in the patient populations that we see in a tertiary referral center, we tend to use a fair bit of atherectomy. However, it may be more of a niche product for many physicians who want to use it just for short focal calcification or for no-stent zones.

Niche Use

Dr. Scheinert: The utilization of atherectomy in Europe and generally outside of the United States is lower than it is in the United States. This is in part related to the early availability of other devices in Europe, which became available at a much later stage in the US. Conceptually, atherectomy is a good way to remove the plaque rather than just pushing it away with a balloon; however, the clinical evidence around this technology is still very limited. Personally, I think atherectomy procedures have certain disadvantages because they prolong the procedure, they can potentially add complications, and they certainly add procedural cost. At the moment, this makes it a niche technology for very select lesion subsets.

BARE-METAL STENTS

Niche Use

Dr. Ansel: Since the first BMS, such as the balloon-expandable Palmaz stent (Cordis Corporation, Bridgewater, NJ), the self-expanding Wallstent (Boston Scientific Corporation, Natick, MA), and IntraCoil stent (no longer available), technology has continued to evolve. Self-expanding tubular nitinol stents demonstrated an improved ability to be placed accurately and demonstrated improved patency for all but simple lesions compared to balloon angioplasty.⁸⁻¹⁰ The next generation of femoropopliteal BMS are focusing on increased radial strength while at the same time adapting to the various external forces exerted on this vascular bed.

The recently released core lab–controlled registry results for the Supera stent (Idev Technologies, Inc., Webster, TX), with a 1-year patency of 80% and no stent fractures, appear very promising.¹¹ Even with the approval of DES, this flexible stent may continue to find utiliza-

tion, especially in very resistive calcified lesions because it resists compression better than all the other currently approved stents. Its shortcoming is primarily centered on the lack of precise placement at the proximal end. Typically, this stent has been utilized in the popliteal and adductor canal areas, where significant calcification and compression are more common.

Workhorse

Dr. Gray: I think BMS technology is clearly still a workhorse for subintimal recanalizations and heavily calcified lesions that require some additional scaffolding. Different types of stents will satisfy a lot of the requirements we have for our interventions today. The question will be, how much better can Zilver PTX improve overall long-term durability? In the Zilver PTX trial, the outcomes were much better than the bare Zilver. But how does that fit in the larger pantheon of BMS that are not Zilver comparators? Clearly a biologic effect is going to displace a lot of BMS use.

Yesterday's Technology

Dr. Scheinert: BMS are certainly still a primary therapy option for the femoropopliteal space. I think the wider use of BMS has certainly contributed to better results in the femoral arteries. More patients are being considered for interventional techniques based on the availability of BMS. However, for longer stented segments, the restenosis rate is still considerably high. It seems to me that we have reached a point where BMS on their own cannot perform well in terms of results.

COVERED STENTS

Workhorse

Dr. Ansel: Stent grafts have undergone a significant change in engineering design and outcomes in the last few years. The randomized VIBRANT trial (Gore & Associates, Flagstaff, AZ) demonstrated focal edge restenosis in the stent graft group, but no improvement was demonstrated in primary or secondary patency compared to bare-metal nitinol stents for long, complex femoropopliteal disease.¹² Since the completion of VIBRANT, stent grafts have undergone design changes and now have a contoured proximal edge (where 60% of restenosis occurs) and added heparin bonding. The VIPER registry trial (Gore & Associates), with similar patient and lesion criteria as the VIBRANT trial, demonstrated an improved primary patency rate of 79% at 1 year. In a retrospective angiographic core lab review, a patency rate of 90% was found when the device was sized appropriately.¹³ Although no difference in acute limb ischemia due to thrombosis was found in the

VIBRANT trial, this concern still appears to hold back universal uptake.

Niche Use

Dr. Gray: A unique aspect of covered stents is that they do not lose patency by length. The patency of a covered stent is not determined the way it is for most other stenting—by the length of the lesion that it is covering; it is determined by vessel preparation and the proximal edge patency. We've used it as a niche tool for aggressive restenotic patients, but there are other people who use it as a workhorse. It depends a little bit on your patient population. In some patient populations, it's difficult to get routine follow-up. I believe that when one of the outcomes of a restenotic stent could be acute thrombosis, that patients should be monitored closely using noninvasive testing. In certain segments of any patient population, patients travel a fair distance for treatment and follow-up, which is one of the reasons that some may hesitate to use covered stents. But it is a good device and has patency effects, especially for the long lesion. In the most recent VIPER trial, the average lesion length was up to 20 cm; in most BMS trials, they're between 5 and 10 cm. For lesions longer than 10 cm, data are largely lacking for BMS, but we have good data on covered stents.

Niche Use

Dr. Scheinert: Covered stents are probably less frequently used in Europe than the United States. One of the main reasons is the associated cost for the devices and limited reimbursement. I think they have great promise for long lesions because the restenosis rate does not seem to be directly related to the lesion length, as it is with other stent devices. I see it more as a niche indication; specifically for long lesions, it is appealing.

DRUG-ELUTING STENTS

Workhorse

Dr. Ansel: With the recent results of the Zilver PTX trial, in which the device demonstrated improved patency compared to both balloon angioplasty and bare-metal stenting, the treatment paradigm is set to change, just as coronary stent treatment did when drug elution became available. Both short- and long-term patency and freedom from target lesion revascularization have been significantly improved at up to 3 years with a > 45% reduction in repeat revascularization.¹⁴ When restenosis does occur, it appears to be more focal and less diffuse, which may lead to simpler repeat procedures.

The effect of lesion length is even more interesting with DES technology. Even though the FAST trial did not

demonstrate improved patency for BMS compared to balloon angioplasty for focal stenoses, the randomized Zilver PTX technology has demonstrated a significant improvement in both patency and target lesion revascularization. Generalization of these results to more complex disease has been looked at in a large multinational study, and the patency and target lesion revascularization curves appear to be very similar to the randomized trial.¹⁵ Subgroup analysis has demonstrated efficacy in patients with diabetes as well as challenging lesions. It is certainly expected that future DES development will follow a pathway similar to that seen in the coronaries, with more flexible stent platforms, newer drugs, and new release mechanisms to be tested.

Workhorse

Dr. Gray: In Europe, they haven't had great penetration, but I'm not sure how much of that is related to the reimbursement landscape. There are good data now from Zilver PTX and the Zilver registry that suggest its utilization should be higher than it is today. While SFA drug-eluting stents have been given a special ICD-9 code for monitoring, there is currently no additional reimbursement over and above other therapies. I think use will pick up if CMS grants additional reimbursement. Where the price ultimately settles will also affect the uptake in the United States.

Workhorse

Dr. Scheinert: I think DES have shown very good results throughout different lesion subsets within randomized trials for short lesions as well as in the world wide registry setting for challenging, real-world lesions. I think they are certainly a first-line treatment option for a wide range of lesions.

DRUG-ELUTING BALLOONS

Workhorse

Dr. Ansel: Multiple DEB platforms have been introduced outside of the United States. Not all of these technologies have been successful, although the majority have demonstrated improved patency in randomized trials compared to balloon angioplasty.^{16,17} This treatment option appears to reduce restenosis by decreasing vascular recoil, vessel atresia, and intimal hyperplasia associated with balloon angioplasty. Unlike DES, there is no scaffold to help with the treatment of dissection, and the exact vessel characteristics that may effectively be treated with this approach have yet to be fully defined.

The available technology in Europe may not always be applicable in the United States, as standards for particulate embolization, coating uniformity, etc., seem

to be more stringent. The first two drug-eluting balloon trials LEVANT 2 trial (Bard Peripheral Vascular, Inc., Tempe, AZ) and IN.PACT (Medtronic, Inc., Minneapolis, MN) have recently completed enrollment, and we await patency results. We will look to our European colleagues to give us early insight as to the potential efficacy of bailout stenting and concomitant atherectomy use with DEB.

Niche Use

Dr. Gray: I think as people gain experience with Zilver PTX and other antiproliferative therapies in the next 3 to 5 years, there will be a shift. The nonantiproliferative, nonbiologic solution for most of what we do today in the SFA and popliteal will become a basic, biologic, antiproliferative solution.

Unfortunately in Europe, physician use of DEB has been limited by the reimbursement environment, which limits our “preview” of these therapies. This is shifting a little, so we’ll hope to have increasing output from them in terms of what they think of the device. Having said that, the European physicians say that they like DEB for a variety of applications typically not requiring stents, such as diffuse disease, shorter length lesions, nonheavily calcified lesions where dissection may not be as big an issue, and dissection is being managed conservatively when it occurs.

There are other technologies that may help potentiate the use of DEB. For example, there is a new device currently in testing in Europe called the Tack-It (Intact Vascular, Wayne, PA), which allows for a very short segment (approximately 6 mm) of stent length. That may be very useful in a segment of DEB where placing a long stent is not preferable, but where it is necessary to secure a short segment of the vessel with dissection.

Workhorse

Dr. Scheinert: DEB are clearly getting more and more traction in the field of peripheral endovascular procedures, particularly in Europe because a variety of devices is commercially available. I think the current evidence mainly refers to shorter lesions where DEBs have been shown to be clearly more effective than plain balloons. However, I think the greatest promise is for longer complex lesions where they might be an important way to improve results and eliminate the need for long, full-metal jacket stenting. Clearly, there is still a lot of need for scientific data specifically looking at those lesion subsets. ■

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