

Challenges Facing Current and Next-Generation SFA Technologies

A discussion of anatomic barriers to treatment, evolving trial designs, and the impact of reimbursement.

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The superficial femoral artery (SFA) is well known for the challenges it poses in achieving favorable and durable revascularization results. The vessel's unique forces and the wide variance in presentations and concomitant factors contribute to this difficulty, but they have also inspired a plethora of potential dedicated device solutions. However, the path to widespread adoption of SFA revascularization devices is also quite challenging. This begins with meeting the demands of the femoropopliteal segment itself, though even proof of safety and efficacy or predicate equivalence is only the beginning for market penetration in 2018 and beyond. This article explores the barriers to entry, including modern regulatory standards, differentiation in a crowded market, and gaining sufficient reimbursement to support adoption.

ANATOMIC BARRIERS TO TREATMENT OF FEMOROPOPLITEAL DISEASE

The femoropopliteal artery is unique in its length and the flexion/extension, torsion, and compressive forces to which it is subjected. These distinctive anatomic features have been well described and are a specific focus of premarket approval (PMA) trials, given the perceived high rate of acute procedural failure and long-term risk of loss of vessel patency. An example of the effect of complex femoropopliteal artery lesion morphologies on acute procedural success is highlighted in the recently reported IN.PACT Global study of “all comers” of claudicants with Rutherford class 2 to 4 femoropopliteal artery disease. A stent/nonstent post hoc subanalysis of the 1,406-patient data set presented by Dr. Gary Ansel at LINC 2018 reported an overall 25.3% provisional stent rate (353 patients with 455 lesions)

and identified three angiographic lesion variables: length, occlusions, and “severe” vessel wall calcification (defined as “bilateral calcium” at the same vessel location involving at least half the total lesion length) as statistically significant predictors of provisional stenting.¹ The analysis noted that high-grade flow-limiting dissections (> type C) and/or a persistent residual stenosis > 50% after drug-coated balloon (DCB) treatment were identified by operators as the indication for stenting. Furthermore, of those patients who received stents, approximately one-third underwent “spot stenting,” one-third underwent partial stenting of the index lesion, and one-third underwent stenting of the entire lesion. However, the big message of the subanalysis was related to the safety of the “standby” stenting algorithm, specifically that there was no difference in clinically driven target lesion revascularization (CD-TLR) at 2 years between patients who received a DCB plus a provisional stent and those who received a DCB alone (80.8% vs 83.9%, respectively; $P = .39$). Importantly, this 2-year endpoint was core lab adjudicated, making this observation that much more substantive. However, this data set did not capture the pattern of loss of patency (stenosis vs occlusion) nor the presence of stent fractures, particularly in long lesion stenting > 20 cm. Finally, whether this excellent observed vessel patency is maintained beyond 2-year follow-up remains to be reported.

Regardless, adjunctive therapies used in concert with DCBs to address these complex lesion subtypes and minimize the need for provisional stenting present an opportunity for those who ascribe to the “nothing left behind” philosophy. Whether an algorithm of vessel preparation with the use of atherectomy prior to DCB

use provides superior or equivalent vessel patency at 1 year and beyond and minimizes the need for adjunct stenting is yet to be fully defined. The ongoing international REALITY study is currently enrolling patients to address these complex lesion subtypes treated with vessel preparation using the HawkOne or TurboHawk atherectomy catheters (Medtronic) prior to the use of the In.Pact Admiral DCB (Medtronic). Otherwise, these complex lesion subtypes may ultimately become the domain of the next generation of drug-eluting nitinol stents that are currently in clinical trials.

MODERN TRIAL DESIGNS

The evolution of regulatory trial designs of next-generation DCBs for the treatment of femoropopliteal disease provides an important example of potential barriers to market entry. DCBs represent one of the most thoroughly studied peripheral endovascular devices to date. Several large randomized controlled trials (RCTs) of DCBs have established that they are as safe as balloon angioplasty and more effective in maintaining vessel patency through long-term follow-up while reducing the need for repeat interventions. It is likely that there will be four or five approved commercially available DCBs in the United States within the next 3 to 5 years.

More recent DCB PMA trial designs have rapidly moved beyond RCT designs versus balloon angioplasty and now seek to establish “noninferiority” in their safety and effectiveness compared to earlier devices (eg, the Ranger DCB [Boston Scientific Corporation] and SurVeil DCB [Surmodics, Inc.] vs In.Pact Admiral DCB) using very similar inclusion/exclusion entry criteria. Given the similarities in the patient cohorts studied in these trials, physicians will have little clinical data to clinically distinguish safety or effectiveness of one DCB over another. It is improbable that industry will pursue appropriately powered head-to-head superiority trials given the cost and the possibility of failure in distinguishing one DCB from another. Unfortunately, physicians will likely have only small unadjudicated multicenter trials with limited clinical follow-up to guide their clinical decision-making, while also formulating their decisions based on marketing claims of theoretic safety and effectiveness of newer coating technologies, paclitaxel formulations, and balloon materials.

Despite the crowded field of new therapies for new drug-eluting platforms (both DCBs and drug-eluting stents) in relatively noncomplex noncalcified femoropopliteal lesions, opportunity remains in the treatment of patients with more complex morphologies. The vessel preparation algorithm that seeks to either modify or remove the barriers to paclitaxel penetra-

tion deeper into the vessel wall without the use of an additional nitinol metallic implant is evolving. The use of various atherectomy devices for vessel preparation prior to the use of a DCB is a compelling element of this algorithm. Despite the increased complexity associated with the use of atherectomy devices prior to DCB use, at present, there are no barriers to use based on reimbursement. The use of atherectomy devices or specialty balloons (eg, the Chocolate balloon [Medtronic] or AngioSculpt balloon [Philips]) prior to DCB use has not been evaluated as a potential solution. The ongoing REALITY trial is an international prospective registry assessing the use of directional atherectomy (HawkOne, TurboHawk) in long, complex, calcified lesions. This clinical events committee- and core lab-adjudicated trial will assess a primary 1-year patency rate and the need for adjunct nitinol stenting postatherectomy plus DCB in the treatment of recoil or flow-limiting dissections. The 1-year primary endpoint assessment is slated for presentation in early 2020.

Close scrutiny of IN.PACT Global and its summary of safety and effectiveness data evaluating adjudicated long lesions details an incremental decline in vessel patency with increasing lesion lengths through 12 months. These data suggest that the 12-month primary patency rate is 75% in lesions 18 to 24 cm, while this rate drops to 63.3% in lesions 30 to 36 cm and 44% in long lesions > 36 cm. Clearly, there is room and opportunity for improvement when addressing long lesions with a stand-alone DCB strategy, even though it is presently an on-label use.

Data from the European DETOUR I study of the Detour system (PQ Bypass, Inc.), the endovascular bypass therapy for treatment of TransAtlantic Inter-Society Consensus II C and D lesions, were recently reported at the Society for Vascular Surgery meeting in June 2018 and demonstrated a 12-month primary patency rate of 72.5% in lesions with a mean length of 37 cm.² The DETOUR II study, an international, single-arm, safety and effectiveness study, is currently enrolling a similar cohort of patients.

EVOLVING ROLE OF POSTMARKET REGISTRY DATA

Postmarketing registry of approved products represents an important adjunct to United States investigational device exemption trials, although careful evaluation of the data derived from these registries is critical. As an example, the ongoing IN.PACT Global registry includes a complex and diverse data set, which is adjudicated by a clinical events committee; however, prespecified cohorts are core lab adjudicated. This is

an important distinction from site-reported data in that it adds another level of diligence and veracity to this data set. Indeed, data directly derived from the IN.PACT Global registry have led to two extensions of the instructions for use for the In.Pact Admiral DCB. Specifically, there are now clearances to address lesion lengths up to 36 cm and treat in-stent restenosis directly.

However, processing large postmarket data sets can take considerable time, and the entirety of the data sets may not be divulged during podium presentations or as published manuscripts. Critical readers of the literature must closely evaluate the definitions of important issues such as lesion length, degree of calcification (which is variably defined), and the length of follow-up. It is important to understand that registries by nature have inherent physician bias, which is sometimes difficult to discern; this bias relates to whether a physician tends to enroll a patient in a registry and the timing of follow-up. Unfortunately, at times, it is difficult to determine whether a registry uses site-reported data, is clinical events committee–adjudicated, or uses a core lab.

Regardless, it is important to understand that head-to-head comparisons of registries using similar, though not identical devices (eg, DCBs), are not possible and should be avoided. Unfortunately, this sometimes evolves into nonadjudicated marketing claims, which should be closely evaluated and scrutinized.

MEDICARE/MEDICAID REIMBURSEMENT

DCBs remain one of the most studied devices to enter the interventional marketplace. Presently, three randomized controlled prospective trials have established the superiority and safety of three DCB devices compared to balloon angioplasty. In all three trials, superior patency extended beyond 1 year and included a reduction in CD-TLR. Despite this established superiority compared to balloon angioplasty, in November 2017, the Centers for Medicare & Medicaid Services (CMS) made public the end date for the transitional pass through (TPT) add-on payment for DCBs, which occurred at the start of 2018. Additionally, CMS did not establish a new ambulatory payment classification rate for DCBs. The ultimate classification of DCBs within a reimbursement scale equivalent to that of angioplasty was met with universal disappointment on the part of individual physicians, societal groups, and industry. Arguably, while not fully realized, the impact of this reimbursement scenario for DCB procedures may ultimately reduce the availability of these devices to the Medicare and Medicaid population, as hospitals would be required to take a loss given the average selling price of DCBs compared to angioplasty balloons. As

such, the importance of governmental reimbursement for these devices and subsequent entrants to the DCB market becomes a potential barrier to device entry into the femoropopliteal endovascular device marketplace. Whether the same fate will await any potential FDA-approved below-the-knee DCB remains unknown.

The Shockwave intravascular lithotripsy (IVL) technology (Shockwave Medical, Inc.) was given the same angioplasty balloon designation by CMS. This device, which is presently CE Mark approved in Europe and cleared under a 510(k) pathway in the United States but not commercially available, is presently being evaluated in a RCT with and without the application of the Shockwave IVL technology plus DCB in calcified SFA morphologies. However, whether this and other such devices aimed treating more complex SFA disease will be able to penetrate the marketplace and provide any benefit to Medicare and Medicaid beneficiaries is uncertain. These specialty devices must not only provide clinical data to clear regulatory hurdles and convince physicians of their utility, they must also gain access to hospital system inventories. Unless administrators and service line managers are willing to take a loss on reimbursement, this may require additional reimbursement provisions.

Adjusting the present methodologies to determine reimbursement may ultimately require lobbying Congress to change the formulas by which CMS makes decisions. The potential results of lobbying efforts by physician groups, professional societies, and industry are uncertain. The expiry of the TPT add-on payment and resultant reimbursement equivalence of DCBs and angioplasty alone is not aligned with the patients' best interests and inhibits value-based care of these patients. Until the merits of each technology are weighed with regard to adjudicated data and clinical outcomes and the impact of potential cost, safety, and efficacy are accounted for, governmental reimbursement may be the ultimate barrier to device entry. ■

1. Ansel G. Outcomes at 2 years in stented vs. non-stented patients post-DCB: a subanalysis from the IN.PACT Global study. Presented at: Leipzig Interventional Course 2018; January 31, 2018; Leipzig, Germany.

2. Krievins D. Fully Percutaneous bypass for treatment of long-segment femoropopliteal disease: 12-month results from the DETOUR I trial. Presented at: Vascular Annual Meeting 2018; June 20–23, 2018; Boston, MA.

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