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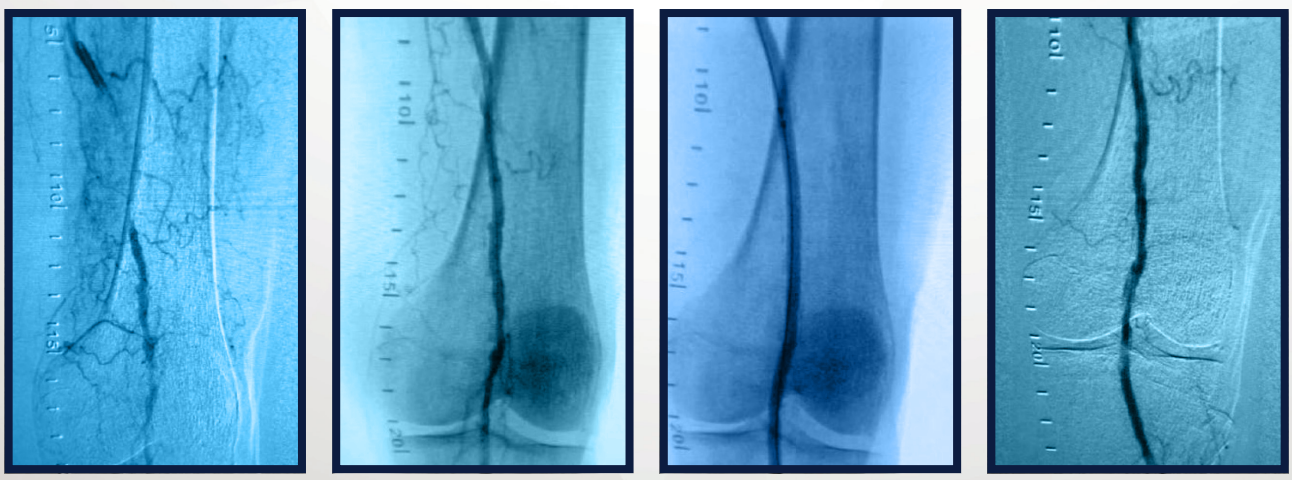
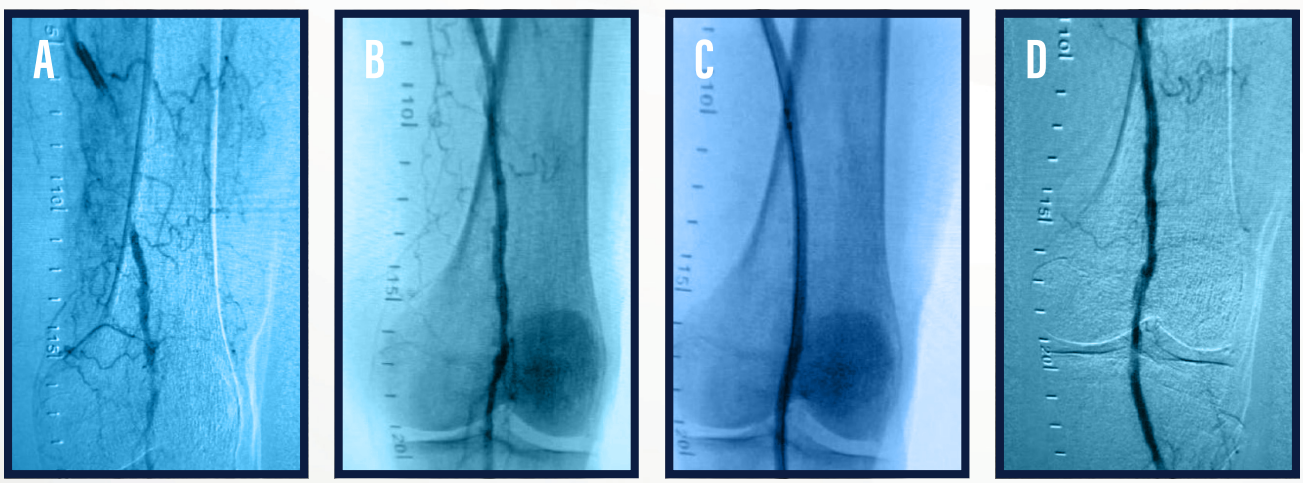
EXTENDING EXPECTATIONS FOR LONG SFA LESIONS



EXTENDING EXPECTATIONS FOR LONG SFA LESIONS



A 96-year-old woman presented with critical limb ischemia and toe wounds on the left foot. She had a chronic total occlusion (CTO) in the left distal superficial femoral artery (SFA) that was approximately 5 cm in length. The anterior tibial artery takeoff had a focal, near-occlusive calcified lesion. There was diffuse calcified disease throughout the distal SFA/popliteal artery (A). Via right femoral access, a 135-cm Trailblazer™ support catheter (Medtronic) and GlideWire (Terumo Interventional Systems) were used to cross the CTO and multiple lesions. A 4-mm SpiderFX™ embolic protection device (Medtronic) was placed in the mid anterior tibial, and multiple passes were made with a HawkOne™-M atherectomy catheter (Medtronic) through the distal SFA and popliteal artery (B). A 3.5- X 120-mm Chocolate™ PTA balloon (Medtronic) was used for predilatation. A 4- X 250-mm IN.PACT™ Admiral™ drug-coated balloon (Medtronic) was inflated at 11 atm for 3 minutes (C). A 2.5- X 40-mm Chocolate PTA balloon was used at the anterior tibial takeoff. Postprocedural angiography showed good results (D).

Case courtesy of Varinder Phangureh, MD.

IN.PACT™ Admiral™ DCB: Safety and Effectiveness in Treating Complex Lesions

Discussing trends demonstrated in existing clinical data and practice for the endovascular treatment of complex femoropopliteal lesions.

BY GARY M. ANSEL, MD, FACC

In relation to femoropopliteal lesions, the term *complex* inspires in each of us our own personal definition, usually comprising morphologic elements of the target lesion such as length, degree of calcium, and presence of an occlusion. Our approach is equally personal, as it is often based on the physician's training, experience, opinion leader presentations, and interpretation of available clinical data. As a result, I am pleased to be accompanied in this supplement by clinicians representing various specialties, each with their own experiences and philosophies, to offer their perspectives on treating complex femoropopliteal lesions.

CURRENT CLINICAL DATA FOR COMPLEX LESIONS

At some point, I expect most physicians will have all seen a graphic similar to Figure 1. I always warn that comparing patency rates across multiple trials is fraught with limitations due to various types of bias as well as variations in populations, lesions, study protocols, definitions, and follow-up, among others. However, Figure 1 does offer us insight into the overall clinical data landscape of core laboratory–adjudicated femoropopliteal studies of FDA class 3 devices and their respective control arms when employed. Since the modest beginning of Figure 1's data points more than 10 years ago, the landscape has certainly evolved, but a few particular trends have become apparent and seem to persist. This article highlights and discusses each of these trends.

DATA EXIST MOSTLY FOR LESIONS ≤ 10 CM

At first glance, we see a majority of data clustered toward shorter lesions. As you might expect, these lesions range from approximately 5 to 12 cm and typically comprise the simple disease process often encountered in investigational device exemption (IDE) studies that device manufacturers are required to perform to gain FDA approval (Figure 1; data points 1-8, 10-16, 23-33, 36-38). However, these lesions are fairly uncommon in many of our own practices, and extrapolating these data sets to longer, more complex lesion types beyond the IDE studies is challenging. Surveying the data for more moderate lesion lengths of approximately 15 to 20 cm, we are limited to five studies consisting of the prespecified in-stent restenosis (ISR) cohort of IN.PACT Global (Figure 1; 17); the randomized ISR cohorts treated with either heparin-bound stent graft or percutaneous transluminal angioplasty (PTA) of the RELINE study (Figure 1; 9, 40); the cohorts of heparin-bound stent graft and nonbound stent graft randomized against their bare-metal stent (BMS) control arms of VIASTAR (Figure 1; 34, 42) and VIBRANT (Figure 1; 35, 41), respectively; and the ZEPHYR single-arm Japan postmarket approval study of a drug-eluting stent (DES) (Figure 1; 39). Beyond 20 cm, the data are similarly sparse, with outcomes reported from four drug-coated balloon (DCB) studies and a single peripheral stent graft study (Figure 1; 18-21, 43). The message here is that although many of us practice in the domain beyond 15 cm, the vast majority of adjudicated outcomes lie below this range.

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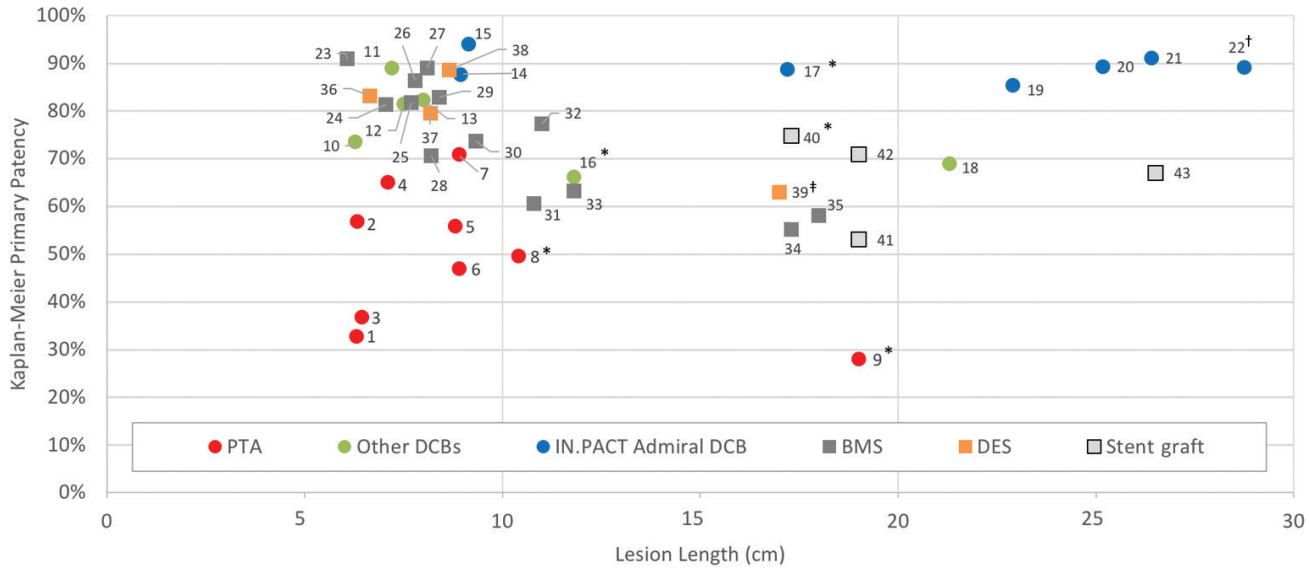
> – Gary M. Ansel, MD, FACC

CONVENTIONAL PTA PATENCY CLUSTERS TOWARD LOW END

Once we dig into the landscape, we see the points representing PTA clustering toward the low patency end of the shorter lesions. Although certainly a variation exists within the PTA cohorts, we have to keep in mind that the study protocols, endpoint definitions, and technical practices evolved during the course of these studies. For instance, compare the two control arms of the Zilver PTX and RESILIENT randomized trials, which

FIGURE 1. CORE LAB-ADJUDICATED 12-MONTH PRIMARY PATENCY BY KAPLAN-MEIER ESTIMATE OF FDA-APPROVED CLASS 3 DEVICES AND THEIR CONTROL ARMS.



Qualitative comparison for illustration purposes only. Not meant for head-to-head comparison.

Data point	Cohort	Patency definition
1	Zilver PTX RCT: PTA arm[1]	PSVR < 2.0 or < 50% stenosis
2	LEVANT II RCT: PTA arm[2]	PSVR < 2.5 and freedom from TLR
3	RESILIENT RCT: PTA arm[3]	PSVR < 2.5 and freedom from TLR
4	ILLUMENATE EU RCT: PTA arm[4]	PSVR ≤ 2.5 and freedom from TLR
5	IN.PACT SFA RCT: PTA arm[5]	PSVR ≤ 2.4 and freedom from CD-TLR
6	IN.PACT Japan RCT: PTA arm[6]	PSVR ≤ 2.4 and freedom from CD-TLR
7	ILLUMENATE Pivotal RCT: PTA arm[7]	PSVR ≤ 2.5 and freedom from TLR
8*	SFA ISR IDE RCT: PTA arm[8]	Freedom from restenosis and CD-TLR
9*	RELINE RCT: PTA arm[9]	PSVR < 2.5 and freedom from TLR
10	LEVANT II RCT: Lutonix 035 DCB (BD Interventional) arm[2]	PSVR < 2.5 and freedom from TLR
11	ILLUMENATE EU RCT: Stellarex DCB (Philips) arm[4]	PSVR ≤ 2.5 and freedom from TLR
12	ILLUMENATE Global: Stellarex DCB[10]	PSVR ≤ 2.5 and freedom from TLR
13	ILLUMENATE Pivotal RCT: Stellarex DCB arm[7]	PSVR ≤ 2.5 and freedom from TLR
14	IN.PACT SFA RCT: IN.PACT™ Admiral™ DCB arm[5]	PSVR ≤ 2.4 and freedom from CD-TLR
15	IN.PACT Japan RCT: IN.PACT™ Admiral™ DCB arm[6]	PSVR ≤ 2.4 and freedom from CD-TLR
16*	SFA ISR IDE RCT: Lutonix 035 DCB arm[8]	Freedom from restenosis and CD-TLR
17*	IN.PACT Global - ISR: IN.PACT™ Admiral™ DCB[11]	PSVR ≤ 2.4 and freedom from TLR
18	Lutonix Long Lesion: Lutonix 035 DCB[8]	Freedom from restenosis and CD-TLR
19	IN.PACT Global - CTO: IN.PACT™ Admiral™ DCB[12]	PSVR ≤ 2.4 and freedom from CD-TLR
20	SFA-Long Study: IN.PACT™ Admiral™ DCB[13]	Freedom from > 50% restenosis and CD-TLR
21	IN.PACT Global - Long Lesion: IN.PACT™ Admiral™ DCB[14]	PSVR ≤ 2.4 and freedom from CD-TLR
22†	IN.PACT Global - Complex Lesion post-hoc subset: IN.PACT™ Admiral™ DCB[5]	PSVR ≤ 2.4 and freedom from CD-TLR
23	Complete SE SFA - Complete SE Stent[15]	PSVR < 2.0 and freedom from revascularization
24	RESILIENT RCT: LifeStent stent (BD Interventional) arm[3]	PSVR < 2.5 and freedom from TLR
25	STROLL: SMART stent (Cordis, a Cardinal Health company)[16]	PSVR < 2.5/50% diameter stenosis and freedom from TLR
26	SUPERB: Supera stent (Abbott Vascular)[17]	PSVR ≤ 2.0 and freedom from TLR
27	SIROCCO RCT: SMART stent arm[18]	≤ 50% stenosis by angiography
28	BioFlex 1: Astron and Pulsar stents (Biotronik)[19]	PSVR ≤ 2.4 and freedom from CD-TLR
29	OSPREY: Misago stent (Terumo Europe)[20]	PSVR < 2.5 and freedom from TLR
30	SuperNOVA: Innova stent (Boston Scientific Corporation)[21]	PSVR < 2.4 and freedom from TLR
31	TIGRIS RCT: Tigris stent (Gore & Associates) arm[22]	PSVR ≤ 2.5 and freedom from TLR
32	DURABILITY II: Protégé EverFlex stent (Medtronic)[23]	PSVR < 2.0 and freedom from CD-TLR
33	TIGRIS RCT: LifeStent stent arm[22]	PSVR ≤ 2.5 and freedom from TLR
34	VIASTAR RCT: BMS arm[24]	PSVR ≤ 2.5 or < 50% stenosis
35	VIBRANT RCT: BMS arm[25]	PSVR < 2.5 and freedom from TLR
36	Zilver PTX RCT: Zilver PTX DES (Cook Medical) arm[1]	PSVR < 2.0 or < 50% stenosis
37	IMPERIAL RCT: Zilver PTX DES arm[26]	PSVR ≤ 2.4 and freedom from CD-TLR
38	IMPERIAL RCT: Eluvia DES (Boston Scientific Corporation) arm[26]	PSVR ≤ 2.4 and freedom from CD-TLR
39‡	ZEPHYR: Zilver PTX DES[27]	PSVR ≤ 2.4 or < 50% stenosis
40*	RELINE RCT: Viabahn heparin-bonded stent-graft (Gore & Associates) arm[9]	PSVR < 2.5 and freedom from TLR
41	VIBRANT RCT: Viabahn stent-graft arm[25]	PSVR < 2.5 and freedom from TLR
42	VIASTAR RCT: Viabahn heparin-bonded stent-graft arm[24]	PSVR ≤ 2.5 or < 50% stenosis
43	Viabahn-25cm: Viabahn heparin-bonded stent-graft[28]	PSVR ≤ 2.5 and freedom from TLR

*In-stent restenosis studies.

†Subset analysis of previously reported data. IN.PACT Global Complex Lesion cohort consists of 227 subjects enrolled in the three IN.PACT Global prespecified imaging cohorts (long lesion, CTO, and in-stent restenosis) exhibiting lesion lengths > 18 cm.

‡Report proportion-based patency of the ZEPHYR study.

Abbreviations: BMS, bare-metal stent; CD-TLR, clinically driven target lesion revascularization; CTO, chronic total occlusion; DCB, drug-coated balloon; DES, drug-eluting stent; PTA, percutaneous transluminal angioplasty; PSVR, peak systolic velocity ratio; RCT, randomized controlled trial; SFA, superficial femoral artery.

posted PTA patency rates of 32.8% and 36.7%, respectively (Figure 1; 1, 3), in lesions of approximately 6.5 cm, against a contemporary DCB control arm such as the ILLUMENATE Pivotal trial control patency rate of 70.9% (Figure 1; 7). In doing so, we see how factors such as randomization after successful predilatation and sustained balloon inflation complicate comparisons across studies. Despite this variability, PTA clearly occupies the low end of the patency spectrum.

PRIMARY PATENCY IS INVERSELY PROPORTIONAL TO LESION LENGTH

The next trend we see is the declining patency rate associated with increasing lesion length, underscoring a pitfall of extrapolating data captured in short-lesion studies to our own practices, where much longer lesions are commonplace. Less is known about length-dependent performance of DESs given the lack of available data. The core lab–adjudicated ZEPHYR DES study reports positive 12-month outcomes in a challenging population exhibiting a mean lesion length of 17 cm (Figure 1; 39), which adds to the experience of shorter-lesion DES cohorts studied as part of the Zilver PTX and IMPERIAL trials (Figure 1; 36-38). Diverging from independently adjudicated patency outcomes, both the all-comers Japan Zilver PTX postmarket surveillance study and a single-center retrospective analysis demonstrate patency consistent with outcomes observed in the shorter-lesion randomized controlled trial (RCT) despite reported mean lesion lengths of 14.7 and 24.2 cm, respectively.[29,30] Importantly, further analysis of Phillips et al did discern higher patency in DES-treated lesions ≤ 20 cm compared with those > 20 cm, which also exhibited a higher proportion of occlusions. This once again suggests a length-dependency effect on patency for lesions treated with DESs.[30] However, as stent length increases, the discussion of stent fracture cannot be totally ignored. Consider 12-month outcomes of two cohorts employing the same stent: the RESILIENT study's BMS arm reported a fracture rate of 3.1% for lesions averaging 7.1 cm (Figure 1; 24) compared with a fracture rate of 27.1% for lesions averaging 11.8 cm in the TIGRIS study BMS arm (Figure 1; 33). Despite being a well-known phenomenon,[31] the consequences of lesion length and fracture are not fully understood or consistent between stent designs.

IN.PACT GLOBAL PRESPECIFIED IMAGING COHORTS BUCK THE TREND IN LESION LENGTH

Very few adjudicated data exist for treatment of lesion lengths > 20 cm; the only data available is composed of four DCB cohorts (Figure 1; 18-21) and a single heparin-bound stent graft study (Figure 1; 43). Historically, studies in this range came late in the evolution of these data. Zeller et al reported the outcomes associated with the 25-cm heparin-bound stent graft in lesions averaging 26.5 cm, (Figure 1; 43) with interestingly non–length-dependent patency rates similar to those reported in the RELINE and VIASTAR studies (Figure 1; 40,42). For the DCB cohorts, the Lutonix Long Lesion study reported a mean lesion length of 21.3 cm (Figure 1; 18), the chronic total occlusion and long lesion prespecified imaging cohorts of the IN.PACT Global study posted mean lesion lengths of 22.8 and 26.4 cm, respectively (Figure 1; 19, 20), and the SFA-Long Study performed by Micari et al averaged 25.2-cm lesion lengths (Figure 1; 20). Importantly, when considering the IN.PACT™ Admiral™ DCB (Medtronic) cohorts, the patency definition is identical across the two RCTs and the three prespecified imaging cohorts of IN.PACT Global, therefore facilitating patency comparisons across cohorts and underscoring the consistency in patency beyond 20-cm lesions, despite variation in study populations and lesion morphologies. However, it is also worth highlighting that these long-lesion DCB studies are not without significant stent usage; in three of these four cohorts, provisional stent rates of approximately 40% and higher are reported (Figure 1; 18, 19, 21). The one exception to this trend of provisional stenting is reported by the SFA-Long study that demonstrated similar patency results while only resorting to stenting in 10.5% of their lesions (Figure 1; 20). In this supplement, we have commentary from Prof. Micari on his approach to PTA vessel preparation and minimizing stent use when employing DCB in challenging lesions.

> **DCBs and, if needed, provisional stent optimization may yield consistent patency with apparently less lesion length dependence.**
>
> – Gary M. Ansel, MD, FACC

SUPPORT FOR EXPANDING INDICATION

Finally, to support recent FDA indication expansion of the IN.PACT Admiral DCB to lesion lengths up to 36 cm, a post hoc analysis was performed on all core lab–adjudicated IN.PACT Global subjects exhibiting lesions ≥ 18 cm, including ISR subjects (Figure 1; 22). The outcomes

are consistent with the other IN.PACT Admiral DCB trends as demonstrated in Figure 1, and 96 (42.5%) of 227 patients received provisional stenting of various lengths. This observation indicates that a DCB with optimal use of stents led to patency similar to the simpler lesions treated with DCBs alone.

CONCLUSION

From the simple, single-digit lesion lengths to the truly long lesions, we certainly have more insight today than 10 years ago. Each of us is left with our own interpretation of these data, but a few trends are evident: (1) PTA is at the low end of the performance range; (2) length-dependent patency is a consistent observation for PTA and BMSs; and (3) DCBs and, if needed, provisional stent optimization may yield consistent patency with apparently less lesion length dependence. Of course, the data continue to evolve, and we hope it will not take us another 10 years to identify new trends, possibly aided by the evolution of lesion preparation with new specialty balloon technologies, atherectomy, and yet-to-be-developed devices that may be used prior to DCBs. For now, we will leave Figure 1 behind, and begin our panel discussion to explore individual opinions on complex lesion treatment. ■

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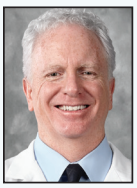
Role of DCB Plus Provisional Stenting in Treating Complex Lesions

Reactions from experts on IN.PACT Global data and what they mean for treatment options.

WITH GARY M. ANSEL, MD, FACC; JOHN R. LAIRD, MD; GUNNAR TEPE, MD, PHD; AND THOMAS ZELLER, MD, PHD



This past winter at the Leipzig Interventional Course (LINC) 2018, I presented the first comparison data from the IN.PACT Global study between patients treated with a stand-alone IN.PACT™ Admiral™ drug-coated balloon (DCB) (Medtronic) and those treated using an IN.PACT Admiral DCB with provisional stenting. IN.PACT Global enrolled more than 1,500 patients and had an overall provisional stent rate of 25.3%.[1] Comparing the 1,044 nonstented DCB patients with the 353 patients who did receive stents afforded a statistically meaningful retrospective examination to gain insight into questions many interventionalists have regarding DCB use: "When do I need a stent?" and "What will be the outcomes if I do stent?" Ideally, we'd like to have data derived from randomized controlled trials (RCTs) for these types of questions, but in the absence of those data, IN.PACT Global gives us the first high-quality glimpse into factors affecting provisional stent use and anticipated outcomes with the IN.PACT Admiral DCB.

Baseline clinical characteristics between the IN.PACT Global stented and nonstented cohorts were fairly well matched, but the cohorts diverged considerably when examining baseline lesion characteristics. The stented lesions demonstrated longer lengths, more total occlusions, longer occluded lengths, higher grade stenoses, and more severe calcification than the nonstented lesions. This is not surprising considering the operators at the time of the procedure were more likely using provisional stents to treat the more complex nature of the lesion, most often using stenting to mitigate recoil and dissection. Surprisingly, after 2 years of follow-up, rates of freedom from clinically driven target lesion revascularization (CD-TLR) were not statistically different with the stented and nonstented cohorts (Kaplan-Meier estimate of 80.8% and 83.9%, respectively).[1] Furthermore, no differences in safety outcomes were observed.

The take-away messages here are that provisional stenting plays a key role in DCB treatment of long, complex disease and that IN.PACT Admiral DCB used in conjunction with provisional stenting demonstrates consistent outcomes at 2 years despite vastly different lesions. In this article, I am joined by my esteemed peers for their reflections on these outcomes.

— Gary M. Ansel, MD, FACC

Provisional stenting following balloon angioplasty to treat significant elastic recoil or flow-limiting dissection is a necessary consequence of balloon angioplasty. RCTs with percutaneous transluminal angioplasty (PTA) control groups have demonstrated provisional stent rates from as low as 6.9% (LEVANT 2) to as high as 50.4% (ZILVER PTX).[2-4] In the IN.PACT SFA Trial, provisional stenting was necessary in 12.6% of cases in the PTA arm and 7.3% of cases in the DCB arm of the trial.[5] Provisional stenting rates rise with increasing lesion complexity, as seen in the IN.PACT Global study.[1] The efficacy of DCB with provisional stent implantation was not well elucidated until recently.

The IN.PACT Global study enrolled 1,535 patients at 64 sites around the world. There was independent adjudication by a clinical events committee and prospective subset analysis with core lab–reported results. There was a 25.3% provisional stent rate in the IN.PACT Global study with the following reasons for stenting: persistent residual stenosis ≥ 50% (59.2%), flow-limiting dissection (53.6%), translesion pressure gradient ≥ 10 mm Hg (0.5%), or other (5.1%). Not surprisingly, lesion lengths were greater in the stented versus nonstented group (15.37 vs 10.97 cm). Additionally, total occlusions were almost twice as common (54.7% vs 28.6%), and severe calcification was more frequently present (14.7% vs 8.7%) in the stented versus nonstented group, respectively. When provisional stenting was required, spot stenting

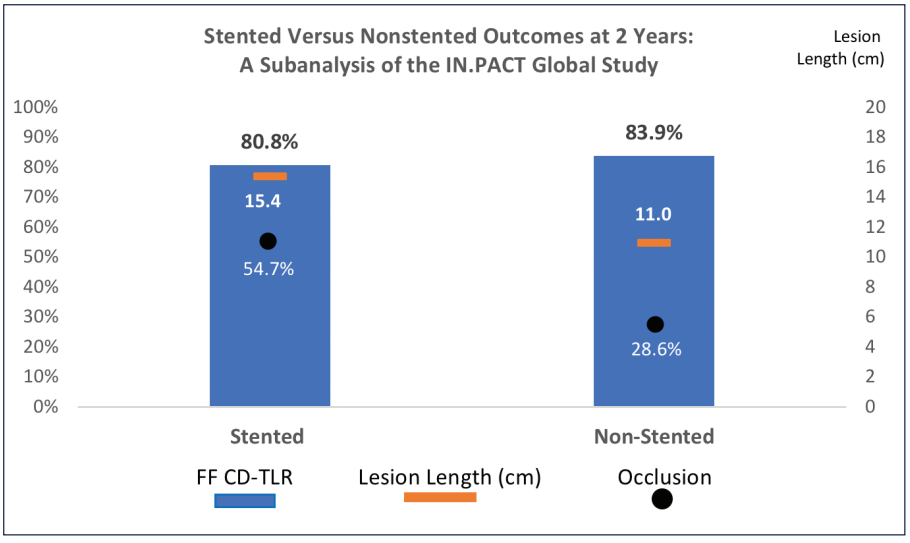


Figure 1. IN.PACT Global subanalysis of stented versus nonstented patients at 2 years. Abbreviations: FF CD-TLR, freedom from clinically driven target lesion revascularization.

> Freedom from CD-TLR in the stented group at 1 and 2 years was excellent (92.1% and 80.8%) and did not differ from the nonstented group despite the increased complexity of lesions in the stent group.
>
> – John R. Laird, MD

(24.4%) or partial lesion coverage (37.8%) were performed in the majority of cases, thus avoiding the dreaded full metal jacket. Freedom from CD-TLR in the stented group at 1 and 2 years was excellent (92.1% and 80.8%) and did not differ from the nonstented group despite the increased complexity of lesions in the stent group (Figure 1). There were no differences between the stented and nonstented groups with regards to any of the safety outcomes.[1]

—John R. Laird, MD

What are your impressions of these data and have they changed your daily practice?

Dr. Laird: I find these data very useful and reassuring. They support the approach that I have adopted in my own clinical practice using DCB angioplasty as a primary treatment strategy for almost all femoropopliteal lesions, followed by provisional stenting as necessary for suboptimal DCB results. When stenting is required, spot stenting or use of stents shorter than the original lesion length are employed. With careful technique and prolonged balloon inflations, the rate of provisional stenting can be surprisingly low even in complex lesions. Nonetheless, it is reassuring to know that there is no "downside" with regard to safety and long-term patency when provisional stenting is performed.

Prof. Tepe: These are great data showing a low TLR rate with the IN.PACT Admiral DCB. Even in more complicated and longer lesions where a stent was needed, the same outcome as stand-alone IN.PACT Admiral DCB can be reached if stents are placed after the IN.PACT Admiral DCB is used.[1] For me, this means that a decision around the question, "Is this a primary PTA/DCB patient or will this be a stent patient?" is not mandatory. I can start with the decision to use an IN.PACT Admiral DCB in order to enhance the patency. In cases where a stent is necessary, the outcome is the same with the combination therapy; therefore, a decision about a stent can be made later. This will allow me to use fewer stents.

Additionally, aside from all the subgroups, the long-term data of the IN.PACT SFA Trial are very important to me because they show that we can either prevent or delay a TLR by using IN.PACT Admiral DCBs.[6-8]

Prof. Zeller: First, stenting does not negatively impact longer-term outcomes of DCB angioplasty. This was an initial concern regarding stent implantation following DCB angioplasty due to the chronic outward force of the nitinol stent applied to the vessel wall, potentially creating chronic vessel trauma. It was unknown if this trauma may overcome the short-term effect of the antiproliferative drug applied by the DCB. Second, DCBs represent a vehicle for drug transfer and do not resolve the general limitations of balloon angioplasty such as mechanical recoil and dissection. Even if we favor the approach of "leave nothing behind," stents are essential to salvage acute treatment success in lesions with increased complexity, as shown in the study. Lesions receiving a stent were longer, more calcified, and had a higher percentage of chronic total occlusions (CTOs). Third, the analysis demonstrates that an optimal DCB result, which was present in nearly three out of four cases, does not deserve stent placement.

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In regard to daily practice, the lesson learned is that a good DCB result, even in complex femoropopliteal lesions including the entire popliteal artery, does not need a scaffold to achieve outstanding clinical results. However, selective stent placement does salvage insufficient balloon and DCB angioplasty outcomes and results in the same 2-year performance as compared with lesions treated with plain DCB angioplasty. This study outcome has the potential to reduce costs for the treatment of complex femoropopliteal lesions.

Dr. Ansel: These types of real-world data from a multicenter study with independent adjudication are important. Regulatory trials are typically completed in such restricted populations that generalization to the more commonly treated patients can often be difficult for the practicing physician. We have wondered how effective DCBs are in complex disease, where we often need to optimize with stents, and now we know DCBs can be very valuable. Providing 2-year outcomes in complex disease by optimizing with provisional stents equal to stand-alone DCBs for simple disease is a great outcome. We currently have compelling 5-year data from the Zilver PTX drug-eluting stent (DES) (Cook Medical),[9] but evaluating bare-metal stent (BMS) use after DCB therapy is important as we try to compare the two treatment modalities.

In my opinion, the 5-year DES data support its expanded use in femoropopliteal disease treatment. Now, with evolving DCB data, especially in conjunction with provisional stent use for the treatment of long, complex disease, we have additional evidence supporting further adoption of drug technologies. These are very promising results but we still are chasing the types of outcomes we see in the coronary vessels. I hope continued investment, research, development, and improvements are still on the horizon.

How do the DCB plus provisional stenting data compare with the results of the BMS results in long lesions?

Dr. Laird: The results of DCB plus provisional stenting from the IN.PACT Global study compare very favorably with the results of BMS for long lesions in the published literature. In the recently published TIGRIS trial, two different bare-nitinol stents (Tigris vascular stent, Gore & Associates; LifeStent, BD Interventional) were compared for similar-length superficial femoral artery (SFA) lesions (10.8 and 11.8 cm, respectively).[10] Freedom from TLR at 2 years for the Tigris and LifeStent were 70.5% and 67.2%, respectively, compared with the 2-year freedom from TLR rate of 80.8% for the IN.PACT Global stent group.[1,10]

What do you see as the benefits or drawbacks of DCB plus provisional stenting in comparison to a primary BMS approach?

Prof. Zeller: A primary BMS full metal jacket approach, particularly in long lesions, is characterized by reduced patency rates and an increased risk for stent fractures.[11,12] DCB angioplasty plus provisional stent placement potentially reduces both risks. The only indication for a full metal jacket is the severely calcified CTO, which would indicate the need for a dedicated interwoven stent offering high compression resistance.

Dr. Laird: There are a number of pitfalls to the primary BMS approach to femoropopliteal lesions. Long-segment SFA stenting is associated with higher restenosis rates as well as higher rates of stent fracture. In the TIGRIS trial, use of the LifeStent for long SFA lesions was associated with a 32.7% fracture rate at 2 years.[10] Many of these fractures were complex grade 4 and 5 fractures. There is a growing understanding that a primary BMS approach that leads to full metal jacket stenting is not a desirable outcome.

The Viabahn stent graft (Gore & Associates) has been shown to be an effective alternative for long femoropopliteal lesions and was shown to be superior to BMSs for long lesions in the VIASTAR trial. In the VIASTAR trial, 1-year freedom from CD-TLR was 84.6% following treatment of long lesions with the Viabahn stent graft (mean lesion length, 19.0 cm).[13] In the IN.PACT Global study, 1-year freedom from CD-TLR following treatment of patients treated in the stented group (mean lesion length, 15.37 cm) was 92.1%.[1] Despite favorable

outcomes with the Viabahn stent graft compared with BMS, there are pitfalls to the use of the Viabahn stent graft. Because the failure mode is often stent graft thrombosis, treatment of Viabahn failure is more complicated and entails the use of thrombolytic agents and thrombectomy devices.

From your experience, what are the advantages/disadvantages of the DCB plus provisional stenting approach in treating CTOs?

Prof. Tepe: This approach allows me to treat CTOs without stents, and in cases where a stent may be needed, I can treat with spot stenting only.

Dr. Ansel: Severely calcified lesions and CTOs are the two most challenging subsets of femoropopliteal disease that we may be faced with treating. These data add support for treating CTOs with DCBs and provisional stenting if necessary. One of the current disadvantages is that Medicare reimbursement does not optimally cover the current cost of treatment for this DCB-based approach, especially for longer lesion disease where multiple balloons and some stenting may occur (even though DCB lengths up to 250 mm are now commercially available to improve this gap).

What are the advantages of using the IN.PACT Admiral DCB versus full metal coverage with a DES?

Dr. Ansel: We recently published our center's experience with the Zilver PTX DES for treating lesion lengths > 20 cm.[14] This was a single-center registry with all the shortcomings and biases that may be present for this type of study, and it was completed before DES devices beyond 8 cm were available. Our experience is that DESs perform better than our historic bare-metal, tubular nitinol stent results but are not as good as the results published on lesion lengths < 20 cm. My personal bias is that very long-segment tubular nitinol stenting is a chronic stimulus for restenosis due to the severe effect on native vessel compliance. This is supported by the improved longer-term restenosis patterns seen in the braided nitinol stent and randomized swirl stent data sets.[15,16] Full metal coverage may be acceptable as we evolve with future stent lines. The current commodity pricing for BMSs may go away as these newer designs become more widely available.

Prof. Tepe: With the IN.PACT Admiral DCB plus provisional stenting approach, we prevent the full metal coverage, which means in case of a TLR, the procedure may be easier and the outcome may be better. Additionally, the issue of stent fractures is minimized.

Do you think the provisional stent rates could be further lowered by a vessel preparation strategy?

Prof. Tepe: If there is less plaque and calcium burden and less tendency for recoil, a DCB-only strategy may be more successful. Nevertheless, to lower stent rates, the approach of a second long inflation PTA has to be mentioned.

Dr. Ansel: Certainly, there are many variables that lead to stenting. The first is the physician's comfort with the various levels of dissection that may lead to unnecessary stenting. Prolonged balloon inflation, vessel preparation devices, and improved balloon design could all lead to less provisional stenting. However, although we may decrease stenting, I feel there will be cases—especially long lesion disease associated with recoil, significant calcification, and extensive dissection—that will necessitate stents. We see in this data set that stenting appears to be very acceptable, and as we move on to newer generations of improved stent designs, this may even be beneficial as seen in the coronary vessels. The use of expensive vessel preparation, which is not currently universally reimbursed, will require the development of some randomized data sets or those operators may face difficulties as we experience continuing efforts for cost-effective, value-based health care.

What do you see as the strength of DCB plus provisional spot stenting versus partial stenting versus a full metal jacket approach?

Prof. Zeller: A full metal jacket after DCB angioplasty is only indicated if the entire lesion mechanically deserves scaffolding (eg, in some CTOs with severe intraluminal calcification). All other lesion types can be treated with a stent length shorter than the index lesion length (spot or partial stenting). Reducing stent length preserves, at least in part, the natural vessel anatomy and facilitates retreatment if indicated. In-stent restenosis still represents one major challenge of endovascular therapy. In addition, positive vessel remodeling frequently seen after DCB angioplasty, particularly in dissected areas, may lead to incomplete wall apposition of stents, which is a risk factor for acute arterial thrombosis.

What are the implications of these data vis-à-vis a primary DES approach?

Dr. Laird: The ultimate question is how the approach of DCB plus provisional stent implantation compares with the approach of primary DES implantation. We do not currently have sufficient data comparing these two approaches. The landscape is also changing with the addition of a second DES into clinical practice both inside and outside of the United States. Until good comparative

> **IN.PACT Admiral DCB represents a benchmark even in the European market where almost 20 different DCBs are commercially available.**
>
> – Thomas Zeller, MD, PhD

data are available, there will likely be strong advocates for both approaches. One potential downside of the primary DES approach is that it will result in a permanent metal implant in all cases, and in some cases, extensive full metal jacket stenting. For those who favor a "leave nothing behind" or "leave as little behind as possible" strategy, a DCB plus provisional stent strategy will remain popular.

Prof. Zeller: Treatment of complex femoropopliteal lesions with DESs means full lesion coverage with stents; the strategy is to implant DESs from healthy to healthy vessel segments, proximal and distal to a lesion. This impacts the biomechanical properties of the treated vessel with unknown consequences. A primary DES approach can be considered in patients with limited compliance during the intervention in order to keep treatment time as short as possible and elderly patients with limited life expectancy. In younger patients, I would favor leaving less metal behind.

Have these data changed your views on a "leave nothing behind" approach?

Prof. Tepe: No, the data are a confirmation of my approach I followed during the past few years. However, one topic is still unknown. Stents are always placed by the decision of the operator. There are no clear rules. With DCB use, a lot of dissections might be "melted away" because of the remodeling effect of the local drug.[17] Therefore, fewer stents are mandatory compared with what is often used in daily practice, at least in the case of dissections.

Prof. Zeller: In complex lesions, the strategy should be modified into "leave no more behind than necessary." The good news is that the mechanical durability of modern nitinol stents is significantly improved, and severe stent fractures are no longer a serious concern, which previously was a reason for avoiding stent placement. An alternative for spot or partial stenting could be spot directional atherectomy, in a sense that lesion areas not responsive to predilatation could be treated with directional atherectomy before DCB inflation as a substitute for spot stenting. This strategy would allow users to still follow a "leave nothing behind" strategy even in most complex lesions.

Dr. Ansel: Although not leaving a prosthetic device behind is often a goal in medical treatments, I personally have been more focused on longer-term clinical outcomes. Now, we have these important data from IN.PACT Global and we see that if we need to treat dissection, recoil, etc., with a stent, the outcomes are similar to optimal DCB results at 2 years. The multiple data sets on DESs even at 5 years have demonstrated low stent fracture rates, a less aggressive pattern of restenosis, and continuing benefit.[9,18] I think the mantra should be "leave what is best behind" and focus on getting a great up-front result. If that can be done with a stand-alone DCB, great; if that means adding a BMS or using DESs up-front to treat a poor acute result, then the data currently support those choices.

How, if at all, have the data shifted your view toward IN.PACT Admiral DCB as a primary therapy for complex lesions?

Dr. Laird: The excellent results of DCB plus provisional stenting in the IN.PACT Global study should provide reassurance to those interventionalists who have adopted a strategy of primary DCB angioplasty for even the most complex femoropopliteal lesions. If provisional stenting is required, there does not appear to be a negative impact with regards to safety or long-term efficacy. Spot stenting or partial lesion coverage can be performed with the expectation that future TLR rates will be low. The IN.PACT Global study has taught us that DCBs can be effective for long lesions, total occlusions, and complex in-stent restenosis.

Dr. Ansel: These data reinforce our use of the IN.PACT Admiral DCB even in complex long lesion disease. These are very good data sets. Furthermore, although economically troublesome, I am a true advocate for doing what is best for the patient. Although the addition of DCBs up to 250 mm in length may help to manage the cost in patients who historically required multiple shorter balloons, I do hope that the hospitals, Medicare, and other payors can identify pathways to optimize the physician drivers as well.

Prof. Tepe: Based on the large amount of data from the IN.PACT Global study, I am confident that this DCB can be used as a primary strategy in almost every patient. It is our primary choice in the SFA and femoropopliteal artery.

Prof. Zeller: The data simply confirm and justify my own treatment strategy I have followed since the very beginning

of the DCB era: Not withholding from patients the potential benefits of DCBs, independent of the TASC classification of the lesion. Simple lesions, mainly TASC A and B, perform well with stand-alone DCB angioplasty;[5,6,19] however, even complex TASC C and D lesions show excellent 2-year outcomes if the DCB is combined with provisional stent placement.[7,8,20] IN.PACT Admiral DCB represents a benchmark even in the European market where almost 20 different DCBs are commercially available. ■

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Vessel Preparation Strategies and Impact on Outcomes in Complex Lesions

A roundtable discussion on the various devices, methods, and data surrounding challenging PAD in the SFA.

WITH BRIAN G. DERUBERTIS, MD, FACS; BRYAN T. FISHER, MD; LOUIS LOPEZ, MD; ANTONIO MICARI, MD, PHD; GEORGE A. PLIAGAS, MD; ERIC C. SCOTT, MD; GREGORY A. STANLEY, MD; AND ERIK G. STILP, MD, FACC, RPVI

Drug-coated balloons (DCBs) have become a critical component of the armamentarium of most operators, as these devices have been shown in several randomized controlled trials to reduce restenosis and result in superior primary patency compared to standard percutaneous transluminal angioplasty (PTA) alone.[1-8] Although head-to-head comparisons are lacking between DCBs and stents, DCBs have shown primary patency rates that are similar to those historically achieved with stents, and there are now good data to support treatment of the superficial femoral artery (SFA) without the need for a permanent scaffold. However, as the IN.PACT Global Registry imaging cohorts and other prospective registries have shown us, increasing lesion complexity (beyond those lesions represented in the investigational device exemption trials for our available DCBs) is associated with higher rates of bailout stent usage, up to 46% in some series.[9] The intuitive explanation for this is that DCBs will address the issue of biologic restenosis, but cannot alter the morphology of the plaque itself, and therefore dissections or the residual plaque burden left behind can result in the need for bailout stenting and can impact patency rates. In the following article, my colleagues and I will delve into a panel discussion regarding how the proper use of vessel prep tools and techniques can be used to minimize dissection and therefore the need for bailout stenting.

— Brian G. DeRubertis, MD, FACS

DIRECTIONAL ATHERECTOMY

With Brian G. DeRubertis, MD, FACS; Louis Lopez, MD; Eric C. Scott, MD; and Gregory A. Stanley, MD

Why do you predominantly use directional atherectomy for vessel prep? What factors drive your decision?

Dr. DeRubertis: The term *vessel prep* can refer to any number of different strategies for altering the properties of a vessel before delivering a definitive therapy, and the choice of vessel preparation may change depending on whether the ultimate therapy is a permanent implant, a drug-eluting stent (DES), or delivery of drug by a DCB. However, atherectomy is rapidly becoming a standard for vessel preparation due to its ability to achieve luminal gain and reduce the residual mechanical forces that act on the lumen of the vessel. Although the term *atherectomy* is broadly applied to a number of different devices, directional atherectomy (also referred to as excisional atherectomy) is particularly suited for vessel preparation due to its ability to act focally, and even eccentrically, in regions of heavy plaque burden. It has a unique ability to achieve dramatic lumen gain in heterogeneous types of plaque, including organized thrombus, restenotic intimal hyperplastic tissue, soft atherosclerotic plaque, and calcium.

Most complex lesions have a variety of plaque morphologies, and it is important to be able to

address these with a single device, the way directional atherectomy can. In my experience, an important predictor of patency is luminal gain, which is accomplished to a greater degree with directional atherectomy than other atherectomy devices.

Dr. Scott: I use vessel prep in hopes that following DCB use, I will attain maximal lumen gain without need for stenting and have no significant residual stenosis or dissection. If vessel prep alone or in conjunction with PTA can provide satisfactory lumen gain with a low risk of dissection, then stenting is unnecessary. I think of directional atherectomy as my "endovascular scalpel"—it can provide a very tailored and lesion-specific therapy in a wide range of lesion morphologies. It's a powerful tool for lumen gain.

Dr. Stanley: I use primary directional atherectomy because of its wide versatility, including the ability to effectively treat calcium. There are few lesions that cannot be adequately addressed with directional atherectomy, whether I'm approaching a focal eccentric lesion, chronic total occlusion (CTO), patent diffuse calcific plaque, or a long-segment heavily calcified CTO. The design characteristics of the latest-generation directional atherectomy catheters (HawkOne™ LX, LS, M, and S atherectomy devices, Medtronic) highlight this versatility: blade rotation speed and catheter wall apposition increases efficiency, contoured teeth on the cutter blade effectively cut/remove calcium, and several individual catheters that can safely address multilevel disease.[10]

I find tremendous benefit in controlling the outcome of the procedure—I actively decide exactly where to remove plaque and how much to remove in real time during the case. There is incremental benefit to making each additional cut with a directional atherectomy catheter, and therefore I can choose when the case is a success.

When you use vessel prep, what are the steps you take and how do you define success?

Dr. Scott: I use vessel prep primarily as a tool for anticipated DCB use, in the hopes that DCB will be the final therapy delivered and that stenting will be unnecessary. If I didn't care about femoropopliteal stent usage, I wouldn't care about vessel prep either. If you look at rates of stenting in our real-world data sets of DCB, you will find bailout stent rates of 20% to 40% in longer lesions.[11-13] To me that is too high. These figures point to the real potential for vessel prep techniques to significantly lower these percentages. One day, I think we will judge differing vessel prep tools specifically on their ability to lower stent utilization in the femoropopliteal segment. When you excise plaque to achieve lumen gain, the risk of dissection becomes very low, as does the need for stenting (2.3% flow-limiting dissection rate, 3.2% provisional stenting rate in the DEFINITIVE LE trial).[14] In my practice, I keep stenting in this segment to < 10% by primarily using directional atherectomy as a vessel prep tool prior to finishing with DCB.

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>
> — Eric C. Scott, MD

> I find tremendous benefit in controlling the outcome of the procedure, meaning I actively decide exactly where to remove plaque and how much to remove in real time during the case.
>
> — Gregory A. Stanley, MD

Dr. Stanley: I define procedural success as the re-establishment of a lumen to < 20% residual stenosis with atherectomy alone. To achieve this result, I employ the techniques described in a case report of a patient with claudication who was treated with directional atherectomy to revascularize the SFA.[15] I obtain diagnostic images and begin atherectomy with the image intensifier in the contralateral oblique position (~30°) and excise the plaque to < 20% residual stenosis angiographically in this view. A standard angioplasty balloon sized 1:1 to the reference vessel diameter is then inflated in the treated segment to low pressure (1 to 2 atm only), demonstrating either residual plaque that must be excised with additional atherectomy or an adequate result.

Once residual stenosis is < 20% in this view, the image intensifier is rotated to an ipsilateral oblique

KEY TAKEAWAYS FROM DEFINITIVE LE[14]

Patient Demographics and Primary Endpoints	• Singe-arm, multicenter, prospective evaluation of 800 patients treated with directional atherectomy as a primary modality • Enrolled 598 claudicants with primary endpoint of primary patency at 12 months • Enrolled 201 CLI patients with a primary endpoint of freedom from major unplanned amputation of target limb at 12 months

Results	• Device success (defined as ≤ 30% residual angiographic stenosis after directional atherectomy without adjunctive interventions): 75%
	  • Following postdilatation: 89%
	• Bailout stent rate: 3.2%
	• Primary patency at 1 year in claudicants: 78%
	  • No significant difference in primary patency between diabetics and non-diabetics (77% vs 78%, *P* > .001 when testing for noninferiority)
	  • Limb salvage at 1 year in CLI patients: 95%
	• Primary patency of tibial lesions treated with directional atherectomy in claudicants: 90%
	  • Primary patency of tibial lesions treated with directional atherectomy in CLI patients: 78%
	• Flow-limiting dissections (2.3%) were universally treated endovascularly

view (~30°). Any remaining plaque in this orientation is removed with the atherectomy catheter, again to < 20% residual stenosis. Another low-pressure balloon inflation confirms I have restored the lumen to near reference vessel area (validated with intravascular ultrasound [IVUS], angiography, intra-arterial pressure measurements, and intra-arterial waveforms). With minimal remaining plaque, the risk of dissection during postdilatation with either a DCB or standard angioplasty balloon is insignificant. This technique is identical for the femoropopliteal and tibial segments.

What data drive your decision to use directional atherectomy?

Dr. Lopez: The question remains: does pretreatment with atherectomy provide enhanced vessel patency compared to DCB alone? Dr. Zeller's DEFINITIVE AR study showed an incremental benefit to pretreatment with atherectomy prior to DCB, especially in heavily calcified arteries.[16] The REALITY trial (NCT02850107) is currently enrolling patients for that specific lesion set.

In my own experience, I have documented excellent patency rates in remarkably complex lesions using atherectomy followed by IN.PACT™ Admiral™ DCB (Medtronic). I studied 120 sequential patients; the average lesion length was 23 cm, 29% were CTOs, 59% had diabetes, and 49% were restenosis lesions. One-year patency with directional atherectomy followed by DCB was 87.5%, which was equivalent to the randomized IN.PACT SFA Trial but comprised a much more complex subset of patients with much longer lesions.[2,17] Pretreatment with atherectomy allowed me to avoid dissections, and I had no bailout stenting.

As our treatment options have evolved and our data on outcomes grows, many operators attempt to leave nothing behind. Stents are metal. All metal eventually fatigues, and when it does, stent struts can fracture. This is a well-known mechanism of restenosis and can create a challenging lesion to correct.[18] Vessel prep with atherectomy virtually eliminates this issue. That said, I also acknowledge that stent design is improving. Drug elution for peripheral stents is improving and stents will continue to serve a need in the interventional lab.

Dr. Stanley: The DEFINITIVE LE[14] data support that directional atherectomy is safe and effective in both the femoral-popliteal and tibial segments, is equally effective in diabetics, and has very good efficacy in the setting of critical limb ischemia (CLI). Additional data with longer follow-up, more complex lesions, and comparative treatment arms is highly needed to further define this technology within the current peripheral artery disease (PAD) treatment landscape.

How is the directionality and versatility of directional atherectomy helpful in treating complex lesions?

Dr. DeRubertis: The different devices that are collectively described as atherectomy catheters vary considerably in their technical properties, clinical benefits, and safety profiles. While some are more suited to calcified lesions, and others are more apt to perform well in soft or thrombotic lesions, I believe that the versatility of directional atherectomy is most useful across a range of patients and lesion types. Directional atherectomy has the benefit of allowing the operator to focus the excisional cuts toward the region of plaque burden and allows for repeated cuts until the lesion has adequately been debulked without affecting adjacent normal tissues. The inherent directionality of the catheter allows for treatment of eccentric and concentric lesions of various plaque compositions.

Although focal lesions can easily be treated with directional atherectomy, these catheters perform safely even in long-segment occlusions, as the harvested atherosclerotic debris can be efficiently contained in the nose-cone of the device and removed without significant risk of embolization when used properly. This combination of properties makes these devices useful in simple focal disease or challenging complex lesions.

Dr. Lopez: Many operators prefer to find one device and apply it to all cases. Diversity of lesions and anatomy simply do not allow that, but directional atherectomy does provide a broad range of applications. It is effective in both soft and heavily calcified plaque. It can be used to literally cut out a dissection flap. It is safe and effective in total occlusions, even if the wire crossing was subintimal. When subintimal, extra care should be given to direct the cutting blade toward the true lumen, which can be visualized via fluorography as the wire will tend to bias towards the advential side of the vessel—often a change in fluoro orientation is needed to optimize the view of the vessel. Directional atherectomy also allows one to directly treat a recalcitrant area in a vessel until an acceptable reduction in residual stenosis has been obtained.

The device is easy to deploy even when traversing severe tortuosity in the aortoiliacs. It captures the plaque for removal from the body rather than sending particulate matter into the distal microvasculature. Ability to directionally remove plaque and the efficiency of the cutter enables the operator to achieve optimal reduction in plaque burden and ability to achieve < 30% residual stenosis. Directional atherectomy is limited by the fact that it is a rear-cutting device and requires a fair-sized landing zone if one wishes to use a distal embolic protection filter.

> **The versatility of directional atherectomy allows luminal gain even in areas of eccentric calcified plaque, thereby removing the mechanical forces exerted by these lesions on the lumen, a factor that likely contributes to patency loss over time.**
>
> — Brian G. DeRubertis, MD, FACS

Rotational atherectomy is a front-cutting device, which is sometimes needed with heavily calcified disease. By design, rotational atherectomy sends particulate matter downstream. In my own practice, I consistently use distal embolic protection to minimize the possibility of significant distal embolization. Front-cutting devices have the advantage of needing only a tiny landing zone for the filter. Rotational atherectomy is limited in the degree of plaque removal by the size of the rotational atherectomy device. This makes directional atherectomy a better option in large-diameter vessels. Although directional atherectomy and rotational atherectomy are fundamentally different, both are effective at changing vessel compliance and minimizing the chance of a dissection. Both provide excellent pretreatment prior to DCB angioplasty.

Why is it important that directional atherectomy actually removes plaque from the patient?

Dr. DeRubertis: The ability to remove the plaque has two distinct advantages: (1) plaque excision and removal maximizes luminal gain and thus likely impacts patency rates, and (2) plaque storage in the catheter nose-cone followed by removal from the patient limits the risk of embolic complications.

Residual stenosis has been correlated to patency rates in prior studies and is likely the method by which directional atherectomy can attain patency rates similar to stent implantation.[1] Additionally, the versatility of directional atherectomy allows luminal gain even in areas of eccentric calcified plaque, thereby removing the mechanical forces exerted by these lesions on the lumen, a factor that likely contributes to patency loss over time.

Embolic complications are a concern with any percutaneous lower extremity intervention, but

> **Mechanically, optimal atherectomy produces a larger lumen and greater acute gain. Biologically, removing the barrier between the vessel and DCB should allow for improved drug uptake and enhanced drug effect.**
>
> — Louis Lopez, MD

this concern is heightened in procedures involving atherectomy.[19] The DEFINITIVE LE study showed an extremely low rate of distal embolization of 3.8% in cases involving directional atherectomy, and this is likely due to the catheter's ability to contain the excised debris in the device and remove it from the body.[14]

Dr. Scott: I think of plaque excision via directional atherectomy as a completely different way to treat arterial stenosis or occlusion from our two preceding therapies, angioplasty and stenting. If you can fully excise a lesion with atherectomy, you don't need either of those modalities. Admittedly, there are longer lesions where the plaque volume exceeds what any device can fully remove, but even in these circumstances, directional atherectomy can be a helpful adjunct in creating lumen gain and reducing the workload of PTA.[16] We have also seen a trend towards improved patency in DEFINITIVE AR for patients who had directional atherectomy to residual stenosis of ≤ 30% prior to DCB compared to patients who had residual stenosis of > 30% after directional atherectomy prior to DCB.[16] These are interesting early data that indicate DCBs may actually be more effective if atherectomy is used to accomplish substantial lumen gain first. Whether this improvement in patency is a function of lumen gain, enhanced penetration of drug, or both remains to be determined.

Dr. Lopez: Mechanically, optimal atherectomy produces a larger lumen and greater acute gain. That means for a fixed degree of late loss, we retain a larger lumen at 1 year. Biologically, removing the barrier between the vessel and DCB should allow for improved drug uptake and enhanced drug effect. We still need more data on this issue to adequately judge. Pretreatment with atherectomy undeniably reduces dissections, reduces elastic recoil, reduces the need for bailout stenting, and improves vessel compliance, allowing for improved vessel expansion with the DCB.

What do you do in your practice that allows you to be efficient with directional atherectomy in complex lesions?

Dr. DeRubertis: As atherectomy is thought to be more time consuming than primary stent implantation, it is important to be efficient and recognize that certain techniques can facilitate this. Oftentimes, long-segment occlusions are the result of a few focal areas of severe disease that arrest flow through the vessel, while much of the vessel may in fact be patent and "hibernating." This can be demonstrated by passing the catheter through the entire lesion in the "off" position, and then performing an angiogram after this dottering technique. Typically, this results in in-line flow through the previously occluded segment, while the true culprit lesions are unmasked. Alternatively, predilate the lesion with an undersized balloon (eg, long 3- or 4-mm balloon for the SFA). Finally, lesions that are suspected to be highly laden with organized or acute thrombus can be treated with an on-table 20-minute infusion of tissue plasminogen activator (tPA) prior to treatment with atherectomy to clear the underlying thrombus and turn an occluded segment into a series of focal stenoses.

Dr. Scott: I've made several changes over the past few years. First, I use the latest HawkOne atherectomy devices almost solely now. The HawkOne 7-F device is 100 µm smaller in profile than the TurboHawk™ 7-F atherectomy device (Medtronic), has an improved hydrophilic coating, and is directed more easily through sheaths placed over the aortic bifurcation. The cutter is more effective as well due to higher RPM speed, enhanced torque from the redesigned drive shaft, and optimized cutting blade apposition due to the refined curvature (or jog) near the cutting window of the device.

In longer CTOs of the SFA, I often begin with a 4- to 5-mm predilation using the longest balloons on the shelf. Using low pressure only, this often identifies portions of the artery that are most diseased and identifies portions of the CTO that will open nicely by PTA alone. I can target use of the atherectomy device at what I believe were causative lesions of the CTO. I let DCB safely take care of the rest.

Dr. Stanley: Device selection is a key component to maintain efficiency. In complex femoropopliteal lesions, I use the HawkOne LX atherectomy device as much as possible. This is a large-vessel device, making it very efficient in gaining lumen and provides the largest nose-cone capacity available, thus limiting the number of cleanings required during the case. In addition, working in a

proximal to distal orientation allows for lumen creation as the device advances, thereby relieving friction in the proximal segments that can sometimes impede control in more distal segments.

How has your approach with directional atherectomy evolved with the rise of DCBs?

Dr. DeRubertis: Directional atherectomy can work effectively as an adjunctive therapy to DCBs by altering this plaque morphology and removing the mechanical forces that act to reduce patency over time. The adjunctive use of directional atherectomy with DCB offers an opportunity to manage both mechanical forces and biologic restenosis effectively, thus reducing the need for stent placement. Additionally, the effectiveness of DCBs have been shown to be reduced as degree of calcium increases in a lesion, and this may suggest that calcium poses a barrier for drug delivery,[14,15] meaning plaque excision with directional atherectomy may enable improved drug delivery. These are among the questions we are currently exploring in the VIVA-sponsored REALITY trial using the HawkOne atherectomy system and the IN.PACT Admiral DCB.

Atherosclerotic lesions of the lower extremity vary considerably in their composition and complexity, and it remains true that some lesions will ultimately require scaffold implantation to optimize outcomes. We now have improved options (woven nitinol stents and next-generation designs) when stenting is required. However, the advent of atherectomy and DCBs also provides us with ways of treating the SFA that offer excellent clinical outcomes that don't require lining the SFA with a permanent implant, and this practice has certainly fallen out of favor for most experienced interventionalists. Once a permanent implant is placed, the consequences of failure of that implant include stent fractures, in-stent restenosis/occlusion, and loss of potential bypass targets. Each of these issues complicates retreatment of that vessel and limits our future options.

PERCUTANEOUS TRANSLUMINAL ANGIOPLASTY

With Antonio Micari, MD, PhD

Why do you predominantly use optimal PTA for vessel prep? What factors drive your decision?

Dr. Micari: PTA is the most utilized technology for managing symptomatic PAD. Progress in the field has led to its use for complex lesions; however, restenosis occurs frequently. Drug-coated technologies are used to improve results of PTA and achieve long-term patency. The mechanical effect of PTA is crucial for the mid and long-term result of drug-elution techniques. DCBs have the most robust clinical program promoting evidence-based medicine. To transfer paclitaxel to the vessel wall, DCBs need to touch the vessel wall and stay inflated long enough to hopefully overcome challenges such as calcium. It is important to prepare the vessel to enhance the drug-elution process. Optimal PTA has a double effect: mechanical, to obtain the maximum lumen gain; and preparatory, so most of the drug penetrates the vessel wall.

When you use vessel prep, what are the steps you take, and how do you define success?

Dr. Micari: Usually, complex femoropopliteal lesions are long, calcified, and often involve the popliteal segment. After crossing the lesion, I dilate the occlusion with a slightly undersized balloon and maintain inflation for 3 minutes before inflation of a DCB for at least 3 minutes. If the result is suboptimal (residual stenosis or dissection affecting the flow), I use a 1:1 balloon:vessel ratio for more time at low pressure. Sometimes along the lesion, some spot residual lesions or stenoses persist; in this case, I apply a short 1:1 balloon to inflate at that specific point. I have a satisfactory result when I obtain

> We know that the full metal jacket or extensive stenting use in the SFA and popliteal artery is not a winning strategy.
>
> — Antonio Micari, MD, PhD

a reasonable lumen gain in absence of focal calcified residual stenosis and no flow-limiting stenosis.

Could you provide an overview of your DCB Long data, and the efficiency of PTA as vessel prep in long lesions?

Dr. Micari: In our SFA-Long Study (105 patients; mean lesion length, 25 cm), we demonstrated satisfactory patency of 89% and 71% at 1 and 2 years, with a very low stenting rate (10.5%).[21,22] We used stenting as bailout in case of residual stenosis or flow-limiting dissection after aggressive postdilatation. Our data were comparable with other studies and registries in terms of patency results but differed in the rate of bailout stent usage, likely due to our consistent vessel preparation.

When and why do you use more than PTA for vessel prep?

Dr. Micari: Angioplasty alone will not be sufficient to obtain a good vessel preparation in all situations. The real enemy is calcium. Very calcified vessels, especially circumferential calcium, do the worst in terms of acute results or long-term patency results. To treat these vessels effectively, we need to debulk or use a specialty balloon to more effectively address the plaque.

What do you perceive as the value in minimizing metal left behind and why that's important in the SFA/popliteal segment?

Dr. Micari: In complex lesions, reducing the stent usage can be very important. First of all, we know that the full metal jacket or extensive stenting use in the SFA and popliteal artery is not a winning strategy. Claudicant patients are typically in their late 60s with a life expectancy similar to the standard population and the chance to have a reintervention is quite high. Having no permanent prosthesis makes the reintervention easier and safer. Popliteal involvement makes the usage of the stent not desirable being that the stent is placed behind the knee in a bending zone. This is dangerous for stent fracture and may result in thrombosis. Data from the IN.PACT Global study shows no difference between the stented and non-stented subgroups when DCBs are used.[23] My primary treatment goal is to avoid leaving a long stent inside the vessel without compromising long-term outcomes and thereby preserving future treatment options.

SPECIALTY BALLOONS

With Bryan T. Fisher, MD; George A. Pliagas, MD; and Erik G. Stilp, MD, FACC, RPVI

When and where do you use specialty balloons for vessel prep? What factors drive your decision?

Dr. Fisher: Vessel preparation is absolutely key to achieving an optimal and more durable result compared to simple balloon angioplasty. Conceptually, we are ultimately trying to remodel the artery with minimal injury to the adjacent normal vessel with the hopes of pushing the boundaries of patency well beyond the standard 2-year mark.

I prefer to use specialty balloons for advanced complex lesions that are classically resistant to traditional therapy. Lesions with heavy calcification and those that are longer in length tend to fall into this complex category. Especially below the knee, specialty balloons have allowed me to consistently achieve patency long enough for wound healing, though consistent patency beyond 6 to 12 months remains elusive.

> Vessel preparation is absolutely key to achieving an optimal and more durable result compared to simple balloon angioplasty.
>
> — Bryan T. Fisher, MD

Dr. Pliagas: The degree and location of calcification is a huge obstacle in our ability to create microchannels that allow DCB permeation into the internal elastic tissue and the media. This is where specialty balloons and atherectomy devices help to enhance the uptake of the drug by creating a conducive microvascular environment for drug uptake into the media. I use the Chocolate™ PTA balloon (Medtronic),

which incorporates a nitinol-constraining structure, creating a complex pattern of pillows and grooves.[24] Using appropriate insufflation, the Chocolate PTA balloon allows for uniform and atraumatic dilatation. This unique property can be utilized safely in the ostium of the SFA, the junction of the P2 and P3 segments of the popliteal, the P3 segment of the popliteal, and the origins of the tibial vessels. In my experience, the Chocolate PTA balloon has lower rates of dissections compared to other uncoated balloons and bare-metal stents.

Dr. Stilp: PAD is a chronic and debilitating disease that affects both quality and quantity of life on two legs, and specialty balloons have become an essential tool in treating infrainguinal PAD safely and effectively. I consider specialty balloon use in all but primary stent situations, which are now few and far between. The up-front angiographic success and symptom relief seen with infrainguinal stents is often not worth the long-term pain for both patients and operators.

Specialty balloons can allow for more aggressive treatment in "no-stent zones" such as the across-knee popliteal and common femoral arteries. They augment treatment of heavily calcified lesions without as much concern for flow-limiting dissections or perforations and minimize need for bailout stents. They are often successful stand-alone options in tibial arteries, where a preponderance of limb-threatening disease lies but where treatment options in the United States are currently most limited.

When you use vessel prep, what are the steps you take, and how do you define success?

Dr. Fisher: The term *vessel prep* does not have a standard definition. Generally, the operator is trying to fulfill four objectives:

1. Achieve luminal gain (< 20%–30% residual stenosis prior to delivery of definitive therapy)
2. Minimize dissection both within and adjacent to the target lesion
3. Remodel the vessel acutely to change vessel compliance
4. Prepare for the delivery of antiproliferative therapy.

Specifically, I routinely perform IVUS before, during, and after treatment in order to get a definitive idea of whether I have achieved the above-mentioned goals. After assessing the vessel size (including variations along the length of the lesion), depth of my wire, and lesion composition, I then choose an atherectomy device to modify the lesion. Next, I dilate the vessel in a selective fashion with regards to diameter choice as there is often large variation in vessel size and lumen along a complex lesion. Below the knee, specialty balloon use has been especially helpful in treating patients with wounds that require a variable window of increased perfusion to achieve healing.

> I choose to lead with the controlled dilatation of a Chocolate PTA specialty balloon except in the rare circumstances where my procedural plan is primary stenting, or where there isn't any significant fluoroscopic calcium.
>
> — Erik G. Stilp, MD, FACC, RPVI

Dr. Stilp: Success in specialty balloon use in my practice is based largely on three metrics:

1. Do they allow me to dilate otherwise non-dilatable disease? There are simply some lesions that won't expand without them. While it's nice to both expand them and not have to stent, a small subset of lesions just need to dilate in order to get adequate stent expansion and apposition, and specialty balloons allow for this.
2. Do they decrease my bailout stent rate in segments treated with drug? I see DCBs primarily as paclitaxel transporters, and only in the softest of femoropopliteal lesions do they double as safe vessel preparers. Although predilatation is now at the discretion of the physician in currently available DCB instructions for use, I find that predilatation increases procedural success with DCBs and minimizes stenting.
3. Do they minimize flow-limiting dissections in long-segment tibial disease? While the PARADISE trial and others have shown DESs to be an effective option for focal tibial lesions in patients with CLI, until below-the-knee (BTK) DCBs or BTK DESs are proven effective, we're left with atherectomy and PTA as options for these patients.[25] In my view, specialty balloons in tibial disease can minimize the degree of intervention needed and provide for adequate stentless angiographic outcomes.

Please provide a brief overview of the data in support of your specialty balloon choice.

Dr. Pliagas: The ultimate struggles we face in the world of intervention is long-term patency and avoidance of amputation. Limitations of endovascular therapy are many but include the presence of calcium, lesion complexity, and lesion length. An article by Cotroneo et al indicated that cutting balloons were a valuable tool in the endovascular treatment of these lesions with no dissections and improved patency at 12 months and 2 years.[26] Another similar article by Iezzi et al from July 2015 described cutting balloon as a safe and effective tool in the routine treatment of short and ostial infrapopliteal lesions.[27]

Dr. Stilp: Postmarket registry data support the use of specialty balloons in the femoropopliteal space. Femoropopliteal lesions were analyzed after treatment with Chocolate PTA alone, and 93.1% were free of stent afterwards in a cohort that included 32% CLI, 20% severely calcified lesions, and 23% CTOs (n = 263 total subjects).[28] There were no grade E/F flow-limiting dissections after Chocolate PTA. Freedom from target lesion revascularization (TLR) at 12 months was 78.5%.

In a single-center cohort that added DCB angioplasty after Chocolate PTA for 81 patients with femoropopliteal lesions and severe claudication, freedom from TLR at 12 months was 98%.[29] The core lab–adjudicated BTK cohort of the Chocolate BAR registry included 226 patients with CLI who underwent Chocolate PTA. The results, which were recently presented at TCT, showed < 30% residual stenosis and a lack of flow-limiting dissection achieved in 85% of lesions.[30] There was 97% freedom from stenting and 97% freedom from major amputation at 6 months.

When do you lead with a specialty balloon versus use it provisionally?

Dr. Fisher: Cost and overall efficacy have to be considered when using specialty balloons regardless of setting. Below the knee, I prefer the use of Chocolate PTA balloon over plain balloon angioplasty. On completion IVUS, there is a difference in the acute remodeling of the vessel with lesion intrusion of dissection flaps into the newly dilated lumen. Also consistent with previous operators, longer inflation times (> 3 minutes) acutely remodel the vessel, resulting in less luminal flap occlusion. The long-term patency and the clinical significance of this observation is not known.

Dr. Stilp: I choose to lead with the controlled dilatation of a Chocolate PTA specialty balloon except in the rare circumstances where my procedural plan is primary stenting, or where there isn't any significant fluoroscopic calcium. In provisional use, I will typically not continue to inflate standard PTA balloons if there is any fluoroscopic evidence of significant stenosis at the target lesions at nominal pressures, but rather deflate and replace with a specialty balloon to minimize dissections and adequately prepare for DCB therapy.

> **The use of specialty balloons such as Chocolate PTA avoids the torsional, radial, and longitudinal stress of PTA while allowing the pillows to uniformly act on vessel dilatation in a controlled manner.**
>
> — George A. Pliagas, MD

What do you see as the value in minimizing metal left behind in the femoropopliteal segment?

Dr. Fisher: The goal of lower extremity treatment is to cause chronic vessel remodeling that is resistant to recurrence secondary to vessel wall injury during treatment. To this end, bare-metal stenting has not eliminated the need for redo interventions. DCBs, on the other hand, have become a proven tool capable of achieving improved patency compared to PTA and bare-metal stenting used to treat long complex lesions in the SFA and popliteal artery.

Dr. Pliagas: For years, complex femoropopliteal pathology was treated with balloon angioplasty and stenting. The physiologic forces exerted on the nitinol self-expanding stent left behind in the SFA/popliteal location lead to a number of suboptimal results including fractures, restenosis, migrations, and ultimately both early and late occlusions.[31] We may see fewer stents used as new treatment algorithms encompassing vessel preparation techniques and drug-eluting technology becomes common practice. As we proceed into the future with new technologies, it will be important to assess which specific preparatory steps, or perhaps which combinations of preparatory steps, ultimately lead us to the best patency rates and reduced amputations. The next challenge will come when we evaluate and assess all of these technologies in their respective settings both above and below the knee.

Dr. Stilp: Repeat procedures expose our patients to more risk and more expense. They stress our labs and ultimately can make it more difficult to get new patients with urgent revascularization needs treated in a timely fashion. Femoropopliteal stents, especially long-segment and overlapped stents in high-torsion zones, tend to readily fracture, restenose, and thrombose.[31-33] Moreover, PAD patients, especially CLI patients who stand to lose the most from recurrent disease, have a staggering number of comorbidities.[34] Many of these conditions necessitate intermittent cessation of antiplatelet and anticoagulant medications. Stented areas are the first to occlude, often leading to limb-threatening ischemia during these periods. Let's consider the case of an elderly woman who shows up to our lab with foot-threatening ischemia. We find that a bit more effort, time, and potentially product cost to minimize stenting during that elderly woman's initial procedure is worth it, as the likelihood of a getting her through a fall with femoral head fracture or severe diverticular bleed in the future is much greater if she doesn't have metal from her mid-SFA through the P2 popliteal.

Please provide an overview of your single-center experience, data, and tools/techniques.

Dr. Pliagas: Our current treatment protocol incorporates all of the aforementioned techniques. Vessel preparation requires a meticulous vessel- and patient-centered approach. In addition to angiography, the use of IVUS in the assessment of calcium burden allows better focus on the atherectomy technique. Appropriate escalation angioplasty then allows the activation of nitrous oxide, which leads to vasodilatation, endothelial regeneration, and inhibition of smooth muscle cell proliferation.[35] The use of specialty balloons such as Chocolate PTA avoids the torsional, radial, and longitudinal stress of PTA while allowing the pillows to uniformly act on vessel dilatation in a controlled manner. The grooves of the Chocolate balloon allow dispersion of the additional angioplasty forces exerted back by the vessel plaque thereby minimizing dissection.[24] Drug-coated technology can be instituted as necessary following vessel preparation allowing for optimal outcomes.

Dr. Stilp: I find that time spent sizing specialty balloons 1:1 with the arterial segment being treated, especially in tibial intervention, minimizes my dissections and therefore my use of stents, while maximizing luminal gain and longer-term outcomes. Tibial interventions are classically undersized, but with either IVUS or extravascular ultrasound, or tedious attention to serial upsizing of balloons with angiographic guidance, specialty balloons can be utilized to their greatest potential.[36] Enough emphasis cannot be placed on the importance of prolonged low-pressure PTA, after adequate sizing. I will frequently leave a Chocolate PTA balloon, sized 1:1 with IVUS, inflated at nominal pressure across long-segment tibial disease for 8 to 10 minutes; 4 to 5 minutes is certainly a necessity. ■

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Economics and Cost Effectiveness of Managing Complex Lesions

Analyzing data on the cost of drug-coated balloons, drug-eluting stents, percutaneous transluminal angioplasty, and bare-metal stents for the treatment of peripheral artery disease.

BY MAHMOOD K. RAZAVI, MD, FSIR, FSVM

It is difficult to engage in a conversation regarding any aspect of health care and avoid terms such as value, cost effectiveness, and net quality impact. The reason is obvious: inflation in the cost of health care has outpaced the economy at large in many Western countries. In the United States, for example, although the rate of health care inflation has slowed over the past 2 decades, it still remains at an unsustainably high rate of 6% to 7% per year,[1] and the operating expenses of United States facilities continue to outpace revenue.[2] Unfortunately, none of these developments appear to be helping health care consumers obtain consistent quality care. In fact, there is no correlation between cost and quality of care, with some of the highest cost facilities in the United States being among the most mediocre.[3] Despite efforts to curb utilization by payers, medical costs continue to rise. Payers and employers are focusing on price control and costs per benefit gained, which is what has led to the age of "value" and efforts to tie reimbursement to outcomes.

The other prevailing trend in the United States is the rapid expansion of office-based labs (OBLs) or ambulatory surgery centers (ASCs) that are entirely or partially owned by physicians.[4] This ownership has influenced physicians to keep the return on their investment in sharp focus while rendering care. Many physicians practice in environments where the interests of all stakeholders may not always be aligned. Patients expect the best care they can get, physicians want to provide the best treatment available, payers are trying to rein in the costs, and facilities need to operate with reasonable margins to stay financially solvent. Therefore, it is our responsibility to understand what the best available care option for the money is and what is the best "value." How "value" in health care is defined in general and who defines it is outside of the scope of this article. Instead, the focus of this article is on value for patients with peripheral artery disease (PAD) and the endovascular treatment of a symptomatic femoropopliteal segment.

Although the index procedure costs were higher for DCBs, this was offset by the savings due to fewer repeat procedures over 2-year follow-up.

– Mahmood K. Razavi, MD, FSIR, FSVM

UNDERSTANDING VALUE FOR PAD

Given the trends discussed previously, a focus on the best value in the treatment of PAD is particularly timely because the annual cost of treating patients with PAD now exceeds that of coronary artery disease or cancer.[5,6] Fortunately, the literature is fairly clear on this topic. In an analysis of the potential impact of treating superficial femoral artery (SFA) disease on payers and providers in the German and United States health care systems, Pietzsch et al examined the outcome and costs of one of four endovascular strategies of bare-metal stents (BMSs), drug-eluting stents (DESs), percutaneous transluminal angioplasty (PTA), and drug-coated balloons (DCBs).[7] Outcome data were derived from a systemic review of the literature and a decision-analytic model was developed to evaluate the economic consequences of the four treatment strategies as index procedures. The average cost per patient over a 24-month period, including the cost of the index procedure and the applicable costs of a possible reintervention, was lowest for the index strategy of DCBs at $10,214, followed by DESs ($12,904), PTA ($13,114), and BMSs ($13,802). The investigators concluded that DCBs offer the "lowest budget impact and, therefore, the greatest economic value to the payers" in the United States. Similarly, drug-eluting therapies were found to be the least costly strategies to the payers in the German health care system.[7]

In another study, Salisbury et al used the data from the randomized IN.PACT SFA Trial to examine the cost-

The literature shows a consistent cost-effectiveness benefit to DCBs in the treatment of femoropopliteal disease in several models and across multiple national health care systems. The magnitude of this benefit, however, may not be uniform across all DCB platforms and all patients and lesion types.

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effectiveness of the IN.PACT™ Admiral™ DCB (Medtronic) versus standard PTA.[8] Resource utilization data were collected for the index procedure and subsequent hospitalizations for vascular care over a 2-year follow-up, and health utility values were derived from the quality of life data. Although the index procedure costs were higher for DCBs, this was offset by the savings due to fewer repeat procedures over 2-year follow-up. The authors concluded that a strategy of initial DCB angioplasty in the treatment of claudicants with SFA disease is likely to be cost effective (if not economically dominant) compared with standard PTA.[8]

Katsanos et al adopted a similar approach to Pietzsch et al to estimate the per patient cost impact of various therapies for SFA on the United Kingdom's National Health Service (NHS).[9] Researchers systematically reviewed 28 studies utilizing various therapies in the SFA on 5,167 lesions. DCBs were estimated to add 0.011 quality-adjusted life years (QALYs) resulting in an estimated incremental cost effectiveness ratio of £3,983 as compared with £4,534 and £20,719 per QALY gained for DESs and BMSs, respectively. The authors concluded that based on currently available data, "DCBs offer the highest clinical and economic value."[9]

Similar conclusions have been reached regarding the cost effectiveness of DCBs from the perspective of the French and Italian NHSs as well as the United States payers.[10-12]

DISCUSSION

Despite the consistent conclusions of the literature regarding the cost effectiveness of DCBs, two important aspects of these analyses must be kept in mind. First, the degree of benefit of DCBs over PTA has not been consistent in various randomized studies with variable patency and clinically driven target lesion revascularization rates.[13-19] Therefore, it is reasonable to assume that not all DCB platforms may prove cost effective to the same extent. Second, analyses based on data from randomized trials are not always applicable to real-world patients who frequently fall outside of the narrow scope of patients included in randomized trials. As such, cost-effectiveness analyses based on the outcome of prospective registries with core lab–adjudicated data that include more complex patients and lesions will be more illuminating.

The literature shows a consistent cost-effectiveness benefit to DCBs in the treatment of femoropopliteal disease in several models and across multiple national health care systems. The magnitude of this benefit, however, may not be uniform across all DCB platforms and all patients and lesion types. ■

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For United States Audiences Only

HawkOne™
The HawkOne™ peripheral directional atherectomy system is intended for use in atherectomy of the peripheral vasculature. The HawkOne™ catheter is indicated for use in conjunction with the SpiderFX™ embolic protection device in the treatment of severely calcified lesions. The HawkOne™ catheter is not intended for use in the coronary, carotid, iliac or renal vasculature.

HawkOne™ Directional Atherectomy System
Medtronic directional atherectomy products are contraindicated for use in patients with in-stent restenosis.

CAUTION: Federal (USA) law restricts these devices to sale by or on the order of a physician.

IMPORTANT: Indications, contraindications, warnings, and instructions for use can be found in the product labeling supplied with each device.

Chocolate™ PTA balloon catheter
Note: Safety information provided is for the United States. Please refer to your region's Instructions for Use for specific details.

Important Information: Indications, contraindications, warnings and instructions for use can be found in the product labelling supplied with each device.

Indications for Use: The Chocolate PTA balloon catheter is intended for balloon dilatation of lesions in the peripheral vasculature, including the iliac, femoral, ilio-femoral, popliteal, infra-popliteal, and renal arteries.
Caution: Federal (USA) law restricts this product for sale by or on the order of a physician.

IN.PACT™ Admiral™ Drug Coated PTA Balloon Catheter Brief Statement (For USA only)
FTSOP113326-32 Rev. 1G

Indications for Use:
The IN.PACT™ Admiral™ Paclitaxel-coated PTA Balloon Catheter is indicated for percutaneous transluminal angioplasty, after appropriate vessel preparation, of de novo, restenotic, or in-stent restenotic lesions with lengths up to 360 mm in superficial femoral or popliteal arteries with reference vessel diameters of 4-7 mm.

Contraindications
- The IN.PACT Admiral DCB is contraindicated for use in:
- Coronary arteries, renal arteries, and supra-aortic/cerebrovascular arteries
- Patients who cannot receive recommended antiplatelet and/or anticoagulant therapy
- Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the delivery system
- Patients with known allergies or sensitivities to paclitaxel
- Women who are breastfeeding, pregnant or are intending to become pregnant or men intending to father children. It is unknown whether paclitaxel will be excreted in human milk and whether there is a potential for adverse reaction in nursing infants from paclitaxel exposure.

Warnings
- Use the product prior to the Use-by Date specified on the package.
- Contents are supplied sterile. Do not use the product if the inner packaging is damaged or opened.
- Do not use air or any gaseous medium to inflate the balloon. Use only the recommended inflation medium (equal parts contrast medium and saline solution).
- Do not move the guidewire during inflation of the IN.PACT Admiral DCB.
- Do not exceed the rated burst pressure (RBP). The RBP is 14 atm (1419 kPa) for all balloons except the 200 and 250 mm balloons. For the 200 and 250 mm balloons the RBP is 11 atm (1115 kPa). The RBP is based on the results of in vitro testing. Use of pressures higher than RBP may result in a ruptured balloon with possible intimal damage and dissection.
- The safety and effectiveness of using multiple IN.PACT Admiral DCBs with a total drug dosage exceeding 34,854 µg of paclitaxel in a patient has not been clinically evaluated.

Precautions
- This product should only be used by physicians trained in percutaneous transluminal angioplasty (PTA).
- This product is designed for single patient use only. Do not reuse, reprocess, or resterilize this product. Reuse, reprocessing, or resterilization may compromise the structural integrity of the device and/or create a risk of contamination of the device, which could result in patient injury, illness, or death.
- Assess risks and benefits before treating patients with a history of severe reaction to contrast agents.
- The safety and effectiveness of the IN.PACT Admiral DCB used in conjunction with other drug-eluting stents or drug-coated balloons in the same procedure or following treatment failure has not been evaluated.
- The extent of the patient's exposure to the drug coating is directly related to the number of balloons used. Refer to the Instructions for Use (IFU) for details regarding the use of multiple balloons and paclitaxel content.
- The use of this product carries the risks associated with percutaneous transluminal angioplasty, including thrombosis, vascular complications, and/or bleeding events
- Vessel preparation using only pre-dilatation was studied in the clinical study. Other methods of vessel preparation, such as atherectomy, have not been studied clinically with IN.PACT Admiral DCB.
- This product is not intended for the expansion or delivery of a stent.

Potential Adverse Effects
- The potential adverse effects (e.g. complications) associated with the use of the device are: abrupt vessel closure; access site pain; allergic reaction to contrast medium, antiplatelet therapy, or catheter system components (materials, drugs, and excipients); amputation/loss of limb; arrhythmias; arterial aneurysm; arterial thrombosis; arteriovenous (AV) fistula; death; dissection; embolization; fever; hematoma; hemorrhage; hypotension/hypertension; inflammation; ischemia or infarction of tissue/organ; local infection at access site; local or distal embolic events; perforation or rupture of the artery; pseudoaneurysm; renal insufficiency or failure; restenosis of the dilated artery; sepsis or systemic infection; shock; stroke; systemic embolization; vessel spasms or recoil; vessel trauma which requires surgical repair.
- Potential complications of peripheral balloon catheterization include, but are not limited to the following: balloon rupture; detachment of a component of the balloon and/or catheter system; failure of the balloon to perform as intended; failure to cross the lesion.
- Although systemic effects are not anticipated, potential adverse events that may be unique to the paclitaxel drug coating include, but are not limited to: allergic/immunologic reaction; alopecia; anemia; gastrointestinal symptoms; hematologic dyscrasia (including leucopenia, neutropenia, thrombocytopenia); hepatic enzyme changes; histologic changes in vessel wall, including inflammation, cellular damage, or necrosis; myalgia/arthralgia; myelosuppression; peripheral neuropathy.
- Refer to the Physician's Desk Reference for more information on the potential adverse effects observed with paclitaxel. There may be other potential adverse effects that are unforeseen at this time.
- Please reference appropriate product Instructions for Use for a detailed list of indications, warnings, precautions and potential adverse effects. This content is available electronically at www.manuals.medtronic.com.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.

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