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Acute Outcomes With a Novel Plaque Modification System in Real-World Femoropopliteal Lesions

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Abstract

Purpose: To report outcomes of a multicenter feasibility study using the FLEX Vessel Prep (VP) System, a novel technology that facilitates plaque incision and lumen gain in stenosed or occluded femoropopliteal arteries prior to balloon angioplasty.

Materials and Methods: Two hundred fifty-five patients (mean age 71.8±9.1 years) were treated with the FLEX VP System at 38 centers between December 2015 and November 2017. Average lesion length was 133±88 mm. Average baseline stenosis was 92%±11%; 112 (44.3%) of 253 patients presented with a chronic total occlusion. Conventional or drug-coated balloon (DCB) angioplasty was performed in all patients after vessel preparation. Vessel measurements were derived from angiograms acquired at baseline, after FLEX passage, and after subsequent ancillary procedures. Logistic regression analyses were performed to identify baseline or procedure variables that predicted the need for provisional stenting.

Results: Average percent reduction in vessel stenosis following treatment with the FLEX VP System was 27%±17%. No flow-limiting dissection, vessel perforation, or embolization was observed; 15 (5.9%) patients had minor (type A or B) dissections. Provisional stenting was performed in 49 (19.2%) patients. Average stenosis following angioplasty ± stenting was 9.1%±7.4%; 9 (3.6%) patients had significant residual stenosis ≥30%. Logistic regression analyses found that patients with dissections, longer lesions, and those receiving conventional balloon dilation alone were most likely to undergo stenting.

Conclusion: In a real-world patient population with long, complex femoropopliteal lesions, use of the FLEX VP System as vessel preparation for angioplasty improved acute outcomes compared to historical controls. The rate of provisional stenting was low, and no serious vessel complications were observed.

Keywords

Angioplasty, dissection, drug-coated balloon, femoropopliteal segment, lumen gain, plaque modification, popliteal artery, scoring balloon, superficial femoral artery, stent, vessel preparation

Introduction

Peripheral artery disease (PAD) is a manifestation of underlying systemic atherosclerosis, and its prevalence increases dramatically with age.[1-4] Even in asymptomatic cases, lower extremity PAD is correlated with a significantly elevated risk of cardiovascular events, such as myocardial infarction and stroke, in diffuse vascular systems.[5-10] Percutaneous transluminal angioplasty (PTA) with provisional stenting is a currently accepted approach for treatment of symptomatic TransAtlantic Inter-Society Consensus (TASC) A and B lesions in the femoropopliteal arteries.[11,12] The rate of acute technical failure with PTA, whether due to ≥30% residual stenoses, dissections, or other vessel complications, has historically been high, particularly in long or otherwise complex lesions.[13,14] These failures then lead to equally high rates of provisional stenting,[13,15,16] but stenting of long superficial femoral artery (SFA) lesions has been associated with inferior outcomes. Restenosis is a major concern particularly when multiple stents are required.[17-21] Considering the risk of long-term complications with a permanent implant in the SFA, PTA would be a more attractive option if acute technical success could be improved. Drug-coated balloons (DCBs), in particular, are a promising development.[22,23]

Currently, there is a lack of consensus as to the optimal treatment for complex femoropopliteal lesions. As most

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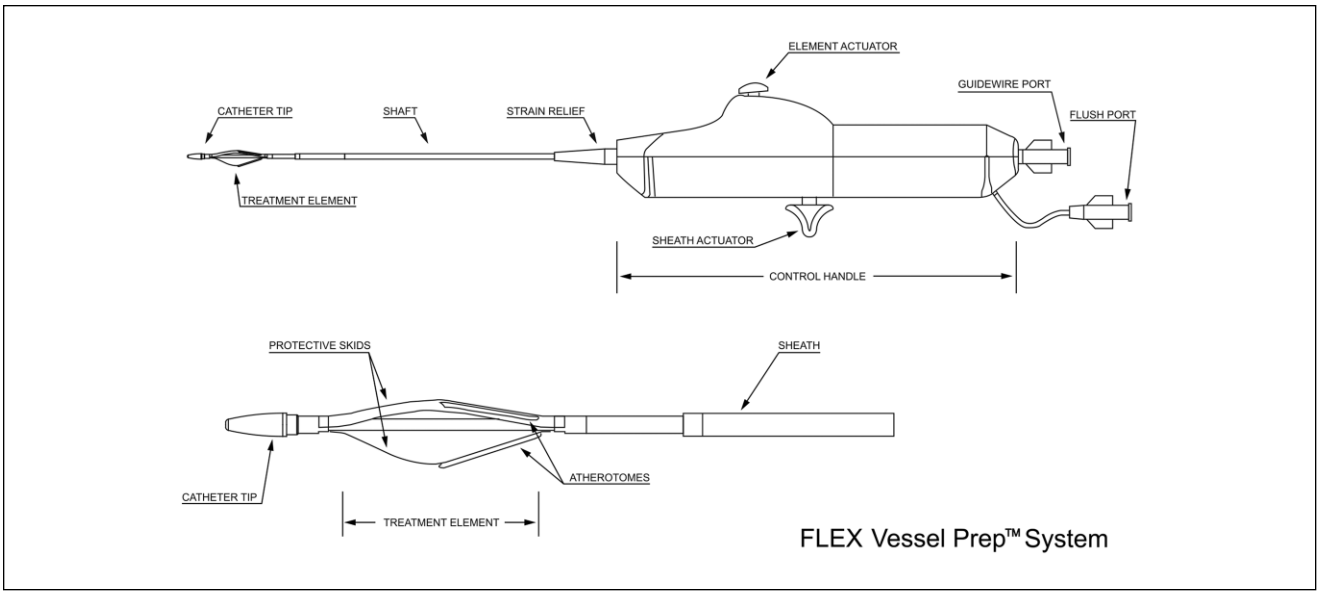

Figure 1. Schematic of the FLEX VP System.

patients with PAD present with long and diffuse lesions localized to this segment, treatment solutions in this area are of critical importance to the vascular interventionist. Nearly 30 years ago, Barath et al[24] conceived of scoring a vessel wall during coronary artery angioplasty to encourage plaque "cracking" along more predictable lines. Historically, scoring devices utilized in the setting of PAD have been cutting-type balloons designed for focal treatment at a set balloon length.[25,26]

The FLEX Vessel Prep System (VentureMed Group, Toledo, OH, USA) is a non-balloon-based vessel prep technology with a one-size-fits-all design distinct from cutting balloons. To our knowledge, it is the only currently manufactured vessel prep technology that provides *continuous* treatment along the lesion, irrespective of length. Though the Flex VP System was approved for the market in June 2016, outcomes with the FLEX System have not been published. The objective of this study was to report real-world acute outcomes with the FLEX VP System and to investigate patient and procedure variables that may be predictive of FLEX and angioplasty success.

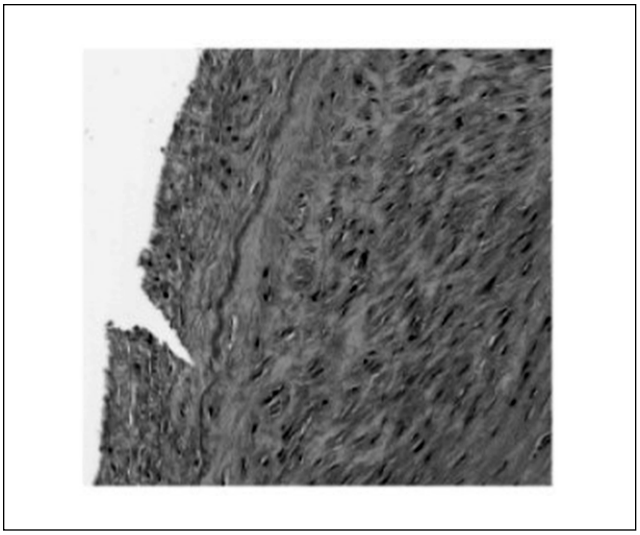

Figure 2. Histology of a microincision created by the FLEX VP System in a human cadaver superficial femoral artery.

Materials and Methods

Device Description

The FLEX VP System was designed to be utilized prior to PTA as a vessel preparation device for femoropopliteal occlusions and stenoses. A single FLEX device (consisting of a sheathed catheter, treatment element, and actuator control handle) can be used for any lesion length, including lesions >100 mm. The FLEX VP System (Figure 1) is 6-F compatible and can be used over a 0.014- or 0.018-inch guidewire. The distal working end has a treatment element comprised of 3 struts radially opposed at 120° with a 0.010-inch-high atherotome mounted perpendicularly on each of the proximal skids. During retrograde pullback of the FLEX System, the treatment element is expanded by pulling back on the actuator, which applies ~1 atm of consistent radial force to allow the atherotomes to longitudinally create continuous parallel microincisions in the vessel wall and enlarge the lumen. The surface area of the skid allows consistent depth of the microincisions (Figure 2) as

the skid "flexes" to the contour of the vessel lumen. Using the control handle, the FLEX can be resheathed, repositioned, and rotated to create multiple incisions during repeat passes; 30° rotation between each pass allows evenly spaced microincisions.

Study Design and Patient Population

Manufacturer-initiated, all-comers, post-market surveillance of patients treated with the FLEX VP System was established in late 2015 at 38 centers (29 US, 9 European) with no inclusion or exclusion criteria applied. Case report forms were collected prospectively and entered into a database, which for this retrospective review was interrogated to identify patients treated from December 2015 through November 2017. Patients gave written informed consent for the procedure per guidelines at each institution; no ethics approval was required for the retrospective review of anonymized data.

The database search found 255 patients (mean age 71.8±9.1 years) treated during the observation period. The FLEX System was applied in 200 (78.4%) SFAs and 27 (10.6%) popliteal arteries (Table 1). Twenty-eight (11.0%) patients were treated with FLEX in target vessels outside the FLEX instructions for use, including iliofemoral and below-the-knee vessels. Average target lesion length in 252 patients was 133±88 mm; 162 (64.3%) patients had lesions ≥100 mm long. More than a third of lesions were chronic total occlusion (CTOs); 21 (8.3%) of 253 patients were treated for in-stent restenosis (ISR).

Calcification severity was assessed by each operator utilizing a modified peripheral artery calcium scoring system (PACCS)[27]: grade 0 – none, grades 1 and 2 – mild, grade 3 – moderate, and grade 4 – severe. Calcium was considered to be severe in 55 (21.7%) of 254 patients, with 166 (65.3%) patients presenting with either mild or moderate calcification. Of 255 patients treated with the FLEX System, 191 (74.9%) presented with CTOs, lesions ≥100 mm, and/or severely calcified lesions.

In this cohort, all patients underwent angioplasty (conventional balloons, DCBs, or both) and provisional stenting following vessel preparation with the FLEX System. The number of passes with the FLEX was decided by the operator. Angiography was performed prior to the procedure, following the application of the FLEX System, and following subsequent endovascular therapy (EVT). All imaging measurements, including degree of stenosis, lesion length, and severity of calcification, were measured by the operator from visual assessment of angiograms.

Definitions

Balloon pressures were of interest to investigate the hypothesis that FLEX usage enhances vessel compliance, enabling lower balloon pressures during subsequent PTA. Thus, in addition to maximum inflation pressure, the lowest inflation pressure needed to attain complete lesion effacement and parallel balloon walls was recorded as the opening balloon pressure. Dissection was classified per standard grades (types A-F) established for the coronary arteries.[28]

Effectiveness of the FLEX System was assessed in 2 ways: lumen gain (baseline percent stenosis – post-FLEX percent stenosis) and post-FLEX reduction in stenosis [(baseline percent stenosis – post-FLEX percent stenosis) ÷ baseline percent stenosis]. Post-FLEX reduction in stenosis differs from lumen gain in that it considers the reduction in stenosis *relative* to the baseline stenosis (the percentage of the whole).

Table 1. Characteristics of 255 Patients Treated With the FLEX VP System at 38 US and European Centers.[a]

Age, y (n=177)	71.8±9.1 (38–97)
Age ≥65 years	150 (84.7)
Men	125/222 (56.3)
Lesion length, mm (n=252)	133.4±87.5 (2–350)
RVD, mm (n=252)	5.4±1.0 (1–8)
Diameter stenosis, % (n=253)	91.9±10.5 (60–100)
Occluded vessel	112/253 (44.3)
In-stent restenosis	21/253 (8.3)
Calcification	
None	33/254 (13.0)
Mild	86/254 (33.9)
Moderate	80/254 (31.5)
Severe	55/254 (21.7)
Target vessel	
SFA	200 (78.4)
Popliteal	27 (10.6)
BTK vessels	22 (8.6)
TPT	8 (3.1)
AT	10 (3.9)
PT	3 (1.2)
Peroneal	1 (0.4)
Iliofemoral vessels	6 (2.3)
Iliac	4 (1.6)
PFA	1 (0.4)
CFA	1 (0.4)
OUS	20 (7.8)

Abbreviations: AT, anterior tibial; BTK, below the knee; CFA, common femoral artery; OUS, outside the United States; PFA, profunda femoral artery; PT, posterior tibial; RVD, reference vessel diameter; SFA, superficial femoral artery; TPT, tibioperoneal trunk; US, United States.
[a]Continuous variables are expressed as mean ± standard deviation (range) and categorical variables are expressed as number/sample (percentage).

Statistical Analyses

This analysis was confined to the SFA and popliteal target vessels in patients treated in the US and European Union after marketing clearance for the FLEX VP System was obtained.

Table 2. Baseline, Post-FLEX, and Postprocedure Measurements of Stenoses.[a]

Baseline diameter stenosis, % (n=253)	91.9±10.5 (60–100)
Post-FLEX stenosis, % (n=245)[b]	66.7±17.3 (10–100)
Post-FLEX lumen gain, % (n=245)[c]	25.2±16.4 (0–89)
Post-FLEX reduction in stenosis, % (n=245)[d]	27.3±17.1 (0–90)
Post-EVT stenosis, % (n=249)[d,e]	9.1±7.4 (0–50)
Post-EVT lumen gain, % (n=249)	82.6±12.1 (50–100)
Post-EVT reduction in stenosis, % (n=249)	90.0±7.9 (50–100)
Significant residual stenosis (>30%)	9 (3.6)

Abbreviations: EVT, endovascular therapy.
[a]Continuous data are presented as the mean ± standard deviation (range); categorical data are given as the number (percentage).
[b]All 255 patients received FLEX treatment; however, only 245 patients had available post-FLEX percent stenosis measurements.
[c]Lumen gain = baseline stenosis − post-FLEX stenosis.
[d]Reduction in stenosis considers final stenosis relative to original stenosis, calculated as [(baseline stenosis − post-FLEX stenosis) ÷ baseline stenosis].
[e]Post-EVT measurements were recorded after angioplasty and provisional stenting.

Continuous data are presented as the mean ± standard deviation; categorical data are given as the number/sample (percentage). Data were site-reported and not adjudicated; missing data were not imputed. Simple and multiple linear regression analyses were conducted to determine whether any patient characteristics (female gender, age, US center, calcification, ISR, baseline stenosis, occlusion, lesion length, reference vessel diameter, lesion location) or procedure variables (opening balloon pressure, maximum inflation pressure, inflation time, number of FLEX passes, post-FLEX stenosis, type of EVT, dissection) were significantly associated with post-FLEX reduction in stenosis. Variables achieving $p<0.15$ in the univariate analysis were entered into the multivariate model. Results are presented as the coefficient of determination (R^2). A positive regression coefficient indicated a positive linear relationship between the independent variable and the dependent outcome of interest (post-FLEX reduction in stenosis).

Exploratory correlation analyses were performed to assess whether relationships existed between those variables identified in linear regression analyses as possible predictors for post-FLEX stenosis reduction with subsequent angioplasty procedure characteristics and outcomes. Strength of the correlation was per established standards, with correlation coefficients (r) ≥0.3 (or less than −0.3) as the threshold for a weak correlative relationship.[29]

Binary logistic regression analyses were conducted to determine which, if any, variables were associated with a need for provisional stenting. Variables achieving $p<0.15$ were entered into the multivariate analysis. Results are presented as the odds ratio with 95% confidence interval (CI). The threshold of statistical significance was $p<0.05$. Analyses were conducted using SPSS software (version 22; IBM Corporation, Armonk, NY, USA).

Results

The average number of passes with the FLEX System was 3.5±1 (range 1–8); 4 (34.1%) passes were most common, followed by 3 (29.0%) passes. Following use of the FLEX device, the average stenosis was reduced from 91.9%±10.5% at baseline to 66.7%±17.3% (Table 2). Average lumen gain following FLEX usage was 25.2%±16.4%. Representative pre-, peri-, and post-FLEX angiographic images are displayed in Figure 3.

All patients underwent conventional and/or DCB angioplasty after FLEX passage; provisional stenting was performed in 49 (19.2%) patients. Average opening and maximum balloon pressures were 4.2±1.5 and 9.2±2.7 atms, respectively (Table 3). Average inflation time was 3.1±2.4 minutes. After EVT, the average stenosis was 9.1%±7.4% (Table 2). Nine (3.6%) patients had significant residual stenosis ≥30%. From baseline to after EVT, the average reduction in stenosis was 90%±8%.

Minor dissections occurred in 15 (6.0%) of 250 patients for whom this outcome was available. Of these, 12 were type A (minor radiolucent areas) and 3 were type B (radiolucent luminal flap parallel to the vessel wall). No flow-limiting dissections, vessel perforations, or embolizations occurred.

Regression and Correlation Analyses

Univariate linear regression analyses were performed to assess the relationship of baseline and FLEX procedure variables with post-FLEX reduction in stenosis (Table 4). Of those variables tested, only patient age was found to be significantly related to a reduction in stenosis following FLEX usage ($p=0.01$). Older patients showed slightly less relative lumen gain with each additional year of age.

Correlation analyses were performed to determine whether post-FLEX reduction in stenosis or patient age was correlated with angioplasty balloon pressures or post-EVT reduction in stenosis. Negligible relationships were identified in all analyses but one. The only significant relationship identified ($r = -0.25$) found that post-FLEX reduction in stenosis was significantly correlated with maximum balloon pressure; that is, patients exhibiting greater reduction

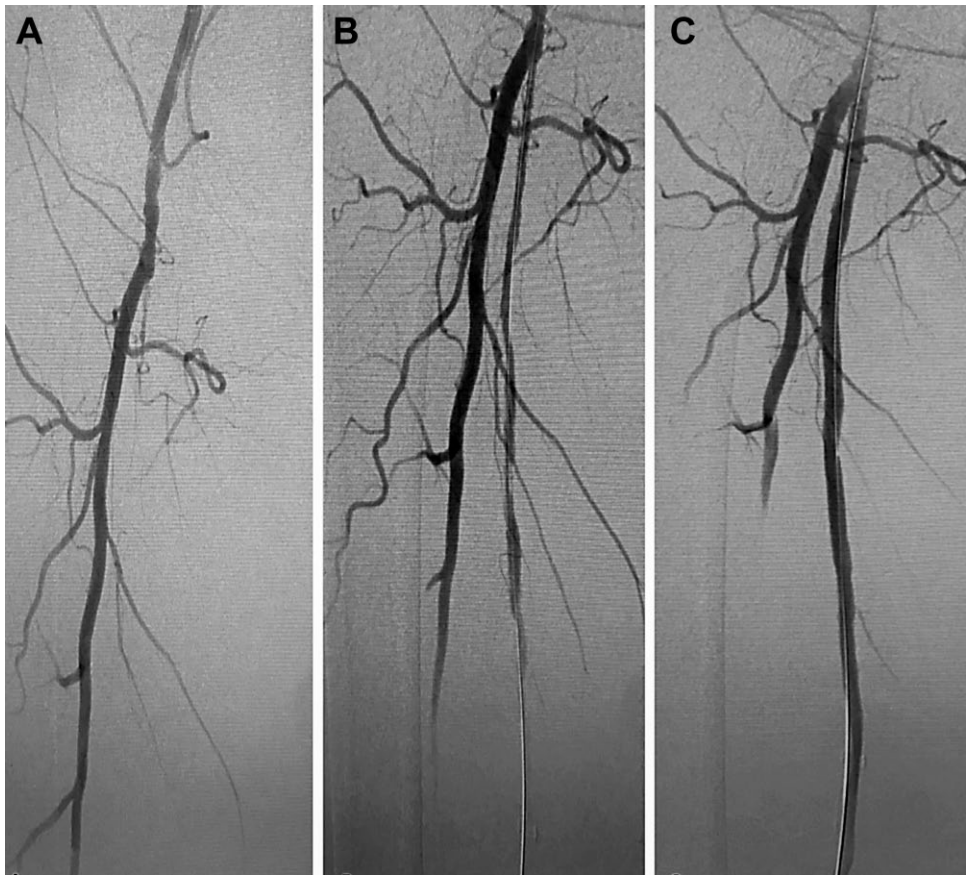

Figure 3. (A) Initial angiogram revealed a long superficial femoral artery chronic total occlusion. (B) Recanalization after FLEX VP System use only. (C) Final angiographic result after drug-coated balloon angioplasty.

Table 3. Post-FLEX Angioplasty and Provisional Stenting Characteristics.

Post-FLEX therapy	
Conventional balloon alone	45/250 (18.0)
DCB alone	90/250 (36.0)
Conventional balloon and DCB	67/250 (26.8)
Conventional balloon and stenting	21/250 (8.4)
DCB and stenting	7/250 (2.8)
Conventional balloon, DCB, and stenting	20/250 (8.0)
Balloon size, mm (n=255)	5.3±0.9 (3–8)
Opening pressure, atm (n=223)	4.2±1.5 (2–12)
Maximum pressure, atm (n=216)	9.2±2.7 (3–18)
Inflation time, min (n=210)	3.1±2.4 (0–15)
Provisional stenting	49/255 (19.2)
Stents per patient	1.4±0.8 (1–4)
Stent diameter, mm	5.8±0.8 (5–8)
Vessel location	
SFA	45/49 (91.8)
Popliteal	3/49 (6.1)
Iliac	1/49 (2.0)

Abbreviations: DCB, drug-coated balloon; SFA, superficial femoral artery. Continuous data are presented as the mean ± standard deviation; categorical data are given as the number/sample (percentage).

in vessel stenosis following use of the FLEX VP System (ie, greater lumen gain) underwent angioplasty with lower maximum balloon pressures ($p<0.001$).

Stenting Subset Analyses

Of the 49 patients who underwent provisional stenting, 21 had undergone conventional balloon angioplasty only, while 20 underwent angioplasty with conventional and DCB balloons and 7 had angioplasty with DCBs alone. The binary logistic regression analyses identified 6 variables in univariate analyses as possible factors (Table 5). In a multivariate model, the most significant predictor of provisional stenting was whether patients underwent conventional balloon angioplasty as opposed to plain + DCB or solely DCB angioplasty. Patients receiving conventional balloon dilation alone were 4.4 times more likely to undergo stenting ($p=0.001$). Patients who experienced minor dissections were 7.2 times more likely to undergo stenting ($p=0.011$). Longer lesions were more likely to be stented. For each millimeter increase in lesion length, patients were 1.005 times

Table 4. Univariate Linear Regression Analysis to Identify Any Relationship Between Patient and Procedure Variables and Post-FLEX Reduction in Stenosis.

Variable	Coefficient[a]	SE	R^2	p
Female sex	−0.03	0.02	0.008	0.18
Age	−0.004	0.001	0.04	0.01
US center[b]	−0.06	0.04	0.008	0.16
Calcification (continuous)[c]	0.01	0.01	0.006	0.23
Severe calcification	0.03	0.03	0.004	0.33
In-stent restenosis	−0.02	0.04	0.001	0.64
Baseline stenosis	0.001	0.001	0.002	0.48
Occlusion	0.02	0.02	0.002	0.48
Lesion length	<0.001	<0.001	0.003	0.97
Vessel diameter	−0.01	0.01	0.004	0.35
Treated vessel				
SFA	−0.01	0.03	0.001	0.67
Popliteal	−0.005	0.04	<0.001	0.89
Other ATK vessels	0.04	0.08	0.001	0.57
Other BTK vessels	0.02	0.04	0.001	0.63
Number of passes with FLEX	0.005	0.009	0.001	0.58

Abbreviations: ATK, above the knee; BTK, below the knee; R^2, coefficient of determination; SE, standard error; SFA, superficial femoral artery; US, United States.
[a]A positive regression coefficient indicates a positive linear relationship between the independent baseline variable and the dependent outcome of interest (post-FLEX reduction in stenosis). Possible predictors were entered into a multivariate model using a cutoff criterion of p<0.15.
[b]Center location was a binary variable in which US was coded as "1". The negative coefficient indicates that patients treated in Europe had greater reduction in stenosis than patients treated in the US.
[c]Univariate regression was run with calcification as a continuous variable in which 0 = no calcification, 1 = mild calcification, 2 = moderate calcification, and 3 = severe calcification.

more likely to receive stenting (p=0.03). A longer balloon inflation time was also found to be associated with a lower risk for stenting, though not to a significant degree (p=0.13).

Discussion

In this retrospective review of a real-world multicenter experience with a vessel preparation device, the FLEX VP System was associated with substantial lumen gain (25% on average) prior to angioplasty. Subsequent dilation was performed at low balloon pressures with no major complications and a low rate of provisional stenting.

Unlike cutting balloons, the FLEX VP System is a non-balloon-based, one-size-fits-all device designed to treat femoropopliteal lesions. Whereas the average lesion length in published reports with cutting balloons ranges from 19 to 34 mm,[25,30,31] treated lesions in the FLEX series were very long, at an average 133 mm. This was a real-world experience in which three-quarters of patients presented with long, heavily calcified, and/or occlusive lesions. In our analyses of factors related to reduction in vessel stenosis following FLEX usage (a surrogate of FLEX technical success), the length of the lesion had no discernible effect on outcome; similarly, the degree of obstruction and calcification did not affect post-FLEX results. These findings suggest that the FLEX System performs equally well irrespective of lesion length, degree of stenosis, or calcium burden. The only predictor for FLEX outcome was age, with slightly less relative lumen gain observed as patient age increased.

There are several different specialty balloons for plaque modification currently marketed for and utilized in the lower extremities. Results with the Cutting Balloon[30,31] (Boston Scientific, Marlborough, MA, USA), AngioSculpt (Spectranetics, Colorado Springs, CO, USA),[25,32,33] and Serranator[34] (Cagent Vascular, Wayne, PA, USA) have shown greatly reduced rates of vessel complications during angioplasty and promising short-term outcomes. However, the Cutting Balloon, initially engineered for the coronary indication, is difficult to utilize in the longer lesions common in the femoropopliteal segment because the 20-mm balloon requires multiple inflation cycles.

Vessel preparation may be particularly beneficial for DCBs, and the high rate of DCB usage in our series (74%) illustrates that interventionists utilize the FLEX as vessel preparation, with 39% transitioning directly from the FLEX to DCB usage. With unmodified plaque, the benefit of costly DCBs is mitigated by the possibility that the drug does not adequately permeate into vessel walls and arrest the inflammatory responses that lead to neointimal hyperplasia and restenosis. For DCBs, vessel preparation has the potential effect of creating more surface area for drug absorption. Further study is required as to whether vessel preparation actually results in later clinical benefit for DCBs. Currently, the immediate benefit of DCBs following FLEX usage was suggested by our analyses of factors related to provisional stenting. Those patients who received solely conventional balloon dilation were significantly more likely to require stenting; this was the most significant predictor for provisional stenting our analyses identified.

In our series, 19% of patients underwent provisional stenting at the operator's discretion. This is substantially lower than rates in the recent Zilver PTX,[35] RESILIENT,[15] and ETAP[36] randomized controlled trials, in which patients randomized to receive angioplasty and provisional stenting underwent stenting at rates of 50%, 40%, and 28%, respectively. Furthermore, this low rate in our current series was observed not in a clinical trial cohort but a real-world population with no anatomic exclusion criteria applied; 75% of patients presented with a CTO, lesion length ≥100 mm, and/or severe calcification, in short, a population more likely to undergo provisional stenting. After review of the case forms, it is unknown whether stenting was chosen due to residual stenosis, to improve a "cosmetic" angiographic result, or due to a general perception that stents improve

Table 5. Univariate and Multivariate Logistic Regression to Assess Predictors of Provisional Stenting.

Variable	Coefficient[a]	SE	Odds Ratio (95% CI)	p
Univariate analysis				
Age	−0.02	0.03	0.98 (0.93 to 1.03)	0.39
Female sex	0.17	0.38	1.2 (0.56 to 2.49)	0.66
Calcification (continuous)	−0.12	0.18	0.89 (0.62 to 1.27)	0.51
Severe calcification	0.09	0.42	1.09 (0.48 to 2.49)	0.84
In-stent restenosis	−0.60	0.77	0.55 (0.12 to 2.51)	0.44
Baseline stenosis	0.02	0.02	1.02 (0.99 to 1.06)	0.22
Lesion length	0.005	0.002	1.005 (1.001 to 1.009)	0.02
Number of passes with FLEX	−0.05	0.14	0.96 (0.72 to 1.27)	0.75
Post-FLEX stenosis	0.003	0.01	1.003 (0.98 to 1.03)	0.75
Post-FLEX reduction in stenosis	0.12	1.10	1.12 (0.13 to 9.9)	0.91
DCB alone	−1.60	0.47	0.20 (0.08 to 0.51)	0.001
Conventional balloon dilation alone	1.57	0.38	4.8 (2.3 to 10.1)	<0.001
Conventional balloon + DCB	−0.009	0.37	0.99 (0.48 to 2.05)	0.98
Opening pressure	0.10	0.13	1.1 (0.86 to 1.42)	0.43
Maximum pressure	0.03	0.08	1.03 (0.88 to 1.2)	0.70
Inflation time	−0.21	0.14	0.81 (0.62 to 1.06)	0.13
Dissection	1.31	0.70	3.7 (0.95 to 14.51)	0.06
Multivariate analysis[b]				
Conventional balloon dilation	1.49	0.47	4.4 (1.8 to 11.1)	0.001
Minor dissection[c]	1.97	0.78	7.2 (1.6 to 33.2)	0.011
Lesion length	0.005	0.002	1.0 (1.0 to 1.0)[b]	0.03
Inflation time	−0.20	0.13	0.82 (0.6 to 1.1)	0.13

Abbreviations: CI, confidence interval; DCB, drug-coated balloon.

[a]To limit the possibility of confounding variables, analyses were restricted to patients in the United States treated for femoropopliteal lesions. A positive regression coefficient indicates a positive relationship between the independent baseline variable and the binary outcome of interest. A positive coefficient for a categorical variable indicates that event of interest (provisional stenting) is more likely with exposure to the predictor variable (eg, female gender). Conversely, a negative coefficient indicates that provisional stenting is less likely with exposure to the predictor variable. For example, patients treated solely with DCBs are less likely to receive stenting than those who received other endovascular treatment (ie, solely conventional balloons or conventional balloons *and* DCBs).

[b]All variables identified as possible predictors in univariate analyses ($p<0.15$) were entered into a multivariate model. Use of DCBs alone and center experience were both removed from the model in backwards stepwise regression.

[c]All 15 (6%) dissections observed in this series were minor (12 type A and 3 type B).

long-term outcomes in longer lesions. Comparatively, in the MASCOT pivotal trial evaluating AngioSculpt,[37] the stent rate was 46%. A more contemporary study involving the use of the Chocolate balloon in femoropopliteal disease cites low rates of dissection (22.5%) and bailout stenting (1.6%), but the lesion lengths were only 83.5 mm on average, with fewer CTOs (23.1%).[38]

Not surprisingly, dissection was associated with a heightened risk for provisional stenting. Historically, the rate of flow-limiting dissection during balloon dilation of peripheral arteries has been high. In a large 2017 analysis, Fujihara et al[16] found that provisional stenting for flow-limiting dissections or residual stenoses >30% occurred in 74% of cases, with over 40% exhibiting severe dissections and 13% exhibiting flow-limiting dissections. No flow-limiting dissection, perforation, or embolization was observed in our series. The mechanism of action of the expanded FLEX treatment element is that it provides a low-force "predilation" of the stenosis prior to balloon angioplasty, which may be the reason behind the low rate of dissections. The FLEX utilizes a non-balloon-based mechanism and therefore can theoretically avoid complications of balloon-based devices such as edge dissections (at the balloon shoulders) and dissections that may occur when supranominal pressures are applied. Outcomes in this study and recent reports with cutting balloons suggest that vessel preparation enhances vessel compliance, enabling lowered balloon pressures and reducing or eliminating the risk of vessel complications.[16,30] Average opening balloon pressure in our series was 4.2 atm and maximum pressure was 9.2 atm; the latter is substantially lower than average pressures in standard angioplasty but in line with maximum pressures associated with available cutting balloons, which have reported similarly reduced or nonexistent serious vessel complications.[26,30] A significant relationship was observed between stenosis reduction after FLEX usage and maximum balloon pressures, with those patients exhibiting greater reduction in stenoses from use of the FLEX VP System subsequently undergoing angioplasty with lower

maximum balloon pressures. A longer inflation time was associated with a reduced risk for stenting, though this was not a significant factor. Zorger et al[39] found that a longer inflation time was associated with improved angioplasty outcome and reduced complications.

Patients with longer lesions were more likely to undergo stenting, though the elevated risk was not extreme or very significant. Calcification and degree of obstruction appeared to have negligible impact on acute outcome; however, it will be critical to assess whether late outcomes will be independent of these well-known risk factors. An analyses by Shammas et al[14] found that the presence of calcification was the most significant factor predictive of provisional stenting following PTA. Six months after treatment of femoropopliteal lesions with DCBs, Tepe et al[40] found that degree of calcification was directly correlated with late lumen loss, with the authors suggesting that vessel preparation to alter or excise plaque may be essential if DCB treatment is to be effective. In our series, severity of baseline obstruction and even severe calcification had no impact on whether provisional stenting was performed. These findings raise the question of whether FLEX may alter the mechanical properties of the vessel, at least in part protecting against the poorer results in calcified and high-grade lesions.

Limitations

The study was limited by its retrospective design and the lack of a control arm. All imaging and data from this real-world experience were site reported, without core laboratory assessment. Estimation of severity of stenoses and calcification was at the discretion of the interventionist. A lack of baseline clinical metrics to delineate the severity of PAD in this patient population was a significant limitation.

The outcome of our analysis indicating that patients undergoing solely conventional balloon dilation (as opposed to DCBs) were more likely to receive stenting must be viewed in the context that some interventionists may have approached angioplasty with an expectation that stenting was likely. As such, they may have selected the less expensive conventional balloon as opposed to a DCB. It is impossible to determine to what extent this influenced the choice of conventional balloon angioplasty vs DCB across the series.

Conclusion

This retrospective analysis suggests that the FLEX VP System may improve acute outcomes achieved with conventional and DCB angioplasty. Vessel preparation facilitated significant predilation lumen gain, and subsequent angioplasty resulted in satisfactory outcome for a majority of patients, with a low rate of provisional stenting and no serious vessel complications. Average opening balloon pressures were low in our series, a possible surrogate of enhanced vessel compliance following FLEX usage. These outcomes were observed in a real-world patient population in which a majority presented with heavily calcified, long, and/or occluded lesions. Further studies with a control arm are warranted.

Declaration of Conflicting Interests

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