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One-Year Outcomes Following Directional Atherectomy of Popliteal Artery Lesions: Subgroup Analysis of the Prospective, Multicenter DEFINITIVE LE Trial

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Abstract

Purpose: To report the effectiveness of directional atherectomy for the treatment of popliteal artery occlusive disease. **Methods:** This subset of the prospective, multicenter, single-arm DEFINITIVE LE trial included 158 patients (mean age 72.0±10.9 years; 82 men) who underwent directional atherectomy in 162 popliteal artery lesions between 2009 and 2011. Forty-eight (30.4%) patients were suffering from critical limb ischemia (CLI). The mean lesion length was 5.8±3.9 cm; 38 (23.5%) arteries were occluded. The primary outcome measure for patients with intermittent claudication (IC) was duplex ultrasound–defined primary patency at 1 year; the outcome for subjects with CLI was freedom from major amputation of the target limb at 1 year. Outcomes and adverse events were independently assessed. **Results:** Procedure success (≤30% residual stenosis) was achieved in 84.4% of treated lesions; adjunctive stenting was required in 6 (3.7%) of the 162 lesions. The 1-year primary patency rate was 75.0% (IC patients 78.2% and CLI patients 67.5%, p=0.118). The freedom from major amputation in both cohorts was 100%. In both IC and CLI patients, significant improvements were demonstrated at 1 year in the Rutherford category, walking distance, and quality of life in comparison to baseline. **Conclusion:** This study indicates that directional atherectomy in popliteal arteries leads to favorable technical and clinical results at 1 year for claudicant as well as CLI patients.

Keywords

amputation, angioplasty, atherectomy, claudication, critical limb ischemia, patency, peripheral artery disease, popliteal artery, stent

Introduction

For patients with symptomatic peripheral artery disease (PAD) refractory to medical and exercise therapy, endovascular intervention is the most frequently recommended course of treatment.[1–3] Randomized trials have established that drug-coated balloons (DCBs), nitinol stents, and drug-eluting stents (DES) are superior to conventional percutaneous transluminal angioplasty (PTA) when treating the superficial femoral artery (SFA) and proximal popliteal artery disease, as demonstrated by lower target lesion revascularization (TLR) rates, improved patency, and clinical improvement.[4–6] However, only 1 randomized, multicenter trial has provided 1-year results after endovascular therapy of isolated popliteal lesions beyond the proximal (P1) segment.[7] In this trial, there was no significant difference

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between primary patency and clinical improvement at 1 year when comparing treatment with PTA and provisional stenting vs primary stenting alone in popliteal artery lesions.

The popliteal artery is subject to significant deformation and biomechanical stress as the knee is flexed, and the clinical implications of these physiologic stresses are not well understood.[8,9] Short-term fracture rates reported for second-generation standard nitinol stents and biomimetic stents in the popliteal artery range from 3.4% to 7% at 12 months following implantation.[7,10–12] However, the link between stent fracture and restenosis is not well characterized, and as such, it is reasonable to avoid primary stent use in the popliteal location.

Percutaneous removal of atherosclerotic plaque through directional atherectomy represents a potential approach to avoid a permanent metal implant. Treatment of infrainguinal lesions using directional atherectomy has been reported to be safe and effective in patients with intermittent claudication (IC) and critical limb ischemia (CLI) in many single-arm studies.[13–17] However, data from larger prospective and independently assessed trials that include CLI patients have been missing. To address this gap, the 1-year outcomes following directional atherectomy in popliteal artery lesions are presented here as a subgroup analysis of the DEFINITIVE LE trial.

Methods

Patient Selection and Study Design

The DEFINITIVE LE trial[18] [Determination of EFfectiveness of the SilverHawk PerIpheral Plaque ExcisioN System (SilverHawk Device) for the Treatment of Infrainguinal VEssels / Lower Extremities] was a prospective, multicenter, single-arm study conducted at 47 medical centers in the United States and Europe in accord with the principles of the Declaration of Helsinki. The study protocol was approved by the ethics committee at each participating institution, and each patient gave written informed consent. An independent Clinical Events Committee (CEC) adjudicated all major adverse events, and core laboratories provided independent analyses for all scheduled and unscheduled duplex ultrasound and angiographic data [VasCore (Massachusetts General Hospital, Boston, MA, USA) and SynvaCor (Springfield, IL, USA), respectively]. Patients were eligible for the study if they were at least 18 years old and suffered from PAD with Rutherford category (RC) ischemia ranging from 1 to 6.

Major exclusion criteria were the presence of severe calcification in the target lesion (defined as radiopacities >1 cm in length on both sides of the arterial wall prior to contrast injection or digital subtraction angiography), in-stent stenosis, previous surgical bypass affecting the target limb, previous amputation above the metatarsal line on the target limb, known systemic coagulopathy, end-stage renal disease requiring hemodialysis for kidney failure, life expectancy <12 months, intolerance to aspirin, clopidogrel, and heparin, and any other factors making follow-up impossible.

Angiographic eligibility for the popliteal artery subcohort required the presence of a de novo or restenotic target lesion (occlusion or stenosis) beginning in the proximal popliteal artery (reference vessel diameter ≥4 and <7 mm) with ≥50% stenosis estimated by angiography. As such, no lesions reported in this study were contiguous with the SFA; however, some lesions encompassed the proximal tibial circulation. According to these parameters, 158 patients (mean age 72.0±10.9 years; 82 men) with 162 popliteal artery lesions qualified for this subgroup analysis. The majority of patients (110, 69.6%) had IC. The comorbidities (Table 1) and lesion characteristics (Table 2) were similar in the IC and CLI cohorts with the exception of diabetes, which was more common in the CLI patients (Table 1). Of the patients with IC, the majority had RC 3 ischemia (71, 64.5%), whereas three-quarters of the CLI patients (36, 75%) had ischemic wounds (RC categories 5/6). Overall, the mean lesion length was 5.8±3.9 cm, with about half the lesions (80, 49.4%) ranging from 4.0 and 9.9 cm; 59 (36.4%) lesions were >10 cm.

Device Description

There were 2 study devices: the SilverHawk and TurboHawk atherectomy catheters (Medtronic, Minneapolis, MN, USA). This single patient use system is designed for the treatment of de novo or restenotic atherosclerotic lesions located in native peripheral arteries. The atherectomy catheter consists of a flexible shaft designed to track over a 0.014-inch guidewire. At the distal end of the device is a small cutting assembly comprised of a rotating inner blade contained within a tubular housing. The proximal end of the catheter contains a connector and positioning lever designed to fit into a small, disposable battery-driven cutter driver, which powers the device. Prior to the initiation of the study, SilverHawk and TurboHawk atherectomy catheters were cleared for commercial use by the Food and Drug Administration and the European Union.

Study Procedures

Arterial access site selection, placement of the introducer sheath, and the initial heparin dose were at the discretion of the investigator. Angiographic images, including runoff circulation, were obtained immediately prior to the procedure. A radiopaque ruler was used to define lesion length and anatomic measurement references. Significant stenosis of the inflow arteries had to be treated successfully prior to enrollment, which occurred when an exchangeable guidewire crossed the most proximal target lesion. Predilation

Table 1. Baseline Patient Characteristics.[a]

Variables	Total (n=158)	Claudicants (n=110)	CLI (n=48)	p
Age, y	72.0±10.9 (158)	72.1±10.7 (110)	71.9±11.5 (48)	0.934
Men	82/158 (51.9)	56/110 (50.9)	26/48 (54.2)	0.732
History/risk factors				
Diabetes	83/158 (52.5)	49/110 (44.5)	34/48 (70.8)	0.003
CHF	20/158 (12.7)	12/110 (10.9)	8/48 (16.7)	0.311
CAD	57/158 (36.1)	40/110 (36.4)	17/48 (35.4)	>0.99
Stroke	15/158 (9.5)	12/110 (10.9)	3/48 (6.3)	0.555
MI	22/158 (13.9)	17/110 (15.5)	5/48 (10.4)	0.436
CABG or PCI	61/158 (38.6)	40/110 (36.4)	21/48 (43.8)	0.381
Hypertension	150/158 (94.9)	106/110 (96.4)	44/48 (91.7)	0.246
Hyperlipidemia	136/158 (86.1)	98/110 (89.1)	38/48 (79.2)	0.132
ESRD requiring HD	36/158 (22.8)	22/110 (20.0)	14/48 (29.2)	0.220
Nonhealing ulcers	38/158 (24.1)	3/110 (2.7)	35/48 (72.9)	<0.001
Current tobacco use	28/158 (17.7)	22/110 (20.0)	6/48 (12.5)	0.365
Rutherford category				<0.001
1. Mild claudication	6/158 (3.8)	6/110 (5.5)	0/48 (0.0)	
2. Moderate claudication	33/158 (20.9)	33/110 (30.0)	0/48 (0.0)	
3. Severe claudication	71/110 (44.9)	71/110 (64.5)	0/48 (0.0)	
4. Rest pain	12/158 (7.6)	0/110 (0.0)	12/48 (25.0)	
5. Minor tissue loss	30/158 (19.0)	0/75 (0.0)	30/48 (62.5)	
6. Major tissue loss	6/158 (3.8)	0/75 (0.0)	6/48 (12.5)	

Abbreviations: CABG, coronary artery bypass graft; CAD, coronary artery disease; CHF, congestive heart failure; CLI, critical limb ischemia; ESRD, end-stage renal disease; HD, hemodialysis; MI, myocardial infarction; PCI, percutaneous coronary intervention.
[a]Continuous data are presented as the means ± standard deviation (N); categorical data are given as the counts/sample (percentage).

Table 2. Lesion Characteristics.[a]

Variables	Total (n=162)	Claudicants (n=114)	CLI (n=48)	p
De novo lesion (site assessed)	149/162 (92.0)	105/114 (92.1)	44/48 (91.7)	>0.99
Lesion length, cm	5.8±3.9	6.0±4.0	5.4±3.6	0.410
≥10.0	23/162 (14.2)	18/114 (15.8)	5/48 (10.4)	0.464
4.0–9.9	80/162 (49.4)	55/114 (48.2)	25/48 (52.1)	0.731
<4	59/162 (36.4)	41/114 (36.0)	18/48 (37.5)	0.859
Baseline stenosis[b]	76.2±18.2 (162)	75.8±17.5 (114)	77.1±19.9 (48)	0.688
Occlusions	38/162 (23.5)	24/114 (21.1)	14/48 (29.9)	0.311
Calcification[b]				
None	117/162 (72.2)	84/114 (73.7)	33/48 (68.8)	0.566
Present or severe	45/162 (27.8)	30/114 (26.3)	15/48 (31.3)	0.566
Severe	8/162 (4.9)	6/114 (5.3)	2/48 (4.2)	>0.99

Abbreviation: CLI, critical limb ischemia.
[a]Continuous data are presented as the means ± standard deviation (N); categorical data are given as the counts/sample (percentage).
[b]Some data are missing as the quality of the captured procedural images was not analyzable by the core laboratory.

was permitted when the atherectomy catheter was unable to cross a lesion. The selection of the atherectomy model, as well as the use of distal protection devices, was at the discretion of the treating physician. In the event of major flow-limiting dissection, perforation, occlusive complication (ie, recoil), or residual stenosis >30% of the target lesion following atherectomy, adjunctive endovascular procedures were allowed. A final angiogram of the target lesion and runoff was captured following all adjunctive procedures (if required). Angiographic results were evaluated by the independent angiographic core laboratory. It was recommended that all subjects receive pre- and postprocedure antiplatelet or antithrombotic therapy as suggested by current guidelines.[1,2]

Follow-up Evaluations

The preintervention evaluation and follow-up visits at 1, 3, 6, and 12 months included clinical examination, calculation of the ankle-brachial index (ABI), determination of the stage of disease according to the RC, target lesion evaluation by duplex (not required at 3 months), quality of life measurements using the EuroQOL 5 Domains (EQ-5D) tool, the Walking Impairment Questionnaire (WIQ) in claudicant patients or wound assessment as applicable in CLI patients, and adverse event evaluation.

Study Endpoints

For subjects with IC (RC 1–3) at baseline, the primary outcome measure was primary patency at 12 months. This was predefined at the beginning of the study based on a duplex-derived peak systolic velocity ratio (PSVR) ≤3.5 at the target lesion with no clinically-driven TLR (CD-TLR). However, this value was less relevant clinically than the now-established ≤2.4 PSVR for restenosis,[19] so all patency values reported in this study are based on a ≤2.4 PSVR. For patients with CLI (RC 4–6) at baseline, the primary endpoint was major unplanned amputation of the target limb at 1 year. Patency using the PSVR as a binary cutpoint was also a secondary outcome in the CLI cohort.

Secondary outcomes included device success (defined as ≤30% residual stenosis following atherectomy as assessed by the angiographic core laboratory and without adjunctive endovascular interventions), secondary patency rate (defined as patency at 1 year following successful TLR), the limb salvage rate at 1 year for the entire cohort, and changes in ABI, RC category, the EQ-5D assessment. Changes in the WIQ scores were assessed for the IC cohort only; for the CLI cohort, an additional secondary outcome was wound healing at 3 months (defined as a decrease of at least one Wagner class grade).

Death, major unplanned amputation of the target limb, and clinically-driven target vessel revascularization (CD-TVR) were defined as major adverse events (MAEs). All major events were determined cumulatively for the 365 days after the index procedure and adjudicated by the independent CEC.

Statistical Analysis

Continuous data were expressed as mean ± standard deviation. Categorical variables were expressed as counts and percentage. Statistical comparisons were performed using the Fisher exact test for categorical data and the Student *t* test for continuous variables. Changes in RC were expressed as the mean (range); comparisons were evaluated using the Wilcoxon signed-rank test. Time-to-event estimates were calculated using the Kaplan-Meier method; groups were compared using the Mantel-Cox log-rank test. The survival analyses for patency and freedom from CD-TLR were based on the number of lesions, while the freedom from MAE was patient based.

The effect of covariates on procedure success was explored using multivariate logistic regression analysis, while their influence on primary patency was tested in Cox proportional hazards models. The significance level for entry of independent variables from the univariate model into the multivariate model was 0.1. The explanatory covariates included gender, age, diabetes, arrhythmia, hypertension, hyperlipidemia, end-stage renal disease requiring hemodialysis, smoking within the past 10 years, IC vs CLI status, lesion length, occluded vs stenosed lesions, reference vessel diameter, calcification, and the TransAtlantic Inter-Society Consensus classification. Results are presented as the odds ratio (OR) or hazard ratio (HR), as appropriate, with 95% confidence intervals (CI). All tests were 2-sided, and $p<0.05$ were deemed statistically significant. All statistical analyses were performed using SAS for Windows (version 9.1 or higher; SAS Institute Inc, Cary, NC, USA).

Results

Acute Outcomes

Device success was achieved in 71.1% of all lesions and did not differ significantly between the IC and CLI cohorts (71.2% vs 70.8%; Table 3). Distal embolic protection via a filter device was used at the discretion of the investigator in 42 (26.6%) subjects. Predilation of the target lesion to allow passage of the atherectomy device was performed in 9 (7.9%) IC and 9 (8.8%) CLI patients (p=0.057). After atherectomy, adjunctive therapy was performed in 63 (38.9%) target lesions, with the majority receiving postdilation (56/162, 34.6%). The adjunctive stent rate was 3.7% (n=6). A total of 33 (20.3%) patients were treated for at least 1 inflow lesion during the index procedure. The majority of treated inflow lesions were in the SFA (28, 77.8%), followed by the iliac (5, 13.8%) and common femoral (3, 8.4%) arteries.

Procedure success, defined as ≤30% residual stenosis adjudicated by the angiographic core laboratory, was achieved in 84.4% of target lesions (87.5% for the IC group vs 77.1% for the CLI group; p=0.10; Table 3). The 23 (15.6%) subjects failing to achieve success had >30% residual stenosis at the end of the procedure.

Periprocedural adverse events were noted in 21 (13.3%) patients (Table 4). Of the 7 (4.4%) patients with an arterial perforation, 2 (1.3%) patients had additional PTA, 4 (2.5%) patients had stenting, and 1 (0.6%) patient had a surgical intervention of the target lesion. Abrupt closure occurred in 4 (2.5%) patients, distal embolization in 9 (5.7%), and flow-limiting dissections in 3 (1.9%) subjects. All events were

Table 3. Procedure Data.[a]

Variables	Total (n=158)	Claudicants (n=110)	CLI (n=48)	p
Procedure time, min	76.4±38 (158)	69.9±36 (110)	91.3±39 (48)	<0.001
Fluoroscopy time, min	20.6±13 (158)	18.5±11 (110)	25.8±17 (48)	0.002
Contrast volume, mL[b]	154.8±86 (157)	152.0±82 (109)	161.0±95 (48)	0.546
Use of embolic protection	42/158 (26.6)	29/110 (26.4)	13/48 (27.1)	>0.99
Device success[b,c]	113/158 (71.1)	79/110 (71.2)	34/48 (70.8)	>0.99
Post-device stenosis, %[b,c]	25.6±15 (158)	26.3±14 (110)	23.9±17 (48)	0.344
Procedure success[b,c]	135/158 (84.4)	98/110 (87.5)	37/48 (77.1)	0.102
Postprocedure stenosis, %[b,c]	19.6±11 (158)	19.7±11 (110)	19.3±13 (48)	0.828

Abbreviation: CLI, critical limb ischemia.
[a]Continuous data are presented as the means ± standard deviation (N); categorical data are given as the counts/sample (percentage).
[b]Missing data were either not reported by the site or not analyzable by the core laboratory.
[c]As assessed by the core laboratory.

Table 4. Events Within 30 Days.[a,b]

Event	Total (n=158)	Claudicants (n=110)	CLI (n=48)	p
Patients with at least 1 event	21 (13.3)	15 (13.6)	6 (12.5)	>0.99
Distal embolization	9 (5.7)	5 (4.5)	4 (8.3)	0.456
PTA required	3	2	1	
Abrupt closure	4 (2.5)	1 (0.9)	3 (6.3)	0.083
Surgery required	2	1	1	
Dissection (flow-limiting)	3 (1.9)	3 (2.7)	0	0.553
Stent required	2	2	0	
Perforation	7 (4.4)	7 (6.4)	0	0.102
PTA/stent/surgery required	2 / 4 / 1	2 / 4 / 1	0 / 0 / 0	

Abbreviations: CLI, critical limb ischemia; PTA, percutaneous transluminal angioplasty.
[a]Data are presented as the counts (percentage).
[b]Patients may have >1 event and appear in multiple rows.

adjudicated by the CEC and reviewed by the angiographic core laboratory.

Follow-up Outcomes

Follow-up compliance was 77.2% at 12 months: 122 patients (91 IC and 31 CLI) completed the study protocol, 26 (16.5%) withdrew, 6 (3.8%) were lost to follow-up, and 4 (2.5%) died (Figure 1).

At 1 year, primary patency overall was 75.0% (95% CI 66.9% to 81.5%); the rates were 78.2% (95% CI 68.7% to 85.1%) for the IC group and 67.5% (95% CI 50.2% to 79.9%) for the CLI group (p=0.118; Figure 2A). Secondary patency for the entire cohort was 93.2% [95.1% for the IC group (95% CI 88.5% to 97.9%) and 88.5% (95% CI 71.7% to 95.6%) for the CLI group; p=0.237]. Multivariate Cox regression analysis revealed smoking within the past 10 years as an independent predictor of primary patency (p=0.007; HR 0.434; 95% CI 0.250 to 0.751). Freedom from CD-TLR at 1 year was 78.8% overall, with 79.1% (95% CI 69.7% to 85.9%) for IC and 78.2% (95% CI 62.0% to 88.1%) for CLI (p=0.509; Figure 2B).

There were 4 deaths, 43 CD-TVRs, and no major amputations in any patient, so the primary outcome measure (freedom from major amputation) of the CLI cohort was 100%. Overall, the 1-year Kaplan-Meier freedom from MAE estimate was 70.1% (95% CI 61.9% to 76.9%), with 72.7% (95% CI 62.9% to 80.3%) for the IC cohort and 63.7% (95% CI 47.6% to 76.1%) for the CLI cohort (p=0.157; Figure 2C). None of the deaths was attributed to the study device or the index procedure by the CEC. Two deaths were due to cancer, while the others were from sepsis and an unrelated bleeding complication. Three of the 4 deaths occurred in the CLI cohort, for 1-year Kaplan-Meier survival estimates of 99.0 % (95% CI 93.2% to 99.9%) for the IC cohort, 93.4% (95% CI 81.0% to 97.8%) for the CLI cohort, and 97.3% (95% CI 93.0% to 99.0%) overall. The 1-year estimates for freedom from CD-TVR were 73.7% (95% CI 63.9% to 81.2%) for the IC patients and 66.9% (95% CI 50.4% to 79.0%) in the CLI cohort.

The mean Rutherford clinical category decreased from 3.3±1.2 at baseline to 1.2±1.4 at 1 year (p<0.001) with significant improvements seen in mean change from baseline for both the IC (–1.6±1.1) and CLI (–3.1±1.8) cohorts (Table 5). The proportion of patients with wounds in the

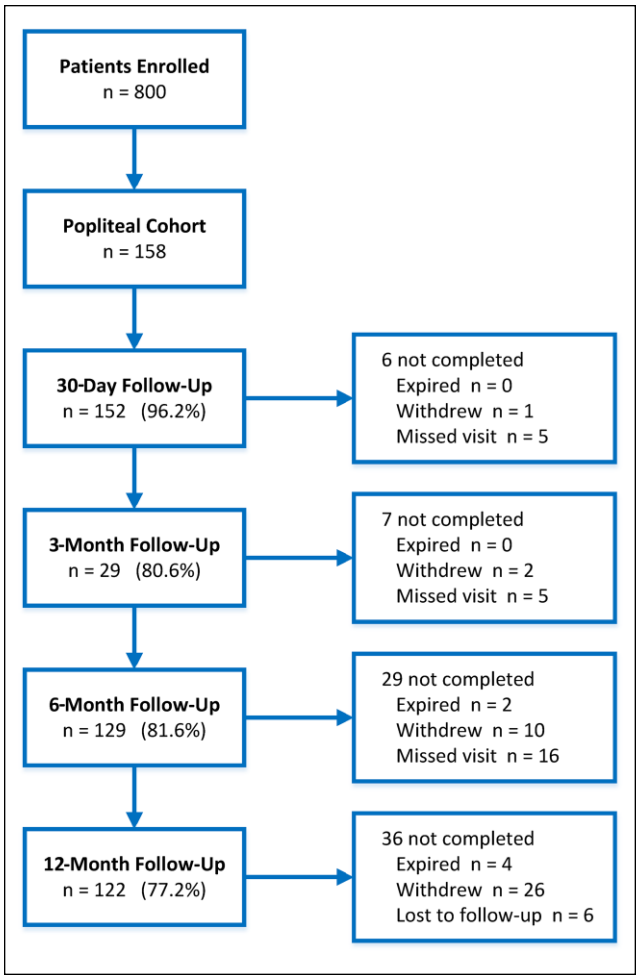

Figure 1. Study profile.

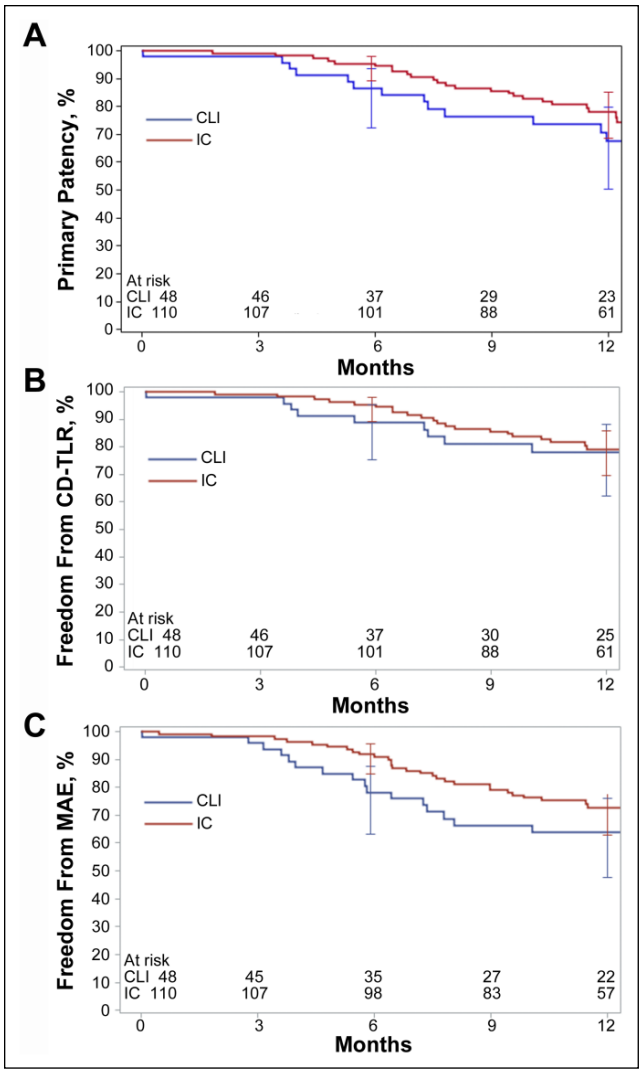

Figure 2. Kaplan-Meier analyses of (A) primary patency, (B) freedom from clinically-driven target lesion revascularization (CD-TLR), and (C) freedom from major adverse events (MAE).

CLI group decreased from 75% (36/48) at baseline to 22.6% (7/31; p<0.001). Mean ABIs improved from 0.7±0.3 at baseline to 0.9±0.2 at 1 year (p<0.001) and were significantly improved for both the IC and the CLI cohorts (+0.2±0.2 and +0.3±0.3, respectively; p<0.001). At 3 months, 57.1% of CLI patients had an improvement of at least 1 category based on their Wagner score.

Quality of life, as measured by the EQ-5D visual analog score, significantly increased from a mean of 64.1±20.1 at baseline to 72.3±17.7 at 1 year (p<0.001). Similarly, a significant improvement was seen in walking distance, as measured by the WIQ in the IC cohort only, with a mean score of 21.0±23.3 at baseline increasing to 48.7±39.2 at 1 year (p<0.001).

Discussion

To date, there are relatively few studies exclusively addressing endovascular treatment options for popliteal artery lesions.[7,10–12,20–25] This study was conducted to report the efficacy and short-term outcomes for directional atherectomy treatment of PAD in the popliteal artery of both IC and CLI patients. All outcomes were determined by independent core laboratories and events were adjudicated by an independent CEC. It is important to emphasize that the procedure success rate of 84.4% reported in this study is the result of a core laboratory analysis. This is in contrast to many studies that report success rates from the sites alone. Unfortunately, investigators often underestimate residual stenosis.

Prior to the DEFINITIVE LE study, Semaan et al[20] compared PTA and directional atherectomy in a retrospective, single-center review of 56 patients with popliteal lesions. Because of residual stenosis or flow-limiting dissection, bailout stenting was performed in 45% of patients treated with PTA compared to 6% of patients treated with directional atherectomy (p=0.005). One-year primary patency

Table 5. Functional Outcomes.[a]

	Total		Claudicants		CLI	
Variable	Baseline	1 Year	Baseline	1 Year	Baseline	1 Year
Rutherford category	3.3±1.2 (1 to 6)	1.2±1.4 (0 to 5) [–2.0±1.5 (–5 to 1)][b]	2.6±0.6 (1 to 3)	1.0±1.1 (0 to 4) [–1.6±1.1 (–3 to 1)][b]	4.9±0.6 (4 to 6)	1.8±1.9 (0 to 5) [–3.1±1.8 (–5 to 0)][b]
Ankle-brachial index	0.7±0.3	0.9±0.2 [0.2±0.2][b]	0.7±0.2	0.9±0.2 [0.2±0.2][b]	0.7±0.3	0.8±0.2 [0.3±0.3][b]

Abbreviation: CLI: critical limb ischemia.
[a]Continuous data are presented as the means ± standard deviation (range) and [mean change from baseline (range if applicable)].
[b]$p<0.001$.

rates showed no significant differences between the study groups (73% vs 75%). Notably, only 21% of the patients had isolated popliteal artery lesions.

In 2 recently published studies, Stavroulakis et al[21,26] evaluated the midterm results of combined directional atherectomy and DCB angioplasty for popliteal artery treatment. Twenty-one patients (18 with IC) were included in the first single-arm prospective study.[21] The bailout stenting rate was 4.8%, and the primary patency rate at 1 year was 95%. Notably, the portion of bailout stenting procedures after directional atherectomy in both studies and the primary patency rate of directional atherectomy at 1 year are comparable with the results of the current DEFINITIVE LE popliteal cohort analysis (3.7% and 75.0%, respectively).

The second study[26] analyzed 2 groups of patients: 31 were treated with DCB alone and 41 were treated with directional atherectomy and DCB. Patency at 12 months was significantly higher in the atherectomy + DCB group (82%) compared with the DCB group alone (65%; p=0.24). In their study, the researchers found that the rate of aneurysm formation in the atherectomy + DCB arm was 7%; in the current study, the CEC found no aneurysms in the popliteal subgroup. Although the primary patency rates of combined directional atherectomy + DCB angioplasty to treat popliteal lesions is promising, these results need to be substantiated by randomized trials with larger patient cohorts.

As the popliteal artery is subject to high biomechanical stress due to repetitive flexion and extension,[8] the fear of stent fractures and restenosis has led to uncertainties in how stenting should be used in optimal treatment of popliteal artery lesions. Though some studies have investigated the use of stents in the popliteal artery, the duration of follow-up has not been sufficient to fully define the characteristics of lesions and patients who will benefit from popliteal artery stenting. In addition, permanent implants can reduce future treatment options.[27]

Scheinert et al[10] published a retrospective, single-center analysis of 101 patients treated with a novel interwoven nitinol stent in popliteal lesion with a mean length of 5.84 cm. One-year primary patency was 87.7%, and the stent fracture rate was 0%. The performance of this particular stent was also investigated in another retrospective registry[11] that included patients with CLI. Primary patency rate at 1 year in the 34 patients eligible for follow-up was 68.4% and the TLR rate was 17.5%. The present study reveals comparable results for directional atherectomy in the CLI cohort, with 1-year primary patency of 67.5% and TLR of 21.8%.

In the prospective, randomized, multicenter ETAP trial,[7] primary nitinol stent placement was compared with PTA in the treatment of popliteal lesions in 246 patients (20.7% with CLI). The target lesions had a mean length of 4.23 cm. The 1-year primary patency rate was significantly higher in the no-stent group (67.4%) than in the PTA patients (44.9%, p=0.002). TLR rates were 14.7% and 44.1%, respectively ($p<0.001$). However, provisional stenting as part of a PTA strategy had equivalent 1-year primary patency in comparison to primary nitinol stent placement (67.4% vs 65.7%). In addition, stent fractures were not correlated to restenosis in this trial.

Parthipun et al[22] investigated the performance of a new hybrid heparin-bonded nitinol ring stent in complex occlusive disease of the popliteal artery in a single-center registry. A total of 54 stents were implanted in 48 patients. Primary patency at 1 year was 69.5% and TLR was 13.9%.

In the current study, multivariate Cox regression analysis revealed smoking within the last 10 years as an independent predictor of primary patency. The reason for this observation remains unclear, but it might be explained by a variant of the "smoker's paradox," which was originally observed in smokers with acute myocardial infarction in whom mortality was reduced. However, this phenomenon is not yet fully understood.[28]

Limitations

The main limitation of this study is the single-arm design without the possibility of a direct comparison of the results to other established endovascular procedures such as PTA, DESs, or DCBs. Moreover, the clinical impact of the inflow and outflow interventions performed during the index procedures remains unclear. Another limitation of this study is the presence of a selection bias due to the exclusion of

patients with severely calcified lesions. Finally, in the current treatment of PAD that utilizes non-stenting technologies, bailout stenting is considered a loss of primary patency and a procedure failure. However, this trial ran from 2009 to 2011 and did not consider bailout stenting to be loss of primary patency. The results of the present study cannot be extrapolated to other atherectomy methods due to fundamental design and performance differences.

Conclusion

The DEFINITIVE LE study has shown that popliteal artery lesions can be treated safely and successfully with directional atherectomy. Additionally, there was no significant difference in primary patency, TLR, or MAE between IC and CLI patients and no significant need for stenting in this challenging anatomic area. This preservation of the native artery increases future treatment options when restenosis occurs. Moreover, the 1-year technical and clinical results are superior to historical PTA results and similar to most stents available on the market. However, randomized trials are needed to clarify the potential of directional atherectomy in comparison to and in combination with other endovascular procedures.

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Authors' Note

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Declaration of Conflicting Interests

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