Different endovascular modalities of treatment for isolated atherosclerotic popliteal artery lesions (EMO-POP) registry

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ABSTRACT

Background: The mid-term results after treatment of isolated popliteal lesions have been limited. The aim of the present study was to report the mid-term outcomes after endovascular treatment of isolated atherosclerotic popliteal artery lesions.

Methods: A multicenter (15 hospitals in five countries) retrospective cohort study was performed. Between June 2016 and June 2021, 651 consecutive patients who had been treated for isolated popliteal lesions using endovascular methods exclusively were included in the present study. Six techniques were identified, including plain balloon angioplasty (PTA; n = 286; 43.9%), drug-coated balloon angioplasty (n = 98; 15.1%), stenting with low-chronic outward force (COF) stents (n = 84; 12.9%), stenting with high-COF stents (n = 76; 11.7%), atherectomy alone (n = 17; 2.6%), and directional atherectomy with drug-coated balloons (n = 90; 13.8%). The primary outcomes measures were primary and secondary patency and freedom from clinically driven target lesion revascularization (F-CDTLR).

Results: The mean patient age was 74.5 years. Most of the patients (n = 409; 62.9%) had had chronic limb-threatening ischemia. Popliteal occlusion was found in 400 cases (61.4%). High-grade calcification was present in 36.7% of cases. Immediate technical success was 94.8%. The median follow-up was 26 months (range, 6-42 months). The actuarial rate for all patients at 26 months (per outcome measure) was as follows: primary patency, 73.9%; secondary patency, 88%; and F-CDTLR, 76.5%. When comparing PTA vs all other treatments in an adjusted regression analysis, the F-CDTLR was 75.2% for PTA vs 76.5% for all other treatment (hazard ratio, 1.06; 95% confidence interval, 0.75-1.48; $P = .46$, adjusted regression). The difference in secondary patency also was not statistically significant (85.7% for PTA vs 88%; $P = .20$). Adjusted Kaplan-Meier analysis revealed that the estimated primary patency was inferior for PTA in pairwise comparisons vs other treatments ($P < .001$ vs atherectomy; $P = .002$ vs directional atherectomy with drug-coated balloons; and $P = .002$ vs low-COF stenting).

Conclusions: The results from our study have shown that endovascular treatment of isolated popliteal lesions is safe and associated with acceptable patency and F-CDTLR in the mid-term. (J Vasc Surg 2022;■:1-10.)

Keywords: Endovascular treatment; Peripheral arterial disease; Popliteal artery

Peripheral arterial disease (PAD) affects >200 million persons worldwide and has remained the leading cause of major lower limb amputations.[1-3] Patients with PAD and intermittent claudication (IC) or chronic limb-threatening ischemia (CLTI) will often have stenotic or occlusive femoropopliteal artery disease. Femoropopliteal revascularization procedures have been the most common procedures performed for patients with IC or CLTI.[2,3]

Isolated atherosclerotic popliteal artery lesions are also common in patients with PAD.[4] Treating isolated popliteal artery lesions using endovascular methods (eg,

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angioplasty, stenting) has been a particular clinical challenge. Because of knee flexion, the popliteal artery is under continuous stress by various biomechanical forces.[5-7] These forces will affect the durability of any endovascular or open surgical technique used in this area because of the potential for plaque formation or stent fractures and postoperative intimal hyperplasia. Furthermore, popliteal lesions will often be severely calcified, further complicating decision-making and the durability of the endovascular revascularization.[8] In recent years, various endovascular modalities have been developed to treat such lesions, in addition to plain balloon angioplasty (PTA), including drug-coated balloon (DCB) angioplasty, atherectomy, stenting (with a variety of devices now available), and even a combination of modalities (eg, atherectomy with DCBs (DAART).[9-15]

Stenting for occlusive lesions of the popliteal artery has been reported to have higher 1-year primary patency compared with PTA in some studies.[9] Treatment of occlusive popliteal lesions with DCB was found to be associated with similar 1-year overall patency and amputation-free survival (AFS) compared with stenting, even for patients with severely calcified lesions.[12] Directional atherectomy in this setting has seems to show favorable outcomes in nonrandomized studies compared with PTA.[10] Furthermore, the use of DAART might be associated with better 1-year primary patency compared with DCB-only treatment.[13] The reported data, however, regarding the outcomes after endovascular treatment of isolated popliteal lesions has some important limitations. Most reports have been single-center studies detailing the outcomes for a specific type of endovascular treatment and have typically included mostly patients with IC, with limited follow-up (usually to 1 year), and no adjustments for lesion length, complexity, or calcification.

Therefore, the aim of the present study was to report the early and mid-term outcomes of endovascular treatment of isolated atherosclerotic popliteal artery lesions using different treatment modalities in the setting of a multicenter cohort study.

ARTICLE HIGHLIGHTS

- **Type of Research:** A multicenter retrospective cohort study under the auspices of the Research Collaborative in Peripheral Arterial Disease, a pan-European scientific collaboration between vascular specialists
- **Key Findings:** A total of 651 consecutive patients who had undergone endovascular treatment of isolated atherosclerotic popliteal artery lesions were included in the present study. Six different techniques were identified. During a median of 26 months, the patency and clinically driven target lesion revascularization rates were acceptable. Plain balloon angioplasty alone was associated with marginally inferior freedom from target lesion revascularization.
- **Take Home Message:** Primary endovascular treatment of isolated popliteal lesions is safe, although plain balloon angioplasty might be associated with inferior patency compared with newer alternative endovascular treatments.

METHODS

Study population

A multicenter retrospective cohort study was conducted under the auspices of the Research Collaborative in Peripheral Arterial Disease, a pan-European scientific collaboration between vascular specialists.[16] A total of 15 departments in five countries participated in the present study (Supplementary Tables I and II, online only).

Given the pragmatic nature of our study, all the departments applied their local and/or regional standardized protocols for pre- and postoperative diagnostic assessments, perioperative medications, and follow-up examinations and/or imaging studies. At least one preoperative diagnostic duplex ultrasound scan (or similar cross-sectional imaging modality; ie, computed tomography or magnetic resonance angiography) was required for inclusion of patients in the study to fully assess the preoperative plaque morphology. Treatment selection was determined by the treating clinician and local multidisciplinary team meeting discussions. All the patients provided written informed consent for the procedure and analysis of their personal data.

Definitions

For the purposes of the present study, the popliteal artery segments were defined as follows: P1 segment, from the intercondylar fossa to the proximal edge of the patella; P2 segment, from the proximal edge of the patella to the level of the knee joint space; P3 segment, from the knee joint space to the ostium (orifice) of the anterior tibial artery. CLTI was defined as presence of PAD (using cross-sectional imaging and/or ankle brachial pressure index) combined with the presence of rest pain, gangrene, and/or lower limb ulceration >2 weeks in duration.[17]

Grading of calcification of the target popliteal artery lesions was performed using the peripheral arterial calcium scoring system (PACSS).[18] High-grade calcification was defined as a lesion PACSS grade of 3 or 4. Runoff status was defined by the number of patent tibial vessels, determined the imaging (diagnostic angiography) findings during the index procedure. Other definitions of clinical events and/or imaging parameters were in accordance with the reporting standards of the Society for Vascular Surgery for PAD.[19]

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Regarding outcomes reporting, primary patency was defined as no evidence of restenosis of the target lesion during follow-up, with a peak systolic velocity ratio ≥2.5 or occlusion of the target lesion, determined using color-coded duplex ultrasound. Secondary patency was defined as target lesion patency maintained by repeat intervention after complete occlusion of the relevant lesion. Freedom from clinically driven target lesion revascularization (F-CDTLR) was defined as no evidence of restenosis of the target lesion with a peak systolic velocity ratio of <1.5 and/or no occlusion of the target lesion. A major lower limb amputation was defined as any amputation ipsilateral to the target lesion and above the level of the ankle joint.

Inclusion and exclusion criteria

The main inclusion criterion was endovascular treatment of a de novo isolated atherosclerotic stenosis or occlusion of the popliteal artery in one or more popliteal artery segments. The exclusion criteria were as follows: repeat procedures, including in-stent restenosis, for isolated popliteal artery disease; popliteal entrapment syndrome; popliteal artery aneurysm; concomitant endovascular or open surgical treatment of the infrainguinal inflow vessels (ie, common femoral artery, superficial femoral artery); and concomitant endovascular or open surgical treatment of the outflow vessels (crural or foot arteries).

Study procedures

Regulatory approval. Ethical and regulatory approval was sought at each individual institution level in accordance with local regulations, given the international nature of our study. The present study complied with the principles of the Declaration of Helsinki. A lead collaborator was identified at each institution who was responsible for the data collection and accuracy, database completion, data exchange, and obtaining local approval. A uniform electronic reporting form was maintained by the lead investigator (N.T.) across all the institutions. Reporting was in accordance with the STROBE (strengthening the reporting of observational studies in epidemiology) guidelines (Supplementary Table II, online only). The study lead investigator (N.T.) was responsible for study conduct and data maintenance.

Data collection. All data related to the patient characteristics and procedures performed were retrospectively collected in a dedicated electronic database, maintained by the lead investigator (N.T.) and the Research Collaborative in Peripheral Arterial Disease collaborative. The patient data were recorded prospectively in each department's local dataset. Subsequently, the follow-up data were collected retrospectively by at least two of us at each site (the lead investigator and key clinical investigator or clinician). On completion of data collection, the data were cleaned by the lead investigator at each site. Two of us (A.S., E.K.) were responsible for overall database maintenance and queried local investigators on completion of data collection regarding erroneous data. The lead local investigator was responsible for data accuracy and auditing at each site in accordance with local regulations. These data included demographics, preoperative cardiovascular risk factors, clinical and diagnostic preoperative assessments, pre- and postoperative medical treatment, intraoperative features and findings, and follow-up outcomes, including all reinterventions, readmissions and major clinical events.

Outcomes

The primary outcomes of interest were primary patency, secondary patency, and F-CDTLR. The secondary outcomes of interest were immediate technical success (defined as flow restoration of the target lesion with residual stenosis <30%), early (30-day) mortality, morbidity (including access site complications, target vessel occlusion, and major adverse cardiovascular events), and AFS at the end of follow-up.

Statistical analysis

Statistical analyses were performed using the R package, version 4.0.5 (R Foundation for Statistical Computing, Vienna, Austria) and SPSS software, version 24.0, for Windows (IBM Corp, Armonk, NY). Two of us (E.K., A.S.) with formal statistical expertise were independently responsible for all analyses, using a predrawn statistical analysis plan. Continuous data are presented as the mean ± standard deviation or median and range, as necessary. Categorical data are presented as absolute numbers and percentages. The Pearson χ^2 test, *t* test, and analysis of variance were used to compare values between groups, depending on the nature of the data and the variables. Six distinct treatment groups were identified according to the procedure performed at baseline (ie, PTA, DCB, primary stenting with high- or low-chronic outward force [COF] devices, atherectomy [alone], and DAART). Patients who had undergone intravascular lithotripsy alone were excluded from analysis because of the low number of patients and short follow-up (<20 patients; <6 months of follow-up).

PTA (ie, reference treatment) was compared for the primary outcomes of interest with the other five more contemporary endovascular treatments using conditional Cox regression, adjusted for medical center, age, sex, CLTI, smoking, diabetes, chronic kidney disease, number of runoff vessels, degree of stenosis preoperatively (baseline), and degree of lesion calcification (key clinical and anatomic parameters). Hazard ratios (HRs) and 95% confidence intervals (CIs) are reported. Given the six different treatment types, a secondary analysis for the primary outcomes of interest was performed using Kaplan-Meier curves until the end of follow-up with an adjusted pairwise comparison that included all the

Table I. Demographic data and preoperative risk factors

Variable	PTA (n = 286)	DCB (n = 98)	Low-COF stent (n = 84)	High-COF stent (n = 76)	Atherectomy (n = 17)	DAART (n = 90)	Total (n = 651)	*P* value
Male sex	143 (50)	50 (51)	44 (52.4)	43 (56.6)	9 (52.9)	53 (58.9)	342 (52.5)	.73
Mean age, years	74.8	73.5	77.3	72.6	77.4	73.4	74.5	.02
Age >80 years	103 (36)	28 (28.6)	39 (46.4)	24 (31.6)	5 (29.4)	25 (27.8)	224 (34.4)	.09
Risk factors								
Current smoking	87 (30.4)	26 (26.5)	17 (20.2)	22 (28.9)	7 (41.2)	40 (44.4)	199 (30.6)	.01
Former smoking	59 (20.6)	20 (20.4)	39 (46.4)	18 (23.7)	2 (11.8)	5 (5.6)	143 (22)	<.001
Hypertension	260 (90.9)	84 (85.7)	66 (78.6)	60 (78.9)	10 (58.8)	76 (84.4)	556 (85.4)	.001
Hypercholesterolemia	185 (64.7)	66 (67.3)	41 (48.8)	45 (59.2)	6 (35.3)	52 (57.8)	395 (60.7)	.02
Diabetes mellitus	123 (43)	39 (39.8)	40 (47.6)	29 (38.2)	9 (52.9)	24 (26.7)	264 (40.6)	.05
Insulin treatment	73 (25.5)	20 (20.4)	21 (25)	17 (13.2)	3 (17.6)	9 (10)	143 (22)	.04
Coronary artery disease	108 (37.8)	35 (35.7)	25 (29.7)	18 (23.7)	10 (58.8)	38 (42.2)	234 (35.9)	.03
Chronic renal failure[a]	34 (11.9)	9 (9.2)	17 (20.2)	8 (10.5)	6 (35.3)	17 (18.9)	91 (14)	.02
Dialysis treatment	10 (3.5)	5 (5.1)	4 (4.8)	2 (2.6)	0	4 (4.4)	25 (3.8)	.90
Rutherford classification								<.001
2 (moderate claudication)	38 (13.3)	15 (15.3)	3 (3.6)	10 (13.2)	1 (5.9)	1 (1.1)	68 (10.4)	
3 (severe claudication)	57 (19.9)	33 (33.7)	10 (11.9)	30 (39.5)	0 (0)	44 (48.9)	174 (26.7)	
4 (rest pain)	69 (24.1)	17 (17.3)	29 (34.5)	16 (21)	9 (52.9)	24 (26.7)	164 (25.2)	
5 (minor tissue loss)	95 (33.2)	28 (28.6)	34 (40.5)	15 (19.7)	5 (29.4)	20 (22.2)	197 (30.3)	
6 (major tissue loss)	27 (9.5)	5 (5.1)	8 (9.5)	5 (6.6)	2 (11.8)	1 (1.1)	48 (7.4)	

COF, Chronic outward force; *DAART,* directional atherectomy with antirestenotic therapy; *DCB,* drug-coated balloon; *PTA,* plain balloon angioplasty. Data presented as number (%), unless noted otherwise.
[a]Glomerular filtration rate <30 mL/min.

following variables: age, sex, Rutherford category at presentation, diabetes, chronic kidney disease, prior stroke or ischemic heart disease, smoking, hypertension, target lesion length, target lesion location (ie, P1, P2, P3, or a combination), number of runoff vessels, and PACSS grade for the target lesion. This allowed for adjusted pairwise comparisons between the six treatment groups for each of the primary outcomes of interest. Given the rarity of clinical events such as major lower limb amputation or death during follow-up in the present study, it was not possible to explore associations between the treatment mode and these clinical outcomes (high probability of error owing to insufficient power) and was beyond the scope of our study. The study provided 90% power to test for differences related to primary patency, comparing PTA with the other five endovascular treatment types, assuming 75% primary patency for PTA ($\alpha = 0.5$). A power analysis was performed to detect a 10% change in patency (85%). Statistical significance was set at the $P < .05$ level.

RESULTS

A total of 671 consecutive patients who had undergone treatment of de novo isolated atherosclerotic popliteal artery lesions from June 2016 to June 2021 using endovascular methods exclusively were enrolled. The 20 patients who had undergone intravascular lithotripsy alone were excluded (insufficient follow-up period [ie, <6 months]). Therefore, the study population included 651 patients. Six distinct endovascular techniques were identified: PTA (n = 286; 43.9%), DCB (n = 98; 15.1%), stenting with low-COF stents (n = 84; 12.9%), stenting with high-COF stents (n = 76; 11.7%), atherectomy alone (n = 17; 2.6%), and DAART (n = 90; 13.8%).

Demographic and morphologic data. The baseline characteristics for the study cohort are presented in Table I. The cardiovascular risk factors were standard for a population presenting with symptomatic PAD but varied between treatment groups, as expected (Table I). The morphologic characteristics for each target lesion, including location, extent, degree of calcification, and runoff status, are summarized in Table II. In 38.9% of cases, two or more segments of the popliteal artery were involved. High-grade calcification was present in 36.7% of cases (ie, grade 3 or 4 using the PACSS). Overall, 26.9% of patients had had only one runoff vessel. The pre- and postoperative medical therapy, which was typical for an all-comers population with symptomatic PAD, is presented in Table III.

Intraprocedural outcomes. Overall, immediate procedural technical success was achieved in 94.8% of cases. The overall median stent or balloon diameter and length used to perform the procedure were 5.1 mm (range, 3-

Table II. Target lesion characteristics

Characteristic	PTA (n = 286)	DCB (n = 98)	Low-COF stent (n = 84)	High-COF stent (n = 76)	Atherectomy (n = 17)	DAART (n = 90)	Total (n = 651)	*P* value
Lesion type								.003
Occlusion	162 (56.6)	54 (55.1)	67 (79.8)	50 (65.8)	11 (64.7)	56 (62.2)	400 (61.4)	
Stenosis	124 (43.4)	44 (44.9)	17 (20.2)	26 (34.2)	6 (35.3)	34 (37.8)	251 (38.6)	
PACSS grade								.001
0	35 (12.2)	7 (7.1)	15 (17.9)	10 (13.2)	1 (5.9)	1 (1.1)	69 (10.6)	
1	58 (20.3)	13 (13.3)	14 (16.7)	14 (18.4)	2 (11.8)	10 (11.1)	111 (17.1)	
2	94 (32.9)	45 (45.9)	23 (27.4)	26 (34.2)	5 (29.4)	39 (43.3)	232 (35.6)	
3	67 (23.4)	17 (17.4)	23 (27.4)	16 (21)	4 (23.5)	17 (18.9)	144 (22.1)	
4	32 (11.2)	16 (16.3)	9 (10.6)	10 (13.32)	5 (29.4)	23 (25.6)	95 (14.6)	
Popliteal artery								.80
P1	71 (24.8)	24 (24.5)	24 (28.6)	15 (19.7)	6 (35.3)	24 (26.7)	164 (25.2)	
P1, P2	49 (17.1)	20 (20.4)	18 (21.4)	21 (27.7)	2 (11.7)	22 (24.3)	132 (20.3)	
P1, P2, P3	28 (9.8)	5 (5.1)	10 (11.9)	6 (7.9)	1 (5.9)	10 (11.1)	60 (9.2)	
P1, P3	2 (0.7)	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	3 (0.5)	
P2	95 (33.2)	30 (30.6)	18 (21.4)	19 (25)	6 (35.3)	23 (25.6)	191 (29.3)	
P2, P3	22 (7.7)	11 (11.2)	11 (13.1)	7 (9.2)	1 (5.9)	6 (6.7)	58 (8.9)	
P3	19 (6.7)	7 (7.1)	3 (3.6)	8 (10.5)	1 (5.9)	5 (5.6)	43 (6.6)	
Runoff BTK vessels								<.001
1	98 (34.3)	23 (23.5)	21 (25)	18 (23.7)	5 (29.4)	10 (11.1)	175 (26.9)	
2	126 (44)	46 (46.9)	53 (63.1)	39 (51.3)	10 (58.8)	57 (63.3)	331 (50.8)	
3	62 (21.7)	29 (29.6)	10 (11.9)	19 (25)	2 (11.8)	23 (25.6)	145 (22.3)	

BTK, Below-the-knee; *COF*, chronic outward force; *DAART*, directional atherectomy with antirestenotic therapy; *DCB*, drug-coated balloon; *PACSS*, peripheral arterial calcium scoring system (proposed); *PTA*, plain balloon angioplasty.
Data presented as number (%).

7 mm), and 84.3 mm (range, 13-250 mm), respectively. In eight cases (1.2%), distal embolization had occurred intraprocedurally. A filter had not been used in any of these cases because these patients had undergone PTA. The runoff vessels were restored in all eight patients using endovascular thromboaspiration and/or local infusion of fibrinolytic agents.

In five cases (0.8%), a popliteal artery perforation had occurred, which had been treated successfully with a covered stent in all cases. In one case (0.2%), persistent bleeding had occurred at the site of retrograde access, via the posterior tibial artery, and had been treated with a covered coronary stent. In two cases (0.3%), low-flow popliteal arteriovenous fistulas were detected and treated conservatively. None of the included patients had required bypass because of treatment failure.

Follow-up at 30 days. The median hospital stay was 3.4 days (range, 1-40 days). Access site complications requiring intervention occurred in 25 patients (3.8%) during the hospital stay. At 30 days of follow-up, the overall mortality and major adverse cardiovascular events rates were 0.9% and 0.5%, respectively.

After discharge and within 30 days, 32 patients (4.9%) had required surgery to treat an access site complication (6 patients) or target vessel occlusion (26 patients; 4%). All these cases were managed endovascularly.

Medium-term follow-up. Follow-up data were available for all patients at a median of 26 months (range, 6-42 months). The estimated 5-year overall survival (Kaplan-Meier) was 70.9%. The actuarial survival for each outcome of interest for the whole cohort at the end of follow-up was as follows: primary patency, 73.89%; secondary patency, 88%; and F-CDTLR, 76.47%. The actuarial outcomes for the primary outcomes of interest (ie, primary patency, secondary patency, F-CDTLR) for each treatment modality group are summarized in Table IV.

The presence of a popliteal occlusion (HR, 1.28; 95% CI, 1.01-1.34; $P < .001$) and poor runoff status (HR, 1.38; 95% CI, 1.04-1.58; $P < .001$) were associated with lower F-CDTLR during the 26-month follow-up (adjusted Cox regression). No other baseline parameters were associated with F-CDTLR during the 26-month follow-up period in the same adjusted model.

The estimated Kaplan-Meier survival at 5 years for the primary outcomes of interest (ie, primary patency, secondary patency, F-CDTLR) for each endovascular treatment is listed in Table V. The results from the adjusted pairwise comparisons (log-rank test *P* values) for the

Table III. Pre- and postoperative medical therapy for whole cohort

Variable	Preoperative, No. (%)	Postoperative, No. (%)	Difference, %
Aspirin	444 (68.2)	507 (77.9)	+9.7
Clopidogrel	127 (19.5)	370 (56.8)	+37.3
Other antiplatelet medication	14 (2.2)	16 (2.5)	+0.3
Warfarin	61 (9.4)	73 (11.2)	+1.8
Direct oral anticoagulant agent	53 (8.1)	66 (10.1)	+2
Statin	384 (59)	409 (62.8)	+3.8
Angiotensin-converting enzyme inhibitor	291 (44.7)	288 (44.2)	−0.5

primary outcomes of interest for each of the six different endovascular treatments are presented in Table VI. Overall, for the estimated primary patency, PTA appeared inferior in the pairwise comparisons to most of the other treatments ($P < .001$ vs atherectomy; $P = .002$ vs DAART; $P = .002$ vs low-COF stenting). However, no significant differences were found for the estimated secondary patency. Supplementary Figs 1-3 (online only) show the adjusted Kaplan-Meier curves for each treatment modality until the end of follow-up for patency (primary and secondary) and F-CDTLR. Overall, in the adjusted Kaplan-Meier analysis, similar to the Cox regression model and subsequent pairwise comparison, PTA seemed to have inferior outcomes for primary patency compared with most of the other more modern endovascular treatments. However, no significant differences were found in secondary patency.

DISCUSSION

To the best of our knowledge, the present study is the largest multicenter series to date to report the midterm outcomes after endovascular treatment of isolated popliteal artery atherosclerotic lesions for a patient population of all-comers, reflecting real-life practice and outcomes. A total of six discreet modes of endovascular treatment were identified. The outcomes were reported for a follow-up period of 26 months. The patient characteristics for both anatomy and comorbidities did differ per treatment group. However, a number of adjusted analyses were performed using two approaches: Cox regression modeling and a more elaborate adjusted analysis using Kaplan-Meier curves and pairwise comparisons between treatment methods. Overall, primary patency, secondary patency, and F-CDTLR were favorable for the whole cohort (all endovascular treatments combined). The present series has provided real-world contemporary evidence that endovascular treatment of isolated popliteal lesions, even those with high calcium loads, is both feasible and safe in the medium term. No major differences were found between treatments modes. PTA seemed to have inferior primary patency compared with all other treatments combined and in pairwise-adjusted comparisons, albeit with only a small absolute risk increase. Secondary patency, however, was still relatively high, especially with the complex nature of isolated popliteal lesions and that ours was an all-comers series.

The popliteal artery is often involved in patients with lower limb multilevel atherosclerotic disease. However, only scarce evidence has been reported regarding the outcomes after endovascular treatment of isolated popliteal lesions.[4] The popliteal artery is subject to very considerable forces during ambulation. Furthermore, popliteal atherosclerotic lesions will often be calcified. Such calcification poses considerable challenges for any form of endovascular treatment. External forces onto the popliteal artery can lead to stent fractures, and heavy calcification is always a challenge to address when performing angioplasty. Angioplasty with selective stenting seems to be a feasible and safe therapy for this anatomic segment and has traditionally been the first-line endovascular treatment of these lesions.[20] The rate of stent fracture has not been negligible, however, ranging from 3.4% to 7.1%.[9,20] The use of newer generation biomimetic stents might be associated with considerably fewer stent fractures at 1 year of follow-up compared with older generation devices.[21] In addition to biomimetic stents, a number of newer devices are now available in the market. They aim to address some of the particular challenges faced when treating isolated popliteal lesions, including avoiding the use of stents, managing recoil and neointimal hyperplasia, and addressing the heavy burden of calcium. These include DCBs, drug-eluting stents, atherectomy with or without the additional use of DCBs, biomimetic interwoven nitinol stents, and combinations of these.

Owing to the inherent challenge of the small numbers of patients with isolated popliteal artery disease treated at each center and the use of a multitude of different endovascular treatment options, very few comparative studies have been reported thus far in this clinical context.[9-13,22] Only one randomized controlled trial

Table IV. Actuarial outcomes at end of follow-up (median, 26 months)

Outcome of interest	PTA (n = 286), %	DCB (n = 98), %	Low-COF stent (n = 84), %	High-COF stent (n = 76), %	Atherectomy (n = 17), %	DAART (n = 90), %	All patients, %
Primary patency	77.4	69.3	65.3	70.3	89.5	61.5	73.9
Secondary patency	85.7	89.6	84	91.9	94.7	84.6	88
F-TLR	75.2	77.9	68	73	89.5	76.9	76.5
AFS	95.2	97.5	97.3	94.6	97.4	100	96.4

AFS, Amputation-free survival; *COF,* chronic outward force; *DAART,* directional atherectomy with antirestenotic therapy; *DCB,* drug-coated balloon; *F-TLR,* freedom from target lesion revascularization; *PTA,* plain balloon angioplasty.

Table V. Estimated Kaplan-Meier survival analysis for 5-year outcomes

Outcome	PTA (n = 265)	DCB (n = 105)	Low-COF stent (n = 96)	High-COF stent (n = 82)	DAART (n = 103)	Atherectomy[a]	Total (all patients)
Clinical improvement	63.5 ± 3	70.6 ± 6.7	71.1 ± 6.4	67.8 ± 8.1	86.7 ± 4.3	NA	68.7 ± 2.9
Primary patency	50.7 ± 6.1	50 ± 7.7	56.6 ± 7.9	56.5 ± 8.6	58.2 ± 12.5	NA	53.9 ± 3.6
Secondary patency	66.9 ± 5.4	72.5 ± 6.8	80.7 ± 5	85 ± 6.5	79.5 ± 8.4	NA	74.8 ± 2.9
F-TLR	51.9 ± 5.4	46.1 ± 7.8	46.7 ± 8.5	52.3 ± 8.5	59.3 ± 12.3	NA	51.1 ± 3.6
AFS	88.7 ± 3.3	91 ± 4.7	95.1 ± 2.9	96.7 ± 2.3	96.1 ± 2.8	NA	92.3 ± 1.7

AFS, Amputation-free survival; *COF,* chronic outward force; *DAART,* directional atherectomy with antirestenotic therapy; *DCB,* drug-coated balloon; *F-TLR,* freedom from target lesion revascularization; *NA,* not available; *PTA,* plain balloon angioplasty.
Data presented as mean percentage ± standard error.
[a]Only 17 patients with available data; therefore, it was not possible to report the Kaplan-Meier estimated outcomes for atherectomy alone.

comparing PTA and stenting has been reported in this context.[9] Furthermore, the results after endovascular revascularization of isolated popliteal lesions using the latest generation devices have not yet been well described, especially in a real-world clinical setting.

To address this gap, we developed a collaboration between 15 European centers to evaluate the performance of modern endovascular treatment for patients with isolated popliteal artery disease using real-world data (all-comers). The treatments used in the present study largely reflected some previous smaller reports of isolated popliteal lesions, such as the series by Chang et al,[23] who reported a 35.6% stenting rate when treating popliteal lesions with PTA. Of the lesions, 45% were popliteal occlusions, and 26% of the lesions were severely calcified.[23]

The population described in the present series is also reflective of routine clinical practice. The included patients were all-comers (consecutive patients identified locally at each participating center). Of the included patients, 37% had had tissue loss and 25% had reported rest pain at baseline. Also, most patients had had at least moderately calcified lesions, which were assessed using detailed analysis and reporting (PACSS grade). In addition to calcium, the lesions were characterized in detail, including length and runoff status. This allowed for careful adjustments when reporting the outcomes and comparing the different endovascular treatments. We found that the previous literature had not carefully adjusted for such detailed anatomic parameters.

All the treatments described in the present series appeared to be safe and feasible. Immediate technical success was satisfactory, and distal embolization seldom occurred in our patients (1.2%), in contrast to that reported in some previous studies.[22] The incidence of embolization was low even in the atherectomy and DAART groups (filter use was not standard). However, we could not perform any adjustments or determine any associations regarding filter use because such use had not been reported uniformly.

Although direct comparisons between the treatments were not easy owing to the number of different endovascular treatments the 651 patients had undergone in the present study, we did not observe any major safety or patency issues with the more contemporary endovascular techniques. PTA might be inferior to some of the other techniques regarding the need for reintervention; however, these differences were fairly minor. Similar results have been reported by previous smaller studies in this clinical context. Semaan et al[22] have previously demonstrated that PTA is associated with similar medium-term patency, limb salvage, and F-CDTLR compared with atherectomy. Rastan et al[9] reported the superiority of stenting vs PTA in terms of acute technical success and 1-year primary patency. None of these series, including the present study, was designed or powered to detect AFS in the long term. Strict long-term follow-up is required for a number of years, using uniform protocols, to be able to assess the potential associations with specific clinical outcomes (eg, death, amputation) in the longer term for patients with isolated popliteal lesions.

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Table VI. Adjusted pairwise comparisons (log-rank test) among six different endovascular treatment methods at last available follow-up

	P value, log-rank test					
Outcome	Atherectomy	DAART	DCB	High-COF	Low-COF	PTA
Primary patency						
Atherectomy	–	–	–	–	–	–
DAART	**.02**	–	–	–	–	–
DCB	**<.001**	**.02**	–	–	–	–
High-COF	**<.001**	.19	.31	–	–	–
Low-COF	**<.001**	.55	**.03**	.35	–	–
PTA	**<.001**	**.002**	.41	**.06**	**.002**	–
Secondary patency						
Atherectomy	–	–	–	–	–	–
DAART	.01	–	–	–	–	–
DCB	.32	.11	–	–	–	–
High-COF	.18	.25	.36	–	–	–
Low-COF	.002	.74	.81	.77	–	–
PTA	.18	.11	.76	.82	.66	–
TLR						
Atherectomy	–	–	–	–	–	–
DAART	.99	–	–	–	–	–
DCB	.42	.32	–	–	–	–
High-COF	.65	.32	.99	–	–	–
Low-COF	.41	.61	.63	.99	–	–
PTA	.57	.29	.51	.99	.99	–

COF, Chronic outward force; *DAART,* directional atherectomy with antirestenotic therapy; *DCB,* drug-coated balloon; *PTA,* plain balloon angioplasty; *TLR,* target lesion revascularization.
Boldface *P* values represent statistical significance.

The presence of a popliteal occlusion (HR, 1.28; 95% CI, 1.01-1.34; $P < .001$) and poor runoff status (HR, 1.38; 95% CI, 1.04-1.58; $P < .001$) were associated with lower F-CDTLR during follow-up (adjusted Cox regression) in our series. No other baseline parameters were associated with CDTLR during follow-up in the same model. Performing further explorations of the dataset for potential associations with other baseline parameters was beyond the scope of the present study, and the cohort was underpowered to detect further associations. Spiliopoulos et al[4] also previously demonstrated that a popliteal occlusion was associated with significantly worse F-CDTLR for patients who had undergone endovascular treatment of isolated popliteal artery lesions. Watanabe et al[24] also demonstrated that the state of distal runoff predicts for the clinical outcomes in patients undergoing femoropopliteal interventions.

The present study had some limitations. We performed a retrospective nonrandomized analysis of patients who had been treated with different techniques at various vascular centers. The presence of a selection and reporting bias was, therefore, inevitable. Thus, we reported the results from two different types of adjusted analysis to assess the main outcomes of interest. Considerable differences were present between the various groups of patients, reflecting the real-world clinical practice and pragmatic design of our study. We attempted to adjust for as many comorbidities and anatomic details as possible. In addition, we used two different statistical approaches (adjusted Cox regression and pairwise comparison using adjusted Kaplan-Meier analysis and log-rank tests), supported by a predrawn analysis plan with independent statistical input (E.K., A.S.). However, these cannot replace randomization. Randomization, however, can be very difficult in this clinical context, owing to the availability of many different endovascular treatments and the fairly rare presentation of patients with isolated popliteal disease. Furthermore, the present study was not powered to detect differences in clinical end points such as AFS or ulcer healing rates. These could not be addressed fully using a study of this nature. Furthermore, the study design did not provide sufficient power to allow for the report of separate regressions or adjusted analyses for each type of concomitant medical therapy and the potential interactions with outcomes. Finally, patient satisfaction or quality of life also could not be assessed from our series.

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CONCLUSIONS

The results from our study have shown that endovascular treatment of isolated popliteal lesions using modern techniques is safe and associated with acceptable mid-term outcomes for primary and secondary patency and F-CDTLR. Immediate technical success was high, and perioperative major complications were rare in the present series across all different treatment modalities. Given the frequent introduction of more endovascular treatments for these lesions, carefully designed prospective multicenter registries with uniform long-term follow-up are warranted in the future.

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AUTHOR CONTRIBUTIONS

Conception and design: NT, AS, KS, HZ, GT
Analysis and interpretation: NT, AS, EK, RB, HZ, GT
Data collection: NT, AS, KS, RB, GT
Writing the article: NT, AS
Critical revision of the article: NT, AS, EK, KS, RB, HZ, GT
Final approval of the article: NT, AS, EK, KS, RB, HZ, GT
Statistical analysis: NT, AS, EK
Obtained funding: Not applicable
Overall responsibility: NT

NT and AS contributed equally to this article and share co-first authorship.

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Additional material for this article may be found online at www.jvascsurg.org.

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Supplementary Table I (online only). Endovascular modalities of treatment for isolated atherosclerotic popliteal artery lesions (EMO-POP) registry collaborative group

Center	Local principal investigator	Patients, No.
St. Franziskus Hospital, Münster, Germany	Giovanni Torsello	139
University of Pisa, Pisa, Italy	Nicola Troisi	101
Deutsches Krankenhausinstitut, Dusseldorf, Germany	Denise Özdemir-van Brunschot	98
Glenfield Hospital, Leicester, United Kingdom	Athanasios Saratzis	56
Centre Hospitalier d'Arras, Arras, France	Teresa Martín González	40
Akademisches Lehrkrankenhaus, Weinheim, Germany	Grigorios Korosoglou	35
University Hospital of Perugia, Perugia, Italy	Giacomo Isernia	34
San Giovanni di Dio Hospital, Florence, Italy	Stefano Michelagnoli	29
Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy	Antonio Nicola Giordano	26
Asklepios Clinic Langen, University of Frankfurt, Langen, Germany	Konstantinos Donas	25
National and Kapodistrian University of Athens, Attikon University Hospital, Athens, Greece	Stavros Spiliopoulos	18
IRCCS Multimedica, Sesto San Giovanni, Italy	Massimiliano Martelli	15
Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy	Alberto Maria Settembrini	15
University Hospital of Trieste, Trieste, Italy	Mario D'Oria	13
Ludwig Maximilian University Hospital of Munich, Munich, Germany	Konstantinos Stavroulakis	7

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Supplementary Table II (online only). STROBE statement—checklist of items that should be included in reports of observational studies[a]

No.	Item	Recommendation	Location in present study
1	Title and abstract		
1a		Indicate study design with commonly used term in title or abstract	Identified in abstract and methods section
1b		Provide in abstract, informative and balanced summary of what was done and what was found	Provided in abstract
	Introduction		
2	Background; rationale	Explain scientific background and rationale for investigation	Stated in introduction
3	Objectives	State specific objectives, including any prespecified hypotheses	Stated in introduction
	Methods		Information for items 4-12 provided in methods section
4	Study design	Present key elements of study design early in report	
5	Setting	Describe setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	
6	Participants		
6a		Cohort study—describe eligibility criteria, sources and methods of participant selection, and methods of follow-up	
6a		Case-control study—describe eligibility criteria, sources and methods of case ascertainment and control selection, and rationale for choice of cases and controls	
6a		Cross-sectional study—describe eligibility criteria, sources and methods of participant selection	
6b		Cohort study—for matched studies, give matching criteria and number of exposed and unexposed	
6b		Case-control study—for matched studies, give matching criteria and number of controls per case	
7	Variables	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers, and provide diagnostic criteria, if applicable	
8[b]	Data sources and measurement	For each variable of interest, provide sources of data and details of methods of assessment (measurement); describe comparability of assessment methods if >1 group included	
9	Bias	Describe any efforts to address potential sources of bias	
10	Study size	Explain determination of study size	
11	Quantitative variables	Explain how quantitative variables were managed in analyses; if applicable, describe which groups were chosen and why	
12	Statistical methods		
12a		Describe all statistical methods, including those used to control for confounding	
12b		Describe methods used to examine subgroups and interactions	
12c		Explain how missing data were addressed	
12d		Cohort study—if applicable, explain how loss to follow-up was addressed	
12d		Case-control study—if applicable, explain how matching of cases and controls was addressed	
12d		Cross-sectional study—if applicable, describe analytical methods used to account for sampling strategy	

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Supplementary Table II (online only). Continued.

No.	Item	Recommendation	Location in present study
12e		Describe any sensitivity analyses	
	Results		Data for items 13-17 presented in results section in order suggested by STROBE guidelines
13[b]	Participants		
13a		Report numbers of individuals at each stage of study (eg, numbers potentially eligible, examined for eligibility, confirmed eligible, included in study, completed follow-up, analyzed)	
13b		Give reasons for nonparticipation at each stage	
13c		Consider use of a flow diagram	
14[b]	Descriptive data		
14a		Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	
14b		Indicate number of participants with missing data for each variable of interest	
14c		Cohort study—summarize follow-up time (eg, average, total)	
15[b]	Outcomes data		
		Cohort study—report numbers of outcome events or summary measures over time	
		Case-control study—report numbers in each exposure category or summary measures of exposure	
		Cross-sectional study—report numbers of outcome events or summary measures	
16	Main results		
16a		Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% CI); ensure clarity regarding which confounders were adjusted for and why they were included	
16b		Report category boundaries when continuous variables were categorized	
16c		If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
17	Other analyses	Report other analyses performed (eg, analyses of subgroups and interactions, sensitivity analyses)	
	Discussion		Data for items 18-21 included in discussion section
18	Key results	Summarize key results with reference to study objectives	
19	Limitations	Discuss limitations of study, including sources of potential bias or imprecision; discuss both direction and magnitude of any potential bias	
20	Interpretation	Give cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	
21	Generalizability	Discuss generalizability (external validity) of study results	
	Other information		Funding and conflicts of interest detailed as required by the Journal
22	Funding	Give source of funding and role of funders for present study and, if applicable, for original study on which the present report was based	

CI, Confidence interval; *STROBE*, strengthening the reporting of observational studies in epidemiology.
[a]An explanation and elaboration report provides details for each checklist item, the methodologic background, and published examples of transparent reporting; the STROBE checklist is best used in conjunction with that report (available at: http://www.plosmedicine.org/, http://www.annals.org/, and http://www.epidem.com/); information on the STROBE Initiative is available at www.strobe-statement.org.
[b]Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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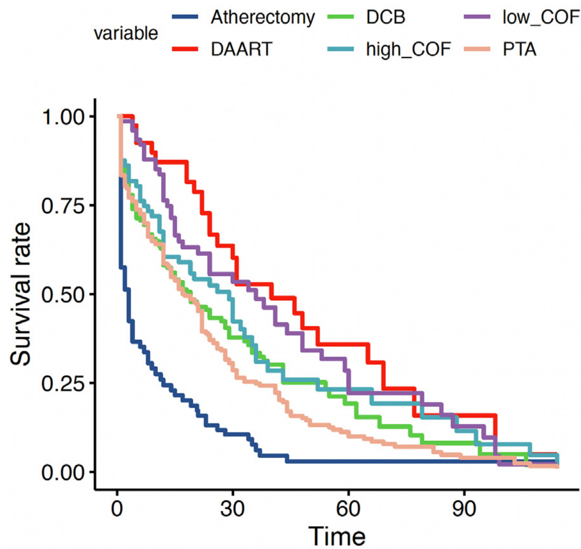
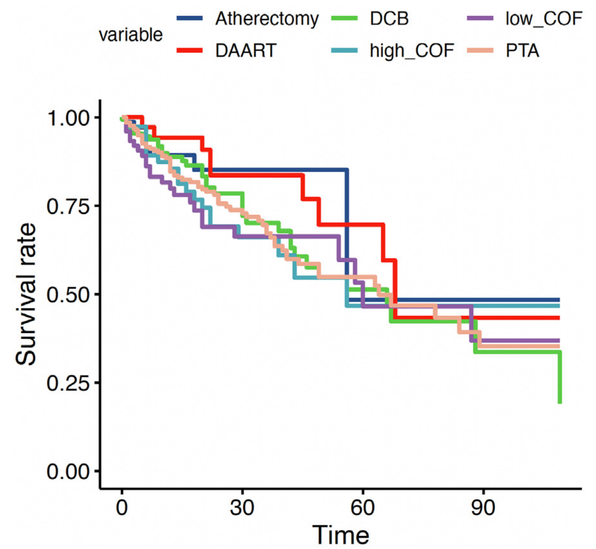
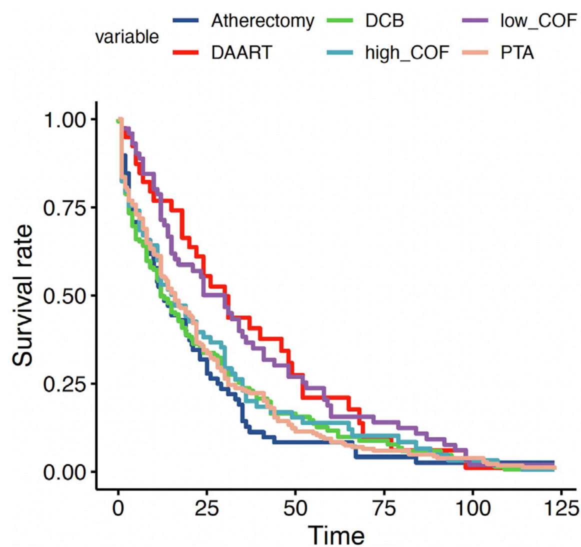


Supplementary Fig 1 (online only). Adjusted Kaplan-Meier curves for pairwise comparisons (log-rank test) of primary patency. *COF,* Chronic outward force; *DAART,* directional atherectomy with antirestenotic therapy; *DCB,* drug-coated balloon; *PTA,* plain balloon angioplasty.



Supplementary Fig 3 (online only). Adjusted Kaplan-Meier curves for pairwise comparisons (log-rank test) of freedom from target lesion revascularization. *COF,* Chronic outward force; *DAART,* directional atherectomy with antirestenotic therapy; *DCB,* drug-coated balloon; *PTA,* plain balloon angioplasty.



Supplementary Fig 2 (online only). Adjusted Kaplan-Meier curves for pairwise comparisons (log-rank test) of secondary patency. *COF,* Chronic outward force; *DAART,* directional atherectomy with antirestenotic therapy; *DCB,* drug-coated balloon; *PTA,* plain balloon angioplasty.