EuroIntervention
2024;20:e1154-e1162
published online e-edition September 2024
DOI: 10.4244/EIJ-D-24-00037

ORIGINAL RESEARCH

Treatment extent of femoropopliteal disease and clinical outcomes following endovascular therapy

Yong-Hoon Yoon[1], MD, PhD; Jae-Hwan Lee[1]*, MD, PhD; Won-Mook Hwang[1], MD; Hyun-Woong Park[1], MD, PhD; Jae-Hyung Roh[1], MD, PhD; Seung-Jun Lee[2], MD, PhD; Young-Guk Ko[2], MD, PhD; Chul-Min Ahn[2], MD, PhD; Cheol Woong Yu[3], MD, PhD; Seung-Whan Lee[4], MD, PhD; Young Jin Youn[5], MD, PhD; Jong Kwan Park[6], MD, PhD; Chang-Hwan Yoon[7,8], MD, PhD; Seung-Woon Rha[9], MD, PhD; Pil-Ki Min[10], MD, PhD; Seung-Hyuk Choi[11], MD, PhD; In-Ho Chae[7,8], MD, PhD; Donghoon Choi[2], MD, PhD; on behalf of the K-VIS investigators

**Corresponding author: Department of Cardiology, Chungnam National University Sejong Hospital, 20 Bodeum 7-ro, Sejong, Republic of Korea. E-mail: myheart@cnu.ac.kr*

This paper also includes supplementary data published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-24-00037

ABSTRACT

BACKGROUND: Endovascular therapy (EVT) has become the preferred treatment modality for femoropopliteal disease. However, there is limited evidence regarding its procedural and clinical outcomes according to the affected area.

AIMS: The aim of this study is to investigate clinical outcomes and device effectiveness according to treatment extent in the superficial femoral artery (SFA), popliteal artery (PA), or both.

METHODS: In this study, we analysed EVT for SFA (2,404 limbs), PA (155 limbs), SFA/PA (383 limbs) using the population in the K-VIS ELLA (Korean Vascular Intervention Society Endovascular Therapy in Lower Limb Artery Diseases) registry. The primary endpoint was target lesion revascularisation (TLR) at 2 years.

RESULTS: The SFA/PA group exhibited a higher prevalence of anatomical complexity, characterised by long lesions, moderate to severe calcification, and total occlusion. The procedures were successful in 97.2% of SFA, 92.9% of PA, and 95.6% of SFA/PA EVTs. The 2-year TLR rates were 21.1%, 18.6%, and 32.7% in the SFA, PA, and SFA/PA groups, respectively. SFA/PA EVT was associated with a significantly increased risk for TLR compared to the SFA group (adjusted hazard ratio [HR] 1.48 [1.09-2.00]; p=0.008) and a trend towards an increased risk compared to the PA group (adjusted HR 1.80 [1.00-3.27]; p=0.052). After overlap weighting, the use of a drug-coated balloon (DCB) was shown to be beneficial, with the lowest TLR rate after SFA and SFA/PA EVT.

CONCLUSIONS: In this large real-world registry, SFA/PA EVT was associated with an increased risk for TLR at 2 years compared to the SFA or PA EVT groups, with favourable outcomes when using a DCB or drug-eluting stent in the SFA/PA EVT group.

KEYWORDS: drug-coated balloon; drug-eluting stent; femoropopliteal disease; treatment extent

SUBMITTED ON 15/01/2024 - REVISION RECEIVED ON 1st 23/04/2024 / 2nd 10/06/2024 - ACCEPTED ON 18/06/2024

Peripheral artery disease (PAD) affects more than 230 million people worldwide and is increasingly recognised as a major comorbidity resulting in serious health conditions, including claudication, amputation, and mortality[1]. Endovascular therapy (EVT) has emerged as an important treatment modality for patients with peripheral artery disease due to its less invasive nature and acceptable efficacy[2].

EVT for femoropopliteal disease has evolved rapidly over the last decade. A newer class of treatment devices, including drug-coated balloons (DCB) and drug-eluting stents (DES), has improved clinical outcomes after EVT for femoropopliteal disease[3-6]. In clinical trials and real-world registries, femoropopliteal disease has generally been treated as a single entity. However, anatomical and physiological differences between the superficial femoral artery (SFA) and popliteal artery (PA) clearly exist, and these differences can possibly affect the interventional approach, procedural success, and long-term clinical outcomes in patients undergoing EVT for femoropopliteal disease[7].

Nonetheless, there is limited evidence regarding the clinical impact of the location of the disease (SFA, PA or both) on procedural and long-term clinical outcomes after EVT. Furthermore, controversy still exists about the effectiveness of various final treatment devices according to the extent of femoropopliteal disease. Therefore, we investigated the clinical significance of treatment extent in patients undergoing EVT for femoropopliteal disease on periprocedural and long-term clinical outcomes and compared the effectiveness of final treatment devices at each treatment extent level.

Impact on daily practice

This study provides demographic and procedural characteristics and clinical outcomes following endovascular therapy (EVT) for femoropopliteal disease based on treatment extent. Patients undergoing superficial femoral artery (SFA)/popliteal artery (PA) EVT who suffer from extensive atherosclerotic burden had the highest target lesion revascularisation (TLR) events over 2 years. The stratified analysis based on treatment extent showed that drug-eluting devices, including drug-coated balloons or drug-eluting stents, had the lowest TLR events in these SFA/PA patients. This result suggests that these drug-eluting devices could be the most effective treatment modality for those with long, diffuse femoropopliteal disease involving both the SFA and the PA.

Methods

STUDY DESIGN AND POPULATION

The K-VIS ELLA (Korean Vascular Intervention Society Endovascular Therapy in Lower Limb Artery Diseases) registry enrolled patients diagnosed with lower extremity PAD undergoing EVT at 19 cardiovascular centres in the Republic of Korea since 2006 (ClinicalTrials.gov: NCT02748226). A comprehensive description of the study's design and the criteria for inclusion/exclusion have been previously published[8]. Overall, 4,393 limbs (2,951 patients) were included in this registry. After excluding patients who did not receive EVT for SFA or PA lesions, including those with in-stent restenosis lesions, prior lower extremity amputation, who lacked follow-up data, or those with insufficient data regarding the mode of EVT, a final cohort of 2,942 limbs from 2,275 patients was subjected to analysis for this study **(Figure 1)**.

The study population was subsequently divided into three distinct groups based on the extent of EVT in the target limbs: (1) EVT for the SFA (SFA group: 2,404 limbs [1,868 patients]), (2) EVT for the PA (PA group: 155 limbs [122 patients]), and (3) EVT for both SFA and PA (SFA/PA group: 383 limbs [285 patients]). The study protocol received approval from the institutional review board at each participating centre and was executed in compliance with the principles outlined in the Declaration of Helsinki. Informed consent was obtained from all patients, except those whose data were collected retrospectively.

PROCEDURES AND FOLLOW-UP

Clinical, imaging, and procedural data were obtained from electronic medical records or telephone interviews. The grading of calcification on angiography was determined based on the peripheral arterial calcium scoring system[9]. Moderate to severe calcification was defined as a calcification grade of 3 or 4. All EVT procedures were conducted by experienced interventional cardiologists. The selection of the treatment strategy, which included factors such as the choice of access route, wire type, wiring technique, the utilisation and type of atherectomy, the use of intravascular imaging, and the final treatment device, was at the discretion of the operator, based on the clinical and anatomical characteristics of each patient. Following balloon angioplasty with either a plain balloon (PB) or DCB, provisional stenting was performed in cases of flow-limiting dissection or residual stenosis greater than 30%. In such cases, patients were categorised into the DCB treatment group. After the initial procedure, patients underwent follow-up evaluations at 6, 12, and 24 months. During the follow-up period, optimal medical treatment, such as antithrombotic agents or lipid-lowering medications, was prescribed by the attending physician.

DEFINITIONS AND CLINICAL OUTCOMES

The success of the EVT procedure was determined by the presence of residual stenosis measuring less than 30% without any flow-limiting dissection. The primary endpoint of the

Abbreviations

BMS	bare metal stent	**PA**	popliteal artery
DCB	drug-coated balloon	**PB**	plain balloon
DES	drug-eluting stent	**SFA**	superficial femoral artery
EVT	endovascular therapy	**TLR**	target lesion revascularisation

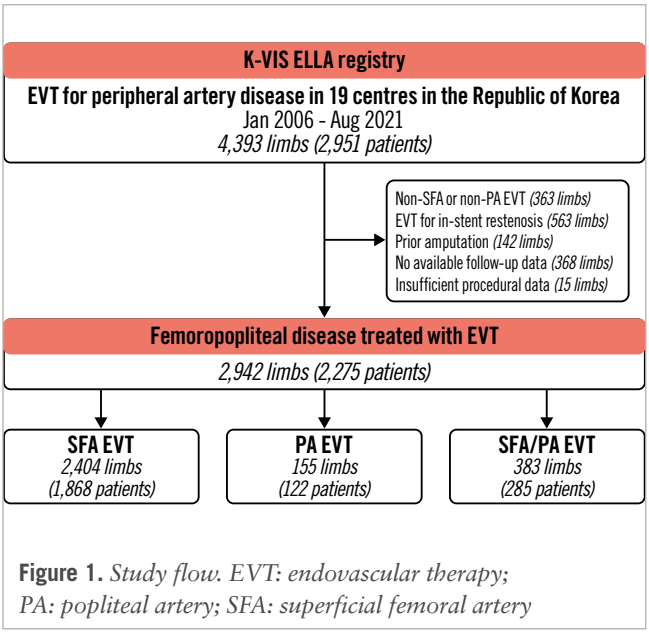


Figure 1. *Study flow. EVT: endovascular therapy; PA: popliteal artery; SFA: superficial femoral artery*

study was target lesion revascularisation (TLR), defined as any subsequent intervention performed within a 5 mm segment proximal or distal to the initially treated target segment during follow-up, with more than 50% angiographic diameter stenosis, accompanied by worsening symptoms and a decline >0.15 in the ankle-brachial index in comparison to the immediate postprocedural ankle-brachial index. Major amputation was defined as amputation of the index limb occurring above the ankle level. Loss of patency was identified when patency, assessed via physiological means (a decrease in ankle-brachial index >0.15) or imaging modalities (such as duplex ultrasound, computed tomography, or angiography), was no longer maintained with symptom aggravation by at least 1 Rutherford category change. A major adverse limb event (MALE) was defined as a composite of TLR or major amputation of the target limb.

STATISTICAL ANALYSIS

Continuous variables are expressed as mean±standard deviation and compared using either one-way analysis of variance or the Kruskal-Wallis test. Categorical variables are presented as counts (%) and analysed using the chi-square or Fisher's exact test, as appropriate. Clinical events observed during follow-up were also assessed, and cumulative event rates and survival curves were generated using the Kaplan-Meier method. All clinical outcomes were reported based on limb-level data, except for mortality, which was analysed based on patient-level data. The follow-up duration was censored either at the time of a clinical event or at the last follow-up, whichever came first. Cox proportional hazards models were used to adjust for confounding factors, including age, sex, body mass index, smoking status, hypertension, diabetes, dyslipidaemia, chronic kidney disease, coronary artery disease, prior EVT, chronic limb-threatening ischaemia, concomitant interventions involving common femoral, iliac, or infrapopliteal lesions, lesion characteristics including total occlusion, TransAtlantic Inter-Society Consensus (TASC) II classification, lesion length, calcification, the final treatment device, medications at discharge (aspirin, clopidogrel, cilostazol, statin), and the year of procedure. Multiple comparisons of Cox proportional hazards models were conducted using the Tukey method to compare clinical outcomes between the three groups defined by femoropopliteal treatment extent. Moreover, the separated propensity scores were calculated for each treatment location group to compare the effectiveness of the final treatment devices (PB, bare metal stent [BMS], DCB, and DES). The propensity score was utilised to estimate the overlap weighting that highlights the target population with the most overlap in observed characteristics between treatments by continuously reducing the weight of units at the tails of the propensity score distribution[10,11]. The standardised mean differences were calculated to assess the balance between plain device and drug-eluting device treatment groups. The cumulative event rates, survival curves, and hazard ratios (HRs) were estimated using the weighted Kaplan-Meier method, and Cox proportional hazards models were additionally adjusted for medications at discharge and the year of procedure to compare the device effectiveness. All reported p-values are two-sided, and statistical significance was defined as $p<0.05$. The statistical analyses were performed using R software, version 4.2.3 (R Foundation for Statistical Computing).

Results

BASELINE CHARACTERISTICS

The mean age of the study population was 69.4 years, with 2,397 (81.5%) male patients, based on limb-level data. In the comparison between groups, the SFA group exhibited the highest percentage of male patients, as well as the highest prevalence of current smokers and individuals with coronary artery disease **(Table 1, Supplementary Table 1)**. The SFA/PA group had the highest prevalence of chronic kidney disease. There were no significant differences in the prevalence of hypertension, diabetes, or dyslipidaemia among the groups. The PA group and SFA/PA group had a history of more chronic kidney disease and prior EVT procedures. Additionally, challenging anatomical characteristics, such as TASC classification C or D, long lesions, total occlusions, and moderate or greater calcification, were most prevalent in the SFA/PA group.

PROCEDURAL OUTCOMES

Table 2 and **Supplementary Table 2** provide an overview of the procedural characteristics of the study population based on limb-level and patient-level data. Intraluminal wiring was the primary method used in the three groups. Atherectomy was most frequently employed in the SFA/PA group (15.4%), with a higher proportion of rotational atherectomy use observed in both the SFA/PA and PA groups compared to the SFA group. Regarding drug-eluting devices, DCB and DES were utilised in 24.3% and 8.0% of cases, respectively, in the SFA group, and 43.6% and 6.8% in the SFA/PA group ($p<0.001$). Notably, DCB (35.5%) were the exclusive drug-eluting devices used in the PA group, whereas DES were not used. The technical success rates were 97.2%, 92.9%, and 95.6% in the SFA, PA, and SFA/PA groups, respectively ($p=0.006$). Vascular rupture and bleeding were most frequently observed in the SFA/PA group. There were no significant differences

Table 1. Baseline demographics.

	Total (N=2,942)	SFA (N=2,404)	PA (N=155)	SFA/PA (N=383)	*p*-value
Age, years	69.4±10.4	69.5±10.1	68.3±10.5	69.1±12.2	0.305
Male	2,397 (81.5)	1,984 (82.5)	121 (78.1)	292 (76.2)	0.007
Body mass index, kg/m^2	23.3±3.4	23.3±3.4	23.8±3.2	23.0±3.6	0.046
Current smoker	804 (27.3)	675 (28.1)	38 (24.5)	91 (23.8)	0.153
Hypertension	2,220 (75.5)	1,831 (76.2)	114 (73.5)	275 (71.8)	0.156
Diabetes	1,865 (63.4)	1,524 (63.4)	99 (63.9)	242 (63.2)	0.989
Diabetes on insulin	482 (16.4)	403 (16.8)	29 (18.7)	50 (13.1)	0.138
Dyslipidaemia	1,715 (58.3)	1,398 (58.2)	90 (58.1)	227 (59.3)	0.917
Chronic kidney disease	755 (25.7)	595 (24.8)	43 (27.7)	117 (30.5)	0.045
End stage renal disease	404 (13.7)	306 (12.7)	29 (18.7)	69 (18.0)	0.004
Coronary artery disease	1,385 (47.1)	1,189 (49.5)	53 (34.2)	143 (37.3)	<0.001
Chronic obstructive lung disease	104 (3.5)	92 (3.8)	1 (0.6)	11 (2.9)	0.087
Prior stroke	515 (17.5)	429 (17.8)	28 (18.1)	58 (15.1)	0.426
Prior endovascular therapy	926 (31.5)	735 (30.6)	54 (34.8)	137 (35.8)	0.082
Chronic limb-threatening ischaemia	1,161 (39.5)	888 (36.9)	73 (47.1)	200 (52.2)	<0.001
TASC II type C or D	1,675 (56.9)	1,363 (56.7)	64 (41.3)	248 (64.8)	<0.001
Lesion length ≥150 mm	1,281 (43.5)	1,048 (43.6)	11 (7.1)	222 (58.0)	<0.001
Total occlusion	1,480 (50.3)	1,159 (48.2)	83 (53.5)	238 (62.1)	<0.001
Moderate/severe calcification	920 (31.3)	743 (30.9)	33 (21.3)	144 (37.6)	0.001

Data are presented as mean±standard deviation or n (%). PA: popliteal artery; SFA: superficial femoral artery; TASC: TransAtlantic Inter-Society Consensus

in the use of antithrombotic and antidyslipidaemia agents at discharge, except for cilostazol, which was administered more often in the SFA group.

Clinical outcomes

During the 2 years of follow-up, TLR occurred in 361 limbs (21.1%) in the SFA group, 20 limbs (18.6%) in the PA group, and 83 limbs (32.7%) in the SFA/PA group (p<0.001) **(Central illustration, Supplementary Table 3)**. In addition, the incidence of loss of patency and MALE were highest in the SFA/PA group (73.4% and 33.1%), whereas those rates were similar between the SFA group (61.2% and 21.7%) and PA group (60.7% and 19.9%). All-cause death occurred least in patients in the SFA group. The incidence of major amputation was remarkably low in all groups, without a significant difference.

In a multivariable Cox proportional model with multiple comparisons **(Table 3)**, the SFA/PA group was associated with an increased risk of TLR compared to the SFA group (adjusted HR 1.48, 95% CI: 1.09-2.00; p=0.008) and the PA group (adjusted HR 1.80, 95% CI: 1.00-3.27; p=0.052). There was no difference in the risk of TLR between the SFA and PA groups. The SFA/PA group also showed a significantly increased risk of loss of patency compared to the SFA group and the PA group. There were no differences in all-cause mortality nor in the rate of major amputation between these groups.

Supplementary Table 4 shows the baseline and procedural characteristics between final treatment devices stratified by femoropopliteal treatment extent. The prevalence of concomitant infrapopliteal treatment and chronic limb-threatening ischaemia were highest in those treated with PB for all three treatment groups. The total occlusion rate was highest in the DES group for SFA EVT and in the BMS group for SFA/PA EVT. Long lesions were mostly treated with DES in SFA and SFA/PA EVT and with DCB in PA EVT. After overlap weighting, all baseline and procedural characteristics were well balanced **(Supplementary Table 5)**. The crude and weighted comparison of treated devices are presented in **Supplementary Figure 1**, **Figure 2**, and **Supplementary Table 6**. Generally, the use of drug-eluting devices including DCB and DES was associated with lower TLR rates in SFA and SFA/PA EVT in the weighted analysis. The weighted TLR rates were lowest in the DCB group in the SFA EVT (weighted HR 0.45, 95% CI: 0.31-0.64; p<0.001, compared to the PB group). There was no difference in the treatment effect between devices in PA EVT, with the lowest TLR rate in the BMS group. In SFA/PA EVT, the TLR rate was lowest in the DCB group, while the TLR rate was numerically higher in the BMS group compared to the PB group.

Discussion

This study investigated the procedural and clinical impact of the treatment extent in patients with femoropopliteal disease undergoing EVT. The study results are summarised as follows: (1) Challenging anatomical characteristics were most prevalent in the SFA/PA group. (2) The technical success rate was lowest in the PA group, and drug-eluting devices including DCB or DES were used most in SFA/PA disease. (3) The prevalence of TLR at 2 years was highest in patients selected for SFA/PA EVT. (4) In multiple comparison analyses, the patients selected for undergoing SFA/PA EVT showed a significantly higher risk for TLR than those undergoing SFA EVT. There was also a trend toward a higher TLR

Table 2. Procedural characteristics.

	Total (N=2,942)	SFA (N=2,404)	PA (N=155)	SFA/PA (N=383)	*p*-value
Wiring approach					0.062
Intraluminal	2,396 (82.3)	1,960 (82.4)	135 (87.7)	301 (79.2)	
Subintimal	516 (17.7)	418 (17.6)	19 (12.3)	79 (20.8)	
Atherectomy					<0.001
Not used	2,716 (92.3)	2,252 (93.7)	140 (90.3)	324 (84.6)	
Rotational	119 (4.0)	70 (2.9)	10 (6.5)	39 (10.2)	
Directional	107 (3.6)	82 (3.4)	5 (3.2)	20 (5.2)	
Final treatment					<0.001
Plain balloon	922 (31.3)	736 (30.6)	75 (48.4)	111 (29.0)	
Bare metal stent	996 (33.9)	892 (37.1)	25 (16.1)	79 (20.6)	
Drug-coated balloon	805 (27.4)	583 (24.3)	55 (35.5)	167 (43.6)	
Drug-eluting stent	219 (7.4)	193 (8.0)	0 (0)	26 (6.8)	
Concomitant treatment					
Common femoral lesion	96 (3.3)	50 (2.1)	2 (1.3)	44 (11.5)	<0.001
Infrapopliteal lesion	668 (22.7)	454 (18.9)	68 (43.9)	146 (38.1)	<0.001
Iliac lesion	422 (14.3)	353 (14.7)	18 (11.6)	51 (13.3)	0.473
Technical success	2,846 (96.7)	2,336 (97.2)	144 (92.9)	366 (95.6)	0.006
Complications					
Distal embolisation	14 (0.5)	11 (0.5)	0 (0)	3 (0.8)	0.467
Vascular rupture	33 (1.1)	19 (0.8)	3 (1.9)	11 (2.9)	0.001
Bleeding	81 (2.8)	58 (2.4)	6 (3.9)	17 (4.4)	0.054
In-hospital death	15 (0.5)	14 (0.6)	1 (0.6)	0 (0)	0.322
Discharge medications					
Aspirin	2,291 (77.9)	1,887 (78.5)	112 (72.3)	292 (76.2)	0.138
Clopidogrel	2,397 (81.5)	1,972 (82.0)	121 (78.1)	304 (79.4)	0.246
Cilostazol	904 (30.7)	775 (32.2)	38 (24.5)	91 (23.8)	0.001
Statin	2,153 (73.2)	1,762 (73.3)	114 (73.5)	277 (72.3)	0.919

Data are presented as n (%). PA: popliteal artery; SFA: superficial femoral artery

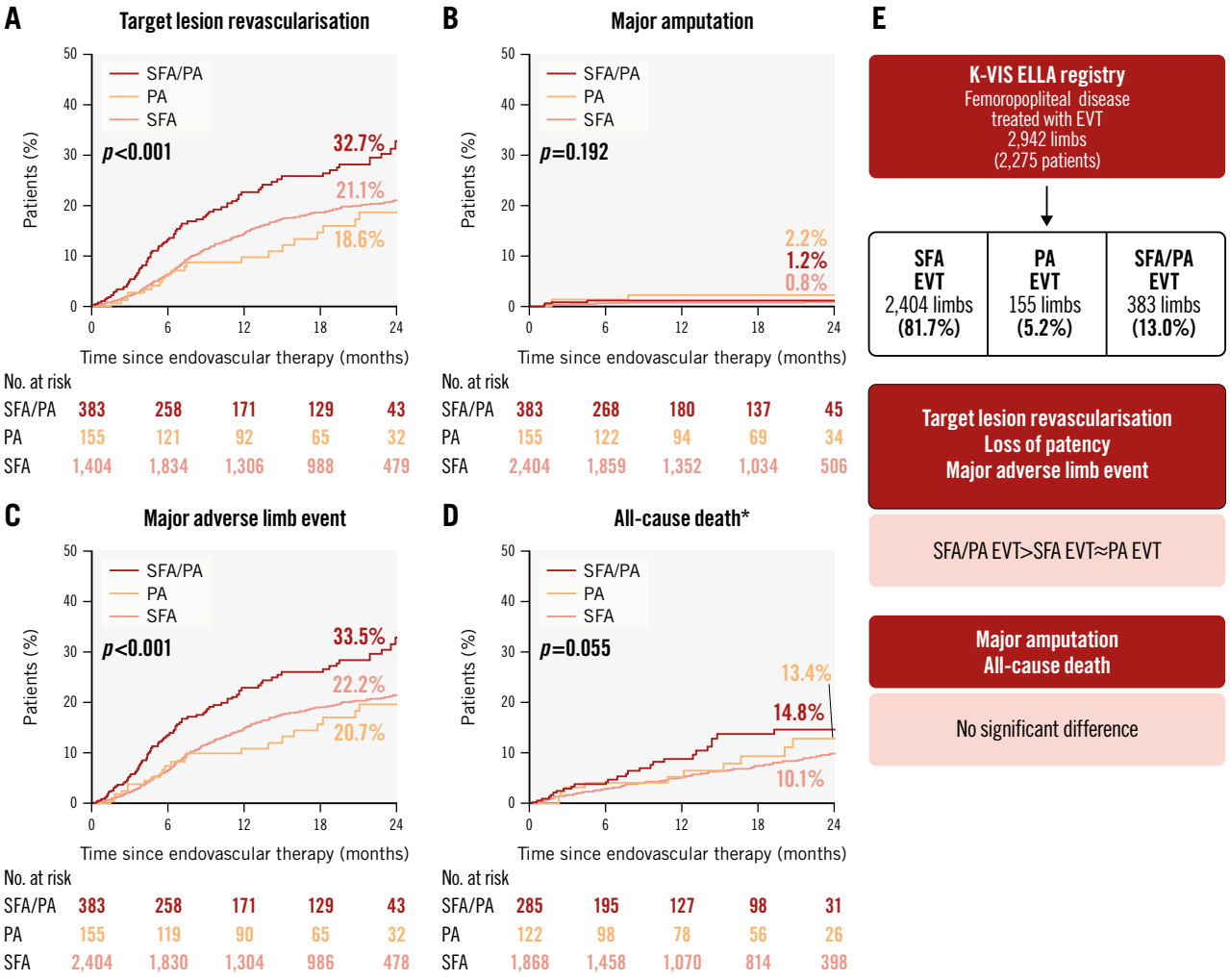
risk in patients undergoing SFA/PA EVT compared to those undergoing PA EVT. (5) In stratified analysis according to femoropopliteal treatment extent, the TLR rate was lowest in the DCB groups in SFA and SFA/PA EVT.

The outcomes of EVT for SFA and PA disease have been evaluated together as femoropopliteal lesions in most published studies. However, in a long segment of femoropopliteal disease, anatomical and physiological differences between the SFA and the popliteal artery exist[7,12,13]. The SFA is long and straight, with a larger diameter and less external compression, while the PA is relatively short with important branches running below the knee level. Additionally, the popliteal artery is uniquely compressed by an external mechanical force while bending the knee joint. These factors result in differences in procedural approach, techniques, and selection of final devices between SFA and PA EVT. Real-world data indicate that PA EVT is characterised by less use of stents compared to SFA EVT[14]. In our study, PA EVT showed more concomitant treatment for infrapopliteal lesions, little use of stents, and a lower immediate technical success rate compared to SFA EVT. The strategy of avoiding stents could be one of the reasons for the lower success rate in PA EVT[15]. To overcome these difficulties, recent studies have investigated the role of atherectomy with antirestenotic therapy using a DCB or an interwoven nitinol stent in PA EVT. The success rate was significantly improved by using an interwoven nitinol stent in PA EVT, with 25% of patients undergoing EVT with PB needing immediate stenting due to a failure to achieve adequate lumen gain[16,17]. However, there is still controversy regarding whether directional atherectomy with antirestenotic therapy could improve technical success in PA EVT[15,18]. All studies about PA EVT have been relatively small; therefore, further studies with large populations are required.

The extent of femoropopliteal disease can vary widely, and thus many factors can affect clinical outcomes after EVT. Lesion length is known to be associated with long-term clinical outcomes after EVT for femoropopliteal disease[19,20]. However, evidence regarding the relevance of disease or treatment extent on long-term outcomes is currently limited. The IN.PACT Global Clinical Study, involving 1,406 patients, reported the lowest freedom from TLR in the SFA/PA EVT group (69.2%) compared to SFA EVT (79.7%) or PA EVT (76.5%) at 3 years using DCB,

EuroIntervention — Central Illustration

Clinical outcomes of endovascular therapy for femoropopliteal disease over a 2-year period based on treatment extent.



Yong-Hoon Yoon *et al.* • *EuroIntervention* 2024;20:e1154-e1162 • DOI: 10.4244/EIJ-D-24-00037

**Analysis based on patient-level data. Kaplan-Meier curves for the following clinical outcomes: target lesion revascularisation (A), major amputation (B), major adverse limb event (C), and all-cause death (D). E) summarises the study results. EVT: endovascular therapy; PA: popliteal artery; SFA: superficial femoral artery*

with a consistent effect after adjusting for lesion length in multivariable analysis[21]. On the other hand, EVT with the interwoven nitinol stent showed similar 3-year TLR-free rates (69.5%) in patients with SFA disease with or without PA involvement[22]. A recent large registry involving 19,324 patients undergoing femoropopliteal EVT for patients with claudication showed the highest index limb revascularisation rate in the SFA/PA EVT group and the highest index limb amputation rate in the PA EVT group. Our real-world data include EVTs with all treatment devices and showed the highest TLR rate in the SFA/PA EVT group with similar TLR rates between the SFA and PA EVT groups at 2 years of follow-up. The higher atherosclerotic burden in the SFA/PA group might play a role in developing restenosis after EVT; furthermore, over- or undersizing a DCB in diffuse disease could lead to inadequate acute lumen gain[21].

The "leave nothing behind" strategy using DCB has recently emerged as an effective and safe treatment option for femoropopliteal EVT[23-25]. Our data showed that DCB and DES showed relatively lower TLR rates in the SFA and SFA/PA groups. These results are consistent with previous randomised trials and real-world registry data assessing SFA and PA lesions together. EVT with DCB was associated with a significant improvement in primary patency at 1 year compared to EVT with PB[3,4]. EVT with DCB was also compared to EVT with DES, and the results showed a similar patency rate in both groups[5,6]. In addition, EVT with BMS was associated with a higher TLR rate compared to PB in SFA/PA

Table 3. Multiple comparisons of femoropopliteal treatment location and clinical outcomes.

	Adjusted hazard ratio (95% confidence interval)	*p*-value
Target lesion revascularisation		
PA vs SFA	0.82 (0.47-1.42)	0.667
SFA/PA vs SFA	1.48 (1.09-2.00)	0.008
SFA/PA vs PA	1.80 (1.00-3.27)	0.052
Major amputation		
PA vs SFA	3.39 (0.61-18.70)	0.213
SFA/PA vs SFA	1.36 (0.34-5.42)	0.859
SFA/PA vs PA	0.40 (0.06-2.92)	0.525
Loss of patency		
PA vs SFA	0.93 (0.70-1.25)	0.841
SFA/PA vs SFA	1.30 (1.08-1.56)	0.002
SFA/PA vs PA	1.39 (1.01-1.92)	0.043
Major adverse limb event		
PA vs SFA	0.87 (0.51-1.48)	0.809
SFA/PA vs SFA	1.43 (1.06-1.92)	0.015
SFA/PA vs PA	1.64 (0.92-2.90)	0.106
All-cause death*		
PA vs SFA	1.31 (0.60-2.84)	0.695
SFA/PA vs SFA	1.07 (0.62-1.85)	0.957
SFA/PA vs PA	0.82 (0.33-2.02)	0.858

*Analysis based on patient-level data. PA: popliteal artery; SFA: superficial femoral artery

EVT in this study. This association is believed to be linked to a higher restenosis risk with BMS in extensive atherosclerotic burden due to the metallic scaffold not being coated in an antiproliferative drug. Therefore, the "leave nothing behind" strategy with a drug-eluting device is preferable, especially in the management of extensive femoropopliteal disease. In PA EVT, on the other hand, there were no differences between the three treatment modalities in our study. Not only could the small size of this population mitigate the difference in effect between treatment modalities, but also, the anatomical and procedural differences could affect device effectiveness in isolated PA EVT. Similarly, most previous research is based either on a small number of patients or single-arm studies. If rescue stenting was ignored, 1-year comparisons patency was similar between EVT with PB and BMS[17]. DCB showed an acceptable 1-year patency[21], and there was a trend that the combined treatment of DCB with atherectomy improved 1-year patency compared to EVT with DCB alone[15]. The lower prevalence of PA involvement in femoropopliteal disease might limit the vigorous investigation of long-term treatment effects between various strategies.

Currently, most evidence with respect to femoropopliteal EVT is limited to midterm follow-up. Therefore, further studies with long-term follow-up comparing the clinical efficacy of different devices in each segment of long femoropopliteal disease are needed. This will enhance understanding of the long-term effect of EVT and clarify the best treatment strategies for each disease segment in femoropopliteal disease.

Limitations

There are several limitations in this study. First, our study primarily serves as a hypothesis-generating investigation because this was an observational study. Therefore, further validation in

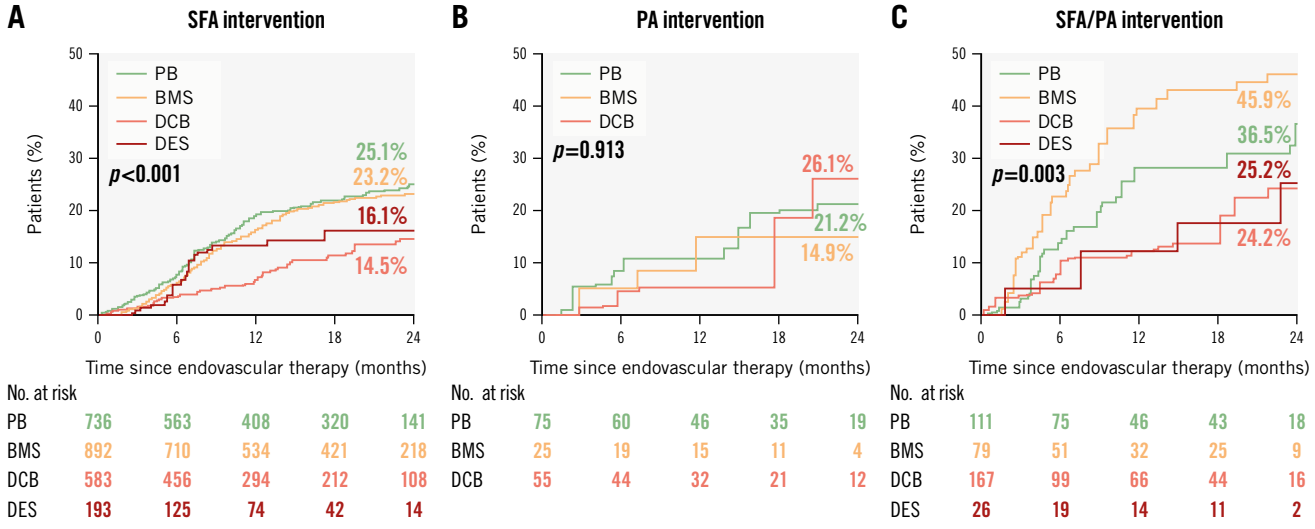


Figure 2. **Analysis based on patient-level data. Kaplan-Meier curves of target lesion revascularisation using overlap weighting between final treatment device groups, stratified by femoropopliteal treatment extent. The curves represent SFA intervention (A), PA intervention (B), and combined SFA/PA intervention (C). BMS: bare metal stent; DCB: drug-coated balloon; DES: drug-eluting stent; PA: popliteal artery; PB: plain balloon; SFA: superficial femoral artery*

larger and more diverse cohorts is needed. Second, all analyses were based on treatment extent rather than the area affected by femoropopliteal disease. This fact could limit the proper interpretation of our results because the attending physician determined the treatment extent, which may not have reflected the true atherosclerotic burden and the extent of femoropopliteal disease. Complex SFA/PA disease could have been treated only in the SFA or the PA for simpler procedures, resulting in different procedural and clinical outcomes. Third, in cases where flow-limiting dissection occurred after balloon angioplasty, subsequent treatment strategies may have varied among operators and centres. Our dataset does not provide information regarding the number of bailout stenting procedures following flow-limiting dissection. However, all bailout stenting procedures undergo review by the national health insurance system in the Republic of Korea. The reimbursement criteria are stringent, potentially limiting the number of exceptional cases. Fourth, our data did not include specific treatment information about each segment in the SFA/PA group. There is a possibility of heterogeneous use of devices in limbs with long disease involvement. In addition, there was no uniform indication across the participating centres for the debulking strategy prior to use of the final device, resulting in additional bias in interpreting the effect of the final device. Fifth, small numbers of patients, especially in the PA group, limited the assessment of the effectiveness of various devices. Sixth, TLR events were determined by the attending physician, and the demographic and anatomical characteristics could have affected the decision-making about reintervention for the patients. Seventh, medical treatment following the index EVT was at the discretion of the attending physicians. Lastly, imaging studies and functional assessment to assess patency were not routinely performed for all patients.

Conclusions

In this real-world registry involving a large population undergoing EVT for femoropopliteal disease, SFA/PA EVT was associated with acceptable immediate periprocedural outcomes despite the higher prevalence of anatomical complexity. However, SFA/PA EVT was associated with an increased risk of TLR at 2 years of follow-up compared to the SFA or PA EVT groups. The use of drug-eluting devices including DCB or DES showed favourable outcomes compared to EVT with PB in patients selected for SFA and SFA/PA intervention.

Authors' affiliations

1. Department of Cardiology, Chungnam National University Sejong Hospital, Chungnam National University School of Medicine, Sejong, Republic of Korea; 2. Severance Cardiovascular Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea; 3. Department of Cardiology, Cardiovascular Center, Korea University, Anam Hospital, Korea University College of Medicine, Seoul, Republic of Korea; 4. Department of Cardiology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; 5. Division of Cardiology, Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, Republic of Korea; 6. Division of Cardiology, Department of Internal Medicine, National Health Insurance Service Ilsan Hospital, Goyang, Republic of Korea; 7. Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea; 8. Department of Cardiology, Seoul National University Bundang Hospital, Seongnam, Republic of Korea; 9. Cardiovascular Center, Division of Cardiology, Department of Internal Medicine, Korea University Guro Hospital, Korea University College of Medicine, Seoul, Republic of Korea; 10. Division of Cardiology, Department of Internal Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea; 11. Division of Cardiology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Funding

This study was supported by grants from the Patient-Centered Clinical Research Coordinating Center funded by the Ministry of Health and Welfare, Republic of Korea (grant HC20C0081).

Conflict of interest statement

The authors have no conflicts of interest relevant to this article to declare.

References

1. Aday AW, Matsushita K. Epidemiology of Peripheral Artery Disease and Polyvascular Disease. *Circ Res.* 2021;128:1818-32.

2. Aboyans V, Ricco JB, Bartelink MEL, Björck M, Brodmann M, Cohnert T, Collet JP, Czerny M, De Carlo M, Debus S, Espinola-Klein C, Kahan T, Kownator S, Mazzolai L, Naylor AR, Roffi M, Röther J, Sprynger M, Tendera M, Tepe G, Venermo M, Vlachopoulos C, Desormais I; ESC Scientific Document Group. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteriesEndorsed by: the European Stroke Organization (ESO)The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). *Eur Heart J.* 2018;39:763-816.

3. Tepe G, Laird J, Schneider P, Brodmann M, Krishnan P, Micari A, Metzger C, Scheinert D, Zeller T, Cohen DJ, Snead DB, Alexander B, Landini M, Jaff MR; IN.PACT SFA Trial Investigators. Drug-coated balloon versus standard percutaneous transluminal angioplasty for the treatment of superficial femoral and popliteal peripheral artery disease: 12-month results from the IN.PACT SFA randomized trial. *Circulation.* 2015;131:495-502.

4. Rosenfield K, Jaff MR, White CJ, Rocha-Singh K, Mena-Hurtado C, Metzger DC, Brodmann M, Pilger E, Zeller T, Krishnan P, Gammon R, Müller-Hülsbeck S, Nehler MR, Benenati JF, Scheinert D; LEVANT 2 Investigators. Trial of a Paclitaxel-Coated Balloon for Femoropopliteal Artery Disease. *N Engl J Med.* 2015;373:145-53.

5. Liistro F, Angioli P, Porto I, Ducci K, Falsini G, Ventoruzzo G, Ricci L, Scatena A, Grotti S, Bolognese L. Drug-Eluting Balloon Versus Drug-Eluting Stent for Complex Femoropopliteal Arterial Lesions: The DRASTICO Study. *J Am Coll Cardiol.* 2019;74:205-15.

6. Bausback Y, Wittig T, Schmidt A, Zeller T, Bosiers M, Peeters P, Brucks S, Lottes AE, Scheinert D, Steiner S. Drug-Eluting Stent Versus Drug-Coated Balloon Revascularization in Patients With Femoropopliteal Arterial Disease. *J Am Coll Cardiol.* 2019;73:667-79.

7. Jadidi M, Razian SA, Anttila E, Doan T, Adamson J, Pipinos M, Kamenskiy A. Comparison of morphometric, structural, mechanical, and physiologic characteristics of human superficial femoral and popliteal arteries. *Acta Biomater.* 2021;121:431-43.

8. Lee SJ, Lee HH, Ko YG, Ahn CM, Lee YJ, Kim JS, Kim BK, Hong MK, Chang Kim H, Yu CW, Lee JH, Lee SW, Youn YJ, Park JK, Yoon CH, Rha SW, Min PK, Choi SH, Chae IH, Choi D; K-VIS Investigators. Device Effectiveness for Femoropopliteal Artery Disease Treatment: An Analysis of K-VIS ELLA Registry. *JACC Cardiovasc Interv.* 2023;16:1640-50.

9. Rocha-Singh KJ, Zeller T, Jaff MR. Peripheral arterial calcification: prevalence, mechanism, detection, and clinical implications. *Catheter Cardiovasc Interv.* 2014;83:E212-20.

10. Li F, Thomas LE, Li F. Addressing Extreme Propensity Scores via the Overlap Weights. *Am J Epidemiol.* 2019;188:250-7.

11. Zhou T, Tong G, Li F, Thomas LE, Li F. PSweight: An R Package for Propensity Score Weighting Analysis. *The R Journal.* 2022;14:282-99.

12. Semaan E, Hamburg N, Nasr W, Shaw P, Eberhardt R, Woodson J, Doros G, Rybin D, Farber A. Endovascular management of the popliteal artery: comparison of atherectomy and angioplasty. *Vasc Endovascular Surg.* 2010;44:25-31.

13. Kröger K, Santosa F, Goyen M. Biomechanical incompatibility of popliteal stent placement. *J Endovasc Ther.* 2004;11:686-94.

14. Altin SE, Parise H, Hess CN, Rosenthal NA, Creager MA, Aronow HD, Curtis JP. Long-Term Patient Outcomes After Femoropopliteal Peripheral Vascular Intervention in Patients With Intermittent Claudication. *JACC Cardiovasc Interv.* 2023;16:1668-78.

15. Stavroulakis K, Schwindt A, Torsello G, Stachmann A, Hericks C, Bosiers MJ, Beropoulis E, Stahlhoff S, Bisdas T. Directional Atherectomy With Antirestenotic Therapy vs Drug-Coated Balloon Angioplasty Alone for Isolated Popliteal Artery Lesions. *J Endovasc Ther.* 2017;24:181-8.

16. Scheinert D, Werner M, Scheinert S, Paetzold A, Banning-Eichenseer U, Piorkowski M, Ulrich M, Bausback Y, Bräunlich S, Schmidt A. Treatment of complex atherosclerotic popliteal artery disease with a new self-expanding interwoven nitinol stent: 12-month results of the Leipzig SUPERA popliteal artery stent registry. *JACC Cardiovasc Interv.* 2013;6:65-71.

17. Rastan A, Krankenberg H, Baumgartner I, Blessing E, Müller-Hülsbeck S, Pilger E, Scheinert D, Lammer J, Gißler M, Noory E, Neumann FJ, Zeller T. Stent placement versus balloon angioplasty for the treatment of obstructive lesions of the popliteal artery: a prospective, multicenter, randomized trial. *Circulation.* 2013;127:2535-41.

18. Rastan A, McKinsey JF, Garcia LA, Rocha-Singh KJ, Jaff MR, Noory E, Zeller T; DEFINITIVE LE Investigators. One-Year Outcomes Following Directional Atherectomy of Infrapopliteal Artery Lesions: Subgroup Results of the Prospective, Multicenter DEFINITIVE LE Trial. *J Endovasc Ther.* 2015;22:839-46.

19. Yoshioka N, Tokuda T, Koyama A, Yamada T, Nishikawa R, Shimamura K, Takagi K, Morita Y, Tanaka A, Ishii H, Morishima I, Murohara T; on the ASIGARU PAD investigators. Clinical outcomes and predictors of restenosis in patients with femoropopliteal artery disease treated using polymer-coated paclitaxel-eluting stents or drug-coated balloons. *Heart Vessels.* 2022;37:555-66.

20. Soga Y, Takahara M, Iida O, Suzuki K, Hirano K, Kawasaki D, Shintani Y, Yamaoka T, Ando K. Relationship Between Primary Patency and Lesion Length Following Bare Nitinol Stent Placement for Femoropopliteal Disease. *J Endovasc Ther.* 2015;22:862-7.

21. Torsello G, Stavroulakis K, Brodmann M, Micari A, Tepe G, Veroux P, Benko A, Choi D, Vermassen FEG, Jaff MR, Guo J, Dobranszki R, Zeller T; IN.PACT Global Investigators. Three-Year Sustained Clinical Efficacy of Drug-Coated Balloon Angioplasty in a Real-World Femoropopliteal Cohort. *J Endovasc Ther.* 2020;27:693-705.

22. Guzzardi G, Spinazzola A, Cangiano G, Natrella M, Paladini A, Porta C, Boccalon L, Negroni D, Leati G, Laganà D, Guglielmi R, Carriero A. Endovascular treatment of femoro-popliteal disease with the Supera stent: results of a multicenter study. *J Public Health Res.* 2021;11:2360.

23. Zeller T, Brodmann M, Ansel GM, Scheinert D, Choi D, Tepe G, Menk J, Micari A. Paclitaxel-coated balloons for femoropopliteal peripheral arterial disease: final five-year results of the IN.PACT Global Study. *EuroIntervention.* 2022;18:e940-8.

24. Thieme M, Von Bilderling P, Paetzel C, Karnabatidis D, Perez Delgado J, Lichtenberg M; Lutonix Global SFA Registry Investigators. The 24-Month Results of the Lutonix Global SFA Registry: Worldwide Experience With Lutonix Drug-Coated Balloon. *JACC Cardiovasc Interv.* 2017;10:1682-90.

25. Giacoppo D, Cassese S, Harada Y, Colleran R, Michel J, Fusaro M, Kastrati A, Byrne RA. Drug-Coated Balloon Versus Plain Balloon Angioplasty for the Treatment of Femoropopliteal Artery Disease: An Updated Systematic Review and Meta-Analysis of Randomized Clinical Trials. *JACC Cardiovasc Interv.* 2016;9:1731-42.

Supplementary data

Supplementary Table 1. Baseline demographics based on patient-level data.

Supplementary Table 2. Procedural characteristics based on patient-level data.

Supplementary Table 3. Clinical outcomes at 1 and 2 years.

Supplementary Table 4. Baseline and procedural characteristics between final treatment device groups, stratified by femoropopliteal treatment extent.

Supplementary Table 5. Adjusted baseline and procedural characteristics between final treatment device groups using overlap weighting, stratified by femoropopliteal treatment extent.

Supplementary Table 6. The risk of target lesion revascularisation between final treatment device groups using unadjusted, multivariable adjusted, and overlap weighting analysis, stratified by femoropopliteal treatment extent.

Supplementary Figure 1. Kaplan-Meier curves of target lesion revascularisation between final treatment device groups, stratified by femoropopliteal treatment extent.

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-24-00037

Supplementary data

Supplementary Table 1. Baseline demographics based on patient-level data.

	Total (N=2275)	SFA (N=1868)	PA (N=122)	SFA/PA (N=285)	P
Age, year	69.4±10.4	69.7±10.1	67.5±10.4	68.8±12.1	0.044
Male	1848 (81.2)	1540 (82.4)	95 (77.9)	213 (74.7)	0.005
Body mass index, kg/m^2	23.3±3.4	23.3±3.4	23.9±3.2	22.8±3.5	0.004
Current smoker	641 (28.2)	541 (29.0)	28 (23.0)	72 (25.3)	0.182
Hypertension	1711 (75.2)	1420 (76.0)	86 (70.5)	205 (71.9)	0.153
Diabetes	1430 (62.9)	1175 (62.9)	74 (60.7)	181 (63.5)	0.858
Diabetes on insulin	363 (16.0)	308 (16.5)	23 (18.9)	32 (11.2)	0.052
Dyslipidemia	1281 (56.3)	1054 (56.4)	69 (56.6)	158 (55.4)	0.951
Chronic kidney disease	575 (25.3)	453 (24.3)	33 (27.0)	89 (31.2)	0.037
End stage renal disease	299 (13.1)	222 (11.9)	22 (18.0)	55 (19.3)	0.001
Coronary artery disease	1058 (46.5)	923 (49.4)	39 (32.0)	96 (33.7)	<0.001
Chronic obstructive lung disease	81 (3.6)	71 (3.8)	1 (0.8)	9 (3.2)	0.210
Prior stroke	394 (17.3)	333 (17.8)	21 (17.2)	40 (14.0)	0.289
Prior endovascular therapy	484 (21.3)	390 (20.9)	28 (23.0)	66 (23.2)	0.612
Chronic limb-threatening ischemia	897 (39.4)	681 (36.5)	56 (45.9)	160 (56.1)	<0.001
TASC-II types, C or D	1272 (55.9)	1032 (55.2)	49 (40.2)	191 (67.0)	<0.001
Lesion length ≥150 mm	953 (41.9)	790 (42.3)	5 (4.1)	158 (55.4)	<0.001
Total occlusion	1165 (51.2)	920 (49.3)	61 (50.0)	184 (64.6)	<0.001
Moderate/severe calcification	715 (31.4)	589 (31.5)	23 (18.9)	103 (36.1)	0.003

PA, popliteal artery; SFA, superficial femoral artery; TASC, Trans-Atlantic Inter-Society Consensus Document

Supplementary Table 2. Procedural characteristics based on patient-level data.

	Total (N=2275)	SFA (N=1868)	PA (N=122)	SFA/PA (N=285)	P
Wiring approach					0.118
Intraluminal	1848 (82.1)	1519 (82.2)	106 (87.6)	223 (79.1)	
Subintimal	402 (17.9)	328 (17.8)	15 (12.4)	59 (20.9)	
Atherectomy					<0.001
Not used	2105 (92.5)	1752 (93.8)	110 (90.2)	243 (85.3)	
Rotational	96 (4.2)	59 (3.2)	7 (5.7)	30 (10.5)	
Directional	74 (3.3)	57 (3.1)	5 (4.1)	12 (4.2)	
Final treatment					<0.001
Plain balloon	698 (30.7)	554 (29.7)	60 (49.2)	84 (29.5)	
Bare metal stent	798 (35.1)	721 (38.6)	18 (14.8)	59 (20.7)	
Drug-coated balloon	616 (27.1)	448 (24.0)	44 (36.1)	124 (43.5)	
Drug-eluting stent	163 (7.2)	145 (7.8)	0	18 (6.3)	
Concomitant treatment					
Common femoral lesion	69 (3.0)	37 (2.0)	0	32 (11.2)	<0.001
Infrapopliteal lesion	530 (23.3)	365 (19.5)	52 (42.6)	113 (39.6)	<0.001
Iliac lesion	346 (15.2)	294 (15.7)	16 (13.1)	36 (12.6)	0.318
Technical success	2191 (96.3)	1807 (96.7)	114 (93.4)	270 (94.7)	0.056
Complications					
Distal embolization	11 (0.5)	10 (0.5)	0	1 (0.4)	0.670
Vascular rupture	28 (1.2)	17 (0.9)	2 (1.6)	9 (3.2)	0.005
Bleeding	58 (2.5)	42 (2.2)	4 (3.3)	12 (4.2)	0.128
In-hospital death	10 (0.4)	9 (0.5)	1 (0.8)	0	0.420
Discharge medications					
Aspirin	1769 (77.8)	1464 (78.4)	89 (73.0)	216 (75.8)	0.262
Clopidogrel	1830 (80.4)	1513 (81.0)	95 (77.9)	222 (77.9)	0.358
Cilostazol	694 (30.5)	603 (32.3)	29 (23.8)	62 (21.8)	<0.001
Statin	1651 (72.6)	1364 (73.0)	86 (70.5)	201 (70.5)	0.591

PA, popliteal artery; SFA, superficial femoral artery

Supplementary Table 3. Clinical outcomes at 1 and 2 years.

	Event number(rate) at 1 year				Event number(rate) at 2 year			
	SFA	PA	SFA/PA	P	SFA	PA	SFA/PA	P
Target lesion revascularization	280 (14.5)	13 (9.7)	68 (22.7)	<0.001	361 (21.1)	20 (18.6)	83 (32.7)	<0.001
Major amputation	15 (0.7)	3 (2.2)	4 (1.2)	0.150	16 (0.8)	3 (2.2)	4 (1.2)	0.192
Loss of patency	941 (45.8)	56 (40.4)	188 (58.5)	<0.001	1158 (61.2)	75 (60.7)	219 (73.4)	<0.001
Major adverse limb event	293 (15.1)	15 (11.0)	70 (23.1)	<0.001	375 (21.7)	22 (19.9)	85 (33.1)	<0.001
All-cause death*	81 (5.2)	6 (5.4)	19 (9.0)	0.095	122 (9.9)	11 (13.0)	26 (14.9)	0.055

PA, popliteal artery; SFA, superficial femoral artery

* Analysis based on patient-level data

Supplementary Table 4. Baseline and procedural characteristics between final treatment device groups, stratified by femoropopliteal treatment extent.

	SFA intervention					PA intervention				SFA/PA intervention				
	PB (N=736)	BMS (N=892)	DCB (N=583)	DES (N=193)	P	PB (N=75)	BMS (N=25)	DCB (N=55)	P	PB (N=111)	BMS (N=79)	DCB (N=167)	DES (N=26)	P
Age, year	68.6±10.6	70.1±9.4	69.4±10.6	70.6±9.5	0.011	69.8±10.3	65.7±11.8	67.4±10.0	0.170	67.4±13.8	69.5±10.9	69.7±11.6	71.7±12.5	0.272
Male	584 (79.3)	754 (84.5)	487 (83.5)	159 (82.4)	0.045	60 (80.0)	19 (76.0)	42 (76.4)	0.852	79 (71.2)	60 (75.9)	134 (80.2)	19 (73.1)	0.362
Body mass index, kg/m^2	23.1±3.4	23.1±3.3	23.6±3.2	23.6±4.1	0.019	23.7±3.4	24.0±3.3	23.9±2.8	0.823	22.5±2.9	23.1±3.8	23.2±3.6	23.7±4.8	0.227
Current smoker	174 (23.6)	284 (31.8)	157 (26.9)	60 (31.1)	0.002	20 (26.7)	5 (20.0)	13 (23.6)	0.784	23 (20.7)	22 (27.8)	38 (22.8)	8 (30.8)	0.553
Hypertension	570 (77.4)	683 (76.6)	440 (75.5)	138 (71.5)	0.360	57 (76.0)	18 (72.0)	39 (70.9)	0.795	76 (68.5)	53 (67.1)	125 (74.9)	21 (80.8)	0.351
Diabetes	477 (64.8)	552 (61.9)	385 (66.0)	110 (57.0)	0.083	48 (64.0)	15 (60.0)	36 (65.5)	0.895	70 (63.1)	48 (60.8)	111 (66.5)	13 (50.0)	0.405
Dyslipidemia	424 (57.6)	482 (54.0)	369 (63.3)	123 (63.7)	0.002	44 (58.7)	13 (52.0)	33 (60.0)	0.789	59 (53.2)	43 (54.4)	109 (65.3)	16 (61.5)	0.169
Chronic kidney disease	198 (26.9)	179 (20.1)	164 (28.1)	54 (28.0)	0.001	21 (28.0)	8 (32.0)	14 (25.5)	0.830	39 (35.1)	23 (29.1)	47 (28.1)	8 (30.8)	0.652
Coronary artery disease	351 (47.7)	475 (53.3)	268 (46.0)	95 (49.2)	0.031	33 (44.0)	6 (24.0)	14 (25.5)	0.044	39 (35.1)	29 (36.7)	69 (41.3)	6 (23.1)	0.304
Prior endovascular therapy	235 (31.9)	236 (26.5)	208 (35.7)	56 (29.0)	0.002	28 (37.3)	7 (28.0)	19 (34.5)	0.697	36 (32.4)	28 (35.4)	63 (37.7)	10 (38.5)	0.825
Common femoral lesion	9 (1.2)	11 (1.2)	28 (4.8)	2 (1.0)	<0.001	1 (1.3)	1 (4.0)	0	0.339	13 (11.7)	6 (7.6)	20 (12.0)	5 (19.2)	0.431
Iliac lesion	79 (10.7)	159 (17.8)	82 (14.1)	33 (17.1)	0.001	9 (12.0)	5 (20.0)	4 (7.3)	0.255	8 (7.2)	13 (16.5)	25 (15.0)	5 (19.2)	0.142
Infrapopliteal lesion	189 (25.7)	125 (14.0)	115 (19.7)	25 (13.0)	<0.001	43 (57.3)	6 (24.0)	19 (34.5)	0.003	55 (49.5)	31 (39.2)	50 (29.9)	10 (38.5)	0.012
Total occlusion	326 (44.3)	462 (51.8)	259 (44.4)	112 (58.0)	<0.001	44 (58.7)	14 (56.0)	25 (45.5)	0.317	70 (63.1)	62 (78.5)	87 (52.1)	19 (73.1)	0.001
TASC-II type, C or D	406 (55.2)	543 (60.9)	303 (52.0)	111 (57.5)	0.006	33 (44.0)	10 (40.0)	21 (38.2)	0.793	84 (75.7)	56 (70.9)	88 (52.7)	20 (76.9)	<0.001
Chronic limb-threatening ischemia	324 (44.0)	307 (34.4)	201 (34.5)	56 (29.0)	<0.001	45 (60.0)	13 (52.0)	15 (27.3)	0.001	70 (63.1)	46 (58.2)	69 (41.3)	15 (57.7)	0.002

Lesion length	≥150 mm	295 (40.1)	369 (41.4)	285 (48.9)	99 (51.3)	0.001	4 (5.3)	2 (8.0)	5 (9.1)	0.699	59 (53.2)	42 (53.2)	103 (61.7)	18 (69.2)	0.251
Moderate/severe calcification		220 (29.9)	282 (31.6)	177 (30.4)	64 (33.2)	0.776	15 (20.0)	6 (24.0)	12 (21.8)	0.908	38 (34.2)	24 (30.4)	71 (42.5)	11 (42.3)	0.235

BMS, bare-metal stent; DCB, drug-coated balloon; DES, drug-eluting stent; PA, popliteal artery; PB, plain balloon; SFA, superficial femoral artery; TASC, Trans-Atlantic Inter-Society Consensus Document

Supplementary Table 5. Adjusted baseline and procedural characteristics between final treatment device groups using overlap weighting, stratified by femoropopliteal treatment extent.

	SFA intervention					PA intervention				SFA/PA intervention				
	PB	BMS	DCB	DES	SMD	PB	BMS	DCB	SMD	PB	BMS	DCB	DES	SMD
Age, year	70.0	70.0	69.9	69.9	0.01	67.2	65.8	67.0	0.08	71.2	70.0	69.8	71.4	0.08
Male	0.82	0.82	0.82	0.82	<0.01	0.77	0.73	0.75	0.06	0.74	0.79	0.75	0.75	0.05
Body mass index, kg/m^2	23.5	23.6	23.5	23.4	0.02	24.5	24.3	24.0	0.10	22.6	23.4	23.4	22.9	0.14
Current smoker	0.31	0.29	0.29	0.29	0.02	0.24	0.23	0.20	0.06	0.29	0.23	0.27	0.25	0.08
Hypertension	0.72	0.74	0.75	0.74	0.03	0.78	0.73	0.69	0.14	0.74	0.79	0.76	0.76	0.05
Diabetes	0.60	0.60	0.60	0.61	0.01	0.59	0.66	0.67	0.11	0.58	0.57	0.59	0.60	0.04
Dyslipidemia	0.62	0.62	0.61	0.61	0.01	0.62	0.56	0.59	0.09	0.56	0.58	0.61	0.55	0.06
Chronic kidney disease	0.25	0.27	0.27	0.27	0.03	0.32	0.31	0.29	0.05	0.28	0.32	0.37	0.33	0.09
Coronary artery disease	0.50	0.49	0.49	0.48	0.02	0.29	0.26	0.29	0.04	0.28	0.30	0.28	0.27	0.04
Prior endovascular therapy	0.30	0.30	0.30	0.29	0.01	0.31	0.28	0.23	0.11	0.33	0.35	0.32	0.33	0.03
Common femoral lesion	0.01	0.01	0.01	0.01	0.02	0	0	0	<0.01	0.10	0.11	0.12	0.11	0.03
Iliac lesion	0.16	0.15	0.15	0.15	0.01	0.16	0.16	0.19	0.06	0.14	0.15	0.17	0.13	0.06
Infrapopliteal lesion	0.15	0.15	0.16	0.15	0.01	0.31	0.33	0.37	0.09	0.42	0.42	0.42	0.42	0.01
Total occlusion	0.54	0.54	0.53	0.53	<0.01	0.59	0.55	0.52	0.11	0.72	0.70	0.72	0.72	0.03
TASC-II type, C or D	0.59	0.54	0.58	0.56	0.05	0.43	0.39	0.43	0.05	0.76	0.74	0.78	0.78	0.05
Chronic limb-threatening ischemia	0.32	0.32	0.33	0.32	0.01	0.41	0.47	0.50	0.11	0.66	0.53	0.58	0.54	0.15
Lesion length ≥150 mm	0.48	0.47	0.48	0.48	0.01	0.04	0.02	0.04	0.09	0.64	0.69	0.63	0.67	0.07
Moderate/severe calcification	0.32	0.31	0.32	0.31	0.01	0.25	0.31	0.21	0.16	0.38	0.44	0.40	0.39	0.06

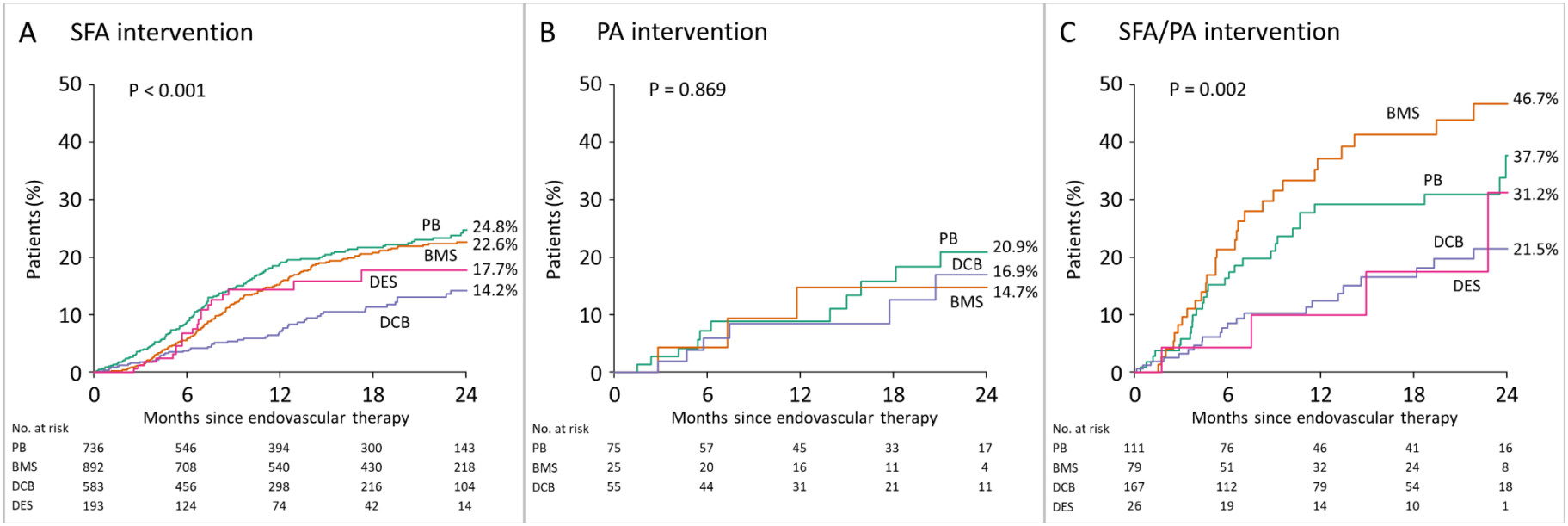
BMS, bare-metal stent; DCB, drug-coated balloon; DES, drug-eluting stent; PA, popliteal artery; PB, plain balloon; SFA, superficial femoral artery; SMD, standardized mean difference; TASC, Trans-Atlantic Inter-Society Consensus Document

Supplementary Table 6. The risk of target lesion revascularisation between final treatment device groups using unadjusted, multivariable adjusted, and overlap weighting analysis, stratified by femoropopliteal treatment extent.

	Unadjusted			Multivariable adjusted		Overlap weighting	
	Event (rate)	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
SFA intervention							
Plain balloon	134 (24.8)	Reference				Reference	
Bare metal stent	155 (22.6)	0.87 (0.69–1.10)	0.235	0.90 (0.70–1.16)	0.398	0.94 (0.73–1.19)	0.588
Drug-coated balloon	51 (14.2)	0.48 (0.34–0.66)	<0.001	0.47 (0.32–0.67)	<0.001	0.45 (0.31–0.64)	<0.001
Drug-eluting stent	21 (17.7)	0.75 (0.47–1.19)	0.218	0.66 (0.40–1.11)	0.119	0.72 (0.44–1.18)	0.194
POP intervention							
Plain balloon	11 (20.9)	Reference					
Bare metal stent	3 (14.7)	0.81 (0.23–2.92)	0.751	0.74 (0.13–4.12)	0.732	1.27 (0.20–8.07)	0.798
Drug-coated balloon	6 (16.9)	0.78 (0.29–2.11)	0.621	1.02 (0.22–4.79)	0.982	1.81 (0.48–6.83)	0.382
SFA/PA intervention							
Plain balloon	29 (37.7)	Reference				Reference	
Bare metal stent	28 (46.7)	1.43 (0.85–2.41)	0.173	1.82 (0.98–3.38)	0.057	1.61 (0.90–2.88)	0.111
Drug-coated balloon	22 (21.5)	0.51 (0.29–0.89)	0.017	0.52 (0.26–1.04)	0.065	0.57 (0.30–1.10)	0.095
Drug-eluting stent	4 (31.2)	0.56 (0.20–1.60)	0.278	0.49 (0.15–1.61)	0.243	0.64 (0.21–1.97)	0.434

CI, confidence interval; HR, hazard ratio; PA, popliteal artery; SFA, superficial femoral artery

The reference of hazard ratios is the plain balloon group.



Supplementary Figure 1. Kaplan-Meier curves of target lesion revascularisation between final treatment device groups, stratified by femoropopliteal treatment extent.

BMS, bare-metal stent; DCB, drug-coated balloon; DES, drug-eluting stent; PA, popliteal artery; PB, plain balloon; SFA, superficial femoral artery