

## Original Research



## OPEN ACCESS

**Received:** Jan 3, 2024

**Revised:** Mar 1, 2024

**Accepted:** Apr 4, 2024

**Published online:** Apr 29, 2024

### Correspondence to

**Young-Guk Ko, MD**

Division of Cardiology, Severance Cardiovascular Hospital, Yonsei University College of Medicine, 50, Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea.  
Email: ygko@yuhs.ac

### Donghoon Choi, MD, PhD

Division of Cardiology, Severance Cardiovascular Hospital, Yonsei University College of Medicine, 50, Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea.  
Email: cdhlyj@yuhs.ac

\*These authors have contributed equally to this work.

Copyright © 2024. The Korean Society of Cardiology

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

### ORCID iDs

Jong-Il Park  <https://orcid.org/0000-0002-4337-4550>  
Young-Guk Ko  <https://orcid.org/0000-0001-7748-5788>  
Seung-Jun Lee  <https://orcid.org/0000-0002-9201-4818>  
Chul-Min Ahn  <https://orcid.org/0000-0002-7071-4370>

<https://e-kcj.org>

# Clinical Outcomes After Drug-Coated Balloon Treatment in Popliteal Artery Disease: K-POP Registry 12-Month Results

Jong-Il Park  MD<sup>1</sup>, Young-Guk Ko  MD<sup>2,\*</sup>, Seung-Jun Lee  MD<sup>2</sup>, Chul-Min Ahn  MD<sup>2</sup>, Seung-Woon Rha  MD<sup>3</sup>, Cheol-Woong Yu  MD<sup>4</sup>, Jong Kwan Park  MD<sup>5</sup>, Sang-Ho Park  MD<sup>6</sup>, Jae-Hwan Lee  MD<sup>7</sup>, Su-Hong Kim  MD<sup>8</sup>, Yong-Joon Lee  MD<sup>2</sup>, Sung-Jin Hong  MD<sup>2</sup>, Jung-Sun Kim  MD<sup>2</sup>, Byeong-Keuk Kim  MD<sup>2</sup>, Myeong-Ki Hong  MD<sup>2</sup>, and Donghoon Choi  MD, PhD<sup>2,\*</sup>

<sup>1</sup>Division of Cardiology, Yeungnam University Medical Center, Yeungnam University College of Medicine, Daegu, Korea

<sup>2</sup>Division of Cardiology, Severance Cardiovascular Hospital, Yonsei University College of Medicine, Seoul, Korea

<sup>3</sup>Division of Cardiology, Korea University Guro Hospital, Seoul, Korea

<sup>4</sup>Division of Cardiology, Korea University Anam Hospital, Seoul, Korea

<sup>5</sup>Division of Cardiology, National Health Insurance Service Ilsan Hospital, Goyang, Korea

<sup>6</sup>Division of Cardiology, Soonchunhyang University Cheonan Hospital, Cheonan, Korea

<sup>7</sup>Division of Cardiology, Chungnam National University Sejong Hospital, Sejong, Korea

<sup>8</sup>Division of Cardiology, Busan Veterans Hospital, Busan, Korea

## AUTHOR'S SUMMARY

This study evaluated the 12-month outcomes of drug-coated balloon (DCB) treatment for atherosclerotic popliteal artery disease. A prospective multicenter registry enrolled 100 patients who underwent endovascular therapy using the IN.PACT DCB. Technical success was achieved in all patients, with combined atherectomy performed in 17% and provisional stenting required in 11%. The clinical primary patency and clinically driven target lesion revascularization-free rates at 12 months were 76.0% and 87.2%, respectively. Female and longer lesion length were the significant predictors of loss of patency. In conclusion, DCB treatment demonstrated favorable 12-month clinical outcomes in patients with popliteal artery disease.

## ABSTRACT

**Background and Objectives:** The popliteal artery is generally regarded as a “no-stent zone.” Limited data are available on the outcomes of drug-coated balloons (DCBs) for popliteal artery disease. This study aimed to evaluate the 12-month clinical outcomes among patients who received DCB treatment for atherosclerotic popliteal artery disease.

**Methods:** This prospective, multicenter registry study enrolled 100 patients from 7 Korean endovascular centers who underwent endovascular therapy using IN.PACT DCB (Medtronic) for symptomatic atherosclerotic popliteal artery disease. The primary endpoint was 12-month clinical primary patency and the secondary endpoint was clinically driven target lesion revascularization (TLR)-free rate.

Seung-Woon Rha   
<https://orcid.org/0000-0001-9456-9852>  
 Cheol-Woong Yu   
<https://orcid.org/0000-0002-5871-4562>  
 Jong Kwan Park   
<https://orcid.org/0000-0002-5506-1412>  
 Sang-Ho Park   
<https://orcid.org/0000-0001-7912-0336>  
 Jae-Hwan Lee   
<https://orcid.org/0000-0002-6561-7760>  
 Su-Hong Kim   
<https://orcid.org/0000-0001-5173-5304>  
 Yong-Joon Lee   
<https://orcid.org/0000-0003-4526-6120>  
 Sung-Jin Hong   
<https://orcid.org/0000-0003-4893-039X>  
 Jung-Sun Kim   
<https://orcid.org/0000-0003-2263-3274>  
 Byeong-Keuk Kim   
<https://orcid.org/0000-0003-2493-066X>  
 Myeong-Ki Hong   
<https://orcid.org/0000-0002-2090-2031>  
 Donghoon Choi   
<https://orcid.org/0000-0002-2009-9760>

#### Trial Registration

ClinicalTrials.gov Identifier: [NCT02698345](https://clinicaltrials.gov/ct2/show/study/NCT02698345)

#### Funding

This study was supported by grants from Medtronic (Santa Rosa, CA, USA); the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI) (No. HI20C1566) and the Bio & Medical Technology Development Program of the National Research Foundation & MSIT (No.2020M3A9I4038455); the Patient-Centered Clinical Research Coordinating Center (PACEN), funded by the Ministry of Health & Welfare, Republic of Korea (HC20C0081); and the Korea Medical Device Development Fund, funded by the Korean government (202011B29-03, 202011D12-02) and the Cardiovascular Research Center (Seoul, Korea).

#### Conflict of Interest

Dr. Ko and Dr. Choi received research grants from Medtronic, Boston Scientific, Samjin Pharm, Korea United Pharm, Dong-A Pharm, and Otsuka, Korea. None of these companies, including Medtronic, were involved in developing the study protocols or procedures for the K-POP study. All other authors report no relationships relevant to the contents of this paper.

**Results:** The mean age of the study cohort was 65.7±10.8 years, and 77% of enrolled patients were men. The mean lesion length was 93.7±53.7 mm, and total occlusions were present in 45% of patients. Technical success was achieved in all patients. Combined atherectomy was performed in 17% and provisional stenting was required in 11%. Out of the enrolled patients, 91 patients completed the 12-month follow-up. Clinical primary patency and TLR-free survival rates at 12 months were 76.0% and 87.2%, respectively. A multivariate Cox regression analysis identified female and longer lesion length as the significant independent predictors of loss of patency.

**Conclusions:** DCB treatment yielded favorable 12-month clinical primary patency and TLR-free survival outcomes in patients with popliteal artery disease.

**Trial Registration:** ClinicalTrials.gov Identifier: [NCT02698345](https://clinicaltrials.gov/ct2/show/study/NCT02698345)

**Keywords:** Popliteal artery; Atherosclerosis; Angioplasty

## INTRODUCTION

The treatment of popliteal artery disease with endovascular therapy (EVT) poses challenges due to the biomechanical forces exerted on the artery during knee joint movements, which negatively impact treatment outcomes.<sup>1,2)</sup> In particular, conventional inflexible stents in the popliteal artery can cause vessel kinking, compromising blood flow and patency.<sup>3,4)</sup> Additionally, stents are prone to restenosis and fractures due to repetitive compression and bending.<sup>5,6)</sup> As a result, the popliteal artery is generally considered unsuitable for stenting. Recently, drug-coated balloons (DCBs) have shown promising results in achieving high patency rates for femoropopliteal artery lesions in various clinical trials.<sup>7-9)</sup> Furthermore, atherectomy prior to DCB treatment has also been reported to enhance success rates in complex lesions.<sup>10)</sup> Despite the theoretical advantages of DCB, which involves the concept of leaving nothing behind, there is a limited amount of data available on the outcomes of EVT using DCBs for popliteal artery disease. Thus, this study aims to investigate the outcomes of IN.PACT DCB (Medtronic, Santa Rosa, CA, USA) in patients undergoing EVT for popliteal artery disease.

## METHODS

### Ethical statement

The K-POP study adhered to the ethical principles of the Declaration of Helsinki (2013), was approved by the Institutional Review Board at each participating center and was registered at [www.ClinicalTrials.gov](https://www.clinicaltrials.gov/ct2/show/study/NCT02698345) (NCT02698345). Informed consent was obtained from all the patients.

### Study design

The Korean Multicenter Prospective Registry of IN.PACT DCB for Popliteal Artery Disease (K-POP Study) was an investigator-initiated, prospective, multicenter, single-arm registry for patients with symptomatic atherosclerotic popliteal artery disease. The major inclusion criteria were intermittent claudication; symptoms of critical limb-threatening ischemia (CLTI, Rutherford categories 2–5); and popliteal artery lesions with >50% stenosis and atherosclerotic etiology. The major exclusion criteria were age >85 years; severe CLTI (Rutherford category 6); acute limb ischemia; previous bypass surgery or stenting of the popliteal artery; untreated inflow disease of the ipsilateral pelvic or femoral arteries (>50% stenosis or occlusion); congestive heart failure with left ventricular ejection fraction <40%; severe hepatic failure; or life expectancy <1 year due to comorbidity.

### Data Sharing Statement

The data generated in this study is available from the corresponding authors upon reasonable request.

### Author Contributions

Conceptualization: Ko YG, Choi D; Data curation: Park JI, Ko YG; Formal analysis: Park JI, Ko YG; Funding acquisition: Ko YG, Choi D; Investigation: Ko YG, Lee SJ, Ahn CM, Rha SW, Yu CW, Park JK, Park SH, Lee JH, Kim SH, Lee YJ, Hong SJ, Kim JS, Kim BK, Hong MK, Choi D; Methodology: Park JI, Ko YG; Supervision: Ko YG, Choi D; Writing - original draft: Park JI, Ko YG; Writing - review & editing: Park JI, Ko YG.

### Interventions

For all procedures, patients received local anesthesia, supplemented with intravenous sedation and analgesia as necessary. Intervention was performed percutaneously via ipsilateral or contralateral femoral puncture, depending on the location of the lesions to treat. A 6F or 7F introducer sheath (Terumo, Tokyo, Japan) was used for the ipsilateral approach, whereas a 6F or 7F long, curved sheath (Balkin or Ansel; Cook Inc., Bloomington, IN, USA) was employed for the contralateral approach. Prior to the procedure, angiography was performed to evaluate lesion morphology, inflow disease (occlusion or stenosis of the femoral or popliteal arteries), and run-off vessels from the upper iliac artery to the lower tibial artery. In cases of total occlusion, both intraluminal and subintimal approaches for recanalization were allowed. After successful guidewire passage, the target lesion was pre-dilated using a plain balloon prior to DCB angioplasty. In the present study, only the IN.PACT Admiral DCB (Medtronic) was used. At the operator's discretion, atherectomy using HwakOne (Medtronic), Jetstream (Boston Scientific, Marlborough, MA, USA), or Rotarex (BD, Franklin Lakes, NJ, USA) was performed prior to DCB angioplasty in patients with calcified plaques following successful intraluminal wire passage. The DCB was applied to the target lesion for 3 minutes. Provisional stenting was performed if residual stenosis was >50% or if dissection resulted in impaired blood flow despite additional post-dilation. Only non-drug-eluting, self-expanding nitinol stents were permitted for provisional stenting. After the procedure, aspirin (100 mg/day) was maintained indefinitely, and clopidogrel (75 mg/day) was prescribed for at least 6 months.

### Follow-up

Patients were followed clinically 1, 3, 6, 9, and 12 months after the procedure, according to the study schedule. Post-procedural ankle-brachial index (ABI) values were obtained at the time of discharge and at 6- and 12-month follow-up. Imaging, such as intra-arterial angiography, computed tomography angiography (CTA), or duplex ultrasound, was recommended at 12-month follow-up. In addition, imaging was required before 12 months if symptoms worsened, as defined by a decrease in ABI value of 0.15 or a change in the Rutherford category.

### Study endpoints and definitions

Popliteal artery segments were defined as follows: P1, from the intercondylar fossa to the proximal edge of the patella; P2, from the proximal part of the patella to the center of the knee joint space; and P3, from the center of the knee joint space to the origin of the anterior tibial artery (**Supplementary Figure 1**). Procedural success was defined as the recanalization of the target lesion with residual stenosis  $\leq 30\%$  and no presence of flow-limiting dissection. The primary endpoint was clinical primary patency, defined as the time from the procedure to the time of symptom aggravation, as indicated by an increase in the Rutherford category accompanied by a decrease of at least 0.15 in ABI or restenosis greater than 50% on imaging (e.g., duplex ultrasound, CTA, or intra-arterial angiography). A lesion or adjacent segment velocity ratio greater than 2.4, as measured by duplex ultrasound, was considered indicative of greater than 50% restenosis. The secondary endpoint was freedom from clinically driven target lesion revascularization (TLR), defined as any repeated intervention or surgical treatment for restenotic lesions characterized by both worsening symptoms and a decrease of at least 0.15 in ABI. Major complications were defined as any events that were fatal, required surgical treatment, or resulted in re-hospitalization during the 30 days following the procedure.

### Statistical analysis

Categorical variables are reported as the number (percentage). Continuous variables are reported as the mean  $\pm$  standard deviation. The primary and secondary endpoints were estimated using Kaplan–Meier survival analysis and subgroups were compared using the log-rank test. We performed univariate Cox proportional hazards regression analysis to identify potential risk factors (clinical and procedural variables) for restenosis 1 year after the procedure. Variables with  $p < 0.20$  in the univariate analysis were included in the multivariate analysis. Significance was established at  $p < 0.05$ . All statistical analyses were performed using SPSS (version 26.0; IBM Corp., Armonk, NY, USA).

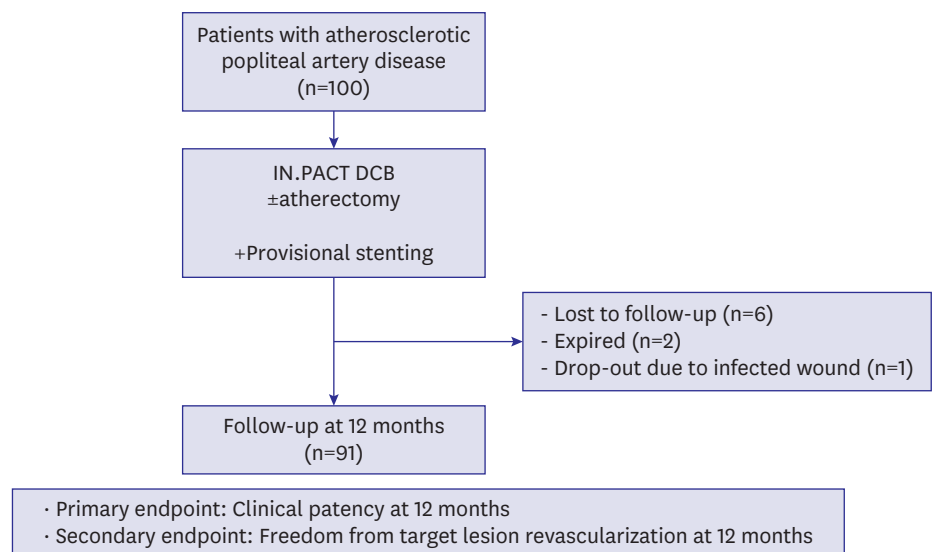
## RESULTS

### Baseline clinical data

From March 2016 through January 2019, a total of 100 patients with atherosclerotic popliteal artery disease were enrolled in this study (**Figure 1**). The baseline clinical characteristics of the study cohort are summarized in **Table 1**. The mean age of study participants was  $65.7 \pm 10.8$  years, and the majority (77.0%) were men. Diabetes mellitus and chronic kidney disease were present in 65.0% and 28.0% of patients, respectively. Previous EVT experience was reported by 29.0% of patients. Claudication was the most common clinical manifestation (63.0%), and the pre-procedural ABI in the target limb was  $0.71 \pm 0.25$ . Further analysis of baseline clinical characteristics by sex, as detailed in **Supplementary Table 1**, showed that females exhibited a higher prevalence of diabetes mellitus (82.6% vs. 59.7%,  $p = 0.035$ ), chronic kidney disease (52.2% vs. 20.8%,  $p = 0.005$ ), end-stage renal dysfunction requiring dialysis (34.8% vs. 10.4%,  $p = 0.009$ ) compared to males. Additionally, it was found that the proportion of current smokers was lower among females compared to males (4.3% vs. 24.7%,  $p < 0.001$ ).

### Lesion and procedural data

The lesion and procedural characteristics of the study cohort are presented in **Table 2**. The mean lesion length was  $93.7 \pm 53.7$  mm. The most commonly involved popliteal artery



**Figure 1.** Patient flow diagram.  
DCB = drug-coated balloon.

**Table 1.** Baseline clinical characteristics

Characteristics	Values (n=100)
Age (years)	65.7±10.8
Male	77 (77.0)
Body mass index (kg/m <sup>2</sup> )	24.18±3.0
Hypertension	69 (69.0)
Diabetes mellitus	65 (65.0)
Dyslipidemia	44 (44.0)
Chronic kidney disease (creatinine >1.5 mg/dL)	28 (28.0)
Dialysis	16 (16.0)
Coronary artery disease	31 (31.0)
Previous percutaneous coronary intervention	24 (24.0)
Previous myocardial infarction	3 (3.0)
Previous coronary bypass surgery	6 (6.0)
Heart failure (ejection fraction <40%)	1 (1.0)
Previous stroke	8 (8.0)
Current smoker	20 (20.0)
Previous percutaneous transluminal angioplasty	29 (29.0)
Rutherford (category)	
2/3	63 (63.0)
4	10 (10.0)
5	23 (23.0)
Pre-procedural ABI	0.71±0.25

Data are presented as the number (%) or the mean ± standard deviation.  
 ABI = ankle-brachial index.

segment was P2 (76%). Total occlusion and severely calcified lesions were detected in 45% and 23% of patients, respectively. Trans-Atlantic Inter-Society Consensus (TASC) II Type D lesions, including total popliteal artery occlusion and proximal trifurcation vessels, were identified in 21% of patients. In 35% of patients, only one or no run-off vessels were detected.

The procedure was successful for all patients. In 15% of patients, revascularization was performed using the intentional subintimal approach. In 17% of patients, atherectomy was performed prior to DCB application. Provisional stenting was required in 11% of patients using bare, self-expanding nitinol stents. The mean diameter of the DCBs used was 5.2±0.8 mm. The ratio of the DCB diameter to the proximal reference diameter was 1.0±0.2 mm, while the ratio of the DCB diameter to the distal reference diameter was found to be 1.2±0.3 mm.

No major complications occurred; however, minor complications were found in 4 patients, including 1 case of access site hematoma, 1 case of popliteal artery perforation related to the use of the atherectomy device, and 2 cases of other artery perforations caused by wiring or balloon dilation. All perforations were managed through EVT.

### Clinical outcomes

Of the 100 patients who were enrolled and underwent the procedure, 91 patients completed the 12-month follow-up (**Figure 1**). Two deaths occurred due to non-cardiovascular causes, 6 patients were lost to follow-up, and 1 patient withdrew due to an uncontrolled wound infection. Imaging studies were performed for 46 patients at the 12-month follow-up visit. The distribution of Rutherford categories at 12-month follow-up showed significant improvements in symptom status compared with the distribution at baseline ( $p < 0.001$ ; **Figure 2**). The 12-month clinical primary patency rate was 76.0%, and the 12-month clinically driven TLR-free survival rate was 87.2% (**Figure 3**). All 12 patients who required TLR were managed with repeat EVT.

**Table 2.** Procedural and lesion characteristics

Characteristics	Values (n=100)
Distal 1/3 of superficial femoral artery involvement	44 (44.0)
Combined targets	
Iliac artery	4 (4.0)
Common femoral artery	5 (5.0)
Superficial femoral artery (distal)	16 (16.0)
Infrapopliteal artery	33 (33.0)
Popliteal artery	
P1 involvement	74 (74.0)
P2 involvement	76 (76.0)
P3 involvement	48 (48.0)
Lesion length (mm)	93.7±53.7
Proximal ref. diameter (mm)	5.2±0.8
Distal ref. diameter (mm)	4.9±3.8
Total occlusion	45 (45.0)
Severe calcification	23 (23.0)
TASC II lesion type	
B	50 (50.0)
C	11 (11.0)
D	21 (21.0)
Run-off vessel ≤1	35 (35.0)
Wiring approach	
Intraluminal	85 (85.0)
Subintimal	15 (15.0)
DCB diameter (mm)	5.2±0.8
Additional treatment	28 (28.0)
Atherectomy	17 (17.0)
HawkOne	7 (7.0)
Jetstream	8 (8.0)
Rotarex	2 (1.2)
Provisional stenting	11 (11.0)
Procedural success	100 (100.0)
Post-procedural ABI	0.93±0.15
Major complications	0 (0.0)
Minor complications	4 (4.0)
Access site hematoma	1 (1.2)
Popliteal artery perforation	1 (1.2)
Other artery perforation	2 (2.0)
Macroembolism	0 (0.0)

Data are presented as number (%) or mean ± standard deviation.

ABI = ankle-brachial index; DCB = drug-coated balloon; TASC = Trans-Atlantic Inter-Society Consensus.

The application of atherectomy prior to DCB did not appear to affect clinical primary patency or TLR-free survival rates (**Figure 4A and B**). Baseline clinical and lesion characteristics did not differ between the DCB alone group and the combined atherectomy and DCB group. However, severely calcified lesions were more frequently present in the latter group (14.5% vs. 64.7%,  $p < 0.001$ ) (**Supplementary Table 2**). The use of provisional stenting also had no significant impact on primary patency or TLR-free survival rates (**Figure 4C and D**). The total occlusion subgroup had a primary patency rate of 66.3%, significantly lower than the 84.5% observed in the non-total occlusion subgroup ( $p = 0.043$ ), indicating worse outcomes in the total occlusion subgroup (**Supplementary Figure 2**).

A multivariate Cox proportional hazards regression analysis (**Table 3**) identified female (hazard ratio [HR], 2.71; 95% confidence interval [CI], 1.08–6.85;  $p = 0.034$ ) and longer lesion length (HR, 1.01; 95% CI, 1.00–1.02;  $p = 0.025$ ) as the significant independent predictors of loss of patency 12-month post-procedure. Although total occlusion (HR, 2.32; 95% CI, 0.93–

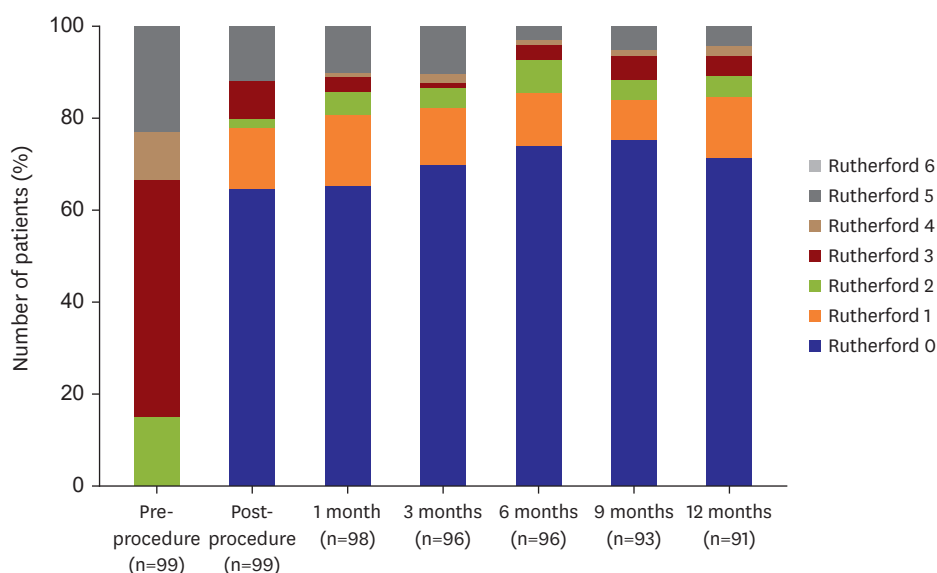


Figure 2. Distribution of Rutherford categories at different follow-up intervals.

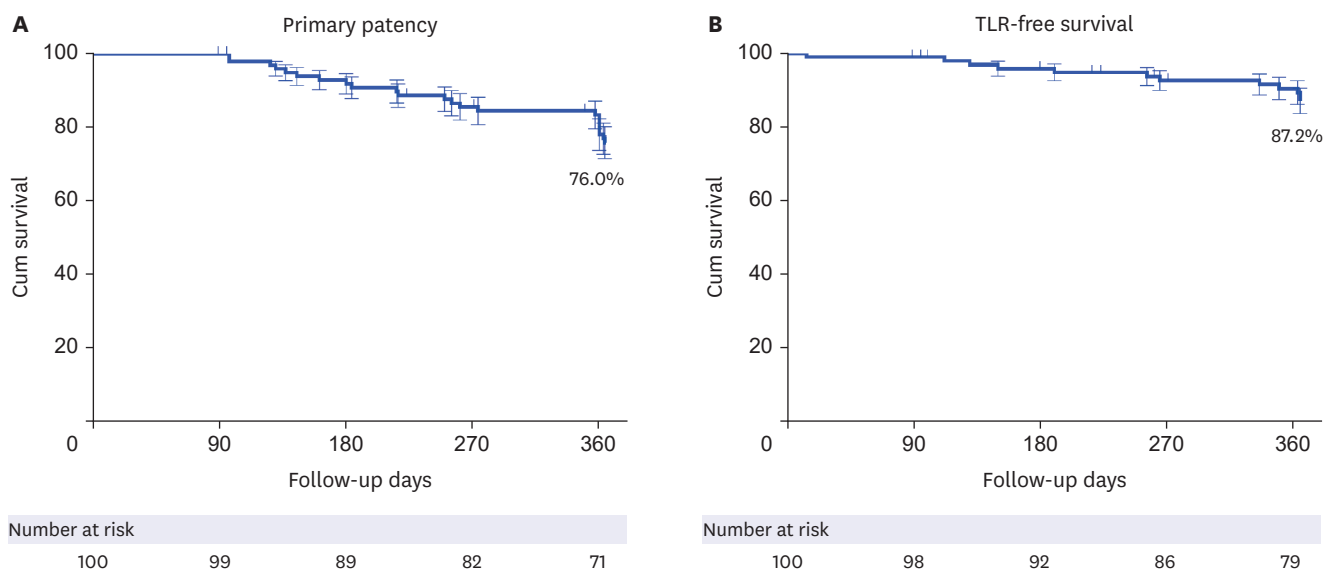
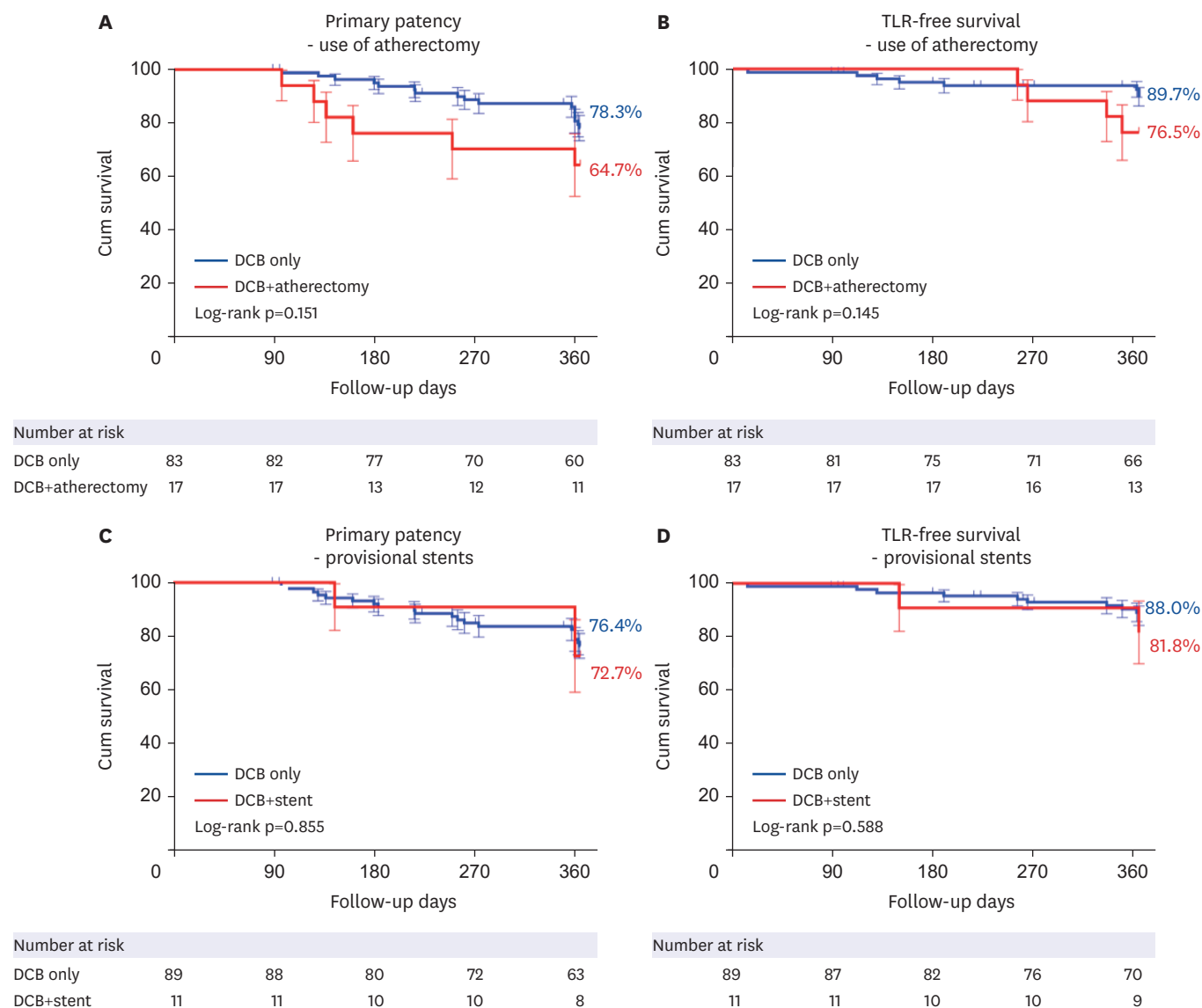


Figure 3. Kaplan-Meier survival curves for clinical outcomes at 1 year. TLR = target lesion revascularization; Cum = cumulative.

5.75;  $p=0.064$ ) and younger age (HR, 0.96; 95% CI, 0.93–1.00;  $p=0.054$ ) were not statistically significant in this analysis, however, given the relatively hazard ratio and small sample size, these 2 variables may be considered significant risk factors of loss of patency.<sup>11)</sup>

## DISCUSSION

In the present study, the application of IN.PACT DCB to treat patients with atherosclerotic popliteal artery lesions achieved 12-month clinical primary patency in 76.0% of cases and 12-month clinically driven TLR-free survival in 87.2% of cases. Total occlusion was identified as an independent predictor of loss of patency within 12 months following the DCB procedure.



**Figure 4.** Kaplan–Meier survival curves according to atherectomy and provisional stent use. Kaplan–Meier survival curves at 1 year are presented according to atherectomy and provisional stent use. (A) Clinical primary patency for the use of atherectomy. (B) TLR-free survival for the use of atherectomy. (C) Clinical primary patency for the use of provisional stents. (D) TLR-free survival for the use of provisional stents. Cum = cumulative; DCB = drug-coated balloon; TLR = target lesion revascularization.

Limited data exist regarding the outcomes of EVT in popliteal artery disease. A randomized controlled trial of patients with popliteal artery lesions showed that primary stenting using bare nitinol stents significantly increased the 1-year patency rate (67.4%) compared with balloon angioplasty (44.9%).<sup>12</sup> However, the 1-year patency rate for stents remains unsatisfactory. The reported outcomes for the use of the more flexible nitinol interwoven stent (SUPERA™; Abbott Vascular, Santa Clara, CA, USA) in popliteal artery disease have been inconsistent and limited to small-volume studies.<sup>12-14</sup> A small (n=50), single-arm, prospective study reported a 1-year primary patency rate of 89.6% for nitinol interwoven stents,<sup>13</sup> similar to the 87.7% 1-year primary patency rate reported by a retrospective study (n=48).<sup>14</sup> However, a separate retrospective study (n=40) reported a 1-year primary patency rate of only 68.4% for nitinol interwoven stents.<sup>15</sup>



**Table 3.** Predictors for loss of patency at 1 year in Cox proportional hazards regression analysis

Factor	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p value	HR (95% CI)	p value
Age	0.97 (0.94–1.01)	0.166	0.96 (0.93–1.00)	0.054
Female	1.88 (0.80–4.43)	0.151	2.71 (1.08–6.85)	0.034
Body mass index	1.06 (0.92–1.22)	0.455		
Hypertension	0.99 (0.41–2.42)	0.995		
Diabetes mellitus	0.86 (0.37–1.99)	0.726		
Hypercholesterolemia	1.12 (0.49–2.54)	0.787		
Current smokers	0.95 (0.59–1.51)	0.818		
Chronic kidney disease	1.16 (0.48–2.83)	0.738		
Coronary artery disease	0.89 (0.37–2.16)	0.792		
Pre-procedure ABI	0.35 (0.06–2.21)	0.264		
Distal 1/3 of SFA involvement	1.88 (0.82–4.28)	0.135	1.77 (0.69–4.57)	0.239
P3 involvement	1.18 (0.52–2.67)	0.694		
Lesion length (mm)	1.01 (1.00–1.02)	0.019	1.01 (1.00–1.02)	0.025
Total occlusion	2.35 (0.99–5.55)	0.051	2.32 (0.93–5.75)	0.064
TASC II D lesion	2.04 (0.87–4.83)	0.103	1.90 (0.72–5.03)	0.198
Subintimal approach	1.26 (0.43–3.71)	0.673		
Run-off vessel $\leq 1$	1.27 (0.55–2.94)	0.575		
Atherectomy	1.95 (0.77–4.94)	0.161	2.33 (0.90–6.01)	0.108
Provisional stenting	1.12 (0.33–3.77)	0.856		
Post-procedure ABI	2.40 (0.71–8.11)	0.436		

ABI = ankle-brachial index; CI = confidence interval; HR = hazard ratio; SFA = superficial femoral artery; TASC = Trans-Atlantic Inter-Society Consensus.

Few studies have reported the outcomes of DCB treatment in patients with popliteal artery disease. A small, retrospective study including 48 patients treated with paclitaxel-coated DCBs found a 1-year primary patency rate of 72.6%.<sup>16)</sup> In a retrospective analysis of 266 patients with lesions with popliteal artery involvement, DCB angioplasty using primarily the IN.PACT DCB achieved a 1-year primary patency rate of 77.4%; however, most of the included cases involved both the superficial femoral artery (SFA) and the popliteal artery, with only 12% of cases involving isolated popliteal lesions. Among the population examined in this study, the patency rate was lowest (57.8%) for lesions extending from the SFA to the infrapopliteal arteries. A subgroup analysis of the IN.PACT Global Study reported a 3-year TLR-free survival rate of 76.5% for isolated popliteal artery lesions, similar to the rate for isolated SFA lesions (79.7%).<sup>17)</sup> Thus, the 1-year primary patency rate of 76.0% and the 1-year TLR-free survival rate of 87.2% for popliteal artery lesions in the present study are consistent with previously reported results, offering further evidence that IN.PACT DCBs result in more favorable outcomes than non-drug-coated balloons or bare nitinol stents.

Few studies have examined the outcomes of combined atherectomy plus DCB therapy for popliteal artery lesions. A retrospective study comparing the use of DCB alone with directional atherectomy with antirestenotic therapy (DAART) for the treatment of isolated popliteal artery lesions found the DAART group achieved a higher 1-year primary patency rate than the DCB alone group (82% vs. 65%,  $p=0.021$ ).<sup>18)</sup> The DAART group had improved TLR-free survival compared with the DCB alone group, although this difference was not significant (94% vs. 82%,  $p=0.072$ ). Similarly, a subgroup analysis of isolated popliteal artery cases in the Determination of Effectiveness of the SilverHawk® Peripheral Plaque Excision System (SilverHawk Device, New Delhi, India) for the Treatment of Infringuinal Vessel/Lower Extremities study indicated that directional atherectomy in isolated popliteal artery lesions resulted in favorable 1-year outcomes.<sup>19)20)</sup> In the present study, combination atherectomy plus DCB therapy was only performed in 17.0% of cases, and the number of cases is insufficient to provide statistical power for data interpretation. The limited number

of patients treated with atherectomy and DCB emphasized the preliminary nature of our findings regarding this treatment. The presence of calcified lesions among these patients indicated a focus on more complex cases, which may affect the outcomes. Therefore, the results from these treatment strategies should be interpreted with caution. Despite these limitations, our study contributed valuable insights into popliteal artery disease treatment, emphasizing the importance of tailored approaches.

In the current study, the female sex, lesion length, total occlusion, and younger age were predictors for loss of patency after DCB treatment for popliteal artery disease. These findings were in agreement with similar observations reported in previous studies.<sup>16)21)22)</sup> Referring to the results of the IN.PACT DCB for femoropopliteal study, it was noted that, although not statistically significant, females exhibited less favorable clinical outcomes compared to males.<sup>22)</sup> This underscores the importance of considering sex as a potential factor influencing the outcomes of DCB treatment for popliteal artery disease. Previous research also highlighted the role of lesion length and total occlusion as predictors in popliteal artery disease.<sup>16)</sup> The consistency of our study's findings with this previous report emphasizes the significance of lesion characteristics in the development of treatment strategies and predictive models for popliteal artery disease. Understanding these factors is crucial for tailoring treatment plans and follow-up strategies, offering clinicians a more nuanced approach to optimizing patient outcomes. Thus, our study contributes to a deeper understanding of the outcomes of DCB treatment for popliteal artery disease, highlighting the necessity of tailored treatment approaches that take into account patient sex and lesion characteristics.

This study has several limitations. First, due to the non-randomized, single-arm study design and the small study population, subgroup analyses were limited. Second, not all patients received 12-month follow-up imaging, which may have resulted in the overestimation of the primary patency rate. Third, the 12-month follow-up duration was likely too short to evaluate the overall efficacy and safety of DCB therapy for popliteal artery disease. Fourth, our study did not include an analysis of residual stenosis or the utilization of intravascular ultrasound guidance, both of which are factors that may influence clinical outcomes in the treatment of popliteal artery lesions with DCB. A large-scale study with a long-term follow-up period remains necessary to validate the findings of the present study.

DCB treatment for popliteal artery disease achieved favorable 12-month clinical primary patency and clinically driven TLR-free survival outcomes.

## SUPPLEMENTARY MATERIALS

### Supplementary Table 1

Baseline clinical characteristics in terms of sex

### Supplementary Table 2

Procedural and lesion characteristics according to use of atherectomy

### Supplementary Figure 1

The segments of popliteal artery.

## Supplementary Figure 2

Kaplan–Meier survival curves regarding to the chronic total occlusion.

## REFERENCES

1. Kröger K, Santosa F, Goyen M. Biomechanical incompatibility of popliteal stent placement. *J Endovasc Ther* 2004;11:686-94. [PUBMED](#) | [CROSSREF](#)
2. Hoffmann U, Vetter J, Rainoni L, Leu AJ, Bollinger A. Popliteal artery compression and force of active plantar flexion in young healthy volunteers. *J Vasc Surg* 1997;26:281-7. [PUBMED](#) | [CROSSREF](#)
3. Tamashiro GA, Tamashiro A, Villegas MO, et al. Flexions of the popliteal artery: technical considerations of femoropopliteal stenting. *J Invasive Cardiol* 2011;23:431-3. [PUBMED](#)
4. Poulson W, Kamenskiy A, Seas A, Deegan P, Lomneth C, MacTaggart J. Limb flexion-induced axial compression and bending in human femoropopliteal artery segments. *J Vasc Surg* 2018;67:607-13. [PUBMED](#) | [CROSSREF](#)
5. Gökçöl C, Diehm N, Kara L, Büchler P. Quantification of popliteal artery deformation during leg flexion in subjects with peripheral artery disease: a pilot study. *J Endovasc Ther* 2013;20:828-35. [PUBMED](#) | [CROSSREF](#)
6. Tosaka A, Soga Y, Iida O, et al. Classification and clinical impact of restenosis after femoropopliteal stenting. *J Am Coll Cardiol* 2012;59:16-23. [PUBMED](#) | [CROSSREF](#)
7. Tepe G, Laird J, Schneider P, et al. 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. [PUBMED](#) | [CROSSREF](#)
8. Giacoppo D, Cassese S, Harada Y, et al. 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. [PUBMED](#) | [CROSSREF](#)
9. Caradu C, Lakhlifi E, Colacchio EC, et al. Systematic review and updated meta-analysis of the use of drug-coated balloon angioplasty versus plain old balloon angioplasty for femoropopliteal arterial disease. *J Vasc Surg* 2019;70:981-995.e10. [PUBMED](#) | [CROSSREF](#)
10. Cha JJ, Lee JH, Ko YG, et al. Clinical outcomes of atherectomy plus drug-coated balloon versus drug-coated balloon alone in the treatment of femoropopliteal artery disease. *Korean Circ J* 2022;52:123-33. [PUBMED](#) | [CROSSREF](#)
11. Cummings P, Rivara FP, Koepsell TD. Writing informative abstracts for journal articles. *Arch Pediatr Adolesc Med* 2004;158:1086-8. [PUBMED](#) | [CROSSREF](#)
12. Rastan A, Krankenberg H, Baumgartner I, et al. 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. [PUBMED](#) | [CROSSREF](#)
13. San Norberto EM, Flota CM, Fidalgo-Domingos L, Taylor JH, Vaquero C. Real-world results of Supera stent implantation for popliteal artery atherosclerotic lesions: 3-year outcome. *Ann Vasc Surg* 2020;62:397-405. [PUBMED](#) | [CROSSREF](#)
14. Scheinert D, Werner M, Scheinert S, et al. 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. [PUBMED](#) | [CROSSREF](#)
15. Goltz JP, Ritter CO, Kellersmann R, Klein D, Hahn D, Kickuth R. Endovascular treatment of popliteal artery segments P1 and P2 in patients with critical limb ischemia: initial experience using a helical nitinol stent with increased radial force. *J Endovasc Ther* 2012;19:450-6. [PUBMED](#) | [CROSSREF](#)
16. Wu X, Peng Z, Qin J, Yang X, Lu X, Ye K. Outcomes of drug-coated balloon angioplasty for isolated chronic occlusion of the popliteal artery: a retrospective single-institution study. *J Vasc Interv Radiol* 2021;32:593-601. [PUBMED](#) | [CROSSREF](#)
17. Torsello G, Stavroulakis K, Brodmann M, et al. Three-year sustained clinical efficacy of drug-coated balloon angioplasty in a real-world femoropopliteal cohort. *J Endovasc Ther* 2020;27:693-705. [PUBMED](#) | [CROSSREF](#)
18. Stavroulakis K, Schwindt A, Torsello G, et al. Directional atherectomy with antirestenotic therapy vs drug-coated balloon angioplasty alone for isolated popliteal artery lesions. *J Endovasc Ther* 2017;24:181-8. [PUBMED](#) | [CROSSREF](#)

19. Rastan A, McKinsey JF, Garcia LA, et al. One-year outcomes following directional atherectomy of popliteal artery lesions: subgroup analysis of the prospective, multicenter DEFINITIVE LE trial. *J Endovasc Ther* 2018;25:100-8. [PUBMED](#) | [CROSSREF](#)
20. McKinsey JF, Zeller T, Rocha-Singh KJ, Jaff MR, Garcia LA; DEFINITIVE LE Investigators. Lower extremity revascularization using directional atherectomy: 12-month prospective results of the DEFINITIVE LE study. *JACC Cardiovasc Interv* 2014;7:923-33. [PUBMED](#) | [CROSSREF](#)
21. Spiliopoulos S, Kitrou P, Galanakis N, et al. Incidence and endovascular treatment of isolated atherosclerotic popliteal artery disease: outcomes from the IPAD multicenter study. *Cardiovasc Intervent Radiol* 2018;41:1481-7. [PUBMED](#) | [CROSSREF](#)
22. Kohi MP, Brodmann M, Zeller T, et al. Sex-related differences in the long-term outcomes of patients with femoropopliteal arterial disease treated with the IN.PACT drug-coated balloon in the IN.PACT SFA randomized controlled trial: a post hoc analysis. *J Vasc Interv Radiol* 2020;31:1410-1418.e10. [PUBMED](#) | [CROSSREF](#)