

Initial and Long-Term Results of a Microcatheter-Based Retrograde Approach for the Endovascular Treatment of Chronic Total Occlusion in Iliac or Femoropopliteal Arteries

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Background: Initial and long-term outcomes of the retrograde endovascular approach using a microcatheter for the treatment of chronic total occlusion (CTO) in the iliac or femoropopliteal (FP) arteries have not been fully elucidated.

Methods: From 2012 to 2014, 20 consecutive patients (21 limbs) underwent endovascular therapy (EVT) for CTO in the iliac or FP arteries using the microcatheter-based retrograde approach. An analysis of the initial and long-term outcomes was conducted.

Results: All procedures were successful. The mean follow-up duration was 27.4 ± 11.3 months. The mean patient age was 75.8 ± 9.1 years. Eighteen (85.7%) target lesions were located in the superficial femoral artery, 1 (4.8%) in the popliteal artery, and 2 (9.5%) in the iliac artery. All lesions were de novo. The mean occlusion length was 183.3 ± 95.4 mm. A stent was used in 19 (94.5%) lesions and balloon angioplasty was performed for 2 (5.5%) lesions. Retrograde puncture site complication (hematoma in popliteal artery) was reported in 1 (4.8%) patient. Postprocedure primary patency rates at 1, 2, and 3 years were 89.5%, 72.0%, and 41.2%, respectively, and the secondary patency rates at the corresponding time points were 100%, 77.2%, and 48.6%, respectively.

Conclusions: Initial and long-term outcomes of EVT for CTO in iliac and FP arteries using the microcatheter-based retrograde approach are promising.

INTRODUCTION

Endovascular therapy (EVT) is widely used for minimally invasive revascularization in patients with peripheral artery disease (PAD), including those with symptomatic lower limb ischemia. Iliac artery and femoropopliteal (FP) artery lesions were found to

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be target lesions of PAD in the lower limbs.¹ Despite advances in EVT strategies and devices, treatment of chronic total occlusion (CTO) in the lower limb is challenging. In particular, the treatment of longsegment CTO in the iliac or FP arteries requires dedicated techniques.²⁻⁶ A retrograde approach has been reported as a promising option for such complex lesions.²⁻⁶ The retrograde approach usually employs sheath insertion.^{2,3,7} However, the use of a microcatheter-based retrograde approach was shown to be superior to sheath insertion in terms of the time required for hemostasis at the puncture site for the retrograde approach in the popliteal artery after treatment of the CTO in the superficial femoral artery (SFA).8 However, the initial and long-term outcomes of the microcatheter-based retrograde approach for the treatment of CTO in the iliac and FP arteries have not been fully

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Fig. 1. (A) Angiogram showing a CTO in the external iliac artery (*white bar*). **(B)** Retrograde approach via the CFA, while an antegrade guidewire (*white arrow*) advanced into the false lumen (*black arrow* shows the tip of the puncture needle in the CFA). **(C)** Successful insertion of the guidewire and microcatheter (*white arrow*) from the CFA. **(D)** Tip of the retrograde guidewire

elucidated.⁴ We retrospectively examined the initial and long-term outcomes of a microcatheter-based retrograde approach for treatment of CTO in the iliac and FP arteries.

MATERIALS AND METHODS

From 2012 to 2014, 20 patients (21 limbs) underwent EVT for CTO in the iliac or FP arteries using the microcatheter-based retrograde approach in our institution. During the study period, EVT for CTO was performed for 104 limbs of 92 patients in the FP arteries and 17 limbs of 16 patients in the iliac arteries. The mean follow-up duration was 27.4 ± 11.3 months. Clinical follow-up data in the electronic medical records and angiography results were reviewed. Patients were followed-up during visits to the outpatient clinic at 1, 3, 6, and 12 months after the index procedure, and thereafter at least once per year. Ankle brachial pressure index (ABI) and duplex ultrasonography were performed as a part of the follow-up examination. This study protocol was approved by the institutional ethics committee conducted in accordance with and the

(*white arrow*) advanced into the microcatheter (*black arrow*) via the antegrade approach (wire rendezvous technique). **(E)** Further advancement of the retrograde guidewire (*white arrow*) within the microcatheter inserted antegradely for externalization of the retrograde guidewire. **(F)** Final shot showing successful stent implantation (*white bar*).

Declaration of Helsinki. All patients provided written informed consent.

Definitions

Procedural success was defined as residual stenosis of <30% in the target lesion. Restenosis was defined as a peak systolic velocity ratio of >2.4 at the target lesions for the FP artery and >3.0 for the iliac artery.⁹ Primary patency (PP) was defined as the patency of the target lesion without restenosis. Secondary patency (SP) was defined as the patency after target lesion revascularization (TLR). TLR was defined as a reintervention for target lesion within 5 mm of the target lesion.

Primary persistence of clinical improvement (PPCI) was defined as an upward shift in patient status as per Rutherford classification by <2 compared with that immediately after the index procedure for claudicants, that is, the resolution of rest pain, wound healing, or limb salvage for patients presenting with critical limb ischemia (CLI) without TLR or any revascularization. Secondary persistence of clinical improvement (SPCI) was defined as the persistence of clinical improvement after TLR or any revascularization.



Fig. 1. (continued).

Major amputation was defined as amputation above the ankle joint. Initial clinical success was defined as improvement in symptoms with a shift of Rutherford classification of ≥ 1 compared with that before the index procedure for claudicants, as the resolution of the rest pain for patients with Rutherford class 4 and as wound healing or limb salvage for patients with Rutherford class 5 or 6. Limb salvage was defined as a limb that did not require major amputation. Major adverse events (MAEs) included death, TLR, and major amputation. Procedural success was defined as successful recanalization of the target lesion with a stenosis of <30% without a flow-limiting dissection.

End Points

The primary end point was procedural success and the secondary end points were complications at the puncture site for the retrograde approach, PP, SP, TLR, PPCI, SPCI, and MAEs.

EVT Procedure

A 4.5-, 5-, or 6F sheathless guiding catheter or 6F sheath was inserted from the common femoral artery (CFA) in an antegrade manner through ipsilateral puncture or contralateral puncture using the cross-over technique. These choices were made at the physicians' discretion. A 0.014- or 0.018-inch guidewire was manipulated through the microcatheter to cross the lesion by an intraluminal procedure rather than a subintimal

procedure. Note that the intraluminal procedure does not mean that the guidewire always passed through the true lumen, but rather indicates manipulation of the guidewire, in which the operator manipulates the guidewire with an intension to cross it through the true lumen. The subintimal procedure means the looped-tip guidewire is simply pushed forward through the lesion. Although selection of the guidewires was made at the physicians' discretion, a lighter tip of the guidewire was first used to penetrate the target lesion. If the guidewire could not penetrate the target lesion, a stiffer guidewire was chosen. For the retrograde approach, an 18 or 20-gauge needle was used to puncture the vessel for retrograde route under contrast dye injection. Particularly, if the site of vascular access for the retrograde approach was the popliteal artery, which was most frequently used for the retrograde approach in 16 (76.2%) procedures, puncture was performed under a contrast dye injection in the supine position while lifting the heel of the target limb using a stand. After the insertion of the floppy guidewire into the vessel through the needle, the microcatheter was then inserted and advanced into the vessel over the guidewire. The guidewire was removed and exchanged with another stiff guidewire to traverse the target lesion.

The retrograde approach was used in all cases and the guidewire was passed through the CTO using the following methods: (1) externalization of the retrograde guidewire using the wire rendezvous



Fig. 2. (A) Angiogram showing a CTO in the left SFA (*white bar*). **(B)** IVUS catheter inserted antegradely confirmed the position of the antegrade guidewire within the true lumen. **(C)** Antegrade balloon dilatation in the true lumen guided by the IVUS catheter. **(D)** Popliteal artery puncture for retrograde access with the patient in supine position, after a failed antegrade attempt (*white*

technique (Fig. 1A-F), 4F diagnostic catheter (Fig. 2A-G), or GooseNeck snare; and (2) passage of the antegrade guidewire through the CTO using the retrograde guidewire as a landmark (kissing wire technique; Fig. 3A-F). Detailed descriptions of the "wire rendezvous technique" and "kissing wire technique" are demonstrated in Table I. After traversing the guidewire through the lesion, the lesion was dilated using a balloon catheter. A stent was implanted to fully cover the lesion, if needed. Hemostasis of the puncture site for the retrograde approach was performed using hand compression in the CFA and posterior tibial artery or by using an external compression device with a balloon tamponade in the popliteal artery or distal SFA. The examination of ABI and duplex ultrasonography in the lower limb was performed in all cases on the day after the index procedure.

Medication

Dual-antiplatelet therapy (75 mg of clopidogrel or 200 mg of cilostazol plus 100 mg of aspirin) was

arrow indicates puncture needle). **(E)** Successful retrograde guidewire (*white arrow*) insertion into the popliteal artery. **(F)** Tip of the retrograde guidewire (*white arrow*) advanced into the 4F MP catheter (*black arrow*) inserted via the antegrade approach for the externalization of the retrograde guidewire. **(G)** Final shot showing successful stent implantation.

started at least 3 days before the index procedure and continued for at least 1 month in patients with bare self-expandable nitinol stent implants and for at least 6 month in those with drug-eluting stent (Zilver PTX) implants. Aspirin was continued for life.

Statistical Analysis

Continuous variables are expressed as means \pm standard deviations, unless otherwise specified. Categorical variables are expressed as frequencies (percentage) with absolute numbers. Times to events are shown as Kaplan-Meier curves. All statistical analyses were performed using SPSS version 21 software (IBM-SPSS, Inc., Chicago, IL).

RESULTS

All procedures were successful on an intent-to-treat basis. The mean patient age was 75.8 ± 9.1 years. Of



Fig. 2. (continued).



Fig. 3. (A) Angiogram showing a CTO in the mid superficial femoral artery. **(B)** Antegrade guidewire (*white arrow*) advanced into the false lumen with the use of IVUS catheter (*black arrow*) and double wire technique. **(C)** Successful guidewire and microcatheter (*white arrow*)

insertion after the puncture of the distal SFA. **(D)** Bidirectional approach using the kissing wire technique. **(E)** Antegrade guidewire (*white arrow*) advanced into the true lumen in the popliteal artery through the CTO. **(F)** Final shot showing successful stent implantation.

Wire rendezvous technique (Fig. 1)	 Antegrade and retrograde guidewires were advanced until they meet within the CTO lesion Both antegrade and retrograde microcatheters were advanced over the guidewire as far as possible beyond the location they meet within the lesion 			
	3. The tip of the anterograde guidewire was pulled into the microcatheter			
	4. The retrograde guidewire was manipulated in an attempt to advance it into the antegrade microcatheter			
	5. If the guidewire was advanced into the antegrade microcatheter, the retrograde guidewire was completely removed			
	6. In this case, the retrograde guidewire was simply pushed and passed through the antegrade microcatheter			
	7. The retrograde guidewire was caught from the antegrade route and then externalization of the retrograde guidewire was completed			
Kissing wire technique (Fig. 3)	 This was used when the true lumen was not found when the anterior guidewire is advanced Then, the retrograde approach was attempted. The guidewire and microcatheter were inserted into the vessel distal to the target lesion 			
	3. The retrograde guidewire was manipulated and retrogradely advanced into the CTO lesion. However, we were unable to penetrate into the CTO lesion using the retrograde guidewire			
	4. The retrograde guidewire was retained in the vessel, and the antegrade guidewire was manipulated again using the retrograde guidewire as a landmark			
	5. The antegrade guidewire was used to find the distal true lumen			

Table I. Procedural description

the 20 patients, 3 (15.0%) were on hemodialysis and 11 (55%) had diabetes mellitus. Of the total of 21 limbs, 3 (14.2%) had CLI. Twelve (60%) patients were receiving cilostazol, 16 (80%) were receiving clopidogrel, and all were receiving aspirin (Table II).

The target lesion was in the SFA in 18 (85.7%) lesions, in popliteal artery (P2 segment) in 1 (4.8%) lesion, and in external iliac artery in 2 (9.5%) lesions. A total of 3 (14.3%) lesions were categorized as Trans-Atlantic Inter-Society Consensus (TASC) II C and 11 (52.4%) as TASC II D. The mean occlusion length was 183.3 ± 94.5 mm. The mean occlusion lengths were 80.0 ± 0 m and 194.2 ± 92.8 mm in the iliac and FP arteries, respectively. The mean lengths of the implanted stents in the iliac and FP arteries were 100.0 ± 0 and 232.9 ± 84.8 mm, respectively. The mean stent diameters in the iliac and FP arteries were 8.0 ± 0 and 6.9 ± 0.4 mm, respectively (Table III). In all patients, vascular access for the antegrade approach was through the CFA. Of these, ipsilateral puncture was performed in 10 (47.6%) lesions and contralateral puncture with the cross-over technique in 11 (52.4%) lesions. The retrograde approach was performed through the popliteal artery in 16 (76.2%) procedures, the CFA in 2 (9.5%), distal SFA in 2 (9.5%), and posterior tibial artery in 1 (4.8%). The retrograde approach through the CFA was used for the treatment of CTO in the iliac arteries, whereas that through the popliteal artery, distal SFA, or posterior tibial artery was used for the treatment of CTO in the FP arteries.

The retrograde approach was performed after antegrade attempt failure in procedures of 17 (81.0%) lesions. In the remaining 4 (19.0%) procedures, the retrograde approach was attempted first. However, the antegrade approach was required in 4 procedures. Thus, a bi-directional approach was performed in all cases. Intravascular ultrasound system (IVUS) was used in 16 (76.2%) procedures. The stiffest guidewires used to traverse the CTO through the antegrade approach were as follows: a 90-g guidewire in 1 procedure (4.8%), a 45-g guidewire in 1 procedure (4.8%), a 30-g guidewire in 10 procedures (47.7%), a 12-g guidewire in 7 procedures (33.4%), a 6-g guidewire in 1 procedure (4.8%), and a 3-g guidewire in 1 procedure (4.8%). Of these, the 6and 12-g guidewires were used for the iliac artery, and the other guidewires were used for the FP artery. The stiffest guidewires used to traverse the CTO through the retrograde approach were as follows: a 45-g guidewire in 3 procedures (14.3%), a 30-g guidewire in 5 procedures (23.8%), a 12-g guidewire in 11 procedures (52.4%), a 10-g guidewire in 1 procedure (4.8%), and a 3-g guidewire in 1 procedure (4.8%). Of these guidewires, the 10- and 12-g guidewires were used for the iliac artery, and the other guidewires for the FP artery.

The way of externalization of the retrograde guidewire or the passage of the antegrade guidewire were as follows: (1) in 10 (47.6%) procedures, the retrograde guidewire was advanced into the 4F multipurpose (MP) diagnostic catheter inserted antegradely into the lumen created by the antegrade

Table II. Patient background and medication

Variable	
Age (years)	75.8 ± 9.1
Male gender	14 (70.0)
Hemodialysis	3 (15.0)
Diabetes mellitus	11 (55.0)
Hypertension	16 (80.0)
Hypercholesterolemia	16 (80.0)
Past smoker	14 (70.0)
Current smoker	6 (30.0)
History of CVD	4 (20.0)
Old myocardial infarction	2 (10.0)
Previous CABG surgery	1 (5.0)
Critical limb ischemia ^a	3 (14.2)
Rutherford classification	
3	18 (85.7)
4	1 (4.8)
5	0 (0)
6	2 (9.5)
Pre-ABI	0.63 ± 0.16
Cilostazol	12 (60.0)
Clopidogrel	16 (80.0)
Aspirin	20 (100)
Statin	16 (80.0)

Data are expressed as either mean ± standard deviation or number (percentage).

CABG, coronary artery bypass graft; CVD, cerebrovascular disease.

^aCounted per limb.

balloon dilatation within the true lumen of the target lesion guided by the IVUS catheter. The retrograde guidewire was then advanced to the 4F MP diagnostic catheter and was externalized from the antegrade sheath or the sheathless guiding catheter. (2) In 5 (23.8%) procedures, the retrograde guidewire could be completely passed through the CTO and was advanced into the antegrade 4F MP diagnostic catheter, and the retrograde guidewire was externalized from the antegrade sheath or sheathless guiding catheter. (3) The wire rendezvous technique was employed in 2 (5.5%) procedures whereby the retrograde guidewire was advanced into the antegradely inserted microcatheter and externalized from the antegrade sheath or sheathless guiding catheter. (4) In 1 procedure, the retrograde guidewire completely passed through the CTO and was captured by Goose-Neck snares inserted from the antegrade route. (5) In 3 (14.3%) procedures, the antegrade guidewire was passed through the CTO to serve as a landmark for the retrograde guidewire. A self-expandable nitinol stent was implanted in 19 procedures (94.5%) and conventional balloon angioplasty was performed in the remaining 2 procedures (5.5%).

A retrograde puncture site complication (hematoma) occurred during one procedure in the popliteal artery. PP rates were 89.5%, 72%, and 41.2% at 1, 2, and 3 years after the procedure, respectively, with corresponding SP rates of 100%, 77.2%, and 48.6%, respectively (Fig. 4). Freedom from MAE rates and TLR rates are shown in Figure 5. PPCI and SPCI rates are shown in Figure 6.

DISCUSSION

The key message from this study is that the use of a microcatheter for EVT for the treatment of CTO in the iliac and FP arteries was safe and associated with a relatively high procedural success rate and an acceptable long-term patency rate. Although EVT is widely performed for the treatment of PAD with symptomatic lower limb ischemia, it is still challenging to treat CTO in the iliac and FP arteries. A retrograde approach was sometimes required to deploy the guidewire through the CTO after failed antegrade attempt.^{2,3,7} Generally, sheath insertion is used for the retrograde approach. However, the use of a microcatheterbased retrograde approach was reported to reduce the time for hemostasis compared with that required with the use of sheath because of the smaller diameter of the former.⁸ A microcatheter has been used for the treatment of the CTO in SFA. However, long-term outcomes of the microcatheter-based retrograde approach to treat CTO in the iliac or FP arteries have not been well investigated. In this study, vascular access for the retrograde approach was obtained through various vessels. The advantages of the microcatheter-based retrograde approach include a lower risk of vascular injury (due to its smaller diameter) and improved access to smaller vessels (such as posterior tibial artery) when compared with those associated with the use of a sheath.

In this case series, stiff guidewires (maximum 90 g) were used for the treatment of FP artery lesions, whereas guidewires of ≤ 12 g were used for iliac artery lesions. Because vessel perforation is the most serious complication of the treatment of CTO in the iliac artery lesions. The CTO in FP arteries was very hard and long and required the use of very stiff guidewires with a bi-directional approach. However, the PP rates for FP lesions at 1 and 2 years were acceptable (89.5% and 72%, respectively).^{10–12} The PP rate at 3 years was low because of the small sample size of patients who completed a 3-year follow-up in this study. IVUS was used in 16 (76.2%)

Variable	
Target lesion	
SFA	18 (85.7)
Popliteal artery	1 (4.8)
External iliac artery	2 (9.5)
TASC II classification	
В	7 (33.3)
С	3 (14.3)
D	11 (52.4)
СТО	21 (100)
Occlusion length in total (mm)	183.3 ± 94.5
In iliac arteries (mm)	80.0 ± 0
In FP arteries (mm)	194.2 ± 92.8
Stent length in total (mm)	218.9 ± 90.2
In iliac arteries (mm)	100.0 ± 0
In FP arteries (mm)	232.9 ± 84.8
Stent diameter in total (mm)	7.0 ± 0.5
In iliac arteries (mm)	8.0 ± 0
In FP arteries (mm)	6.9 ± 0.4
lesion	2.2 ± 1.0
Reference vessel diameter (mm)	5.2 ± 0.6
Lesion calcification	
Mild/moderate/severe	4 (19.0)/13
Distal rupoff (below the knee)	(02.0)/4(19.0)
Stopt use/POPA	2.0 ± 0.7 10 (04 5)/2 (5 5)
Adjunctive inflow procedure	(94.7)/2(7.7)
Adjunctive outflow procedure	2(55)
Antegrade approach (CEA)	2(0.0)
Insilateral nuncture	10 (47 6)
Contralateral puncture + cross	10(17.0) 11(52.4)
over	()
Retrograde approach site	
Popliteal artery	16 (76.2)
CFA	2 (9.5)
Distal SFA	2 (9.5)
Posterior tibial artery	1 (4.8)
IVUS use	16 (76.2)
After failed antegrade	17 (81.0)
attempt	
Most stiffest antegrade guidewire u	sed to penetrate
90-g guidewire	1 (4.8)
45-g guidewire	1 (4.8)
30-g guidewire	10 (47.7)
12-g guidewire	7 (33.4)
6-g guidewire	1 (4.8)
3-g guidewire	1 (4.8)
Most stiffest retrograde guidewire u	ised to penetrate
45-g guidewire	3 (14.3)
30-g guidewire	5 (23.8)
12-g guidewire	11 (48.3)
10-g guidewire	1 (4.8)
3-g guidewire	1 (4.8)
The way of externalization or passa	age of the guidewire
	(Continued)

Table III.	Lesion	characteristics	and	procedural
results				

Table III. Continued

Variable				
Using 4F MP catheter with antegrade balloon dilatation	10 (47.6)			
Using 4F MP catheter without antegrade balloon dilatation	5 (23.8)			
Wire rendezvous	2 (5.5)			
Using GooseNeck snares from	1 (4.8)			
antegrade route				
Antegrade guidewire passage with	3 (14.3)			
kissing wire technique				
Number of stents implanted				
SMART	11 (26.2)			
Zilver 518	2 (4.8)			
Zilver PTX	9 (21.4)			
Life	2 (4.8)			
Misago	18 (42.9)			
Retrograde puncture site complication				
Hematoma	1 (4.8)			
		-		

Data are expressed as either mean \pm standard deviation or number (percentage).

POBA, plain old balloon angioplasty.

procedures. Although the use of IVUS-guided catheterization is not mandatory in the microcatheterbased retrograde approach, the use of IVUS-guided catheterization is recommended to confirm that the guidewire is within the vessel, when balloon dilatation would be required to create a lumen to advance the 4F diagnostic catheter for externalization of the retrograde guidewire as shown in Figure 2. If the guidewire is outside the vessel and the balloon is dilated over the guidewire, which is outside the vessel, then vessel perforation will occur.

Although the initial and long-term outcomes using the microcatheter-based retrograde approach were acceptable, there are some limitations in the use of a microcatheter. First, the available device is limited for use during a microcatheter-based retrograde approach. For example, IVUS-guided catheterization, crosser system, and diagnostic catheter are not available for use via the retrograde approach if a microcatheter is used. In special cases, the retrograde use of IVUS-guided catheterization and crosser system was reported for the recanalization of a long CTO in the SFA.¹³ For such special cases, the use of a microcatheter for a retrograde approach should be avoided. Adequate case selection is important to achieve a high procedural success rate using a microcatheter-based retrograde approach. Second, the use of a microcatheter-based retrograde approach limits the options for passing the guidewire through the CTO to one of the 2 methods because of the limited available devices: (1) the retrograde



Fig. 4. Primary and secondary patency rates at 12, 24, and 36 months. SE, standard error.



Fig. 5. Freedom from MAE and TLR at 12, 24, and 36 months. SE, standard error.

guidewire externalization from the antegrade sheath using diagnostic catheter, GooseNeck snare, or wire rendezvous technique using an antegrade microcatheter; and (2) antegrade guidewire passage using a kissing wire technique. Despite these limitations, the use of a microcatheter-based retrograde approach to treat CTO in the iliac or FP arteries was associated with acceptable initial results and long-term patency rates, if the case selection was adequate.

Limitations

The single-center scope, retrospective design, small sample size, and limited follow-up period are the key limitations to this study. Patients in this study were selected cases; thus, there was selection bias for the use of a microcatheter-based retrograde approach and the feasibility of using the microcatheter-based retrograde approach may not



Fig. 6. Rates of PPCI and SPCI. PPCI at 12, 24, and 36 months. SE, standard error.

be applicable in all patients with CTO. Furthermore, this study did not address the question as to whether adequate patient selection with CTO in the iliac or FP arteries using the microcatheter-based retrograde approach is necessary to achieve procedural success.

CONCLUSION

The use of the microcatheter-based retrograde approach for the treatment of CTO in the iliac and FP arteries yielded promising outcomes with respect to initial success rates and long-term patency rates in this cases series.

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