

IVUS-Guided Wiring Improves the Clinical Outcomes of Angioplasty for Long Femoropopliteal CTO Compared with the Conventional Intraluminal Approach

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Aims: This study aimed to assess the clinical efficacy of intravascular ultrasound (IVUS)-guided intraplaque wiring for femoropopliteal (FP) chronic total occlusion (CTO).

Methods: This single-center, retrospective, observational study was performed at the Japanese Red Cross Kyoto Daini Hospital. From March 2013 to June 2017, a total of 75 consecutive patients (mean age: 75.4 ± 8.5 years; 59 males), who underwent endovascular treatment (EVT), having 82 de novo FP-CTO lesions, were enrolled in this study. Eleven of the lesions that met the exclusion criteria were excluded, and the remaining 71 lesions were divided into the IVUS-guided wiring group ($n=34$) and non-IVUS-guided wiring group ($n=37$). Primary patency, defined as a peak systolic velocity ratio of <2.4 on duplex ultrasonography, and freedom from clinically driven target lesion revascularization (CD-TLR) at 12 months were the primary outcomes.

Results: The mean lesion length was 21.6 ± 8.9 cm. The frequencies of primary patency and freedom from CD-TLR were significantly higher in the IVUS-guided wiring group than in the non-IVUS-guided wiring group (70.0% vs. 52.2%, $p=0.045$; 83.9% vs. 62.8%, $p=0.036$, respectively). The complete clinically true lumen angioplasty rate was also higher in the IVUS-guided wiring group than in the non-IVUS-guided wiring group (91.1% vs. 51.3%, $p<0.001$, respectively). The clinically true and false wire passage rates were respectively 97.3% and 2.7% in the IVUS-guided wiring group.

Conclusion: IVUS-guided wiring improves the clinical outcomes of EVT for FP-CTO by achieving a high clinically true lumen wire passage rate.

Key words: Chronic total occlusion, Endovascular treatment, Femoropopliteal segment, Intravascular ultrasound, Restenosis

Introduction

Recently issued guidelines regarding peripheral arterial disease recommend an endovascular-first strategy for femoropopliteal (FP) lesions of <25 cm in length, including cases of chronic total occlusion (CTO)¹. However, there is no consensus regarding the optimal wire passage route for the recanalization of FP-CTO. Previous studies have demonstrated that the intraluminal approach did not improve the clinical outcomes of endovascular treatment (EVT) for FP-

CTO lesions compared with the subintimal approach²⁻⁴. Recently, Kawasaki *et al.* proposed that CTO wire passage routes should be classified into the intraplaque, subintimal, and intramedial routes based on intravascular ultrasound (IVUS) examinations (Fig. 1)⁵. They demonstrated that attempts to perform the wire loop technique with a 0.035 inch guide-wire via the subintimal approach did not always result in the subintimal or intramedial route being taken. Conversely, Mori *et al.* reported that attempts to perform the drilling technique using a 0.014 inch guide-

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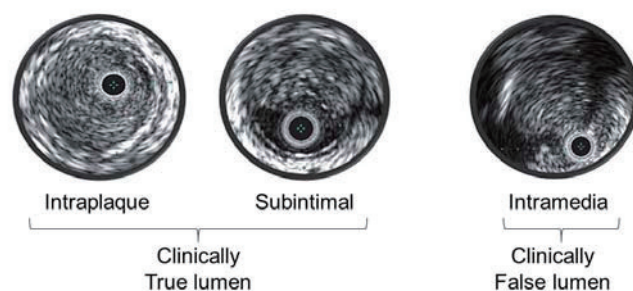


Fig. 1. Definition of the wire passage route

Clinically true lumen: Intraplaque and subintimal

Clinically false lumen: Intramedia

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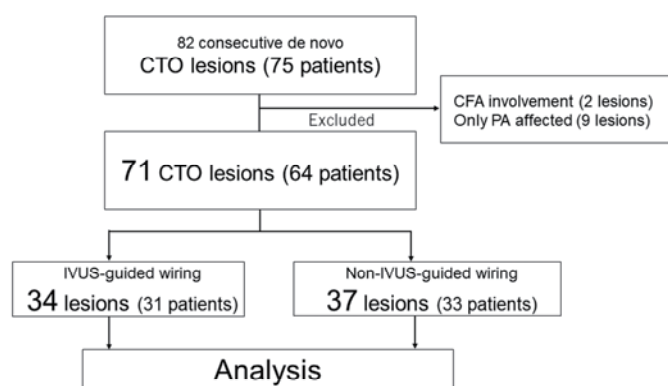


Fig. 2. Study flow chart

CTO, chronic total occlusion; IVUS, intravascular ultrasound;
CFA, common femoral artery; PA, popliteal artery

wire via the intraluminal approach did not always result in the intraplaque route being taken⁶). They also revealed that the intramedial CTO wire passage route is an independent risk factor for restenosis. There have not been any reports about the usefulness of IVUS-guided wiring for FP-CTO lesions with regard to the IVUS-guided approach.

Aim

In this study, we examined the clinical usefulness of an IVUS-guided wiring technique. We also investigated how often an intraplaque or subintimal wire passage route was achieved and intramedial route was avoided when this technique was performed.

Methods

Study Design and Patient Population

This single-center, retrospective, observational study was performed at the Japanese Red Cross Kyoto Daini Hospital. The study protocol was developed

according to the Declaration of Helsinki and was approved by the ethics committee of our hospital. Written informed consent for the EVT was obtained from all patients who were enrolled in this study.

From March 2013 to June 2017, a total of 75 consecutive patients having 82 de novo CTO lesions were retrospectively enrolled in this study. The inclusion criteria were symptomatic patients with Rutherford class categories 2 to 5 disease, who presented with de novo CTO of the FP segment. The exclusion criteria were comorbid common femoral artery (CFA) stenosis and isolated popliteal artery occlusion. Eleven of the lesions that met the exclusion criteria were excluded. The remaining 71 lesions (64 patients) were divided into the following two subgroups according to whether or not IVUS-guided wiring was performed: the IVUS-guided wiring group (34 lesions in 31 patients) and the non-IVUS-guided wiring group (37 lesions in 33 patients) (Fig. 2).

Definitions

Regarding the wire passage route, intraplaque,

inside the plaque; subintimal; between the plaque and media; intramedia; and between the media and adventitia were the original Kawasaki's classification. However, the three classifications are slightly complicated for clinical use, and the clinical significance of the intraplaque and the subintimal wire passage route are difficult to differentiate. Therefore, in this study, this classification was reclassified into two subgroups: clinically true lumen, intraplaque and subintimal, and clinically false lumen, intramedia.

Procedure

All of the patients received dual antiplatelet therapy (100 mg/day aspirin and 75 mg/day clopidogrel or 200 mg/day cilostazol) before the procedure. The EVT procedures were performed by interventional cardiologists that had been certified by the Japanese Association of Cardiovascular Intervention and Therapeutics. The initial antegrade approach site was the contralateral or ipsilateral CFA, and a 6-F sheath was inserted. Five thousand units of unfractionated heparin (UH) was injected via the inserted sheath, and additional UH was administered every 60 min to maintain an activated clotting time of 250 to 300 s. To cross the target lesion, a 0.014 inch guidewire was used with the support of a 5.5- or 6-F guiding catheter for the IVUS-guided wiring and a microcatheter for the non-IVUS-guided wiring. If the antegrade approach failed, a retrograde approach was applied using a distal puncture or transcatheter angioplasty, as described previously⁷⁻¹¹. In the retrograde approach, the wire rendezvous technique was used to achieve wire externalization¹². After a guidewire had been passed through the target lesion, pre-dilation was performed using a 2.0 or 3.0 mm balloon, before an IVUS evaluation was conducted. The lesions were treated using balloon angioplasty with an optimally sized balloon or provisional stenting with a bare Nitinol stent (BNS), drug-coated stent (DCS), or a stent graft. The size of the balloon or stent was determined based on the external elastic membrane (EEM) area at the distal reference site. Post-dilation was performed if residual stenosis of >50% was present.

Guidewire Selection

In both wiring strategies, a polymer jacketed guidewire with low penetration force (tip load: 1–3 g) was used as an initial guidewire. If this could not advance because of the hard plaque, guidewire escalation to an intermediate (tip load: 6–12 g) or high penetration (tip load: 15–45 g) force with hydro coating was performed. In the case of IVUS-guided parallel wiring, tapered intermediate or high penetration force guidewire was used to advance the guidewire forcibly

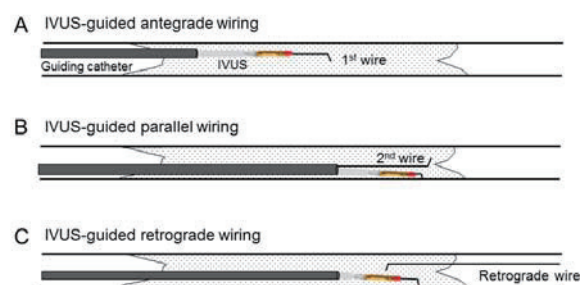


Fig. 3. Schema of the IVUS-guided wiring

IVUS, intravascular ultrasound

(A) IVUS-guided antegrade wiring technique

(B) IVUS-guided parallel wiring technique.

(C) IVUS-guided retrograde wiring technique

in the intended direction.

IVUS-Guided Wiring

The IVUS-guided wiring strategy is shown in **Fig. 3**. In the first step, a 0.014 inch guidewire with an IVUS catheter (Eagle Eye short tip; Volcano Corporation, Rancho Cordova, CA, USA) inside a 5.5- or 6-F guiding catheter was advanced using the drilling technique, and then, an IVUS examination was performed immediately. If the IVUS catheter and/or the guiding catheter could not advance, the balloon anchor technique¹³ was then performed using a 2.0 or 3.0 mm short balloon to advance the system. When the first system entered into the subintimal or intramedial space, the IVUS-guided parallel wiring technique was applied to advance a second guidewire into the intraplaque region using IVUS images obtained via the first wire. If the second step failed, retrograde wiring was performed using a 0.014 inch guidewire with a microcatheter under antegrade IVUS guidance.

IVUS Data Analysis

The IVUS data analysis was performed by two experienced cardiologists using the s5 Imaging System (Volcano Corporation, Rancho Cordova, CA, USA). Regardless of whether IVUS guide wiring was performed or not, IVUS evaluation of the following vascular parameters was performed for all lesions after passing through the guidewire as described previously^{5, 6}. Briefly, the IVUS catheter was manually pulled back at 1 cm/s under fluoroscopy with reference to a ruler. Fluoroscopy at the time of IVUS recording was stored so that the positional relationship between the IVUS catheter and the lesion could be known at the time of analysis. The measured IVUS parameters were the CTO wire passage route, which was classified into the intraplaque, subintimal, and intramedial routes; the cross-sectional EEM area at the

Table 1. Frequencies of the antegrade and bidirectional approaches

	Overall (<i>n</i> = 71)	IVUS-guided cohort (<i>n</i> = 34)	Non-IVUS-guided cohort (<i>n</i> = 37)	<i>P</i> -value
Antegrade approach, % (<i>n</i>)	69.0 (49)	82.3 (28)	56.7 (21)	<0.001
Bidirectional approach, % (<i>n</i>)	30.9 (22)	16.7 (6)	42.1 (16)	

Data are shown as absolute (percentage) values.

IVUS, intravascular ultrasound

proximal and distal reference sites; the post-procedural minimum lumen area (MLA); and post-procedural axial lumen eccentricity ratio (the ratio of the long-axis diameter to the short-axis diameter).

Outcomes

The primary outcomes of this study were the primary patency rate, which was defined as a peak systolic velocity ratio of <2.4 on duplex ultrasound, and the percentage of patients that were freedom from clinically driven target lesion revascularization (CD-TLR) at 12 months after the initial treatment. The other examined outcomes included the procedure time, radiation exposure time, the frequency of retrograde access, and the amount of contrast media used. These parameters were compared between the IVUS-guided and non-IVUS-guided wiring groups.

Statistical Analyses

The statistical analyses were performed on an intention-to-treat basis. Continuous variables are reported as mean \pm SD values. Categorical variables are shown as percentages. Continuous variables were compared using the unpaired Student's *t*-test, and categorical variables were compared using the chi-square test or Fisher's exact test. Time-dependent parameters were analyzed using the Kaplan–Meier method. For the analyses of primary and other outcomes, the groups were compared using the log-rank test. Statistical significance was defined as a *p*-value of <0.05. All statistical analyses were performed using JMP software (version 10.0.0, SAS Institute, Cary, NC, USA).

Results

The overall success rate of the procedure was 95.9%. The success rates of the IVUS-guided wiring group and non-IVUS-guided wiring group were 97.1% and 94.8%, respectively (*p* = 0.487). Moreover, the success rate of antegrade wiring was higher in the IVUS-guided wiring group than in the non-IVUS-guided wiring group (82.3% vs. 56.7%, *p* < 0.001) (Table 1). Among all 22 bidirectional wiring cases, distal puncture was performed in 19 cases (distal

superficial femoral artery [SFA]: 10 cases, popliteal artery [POP]: eight cases, high-tibial puncture: one case), and the transcollateral approach was applied in three cases.

Patients and Lesion Characteristics

The patients' background data are shown in Table 2. The patients' mean age was 75.3 \pm 8.7 years. Regarding the patients' underlying conditions, 48% of patients had diabetes mellitus, 17% of patients had chronic kidney disease, and 32% of patients presented with chronic limb-threatening ischemia. These variables did not differ significantly between the IVUS-guided and non-IVUS-guided wiring groups. The characteristics of the lesions are presented in Table 3. The mean lesion length, CTO length, and reference site diameter were 21.6 \pm 8.9 cm, 16.4 \pm 9.6 cm, and 5.5 \pm 0.7 mm, respectively. The frequencies of Trans-Atlantic Inter-Society Consensus (TASC II) type C or D lesions and severe calcification, which was defined as peripheral arterial calcium scoring system¹⁴⁾ grade 3 or 4 calcification, were 76% and 31%, respectively. The mean pre-procedural and post-procedural ankle–brachial index values were 0.56 \pm 0.14 and 0.90 \pm 0.14, respectively. There were no significant differences in these variables between the two groups. Regarding the final devices used, plain old balloon angioplasty (POBA), BNS, and DCS were applied in 8%, 75%, and 14% of cases, respectively. The frequency of BNS use tended to be higher in the non-IVUS-guided group; however, the difference was not statistically significant (*p* = 0.135).

IVUS Findings

The IVUS findings are shown in Table 4. The cross-sectional EEM area, post-procedural MLA, and post-procedural axial lumen eccentricity ratio did not differ between the IVUS-guided and non-IVUS-guided wiring groups (proximal EEM: 35.6 \pm 13.8 vs. 34.6 \pm 15.1 mm², *p* = 0.773; distal EEM: 25.6 \pm 9.4 vs. 25.9 \pm 11.2 mm², *p* = 0.926; post-procedural MLA: 15.0 \pm 3.5 vs. 15.7 \pm 5.2 mm², *p* = 0.579; axial lumen eccentricity ratio: 1.4 \pm 0.6 vs. 1.5 \pm 0.4, *p* = 0.926). Regarding the wire passage route, a clinically true

Table 2. Baseline patient characteristics

	Overall (<i>n</i> = 71)	IVUS-guided cohort (<i>n</i> = 34)	Non-IVUS-guided cohort (<i>n</i> = 37)	<i>P</i> -value
Age (years)	75.3 ± 8.7	75.1 ± 8.3	75.6 ± 9.3	0.822
Male, % (<i>n</i>)	73.2 (52)	79.4 (27)	67.6 (25)	0.113
Diabetes mellitus, % (<i>n</i>)	47.8 (34)	52.9 (18)	43.2 (16)	0.251
Hypertension, % (<i>n</i>)	80.2 (57)	82.4 (28)	78.4 (29)	0.554
Dyslipidemia, % (<i>n</i>)	63.3 (45)	70.6 (24)	56.8 (21)	0.089
CKD (<60 mL/min/1.73 m ²), % (<i>n</i>)	16.9 (12)	20.6 (7)	13.5 (5)	0.264
Daily hemodialysis, % (<i>n</i>)	5.6 (4)	8.8 (3)	2.7 (1)	0.116
History of smoking, % (<i>n</i>)	42.2 (30)	44.1 (15)	40.5 (15)	0.668
History of CAD, % (<i>n</i>)	60.5 (43)	67.6 (23)	54.4 (20)	0.100
History of CVD, % (<i>n</i>)	28.1 (20)	20.6 (7)	35.1 (13)	0.055
CLTI, % (<i>n</i>)	32.3 (23)	26.5 (9)	37.8 (14)	0.151

Continuous data are presented as the mean ± standard deviation.

Categorical data are shown as absolute (percentage) values.

IVUS, intravascular ultrasound; CKD, chronic kidney disease; CAD, coronary artery disease²; CVD, cerebrovascular disease; CLTI, chronic limb-threatening ischemia

Table 3. Lesional, procedural, and clinical characteristics

	Overall (<i>n</i> = 71)	IVUS-guided cohort (<i>n</i> = 34)	Non-IVUS-guided cohort (<i>n</i> = 37)	<i>P</i> -value
Lesion characteristics				
Lesion length, cm	21.6 ± 8.9	22.3 ± 9.8	20.9 ± 8.2	0.522
CTO length, cm	16.4 ± 9.6	16.7 ± 11.1	16.0 ± 8.2	0.756
Reference site diameter, mm	5.5 ± 0.7	5.7 ± 0.8	5.3 ± 0.7	0.052
TASC II C/D lesion, % (<i>n</i>)	76.0 (54)	82.4 (28)	70.3 (26)	0.094
Severely calcified, % (<i>n</i>)	30.9 (22)	32.4 (11)	29.7 (11)	0.737
BTK runoff	1.9 ± 0.8	1.8 ± 0.8	2.0 ± 0.8	0.460
Final device				
POBA, % (<i>n</i>)	8.4 (6)	14.7 (5)	2.7 (1)	0.135
BNS, % (<i>n</i>)	74.6 (53)	52.9 (18)	94.6 (35)	
DCS, % (<i>n</i>)	14.0 (10)	26.5 (9)	2.7 (1)	
Stent graft, % (<i>n</i>)	2.8 (2)	5.9 (2)	0.0 (0)	
Pre-ABI	0.56 ± 0.14	0.54 ± 0.13	0.57 ± 0.14	0.355
Post-ABI	0.90 ± 0.14	0.91 ± 0.11	0.89 ± 0.16	0.702

Data are shown as absolute (percentage) values.

IVUS, intravascular ultrasound; CTO, chronic total occlusion; TASC, trans-Atlantic Inter Society Consensus; BTK, below the knee; POBA, plain old balloon angioplasty; BNS, bare Nitinol stent; DCS, drug-coated stent; ABI, ankle-brachial pressure index

lumen wire routes, including the intraplaque and sub-intimal routes, were achieved in 97.3% in the IVUS-guided group and 70.8% in the non-IVUS-guided group ($p=0.010$), whereas clinically false lumen wire route was taken in 2.7% in the IVUS-guided group and 29.2% in the non-IVUS-guided group. Complete clinically true lumen route (CTLR) was achieved in 91.1% (31 lesions) of cases in the IVUS-guided wiring group and 51.3% (19 lesions) of cases in the non-IVUS-guided group ($p<0.001$).

Clinical Outcomes

The clinical outcomes of the examined cases are shown in **Fig. 4**. The primary patency rate at 12 months was significantly higher in the IVUS-guided group than in the non-IVUS-guided group (70.0% vs. 52.2%, ($p=0.045$)) (**Fig. 5A**). The percentage of patients that were freedom from clinically driven TLR at 12 months was also higher in the IVUS-guided group than in the non-IVUS group (83.9% vs. 62.8%, $p=0.036$) (**Fig. 5B**).

Table 4. IVUS findings

	Overall (<i>n</i> = 71)	IVUS-guided cohort (<i>n</i> = 34)	Non-IVUS-guided cohort (<i>n</i> = 37)	<i>P</i> -value
Proximal lumen EEM, mm ²	35.2 ± 14.4	35.6 ± 13.8	34.6 ± 15.1	0.773
Distal lumen EEM, mm ²	25.7 ± 10.2	25.6 ± 9.4	25.9 ± 11.2	0.926
Post-procedural MLA, mm ²	15.3 ± 4.3	15.0 ± 3.5	15.7 ± 5.2	0.579
Post-procedural ALE	1.5 ± 0.6	1.4 ± 0.6	1.5 ± 0.4	0.926
Wire-passage route				0.010
Clinically true lumen Intraplaque, %	77.8	94.0	58.3	
Subintimal, %	7.5	3.3	12.5	
Clinically false lumen Intramedia, %	14.7	2.7	29.2	
Complete CTRLR, % (<i>n</i>)	70.4 (50)	91.1 (31)	51.3 (19)	< 0.001

Continuous data are presented as the mean ± standard deviation.

Categorical data are shown as absolute (percentage) values.

IVUS, intravascular ultrasound; EEM, external elastic membrane; MLA, minimum lumen area; ALE, axial lumen eccentricity; CTRLR, clinically true lumen route

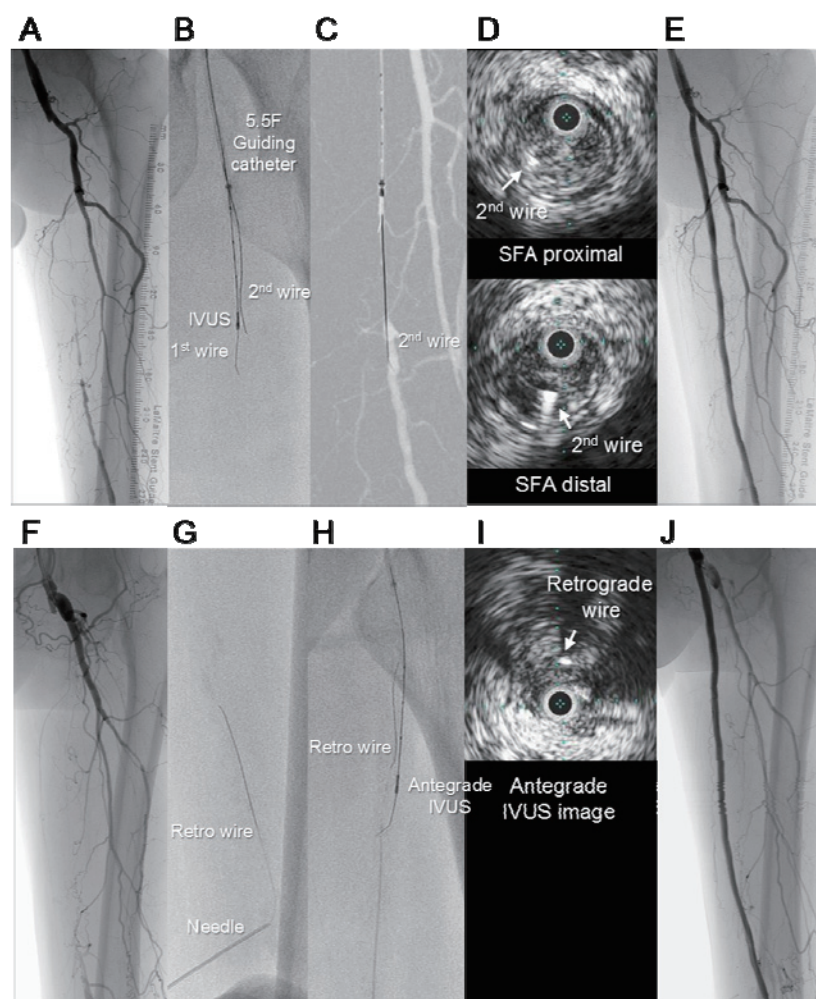


Fig. 4. Representative cases in which IVUS-guided wiring was performed

DSA, digital subtraction angiography; IVUS, intravascular ultrasound; CTO, chronic total occlusion; SFA, superficial femoral artery

Case 1.

(A) DSA showing CTO of the left SFA

(B) A fluoroscopic image of the IVUS-guided parallel wiring technique

(C) Image of a guidewire

The guidewire, which was located in the intraplaque region, could easily pass into the distal true lumen.

(D) IVUS images of the subintimal space

The second guidewire was clearly visible in the intraplaque region.

(E) Completion angiography

Case 2.

(F) DSA showing CTO of the left SFA

(G) Frontal SFA puncture

(H) A fluoroscopic image of IVUS-guided retrograde wiring

(I) Antegrade IVUS imaging

A retrograde guidewire was found in the intraplaque region.

(J) Completion angiography

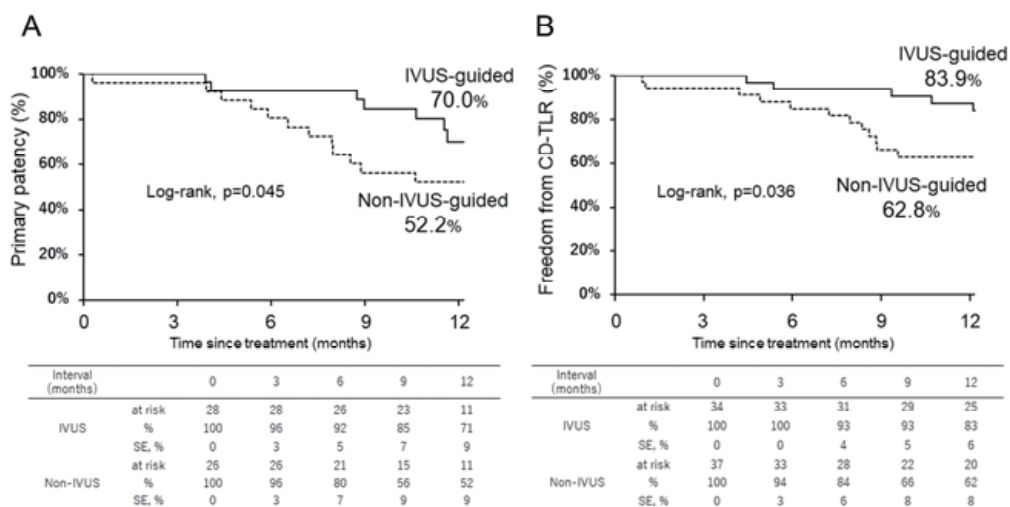


Fig. 5. Kaplan–Meier analysis of the patients’ clinical outcomes

CD-TLR, clinically driven total lesion revascularization

(A) Primary patency at 12 months

(B) Freedom from CD-TLR at 12 months

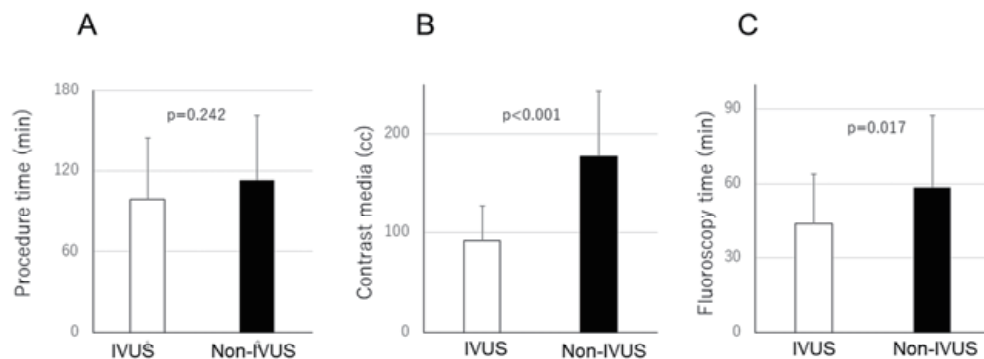


Fig. 6. Technical factors

IVUS, intravascular ultrasound

(A) Procedure time

(B) The amount of contrast media used

(C) Fluoroscopy time

In procedural factors, although the procedure time did not differ significantly between the two groups (99.2 vs. 113.4 min, $p=0.242$), the amount of contrast media used was significantly lower (96.1 ± 39.5 vs. 178.6 ± 66.0 cm³, $p<0.001$), and the fluoroscopy time was significantly shorter (48.5 ± 23.6 vs. 58.2 ± 29.1 min, $p=0.017$) in the IVUS-guided wiring group than in the non-IVUS-guided wiring group (**Fig. 6**).

Subgroup Analysis

To investigate the efficacy of the clinically true lumen wiring, complete CTRR subgroup and incomplete CTRR subgroup in which intramedial route

remained, were created and the IVUS findings of these subgroups were compared. IVUS analysis showed that the post-procedural MLA was significantly larger in the complete CTRR group than in the incomplete CTRR group (16.4 ± 4.0 vs. 12.4 ± 3.5 mm², $p=0.044$). Moreover, the post-procedural axial lumen eccentricity ratio was significantly lower in the complete CTRR group than in the incomplete CTRR group (1.4 ± 0.3 vs. 1.8 ± 0.5 , $p=0.005$) (**Table 5**).

Discussion

In this study, IVUS-guided wiring improved the rates of primary patency and freedom from clinically

Table 5. IVUS findings of subgroup analysis

	Overall (<i>n</i> = 71)	Complete CTRL cohort (<i>n</i> = 50)	Incomplete CTRL cohort (<i>n</i> = 21)	<i>P</i> -value
Proximal lumen EEM, mm ²	35.4 ± 14.5	35.0 ± 13.3	36.2 ± 17.1	0.773
Distal lumen EEM, mm ²	25.9 ± 10.2	26.3 ± 10.7	25.1 ± 9.5	0.667
Post-procedural MLA, mm ²	15.5 ± 4.6	16.4 ± 4.0	12.4 ± 3.5	0.044
Post-procedural ALE	1.6 ± 0.6	1.4 ± 0.3	1.8 ± 0.5	0.005

Continuous data are presented as the mean ± standard deviation.

CTRL, clinically true lumen route

EEM, external elastic membrane

MLA, minimum lumen area

ALE, axial lumen eccentricity

driven TLR at 12 months after EVT for FP-CTO by achieving high rate of CTRL. Moreover, IVUS-guided wiring has several other advantages, e.g., it reduces radiation exposure, the amount of contrast media used, and the frequency of distal puncture procedures.

Previous studies have failed to prove that the intraluminal approach has a clinical benefit compared with the subintimal approach²⁻⁴. However, in these studies, intraluminal and subintimal approaches were classified based on the wiring method and/or the size of the guidewire. Furthermore, these studies did not investigate the wire passage route using IVUS. The wire passage route cannot be defined based on the wiring method, which typically involves the drilling method or knuckle loop technique, or the size of the guidewire (0.014, 0.018, or 0.035 inch), as described in previous reports^{5,6}.

Although Ishihara *et al.* compared intraluminal and subintimal angioplasty on the basis of IVUS evaluations performed after guidewire insertion, they only conducted a qualitative analysis and a not-quantitative analysis of the wire passage route⁴. Conversely, on the basis of a quantitative analysis of IVUS examinations, Mori *et al.* revealed that the intramedial wire passage route being used to place >14% stents is an independent risk factor for restenosis after EVT for FP-CTO lesions⁶. In our study, IVUS-guided wiring reduced the frequency of intramedial wire insertion and consequently improved the clinical outcomes of interventions for FP-CTO lesions. The following can be considered as mechanisms by which IVUS-guided wiring improves clinical outcomes. Generally, balloon dilation or stent placement in the intramedial space can cause under expansion. In this study, there were no differences in the MLA in the acute phase between the IVUS-guided and non-IVUS-guided wiring groups. This might have been because IVUS optimization was performed after balloon dilation or stent placement, which might have offset any differences between the two groups. However, our subgroup analysis showed

that, despite the proximal and distal reference diameters were similar between both groups, the post-procedural MLA was significantly larger and axial lumen eccentricity ratio was lower in the complete CTRL group than in the incomplete CTRL group. Post-procedural smaller MLA has been reported as a risk factor for restenosis both balloon angioplasty and stenting strategy¹⁵⁻¹⁷. Moreover, post-treatment asymmetry has been reported to increase the risk of restenosis after FP DCS placement¹⁸, and the clinical results of our study might be affected by post-treatment MLA and asymmetry. Moreover, even if an acute gain is achieved, it has been reported that Nitinol stents can cause recoil in the chronic phase, leading to restenosis, not only in the coronary arteries but also in FP lesions, and POBA or stenting of the intramedial space might cause recoil in the chronic phase after treatment^{19, 20}. Another possible cause of restenosis is medial inflammation. Expanding the intramedial space is considered to cause medial injuries, and previous studies have shown that medial injuries induce inflammatory cell migration and endothelial cell and smooth muscle cell proliferation, leading to vessel restenosis²¹⁻²³.

The main limitations of IVUS-guided wiring are that a CTRL is not always achieved and that the procedure itself requires skill and has not been standardized. Moreover, the second wire can become difficult to see because of acoustic shadows in severely calcified lesions. Regarding this issue, the development of appropriate devices, such as guiding catheters, IVUS catheters, and guidewires, is expected in the future. However, when using a debulking device, confirming the route with IVUS might improve the effectiveness of the device and the safety of the procedure. Moreover, to analyze whether there were differences in clinical outcomes between the intraplaque and subintimal routes was not possible because of the relatively small number of wires that passed via these routes in this study. This will be clarified in future well-designed prospective multicenter large-scale studies.

Limitations

1. Since this was a pilot study, it was relatively small scale, single-center, and retrospective. It has been reported that, depending on the number of cases performed each year, EVT results vary from institution to institution²⁴; hence, the results of this study cannot always be generalized. To confirm the results of this study, further investigation (RCT or well-designed prospective multicenter trial with a larger cohort) is necessary to clarify the reason for this clinical benefit.

2. The angiographic and IVUS data were not analyzed in a core laboratory.

3. It cannot be denied that the differences in the final devices used between the two groups affected the results.

4. In this study, relatively old-generation devices that did not show sufficient results in TASC II type C or D lesions^{16, 25, 26} were mainly used, and further investigation is necessary to investigate whether IVUS-guided wiring is effective for the new-generation DES and DCB.

Conclusion

The IVUS-guided wiring strategy improves the clinical outcomes of angioplasty for FP-CTO lesions by achieving a high clinically true lumen wire passage route rate. This strategy might also be useful in reducing patients' radiation exposure, the amount of contrast media used, and the frequency of the retrograde approach.

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