ESC European Society of Cardiology

European Heart Journal - Case Reports (2023) **7**, 1–8
https://doi.org/10.1093/ehjcr/ytad518

CASE SERIES
Cardiovascular imaging

The observation of below-the-knee artery by optical frequency domain image and angioscopy: a case series

Haruya Yamane, Yasunori Ueda *, Kuniyasu Ikeoka, Shumpei Kosugi, Haruhiko Abe, Tsuyoshi Mishima, Koichi Inoue, and Yasushi Matsumura

Cardiovascular Division, NHO Osaka National Hospital, 2-1-14 Hoenzaka, Chuo-ku, Osaka, Osaka 540-0006, Japan

Received 25 January 2023; revised 5 October 2023; accepted 16 October 2023; online publish-ahead-of-print 18 October 2023

Background Endovascular treatment (EVT) is a well-established treatment for patients with chronic limb-threatening ischaemia, and below-the-knee (BTK) artery is its main target, although the re-intervention rate is still high. Understanding of the characteristics of BTK artery atherosclerosis would be required to overcome this issue. In this case series, we elucidated the characteristics of non-stenotic BTK artery atherosclerosis in the patients who received EVT of the superficial femoral artery (SFA) using optical frequency domain imaging (OFDI) and angioscopy.

Case summary We presented five patients who underwent EVT of SFA and subsequent observation of ipsilateral BTK artery using OFDI and angioscopy. Patients one and two had advanced atherosclerosis; however, patients three, four, and five had only mild atherosclerosis.

Discussion All patients had multiple risk factors for atherosclerosis and stenosis/occlusion of the SFA and ipsilateral BTK arteries. Furthermore, some patients had several other atherosclerotic vascular diseases suggesting the presence of advanced systemic atherosclerosis. On the other hand, some patients with multiple BTK artery stenosis/occlusion did not have advanced atherosclerosis in the examined BTK artery. The absence of significant atherosclerosis in a BTK artery in patients with multiple stenoses or occlusion in other ipsilateral BTK arteries may suggest some mechanism of vessel occlusion other than atherosclerosis. Further investigations are needed to clarify the mechanism.

Keywords Lower extremity artery disease • Below-the-knee artery • Optical frequency domain imaging • Angioscopy • Case report

ESC curriculum 2.1 Imaging modalities • 9.3 Peripheral artery disease

Learning points

- To understand the characteristics of below-the-knee (BTK) artery atherosclerosis by multiple imaging.
- To know that non-stenotic BTK artery does not always have advanced atherosclerosis in the patients with stenotic/occluded ipsilateral superficial femoral artery and BTK arteries.

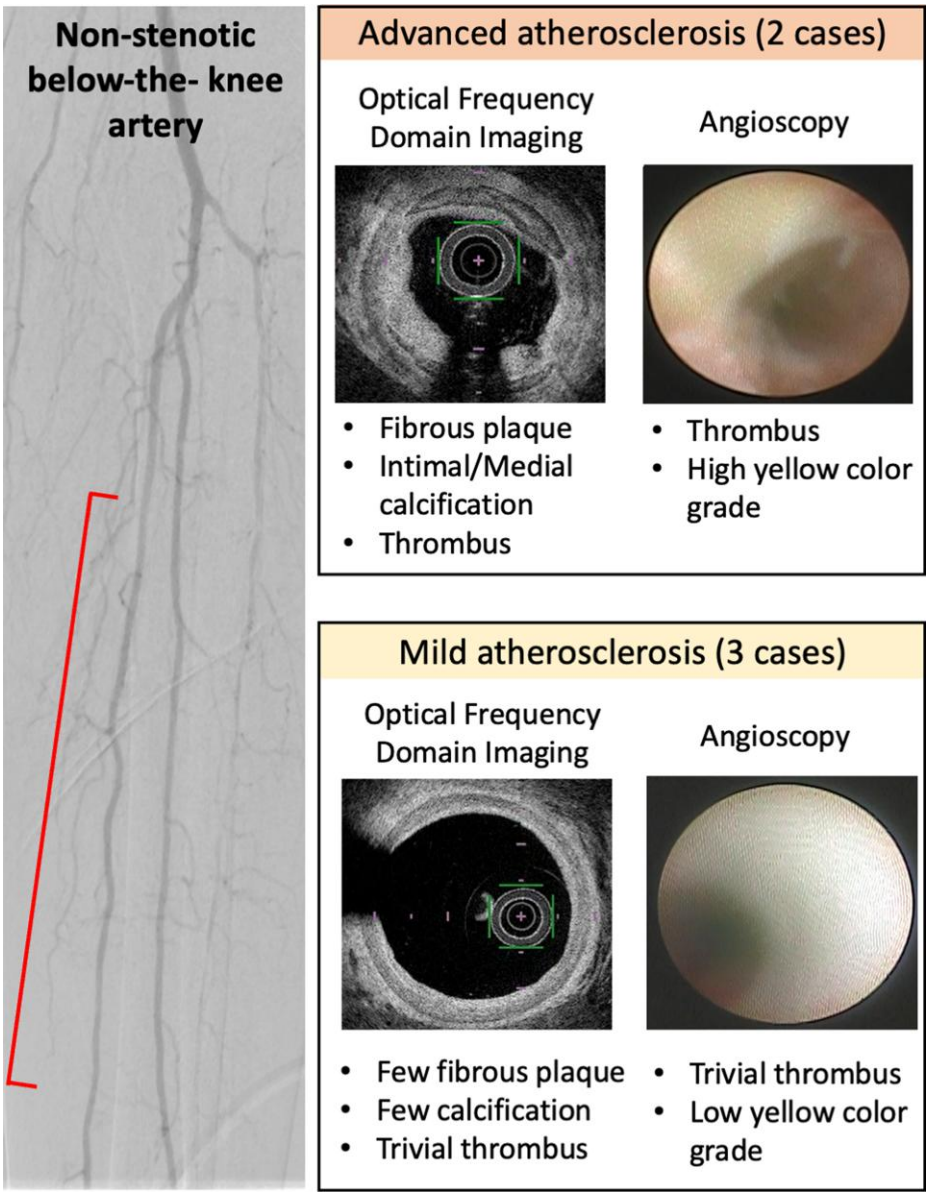
Introduction

Endovascular treatment (EVT) is a well-established treatment for chronic limb-threatening ischaemia with a high technical success rate and good wound healing rate.[1,2] Although the below-the-knee (BTK) artery is its main target, the re-intervention rate is still high.[3] The development of treatment devices and understanding of BTK artery atherosclerosis is needed to overcome this issue. Although previous pathological reports showed that fibrous plaque and intimal/medial calcification are the main characteristics of BTK artery atherosclerosis and

* Corresponding author. Tel: +81 6 6942 1331, Fax: +81 6 6943 6467, Email: yellowplaque@gmail.com
Handling Editor: Vincenzo Nuzzi
Peer-reviewers: Ryaan El-Andari; Lina Ya'qoub; Sumit Sohal; Rafal Wolny
Compliance Editor: Polyvios Demetriades

that atheromatous plaque, calcified nodules, and ruptured plaque are rarely observed,[4,5] there are few reports of the characteristics of BTK artery atherosclerosis in living patients. In this case series, the characteristics of non-stenotic BTK artery atherosclerosis in patients who underwent EVT of a superficial femoral artery (SFA) using optical frequency domain imaging (OFDI) and angioscopy are presented. OFDI is a high-resolution intravascular imaging modality with which one can evaluate the vessel lumen microscopically.[6] By measuring the intensity of reflected light waves and interpreting these optical echoes, OFDI constructs cross-sectional images.[7] Its resolution is approximately 10 times greater than that of conventional intravascular ultrasound.[6]

Summary figure



Case presentations

Patient 1

A 67-year-old man was admitted with intermittent claudication. He was diagnosed with lower extremity artery disease (LEAD) because the left popliteal artery pulse was not palpable, and contrast-enhanced computed tomography showed occlusion of his left SFA. He had hypertension (HT) and diabetes mellitus (DM), was on haemodialysis (HD), and had a history of right SFA, right subclavian artery (SCA), and coronary artery (CA) catheter interventions. His laboratory results and medications are presented in *Table 1*. The initial angiogram showed that the left SFA was occluded, and the left anterior tibial artery (ATA) had severe stenosis, but the left posterior tibial artery (PTA) and peroneal artery

Table 1 Summary of risk factors, laboratory data, and medications

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Risk factors	HT, DM, HD	HT, DM, DL	HT, DM, Smoking	HT, DM	HT, DM, HD
Laboratory data					
Triglyceride (mg/dL)	152	186	88	92	46
HDL-c (mg/dL)	48	43	60	36	46
LDL-c (mg/dL)	39	67	113	90	71
HbA1c (mg/dL)	5.6	8.1	7.2	7.5	5.1
Medications					
Dual	Aspirin	Aspirin	Aspirin	Aspirin	Aspirin
anti-platelet therapy[a]	Prasugrel	Cilostazol	Clopidogrel	Clopidogrel	Clopidogrel
Blood pressure lowering medicine	Olmesartan	Azilsartan	Amlodipine	Irbesaltan	Azilsartan
	20 mg	40 mg	5 mg	100 mg	40 mg
		Cilnidipine		Amlodipine	Amlodipine
		5 mg		5 mg	10 mg
Lipid-lowering drug	Rosuvastatin	Atorvastatin	None	Atorvastatin	Rosuvastatin
	5 mg	10 mg		10 mg	5 mg
Oral hypoglycaemic drug	Teneligliptin	Metformin	Alogliptin	Metformin	Metformin
	20 mg	1000 mg	12.5 mg	500 mg	1000 mg
		Repaglinide		Sitagliptin	
		1 mg		50 mg	

DL, dyslipidemia; DM, diabetes mellitus; HbA1c, haemoglobin A1c; HD, haemodialysis; HDL-c, high density lipoprotein cholesterol; HT, hypertension; LDL-c, low density lipoprotein cholesterol.
[a]Anticoagulation was not performed in any patient.

(PA) had no stenoses (*Figure 1* A1, A2). The guidewire was passed through the occluded lesion in the left SFA using bi-directional wiring, and successful EVT was achieved by 6.0-mm balloon angioplasty and the application of a drug-coated balloon (DCB).

After EVT, the left PTA was examined by OFDI and non-obstructive general angioscopy. Cross-sectional OFDI images were evaluated at 2.0-mm intervals. Areas of fibrous plaque, atheromatous plaque, intimal/medial calcification, and thrombus were counted. The maximum yellow colour grade and the amount of white or red thrombus were evaluated by angioscopy.[8] The observed vessel was divided into three sections (proximal, mid, and distal) to present the findings (*Table 2*).

Abundant fibrous plaques, calcification, and thrombus were detected, whereas no atheromatous plaques were detected by OFDI (*Figure 1* B1–D1). Grade 2–3 yellow plaques and a moderate amount of white thrombus were detected by angioscopy (*Figure 1* B2–D2). In summary, advanced atherosclerosis with thrombus, indicating plaque disruption, was detected.

His intermittent claudication disappeared after EVT, and he was discharged 3 days later without any complications. At 1-year follow-up, ultrasonography demonstrated restenosis of the target lesion.

Patient 2

A 73-year-old man diagnosed with LEAD underwent successful EVT of left SFA stenosis using DCB (*Figure 2* A1). He had DM and a history of femoro-popliteal bypass for right SFA occlusion 5 years earlier. The initial angiogram showed that the left PTA had a diffuse stenosis, but the left ATA and PA had no stenoses (*Figure 2* A2). The guidewire was passed through the stenotic lesion in the left SFA, and successful EVT was achieved by 6.0-mm balloon angioplasty and the application of DCB.

The left ATA was examined by intravascular imaging. Abundant fibrous plaques, calcification, thrombus, and atheromatous plaques were detected by OFDI (*Figure 2* B1–D1). In grades 2–3 yellow plaques and moderate amounts of white and red thrombi were detected by angioscopy (*Figure 2* B2–D2). In summary, advanced atherosclerosis with thrombus, indicating plaque disruption was detected.

Patient 3

A 72-year-old man diagnosed with LEAD underwent successful EVT of left SFA occlusion using DCB (*Figure 3* A1). He had HT and DM and was a current smoker. The initial angiogram showed that the left ATA and PA were occluded, but the PTA had no stenosis (*Figure 3* A2). The guidewire was passed antegrade through the occluded lesion in the left SFA, and successful EVT was achieved by 5.0-mm balloon angioplasty and the application of DCB.

The left PTA was examined by intravascular imaging. Few fibrous plaques and calcification were detected by OFDI (*Figure 3* B1–D1). No yellow plaque or thrombus was detected by angioscopy (*Figure 3* B2–D2). In summary, atherosclerotic change was mild.

Patient 4

A 70-year-old man diagnosed with LEAD underwent successful EVT of left SFA occlusion using DCB (*Figure 4* A1). He had HT, DM, and dyslipidemia. The initial angiogram showed that the left ATA was occluded,

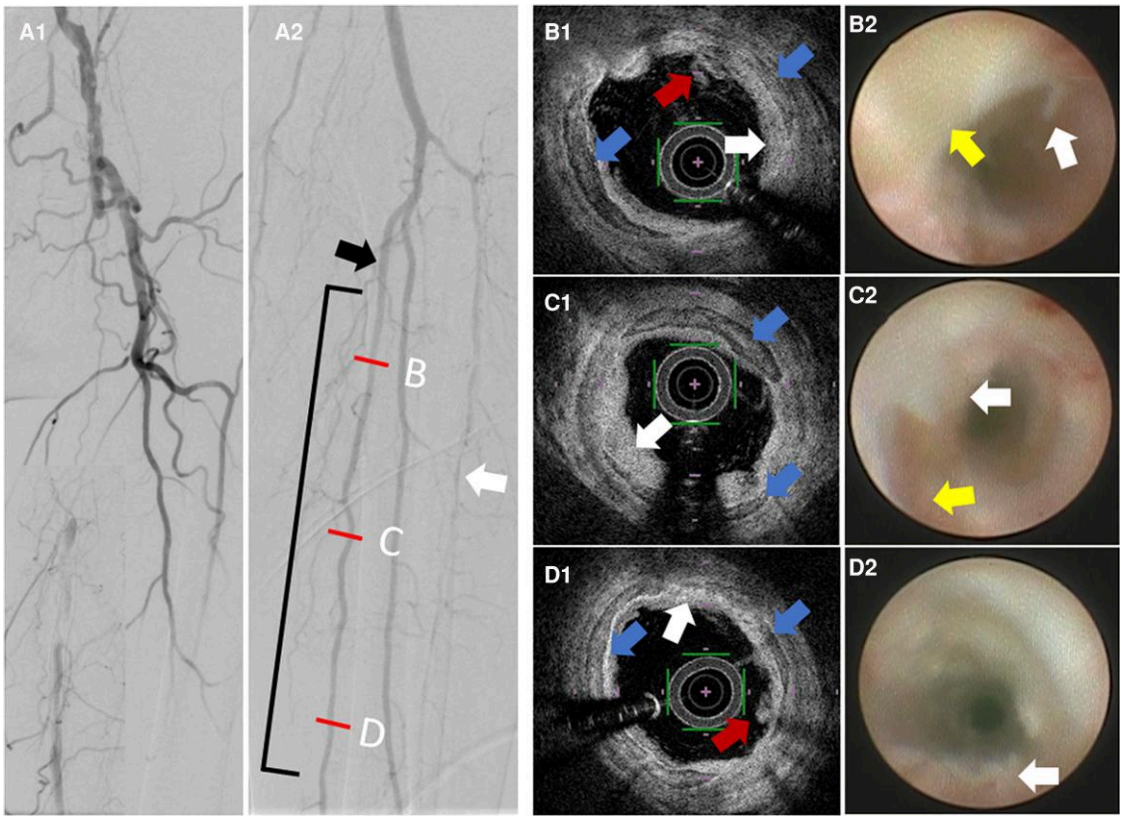


Figure 1 Initial angiogram, below-the-knee arterial images of optical frequency domain imaging and angioscopy in patient 1. The left superficial femoral artery was occluded (*A*1) and ipsilateral posterior tibial artery (*A*2, black arrow) was examined (black line). Optical frequency domain imaging (*B*1, *C*1, *D*1) detected fibrous plaques (white arrow), medial calcification (blue arrow) and thrombus (red arrow). Angioscopy (*B*2, *C*2, *D*2) detected yellow plaques (yellow arrow) and white thrombus (white arrow). See Supplementary material online, Videos *S1* and *S2*.

Table 2 Summary of findings of below-the-knee artery by optical frequency domain image and angioscopy

		Optical frequency domain image				Angioscopy			
		Fibrous plaque (%)	Atheromatous plaque (%)	Intimal or medial calcification (%)	Thrombus (%)	Maximum yellow colour grade	White thrombus	Red thrombus	Thrombus volume
Patient 1	Proximal	73	0	100	68	3	+	—	Moderate
	Mid	59	0	100	64	2	+	—	Mild
	Distal	27	0	100	36	2	+	—	Mild
Patient 2	Proximal	32	4	100	9	3	+	—	Mild
	Mid	35	0	100	0	3	+	+	Mild
	Distal	64	0	100	0	2	+	+	Moderate
Patient 3	Proximal	0	0	0	0	0	—	—	None
	Mid	0	0	0	0	0	—	—	None
	Distal	12	0	8	0	0	—	—	None
Patient 4	Proximal	0	0	0	8	1	+	—	Mild
	Mid	0	0	0	0	0	—	—	None
	Distal	0	0	0	0	0	+	—	Mild
Patient 5	Proximal	80	0	20	4	2	+	+	Mild
	Mid	12	0	8	0	1	—	+	Mild
	Distal	28	0	8	0	2	+	—	Mild

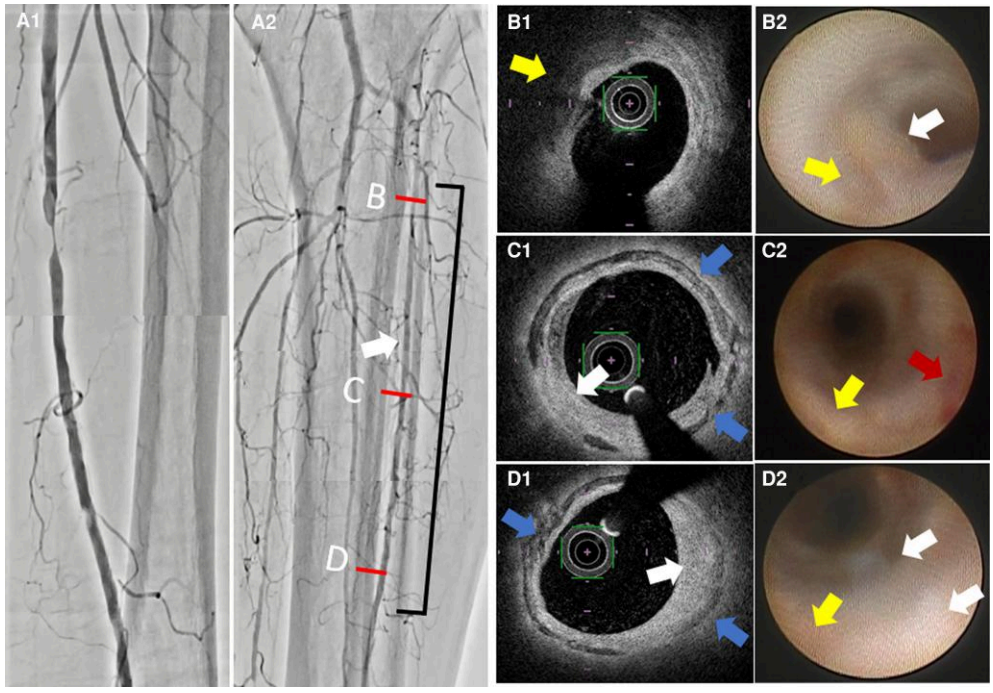


Figure 2 Initial angiogram, below-the-knee arterial images of optical frequency domain imaging and angioscopy in patient 2. Left superficial femoral artery had severe stenosis (*A*1) and ipsilateral anterior tibial artery (*A*2, white arrow) was examined (black line). Optical frequency domain imaging (*B*1, *C*1, *D*1) detected atheromatous plaque (yellow arrow), fibrous plaques (white arrow), medial calcification (blue arrow), and thrombus (red arrow). Angioscopy (*B*2, *C*2, *D*2) detected yellow plaques (yellow arrow), and white (white arrow) and red (red arrow) thrombus. See Supplementary material online, video *S3* and *S4*.

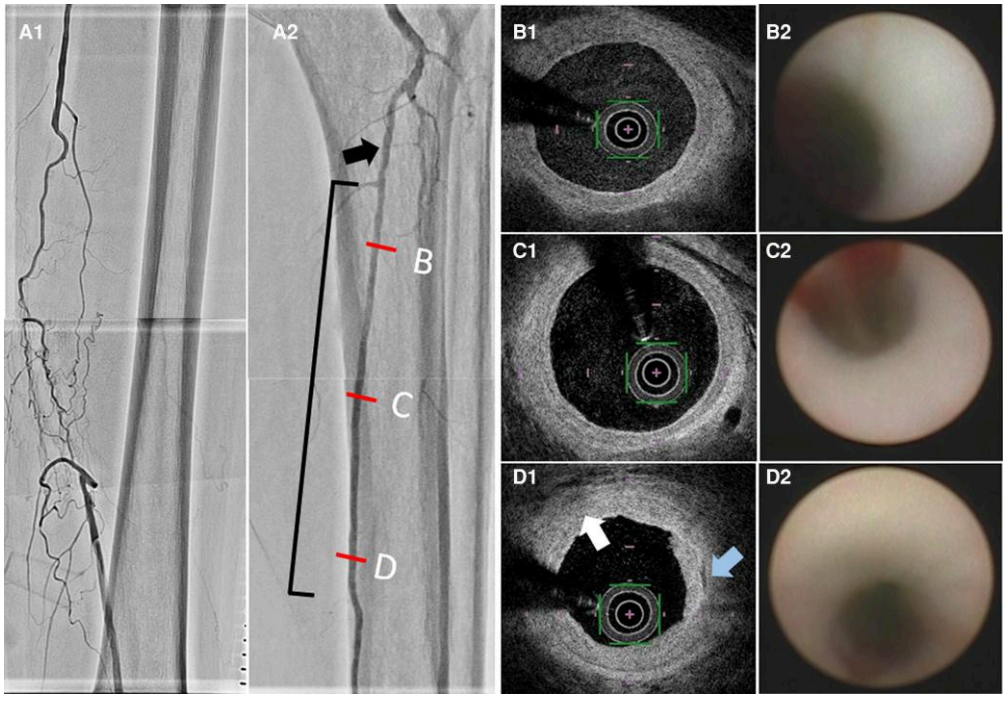


Figure 3 Initial angiogram, below-the-knee arterial images of optical frequency domain imaging and angioscopy in patient 3. The left superficial femoral artery was occluded (*A*1) and ipsilateral posterior tibial artery (*A*2, black arrow) was examined (black line). Optical frequency domain imaging (*B*1, *C*1, *D*1) detected mild fibrous plaques (white arrow) and medial calcifications (blue arrow). Angioscopy (*B*2, *C*2, *D*2) detected no yellow plaque or thrombus. See Supplementary material online, Videos *S5* and *S6*.

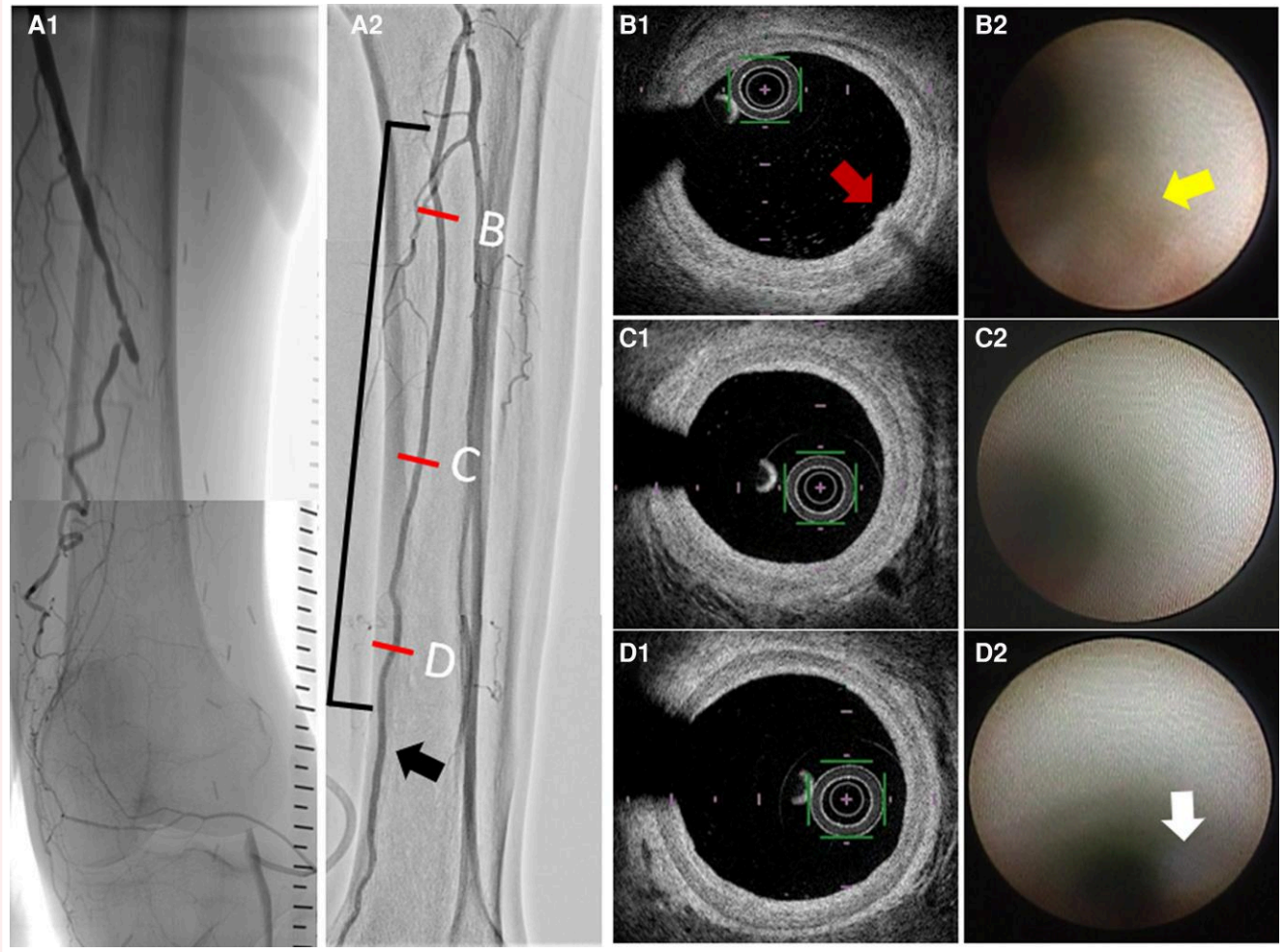


Figure 4 Initial angiogram, below-the-knee arterial images of optical frequency domain imaging and angioscopy in patient 4. Left superficial femoral artery was occluded (*A*1) and ipsilateral posterior tibial artery (*A*2, black arrow) was examined (black line). Optical frequency domain imaging (*B*1, *C*1, *D*1) detected a trivial thrombus (red arrow). Angioscopy (*B*2, *C*2, *D*2) detected grade 1 yellow plaque (yellow arrow) and white thrombus (white arrow). See Supplementary material online, Videos *S7* and *S8*.

but the PTA and PA had no stenoses (*Figure 4* *A*2). The guidewire was passed retrogradely through the occluded lesion in the left SFA, and successful EVT was achieved by 5.0-mm balloon angioplasty and the application of DCB.

The left PTA was examined by intravascular imaging. There was no plaque or calcification, but a trivial thrombus was seen on OFDI (*Figure 4* *B*1–*D*1). Grade 1 yellow plaque and a small amount of white thrombus were detected by angioscopy (*Figure 4* *B*2–*D*2). In summary, atherosclerotic change was mild.

Patient 5

An 81-year-old man diagnosed with LEAD underwent successful EVT of right SFA occlusion using DCB (*Figure 5* *A*1). He had HT and DM, and was on HD. The initial angiogram showed that the right ATA was occluded, but the PTA and PA had no stenoses (*Figure 5* *A*2). The guidewire was passed through the occluded lesion in the right SFA using bi-directional wiring, and successful EVT was achieved by 5.0-mm balloon angioplasty and the application of DCB.

The right PTA was examined by intravascular imaging. Abundant fibrous plaques, mild calcification, and a small amount of thrombus were detected by OFDI (*Figure 5* *B*1–*D*1). In grades 1–2 yellow plaques and small amounts of white and red thrombi were detected by angioscopy (*Figure 5* *B*2–*D*2). In summary, atherosclerotic change was mild.

Discussion

This is the first report of the evaluation of atherosclerosis by OFDI and angioscopy in non-stenotic BTK arteries. Five patients who underwent SFA EVT and examinations of the non-stenotic ipsilateral BTK artery by OFDI and angioscopy were presented. All patients had multiple risk factors for atherosclerosis and stenosis/occlusion of the SFA and ipsilateral BTK arteries. Furthermore, some patients (patients 1 and 2) had several other atherosclerotic vascular diseases (CA disease, upper extremity artery disease, or contralateral LEAD), suggesting the presence of advanced systemic atherosclerosis. A summary of lower-limb and other vascular diseases is presented in *Table 3*. All patients were on dual anti-

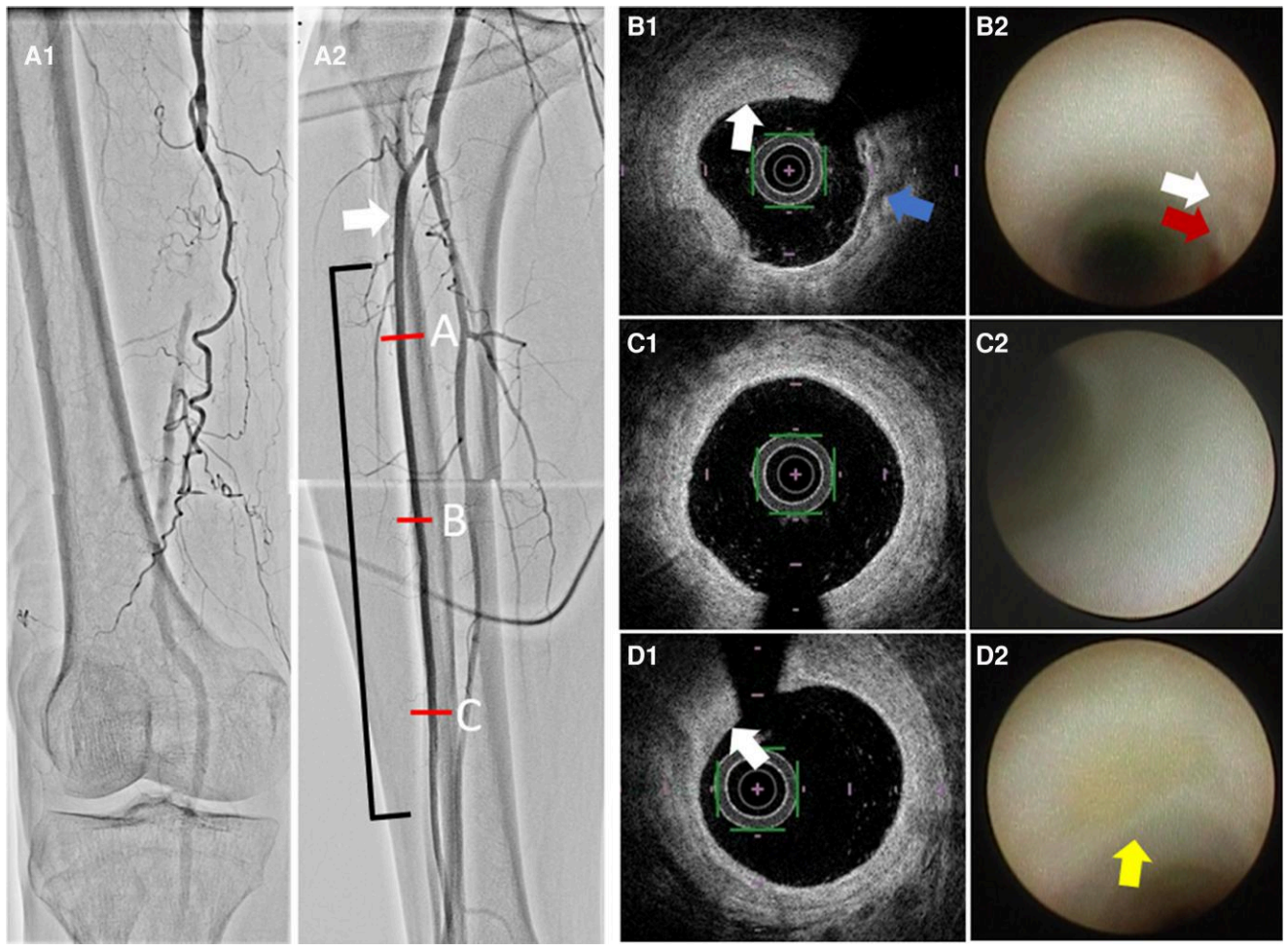


Figure 5 Initial angiogram, below-the-knee arterial images of optical frequency domain imaging and angioscopy in patient 5. Right superficial femoral artery was occluded (*A*1) and ipsilateral anterior tibial artery (*A*2, white arrow) was examined (black line). Optical frequency domain imaging (*B*1, *C*1, *D*1) detected fibrous plaques (white arrow) and intimal calcification (blue arrow). Angioscopy (*B*2, *C*2, *D*2) detected yellow plaques (yellow arrow), white (white arrow), and red (red arrow) thrombus. See Supplementary material online, Videos *S9* and *S10*.

platelet therapy, but none were on anticoagulation therapy. All OFDI and angioscopy images were recorded after the SFA interventions, which were performed by the antegrade approach in patient 3 and by the retrograde approach in all other patients.

The examined BTK artery had advanced atherosclerosis in patients 1 and 2, but only mild atherosclerosis in patients 3–5.

The characteristics of BTK atherosclerosis were seen as fibrous plaques, intimal/medial calcification, and thrombus by OFDI and as disrupted or non-disrupted yellow plaques by angioscopy. Thrombus adhesion indicates plaque disruption, which was usually detected on yellow plaques by angioscopy, whereas underlying plaques were not necessarily atheromatous plaques on OFDI. A plausible explanation would be that superficial deposition of lipid detected as yellow plaque by angioscopy may be thrombogenic, although it is not detected as atheromatous plaque by OFDI. Plaque disruption includes plaque rupture, plaque erosion, and functional disruption of intimal anti-thrombotic function. Although ruptured plaques are frequently observed in the coronary arteries,[9,10] ruptured plaques were not detected in the BTK arteries in the present study.

The patients with advanced atherosclerosis (patients 1 and 2) had several other systemic atherosclerotic vascular diseases, but those with mild atherosclerosis (patients 3–5) did not. On the other hand, the patients with mild atherosclerosis in BTK arteries (patients 3–5) had stenosis/occlusion in other ipsilateral BTK arteries. The absence of significant atherosclerosis in patients with multiple stenoses or occlusion may suggest some mechanism of vessel occlusion other than atherosclerosis. However, since the presence or absence of atherosclerosis in the stenotic/occluded BTK arteries was not directly examined in this study, further investigations are needed to clarify the mechanism of BTK stenosis/occlusion. Previous pathological studies suggested that BTK stenosis/occlusion is predominantly caused by thromboembolism rather than atherosclerosis.[4,5] By direct examination of stenotic/occluded BTK arteries with intravascular imaging, it may be possible to clarify the mechanism of vessel stenosis/occlusion in each patient and improve the treatment strategy for each patient.

Table 3 Summary of lower-limb and other vascular diseases

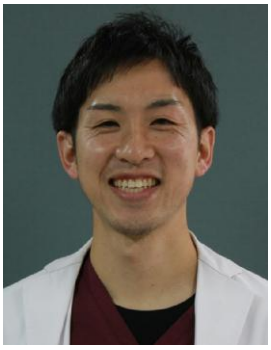
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age (years)	67	70	72	70	81
Rutherford classification	2	3	3	2	2
Target lesion of EVT	Left SFA	Left SFA	Left SFA	Left SFA	Right SFA
Lesion length (cm)	20	8	15	20	10
Ipsilateral BTK artery					
ATA	Stenosis	Patent	Occlusion	Occlusion	Patent
PTA	Patent	Stenosis	Patent	Patent	Occlusion
PA	Patent	Patent	Occlusion	Patent	Patent
Examined BTK	Left PTA	Left ATA	Left PTA	Left PTA	Right ATA
Contralateral BTK artery					
ATA	Patent	Patent	Patent	Unknown	Stenosis
PTA	Patent	Patent	Occlusion		Occlusion
PA	Patent	Patent	Patent		Occlusion
Other vascular disease	CA, right SCA, right SFA	Right SFA	None	None	CA
1-year follow-up of target lesion	Restenosis	Restenosis	Patent	Patent	Patent

ATA, anterior tibial artery; BTK, below-the-knee; CA, coronary artery; EVT, endovascular treatment; PA, peroneal artery; PTA, posterior tibial artery; SCA, subclavian artery; SFA, superficial femoral artery.

Conclusion

The characteristics of non-stenotic BTK artery atherosclerosis in patients who underwent SFA EVT were elucidated by OFDI and angioscopy. Some patients had advanced atherosclerosis with plaque disruption, but others had only mild atherosclerosis, although they all had ipsilateral BTK artery occlusion.

Lead author biography



Dr. Haruya Yamane, MD currently works as a Cardiologist at NHO Osaka National Hospital, Osaka, Japan.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: Ueda Y: Research grant from Abbott, Daiichi-Sankyo, Teijin, Japan Lifeline, OrbusNeich, Janssen, Otsuka, Ono, Eli Lilly, Astellas, Amgen, Boehringer Ingelheim, and Novartis. Lecture fees from Abbott, Kowa, Bayer, Daiichi-Sankyo, Nipro, Takeda, AstraZeneca, Japan Lifeline, Novartis, Ono, Boehringer Ingelheim, and Amgen. Others: none.

Funding: None declared.

Data availability

The data underlying this article are available in the article and in its online supplementary material .

References

1. Conte MS, Bradbury AW, Kolh P, White JV, Dick F, Fitridge R, *et al.* Global vascular guidelines on the management of chronic limb-threatening ischemia. *Eur J Vasc Endovasc Surg* 2019;**58**:S1–S109.e33.
2. Iida O, Takahara M, Soga Y, Kodama A, Terashi H, Azuma N, *et al.* Three-Year outcomes of surgical versus endovascular revascularization for critical limb ischemia: the SPINACH study (surgical reconstruction versus peripheral intervention in patients with critical limb ischemia). *Circ Cardiovasc Interv* 2017;**10**:e005531.
3. Iida O, Nakamura M, Yamauchi Y, Kawasaki D, Yokoi Y, Yokoi H, *et al.* Endovascular treatment for infrainguinal vessels in patients with critical limb ischemia: OLIVE registry, a prospective, multicenter study in Japan with 12-month follow-up. *Circ Cardiovasc Interv* 2013;**6**:68–76.
4. Narula N, Dannenberg AJ, Olin JW, Bhatt DL, Johnson KW, Nadkarni G, *et al.* Pathology of peripheral artery disease in patients with critical limb ischemia. *J Am Coll Cardiol* 2018;**72**:2152–2163.
5. Torii S, Mustapha JA, Narula J, Mori H, Saab F, Jinnouchi H, *et al.* Histopathologic characterization of peripheral arteries in subjects with abundant risk factors: correlating imaging with pathology. *JACC Cardiovasc Imaging* 2019;**12**:1501–1513.
6. Otsuka K, Shimada K, Ishikawa H, Nakamura H, Katayama H, Takeda H, *et al.* Usefulness of pre- and post-stent optical frequency domain imaging fndings in the prediction of periprocedural cardiac troponin elevation in patients with coronary artery disease. *Heart Vessels* 2020;**35**:451–462.
7. Kawamori H, Konishi A, Shinke T, Akahori H, Ishihara M, Tsujita H, *et al.* Efficacy of optical frequency domain imaging in detecting peripheral artery disease: the result of a multi-center, open label, single -arm study. *Heart Vessels* 2021;**36**:818–826.
8. Yamane H, Ueda Y, Ikeoka K, Kosugi S. Case report of a peripheral artery disease patient with its aetiology clarified by retrograde angioscopy. *Eur Heart J Case Rep* 2022;**6**:ytac393.
9. Masumura Y, Ueda Y, Matsuo K, Akazawa Y, Nishio M, Hirata A, *et al.* Frequency and location of yellow and disrupted coronary plaques in patients as detected by angioscopy. *Circ J* 2011;**75**:603–612.
10. Kimura S, Cho S, Misu Y, Ohmori M, Tateishi R, Kaneda T, *et al.* Optical coherence tomography and coronary angioscopy assessment of healed coronary plaque components. *Int J Cardiovasc Imaging* 2021;**37**:2849–2859.