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CASE REPORT
Other

Efficacy of pressure gradient measurement using peripheral fractional flow reserve in common femoral artery: a case report

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Background The severity of peripheral artery disease (PAD) is usually diagnosed by physiological assessments, such as the ankle brachial index (ABI) or peak systolic velocity (PSV) on ultrasonography. We examined peripheral fractional flow reserve (pFFR: distal mean pressure divided by proximal mean pressure) measured by a pressure wire and pressure gradient to diagnose PAD patients who do not have lowered ABI or high PSV on ultrasonography.

Case summary An 84-year-old woman with intermittent claudication in her left leg had severe calcification in the left common femoral artery (CFA) on angiography. The exercise-stress ABI of pre-endovascular therapy (EVT) was 1.05/0.98. In addition, the PSV of the left CFA on ultrasonography was 230 cm/s. However, the pFFR using papaverine and alprostadil in the left CFA was 0.86, which was a significant score. In addition, the systolic pressure gradient between the distal and proximal regions was >20 mmHg. We performed EVT for the lesion, and the pFFR improved to 0.96. The systolic pressure gradient was only 1 mmHg at the lesion.

Discussion Symptomatic PAD patients whose ABI or PSV on ultrasonography is insufficient for EVT could be diagnosed with ischaemia using a pressure gradient and pFFR.

Keywords Peripheral artery disease • Fractional flow reserve • Endovascular treatment • Ankle brachial index • Case report

ESC Curriculum 9.3 Peripheral artery disease • 8.6 Secondary prevention

Learning points

- Physiological assessments (such as ankle brachial index or ultrasound) in isolation are often insufficient to exclude the requirement of endovascular treatment.
- In symptomatic peripheral arterial disease, the measurement of pressure gradient and peripheral blood flow reserve can be an effective means of assessing disease severity.

Introduction

The diagnosis and severity of peripheral artery disease (PAD) is typically determined using the lowered ankle brachial index (ABI) or high peak systolic velocity (PSV) in ultrasonography. An ABI <0.90 or PSV in ultrasound >300 cm/s is useful for diagnosing PAD.[1] Fractional flow reserve (FFR: distal mean pressure divided by proximal mean pressure) examination is widely used in coronary vessel disease and is being adapted to PAD.[2,3] However, PAD cases diagnosed with the peripheral FFR (pFFR) have not yet been reported. We encountered a patient with

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symptomatic PAD whose physiological examinations were thought to be negative for ischaemia. Herein, we report a case in which invasive assessments, such as pressure gradient (PG) and pFFR, were useful.

Timeline

Date	Event
Two months before hospitalization at first medical examination:	Patient complained of intermittent claudication in her left lower extremity (Rutherford classification stage 3)
One week before hospitalization:	Exercise-stress ankle brachial index (ABI) was evaluated and ultrasonography was performed. The ABI was 1.05/0.98, and peak systolic velocity (PSV) of the common femoral artery was 230 cm/s in ultrasonography, which were not conclusive for diagnosis of peripheral artery disease.
Day 1:	Informed the patient about the peripheral fractional flow reserve (FFR) and endovascular therapy (EVT) procedure and obtained her consent
Day 2:	Performed EVT. Peripheral FFR improved from 0.86 to 0.99.
Day 3:	Started rehabilitation
Day 5:	Re-examined ultrasonography. The PSV was 227 cm/s.
	Intermittent claudication disappeared (Rutherford classification stage 0)
Day 7:	Patient was discharged from our hospital
One month later:	Outpatient visit for follow-up. No recurrence of intermittent claudication.
	ABI, 0.97/0.99 and PSV, 217 cm/s.
Three Months Later:	ABI, 0.93/0.94 and PSV, 202 cm/s.

Case presentation

The patient was an 84-year-old woman who experienced intermittent claudication in her left lower extremity after walking for approximately 5 minutes (Rutherford classification stage 3). She had no cold sensation or ulcers in her lower extremities. The left popliteal artery was easy to palpate, but the dorsalis pedis artery was difficult to palpate. She had hypertension and a history of aortic valve replacement owing to severe aortic valve stenosis. A systolic murmur was heard in the left anterior thoracic region. She had no jugular venous dilatation or leg oedema. Moreover, she had adequate cardiac function and no indication of ischaemic heart disease. The ABI after exercise-stress was within the normal range: 1.05 for the right extremity and 0.98 for the left extremity. Ultrasonography revealed severe stenosis with calcification in the left common femoral artery (CFA), and the PSV was 230 cm/s. Although there was no decrease in the ABI, she had lower extremity symptoms, and ultrasonography indicated severe stenosis and an increased PSV. Therefore, we decided to perform endovascular angiography and PG evaluation.

We punctured the right CFA and placed the catheter in the left external iliac artery. Angiography revealed severe calcification in the left CFA and 90% stenosis without flow limitation (*Figure 1A*). We used 40 mg of papaverine and 1 μg of alprostadil to induce maximal hyperaemia, and we examined the pFFR using a pressure guidewire (OmniWire, 0.014 inch, Philips, USA). We equalized the proximal pressure to the left external iliac artery. At rest, the systolic PG was 13 mmHg, and the mean PG was 7 mmHg. In hyperaemia, the systolic PG was 23 mmHg, mean PG was 11 mmHg, and pFFR was 0.86 (*Figure 1B* and Table 1).

First, a guidewire (Jupiter FC3, 300 cm, 0.014 inch, Boston, MA, USA) was advanced to the popliteal artery passing beside the calcification. Subsequently, we discovered that intravascular ultrasound (IVUS) could not pass through the lesion. An attempt to pass the intra-calcification using heavier guidewires and a microcatheter was unsuccessful. Next, we punctured the calcified lesion directly using a 20-G needle (105 mm, Medikit, Tokyo, Japan) and succeeded in passing through the lesion. The guidewire was inserted through the needle that passed through the calcified lesion and pulled through the guide catheter. Calcification was debulked using the CROSSER (Bard Peripheral Vascular Inc., Tempe, AZ, USA), which is a novel penetrating catheter for peripheral chronic total occlusion by using high-frequency mechanical vibration to break through obstructive plaque. Angiography revealed expansion of the lesion. Balloon expansion was performed using a JADE 3.5/80 mm (OrbusNeich, Tokyo, Japan) and a peripheral cutting balloon (6.0/20 mm; Boston, MA, USA). We then performed drug-coated balloon (DCB) expansion using a Ranger 7.0/60 mm (Boston, MA, USA) (*Figure 2A-D*). We observed expansion in the lesion without major dissection on angiography and IVUS (*Figure 3A-B*).

After endovascular therapy (EVT), we re-examined the PG and pFFR. At rest, the systolic PG was 3 mmHg, and the mean PG was 2 mmHg. In hyperaemia, the systolic PG was 2 mmHg, mean PG was 1 mmHg, and pFFR was 0.99. After treatment, the patient's lower extremity symptoms improved to a Rutherford classification grade of 0, without recurrence 3 months later.

Discussion

It is necessary to evaluate the severity of ischaemia in patients with PAD undergoing EVT. Objective evaluation is often performed using the ABI or PSV on ultrasonography. In this case, although the patient had intermittent claudication, she had no remarkable deficiency in exercise-stress ABI or a significant increase in PSV. It was thus challenging to determine the severity of the lesion; however, using a pressure wire, we were able to accurately measure the severity of the lesion. No widespread consensus or cut-off value has been determined regarding the pFFR. In this case, we used papaverine to induce maximum hyperaemia; other drugs to consider include 100 μg of adenosine 5′-triphosphate, 250 μg of isosorbide dinitrate, and 200 μg of nitroglycerine.[2,4,5] This method was considered suitable for two reasons. First, the CFA had severe calcification, which was thought to prevent a guiding catheter from passing through the lesion without a pressure wedge.[4] Second, physiological measurement using a pressure wire could help examine the lesion more accurately due to the absence of flow limitation. Measurement of the pFFR is reportedly a feasible and safe procedure[3] because there are no complications in this drug-stress procedure. Although further assessments are required and the risks for

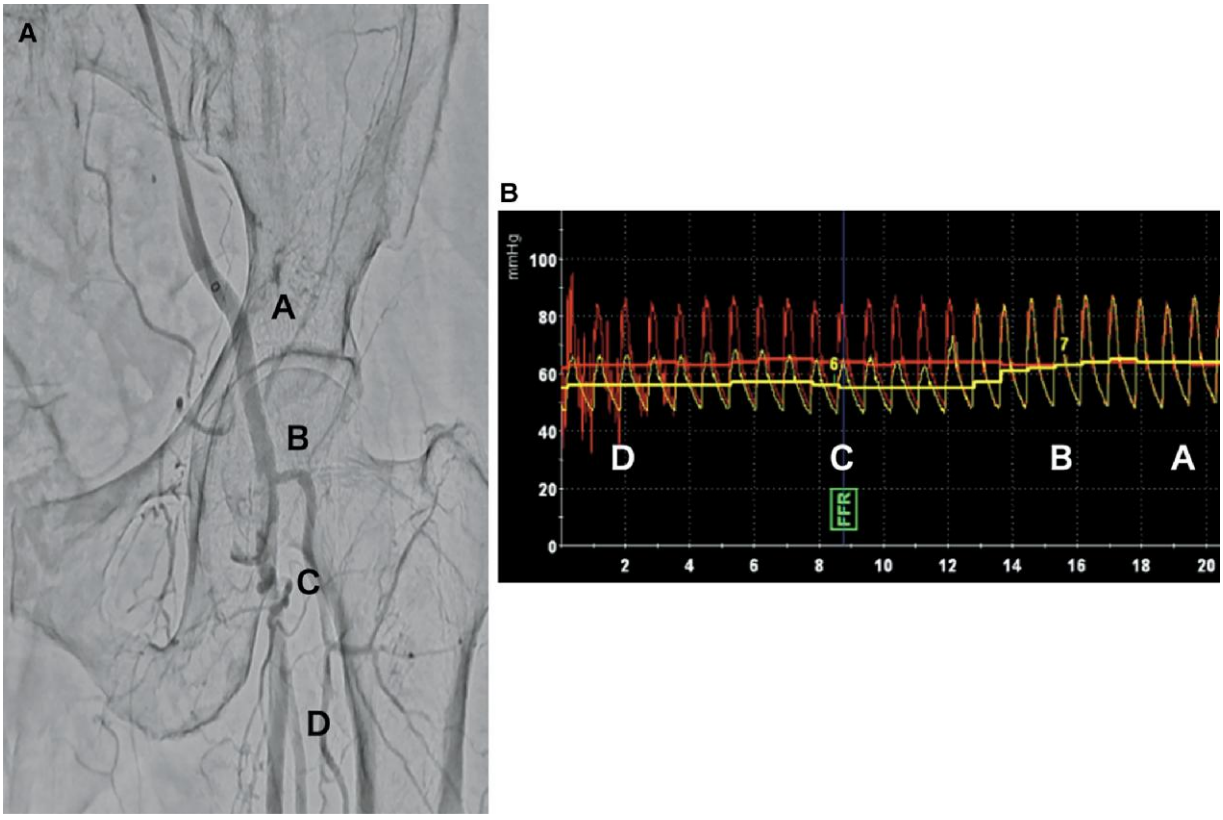

Figure 1 Pre-angiography and assessments of ischaemia, peripheral fractional flow reserve tracing. (*A*) Angiography revealed severe stenosis of the left common femoral artery with a slit. We measured pressure using a pressure guidewire at proximal superficial femoral artery (D), distal (C) and proximal (B) common femoral artery, and external iliac artery (A). In drug-induced hyperaemia, the systolic pressure gradient was 23 mmHg, and the fractional flow reserve measured using a pressure guidewire was 0.86. (*B*) Aortic pressure was shown as the wave above, distal artery pressure was shown as the wave below. Tracing of distal artery pressure/aortic pressure, systolic pressure, and peripheral fractional flow reserve was shown in *Table 1*.

Table 1 Pd/Pa, systolic pressure, pFFR at each point

	Pd/Pa (mmHg)	Systolic pressure (mmHg)	pFFR
A	66/66	90	1.0
B	66/66	90	1.0
C	55/64	67	0.86
D	56/65	66	0.86

Peripheral FFR was calculated by dividing distal mean pressure by proximal mean pressure. We measured pressure using a pressure guidewire at proximal SFA (D), distal (C) and proximal (B) CFA, and EIA (A).
Pa, aortic pressure; Pd, distal artery pressure; pFFR, peripheral fractional flow reserve.

each patient must be considered, including cardiac function or cardiovascular event risks, we recommend this method for the evaluation of the severity of ischaemia.

The significance of the PG for PAD lesions remains controversial. Some reports have suggested that the systolic PG of the lesion at rest is >10 mmHg, and >20 mmHg at maximum hyperaemia, while others have reported that a mean PG of more than 10 mmHg is an indication for stenting.[6,7] It has also been reported that, in the iliac artery, a mean PG <10 mmHg after intervention is an indicator of hemodynamic status.[8]

For reference, in the fractional flow reserve versus angiography for multivessel evaluation 2 trial, percutaneous coronary intervention (PCI) along with optimal medical therapy was associated with fewer composite events and a better prognosis in patients with stable angina pectoris when the FFR value was ≤0.8.[9] Therefore, PCI is now considered when the FFR value is ≤0.8, and medical therapy when the value is >0.8. In another study, the pFFR was reported to be significant if it was <0.85; additional reports are expected in the future.[2] In our case, the systolic PG at hyperaemia was >20 mmHg, which was determined to be a significant stenosis with reactive hyperaemia. The fact that the patient's lower extremity symptoms did not improve with antiplatelet therapy alone was another factor in our decision that EVT was better than drug therapy alone. Some reports have shown that the hyperaemic mean PG and pFFR are both significantly correlated with the PSV ratio,[2] but this was not applicable in this case. In fact, the PGs were remarkably better after EVT, ranging from 1 to 11 mmHg in hyperaemia. In addition, the pFFR improved from 0.86 to 0.99. One month later, the patient's intermittent claudication disappeared when walking over 500–600 metres, and she had no numbness in her feet. The resting ABI was 0.97/0.99, and the exercise-stressed ABI was 1.06/1.10. In addition, the PSV in the CFA was 217 cm/s. All these scores indicate the effectiveness of EVT on the CFA in our case. For reference, in superficial femoral artery (SFA) stenosis, a pFFR <0.92–0.95 may be considered a predictor for future restenosis.[10,11] The application of a pFFR cut-off value for CFA lesions remains controversial and may need resolving in the future. We

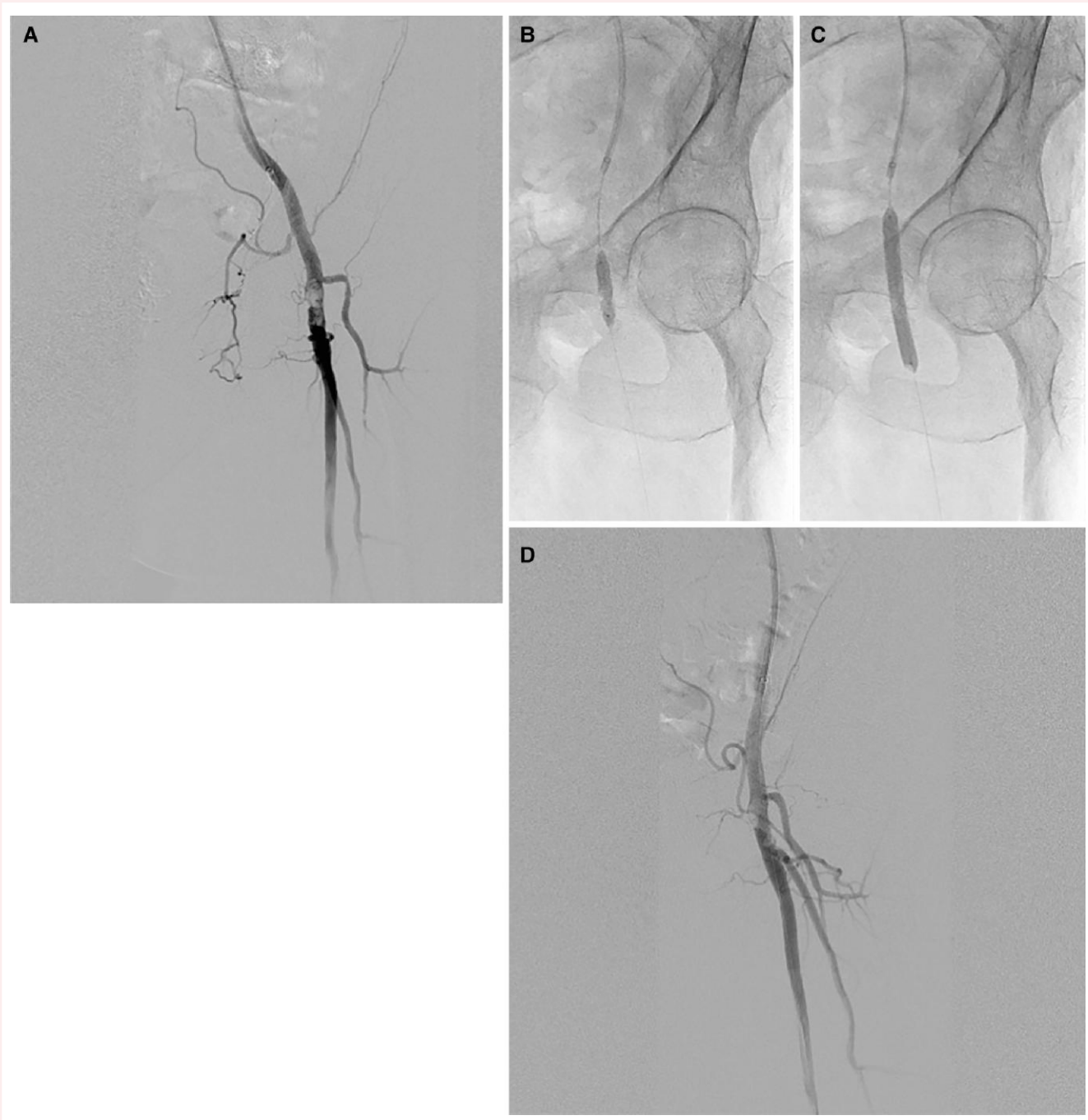

Figure 2 Interventional procedure. (*A*) First angiography from the guided catheter. (*B* and *C*) We performed pre-balloon dilatation and achieved expansion, using the drug-coated balloon strategy. *Figure 2D* The patient's common femoral artery expanded without major dissection or flow limitation.

referred to the SFA data to predict the outcome of EVT on the CFA, which still had calcified plaque after expansion.

The endpoint of the EVT was to perform a balloon expansion in the lesion with a paclitaxel-coated balloon. In CFA lesions, DCB strategies are not inferior to non-DCB strategies in terms of target lesion revascularisation, limb loss, and major adverse limb events at 12 and 24 months of follow-up.[12] Generally, stenting is not suitable for the CFA because of the risk of stent fracture in the bent area. Our patient's CFA expanded after pre-ballooning without major dissection, and the DCB enabled the CFA to obtain sufficient flow without any major dissection or distal embolism.

A limitation of our procedure is that the guiding catheter may have reduced progressive blood flow, which could have led to fluctuations in the PG or pFFR. In the case of diffuse lesions, the proximal mean pressure should be measured more proximally, such as at the terminal aorta, if possible. Moreover, there are few reports of the efficacy of pFFR-computed tomography. In a previous study, it had similar diagnostic value to invasive FFR in aortoiliac lesions.[13] However, as the available

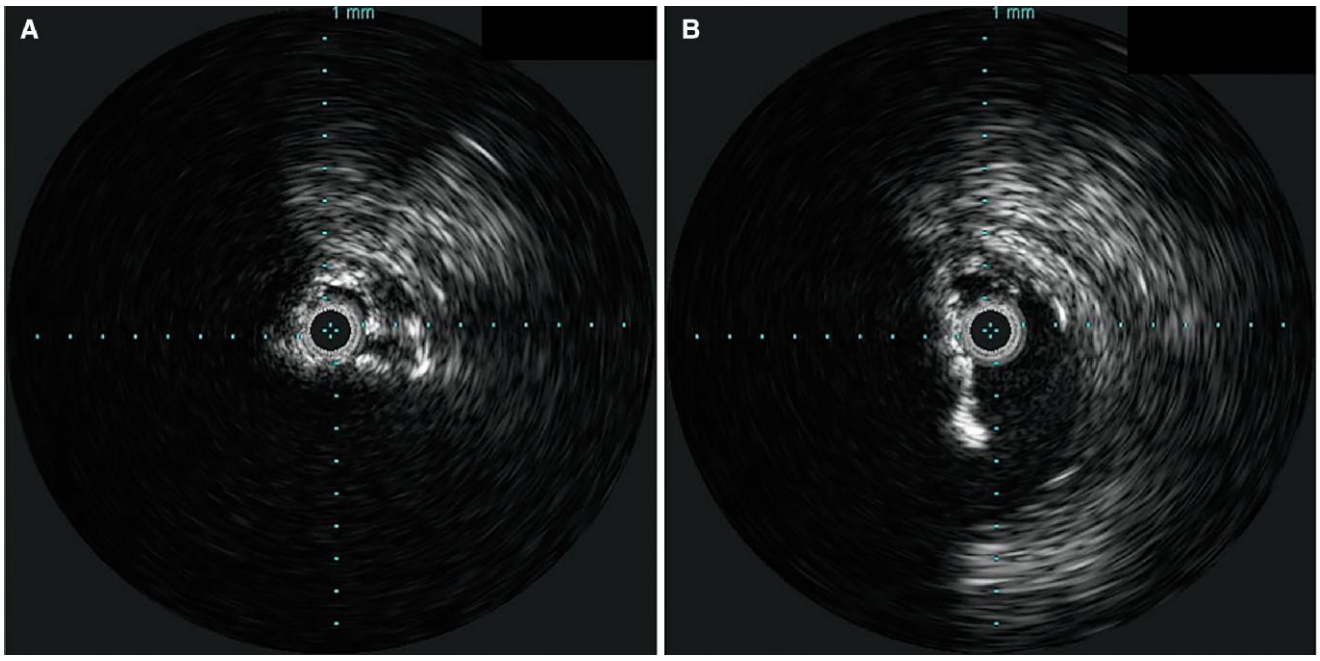

Figure 3 Intravascular ultrasound findings. (*A*) First intravascular ultrasound before dilatation showed more severe stenosis than in angiography, with circumferential calcification. The minimum lumen area was 8.9 mm^2. (*B*) Final intravascular ultrasound showed that expansion was achieved, but that semiperipheral calcification remained. The minimum lumen area was 11.1 mm^2.

evidence is derived from a small number of retrospective reviews, further studies are needed.

Conclusions

It is useful to evaluate the pFFR and PG to perform optimal EVT for patients with PAD. In patients with PAD with a suspected stenotic lesion, evaluation via the pFFR or PG may provide valuable findings, even in the absence of a decrease in ABI or a high PSV.

Lead author biography

Yuki Nakamura was born in Shiga, Japan, in 1989. I received the MD degree from University of Occupational and Environmental Health, Kitakyusyu, Japan in 2017. I completed 2 years of Japanese resident program at Kawasaki Hospital in Kobe (2017–2019). Currently, I am working at Kumamoto Rosai Hospital as an interventional cardiologist.

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

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Data availability

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

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