

# The combination assessment of lipid pool and thrombus by optical coherence tomography can predict the filter no-reflow in primary PCI for ST elevated myocardial infarction

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## Abstract

The usefulness of distal protection devices is still controversial. Moreover, there is no report on thrombus evaluation by using optical coherence tomography (OCT) for determining whether to use a distal protection device. The aim of the present study was to investigate the predictor of filter no-reflow (FNR) by using OCT in primary percutaneous coronary intervention (PCI) for ST-elevated acute myocardial infarction (STEMI).

We performed preinterventional OCT in 25 patients with STEMI who were undergoing primary PCI with Filtrap. FNR was defined as coronary flow decreasing to TIMI flow grade 0 after mechanical dilatation.

FNR was observed in 13 cases (52%). In the comparisons between cases with or without the FNR, the stent length, lipid pool length, lipid pool + thrombus length, and lipid pool + thrombus index showed significant differences. In multivariate analysis, lipid pool + thrombus length was the only independent predictor of FNR (OR 1.438, 95% CI 1.001 - 2.064,  $P < .05$ ). The optimal cut-off value of lipid pool + thrombus length for predicting FNR was 13.1 mm (AUC=0.840, sensitivity 76.9%, specificity 75.0%). Moreover, when adding the evaluation of thrombus length to that of lipid pool length, the prediction accuracy of FNR further increased (IDI 0.14: 0.019–0.25,  $P = .023$ ).

The longitudinal length of the lipid pool plus thrombus was an independent predictor of FNR and the prediction accuracy improved by adding the thrombus to the lipid pool. These results might be useful for making intraoperative judgment about whether filter devices should be applied in primary PCI for STEMI.

**Abbreviations:** AMI = acute myocardial infarction, AUC = area under the ROC curve, DPDs = distal protection devices, FNR = filter no-reflow, IDI = integrated discrimination improvement, IVUS = intravascular ultrasound, OCT = optical coherence tomography, PCI = percutaneous coronary intervention, ROC = receiver-operator characteristic, STEMI = ST-elevated acute myocardial infarction, TCFA = thin-cap fibroatheroma, TIMI = thrombolysis in myocardial infarction.

**Keywords:** filter no-reflow, lipid pool, optical coherence tomography, ST elevated myocardial infarction, thrombus

## 1. Introduction

No-reflow phenomenon during percutaneous coronary intervention (PCI) induces unfavorable clinical outcomes, such as prolonged hospitalization and increased mortality.<sup>[1,2]</sup> No-reflow

is now considered to have multifocal pathogenetic causes.<sup>[3]</sup> During PCI, filter devices have been expected to prevent distal microcirculatory impairment due to atherothrombotic embolism. Although some randomized clinical trials failed to demonstrate

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the efficacy of the routine use of distal protection devices (DPDs) in primary PCI for acute myocardial infarction (AMI),<sup>[4]</sup> some studies have found that DPDs can improve clinical outcomes in selected patients.<sup>[5,6]</sup> In the clinical setting, we sometimes encounter the filter no-reflow (FNR) phenomenon during PCI with filter devices, especially in a high-risk patient. FNR is thought to occur due to capture of thromboembolic materials, which may lead to prevent distal embolism.

Many intravascular ultrasound (IVUS) parameters have been shown to be related to the no-reflow and FNR phenomena.<sup>[7-9]</sup> Recently, optical coherence tomography (OCT) has been widely used as well as IVUS, in the clinical setting. OCT can obtain more detailed information about plaque morphology and thrombus than can IVUS.<sup>[10,11]</sup> Although some OCT parameters are considered to be useful for predicting no-reflow in angina pectoris and AMI,<sup>[12,13]</sup> there has been no reported on which parameters of OCT could predict FNR for ST-elevated myocardial infarction (STEMI). Thus, the aim of the present study was to investigate the predictive values of OCT parameters for FNR during primary PCI in STEMI.

## 2. Methods

### 2.1. Study population

This was a cross-sectional study. Between December 2013 and May 2016, from 184 consecutive patients with STEMI at Komaki City Hospital, 54 patients who underwent primary PCI guided by OCT within 24 hours after symptom onset was included in this study. Of these, patients who needed predilatation before the first OCT imaging ( $n = 11$ ), those with poor OCT image quality ( $n = 4$ ), and/or those without Filtrap use ( $n = 14$ ) were excluded. Finally, the remaining 25 patients were examined in this study (Fig. 1).

STEMI was diagnosed on the basis of typical chest pain lasting  $\geq 30$  minutes, ECG showing ST-segment elevation of  $\geq 1$  mm in at least 2 contiguous limb leads or  $\geq 2$  mm in at least 2 contiguous precordial leads, and elevated serum creatine kinase-MB level (more than 2 times above the upper limit of the reference range of the hospital).

This study was approved by the research and ethics committees of Komaki City Hospital, and was conducted in accordance with the ethical principles of Declaration of Helsinki. Written

informed consent was obtained from all patients before any procedures were conducted.

### 2.2. PCI procedure

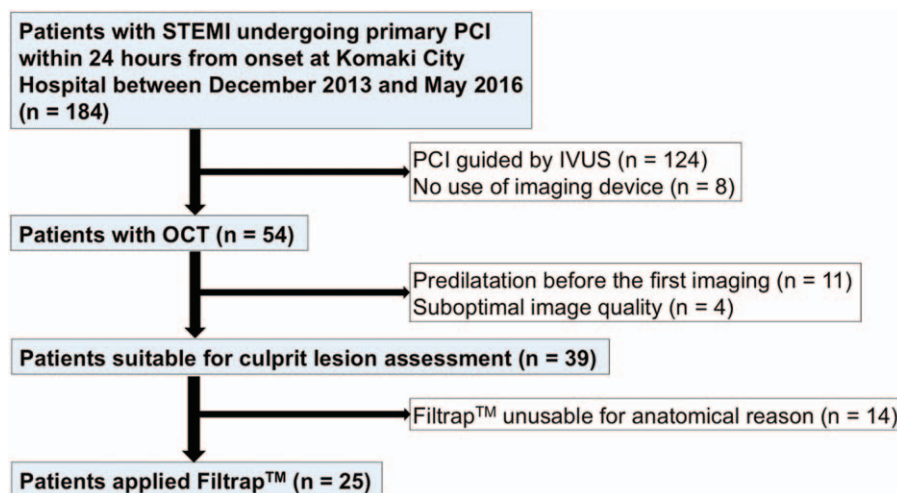
All patients received intravenous heparin and dual antiplatelet therapy was administered at the emergency room. Neither platelet glycoprotein IIb/IIIa receptor inhibitors nor bivalirudin were not administered because they have not been approved in Japan. PCI was performed using a 6 to 7 Fr guiding catheter. After diagnostic angiography, a 0.014-in conventional angioplasty guidewire was advanced across the target lesion. Manual thrombus aspiration was performed with an Eliminate catheter (Terumo Corporation, Tokyo, Japan) if the first angiogram did not show thrombolysis in myocardial infarction (TIMI) flow grade 3. After repeated thrombus aspirations, if the TIMI flow grade was  $< 3$ , balloon dilatation was performed before the OCT procedure, and those patients were excluded from this study. After the first OCT image, the filter-type DPD (Filtrap; Nipro, Japan) was delivered to the distal side of the culprit lesion if the anatomical location was acceptable for this device placement. During DPD placement, routine PCI practices such as balloon dilatation and stent implantation were performed. Coronary angiograms were performed as often as possible immediately after each mechanical dilatation to check the coronary flow.

### 2.3. OCT Procedure

Whether to use OCT as an imaging device depended on the operator's decision. OCT was performed after obtaining TIMI flow grade 3. OCT images were acquired by using a frequency domain OCT system (Dragonfly JP and ILUMIEN OPTIS; St Jude Medical, St Paul, MA). After an intracoronary injection of isosorbide dinitrate, OCT images were obtained with manual injection of Dextran 40 (Low Molecular Dextran L; Otsuka Pharmaceutical Factory, Japan) or a mixture of contrast media and Dextran.<sup>[14]</sup> All OCT images were obtained by using automatic pullback at a rate of 18.0 mm/s from the distal to proximal side of the culprit lesion.

### 2.4. Angiographic analysis

The coronary angiograms were analyzed by an investigator blinded to the clinical and OCT findings. The lesion length,



**Figure 1.** Flow chart of patients included in the study. IVUS=intravascular ultrasound, OCT=optical coherence tomography, PCI=percutaneous coronary intervention, STEMI=ST-elevated acute myocardial infarction.

reference diameter, and percentage of diameter stenosis were measured offline using a contour detection minimum cost algorithm (QCA-CMS Version 3.0; MEDIS, Leiden, the Netherlands). We defined lesions types according to the American Heart Association/American College of Cardiology classification. Coronary flow was assessed according to the TIMI criteria. FNR was defined as coronary flow decreasing to TIMI flow grade 0 after mechanical dilatation during deployment of Filtrap, followed by a sudden increase of >1 TIMI flow grade immediately after device removal, in the absence of dissection, spasm, or 25% residual stenosis. Based on the previous report that the degree of increase in TIMI frame count after DPD removal correlated with the amount of debris captured by DPD, we defined FNR as described above for screening cases that were assumed to have a large amount of debris.<sup>[15]</sup>

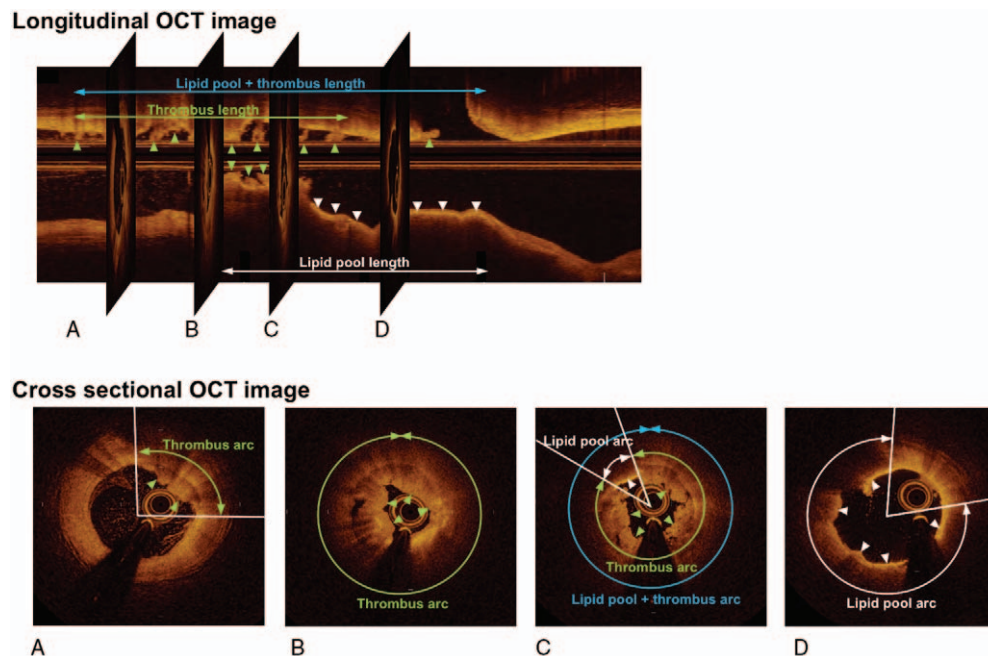
**2.5. OCT Image analysis**

The OCT images were analyzed by 2 experienced investigators who were blinded to the clinical and angiographic data. Preinterventional cross-sectional OCT images were analyzed at every 1-mm interval spanning from 5 mm proximal and 5 mm distal to the culprit lesion. OCT findings were evaluated according to previously validated criteria.<sup>[16-19]</sup> Plaque rupture was defined as fibrous cap discontinuity with the formation of a cavity in the plaque. Plaque erosion was defined as the presence of an attached thrombus overlying an intact and visualized plaque, luminal surface irregularity at the culprit lesion in the absence of a thrombus, or attenuation of the underlying plaque by a thrombus without superficial lipid or calcification immediately proximal or distal to the site of the thrombus. Calcified nodule was defined to

be present when fibrous cap disruption was detected over a calcified plaque, characterized by protruding calcification, superficial calcium, and the presence of substantive calcium proximal and/or distal to the lesion.

Lipid pool was defined as a signal-poor region with poorly defined borders and fast OCT signal drop-off. Thrombus was defined as a mass floating within the vessel lumen or attached to the vessel wall. In this study, we also defined a parameter called lipid pool plus thrombus calculated by treating the lipid pool and the thrombus identically. The arc of lipid pool, thrombus, and lipid pool plus thrombus were measured by using cross-sectional images, and their lengths were measured as their consecutive longitudinal lengths at the culprit lesion (Fig. 2). Index was defined as the mean arc of the target component multiplied by the longitudinal length of the component, and it was calculated for both lipid pool and lipid pool plus thrombus.

Fibrous cap thickness was measured in 3 different times, and the average value was adopted. Thin-cap fibroatheroma (TCFA) was defined as a lipid plaque with lipid content in  $\geq 90^\circ$  in any of the cross-sectional images within the plaque, and when the thinnest part of the fibrous cap measuring  $\leq 65 \mu\text{m}$ . Calcification was defined as a signal poor or heterogeneous region with sharply delineated borders. Spotty calcium was defined as a small calcium deposit within an arc of  $\leq 90^\circ$  in more than one cross-sectional image of the culprit lesion. Cholesterol crystal was defined as liner, highly backscattering structures within the plaque. Macrophages accumulation was defined as signal rich, distinct or confluent punctuate regions with heterogeneous backward shadows. Vasa vasorum was defined as a sharply delineated signal-poor hole visible on multiple contiguous frames.



**Figure 2.** Lipid pool and thrombus assessment by optical coherence tomography. In the longitudinal view, lipid pool (white arrowheads) and thrombus (green arrowheads) are observed, and each length can be measured separately while overlap (white or green 2 direction arrow). However, it is difficult to distinguish the presence of lipid pool in the area where a large amount of thrombus exists. The lipid pool + thrombus length was measured not by adding each length together, but by collecting both of them (blue 2 direction arrow). In the cross-sectional image, lipid pool (white arrowheads) and thrombus (green arrowheads) are observed as well as longitudinal view, and their angles can be measured (white or green double arrows arc). In slices (A) and (D), only thrombus or lipid pool existence is confirmed, and both are recognized in slice (C). In slice (B), thrombus is abundant and lipid pool can not be confirmed. Since the posterior side of the thrombus is not clear by the attenuation effect, it was unknown whether lipid pool existed in that part. The unknown part of lipid pool was not included in the measurement, and the lipid pool + thrombus arc was measured so that it does not overlap like the longitudinal view (blue double arrows arc).

**2.6. Statistical analysis**

Continuous variables are expressed as means ± SD or median (25th, 75th percentiles). Categorical variables are expressed as percentages. Student's *t* test or Mann–Whitney *U*-test was used to compare continuous variables, and the chi-square or Fisher's exact test was used to compare categorical variables when appropriate. To identify independent predictors of FNR, multivariate logistic regression analysis was performed adjusting for onset-reperfusion time, plaque rupture, and lipid pool plus thrombus length. The predictive performance of the parameter with thrombus added to lipid pool was evaluated by calculating c-statistics. Improvements in predictive accuracy were determined by calculating the net reclassification improvement and the integrated discrimination improvement (IDI). A 2-sided *P* value of <.05 was considered to indicate statistical significance. Calculations were performed by blinded investigators by using SPSS version 18.0 (IBM, Armonk, NY) and R 2.13.1 with PredictABEL and pROC packages (R Development Core Team 2011, Vienna, Austria).

**3. Results**

FNR was observed in 12 of 25 patients (48.0%). The clinical characteristics according to the presence or absence of FNR are summarized in Table 1. There were no significant differences in coronary risk factors, clinical states on arrival, laboratory data, and medications between the 2 groups.

**Table 1**  
**Patients' characteristics.**

Variables	Filter no-reflow		<i>P</i>
	(-) n=12	(+) n=13	
<b>Demographics</b>			
Male, n (%)	10 (83.3)	11 (84.6)	.67
Age, years	62.6 ± 11.8	55.9 ± 12.5	.23
BMI, kg/m <sup>2</sup>	23.3 ± 4.3	25.0 ± 4.2	.58
Hypertension, n (%)	5 (41.7)	7 (53.8)	.54
Diabetes, n (%)	5 (41.7)	6 (50.0)	.68
Dyslipidemia, n (%)	8 (66.7)	11 (84.6)	.28
Chronic kidney disease, n (%)	1 (8.3)	1 (7.7)	.74
Current smoker, n (%)	9 (75.0)	11 (84.6)	.46
Prior PCI or CABG or MI, n (%)	2 (16.7)	2 (15.4)	.67
<b>Clinical states on arrival</b>			
sBP, mm Hg	142.5 ± 32.5	149.3 ± 23.1	.37
HR, bpm	81.9 ± 18.6	82.7 ± 24.0	.63
Killip class I/II/III/IV, n	12/0/0/0	11/1/1/0	.57
<b>Laboratory data</b>			
LDL-C, mg/dL	98 [83–116]	109 [102–135]	.12
HDL-C, mg/dL	49.5 ± 16.4	41.2 ± 7.7	.18
Triglycerides, mg/dL	80 [42–117]	152 [71–176]	.12
HbA1c, %	6.2 [5.8–7.4]	5.6 [5.6–6.9]	.17
eGFR, mL/min/1.73 m <sup>2</sup>	81.6 [66.9–95.0]	77.3 [73.0–90.8]	.83
<b>Medications</b>			
ACE-I or ARB, n (%)	3 (25.0)	3 (23.1)	.64
Beta-blocker, n (%)	1 (8.3)	1 (7.7)	.74
Statin, n (%)	5 (41.7)	2 (15.4)	.16
Antithrombotic agents, n (%)	2 (16.7)	1 (7.7)	.47

ACE-I=angiotensin-converting enzyme inhibitors, ARB=angiotensin receptor blocker, BMI=body mass index, CABG=coronary artery bypass grafting, eGFR=estimated glomerular filtration rate, HDL-C=high-density lipoprotein cholesterol, HR=heart rate, LDL-C=low-density lipoprotein cholesterol, MI=myocardial infarction, PCI=percutaneous coronary intervention, sBP=systolic blood pressure. Data are expressed as number (percentages), means ± SD, or median (25th, 75th percentiles).

**Table 2**  
**Coronary angiographical findings.**

Variables	Filter no-reflow		<i>P</i>
	(-) n=12	(+) n=13	
RCA/LAD/LCx, n (%)	7/4/1	6/6/1	.80
ACC/AHA B2 or C, n (%)	10 (83.3)	13 (100)	.22
Initial TIMI flow 0/II/III, n (%)	6/0/6/0	10/0/2/1	.27
Final TIMI III flow, n (%)	12 (100)	12 (92.3)	.52
Predilatation, n (%)	10 (83.3)	12 (92.3)	.47
Stent usage, n (%)	11 (83.3)	12 (92.3)	.74
Stent diameter, mm	3.25 [2.75–3.50]	3.13 [2.75–3.50]	.92
Total stent length, mm	18.9 ± 4.6	25.4 ± 8.4	.03
Postdilatation, n (%)	7 (58.3)	9 (69.2)	.44
Maximum balloon size, mm	3.50 [2.88–3.50]	3.50 [3.00–3.50]	.87
Onset-reperfusion time, hour	3.33 [2.67–12.5]	2.87 [2.38–4.42]	.22
<b>QCA analysis</b>			
Reference vessel diameter, mm	2.89 ± 0.54	3.02 ± 0.56	.59
Minimal lumen diameter, mm	0 [0–0.28]	0 [0–0.14]	.47
Percentage diameter stenosis, %	100 [89–100]	100 [95–100]	.52
Lesion length, mm	16.2 ± 6.1	22.4 ± 10.2	.10

LAD=left anterior descending, LCx=left circumflex, QCA=quantitative coronary angiography, RCA=right coronary artery. Data are expressed as number (percentages), means ± SD, or median (25th, 75th percentiles).

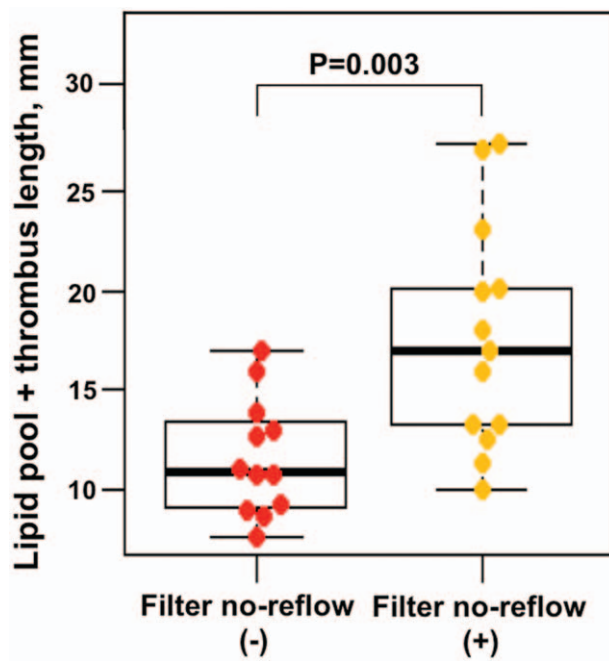
The angiographic and procedural findings are presented in Table 2. There were no significant differences in the culprit lesion characteristics, TIMI coronary flow grade, and PCI procedures between the 2 groups. However, the total stent length was significantly higher in the FNR (+) group (18.9 ± 4.6 mm vs. 25.4 ± 8.4 mm, *P* = .032).

Table 3 shows the OCT characteristics. The lipid pool length and lipid pool plus thrombus length were significantly longer in

**Table 3**  
**Optical coherence tomography findings.**

Variables	Filter no-reflow		<i>P</i>
	(-) n=12	(+) n=13	
Plaque rupture, n (%)	7 (58.3)	11 (84.6)	.16
Erosion, n (%)	5 (41.7)	2 (15.4)	.16
Calcified nodule, n (%)	0 (0)	0 (0)	
Thin cap fibrous atheroma, n (%)	8 (66.7)	9 (69.2)	.61
Minimum cap thickness of fibrous atheroma, μm	60 [50–81]	52 [45–60]	.16
Calcification, n (%)	7 (58.3)	7 (53.8)	.82
Spotty calcium, n (%)	7 (58.3)	8 (61.5)	.60
Cholesterol crystal, n (%)	10 (83.3)	12 (92.3)	.47
Macrophage, n (%)	10 (83.3)	13 (100)	.22
Vasa vasorum, n (%)	6 (50.0)	7 (53.8)	.31
Maximum lipid pool arc, °	126 ± 88	172 ± 105	.25
Lipid pool length, mm	8.5 ± 5.3	14.9 ± 7.5	.02
Thrombus, n (%)	12 (100)	13 (100)	
Maximum thrombus arc, °	216 ± 97	248 ± 114	.46
Maximum thrombus area, mm <sup>2</sup>	2.2 [0.9–3.0]	1.2 [0.9–4.5]	.96
Thrombus length, mm	6.0 ± 3.1	8.7 ± 6.0	.24
Maximum lipid pool + thrombus arc, °	360 [360–360]	360 [345–360]	.39
Lipid pool + thrombus length, mm	11.6 ± 2.9	17.6 ± 5.7	.003
Lipid pool index	344 [127–723]	888 [449–2189]	.06
Lipid pool + thrombus index	902 ± 624	1986 ± 1305	.016

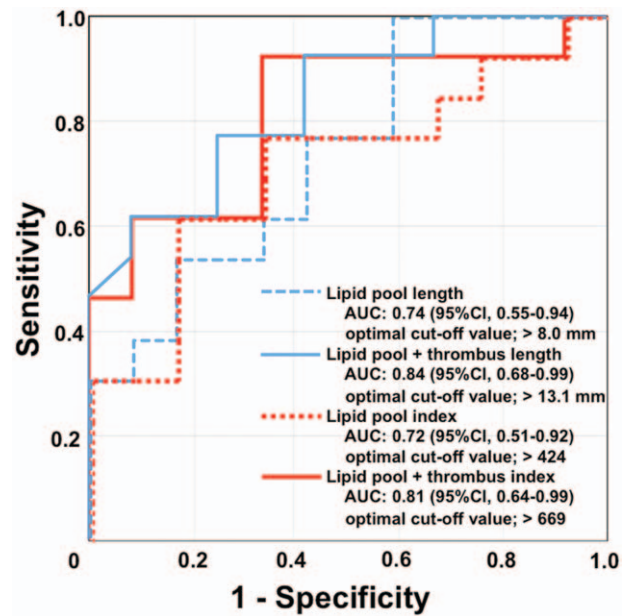
Lipid pool index is defined as the mean lipid pool arc multiplied by the longitudinal length of the lipid pool length. Lipid pool + thrombus index is defined as the mean arc of the lipid pool + thrombus multiplied by the longitudinal length of lipid pool + thrombus. Data are expressed as number (percentages), means ± SD, or median (25th, 75th percentiles).



**Figure 3.** Comparison of the length of lipid pool plus thrombus between the both groups.

the FNR (+) group ( $8.5 \pm 5.3$  mm vs.  $14.9 \pm 7.5$  mm [ $P = .023$ ] and  $11.6 \pm 2.9$  mm vs.  $17.6 \pm 5.7$  mm [ $P = .003$ ], respectively) (Fig. 3). Although the lipid pool index was not statistically significant, the lipid pool plus thrombus index was larger in the FNR (+) group ( $902 \pm 624$  vs.  $1986 \pm 1305$ ,  $P = .016$ ). However, no significant difference was found in the maximum arc of lipid pool, thrombus, and lipid pool plus thrombus. Similarly, the rate of plaque rupture, TCFA, spotty calcium, and cholesterol crystal did not show significant differences between the 2 groups.

The results of the simple and multiple logistic regression analyses for the prediction of FNR are presented in Table 4. Multiple logistic regression analysis revealed that the length of



**Figure 4.** Receiver-operating characteristic curves of lipid pool length, lipid pool plus thrombus length, lipid pool index, and lipid pool plus thrombus index. AUC=area under the curve, CI=confidence interval.

lipid pool plus thrombus was an only independent predictor for FNR during direct PCI in patients with STEMI (odds ratio 1.44, 95% confidence interval 1.001–2.064,  $P < .05$ ). Fig. 4 shows the receiver-operator characteristic (ROC) curves of lipid pool length, lipid pool plus thrombus length, lipid pool index, and lipid pool plus thrombus index with FNR. The best cut-off values for predicting FNR was a lipid pool plus thrombus length  $> 13.1$  mm; sensitivity, 76.9%; specificity, 75.0%; positive predictive value, 76.9%; negative predictive value, 75.0%. The ROC analysis showed that there was no significant difference in the area under the ROC curve (AUC) between the 2 groups (lipid pool length  $AUC = 0.74$  vs. lipid pool plus thrombus length  $AUC = 0.84$  [ $P = .21$ ] and lipid pool index  $AUC = 0.72$  vs. lipid

**Table 4**  
Simple and multiple regression analysis with FNR.

Variables	Simple regression			Multiple regression		
	OR	95% CI	P	OR	95% CI	P
Male	0.96	0.89–1.03	.22			
Age, years	0.97	0.93–1.04	.61			
Hypertension	1.63	0.34–7.95	.54			
Diabetes mellitus	1.40	0.28–7.02	.68			
Dyslipidemia	2.75	0.40–18.88	.3			
Chronic kidney disease	0.92	0.05–16.49	.92			
Current smoking	1.83	0.25–13.47	.55			
Onset-reperfusion time, hour	0.75	0.55–1.03	.07	0.75	0.51–1.10	.14
Reference vessel diameter, mm	1.72	0.38–7.75	.48			
Total stent length, mm	1.17	1.00–1.37	.06			
Plaque rupture	3.93	0.59–26.1	.16	2.34	0.18–30.04	.51
TCFA	1.13	0.21–6.05	.89			
Lipid pool length, mm	1.12	1.01–1.38	.04			
Lipid pool + thrombus length, mm	1.43	1.06–1.93	.02	1.44	1.00–2.06	<.05
Lipid pool index	1.001	1.000–1.002	.10			
Lipid pool + thrombus index	1.001	1.000–1.002	.04			

CI=confidence interval, OR=odds ratio, TCFA=thin-cap fibroatheroma.

**Table 5****Discrimination of each predictive parameter of FNR.**

	AUC (95% CI)	P-value	IDI (95% CI)	P-value	NRI (95% CI)	P-value
Lipid pool length	0.74 (0.55–0.94)	Reference	Reference		Reference	
Lipid pool + thrombus Length	0.84 (0.68–0.99)	.21	0.14 (0.019–0.25)	.023	0.41 (–0.16–0.98)	.16
Lipid pool index	0.72 (0.51–0.92)	Reference	Reference		Reference	
Lipid pool + thrombus index	0.81 (0.64–0.99)	.36	0.082 (–0.044–0.21)	.20	0.26 (–0.31–0.83)	.37

IDI=integrated discrimination improvement, NPV=negative predictive value, NRI=net reclassification improvement, PPV=positive predictive value.

pool plus thrombus index AUC=0.81 [ $P=.36$ ], respectively) (Table 5). However, from the IDI, the predictive accuracy of the FNR was significantly improved by considering thrombus length compared with only the lipid pool length.

#### 4. Discussion

The main findings of the present study were as follows: (i) The longitudinal length of lipid pool plus thrombus was the independent predictor of FNR during primary PCI in STEMI; (ii) The evaluation method in which lipid pool and thrombus were treated identically improved the predictive accuracy for FNR more than that by considering lipid pool alone.

The application of DPDs for the prevention of distal atherothrombotic embolization in routine PCI procedures remains controversial,<sup>[4,20,21]</sup> because DPDs sometimes cause coronary injury and vasospasm.<sup>[22]</sup> Nevertheless, it has been reported that DPDs could reduce major adverse cardiac events in PCI for high-risk lesions of no-reflow such as saphenous vein bypass grafts, and that filter-type DPDs could improve long-term outcomes after PCI for AMI.<sup>[5,23,24]</sup> The slow-flow and no-reflow phenomena resulting in microcirculatory impairment are related to poor clinical outcomes in direct PCI.<sup>[1,2]</sup> Recently mechanisms of the slow flow and no-reflow are considered to be multifactorial, including concretely physical obstruction of distal microcirculation by atherothrombotic embolization, reperfusion injury, spasm of coronary microvessels, and local inflammation.<sup>[3]</sup> These are thought to be related to endothelial dysfunction in the coronary microcirculation and it seems that endothelial dysfunction is an important position as a mechanism of the slow flow and no-reflow. Although not all of the coronary microcirculation is protected by the DPDs, there is also a report that more debris is captured by filter in patients with FNR compared to those without,<sup>[15]</sup> so filter device is thought to be able to protect the distal microcirculation at least from atherothrombotic embolization which causes the slow flow and no-reflow both directly and indirectly. From this point of the view, investigation of the predictors of FNR is considered useful for selecting a good indication of filter device.

Both platelet glycoprotein IIb/IIIa receptor inhibitors and bivalirudin are not used in this study because they have not been approved in Japan. There are several reports on the effect of perioperative myocardial damage reduction and prognosis improvement about these drugs.<sup>[25–27]</sup> Also as Picchi et al<sup>[28]</sup> are trying to show, bivalirudin may have the effect of reducing the thrombus of the culprit lesion to such an amount that OCT imaging can detect in the acute phase of STEMI. These drugs may decrease thrombus volume, improve the quality of OCT image, and further reduce the incidence of FNR. On the other hand, there are concerns of an increase in the risk of bleeding and acute stent thrombosis.<sup>[27,29]</sup> Since DPDs may also cause complications as described above, it is meaningful to decrease cases in which

DPDs should be applied beforehand. However, distal embolism is still a big problem even when antithrombotic therapy is performed, and it is considered important to detect the high risk case of atherothrombotic embolization by performing detailed image evaluation even under antithrombotic therapy.

OCT can obtain more detailed information about plaque morphology and thrombus than can IVUS; however, OCT is not always able to achieve visualization as far as the adventitia because of its tissue penetration power, especially in the presence of a lipid rich plaque or thrombus.<sup>[10,11]</sup> In the clinical setting, it is sometimes difficult for physicians to analyze the area of lipid plaque precisely by using cross-sectional OCT images. In contrast, a longitudinal length of the lipid pool > 9 mm on OCT is associated microvascular no-reflow for STEMI, and a lipid index > 3500 which is a parameter representing the average arc of the lipid plaque on the cross-sectional OCT image multiplied by the longitudinal length, was associated no-reflow for STEMI by ruptured plaque.<sup>[30,31]</sup> In our study, the longitudinal lipid pool length was also associated with FNR; however, the lipid pool index did not show relevance to FNR. Similarly, the lipid pool plus thrombus length was the independent predictor of FNR, but not the lipid pool plus thrombus index. To predict the amount of distal embolism, the index seemed to be more accurate evaluation method than considering the longitudinal length alone, because the concept of the index is closer to volume than the concept of length alone. Although there was little difference in the predictive ability of both parameters, it was taken into consideration in this study that the small sample size might have influenced the result. However, the calculation of the longitudinal length in the OCT image may be simpler than that of the index, and we believe that this is important for making an immediate judgement of whether or not to perform distal protection during primary PCI for STEMI.

On OCT, the image behind the thrombus, especially with red thrombus, becomes unclear owing to the attenuation effect.<sup>[32]</sup> Thus, accurate evaluation of the thrombus volume becomes difficult and evaluation of the plaque behind the thrombus becomes impossible. For this reason, OCT-guided PCI for STEMI, which tends to have a high thrombus volume, seems to have limitations in predicting distal embolism through the evaluation of plaque alone.<sup>[33]</sup> In consideration of these factors, we evaluated the parameter lipid pool plus thrombus, which collectively calculated the lipid pool and the thrombus, and confirmed the improvement of prediction accuracy for FNR over the calculation with lipid pool alone. The parameter of lipid pool plus thrombus length is attractive because it can be easily measured and well adapted to the difficulties of OCT in patients with STEMI.

#### 5. Limitations

This study has several limitations. The major limitation is the small sample size. As each OCT parameter was significantly

confounded, it was difficult to compare them directly by using multivariate analysis. Because whether to use OCT as an imaging device depended on the operator's decision, patient selection bias existed. There were also many cases of difficulty adapting to Filtrap, which also seemed to have rendered selection bias. In many cases, thrombus aspiration was performed before the first OCT imaging, which may have affected the imaging evaluation of plaque morphology and thrombus volume. Furthermore, we did not evaluate IVUS at the same time, and we could not compare the OCT parameters with those of IVUS. Finally, there has been no report that prevention of FNR leads to improved prognosis. Prospective study will be advocated to investigate the usefulness of filter devices for high risk patients of FNR using the findings obtained in the study. The results in the study were limited to STEMI cases with a large amount of unstable plaque and thrombus. This evaluation might be difficult to adapt to the case of stable angina. However, the importance of longitudinal length evaluation for lipid pool, which can be an embolic source, seems to be applicable to other than STEMI cases. In addition, unstable angina pectoris also has thrombosis in many cases, as in STEMI, the evaluation method of this study may be useful.

## 6. Conclusions

In primary PCI for STEMI, FNR could be predicted rapidly by evaluating the OCT image in the long-axis direction, and the prediction ability might be improved by collectively evaluating the lipid pool and the thrombus rather than evaluating only the lipid pool. These results might help operator to decide whether filter devices should be applied for primary PCI in STEMI patients requiring especially quick judgement.

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