Optical coherence tomography assessment of efficacy of thrombus aspiration in patients undergoing a primary percutaneous coronary intervention for acute ST-elevation myocardial infarction

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Objective **We used optical coherence tomography (OCT) to assess the impact of thrombus aspiration before angioplasty on poststenting tissue protrusions in patients undergoing a primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI).**

Methods and results **A total of 188 patients with STEMI who underwent thrombus-aspiration PCI ($n = 113$) or standard PCI ($n = 75$) were examined in this study. OCT was performed immediately after primary PCI to assess lesion morphology in the stented segment. The minimum stent area was similar between the thrombus-aspiration PCI group and the standard PCI group [7.4 interquartile range (IQR): 5.8–9.4 vs. 7.4 IQR: 5.8–8.9 mm^2, $P = 0.788$]. The maximum tissue protrusion area [0.6 (IQR: 0.3–1.1) vs. 1.2 (IQR: 0.8–1.9) mm^2, $P < 0.001$], the mean tissue protrusion area [0.1 (IQR: 0.1–0.2) vs. 0.5 (IQR: 0.3–0.8) mm^2, $P < 0.001$], and tissue protrusion volume [2.3 (IQR: 1.3–4.3) vs. 8.3 (IQR: 5.4–14.6) mm^3, $P < 0.001$] were significantly smaller in the thrombus-aspiration PCI group compared with the standard PCI group. Minimum lumen area was significantly greater in the thrombus-aspiration PCI group compared with the standard PCI group [6.9 (IQR: 5.4–8.8) vs. 6.3 (IQR: 4.6–7.8) mm^2, $P = 0.033$].**

Conclusion **Thrombus aspiration before angioplasty in patients with STEMI was associated with significantly smaller tissue protrusion and larger lumen poststenting compared with standard PCI. Thrombus aspiration in primary PCI favorably influenced lesion morphologies in the stented segment.** *Coron Artery Dis* **26:567–572** **Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.**

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Keywords: acute myocardial infarction, optical coherence tomography, percutaneous coronary intervention, stents, thrombus

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Introduction

Acute myocardial infarction with ST-segment elevation myocardial infarction (STEMI) is caused by intraluminal thrombosis resulting in coronary artery occlusion. Primary percutaneous coronary intervention (PCI) is the standard of care for patients with STEMI and is effective for restoration of coronary blood flow [1,2]. Major complications of primary PCI are related to coronary thrombus. Distal embolization of thrombus leads to coronary no-reflow and increases infarct size [3,4]. In-stent protrusion of residual thrombus has been associated with future adverse events such as stent thrombosis [5]. Thrombus aspiration is a useful adjunctive therapy of primary PCI. Previous studies have shown that thrombus aspiration before angioplasty prevents thrombus embolization, reduces infarct size, and improves clinical outcome in comparison with standard primary PCI [3,4]. However, the efficacy of thrombus aspiration before angioplasty for preventing poststenting tissue protrusion has not been fully elucidated. Optical coherence tomography (OCT) is an optical analogue of intravascular ultrasound (IVUS) that provides high-resolution (10–20 μm) cross-sectional images of coronary arteries. Recent studies have shown that OCT can identify intracoronary thrombus more accurately than conventional imaging methods [6]. Therefore, we used OCT to assess the impact of thrombus aspiration before angioplasty on poststenting tissue protrusions in patients undergoing primary PCI for STEMI.

Methods

Study population

From our OCT registry between April 2011 and March 2013, we retrospectively identified 188 STEMI patients

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who underwent OCT immediately after primary PCI. The enrollment criteria of STEMI in the present study were based on the concurrence of all the following: (a) continuous chest pain for at least 30 min; (b) arrival at our hospital within 6 h from the onset of symptoms; (c) ST-segment elevation at least 0.1 mV in two or more contiguous leads on 12-lead ECG; and (d) elevated myocardial enzyme [plasma creatine-kinase myocardial band (CK-MB) fraction level more than two times higher than normal]. All patients had a de-novo infarct-related lesion in the native coronary artery, which was treated with drug-eluting or bare-metal stents (40 Xience everolimus-eluting stents; Abbott Vascular, Santa Clara, California, USA; 18 Promus everolimus-eluting stents; Boston Scientific, Natrick, Massachusetts, USA; 65 Multi-link Vision bare-metal stents; Abbott Vascular; 33 Driver bare-metal stents; Medtronic, Santa Rosa, California, USA; 18 Duraflex bare-metal stents; Goodman, Nagoya, Japan; and 14 Liberté bare-metal stents; Boston Scientific). The general exclusion criteria for OCT imaging were cardiogenic shock, chronic renal failure, or extremely tortuous vessels. The present study was approved by the institutional review board, and written informed consent was obtained from all patients.

Thrombus aspiration and PCI

All patients were pretreated with aspirin 200 mg, intravenous heparin 100 U/kg, and clopidogrel 300 mg before PCI. No patients received thrombolytic therapy. The decision to perform thrombus aspiration was left to the clinician's discretion. Manual thrombus aspiration was performed before any angioplasty using the Thrombuster III GR catheter (Kaneka Corp., Osaka, Japan). This device is a dual-lumen, monorail design, 6 Fr compatible catheter. The smaller lumen accommodates a 0.014 inch coronary guidewire. The larger extraction lumen allows the removal of thrombus, which is aspirated with a 30 ml locking vacuum syringe. After placement of the guidewire, the aspiration catheter was carefully advanced into the infarct-related coronary artery. Aspiration was started proximal to the infarct-related lesion, gently pushing the catheter through the lesion and then pulling it in a proximal direction, maintaining negative pressure even when the lesion was crossed. Multiple passages of the catheter across the lesion were enforced for aspiration. Withdrawal of the catheter from the coronary artery was performed with permanent negative pressure. Irrespective of the thrombus aspiration, balloon angioplasty and stent implantation were performed in a standard manner. Thrombus aspiration was not performed after stent implantation.

OCT imaging and analysis

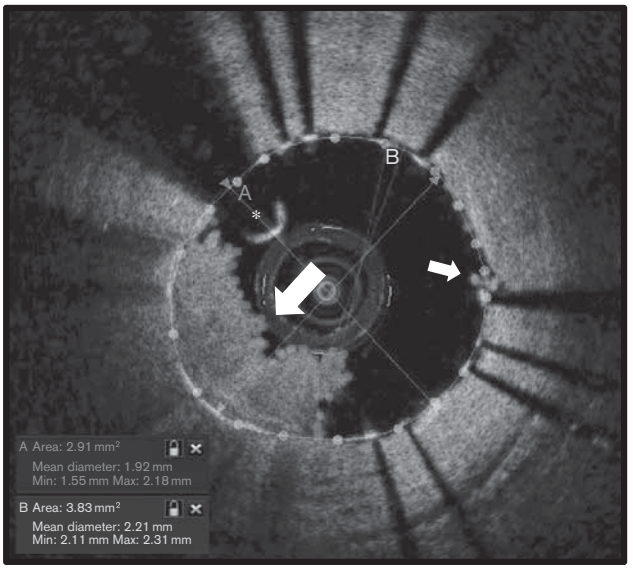
Immediately after primary PCI, OCT was performed using C7-XR/ILUMIEN (St. Jude Medical, St Paul, Minnesota, USA). Following automatic calibration, an OCT catheter was advanced distally to the stented segment over a 0.014 inch conventional angioplasty guidewire. After the catheter placement, preheated contrast media at 37°C were flushed through the guiding catheter at a rate of 3–4 ml/s for ~3–4 s through an injector pump. When a blood-free image was observed, the OCT imaging core was pulled back over a longitudinal distance up to 50 mm at a rate of 20 mm/s using standalone electronic control of the pullback motor. OCT images (100 frames/s) were stored digitally for analysis.

All OCT images were analyzed by an experienced investigator (I.Y.) who was blinded to the clinical information and angiographic findings. The OCT analysis was carried out using a dedicated off-line review system with a semiautomated contour-detection software (St. Jude Medical). Image calibration was adjusted again before the OCT analysis. Tissue protrusion was defined as a tissue prolapse between stent struts extending inside a circular arc [6] (Fig. 1). A malapposed strut was defined as a strut with a distance of greater than 200 μm between the center of the strut blooming and the adjacent lumen border [7]. Cross-sectional areas of the stent, lumen (intrastent lumen + extrastent lumen), and tissue protrusion were measured at longitudinal intervals of 1 mm in the stented segment [8]. Volume measurements were determined using Simpson's rule and also reported as mean areas.

Angiographic analysis

Quantitative coronary angiographic analysis was carried out using a validated automated edge detection algorithm (CAAS-5; Pie Medical, Maastricht, the Netherlands) by

Fig. 1



OCT assessment of stent, lumen, and tissue protrusion area. OCT shows tissue protrusions within the stent (arrows). The tissue protrusion area is calculated as the stent area minus the intrastent lumen area. Outer circle with dots (area B) = stent; inner circle with dots (area A) = intrastent lumen; asterisk = guidewire shadow. OCT, optical coherence tomography.

an experienced investigator (Y.T.) who was blinded to the PCI procedure information and OCT findings. The reference lumen diameter, minimum lumen diameter, and percent diameter stenosis [(1 − minimum lumen diameter/reference lumen diameter) × 100] were measured in the view that was the most severe and not foreshortened. Thrombolysis in myocardial infarction flow grade was assessed as described previously [9]. The no-reflow phenomenon was defined as thrombolysis in myocardial infarction flow grade 0, 1, or 2 without mechanical obstruction on the angiogram immediately after stent implantation or postdilatation [3]. Distal embolization was defined as the angiographic cut-off of the distal branch or vessel at any point during the PCI procedure [3]. Early stent thrombosis was defined as occurring within 30 days of previous stent implantation and confirmed by angiography according to the Academic Research Consortium definitions [10].

Laboratory analysis

Blood samples were obtained on admission, at 3 h intervals during the first 24 h, and at 6 h intervals for the next 2 days after PCI. These samples were analyzed to derive peak CK-MB levels by a fluorometric enzyme immunoassay.

Statistical analysis

Statistical analysis was carried out using Statview 5.0.1 (SAS Institute, Cary, North Carolina, USA). Categorical variables were presented as incidences, with comparison using χ^2 statistics or the Fisher exact test if there was an expected cell value less than 5. Continuous variables were presented as medians and interquartile ranges (IQRs), and were compared using the Mann–Whitney *U*-test. All analyses required a *P* value less than 0.05 for statistical significance.

Results

Patient characteristics

During the study period, 202 STEMI patients underwent primary PCI (thrombus aspiration: $n = 116$; and nonthrombus aspiration: $n = 86$). OCT was not performed in 11 patients according to the exclusion criteria of the OCT imaging. In addition, we excluded three patients from the analysis because of inadequate OCT images. Thus, the final study population included 188 patients. Of 188 patients, 113 patients underwent successful thrombus aspiration before any angioplasty (thrombus-aspiration PCI group) and 75 patients underwent PCI without thrombus aspiration (standard PCI group). Four patients had unsuccessful thrombus aspiration because of a failure to advance the catheter across the lesion in the standard PCI group. The patients' clinical characteristics are summarized in Table 1. There were no significant differences in terms of age, sex, and cardiovascular risk factors between the thrombus-aspiration PCI group and the standard PCI group.

Angiography and PCI

Angiographic findings and PCI procedural characteristics are summarized in Table 2. The time interval from the onset of symptoms to angiography was comparable between the thrombus-aspiration PCI group and the standard PCI group [5 (IQR: 4–6) vs. 5 (IQR: 4–6) h,

Table 1 Patients' clinical characteristics

	Thrombus aspiration PCI ($n = 113$)	Standard PCI ($n = 75$)	*P*-value
Age (years)	68 (59–76)	68 (64–77)	0.196
Male	87 (77)	54 (72)	0.439
Hypertension	86 (76)	52 (69)	0.303
Diabetes mellitus	41 (36)	22 (29)	0.323
Dyslipidemia	58 (51)	39 (52)	0.928
Current smoking	46 (41)	32 (43)	0.790
Obesity	21 (19)	14 (19)	0.989
Family history of IHD	13 (12)	9 (12)	0.918
Previous MI	9 (8)	7 (9)	0.742
Previous PCI	10 (9)	10 (13)	0.443

Values are *n* (%) or median (interquartile range).
IHD, ischemic heart disease; MI, myocardial infarction; PCI, percutaneous coronary intervention.

Table 2 Angiographic findings and PCI procedural characteristics

	Thrombus aspiration PCI ($n = 113$)	Standard PCI ($n = 75$)	*P*-value
Pre-PCI angiography			
Infarct-related vessel			0.969
LAD	48 (42)	33 (44)	
LCX	21 (19)	13 (17)	
RCA	44 (39)	29 (39)	
TIMI flow grade			0.492
Grade 0	72 (64)	42 (56)	
Grade 1	7 (6)	9 (12)	
Grade 2	20 (18)	13 (17)	
Grade 3	14 (12)	11 (15)	
PCI procedure			
Stent diameter (mm)	3.5 (3.0–3.5)	3.5 (3.0–3.5)	0.265
Stent length (mm)	18 (15–20)	18 (15–23)	0.554
Multiple stents	2 (2)	3 (4)	0.389
Prestent ballooning	97 (86)	67 (89)	0.482
Poststent ballooning	57 (50)	41 (55)	0.570
Maximum balloon size (mm)	3.5 (3.0–3.5)	3.5 (3.0–3.5)	0.320
Maximum inflation pressure (atm)	14 (11–16)	14 (10–16)	0.781
Stent-to-artery ratio	1.00 (0.97–1.03)	1.00 (0.95–1.01)	0.211
Drug-eluting stents	30 (27)	28 (37)	0.149
Bare-metal stents	83 (73)	47 (63)	0.149
Post-PCI angiography			
Reference vessel diameter (mm)	3.3 (2.9–3.6)	3.3 (3.1–3.6)	0.821
Minimum lumen diameter (mm)	3.2 (2.8–3.4)	3.1 (2.9–3.5)	0.989
Diameter stenosis (%)	3 (2–4)	4 (2–7)	0.155
Distal embolization	4 (4)	7 (9)	0.119
No-reflow	8 (7)	13 (17)	0.029

Values are *n* (%) or median (interquartile range).
LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; PCI, percutaneous coronary intervention; RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction.

Table 3 OCT findings immediately after PCI

	Thrombus aspiration PCI ($n=113$)	Standard PCI ($n=75$)	*P*-value
Maximum tissue protrusion site (mm^2)			
Stent area	8.2 (6.5–10.4)	8.1 (6.4–9.6)	0.423
Intrastent lumen area	7.5 (5.7–9.3)	6.4 (4.7–8.0)	0.006
Extrastent lumen area	0 (0–0)	0 (0–0)	0.918
Tissue protrusion area	0.6 (0.3–1.1)	1.2 (0.8–1.9)	<0.001
Minimum lumen area site (mm^2)			
Stent area	7.4 (5.8–9.6)	7.8 (5.9–9.1)	0.692
Intrastent lumen area	6.9 (5.4–8.8)	6.3 (4.6–7.8)	0.033
Extrastent lumen area	0 (0–0)	0 (0–0)	0.999
Tissue protrusion area	0.1 (0–0.8)	1.1 (0.6–1.8)	<0.001
Minimum stent area site (mm^2)			
Stent area	7.4 (5.8–9.4)	7.4 (5.8–8.9)	0.788
Intrastent lumen area	6.9 (5.6–8.7)	6.5 (4.9–8.0)	0.091
Extrastent lumen area	0 (0–0)	0 (0–0)	0.999
Tissue protrusion area	0 (0–0.3)	0.6 (0–1.1)	<0.001
Stented segment			
Mean stent area (mm^2)	8.1 (6.5–10.2)	8.7 (6.6–9.9)	0.840
Mean intrastent lumen area (mm^2)	8.0 (6.5–10.0)	7.8 (5.9–9.3)	0.293
Mean extrastent lumen area (mm^2)	0 (0–0)	0 (0–0)	0.767
Mean tissue protrusion area (mm^2)	0.1 (0.1–0.2)	0.5 (0.3–0.8)	<0.001
Stent volume (mm^3)	146.6 (111.4–199.9)	150.8 (110.1–189.7)	0.737
Intrastent lumen volume (mm^3)	144.7 (109.4–194.3)	141.7 (100.6–173.2)	0.191
Extrastent lumen volume (mm^3)	0 (0–0.4)	0 (0–0)	0.719
Tissue protrusion volume (mm^3)	2.3 (1.3–4.3)	8.3 (5.4–14.6)	<0.001

Values are represented as median (interquartile range).
OCT, optical coherence tomography; PCI, percutaneous coronary intervention.

$P=0.863$]. Preprocedural angiographic findings were not different between the two groups. In the thrombus-aspiration PCI group, multiple passages [3 (IQR: 3–3) per patient] of the aspiration catheter across the lesion were performed in all patients. Stent profiles, PCI procedural characteristics, and post-PCI quantitative angiographic measurements were similar in the two groups. Although the frequency of distal embolization was not different between the two groups, the frequency of no-reflow was significantly lower in the thrombus-aspiration PCI group than the standard PCI group (7 vs. 17%, $P=0.029$).

OCT analysis

The OCT findings immediately after PCI are summarized in Table 3. Minimum stent area was similar between the thrombus-aspiration PCI group and the standard PCI group [7.4 (IQR: 5.8–9.4) vs. 7.4 (IQR: 5.8–8.9) mm^2, $P=0.788$]. Maximum tissue protrusion area [0.6 (IQR: 0.3–1.1) vs. 1.2 (IQR: 0.8–1.9) mm^2, $P<0.001$], the mean tissue protrusion area [0.1 (IQR: 0.1–0.2) vs. 0.5 (IQR: 0.3–0.8) mm^2, $P<0.001$], and tissue protrusion volume [2.3 (IQR: 1.3–4.3) vs. 8.3 (IQR: 5.4–14.6) mm^3, $P<0.001$] were significantly smaller in the thrombus-aspiration PCI group compared with the standard PCI group. Minimum lumen area was significantly greater in the thrombus-aspiration PCI group compared with the standard PCI group [6.9 (IQR: 5.4–8.8) vs. 6.3 (IQR: 4.6–7.8) mm^2, $P=0.033$]. The percentage of malapposed struts per stented segment [0 (IQR: 0–0) vs. 0 (IQR: 0–0)%, $P=0.939$] and the frequency of stented segment with any malapposed struts [27 (24%) vs. 18 (24%), $P=0.987$] were not different between the two groups.

Early outcome

There was no difference in the peak CK-MB level between the two groups [138 (IQR: 65–330) vs. 250 (IQR: 82–360) IU/l, $P=0.361$]. Early stent thrombosis occurred in one (0.9%) patient with thrombus-aspiration PCI and in one (1.3%) patient with standard PCI ($P>0.999$).

Discussion

The main finding of the present OCT study is that thrombus aspiration before angioplasty in patients with STEMI was associated with significantly smaller poststenting tissue protrusion and larger lumen compared with those achieved by standard PCI. Thrombus aspiration in primary PCI favorably influenced lesion morphologies in the stented segment.

Clinical impact of thrombus aspiration

There is still a certain amount of controversy as to the clinical effect of thrombus aspiration in primary PCI for STEMI. The VAMPIRE (Vacuum Aspiration Thrombus Removal) trial showed a trend toward lower incidence of no-reflow and a significantly higher rate of myocardial blush grade 3 in patients treated with thrombus aspiration compared with standard primary PCI [11]. The EXPIRA (Thrombectomy with Export Catheter in Infarct-Related Artery during Primary Percutaneous Coronary Intervention) trial showed a decrease in MRI-determined infarct size by thrombus aspiration [12]. The TAPAS (Thrombus Aspiration during Percutaneous Coronary Intervention in Acute Myocardial Infarction Study) showed an almost 50% reduction in 1-year mortality by thrombus aspiration [3,4]. On the basis of these results, the most recent guidelines suggest the routine use of manual

thrombus aspiration in primary PCI (class IIa) [1,2]. However, the TASTE (Thrombus Aspiration in ST-Elevation Myocardial Infarction in Scandinavia) trial recently showed no significant benefit of thrombus aspiration with respect to mortality, reinfarction, stent thrombosis, target-lesion revascularization, and target-vessel revascularization at 30 days [13]. Currently, a large-scale (n=10 700) trial called TOTAL (A Randomized Trial of Routine Aspiration Thrombectomy with PCI versus PCI alone in patients with SATEMI undergoing primary PCI) is in progress [14]. This trial would determine the effect of thrombus aspiration in primary PCI on clinically important outcomes.

Thrombus aspiration and tissue protrusion

When a stent is implanted in a culprit lesion of STEMI, thrombus partially protrudes into the lumen through the mesh of metallic stent struts and limits the coronary flow. In the present study, thrombus aspiration reduced tissue protrusion and then increased lumen after stent implantation. However, in a previous OCT study called TROFI (Randomized Study to Assess the Effect of Thrombus Aspiration on Flow Area in Patients with ST-Elevation Myocardial Infarction), the tissue protrusion and lumen area in the stented segment were not different between the groups with and without thrombus aspiration [15]. The effect of thrombus aspiration is considered to be associated with lesion characteristics, aspiration procedures, and devices. The preprocedural thrombus burden influences the efficacy of thrombus aspiration. The subanalysis in the TROFI trial showed that thrombus aspiration reduced tissue protrusion and increased lumen after stent implantation more effectively in patients with a large thrombus burden than those with a small thrombus [15]. Repeated thrombus aspiration has a benefit for the outcome of tissue protrusion and lumen area. The present study enforced multiple aspirations in all patients, whereas 28% of the patients in the TROFI trial underwent only single aspiration [15]. A larger extraction lumen likely affects the efficacy of the aspiration catheter with respect to thrombectomy. The aspiration catheter used in the present study, which is available only in Japan, has a 20% larger extraction lumen area compared with the device used in the TROFI trial.

Clinical implication of tissue protrusion

There is an IVUS study reporting the clinical outcome of tissue protrusion after stenting in patients with STEMI. The HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) trial showed that IVUS-documented tissue protrusion was associated with early stent thrombosis, but not with late stent restenosis [5,16]. Unfortunately, the present OCT study was not powered to show a correlation between tissue protrusion after stenting and clinical events. Therefore, a further study with a larger population is needed to assess whether the reduction of tissue protrusion volume by thrombus aspiration is associated directly with improvement in clinical outcome in patients undergoing primary PCI for STEMI.

Limitations

The present study has several limitations. First, this was a single-center, nonrandomized, retrospective study with a small sample size. Hence, caution must be exercised when interpreting the results. Second, the study lacks OCT data before thrombus aspiration or stent implantation. OCT cannot provide clear images in the thrombus-occluded coronary artery because of signal attenuation caused by red blood cells. Third, OCT cannot discriminate mural thrombus from plaque tissue; therefore, OCT-documented tissue protrusion might include thrombus protrusion and plaque protrusion. Finally, various types of stents were used in the present study. Tissue protrusion could be influenced by stent designs.

Conclusion

Thrombus aspiration before angioplasty in patients with STEMI prevents poststenting tissue protrusion and preserves luminal area in the treated segment, and it therefore represents a useful adjunctive therapy in primary PCI.

Acknowledgements

Conflicts of interest

Dr Kubo and Dr Akasaka have received lecture fees from St. Jude Medical. For the remaining authors there are no conflicts of interest.

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