EROSION Study (Effective Anti-Thrombotic Therapy Without Stenting: Intravascular Optical Coherence Tomography–Based Management in Plaque Erosion)

A 1-Year Follow-Up Report

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Background—The initial EROSION study (Effective Anti-Thrombotic Therapy Without Stenting: Intravascular Optical Coherence Tomography–Based Management in Plaque Erosion) demonstrated that patients with acute coronary syndrome caused by plaque erosion might be stabilized with aspirin and ticagrelor without stenting for ≤1 month. However, a long-term evaluation of outcomes is lacking. The aim of this study was to assess whether the initial benefit of noninterventional therapy for patients with acute coronary syndrome caused by plaque erosion is maintained for ≤1 year.

Methods and Results—Among 53 patients who completed clinical follow-up, 49 underwent repeat optical coherence tomography imaging at 1 year. Median residual thrombus volume decreased significantly from 1 month to 1 year (0.3 mm^3 (0.0–2.0 mm^3] versus 0.1 mm^3 [0.0–2.0 mm^3]; P=0.001). Almost half of the patients (46.9%) had no residual thrombus at 1 year. Minimal effective flow area remained unchanged (2.1 mm^2 [1.5–3.8 mm^2] versus 2.1 mm^2 [1.6–4.0 mm^2]; P=0.152). Among 53 patients, 49 (92.5%) remained free from major adverse cardiovascular event for ≤1 year: 3 (5.7%) patients required revascularization because of exertional angina and 1 (1.9%) patient had gastrointestinal bleeding.

Conclusions—One-year follow-up optical coherence tomography demonstrated a further decrease in thrombus volume between 1-month and 1-year follow-up. A majority (92.5%) of patients with acute coronary syndrome caused by plaque erosion managed with aspirin and ticagrelor without stenting remained free of major adverse cardiovascular event for ≤1 year.

Clinical Trial Registration—URL: https://www.clinicaltrials.gov. Unique identifier: NCT02041650.

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Key Words: acute coronary syndrome ■ optical coherence tomography ■ thrombosis

Three distinct pathologies are responsible for a majority of acute coronary syndromes (ACS): plaque rupture, plaque erosion, and calcified nodule.[1,2] In current practice, patients with ACS are uniformly treated with an intracoronary stent, irrespective of underlying pathology.[3,4] Although the incidence is low, early and late stent-related complications such as stent thrombosis, restenosis, and neoatherosclerosis remain a major problem.[5–8] In addition, a recent report suggested that stent healing might be impaired in plaque erosion.[9] Previous small retrospective studies suggested that patients with ACS caused by plaque erosion might be stabilized with antiplatelet therapy without stenting.[10,11] In the EROSION study (Effective Anti-Thrombotic Therapy Without Stenting: Intravascular Optical Coherence Tomography–Based Management in Plaque Erosion), we prospectively demonstrated that antiplatelet therapy without stenting in ACS patients with plaque erosion might be safe and feasible ≤1 month.[12] However, the long-term outcome of this noninterventional management is unknown. In this study, we aimed to assess whether the initial benefit of dual antiplatelet therapy without stenting is maintained ≤1 year.

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WHAT IS KNOWN

- Plaque erosion is the underlying pathology in 1 out of 4 patients with acute coronary syndromes.
- Patients with acute coronary syndromes caused by plaque erosion were successfully treated with antiplatelet therapy (aspirin and ticagrelor) without stenting ≤1 month.

WHAT THE STUDY ADDS

- The majority (92.5%) of acute coronary syndromes patients with erosion treated with antiplatelet therapy without stenting remained free from major adverse cardiovascular event ≤1 year.
- This study suggests the possibility of individualized therapy for patients with acute coronary syndromes.

Methods

The data that support the findings of this study are available from the corresponding author on reasonable request.

Study Design and Patients

This is a follow-up report of the previously published EROSION study,[12] which was a single-arm, prospective, proof-of-concept study in ACS patients enrolled between August 2014 and April 2016. Baseline inclusion and exclusion criteria and catheterization procedure were detailed in the appendix and the previous report.[12] The management decision, including use of GPI (glycoprotein IIb/IIIa inhibitor) or manual thrombectomy,was at the discretion of the treating cardiologist. GPI was used in 33 (62.3%) patients, and manual thrombectomy was performed in 44 (83.0%) patients. Fifty-three of the 55 patients who completed 1-month follow-up were continuously treated with aspirin (100 mg/d) and ticagrelor (90 mg twice per day) for ≤1 year. One patient who underwent angiography-driven revascularization at 1-month follow-up and another patient with a penetrating aortic ulcer at 1-month follow-up were excluded. Among 53 patients, 49 patients completed 1-year follow-up angiography and optical coherence tomography (OCT): 3 patients refused repeat catheterization, and 1 patient did not undergo catheterization because of gastrointestinal bleeding at 3 months (ticagrelor was discontinued; Figure 1). Qualitative and quantitative analysis were performed, and these parameters were compared among index, 1-month follow-up, and 1-year follow-up. Coronary angiography was performed via the transradial or transfemoral approach. Imaging of the region of the previous erosion site was performed using frequency domain OCT. Coronary angiogram and OCT analysis methods outlined in the previous EROSION study were implemented (Data Supplement). The clinical end point was major adverse cardiovascular event (MACE), which is defined as the composite of cardiac death, recurrent myocardial infarction, ischemia-driven target lesion revascularization, stroke, and major bleeding. The definitions of the individual components of MACE are summarized in the Data Supplement. This study was approved by the Ethics Committee of the Second Affiliated Hospital of Harbin Medical University (Harbin, China), and all patients provided written informed consent.

Statistical Methods

Statistical analyses were performed with SPSS version 20.0 (SPSS, Inc, Chicago, IL). The final clinical analysis set included all 53 patients, and the imaging analysis set included the 49 patients with repeat angiography and OCT. Data distribution was assessed by the Kolmogorov–Smirnov test. Differences in angiography and OCT measures among baseline, 1-month follow-up, and 1-year follow-up were evaluated using a repeated-measures ANOVA or Fried man test, whichever suits the best depending on the data distribution. Differences in angiography and OCT measures between baseline and 1-year follow-up and between 1-month and 1-year follow-up were evaluated using a paired t test or Wilcoxon signed-rank test. Continuous outcomes were presented as mean±SD for normally distributed data or median (25th–75th percentiles) for non-normally distributed data. Between-group differences were tested using the independent samples t test or the Mann–Whitney U test. Categorical data were presented as counts (proportions) and were compared using the χ^2 test or Fisher exact test. A 2-tailed P value of <0.05 was considered statistically significant. A multivariable logistic regression analysis was performed to find independent predictors for residual thrombus. The variables with a P value <0.10 in univariable logistic regression analysis were entered into the multivariable logistic regression analysis.

Results

Baseline Characteristics and Follow-Up Laboratory Results

Baseline characteristics of patients enrolled in the study are summarized in Table 1. The median age was 53.0 years (43.0–60.5 years), and a majority (86.8%) of patients were male. All patients except 2 presented with ST-segment–elevation myocardial infarction. At 1-year follow-up, total cholesterol, low-density lipoprotein, and high-sensitive C-reactive protein levels were lower compared with those at baseline (all P<0.001) and remained at similar levels compared with those at 1-month follow-up (all P>0.1). Aspirin, ticagrelor, and statin were maintained ≤1 year in all but 1 patient who discontinued ticagrelor because of gastrointestinal bleeding at 3 months.

Angiographic Findings

The lesion distribution and coronary angiography data are listed in Table 1. The left anterior descending artery was most frequently involved. Minimal lumen diameter, reference vessel diameter, and percent diameter stenosis remained unchanged between 1-month follow-up and 1-year follow-up.

OCT Findings

Residual thrombus and minimal flow area were assessed by OCT (Table 2). Thrombus volume significantly decreased from 1 month to 1 year (0.3 mm^3 [0.0–2.0 mm^3] versus

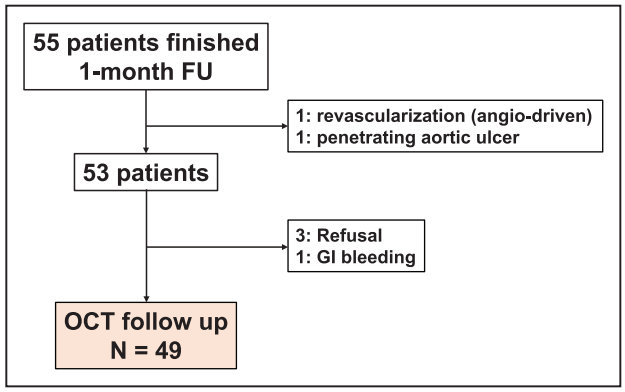

Figure 1. Study flow diagram. FU indicates follow-up; GI, gastrointestinal; and OCT, optical coherence tomography.

Table 1. Baseline Characteristics and Follow-Up Laboratory Results

	Baseline (n=53)	1-mo Follow-Up	12-mo Follow-Up	$P_{BL\ vs\ 1\ mo}$	$P_{BL\ vs\ 12\ mo}$	$P_{1\ mo\ vs\ 12\ mo}$
Age, y	53.0 (43.0–60.5)					
Male	46 (86.8)					
Hypertension	16 (30.2)					
Diabetes mellitus	6 (11.3)					
Smoking	43 (81.1)					
Prior MI	2 (3.8)					
Prior PCI	2 (3.8)					
Presentation						
STEMI	51 (96.2)					
NSTEACS	2 (3.8)					
Laboratory data						
Total cholesterol, mg/dL	167.0 (138.9–191.8)	132.0 (111.7–150.7)	140.5 (120.6–163.3)	<0.001	<0.001	0.29
LDL-C, mg/dL	104.5 (83.6–123.9)	68.9 (59.6–95.7)	76.7 (58.7–97.3)	<0.001	<0.001	0.63
HDL-C, mg/dL	46.8 (38.9–57.0)	44.1 (38.1–51.2)	47.0 (41.0–53.2)	0.35	0.25	0.78
hs-CRP, mg/L	9.6 (3.4–12.1)	1.3 (0.5–4.0)	1.0 (0.6–2.4)	<0.001	<0.001	0.17
Procedure characteristics						
Manual thrombectomy	44 (83.0)					
GPI	33 (62.3)					
Medications						
Aspirin	53 (100.0)					
Ticagrelor	53 (100.0)					
Statin	53 (100.0)					
β-blockers	31 (58.5)					
ACEI or ARB	36 (67.9)					
Angiographic findings	(n=49)					
Lesion location						
LAD	34 (69.4)					
LCx	4 (8.2)					
RCA	11 (22.4)					
MLD, mm	1.3 (1.1–1.6)	1.5 (1.2–1.8)	1.5 (1.2–1.8)	<0.001	<0.001	0.495
RVD, mm	3.0 (2.8–3.3)	3.0 (2.7–3.3)	3.0 (2.7–3.4)	0.54	0.74	0.75
DS, %	57.0 (49.0–64.0)	49.0 (41.5–59.0)	49.0 (39.5–58.5)	<0.001	<0.001	0.84
Lesion length, mm	12.8 (10.8–15.5)	13.0 (10.8–15.3)	12.5 (10.6–15.3)	0.74	0.37	0.40

Values shown are n (%) or median (interquartile range). ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BL, baseline; DS, diameter stenosis; GPI, glycoprotein IIb/IIIa inhibitor; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high-sensitive C-reactive protein; LAD, left anterior descending artery; LCx, left circumflex artery; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; MLD, minimal lumen diameter; NSTEACS, non–ST-segment–elevation acute coronary syndrome; PCI, percutaneous coronary intervention; RCA, right coronary artery; RVD, reference vessel diameter; and STEMI, ST-segment elevation myocardial infarction.

0.1 mm^3 [0.0–2.0 mm^3]; P=0.001). Other thrombus parameters including thrombus burden, thrombus length, and thrombus score also significantly decreased between 1 month and 1 year. The predominant type of thrombus was platelet-rich white thrombus. Among 49 patients, 20 (40.8%) had no residual thrombus at 1-month follow-up. After 1 year of antiplatelet therapy, thrombus disappeared in 3 additional patients, resulting in 23 (46.9%) patients with no residual thrombus. There were no significant differences in baseline clinical characteristics between patients with and without residual thrombus (Table 3). A multivariate analysis showed GPI (tirofiban; odds ratio, 0.09) and thrombus score (odds ratio, 1.05) were independent predictors for residual thrombus (Table I in the Data Supplement). Figure 2 shows representative cases with and without residual thrombus after 1 year of antiplatelet therapy. Finally, the minimal flow area of the culprit lesion remained

Table 2. Thrombus Assessed by Optical Coherence Tomography

	Baseline (n=49)	1-mo Follow-Up	12-mo Follow-Up	*P* Value	$P_{1\ mo\ vs\ 12\ mo}$
Thrombus volume, mm^3					
Median (IQR)	3.7 (1.3–9.9)	0.3 (0.0–2.0)	0.1 (0.0–2.0)	<0.001	0.001
Mean (SD)	9.2 (14.1)	1.5 (2.2)	1.3 (2.0)	<0.001	0.027
Thrombus burden, %					
Median (IQR)	16.1 (9.2–23.1)	3.0 (0.0–9.8)	2.0 (0.0–8.4)	<0.001	0.009
Mean (SD)	17.1 (11.6)	6.2 (8.6)	5.5 (8.0)	<0.001	0.013
Mean thrombus area, mm^2					
Median (IQR)	0.5 (0.3–1.1)	0.2 (0.0–0.4)	0.2 (0.0–0.4)	<0.001	0.063
Mean (SD)	0.8 (0.8)	0.3 (0.5)	0.3 (0.5)	<0.001	0.16
Max thrombus area, mm^2					
Median (IQR)	1.2 (0.6–2.3)	0.3 (0.0–0.8)	0.3 (0.0–0.8)	<0.001	0.053
Mean (SD)	1.7 (1.7)	0.6 (0.8)	0.5 (0.7)	<0.001	0.077
Thrombus length, mm					
Median (IQR)	7.7 (5.9–13.2)	1.4 (0.0–4.2)	1.2 (0.0–4.0)	<0.001	0.001
Mean (SD)	9.2 (5.0)	2.9 (4.3)	2.5 (3.5)	<0.001	0.013
Thrombus score					
Median (IQR)	53 (38–88)	7 (0–23)	5 (0–20)	<0.001	0.002
Mean (SD)	66.1 (46.6)	16.0 (22.2)	13.9 (19.0)	<0.001	0.004
Thrombus type				<0.001	0.61
White	37 (75.5)	28 (57.2)	26 (53.1)		
Red	12 (24.5)	1 (2.0)	0 (0.0)		
No thrombus	0 (0.0)	20 (40.8)	23 (46.9)		
Minimal flow area, mm^2					
Median (IQR)	1.6 (1.4–2.4)	2.1 (1.5–3.8)	2.1 (1.6–4.0)	0.001	0.15
Mean (SD)	2.3 (2.0)	2.8 (2.3)	2.9 (2.3)	<0.001	0.72

Values shown are n (%), median (IQR), or mean (SD). The *P* value was based on 49 patients with paired data. BL indicates baseline; and IQR, interquartile range.

unchanged between 1 month and 1 year (2.1 mm^2 [1.5–3.8] versus 2.1 mm^2 [1.6–4.0 mm^2]; *P*=0.152).

Clinical Follow-Up

Among 53 patients, 49 (92.5%) remained free from MACE for ≤1 year: 3 (5.7%) patients underwent nonurgent revascularization because of exertional angina, and 1 (1.9%) patient had gastrointestinal bleeding at 3 months. Between patients with and without target lesion revascularization, no significant differences in high-sensitive C-reactive protein and white blood cell values were observed (Table II in the Data Supplement).

No cardiac death, recurrent myocardial infarction, or stroke occurred.

Discussion

In this prospective study, we investigated the safety and feasibility of long-term antiplatelet therapy without stenting in patients with ACS caused by plaque erosion. The main findings of the study are (1) 1-year follow-up OCT demonstrated a further decrease in thrombus volume between 1-month and 1-year follow-up, and (2) a majority (92.5%) of the patients remained free from MACE for ≤1 year.

Evolution of the Residual Thrombus

Between 1 month and 1 year, there was a further decrease in thrombus volume potentially because of further thrombus dissolution or thrombus organization. Regardless of the underlying mechanism, OCT findings at 1 year are consistent with more stable condition without protruding thrombus. In our study, among 49 patients, 23 (46.9%) had no residual thrombus after 1 year of antiplatelet therapy. The observation that thrombus disappeared in 3 additional patients during the follow-up period indicated that continuous dissolution of thrombus might be the primary mechanism.

Those 23 patients without residual thrombus had more frequent use of GPIs during the acute phase and had low thrombus volume at baseline. This result implies the importance of effective antiplatelet therapy, particularly during the acute phase preceding thrombus organization.

Table 3. Baseline Characteristics Between Patients With and Without Residual Thrombus

	With Residual Thrombus (n=26)	Without Residual Thrombus (n=23)	*P* Value
Age, y	57.5 (44.5–65.3)	51.0 (42.0–58.0)	0.074
Male	23 (88.5)	19 (82.6)	0.56
Hypertension	6 (23.1)	10 (43.5)	0.13
Diabetes mellitus	3 (11.5)	3 (13.0)	0.87
Smoking	20 (76.9)	19 (82.6)	0.62
Prior MI	2 (7.7)	0 (0.0)	0.17
Prior PCI	2 (7.7)	0 (0.0)	0.17
Presentation			
STEMI	24 (92.3)	23 (100.0)	0.17
NSTEACS	2 (7.7)	0 (0.0)	
Laboratory data			
Total cholesterol, mg/dL	168.0 (137.8–197.8)	162.5 (140.1–185.8)	0.57
LDL-C, mg/dL	109.5 (87.2–131.2)	100.2 (74.3–120.2)	0.16
HDL-C, mg/dL	45.7 (34.4–54.2)	48.4 (42.4–64.6)	0.17
hs-CRP, mg/L	6.7 (3.5–10.9)	11.9 (3.1–13.1)	0.14
Medications			
Aspirin	26 (100.0)	23 (100.0)	…
Ticagrelor	26 (100.0)	23 (100.0)	…
Statin	26 (100.0)	23 (100.0)	…
β-blockers	15 (57.7)	15 (65.2)	0.59
ACEI or ARB	18 (69.2)	15 (65.2)	0.77
Angiographic findings			
Lesion location			0.99
LAD	18 (69.2)	16 (69.6)	
LCx	2 (7.7)	2 (8.7)	
RCA	6 (23.1)	5 (21.7)	
TIMI flow grade 0/1 (prethrombectomy)	15 (57.7)	14 (60.9)	0.91
Manual thrombectomy	20 (76.9)	21 (91.3)	0.17
GPI	13 (50.0)	18 (78.3)	0.04
Quantitative coronary analysis (post-thrombectomy)			
MLD, mm	1.3 (1.0–1.5)	1.3 (1.1–1.7)	0.89
RVD, mm	3.0 (2.7–3.3)	3.2 (2.8–3.6)	0.67
DS, %	59.0 (49.0–63.3)	53.0 (47.0–65.0)	0.82
Lesion length, mm	13.9 (11.1–16.3)	12.3 (9.7–13.7)	0.10
OCT			
Thrombus volume, mm^3	7.7 (3.1–13.6)	3.0 (1.0–3.7)	0.007
Thrombus burden, %	17.6 (9.4–26.8)	13.2 (8.9–18.8)	0.24
Mean thrombus area, mm^2	0.8 (0.3–1.2)	0.4 (0.3–0.6)	0.09
Max thrombus area, mm^2	1.7 (0.8–2.6)	0.9 (0.5–1.8)	0.039
Thrombus length, mm	8.4 (6.6–14.2)	7.1 (4.5–9.2)	0.053
Thrombus score	66 (42–106)	45 (26–66)	0.009
Thrombus type			0.67
White	19 (73.1)	18 (78.3)	
Red	7 (26.9)	5 (21.7)	
Minimal flow area, mm^2	1.5 (1.3–2.4)	1.7 (1.4–2.4)	0.56

Values shown are n (%) or median (IQR). ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; DS, diameter stenosis; GPI, glycoprotein IIb/IIIa inhibitor; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high-sensitive C-reactive protein; LAD, left anterior descending artery; LCx, left circumflex artery; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; MLD, minimal lumen diameter; NSTEACS, non–ST-segment–elevation acute coronary syndrome; OCT, optical coherence tomography; PCI, percutaneous coronary intervention; RCA, right coronary artery; RVD, reference vessel diameter; STEMI, ST-segment elevation myocardial infarction; and TIMI, Thrombolysis in Myocardial Infarction.

Safety and Feasibility of the Noninterventional Management for Plaque Erosion

Management of patients with ACS has continuously evolved from aspirin and heparin, to balloon angioplasty, to bare-metal stents, and ultimately to drug-eluting stents.[13] The current standard of care for ACS patients includes implantation of drug-eluting stents and dual antiplatelet therapy for at least 1 year.[14–16] The 1-year MACE rate with this approach in patients with coronary artery disease ranges from 4.4% to 10.1%,[17–20] which includes target lesion revascularization (≤3.9%), recurrent ACS (≤4.6%), and stent thrombosis (≤1.2%). The MACE rate is higher (≤12.6%) in patients with ACS presentation.[21,22]

It is known that ACS is caused by coronary plaque rupture, plaque erosion, or rarely, calcified nodule, resulting in occlusive thrombus formation.[1,2] Ex vivo and in vivo studies have demonstrated that in approximately one third of patients, the mechanism responsible for ACS is plaque erosion.[23–28] In erosion, the culprit lesion typically has larger lumen, preserved vascular structure, and platelet-rich thrombus.[23–26] These findings have led us to hypothesize that patients with erosion might be managed conservatively with antithrombotic therapy (particularly antiplatelet therapy) without stenting. This

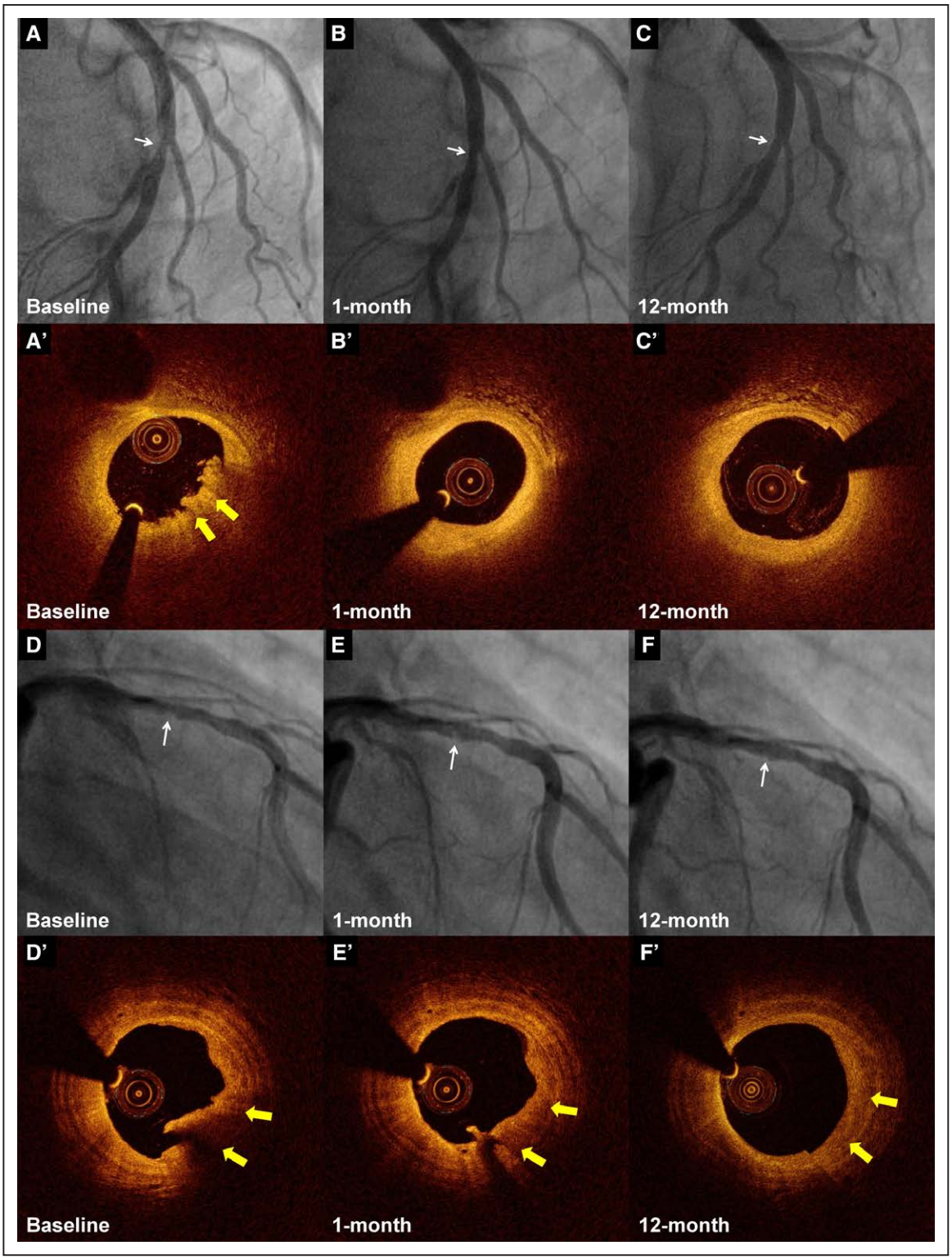

Figure 2. Representative cases with and without residual thrombus. A 37-year-old male patient presented with anterior ST-segment–elevation myocardial infarction (STEMI). Baseline angiogram (**A**) showed a moderate lesion (white arrow) in the left anterior descending artery (LAD) after thrombectomy. Baseline optical coherence tomography (OCT) cross-sectional image (**A**′) of the culprit lesion showed plaque erosion with thrombus (yellow arrows). At 1-month and at 1-year follow-up, angiogram (**B** and **C**) showed mild stenosis, and OCT images (**B**′ and **C**′) showed no residual thrombus. Another 55-year-old male patient presented with STEMI. Baseline angiogram (**D**) showed a mild irregular lesion in the LAD after thrombectomy (white arrow). Baseline OCT cross-sectional image (**D**′) of the culprit lesion indicated plaque erosion with thrombus (yellow arrows). At 1 month and 1 year, a follow-up angiogram showed minimal improvement of the culprit lesion (**E** and **F**). OCT images (**E**′ and **F**′) showed residual thrombus, which looked like organized (yellow arrows).

concept has been supported by several retrospective studies. These studies showed patients with erosion-cause ACS could be stabilized with antiplatelet therapy without stenting.[10,11] In the first prospective proof-of-concept EROSION study, antiplatelet therapy without stenting was effective with significant reduction in thrombus volume in patients with ACS caused by plaque erosion ≤1 month.[12] The aim of the current study was to assess whether the initial benefit of the noninterventional management is maintained for ≤1 year. In the current study, thrombus volume significantly decreased from 1 month to 1 year. In addition, 92.5% of the patients remained free of MACE at 1 year. Three patients underwent nonurgent revascularization because of exercise-induced angina, and none had recurrent ACS.

A recent study reported that very late stent thrombosis was the underlying mechanism for 20% of myocardial infarctions that occurred after drug-eluting stent implantation.[6] The risk of very late stent thrombosis may persist indefinitely after drug-eluting stent implantation. Therefore, avoiding stent implantation will reduce the risks of future stent-related complications.

Implications for Clinical Practice

This 1-year follow-up report on noninterventional approach with antiplatelet therapy without stenting in ACS patients caused by plaque erosion is a proof-of-concept study. Although the number is small, only 5.7% of patients underwent elective revascularization and nobody presented with ACS. The result of this study provides a basis for a potential major shift in the management of patients with ACS caused by plaque erosion.

As the incidence of plaque rupture decreases with widespread use of statins, the relative incidence of plaque erosion is predicted to increase. Therefore, this noninterventional management of ACS patients based on pathophysiology may be of importance in the era of aggressive secondary prevention.

Study Limitations

Several limitations should be acknowledged. First, this was a proof-of-concept study performed at a single center with a small number of patients. Thus, this study was underpowered for the clinical end point. Second, our study was not randomized and did not include a control group of patients treated with stents. Third, investigators and patients were unblinded. Nonetheless, all analyses were performed at an independent core laboratory by investigators who were blinded to patient information. Fourth, the use of GPI and thrombectomy were left at the discretion of the operators. Thrombectomy might have affected lesion morphologies. However, care was taken to avoid excessive mechanical trauma to the vessel wall. Fifth, although all ACS patients were eligible, most patients had ST-segment–elevation myocardial infarction. Finally, the data were acquired in predominantly young Chinese males with a high prevalence of smoking. Therefore, the results may not be generalizable.

Conclusions

One-year follow-up OCT demonstrated a further decrease in thrombus volume between 1 month and 1 year. A majority (92.5%) of patients with ACS caused by plaque erosion managed with aspirin and ticagrelor remained free of MACE for ≤1 year. For patients with ACS caused by plaque erosion, noninterventional management with aspirin and ticagrelor without stenting may be an alternative option. Randomized trials will be needed to replicate this pilot data and to further evaluate the long-term clinical outcomes of this new treatment strategy in patients with ACS caused by plaque erosion.

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Disclosures

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EROSION Study (Effective Anti-Thrombotic Therapy Without Stenting: Intravascular Optical Coherence Tomography–Based Management in Plaque Erosion): A 1-Year Follow-Up Report

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SUPPLEMENTAL MATERIAL

Effective Anti-thrombotic Therapy without Stenting: Intravascular OCT-based Management in Plaque Erosion (the EROSION study): A 1 Year Follow-up Report

Supplemental Methods

1. Catheterization procedures

Patients were treated with aspirin (300mg), ticagrelor (180mg), and unfractionated heparin (100IU/kg) prior to catheterization procedure. Coronary angiography was performed via trans-radial or trans-femoral approach with the use of a 6F or 7F sheath after intracoronary administration of 100–200 mg nitroglycerin. The management decisions, including the use of glycoprotein IIb/IIIa inhibitor (GP IIb/IIIa inhibitor, tirofiban, bolus of 25 mg/kg administered over 3 min followed by continuous intravenous infusion of 0.15 mg/kg/min) or manual aspiration thrombectomy (using the ExportV aspiration catheter, Medtronic CardioVascular, Santa Rosa, CA, USA), were at the discretion of the treating cardiologist. The duration of GP IIb/IIIa inhibitor infusion was 12 - 24 hours. Imaging of the culprit lesion was performed using frequency domain OCT (FD-OCT) after antegrade coronary flow was restored. When plaque erosion was diagnosed by OCT, the residual diameter stenosis (DS) was <70% on angiogram, thrombolysis in myocardial infarction (TIMI) flow grade was 3, and the patient was stable

without symptoms, no stent was implanted. Instead, the patient was continuously treated with the anti-thrombotic therapy.

2. Definitions of major adverse cardiovascular events

Major adverse cardiovascular event (MACE) was defined as the composite of cardiac death, recurrent myocardial infarction, ischemia-driven target lesion revascularization, stroke, and major bleeding. Cardiac death was defined as death in the presence of acute coronary syndrome, significant cardiac arrhythmia, refractory congestive heart failure, or death attributed to cardiovascular cause at post-mortem. Recurrent myocardial infarction was defined as typical chest pain accompanied by a rise of more than two times the upper reference limit of troponins, development of new Q waves on the ECG, or both. Ischemia-driven target lesion revascularization was defined as either percutaneous or surgical revascularization at the culprit lesion site identified at index procedure for angina or angina equivalent symptoms[1]. Stroke was defined as a new acute episode of neurologic dysfunction thought to be vascular in origin, with signs or symptoms lasting more than 24 hours, preferably supported by an imaging procedure such as a computed tomography or magnetic resonance imaging. Major bleeding was defined as any fatal bleed, intracranial bleed, intrapericardial bleed with cardiac tamponade, or hypovolemic shock/severe hypotension caused by bleeding requiring pressor or surgery; a fall in hemoglobin of $\geq$ 5 g/dL; or a need for transfusion of $\geq$ 4 units red cell concentrates. Other major bleeding was defined as significantly disabling bleeding, a fall in hemoglobin of $\geq$ 3 g/dL but <5 g/dl, or a need for transfusion of at least 2 units of red cell concentrates.

3. Coronary angiogram analysis

A quantitative coronary angiography analysis was performed using Cardiovascular Angiography Analysis System (CAAS) 5.10, Pie Medical Imaging B.V., Maastricht, the Netherlands. Minimal lumen diameter, reference vessel diameter, diameter stenosis, and lesion length were measured. Coronary flow was assessed with the thrombolysis in myocardial infarction flow grade classification.

4. Optical coherence tomography image analysis

A commercially available optical coherence tomography (OCT) system (C7 System, LightLab Imaging Inc./St Jude Medical, Inc., Westford, MA, USA) was used. In the C7 system, images are acquired at a rate of 80 frames per second during an automated pullback at a speed of 20 mm/s. The detailed technique of intracoronary OCT imaging has been previously described[2,3]. The OCT images were analyzed by using offline software (LightLab Imaging, Inc./St Jude Medical, Inc.) at Massachusetts General Hospital (MGH) OCT Core Laboratory. Two experienced investigators who were blinded to the clinical information performed analysis using the established criteria. When there was discordance between the observers, a consensus was obtained from a third investigator.

Based on the established OCT diagnostic criteria[4], plaque erosion at baseline was identified by the presence of attached thrombus overlying an intact and visualized plaque, luminal surface irregularity at the culprit lesion in the absence of thrombus, or attenuation of underlying plaque

by thrombus without superficial lipid or calcification immediately proximal or distal to the site of thrombus. OCT does not provide adequate resolution to identify the endothelial lining. Therefore, the definition of plaque erosion is in some ways a diagnosis of exclusion, requiring the absence of fibrous cap rupture. All fiduciary landmarks such as side branch, calcification, microchannel, and stent edge were used to match the location of target lesions and thrombus at baseline and at follow-ups.

5. Thrombus assessment and measurement

Thrombus was also defined as an irregular mass (diameter > 250 μm) either attached to the luminal surface or floating within the lumen. The type of thrombus was categorized as either red or white thrombus. A previous study reported that the half attenuation time of the signal intensity curve, which was defined as the distance from peak intensity to its half intensity, was significantly different between red and white thrombus.[3] Red thrombus was highly backscattering with high attenuation, whereas white thrombus was homogeneous with low attenuation.[4] When the thrombus contained both red and white elements, predominant component was selected as a representative thrombus type.

In previous EROSION study[5] and this study, the thrombus volume was measured on every frame (sampling distance of 250 μm). The quantitative method for thrombus analysis has been previously described[6,7]. In brief, in each OCT frame, lumen area (LA) and flow area (FA) were measured and thrombus area (TA) was calculated as LA minus FA, i.e.

$$TA\ (mm^2) = LA\ (mm^2) - FA\ (mm^2).$$

The thrombus length was measured as the longitudinal distance between the most distal and the most proximal frame that showed intraluminal thrombus. Thrombus volume (TV) was calculated as the mean TA multiplied by the thrombus length, i.e.

$$TV\ (mm^3) = \text{mean TA}\ (mm^2) \times \text{Thrombus length}\ (mm).$$

Luminal border was traced as previously described[6,7]. On image frame where the luminal border was visible in at least three of four quadrants of the image, LA was traced using the 'Area - Multiple points' tool of the proprietary analysis software (St. Jude Medical). When the luminal border was difficult to identify in more than one quadrant, LA was extrapolated from the nearest proximal or distal frame with visible lumen contour. Copy-paste function of the proprietary analysis software was used, supplemented by manual corrections to adjust the copied area to the visible parts of vessel lumen in the frame it was copied to. If needed, additional manual corrections were taken with the assistance of the longitudinal view.

Thrombus burden (TB) was defined as the mean TA divided by the mean LA, i.e.

$$TB\ (\%) = \text{mean TA}\ (mm^2) / \text{mean LA}\ (mm^2) \times 100\%.$$

A semi-quantitative assessment was also performed using the OCT-thrombus score, applying the previously published method[2]. A thrombus was classified as absent (as 0) or subtending 1, 2, 3,

or 4 quadrants in each cross-section, and the OCT-thrombus score was calculated as the sum of each cross-section score.

Supplemental Table 1

	Unadjusted			Adjusted		
	OR	95% CI	p	OR	95% CI	p
Age	1.05	1.00 - 1.12	0.07			0.15
GPI	0.21	0.06 – 0.79	0.02	0.09	0.02 – 0.50	0.006
Thrombus length * per 1mm increase	1.14	1.002 - 1.31	0.047			0.35
Thrombus score * per 1 increase	1.03	1.01 - 1.05	0.012	1.05	1.01 - 1.10	0.02

Supplemental Table 2

	TLR (N = 3)	no TLR (N = 50)	P
Baseline			
WBC, $x10^3/\mu L$	11.8 (8.8, 12.7)	11.4 (9.7, 15.6)	0.66
hs-CRP, mg/L	7.1 (1.1, 13.2)	7.3 (3.1, 11.9)	0.92
1 month follow-up			
WBC, $x10^3/\mu L$	6.7 (5.0, 8.0)	7.2 (5.9, 8.9)	0.44
hs-CRP, mg/L	0.6 (0.2, 5.3)	1.1 (0.4, 3.8)	0.65
12 months follow-up			
WBC, $x10^3/\mu L$	6.0 (4.6, 14.2)	6.8 (5.8, 8.2)	0.74
hs-CRP, mg/L	0.8 (0.4, 1.1)	1.0 (0.5, 2.7)	0.48

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