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FASTTRACK CLINICAL RESEARCH
ESC Hot Line

Acute Coronary Syndromes

Effective anti-thrombotic therapy without stenting: intravascular optical coherence tomography-based management in plaque erosion (the EROSION study)

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Aims Plaque erosion, compared with plaque rupture, has distinctly different underlying pathology and therefore may merit tailored therapy. In this study, we aimed to assess whether patients with acute coronary syndrome (ACS) caused by plaque erosion might be stabilized by anti-thrombotic therapy without stent implantation.

Methods and results This was a single-centre, uncontrolled, prospective, proof-of concept study. Patients with ACS including ST-segment elevation myocardial infarction were prospectively enrolled. If needed, aspiration thrombectomy was performed. Patients diagnosed with plaque erosion by optical coherence tomography (OCT) and residual diameter stenosis <70% on coronary angiogram were treated with anti-thrombotic therapy without stenting. OCT was repeated at 1 month and thrombus volume was measured. The primary endpoint was >50% reduction of thrombus volume at 1 month compared with baseline. The secondary endpoint was a composite of cardiac death, recurrent ischaemia requiring revascularization, stroke, and major bleeding. Among 405 ACS patients with analysable OCT images, plaque erosion was identified in 103 (25.4%) patients. Sixty patients enrolled and 55 patients completed the 1-month follow-up. Forty-seven patients (47/60, 78.3%; 95% confidence interval: 65.8–87.9%) met the primary endpoint, and 22 patients had no visible thrombus at 1 month. Thrombus volume decreased from 3.7 (1.3, 10.9) mm^3 to 0.2 (0.0, 2.0) mm^3. Minimal flow area increased from 1.7 (1.4, 2.4) mm^2 to 2.1 (1.5, 3.8) mm^2. One patient died of gastrointestinal bleeding, and another patient required repeat percutaneous coronary intervention. The rest of the patients remained asymptomatic.

Conclusion For patients with ACS caused by plaque erosion, conservative treatment with anti-thrombotic therapy without stenting may be an option.

Keywords Plaque erosion • Plaque rupture • Anti-thrombotic therapy • Optical coherence tomography • Acute coronary syndrome

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Introduction

Acute coronary syndrome (ACS) including ST-segment elevation myocardial infarction (STEMI) remains a significant global public health problem.[1] Three underlying mechanisms for ACS include plaque rupture, plaque erosion, and calcified nodule.[2] Although plaque rupture is the most common cause (≈60%) of ACS, plaque erosion is responsible for 22–44% of patients.[2,3] Pathology studies demonstrated that, plaque erosion occurs over lesions rich in smooth muscle cells and proteoglycans, with superficial endothelial denudation.[4,5]

Optical coherence tomography (OCT) is a high-resolution (10–15 μm) intracoronary imaging modality that has shown to be able to differentiate the plaque erosion from plaque rupture *in vivo*.[6] The hallmarks of plaque erosion include preserved vascular integrity (intact fibrous cap), larger residual lumen, and platelet-rich thrombus.[4,6–8] On the basis of the distinct pathological features associated with plaque erosion, we hypothesized that patients with ACS caused by plaque erosion might be stabilized by effective anti-thrombotic therapy without stent implantation, thereby abrogating stent related early and late complications. This prospective study was designed to test the feasibility of the conservative approach with anti-thrombotic therapy in patients with ACS caused by plaque erosion.

Methods

Study design and patients

This was a single-arm, uncontrolled, prospective, proof-of-concept study in ACS patients enrolled at a single centre (The 2nd Affiliated Hospital of Harbin Medical University) between August 2014 and April 2016 [NCT02041650]. Patients presenting with ACS and undergoing emergency procedure were screened. Details of inclusion and exclusion criteria are reported in the Supplementary material online.

This study was approved by the Ethics Committee of The 2nd Affiliated Hospital of Harbin Medical University (Harbin, China), and all patients provided written informed consent.

Catheterization procedures

Patients were treated with aspirin (300 mg), ticagrelor (180 mg), and unfractionated heparin (100 IU/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 μg nitroglycerin. The management decisions, including the use of glycoprotein IIb/IIIa inhibitor (GPI, tirofiban, bolus of 25 μg/kg administered over 3 min followed by continuous intravenous infusion of 0.15 μg/kg/min) or manual aspiration thrombectomy (using the Export® aspiration catheter, Medtronic CardioVascular, Santa Rosa, CA, USA), were at the discretion of the treating cardiologist. 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.

Post-catheterization treatment protocol

The patients enrolled in this study were treated with unfractionated heparin (continuous intravenous infusion to maintain aPTT between 50 and 70 s) or low molecular weight heparin (enoxaparin, 1 mg/kg subcutaneously, every 12 h) for 3 days. Dual anti-platelet therapy (DAPT) with aspirin (100 mg/day) and ticagrelor (90 mg, twice per day) was continued. The patients without recurrent ischaemia were discharged on day 5. Repeat angiography and OCT were performed at 1 month.

Endpoints and clinical follow-up

Primary endpoint

The primary endpoint was >50% reduction of thrombus volume measured by OCT at 1 month.

Secondary endpoint

The secondary endpoint was major adverse cardiovascular events (MACEs) defined as the composite of cardiac death, re-infarction, re-hospitalization due to unstable or progressive angina, clinically driven target lesion revascularization, stroke, and major bleeding. Definitions of the individual components of MACE are summarized in the Supplementary material online.

Coronary angiogram analysis (see Supplementary material online)

OCT image analysis (see Supplementary material online)

Statistical methods

Statistical analysis was performed with SPSS version 20.0 (SPSS, Inc., Chicago, IL, USA). The final analysis set included all 60 enrolled patients (i.e. intention to treat). The proportion meeting the primary endpoint was reported with an exact 95% confidence interval (CI) based on Binomial distribution. Data distribution was assessed according to the Kolmogorov–Smirnov test. Continuous variables were shown as mean ± standard deviation (SD) for normally distributed data or as median (25th–75th percentiles) for non-normally distributed data. Between-group differences were tested using an independent sample *t*-test or the Mann–Whitney *U* test. A paired *t*-test or Wilcoxon test was used to compare angiographic and OCT differences between baseline and follow-up (55 patients with paired data). Categorical data were presented as counts (proportions) and were compared using the χ^2 test or Fisher's exact test (if the expected cell value was <5). Intra- and inter-observer reliability of thrombus volume was assessed by intra-class correlation (ICC) and a value >0.9 was defined as excellent correlation. A two-tailed *P* value < 0.05 was considered statistically significant.

Results

Baseline characteristics

The study flow chart is shown in *Figure 1*. Among 405 ACS patients (393 STEMI) with analysable OCT images, plaque erosion was identified as the underlying pathology in 103 subjects (25.4%). Among these patients, 43 cases were not enrolled for the following reasons: DS > 70% ($n = 32$); plaque erosion missed by the treating cardiologist ($n = 11$). From the 60 patients enrolled, an additional four patients were observed with >70% culprit lesion stenosis by the investigators at the core laboratory. One patient died of gastrointestinal bleeding. Fifty-five patients completed a 1-month follow-up.

Baseline clinical characteristics are listed in *Table 1*. The majority (96.7%) of patients had STEMI and thrombectomy was performed in 85.0% of these patients. The time interval between the administration

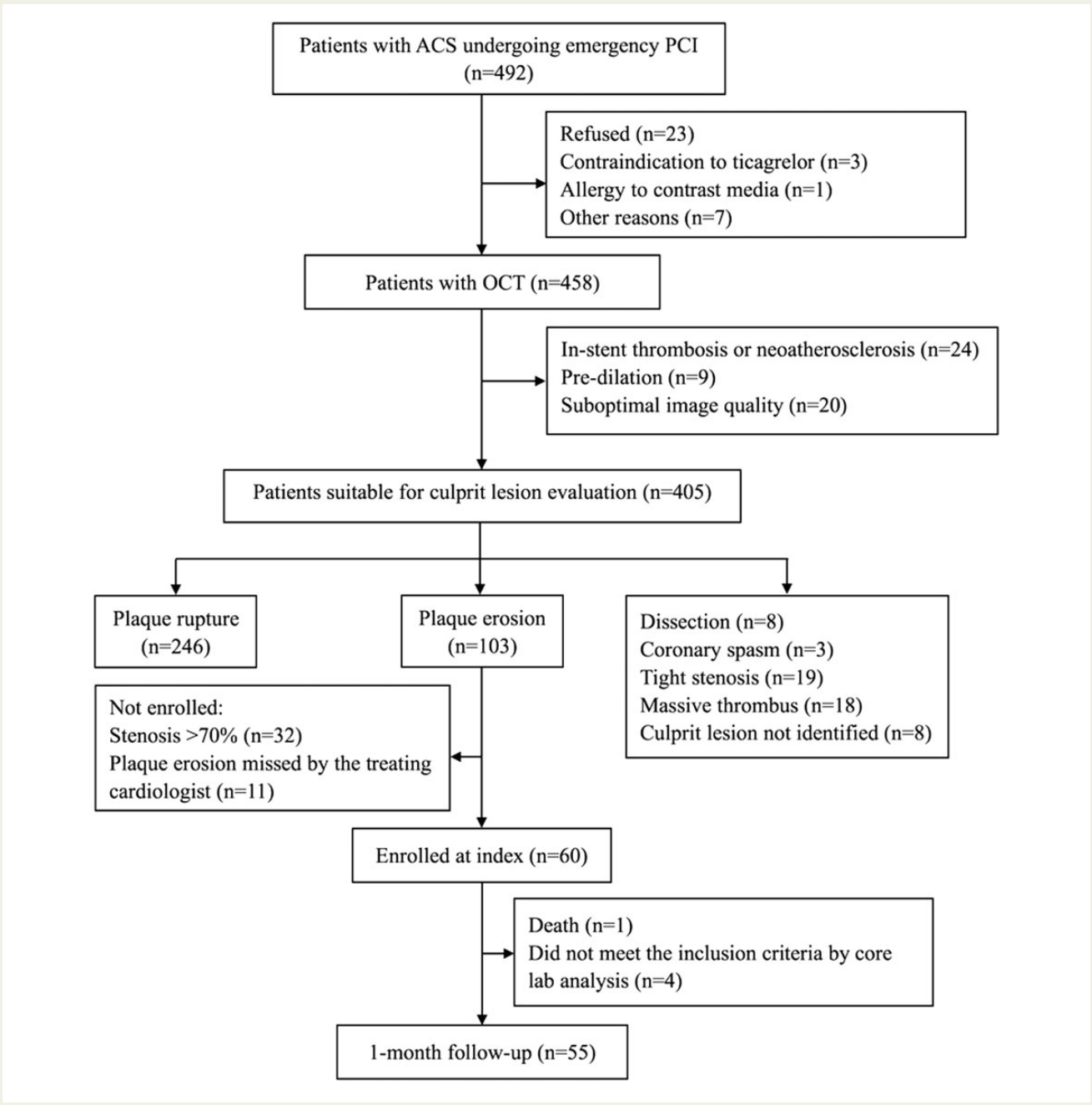

Figure 1 Study flow diagram. ACS, acute coronary syndrome; PCI, percutaneous coronary intervention; OCT, optical coherence tomography.

of loading doses of aspirin and ticagrelor and the procedure was 43 (28, 75) min. Glycoprotein IIb/IIIa inhibitor was used in 63.3%. All patients were treated with DAPT (aspirin and ticagrelor) and statins at discharge. The total ischaemia time was 4.6 (3.1, 8.6) h.

Angiographic findings

The lesion distribution and coronary angiography data are listed in *Table 2*. Plaque erosion was most frequently detected in the left anterior descending artery (66.7%), particularly in the proximal and mid-segments. TIMI flow 0–1 was found in 39 (65.0%) patients on the initial angiography (pre-thrombectomy). After thrombectomy, TIMI 3 flow was achieved in all 60 patients and DS was 56.7 ± 10.4%. At 1 month, minimal lumen diameter increased (from 1.35 ± 0.44 mm to 1.54 ± 0.53 mm: percent change, 13.6 (0.0, 22.9); $P < 0.001$) and DS decreased (from 56.7 ± 10.4% to 50.6 ± 11.8%: percent change, −8.2 (−16.7, 0.0), $P < 0.001$).

OCT findings

The OCT findings are listed in *Table 3* and *Figure 2*. White thrombus (73.3%) was the predominant type of thrombus in patients with

Table 1 Baseline characteristics

Variables	Enrolled patients ($n = 60$)	Completers ($n = 55$)
Age, years	52.9 ± 10.5	52.4 ± 10.4
Male	51 (85.5)	48 (87.3)
Smoking	42 (70.0)	41 (74.5)
Diabetes mellitus	7 (11.7)	7 (12.7)
Hypertension	19 (31.7)	17 (30.9)
Prior-MI	2 (3.3)	2 (3.6)
Prior-PCI	2 (3.3)	2 (3.6)
Presentation		
STEMI	58 (96.7)	53 (96.4)
NSTEACS	2 (3.3)	2 (3.6)
Laboratory data		
LDL-C, mg/dL	108.3 ± 37.6	110.2 ± 38.5
hs-CRP, mg/L	6.8 (2.2, 11.9)	7.3 (2.9, 12.0)
Creatinine, μmol/L	76.7 ± 24.7	76.8 ± 24.4
CK-MB, μg/L	12.8 (1.8, 65.2)	12.4 (1.8, 64.1)
TnI, μg/L	2.0 (0.2, 10.6)	1.6 (0.1, 11.0)
Procedure characteristics		
Manual thrombectomy	51 (85.0)	46 (83.6)
GPI	38 (63.3)	35 (63.6)
Pre-hospital fibrinolysis	3 (5.0)	3 (5.5)
DAPT to procedure, min	43 (28, 75)	44 (28, 78)
Duration of GPI infusion, h	12.0 (0.0, 24.0)	12.0 (0.0, 24.0)
Total ischemic time, h	4.6 (3.1, 8.6)	4.6 (3.0, 8.5)
Symptom onset to OCT, h	4.8 (3.3, 9.1)	4.8 (3.3, 9.0)
Medications at the discharge		
Aspirin	60 (100.0)	55 (100.0)
Ticagrelor	60 (100.0)	55 (100.0)
Statins	60 (100.0)	55 (100.0)
Beta-blockers	33 (55.0)	32 (58.2)
ACE inhibitors or ARB	40 (66.7)	38 (69.1)

Values shown are *n* (%), mean ± SD, or median (interquartile range).
SD, standard deviation; MI, myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; NSTEACS, non-ST-segment elevation acute coronary syndrome; LDL-C, low-density lipoprotein-cholesterol; hs-CRP, high-sensitive C-reactive protein; CK-MB, creatine kinase myocardial band; TnI, troponin I; GPI, glycoprotein IIb/IIIa inhibitor; DAPT, dual anti-platelet therapy; OCT, optical coherence tomography; ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker.

Table 2 Angiographic findings

Angiographic characteristics	No. of patients
Lesion location	$n = 60$
LAD	40 (66.7)
Proximal (CASS 12)	15 (37.5)
Mid (CASS 13)	22 (55.0)
Distal (CASS 14)	3 (7.5)
RCA	14 (23.3)
Proximal (CASS 1)	1 (7.1)
Mid (CASS 2)	5 (35.8)
Distal (CASS 3)	8 (57.1)
LCx	6 (10.0)
Proximal (CASS 18)	4 (66.7)
Distal (CASS 19)	2 (33.3)
Baseline angiography	$n = 60$
Pre-thrombectomy	
TIMI flow grade	
0/1	39 (65.0)
2/3	21 (35.0)
MLD, mm	0.34 ± 0.54
RVD, mm	3.18 ± 0.57
DS, %	89.9 ± 15.5
Lesion length, mm	14.1 ± 2.5
Post-thrombectomy	
TIMI flow 3	60 (100)
MLD, mm	1.35 ± 0.44
RVD, mm	3.13 ± 0.56
DS, %	56.7 ± 10.4
Lesion length, mm	13.4 ± 4.0
Follow-up angiography	$n = 55$
TIMI flow 3	55 (100)
MLD, mm	1.54 ± 0.53
RVD, mm	3.13 ± 0.67
DS, %	50.6 ± 11.8
Lesion length, mm	13.1 ± 3.2

Values shown are *n* (%) or mean ± SD.
SD, standard deviation; LAD, left anterior descending artery; RCA, right coronary artery; LCx, left circumflex artery; CASS, coronary artery surgery segment; TIMI, thrombolysis in myocardial infarction; MLD, minimal lumen diameter; RVD, reference vessel diameter; DS, diameter stenosis.

plaque erosion. Thrombus volume significantly decreased by 94.2% from 3.7 (1.3, 10.9) mm^3 to 0.2 (0.0, 2.0) mm^3 ($P < 0.001$). Intra-observer (ICC = 0.998) and inter-observer (ICC = 0.986) reliabilities were high for the thrombus volume measurement. Other thrombus parameters including thrombus burden, thrombus area, thrombus length, and thrombus score significantly decreased at follow-up (all $P < 0.001$). Forty-seven (47/60, 78.3%; 95% CI: 65.8–87.9%) patients met the primary endpoint (>50% reduction of thrombus volume. Blue area in *Figure 2B*). At 1-month follow-up, 22 patients had no visible thrombus (100.0% reduction in *Figure 2B*). There was no significant difference in baseline clinical characteristics between patients who met the primary endpoint and who did not (see Supplementary material online, *Table S1*). Patients with GPI displayed a greater percentage change in thrombus volume [−100.0 (−100.0, −75.0) vs. −81.0 (−97.3, −51.8), respectively; $P = 0.043$] and a higher incidence of 100.0% thrombus volume reduction (51.4% vs. 20.0%, respectively; $P = 0.022$) than patients without GPI. The minimal flow area of the culprit lesion significantly increased from 1.7 (1.4, 2.4) mm^2 to 2.1 (1.5, 3.8) mm^2 ($P = 0.002$). *Figure 3* shows the representative case with no residual thrombus after 1 month of anti-thrombotic therapy. The underlying plaque characteristics are listed in the Supplementary material online, *Table S2*.

Clinical outcomes

One patient died of gastrointestinal bleeding. Eight days after initial presentation, this patient developed melena and hypotension.

Table 3 Thrombus analysis

Variables	Baseline (n = 60)	Follow-up (n = 55)	Percent change (%)	P
Thrombus type				<0.001
White	44 (73.3)	29 (52.7)		
Red	16 (26.7)	4 (7.3)		
No thrombus	0 (0.0)	22 (40.0)		
Thrombus volume, mm^3				
Median (IQR)	3.7 (1.3, 10.9)	0.2 (0.0, 2.0)	−94.2 (−100.0, −63.7)	<0.001
Mean (SD)	10.0 (17.4)	1.7 (2.8)	−79.2 (27.7)	<0.001
Thrombus burden, %				
Median (IQR)	16.0 (8.9, 21.5)	2.9 (0.0, 9.2)	−85.4 (−100.0, −9.0)	<0.001
Mean (SD)	16.8 (11.4)	6.4 (9.0)	−58.2 (48.3)	<0.001
Mean thrombus area, mm^2				
Median (IQR)	0.5 (0.3, 1.0)	0.2 (0.0, 0.5)	−82.5 (−100.0, −14.2)	<0.001
Mean (SD)	0.8 (0.9)	0.3 (0.4)	−57.2 (48.5)	<0.001
Max thrombus area, mm^2				
Median (IQR)	1.0 (0.6, 2.2)	0.3 (0.0, 1.0)	−83.8 (−100.0, −25.0)	<0.001
Mean (SD)	1.7 (1.8)	0.6 (0.8)	−61.0 (44.9)	<0.001
Thrombus length, mm				
Median (IQR)	7.7 (5.4, 12.8)	1.5 (0.0, 4.9)	−79.7 (−100.0, −54.8)	<0.001
Mean (SD)	9.1 (5.4)	3.2 (4.5)	−70.8 (33.4)	<0.001
Thrombus score				
Median (IQR)	53 (37, 88)	7 (0, 27)	−87.5 (−100.0, −60.0)	<0.001
Mean (SD)	66 (49)	18 (24)	−75.8 (30.8)	<0.001
Minimal flow area, mm^2				
Median (IQR)	1.7 (1.4, 2.4)	2.1 (1.5, 3.8)	15.0 (−8.6, 40.5)	0.002
Mean (SD)	2.3 (1.9)	2.9 (2.2)	27.4 (56.4)	0.001

Values shown are n (%), median (IQR), or mean (SD). The percent change and P value were based on 55 patients with paired data.
IQR, interquartile range, SD, standard deviation.

The haemoglobin decreased from 11.2 to 7.1 g/dL. Repeat coronary angiography showed patent culprit artery (left anterior descending artery). Another patient underwent repeat percutaneous coronary intervention (PCI) for angiographic stenosis but without symptoms or objective evidence of ischaemia. At 1 month, coronary angiogram showed significant stenosis without improvement. His primary cardiologist decided to perform PCI.

Discussion

In this prospective study, we investigated the feasibility and safety of anti-thrombotic therapy without stenting in patients with ACS (the majority were STEMI) caused by plaque erosion. The main findings of this study were (i) plaque erosion was a frequent (25.4%) underlying mechanism in patients with ACS, second only to plaque rupture (60.7%); (ii) thrombus volume significantly decreased (−94.2%) in the 55 patients who were treated with anti-thrombotic therapy and completed their 1-month follow-up. The majority (47/60, 78.3%; 95% CI: 65.8–87.9%) of patients met the primary endpoint (>50% reduction of thrombus volume) and 22 patients had no residual thrombus at 1 month; and (iii) all except two patients treated with anti-thrombotic therapy without stent implantation remained free of MACE.

Prevalence of plaque erosion

Plaque rupture is the most common substrate for coronary occlusive thrombosis in nearly 60% of patients with ACS.[2] However, a significant portion of thrombotic lesions are associated with plaque erosion.[2,3] An overview of post-mortem studies including sudden cardiac death revealed that the incidence of plaque erosion ranged from 22 to 44%.[3] Arbustini *et al.*[9] studied 298 cases dying of acute myocardial infarction (AMI) and showed that plaque erosion was the underlying mechanism in 25% of patients.

Intravascular FD-OCT is an imaging modality that provides superior resolution (10–15 μm), which can be performed quickly (20 mm/s) and safely.[10] It has become possible to make an *in vivo* diagnosis of plaque erosion using an OCT.[6,11] In a recent ACS study, our group reported that the prevalence of plaque erosion was 31%.[6] Subsequently, Higuma *et al.*[12] reported that plaque erosion was responsible in 26.8% of patients with STEMI. In this study, we prospectively studied the prevalence of plaque erosion in ACS patients (97.0% STEMI) and showed that in 25.4% of patients, plaque erosion was the underlying mechanism. This result is consistent with those of the previous autopsy and retrospective studies.

Unique features of plaque erosion

Plaque erosion and plaque rupture are distinctly different entities.[13] Three unique features of plaque erosion indicate that thrombus

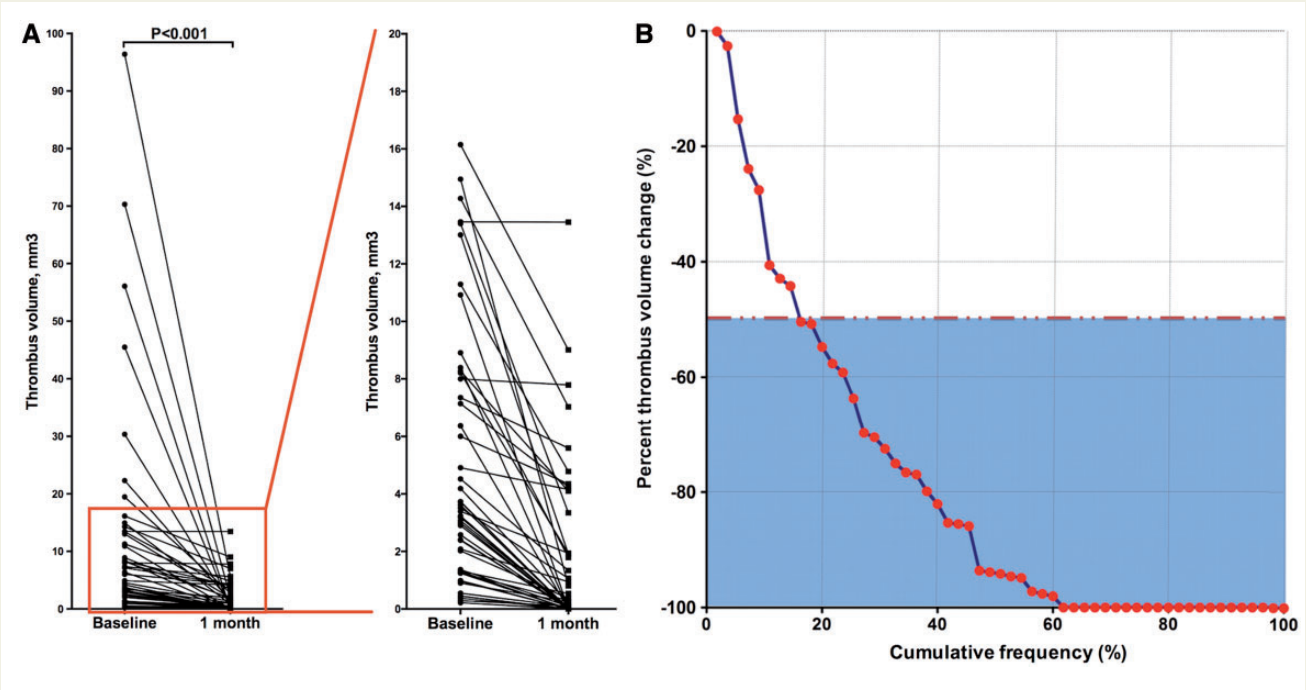

Figure 2 Changes in thrombus volume. (*A*) Absolute change of thrombus volume from baseline to follow-up. (*B*) Percent thrombus volume reduction in 55 individual patients completed 1-month follow-up. Forty-seven patients met the primary endpoint (blue area) and 22 patients had no residual thrombus at 1 month (100.0% reduction).

removal without stent implantation and effective anti-thrombotic therapy may be sufficient to restore coronary artery patency and allow healing of the endothelial layer. First, eroded plaques are typically characterized by either an absent or deeply seated necrotic core with an intact fibrous cap. In contrast, ruptured plaques have a necrotic core which is exposed to circulating blood by a thin fractured fibrous cap (<65μm).[2,4,6] Second, the stenosis of coronary lumen may not always be significant in eroded plaques. According to pathology studies,[4,7] plaque rupture was associated with an average area stenosis of 77%, whereas plaque erosion had an average 70% area stenosis. Kramer *et al.*[7] demonstrated that plaque erosion (60%) had a higher incidence of <75% area stenosis, when compared with plaque rupture (35.4%). Jia *et al.*[6] reported that in plaque erosion, the mean DS was 55.4% and about 70% of patients had DS < 70%. Third, luminal thrombus in plaque erosion has been attributed to apoptosis or denudation of superficial endothelial cells and is rich in platelets but less in fibrin.[5,8,14] In a retrospective study by Prati *et al.*,[15] 12 of 31 STEMI patients with plaque erosion were managed with thrombectomy and DAPT only, whereas others were treated with stenting. Remarkably, after the 2-year follow-up, none of these 12 patients required an additional revascularization. In this study, most (96.4%) of the patients with plaque erosion were stable up to 1 month using the conservative approach.

Evolution of thrombus

The time course of intracoronary thrombus on angiogram in patients with ACS has been previously reported.[16] Recently, several studies demonstrated that the FD-OCT assessment of thrombus volume in ACS patients is feasible and highly reproducible.[17,18] Amabile *et al.*[18] reported that thrombus volume diminished over time under optimal medical therapy and this decrease could be monitored by FD-OCT. The fate of thrombus is largely determined by the balance between platelet activation, pro-coagulant factors, anti-thrombotic therapy, and the fibrinolytic system.[19] Anti-thrombotic therapy including dual anti-platelet and anticoagulation therapy blocks platelets and the coagulation cascade, therefore preventing further thrombus formation, while the endogenous fibrinolytic system promotes the dissolution of existing thrombus.[18] Eroded plaques do not contain a large necrotic core but exhibit a proteoglycan-rich matrix and smooth muscle cells, which have less tissue factor and inflammation (macrophages and C-reactive protein), resulting in lower local thrombogenicity.[4,7,8] Therefore, the potent anti-thrombotic therapy inhibits the thrombus growth and facilitates the endogenous thrombolytic system. In fact, we prospectively demonstrated that thrombus volume decreased significantly at follow-up. The stenotic lesion segment is associated with high shear stress, which can induce platelet aggregation by direct activation of glycoprotein IIb/IIIa receptor.[20] In our study, the addition of a GPI enhanced the anti-thrombotic effect. The minimal flow area increased significantly at follow-up, which is primarily attributable to thrombus dissolution.

Recently, routine aspiration thrombectomy failed to show clinical benefit in patients with STEMI.[21] The proposed explanations include the presence of a large amount of residual thrombus even after thrombectomy, a small amount of thrombus burden, or a limited role of culprit lesion thrombus on infarct size. An OCT sub-study of TOTAL (ThrOmbecTomy vs. PCI Alone) trial demonstrated that thrombectomy did not significantly reduce pre-stent thrombus burden at the culprit lesion compared with PCI alone.[22] In our study, we

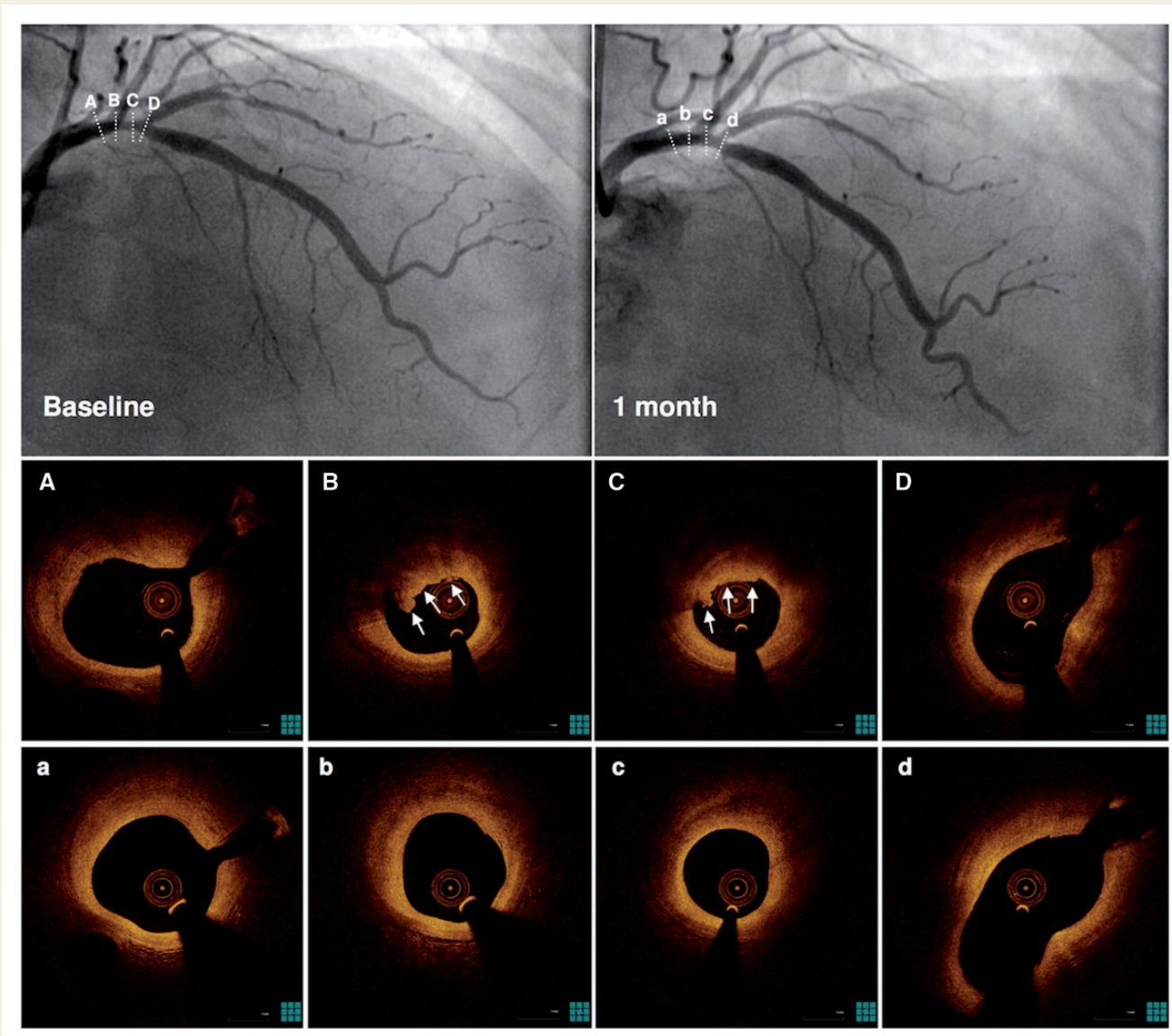

Figure 3 Representative case with no residual thrombus at 1 month. A 65-year-old man presented with ST-segment elevation myocardial infarction (STEMI). Baseline angiogram (upper left) shows a 55% stenosis in the proximal left anterior descending artery (LAD). Serial optical coherence tomography (OCT) cross-sectional images from proximal to distal (*A–D*) of the culprit lesion indicate plaque erosion with white thrombus (arrows). After 1 month of treatment, angiogram (upper right) shows a 45% stenosis, and serial OCT images (*a–d*) showed no visible thrombus overlying a fibrous plaque. The minimal flow area increased from 2.4 to 4.0 mm^2.

also found a substantial amount of residual thrombus after thrombectomy. Further studies should focus on the selective use of the thrombectomy procedure in patients with a large thrombus burden, the effective removal of thrombus, and the identification of subgroups of patients who might derive most benefit from manual thrombectomy.

A new paradigm in the management of ACS patients

Our study results reflect a balance of potential benefits and risks. Leaving an unstented lesion at the site of a previously thrombotic occlusion may put the patient at high risk of re-occlusion, as stenting is associated with low re-occlusion rates of 2%.[23] However, the rate of re-occlusion after successful thrombectomy alone is unknown. Multiple factors play a role in re-occlusion, including local and systemic thrombogenicity, lesion stenosis, slowed blood flow (TIMI flow grade = 2), lesions morphology (ulcerated lesions).[24–26] Potent antithrombotic therapy, distinct pathology characteristics of plaque erosion (less local thrombogenicity), and the strict inclusion criteria (we only chose patients with DS <70% and TIMI flow = 3) probably contributed to the absence of re-occlusion after initial reperfusion in our study. One patient died of gastrointestinal bleeding on DAPT. If this

patient had been stented, he would have been on DAPT and therefore bleeding would not have been avoided. Future studies will need to investigate how to balance the risks of major bleeding and thrombotic events for the patients with plaque erosion managed by antithrombotic therapy without stenting.

Implications for clinical practice

Our strategy of conservative anti-thrombotic therapy without stenting in selected ACS patients caused by plaque erosion represents a potential new treatment paradigm. In our study, DAPT with aspirin and ticagrelor were used during the follow-up period. If this conservative approach without a metallic stent or polymer scaffold proves to be effective and safe, it may become a new treatment paradigm for one-fourth patients with ACS.

Study limitations

There are several limitations that should be acknowledged. First, this study was a single-centre study and was underpowered for the secondary endpoint of MACE because of a small number of patients. However, this study was designed for proof-of-concept. Second, our study design was non-randomized and did not include a control group of patients treated with stent implantation. Third, investigators and patients were unblinded in our study. Nonetheless, all analyses for clinical and imaging data were performed at an independent core laboratory by investigators who were blinded to patient information. Fourth, 11 patients with plaque erosion were missed by the treating cardiologist, which might have induced bias. Fifth, the use of GPI and thrombectomy was non-randomized. Therefore, the results of differential responses in GPI-treated subgroup should be interpreted with caution. Sixth, thrombectomy may have affected lesion morphologies. However, care was taken to avoid excessive mechanical trauma. Seventh, the 50% cutpoint for reduction of thrombus volume was an arbitrary choice, as there was no previously available data. Eighth, the detachment of endothelial cells is a key pathological criterion for erosion. Despite its high resolution, current FD-OCT cannot visualize individual endothelial cells. As a result, the OCT definition of plaque erosion is in some ways a diagnosis of exclusion, requiring the absence of fibrous cap rupture, although it is widely used. Ninth, although all ACS patients were eligible, the majority of patients enrolled had STEMI. Tenth, OCT is the ideal modality to evaluate intracoronary thrombus *in vivo*. However, the signal attenuation caused by a large size red thrombus can potentially mask the vessel wall, obstructing thrombus and underlying plaque measurements. For these cases, we used a previously published method, which showed adequate reproducibility.[17,18] In addition, as platelet-rich (white) thrombus is the predominant type in plaque erosion, we were able to trace the lumen border in the majority cases. Finally, the data were acquired in predominantly young Chinese males with a high prevalence of smoking. Therefore, the results may not be generalizable.

Conclusions

Plaque erosion was the underlying pathology in one-quarter of patients with ACS. Anti-thrombotic therapy without stent implantation effectively reduced thrombus volume and enlarged the flow area without re-occlusion of the culprit lesion at 1 month in predominantly young Chinese males with a high prevalence of smoking. Randomized trials will be needed to reproduce this pilot data and to further evaluate the long-term outcomes of this new treatment strategy in patients with ACS caused by plaque erosion.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

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