Aims: Recent studies suggested plaque erosion with noncritical stenosis could be treated distinctly from that with critical stenosis, but their morphological features remained largely unknown. The present study aimed to investigate morphological features of eroded plaques with different lumen stenosis using optical coherence tomography (OCT).

Methods: A total of 348 ST-segment elevated myocardial infarction patients with culprit OCT-defined plaque erosion (OCT-erosion) were analyzed. Based on the severity of lumen area stenosis, all patients with OCT-erosions were divided into the following three groups: Group A (area stenosis ≤ 50%, n = 50); Group B (50% ≤ area stenosis ≤ 75%, n = 146); Group C (area stenosis ≥ 75%, n = 152).

Results: Compared with patients in Groups A and B, patients in Group C were older (p = 0.008) and had higher prevalence of hypertension (p = 0.029). Angiographic analysis showed that 72.0% of the eroded plaques in Group A were located in the left anterior descending artery, followed by 67.8% in Group B, and 53.9% in Group C (p = 0.039). OCT analysis showed that Group A had the highest prevalence of fibrous plaques (p < 0.001) and nearby bifurcation (p = 0.036), but the lowest prevalence of lipid-rich plaques (p < 0.001), macrophage accumulation (p < 0.001), microvessels (p = 0.009), cholesterol crystals (p < 0.001), and calcification (p = 0.023). Multivariable regression analysis showed fibrous plaque (odds ratio [OR]: 3.014, 95% confidence interval [CI]: 1.932–4.702, p < 0.001) and nearby bifurcation (OR: 1.750, 95% CI: 1.109–2.761, p = 0.016) were independently associated with OCT-erosion with an area stenosis of ≤ 75%.

Conclusions: More than half of OCT-erosions presented with ≤ 75% area stenosis, having distinct morphological features from those of OCT-erosions with critical stenosis. Fibrous plaque and nearby bifurcation were independently associated with noncritically stenotic OCT-erosion, suggesting that eroded plaques might need individualized treatment.

Key words: Bifurcation, Coronary stenosis, Myocardial infarction, Optical coherence tomography, Plaque erosion
stenosis of <75% in sudden death victims\textsuperscript{39}. Recent clinical studies indicate the feasibility and safety of conservative treatment without stenting in patients with plaque erosion and subcritical stenosis\textsuperscript{4,7}). Moreover, accumulative evidence showed that flow disturbance plays a crucial role in mechanisms of plaque erosion\textsuperscript{4, 9}). Local flow disturbance due to coronary lumen narrowing or nearby arterial bifurcation may alter endothelial shear stress and activate platelets\textsuperscript{10}). A recent OCT study demonstrated that in cases with superficial erosion, the composition of the thrombi was related to the degree of luminal narrowing, and the prevalence of fibrin-rich thrombi increased as stenosis severity became milder\textsuperscript{11}). However, morphological features of eroded plaques with mild, moderate, and severe lumen narrowing have not been systemically investigated.

**Aim**

The present study aimed to assess morphological features of OCT-defined plaque erosion (OCT-erosion) lesions with different lumen area stenosis by using intravascular OCT and to investigate the predictors of OCT-erosion with noncritical stenosis.

**Methods**

**Study Population**

Between August 2014 and December 2017, a total of 4284 patients with STEMI were admitted to our hospital. Among them, 1660 patients with STEMI underwent OCT imaging of the culprit lesion during emergency intervention and were prospectively enrolled. Patients with cardiac shock, severe kidney dysfunction, chronic total occlusion, extremely tortuous arteries, left main lesion, allergy to contrast, and other conditions that the investigator considered unsuitable were excluded. All OCT images of the 1660 enrolled patients with STEMI were retrospectively analyzed, and 218 patients were excluded during image analysis due to the following reasons: pre-dilation before OCT imaging (n=31), poor OCT image quality or massive thrombus (n=129), and in-stent thrombosis or neatherosclerosis (n=58). Consequently, 1442 STEMI patients with eligible OCT images of the culprit lesion were analyzed and 348 (24.1%) had OCT-erosion. The study flowchart is shown in Fig. 1.

STEMI was diagnosed when patients had persistent typical chest pain with ST-segment elevation of >0.1 mV in ≥ 2 contiguous leads or new left bundle branch block on the electrocardiograms as well as elevated serum cardiac biomarkers (creatinine-MB or troponin T/I). The culprit lesion was identified by coronary angiography, ST-segment alteration on electrocardiograms, and/or regional wall motion abnormalities on cardiac ultrasound. Clinical characteristics including demographics, traditional coronary risk factors, and pre-intervention laboratory tests were collected. Detailed definitions of traditional coronary risk factors are presented in the Supplementary Methods. This study was approved by the ethic community of our hospital and informed consents were obtained from all patients.

**Coronary Angiography Analysis**

Patients were treated with a loading dose of dual antiplatelet therapy before intervention. Coronary angiography was performed via the radial or femoral approach after intracoronary injection of nitroglycerin. Coronary angiograms were analyzed using a quantitative coronary angiography analysis system (CAAS 5.10.1; Pie Medical Imaging BV, Maastricht, The Netherlands) by an experienced investigator (S.Z.) who was blinded to the patients’ information. Quantitative angiographic data, including distal and proximal reference vessel diameter, minimal vessel diameter, percentage diameter stenosis, and lesion length, were measured post-thrombectomy.

**Optical Coherence Tomography Acquisition and Analysis**

OCT was performed under discretion of an intervention cardiologist with the C7-XR/ILUMIEN OCT system (Abbott Vascular, Santa Clara, CA, USA) after restoration of the anterior blood flow. Manual thrombectomy was performed in the setting of initial thrombolysis in myocardial infarction (TIMI) flow grade of ≤ 1 or extensive thrombus, whereas pre-dilation prior to OCT imaging was not allowed. The OCT imaging catheter was carefully advanced distal to the culprit lesion. The automated pullback was performed while blood was displaced by a short injection of contrast through the guiding catheter. All OCT images were digitally stored and analyzed using off-line review workstation software (Abbott Vascular) in the Intravascular Imaging and Physiology Core Lab of the 2nd Affiliated Hospital of Harbin Medical University by two independent investigators (C.F. and J.D.). When there was discordance between two investigators, a consensus was obtained from a third experienced investigator (J.H.).

All measurements were performed according to previously established consensus and guidelines\textsuperscript{12}). Reference lumen area (RLA) was measured at the largest lumen site proximal or distal to the lesion, but within the same segment with no major intervening
Statistical analyses were performed by an independent statistician (L.L.) using SPSS version 20.0 (SPSS, Chicago, IL, USA). Categorical variables were presented as number (percentage) and continuous variables were presented as mean ± standard deviations when normally distributed and as median (interquartile range) when abnormally distributed after testing for normal distribution by the nonparametric one-sample Kolmogorov–Smirnov test. Categorical variables were compared using the Chi-square or Fisher’s exact test. Bonferroni’s correction was applied for multiple comparisons among the three groups and a \( p < 0.017 \) in a two-group comparison was considered significantly different. Continuous variables were compared with the use of ANOVA or the Kruskal–Wallis \( H \) test when appropriate, and post-hoc test was used only if \( p < 0.05 \). Multivariable logistic regression analysis was used to identify independent predictors of OCT-erosion with noncritical stenosis (<75% lumen area stenosis). Variables with a \( p < 0.1 \) in the univariable analysis were included in the multivariable model. A two-tailed
Results

Clinical Characteristics and Coronary Angiographic Findings of STEMI Patients with OCT-Erosion

Among 348 culprit OCT-erosions in STEMI patients, 14.4% had <50% lumen area stenosis (Group A), 42.0% had 50%–75% (Group B), and 43.7% had ≥75% (Group C) (Fig. 1).

The clinical characteristics and coronary angiographic findings are summarized in Table 1 and Supplementary Table 1. As compared with patients in Groups A and B, those in Group C were the oldest (51.3 ± 12.8 years vs. 53.6 ± 10.0 years vs. 56.3 ± 11.1 years, p < 0.008) and had the highest prevalence of hypertension (22.0% vs. 33.6% vs. 42.1%, p = 0.029). Angiographic analysis showed that 72.0% of plaque erosions in Group A were located in the left anterior descending artery, followed by 67.8% in Group B and 53.9% in Group C (p = 0.039). Diameter stenosis of Groups A, B, and C were 53.7% ± 18.3%, 62.0% ± 13.7%, and 67.8% ± 10.9%, respectively (p < 0.001).

Morphological Characteristics of OCT-Erosions with Different Area Stenosis

OCT findings are shown in Table 2, Supplementary Table 2 and Fig. 2. The prevalence of fibrous plaques was highest in Group A compared with Groups B and C (82.0% vs. 54.8% vs. 34.9%, p < 0.001), whereas lipid-rich plaques (LRPs) were most frequent in Group C (16.0% vs. 43.8% vs. 62.5%, p < 0.001). The prevalence of macrophage accumulation, microvessels, cholesterol crystals, and calcification (including spotty calcification) increased gradually from Group A to Group B to Group C. Notably, nearby bifurcation was most common in Group A, followed by Groups B and C (72.0% vs. 67.1% vs. 55.3%, p = 0.036). The distributions of nearby bifurcation to the site of MLA were similar among the three groups (Supplementary Fig. 2). Layered plaque was least observed in Group A as compared with Groups B and C (22.0% vs. 44.5% vs. 52.0%, p = 0.001), but there was no significant difference in layer thickness and area among the three groups.

Predictors of OCT-Erosion with Noncritical Stenosis

In all 348 STEMI patients with OCT-erosion, the following variables with a p < 0.1 in the univariable analysis (Supplementary Table 3) were tested: age, hypertension, culprit vessel of the left anterior descending artery, multivessel disease, RLA, fibrous plaque, macrophage accumulation, microvessels, cholesterol crystals, calcification, nearby bifurcation, and layered plaque. In multivariable logistic regression analysis, fibrous plaque (odds ratio [OR]: 3.014, 95% confidence interval [CI]: 1.932–4.702, p < 0.001) and nearby bifurcation (OR: 1.750, 95% CI: 1.109–2.761, p = 0.016) were independently associated with OCT-erosion with noncritical stenosis (<75% lumen area stenosis; vs. OCT-erosion with critical stenosis [≥75% area stenosis]) (Fig. 3).

Discussion

The present study provided in vivo evidence of morphological characteristics of culprit eroded plaques with different lumen narrowing in patients with STEMI by using OCT. The main findings were as follows: (1) 56.3% of STEMI patients with culprit OCT-erosion had lumen area stenosis of <75%; and (2) as compared with critical stenotic OCT-erosion, culprit OCT-erosion with noncritical stenosis occurred more in fibrous plaques and more frequently near arterial bifurcation.

Coronary Lumen Stenosis and Plaque Erosion

The present study found that 56.3% of culprit OCT-erosion lesions had a lumen area stenosis of < 75%. Our findings were in line with previous pathological evidence. Kramer et al. reported that 60% (30/50) of culprit erosive plaques were identified with <75% cross-sectional luminal narrowing—defined as (1-lumen area/internal elastic lamina area)*100, where the area of the thrombus was excluded from the calculation of percent stenosis—in cases of sudden cardiac death3). In addition, postmortem studies showed culprit plaque erosion was accompanied with approximately 70% lumen area stenosis (equivalent to a 45% diameter stenosis)5, 14). Consistent with these reports, the present study showed that the average lumen area stenosis for all 348 culprit lesions of OCT-erosion was 67.3% ± 17.7%, corresponding to an estimated diameter stenosis of about 43%. However, our quantitative coronary angiography analysis exhibited an average diameter stenosis of 63.3% ± 14.2%. Similar results were obtained in recent intravascular imaging studies on acute coronary syndrome (ACS) patients; culprit erosive lesions had diameter stenoses ranging from 55% to 77% at the beginning of emergency intervention1, 13, 15, 16). This disparity could be explained by the presence of residual thrombus within the culprit lesion, which may result in an overestimation of stenosis severity. More specifically, the diameter stenosis assessed by coronary angiography consists of stenosis caused by the atherosclerotic plaque (plaque-stenosis) and stenosis caused by the subsequent

p < 0.05 was considered as statistically significant.
Table 1. Clinical characteristics and coronary angiographic findings of STEMI patients with OCT-erosion

| Variables                        | Area stenosis | Group A <50% (n=50) | Group B 50-75% (n=146) | Group C ≥75% (n=152) | p value A vs. B vs. C | A vs. B | B vs. C | A vs. C |
|----------------------------------|---------------|----------------------|------------------------|----------------------|-----------------------|---------|---------|---------|
| Clinical characteristics         |               |                      |                        |                      |                       |         |         |         |
| Age, years                       |               | 51.3 ±12.8           | 53.6 ±10.0             | 56.3 ±11.1           | 0.008 0.195 0.031 0.005 |         |         |         |
| Male                             |               | 42 (84.0)            | 115 (78.8)             | 119 (78.3)           | 0.673 NA NA NA          |         |         |         |
| Smoking status                   |               |                      |                        |                      |                       |         |         |         |
| Never                            |               | 14 (28.0)            | 38 (26.0)              | 49 (32.2)            | 0.226 NA NA NA          |         |         |         |
| Former                           |               | 6 (12.0)             | 7 (4.8)                | 14 (9.2)             |                       |         |         |         |
| Current                          |               | 30 (60.0)            | 101 (69.2)             | 89 (58.6)            |                       |         |         |         |
| Diabetes mellitus                |               | 5 (10.0)             | 21 (14.4)              | 26 (17.1)            | 0.459 NA NA NA          |         |         |         |
| Hypertension                     |               | 11 (22.0)            | 49 (33.6)              | 64 (42.1)            | 0.029 0.126 0.129 0.011 |         |         |         |
| Dyslipidemia                     |               | 21 (42.0)            | 80 (54.8)              | 65 (42.8)            | 0.079 NA NA NA          |         |         |         |
| CKD                              |               | 4 (8.0)              | 7 (4.8)                | 9 (5.9)              | 0.697 NA NA NA          |         |         |         |
| Laboratory test                  |               |                      |                        |                      |                       |         |         |         |
| TC, mg/dL                        |               | 186.3 ±63.7          | 177.8 ±37.4            | 175.6 ±38.7          | 0.306 NA NA NA          |         |         |         |
| TG, mg/dL                        |               | 136.7 ±74.7          | 142.1 ±78.6            | 131.8 ±78.9          | 0.526 NA NA NA          |         |         |         |
| LDL-C, mg/dL                     |               | 109.5 ±33.9          | 117.4 ±45.7            | 109.6 ±34.7          | 0.194 NA NA NA          |         |         |         |
| HDL-C, mg/dL                     |               | 52.0 ±9.7            | 49.7 ±11.7             | 50.3 ±11.4           | 0.469 NA NA NA          |         |         |         |
| cTnI, µg/L                       |               | 2.9 (0.3, 55.1)      | 1.5 (0.2, 8.8)         | 1.5 (0.3, 10.0)      | 0.173 NA NA NA          |         |         |         |
| CK-MB, U/L                       |               | 19.5 (2.0, 149.5)    | 13.2 (1.9, 64.5)       | 14.6 (1.9, 85.0)     | 0.252 NA NA NA          |         |         |         |
| hs-CRP, mg/L                     |               | 6.8 ±5.3             | 6.9 ±5.1               | 6.0 ±4.9             | 0.274 NA NA NA          |         |         |         |
| pro-BNP, pg/mL                   |               | 441.0 (77.5, 1106.5) | 305.0 (79.5, 1376.0)   | 262.0 (60.3, 1242.3) | 0.799 NA NA NA          |         |         |         |
| STEMI onset to OCT imaging time, min |       | 326.0 (210.0, 522.0) | 285.5 (187.8, 456.0)   | 316.0 (205.0, 517.0) | 0.454 NA NA NA          |         |         |         |
| Coronary angiographic findings   |               |                      |                        |                      |                       |         |         |         |
| Culprit vessel                   |               |                      |                        |                      |                       |         |         |         |
| LAD                              |               | 36 (72.0)            | 99 (67.8)              | 82 (53.9)            | 0.039 0.529 0.063 0.076 |         |         |         |
| LCX                              |               | 2 (4.0)              | 13 (8.9)               | 13 (8.6)             |                       |         |         |         |
| RCA                              |               | 12 (24.0)            | 34 (23.3)              | 57 (37.5)            |                       |         |         |         |
| Segment                          |               |                      |                        |                      | 0.201 NA NA NA          |         |         |         |
| Proximal                         |               | 20 (40.0)            | 76 (52.1)              | 63 (41.4)            |                       |         |         |         |
| Mid                              |               | 18 (36.0)            | 51 (34.9)              | 63 (41.4)            |                       |         |         |         |
| Distal                           |               | 12 (24.0)            | 19 (13.0)              | 26 (17.1)            |                       |         |         |         |
| Lesion length, mm                |               | 18.8 ±8.7            | 18.0 ±8.8              | 18.2 ±9.0            | 0.850 NA NA NA          |         |         |         |
| RLD, mm                          |               | 3.2 ±0.6             | 3.1 ±0.6               | 3.1 ±0.5             | 0.231 NA NA NA          |         |         |         |
| MLD, mm                          |               | 1.5 ±0.7             | 1.2 ±0.5               | 1.0 ±0.4             | <0.001 <0.001 <0.002 <0.001 |         |         |         |
| DS, %                            |               | 53.7 ±18.3           | 62.0 ±13.7             | 67.8 ±10.9           | <0.001 <0.001 <0.001 <0.001 |         |         |         |
| Initial TIMI flow 0-1            |               | 31 (62.0)            | 98 (67.1)              | 97 (63.8)            | 0.748 NA NA NA          |         |         |         |
| Multivessel disease              |               | 12 (24.0)            | 44 (30.1)              | 60 (39.5)            | 0.074 NA NA NA          |         |         |         |
| Thrombolysis                     |               | 3 (6.0)              | 7 (4.8)                | 9 (5.9)              | 0.898 NA NA NA          |         |         |         |
| Thrombus aspiration              |               | 36 (72.0)            | 126 (86.3)             | 121 (79.6)           | 0.063 NA NA NA          |         |         |         |

Values expressed as n (%), mean ± SD, or median (25th-75th percentiles). A p-value <0.05 (A vs. B vs. C) or p-value <0.017 (two-group comparison) was considered statistically significant.

CKD, chronic kidney disease; CK-MB, creatine kinase-MB; cTnI, cardiac troponin I; DS, diameter stenosis; 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; MLD, minimal lumen diameter; OCT, optical coherence tomography; pro-BNP, pro-type B natriuretic peptide; RCA, right coronary artery; RLD, reference lumen diameter; TC, total cholesterol; TG, triglyceride; TIMI, thrombolysis in myocardial infarction.
Table 2. Morphological characteristics of plaque erosions with different area stenosis detected by OCT

| Variables                          | Group A <50% (n=50) | Group B 50-75% (n=146) | Group C ≥75% (n=152) | p value                  |
|-----------------------------------|---------------------|-------------------------|----------------------|-------------------------|
| Area stenosis, %                  | 33.3 ± 14.4         | 64.3 ± 7.0              | 81.4 ± 4.1           | <0.001                  |
| MLA, mm²                          | 5.7 ± 3.1           | 2.5 ± 1.1               | 1.5 ± 0.4            | <0.001                  |
| RLA, mm²                          | 8.4 ± 3.7           | 7.2 ± 2.8               | 8.1 ± 2.5            | <0.001                  |
| Fibrous plaque                    | 41 (82.0)           | 80 (54.8)               | 53 (34.9)            | <0.001                  |
| Lipid plaque                      | 9 (18.0)            | 66 (45.2)               | 99 (65.1)            | <0.001                  |
| Lipid length, mm                  | 10.5 ± 7.3          | 10.2 ± 5.3              | 10.6 ± 5.2           | <0.001                  |
| Mean lipid arc, °                 | 207.0 ± 40.3        | 209.7 ± 45.5            | 228.5 ± 50.0         | 0.033                   |
| Maximal lipid arc, °              | 295.3 ± 75.4        | 288.5 ± 61.7            | 310.7 ± 62.8         | 0.084                   |
| Minimal FCT, μm                   | 87.6 ± 28.8         | 94.6 ± 36.1             | 91.0 ± 42.9          | 0.793                   |
| LRP                               | 8 (16.0)            | 64 (43.8)               | 95 (62.5)            | <0.001                  |
| TCFA                              | 2 (4.0)             | 13 (8.9)                | 32 (21.1)            | <0.010                  |
| Macrophage                        | 8 (16.0)            | 82 (56.2)               | 100 (65.8)           | <0.001                  |
| Microvessels                      | 8 (16.0)            | 48 (32.9)               | 60 (39.5)            | <0.001                  |
| Cholesterol crystals              | 3 (6.0)             | 23 (15.8)               | 45 (29.6)            | <0.001                  |
| Calcification                      | 8 (16.0)            | 42 (28.8)               | 55 (36.2)            | 0.023                   |
| Spotty calcification              | 3 (6.0)             | 32 (21.9)               | 42 (27.6)            | 0.006                   |
| Nearby bifurcation                | 36 (72.0)           | 98 (67.1)               | 84 (55.3)            | 0.036                   |
| Distance from bifurcation to MLA, mm | 2.5 ± 1.7         | 2.3 ± 1.5               | 2.4 ± 1.4            | 0.710                   |
| Layered plaque                    | 11 (22.0)           | 65 (44.5)               | 79 (52.0)            | 0.001                   |
| Layer thickness, μm               | 655.0 (505.0, 787.5) | 575.0 (465.0, 775.0)    | 570.0 (435.0, 775.0) | 0.760                   |
| Layer area, mm²                   | 1.4 (1.0, 2.4)      | 1.2 (0.8, 2.1)          | 1.4 (0.9, 2.1)       | 0.573                   |

Values expressed as n (%), mean ± SD, or median (25th-75th percentiles).

A p-value < 0.05 (A vs. B vs. C) or p-value < 0.017 (two-group comparison) was considered statistically significant.

FCT, fibrous cap thickness; LRP, lipid-rich plaque; MLA, minimal lumen area; OCT, optical coherence tomography; RLA, reference lumen area; TCFA, thin cap fibroatheroma.

Fig. 2. Morphological characteristics of OCT-erosion lesions with different area stenosis detected by optical coherence tomography

Compared with Groups B and C, fibrous plaque and nearby bifurcation were most common in Group A. The prevalence of lipid-rich plaque, macrophage accumulation, microvessels, cholesterol crystals, calcification (including spotty calcification), and layered plaque increased gradually from Group A to Group B to Group C. AS, area stenosis; OCT, optical coherence tomography.
demonstrated the prevalence of LRP was lowest in cases of plaque erosion with mild stenosis\(^{11}\). Additionally, the present study revealed a lower level of coronary plaque vulnerability of eroded plaque with noncritical stenosis, such as less frequent LRP, macrophage accumulation, microvessels, cholesterol crystals, calcification (including spotty calcification), and layered plaques. Previous studies suggested that these plaque features reflect the vulnerability of coronary lesions to thrombus formation and are associated with future adverse events\(^{21-26}\). Layered plaques indicated a previous thrombotic event and subsequent healing of the coronary lesion\(^{27}\). With coronary stenosis increasing, the prevalence of layered plaque increased, suggesting a higher risk of recurrent thrombotic event in critical stenotic OCT-erosion.

Nearby Bifurcation and OCT-Erosion

Accumulative evidence has highlighted the role of local flow disturbance in the occurrence of plaque erosion\(^{8, 28, 29}\). As previous experimental work reported that flow disturbance potentiates endothelial cell dysfunction through toll-like receptor 2 stimulation and neutrophil recruitment, which in turn promotes endothelial detachment and acute coronary thrombosis\(^{8, 30, 31}\). For coronary atherosclerotic lesions, local hemodynamic changes can result from coronary lumen stenosis, branches, and vessel bends\(^{32}\). A recent clinical study of STEMI patients suggested that nearby bifurcation, which could give rise to disturbed blood flow, was a local anatomical risk factor of superficial erosion\(^{1}\). The present study found nearby bifurcation independently associated with OCT-erosion with noncritical stenosis\(^{17}\).

A recent OCT study of ACS patients also demonstrated the prevalence of LRP was lowest in cases of plaque erosion with mild stenosis\(^{11}\). Additionally, the present study revealed a lower level of coronary plaque vulnerability of eroded plaque with noncritical stenosis, such as less frequent LRP, macrophage accumulation, microvessels, cholesterol crystals, calcification (including spotty calcification), and layered plaques. Previous studies suggested that these plaque features reflect the vulnerability of coronary lesions to thrombus formation and are associated with future adverse events\(^{21-26}\). Layered plaques indicated a previous thrombotic event and subsequent healing of the coronary lesion\(^{27}\). With coronary stenosis increasing, the prevalence of layered plaque increased, suggesting a higher risk of recurrent thrombotic event in critical stenotic OCT-erosion.

**Underlying Plaque Phenotype of Superficial Erosion**

Pathological and clinical imaging studies suggested plaque erosion was not a homogeneous entity because of the heterogeneous underlying substrates\(^{14, 17-19}\). Unlike plaque rupture merely involving a thin-cap fibroatheroma, plaque erosion occurred in plaques rich in smooth muscle cells and extracellular matrix components such as proteoglycans and hyaluronan, in which a lipid pool was absent or deep-seated\(^{14, 20}\). Our group recently reported that plaque erosion was most frequently detected in fibrous plaques, following thick-cap fibroatheromas, and least in thin-cap fibroatheromas\(^{17}\). Using multiple intravascular imaging modalities, Yamaguchi et al. suggested OCT-erosion lesions had at least two distinct plaque morphologies of different lipid core burden, including fibrous plaque and LRP\(^{18}\). Moreover, in ACS patients, the absence of LRP underneath an eroded plaque predicted better clinical outcomes\(^{19}\). In the present study, fibrous plaque was independently associated with culprit OCT-erosion with noncritical stenosis (<75% lumen area stenosis), whereas lipid plaque related to OCT-erosion with critical stenosis. This is consistent with previous pathological findings that plaque erosion lesion with noncritical stenosis had a smaller necrotic core area and macrophage area than that with critical stenosis\(^{15}\). A recent OCT study of ACS patients also demonstrated the prevalence of LRP was lowest in cases of plaque erosion with mild stenosis\(^{11}\). Additionally, the present study revealed a lower level of coronary plaque vulnerability of eroded plaque with noncritical stenosis, such as less frequent LRP, macrophage accumulation, microvessels, cholesterol crystals, calcification (including spotty calcification), and layered plaques. Previous studies suggested that these plaque features reflect the vulnerability of coronary lesions to thrombus formation and are associated with future adverse events\(^{21-26}\). Layered plaques indicated a previous thrombotic event and subsequent healing of the coronary lesion\(^{27}\). With coronary stenosis increasing, the prevalence of layered plaque increased, suggesting a higher risk of recurrent thrombotic event in critical stenotic OCT-erosion.
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Emergency stent implantation for selected myocardial infarction patients (mild stenosis and good TIMI flow) with culprit plaque erosion. Generally, stent implantation was recommended to improve the artery lumen and flow space in patients with STEMI. However, in lesions with noncritical stenosis, fibrous plaque and nearby bifurcation were more frequent while the plaque vulnerable features (i.e., less frequent LRP, macrophage accumulations, etc.) were less. Conservative medication therapy might be feasible and able to avoid the risk of stenting-related complications, including loss of small branches. Additional research is needed to investigate the detailed mechanism of plaque erosion onset and a more tailored treatment therapy to individual patients.

Limitations

The present study had some limitations. First, this was a single-center, observational study in STEMI patients, and OCT imaging was performed under the discretion of an interventional cardiologist. Thus,
there might have been some selection bias and our conclusions might not be generalizable. Second, the sample size of this study was limited; a large-scale study is needed. Third, the definition of OCT-erosion was somewhat an exclusion diagnosis and has not been validated in pathohistological studies. The current OCT system cannot visualize endothelial cells, making it difficult to distinguish thrombosis caused by tight stenosis from that caused by erosion. However, OCT was the hitherto unique modality to identify in vivo plaque erosion and this definition had high reproducibility, as reported by many previous studies. Fourth, limitations of near-infrared light partially reduced the ability of OCT to detect microstructures underlying a lipid plaque or thrombus, so it might be difficult to distinguish small ruptures filled with thrombus from erosion and to analyze plaque burden and remodeling. The residual thrombus might also influence the measurement of the lumen area. Thus, OCT images were analyzed consecutively to minimize the error. Fifth, due to the large thrombus burden and poor blood flow in most STEMI patients, thrombus aspiration was an efficient procedure to early recanalize the occluded artery and to better assess coronary lesions during emergency intervention. In this study, manual thrombectomy was performed in 81.3% (283/348) of the patients, and a similar prevalence of thrombectomy has been found in previous OCT studies on STEMI patients. The frequency of thrombus aspiration was comparable among the three groups, so the potential effect of thrombus aspiration on lesion morphology was similar among the three groups. Sixth, OCT measurement of thrombus was not performed in consideration of the potential influence of thrombectomy, and those images with massive thrombus influencing OCT analysis were excluded from this study (Fig. 1).

**Conclusion**

In STEMI patients, more than half of OCT-erosion lesions presented with <75% lumen stenosis, which had distinct morphological features from those of OCT-erosion with severe lumen stenosis. Fibrous plaque and nearby bifurcation detected by OCT were independently associated with the presence of noncritically stenotic OCT-erosion. Further studies are warranted to investigate a more tailored treatment therapy to individual patients.

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Supplementary Methods

Definitions of Traditional Coronary Risk Factors
Cigarette smoking status was identified by personal history and was categorized into current smoker (active smoking within 1 month), former smoker (smoking cessation of >1 month), and non-smoker. Hypertension was defined as documented history of hypertension or a systolic blood pressure of ≥ 140 mmHg, diastolic blood pressure of ≥ 90 mmHg, or anti-hypertension therapy at admission. Diabetes mellitus was diagnosed in a patient who met at least one of the following criteria: documented history of diabetes mellitus, use of hypoglycemia agents, fasting glucose of ≥ 126 mg/dL, 2-hour plasma glucose level of ≥ 200 mg/dL in the oral glucose tolerance test, classic symptom with casual plasma glucose level of ≥ 126 mg/dL, or hemoglobin A1c of ≥ 6.5%. Dyslipidemia was diagnosed in patients with a history of hyperlipidemia, receiving lipid-lowering treatment, or newly diagnosed with hyperlipidemia (total cholesterol level of ≥ 220 mg/dL, triglycerides of ≥ 150 mg/dL, low-density lipoprotein cholesterol of ≥ 140 mg/dL, or high-density lipoprotein cholesterol of ≤ 40 mg/dL). We calculated the estimated glomerular filtration rate (eGFR) for each patient using the 2009 Chronic Kidney Disease Epidemiology Collaboration equation, and chronic kidney disease was defined as an eGFR of <60 mL/min per 1.73 m² for ≥ 3 months.

Quantitative and Qualitative Analyses of Plaque Features
The underlying plaque phenotypes were classified as fibrous plaque or lipid plaque. Fibrous plaque was identified using optical coherence tomography (OCT) by a homogeneous high OCT signal region and lipid plaque was identified by a poor OCT signal region with a diffused border. For lipid plaques, the lipid length was measured on the longitudinal view of the culprit lesion and the lipid arc was measured per 1 mm in the lipid segment. Minimal fibrous cap thickness (FCT) was measured three times in the thinnest region of the fibrous cap overlying the lipid pool and a mean value was obtained. A lipid-rich plaque (LRP) was recorded when the lipid arc was > 90°, and a thin-cap fibroatheroma was defined as a LRP with minimal FCT of <65 µm.

The signal-poor or heterogeneous region with a sharply delineated border detected in the plaque was identified as calcification. Spotty calcification was defined as calcification with an arc of <90°. Macrophage accumulation was defined as signal-rich, distinct, or confluent punctate regions with heterogeneous backward shadows in the plaque. Microvessels presented as signal-poor voids sharply delineated with a diameter of 50–300 µm visible in at least three cross-sections. Cholesterol crystals were identified by thin, linear, and signal-rich regions within the plaque. A layered plaque was defined as a plaque with heterogeneous signal-rich layered tissue of different optical signal intensity located close to the luminal surface that was clearly demarcated from the underlying tissue. The maximum thickness and area of the layered tissue was measured on the cross-sectional view.

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Supplementary Fig. 1. Measurement of minimal lumen area

The figure shows an optical coherence tomography representative image of plaque erosion. The arrow points intracoronary thrombus presented on the surface of an atheroma. There is no evidence of intimal disruption. The MLA of this lesion is the area bounded by the luminal border (white dotted line) including the thrombus area.

*represented guidewire artifact. MLA, minimal lumen area.
**Supplementary Table 1.** Clinical and coronary angiographical features of all STEMI patients with OCT-erosion

| Variables                      | Overall (n = 348) |
|-------------------------------|-------------------|
| **Clinical characteristics**  |                   |
| Age, years                    | 54.5 ± 11.0       |
| Male                          | 276 (79.3)        |
| Smoking status                |                   |
| Never                         | 101 (29.0)        |
| Former                        | 27 (7.8)          |
| Current                       | 220 (63.2)        |
| Diabetes mellitus             | 52 (14.9)         |
| Hypertension                  | 124 (35.6)        |
| Dyslipidemia                  | 166 (47.7)        |
| CKD                           | 20 (5.7)          |
| **Laboratory test**           |                   |
| TC, mg/dL                     | 178.0 ± 42.7      |
| TG, mg/dL                     | 136.8 ± 78.1      |
| LDL-C, mg/dL                  | 112.9 ± 39.7      |
| HDL-C, mg/dL                  | 50.3 ± 11.3       |
| cTnI, µg/L                    | 1.6 (0.3, 10.2)   |
| CK-MB, U/L                    | 14.7 (2.0, 87.1)  |
| hs-CRP, mg/L                  | 6.5 ± 5.0         |
| pro-BNP, pg/ml                | 302.0 (69.0, 1257.5) |
| **STEMI onset to OCT imaging time, min** | 300.0 (200.0, 501.5) |
| **Coronary angiographic findings** | \n| Culprit vessel                |                   |
| LAD                           | 217 (62.4)        |
| LCX                           | 28 (8.0)          |
| RCA                           | 103 (29.6)        |
| **Segment**                   |                   |
| Proximal                      | 159 (45.7)        |
| Mid                           | 132 (37.9)        |
| Distal                        | 57 (16.4)         |
| Lesion length, mm             | 18.2 ± 9.0        |
| RLD, mm                       | 3.1 ± 0.5         |
| MLD, mm                       | 1.1 ± 0.5         |
| DS, %                         | 63.3 ± 14.2       |
| Initial TIMI flow 0-1          | 226 (64.9)        |
| Multivessel disease           | 116 (33.3)        |
| Thrombolysis                  | 19 (5.5)          |
| Thrombus aspiration           | 283 (81.3)        |

Values expressed as n (%), mean ± SD, or median (25th-75th percentiles).
A p-value < 0.05 (A vs. B vs. C) or p-value < 0.017 (two-group comparison) was considered statistically significant.
CKD, chronic kidney disease; CK-MB, creatine kinase-MB; cTnI, cardiac troponin I; DS, diameter stenosis; 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; MLD, minimal lumen diameter; OCT, optical coherence tomography; pro-BNP, pro-type B natriuretic peptide; RCA, right coronary artery; RLD, reference lumen diameter; TC, total cholesterol; TG, triglyceride; TIMI, thrombolysis in myocardial infarction.

**Supplementary Table 2.** OCT findings of all OCT-erosions

| Variables                      | Overall (n = 348) |
|-------------------------------|-------------------|
| Area stenosis, %              | 67.4 ± 17.4       |
| MLA, mm²                      | 2.5 ± 2.0         |
| RLA, mm²                      | 7.8 ± 2.9         |
| Fibrous plaque                | 174 (50.0)        |
| Lipid plaque                  | 174 (50.0)        |
| Lipid length, mm              | 10.5 ± 5.2        |
| Mean lipid arc, °             | 220.2 ± 48.6      |
| Maximal lipid arc, °          | 301.4 ± 63.6      |
| Minimal FCT, µm               | 92.2 ± 39.6       |
| LRP                           | 167 (48.0)        |
| TCFA                          | 47 (13.5)         |
| Macrophage                    | 190 (54.6)        |
| Microvessels                  | 116 (33.3)        |
| Cholesterol crystals          | 71 (20.4)         |
| Calcification                 | 105 (30.2)        |
| Spotty calcification          | 77 (22.1)         |
| Nearby bifurcation            | 218 (62.6)        |
| Distance to bifurcation, mm   | 2.4 ± 1.5         |
| Layered plaque                | 155 (44.5)        |
| Layer thickness, µm           | 570.0 (440.0, 770.0) |
| Layer area, mm²               | 1.4 (0.9, 2.1)    |

Values expressed as n (%), mean ± SD, or median (25th-75th percentiles).
A p-value < 0.05(A vs. B vs. C) or p-value < 0.017 (two-group comparison) was considered statistically significant.
FCT, fibrous cap thickness; LRP, lipid-rich plaque; MLA, minimal lumen area; OCT, optical coherence tomography; RLA, reference lumen area; TCFA, thin cap fibroatheroma.
Supplementary Table 3. Univariable logistic regression analysis for OCT-erosion with noncritical stenosis

| Variables                             | Univariable analysis |
|---------------------------------------|----------------------|
|                                       | $P$ value | OR (95% CI)      |
| Age $^a$.                             | 0.006      | 0.972 (0.953-0.992) |
| Male                                  | 0.679      | 1.116 (0.663-1.880) |
| Current smoking                       | 0.113      | 1.427 (0.920-2.213) |
| Diabetes mellitus                     | 0.320      | 0.741 (0.411-1.338) |
| Hypertension                          | 0.027      | 0.607 (0.390-0.944) |
| Dyslipidemia                          | 0.105      | 1.423 (0.929-2.179) |
| CKD                                   | 0.902      | 0.945 (0.381-2.341) |
| TC $^b$.                               | 0.348      | 1.002 (0.997-1.008) |
| TG $^b$.                               | 0.292      | 1.002 (0.999-1.004) |
| LDL-C $^b$.                           | 0.185      | 1.004 (0.998-1.010) |
| HDL-C $^b$.                           | 0.985      | 1.000 (0.981-1.019) |
| LAD                                   | 0.005      | 1.889 (1.217-2.932) |
| Multivessel disease                   | 0.033      | 0.613 (0.391-0.961) |
| Initial TIMI flow 0-1                 | 0.698      | 1.092 (0.701-1.701) |
| Thrombolysis                          | 0.739      | 0.854 (0.338-2.158) |
| Thrombus aspiration                   | 0.470      | 1.221 (0.711-2.096) |
| Lesion length $^c$.                   | 0.364      | 0.984 (0.951-1.018) |
| RLA $^d$.                             | 0.083      | 0.936 (0.869-1.009) |
| Fibrous plaque                        | $<0.001$   | 3.014 (1.939-4.683) |
| Macrophage                            | $<0.001$   | 0.442 (0.285-0.684) |
| Microvessels                          | 0.033      | 0.613 (0.391-0.961) |
| Cholesterol crystals                  | $<0.001$   | 0.364 (0.212-0.624) |
| Calcification                         | 0.032      | 0.604 (0.381-0.958) |
| Nearby bifurcation                    | 0.013      | 1.750 (1.128-2.714) |
| Layered plaque                        | 0.014      | 0.585 (0.381-0.899) |

a. OR for age was calculated for each 1-year increase; b. OR for TC, TG, LDL-C and HDL-C were calculated for each 1.0 mg/dL increase; c. OR for lesion length was calculated for each 1 mm increase; d. OR for RLA was calculated for each 1 mm$^2$ increase.

CI, confidence interval; CKD, chronic kidney disease; HDL-C, high-density lipoprotein cholesterol; LAD, left anterior descending artery; LDL-C, low-density lipoprotein cholesterol; LRP, lipid-rich plaque; OCT, optical coherence tomography; OR, odds ratio; RLA, reference lumen area; TC, total cholesterol; TG, triglyceride; TIMI, thrombolysis in myocardial infarction.

Supplementary Fig. 2. Distribution of nearby bifurcation to the site of minimal lumen area

The red line represents the site of minimal lumen area (MLA). The distributions of nearby bifurcation to the site of MLA were similar among plaque erosions with different area stenosis ($p=0.488$).