Iranian Heart Journal; 2022; 23 (2)

Original Article

Comparison Between Plaque Rupture and Plaque Erosion in the Setting of Acute Coronary Syndrome: Patient Characteristics and Procedural Outcomes

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ABSTRACT

Background: Acute coronary syndrome (ACS) caused by unstable plaque remains the leading cause of mortality and morbidity. The majority of acute coronary occlusion cases are attributed primarily to either plaque rupture or plaque erosion. This study aimed to investigate the effect of unstable plaque morphology on procedural outcomes among patients presenting with ACS.

Methods: This retrospective study enrolled 100 patients with ACS managed by optical coherence tomography (OCT)-guided percutaneous coronary intervention (PCI) in our tertiary center. The demographic and clinical characteristics, as well as angiographic and procedural data, of the study population were recorded. OCT was done before PCI and was repeated after PCI. The patients were thoroughly followed up for 180 days postprocedurally to detect 3 and 6 months' adverse outcomes.

Results: The study population consisted of 100 patients. Men comprised 87% of the studied patients (mean age=53.3 y). Sixty-six patients had ST-segment-elevation myocardial infarction (STEMI), and the left anterior descending was the culprit vessel in 70% of the cases. Plaque rupture was more frequently associated with STEMI presentation, younger age, and white occlusive thrombi. Post-intervention OCT showed a mean minimum stent area of 8 mm^2 and a mean stent expansion of 93.2%. No significant difference was observed between plaque erosion and plaque rupture regarding edge dissection and tissue protrusion. The no-reflow phenomenon was encountered solely among patients with plaque rupture.

Conclusions: OCT is safe and feasible in the setting of ACS. Stent malapposition could be easily missed in angiography. Plaque rupture was associated with more adverse angiographic outcomes in terms of the no-reflow phenomenon. ***(Iranian Heart Journal 2022; 23(2): 75-86)***

KEYWORDS: Acute coronary syndrome, Optical coherence tomography, Plaque rupture, Plaque erosion

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Received: October 15, 2021 **Accepted:** January 16, 2022

Acute myocardial infarction (MI) is caused by plaque rupture, erosion, and very rarely calcified nodules in the setting of atherosclerotic coronary artery disease. Plaque rupture is responsible for 65% of cases with acute coronary thrombotic occlusion, while 30% of cases are attributed to plaque erosion.[1] Plaque rupture is defined as loss of fibrous cap integrity and cavitation within lipid-laden plaques, while plaque erosion is associated with denuded surface endothelia and intact fibrous caps but usually over thicker intima with less inflammation and less luminal narrowing.[1]

Current practice recommends routine interventions on culprit thrombotic lesions by stenting regardless of the primary etiology of the thrombotic occlusion.[2-6] Still, some sub-studies have suggested that this approach fails to provide equivalent benefits in some subgroups such as smokers and women. This hypothesis is based on the pathological features of plaque erosion, which is associated with less luminal obstruction and less aggressive thrombosis. This condition can be medically stabilized using antithrombotic agents with tight risk factor control.[7-9]

In the past decades, intravascular ultrasound (IVUS) and more recently optical coherence tomography (OCT) have been frequently used to optimize percutaneous coronary intervention (PCI) outcomes. IVUS imaging in a pre-intervention setting aids in assessing lesion significance, plaque morphology, need for lesion preparation, and proper stent selection in terms of length and diameter.[10-19] Post-stenting IVUS imaging is extremely beneficial in detecting acute adverse outcomes concerning edge dissection, under-expansion, malapposition, tissue protrusion, and geographic miss, all of which can influence short and long-term outcomes.[20-27]

By comparison with IVUS, not only does frequency-domain OCT have 10 times higher axial resolution and poor tissue penetration (1–2 mm), but also it requires blood clearance. IVUS uses ultrasound, while OCT utilizes infrared light with very short wavelengths (1–3 um), yielding significantly higher resolution but with poor tissue penetration. The wavelength of red blood cells is greater than that of OCT, giving rise to backscattering with OCT in the presence of blood and, consequently, necessitating blood clearance during examinations. A combination of higher resolution and minor penetration can provide a clear distinction between the luminal surface and the atherosclerotic plaque, enabling OCT to be superior in luminal measurement, plaque characterization, and thrombus composition determination.[27-31]

Frequency-domain OCT enables interventionists to investigate the nature of unstable plaques and differentiate plaque rupture from erosion and calcific nodules. Plaque erosion is characterized by a less obstructive atherosclerotic plaque with much preserved vascular integrity.[32-34] Autopsy studies have shown that plaque rupture is frequently significantly occlusive with a large plaque burden and a densely necrotic core with disrupted fibrous caps and more intimal inflammation. Cap disruption exposes the heavily thrombogenic core to circulating blood elements, leading to acute thrombotic coronary occlusion. In contrast, in plaque erosion, luminal thrombi have been attributed to the apoptosis or denudation of the intimal endothelium and, consequently, platelet richness.[35]

The present study aimed to investigate the influence of unstable plaque morphology in terms of rupture versus erosion on procedural outcomes among patients presenting with acute coronary syndrome (ACS) managed by OCT-guided PCI. Between January 2020 and January 2021, 100 consecutive patients, who presented to our tertiary center with ACS and underwent

OCT-guided PCI, were retrospectively enrolled. The exclusion criteria were patients post coronary artery bypass grafting, patients with end-stage renal disease, poor OCT image acquisition, vasospastic angina, and embolic coronary occlusion. Written informed consent was waived due to the retrospective design of this study.

METHODS

All the patients underwent full history taking and thorough clinical examinations. ST-segment-elevation myocardial infarction (STEMI) was defined as persistent chest pain for at least 30 minutes, arrival at a PCI-capable center within 24 hours from symptom onset, ST-segment elevation exceeding 0.1 mV in 2 or more contiguous leads, or a newly discovered left bundle-branch block. NSTEMI was defined as prolonged chest pain with elevated cardiac biomarkers in the absence of ST-segment elevation on the 12-lead surface electrocardiogram.

A culprit lesion was defined as a thrombus-containing lesion and was guided by 12-leads surface electrocardiography and echocardiography to define the affected territory. Hypertension was defined as a systolic blood pressure exceeding 140 mm Hg or a diastolic blood pressure exceeding 90 mm Hg or the current use of antihypertensive medications. Diabetes mellitus was defined as HBa1c exceeding 6.5 or the current use of medications. Dyslipidemia was defined as low-density lipoprotein exceeding 140 mg/dL or the current intake of statins.[36]

During the hospital stay, pre and post-PCI serum creatinine levels were measured, and full echocardiographic analysis was done. Total days of hospital stay were recorded, and immediate post-PCI adverse outcomes were noted. The recruited patients were followed up for 6 months to detect 6 months' adverse events.

Patient Preparation and OCT Techniques

Antiplatelets and antithrombotics were administered according to the latest PCI guidelines. Second and third-generation drug-eluting stents were inserted according to the treating physician's preference. Lesion measurements were done in the worst-looking view, and end-diastolic frames were selected after the administration of 200 μg of nitroglycerin. After PCI, the patients were categorized into 2 groups: plaque rupture and erosion.

A commercially available frequency-domain OCT system (Ilumien System, Light Lab Imaging, Inc, St Jude Medical, Westford, MA, USA) and a 0.014-inch imaging wire (Image Wire, St Jude Medical, Westford, MA, USA) were used. Motorized wire pull-back at 10 mm/s was performed during contrast injection. The PCI procedure was guided by an OCT specialist, who mentored lesion measurements and analyses.[2,37]

Underlying plaque morphology was identified through every frame in the culprit lesion. Plaque rupture was defined as the disruption of the lesion fibrous cap with plaque cavitation. Plaque erosion was defined as luminal irregularities with thrombus formation overlying an intact fibrous cap. Thrombi, if present, were categorized into red and white thrombi guided by their morphology, signal attenuation, and backscattering.[2,38,39]

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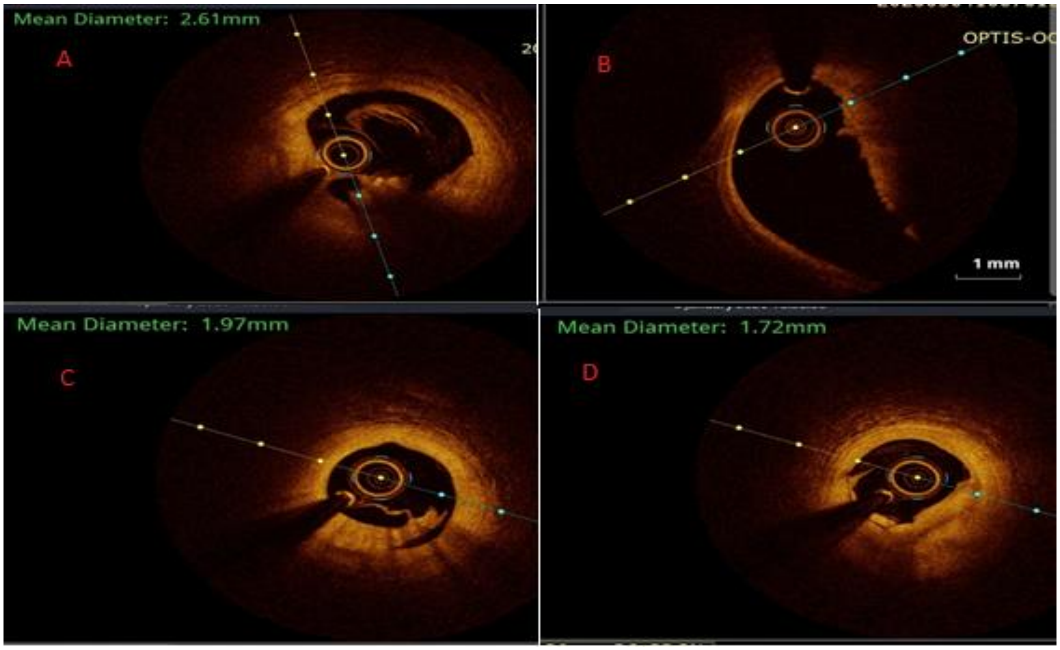

Figure 1: The images illustrate representative OCT snapshots from the studied patients. (A) The image presents the OCT of plaque rupture overlying a fibrocalcific atheroma. (B) The image shows the OCT of plaque erosion with a red thrombus. (C) The OCT image of plaque rupture is illustrated. (D) The image presents the OCT of plaque erosion with a white thrombus.

OCT, Optical coherence tomography

The OCT analysis included lumen areas at proximal and distal references (defined as the frames just proximal or distal to the stent edges), minimum lumen areas in the stented segment, minimum stent areas, and acute luminal gain. We did not use a definite cutoff value for the final minimum stent areas. Final minimum stent areas equal to or greater than 90% are considered optimal and equal to or greater than 80% are considered acceptable in clinical practice. Dissection was defined as the intimal disruption of the luminal surface at the stent edges. Stent malapposition was defined as the presence of a gap between struts and the luminal surface and was considered significant if the stent-lumen distance exceeded 0.2 mm. Tissue prolapse was defined as tissue or thrombus protrusion between stent struts toward the lumen. The thrombolysis in myocardial (TIMI) flow grade following the procedure was documented with special emphasis on cases with the no-reflow phenomenon.[40-44]

Statistical Analysis

Statistical testing was performed using the Statistical Package for Social Sciences (SPSS), version 20. Continuous variables were presented as the mean ± the standard deviation (SD). Categorical variables were expressed as numbers and percentages. The Kolmogorov–Smirnov test for normal distribution was applied to differentiate between parametric and nonparametric data. The ANOVA test was also used to assess the relationship between different variables. Univariate and multivariate analyses were conducted. For all the statistical tests, a *P* value of less than 0.05 was taken to indicate a significant difference.

RESULTS

Demographic Data and Risk Factors

The study population consisted of 100 patients. The baseline demographic and clinical characteristics of the studied patients are summarized in Table 1. Men comprised

86% of the study population, and the mean age was 53.3 years. The average time of symptom onset was 9.7 hours. The most prevalent risk factors were smoking (79%), hypertension (60%), dyslipidemia (48%), and diabetes mellitus (34%). Six patients had previous cerebrovascular accidents.

Culprit Lesion Morphology

The majority of the patients enrolled were in the setting of STEMI (66%). Two patients were in Killip III, and 1 patient was in cardiogenic shock. Plaque rupture was diagnosed in 67 patients, as opposed to 33 patients with plaque erosion. Culprit lesions showed white thrombi in 53 cases, while 47 patients had fibrin-rich red thrombi. Eleven patients developed the no-reflow phenomenon, which was managed successfully intraprocedurally with pharmacological agents. Culprit lesion characteristics are mentioned in Table 2.

Procedural Outcomes

All the studied subjects had drug-eluting stent implantation in the culprit lesion, with single stents in 88 patients and 2 stents in 12 patients. The anatomical distribution of the culprit lesions was 70% in the left anterior descending, 20% in the right coronary artery, 11% in the left circumflex, 4% in the left main trunk, and 2% in the diagonal. Post-intervention OCT study showed a mean stent expansion rate of 93.2% with a final achieved mean minimum stent area of 8 mm^2. Significant edge dissection was encountered in 6 cases, tissue or thrombus prolapse in 38, and significant malapposition necessitating additional optimization in 56 (Table 3).

Table 1: Baseline demographic data and risk factors of the study population

N=100	No.	%	
Sex male female	 86 14	 86 14	
Smoking	79	79	
Hypertension	60	60	
Diabetes mellitus	34	34	
Dyslipidemia	48	48	
Peripheral vascular disease	0	0	
Cerebrovascular accident	6	6	
	mean	± SD	range
Age, y	53.3	± 11.3	28-85
Pain time, h	9.7	± 8.6	2 - 48

Table 2: Culprit lesion characteristics by pre-intervention OCT

N=100	No.	%	95% CI
STEMI Non-STEMI	66 34	66 34	55-75% 24-44%
No-reflow	11	11	5-18%
Plaque rupture	67	67	56-76%
Plaque erosion	33	33	23-43%
Thrombus Type red white	 47 53	 47 53	 36-57% 42-63%
Fibrotic plaque	24	24%	
Fibrocalcific plaque	12	12%	
Necrotic plaque	64	64%	
	mean ± SD	range	
Reference vessel diameter, mm	3.3±0.5	2.2-4.7	
Lesion diameter, mm	1.52±0.3	0.9-3	
MLA, mm^2	2.65±1.0	0.8-8	

OCT, Optical coherence tomography; STEMI, ST-segment-elevation myocardial infarction; MLA, Minimal luminal area

Table 3: OCT study following the intervention

N=100	No.	%
Dissection	6	6
Prolapse	38	38
Malapposition	56	56
	Mean ± SD	range
Expansion %	93.2±4.5	86-114
MSA, mm^2	8.0±2.7	3.7-15.8

OCT, Optical coherence tomography; MSA, Minimal stent area

Plaque Rupture vs Plaque Erosion

The study population was divided according to culprit morphology into 2 groups: plaque rupture (67%) and plaque erosion (33%). Both groups were compared in terms of baseline clinical and demographic data (Table 4). No significant differences existed between sex and the occurrence of plaque rupture or erosion. There was a higher percentage of plaque rupture in the young age group than in the older age group, but the difference was not significant statistically. No statistically significant differences were observed between smokers and nonsmokers as regards plaque rupture or plaque erosion. Patients with plaque erosion had a trend to be hypertensive (38.5%) and diabetics (44.1%), with no significant statistical difference with plaque rupture. Cases with plaque erosion tended to have a longer pain duration than those with plaque rupture, which was statistically significant (12.3±8.6 h vs 8.4±7.6 h). Table 4 shows a higher percentage of plaque rupture among patients with STEMI than in those with non-STEMI (83.3% vs 35.3%), and the difference was highly statistically significant. Patients with STEMI had 9 times the risk of the development of plaque rupture compared with non-STEMI patients.

The procedural outcome was analyzed and compared between the 2 groups of plaque erosion and plaque rupture (Table 5). Patients with plaque erosion had a higher percentage of tissue prolapse (48.5%) than those with plaque rupture (32.8%), which was not significant statistically. The no-reflow phenomenon was encountered exclusively among the plaque rupture group, with 16.4% of these patients developing the no-reflow phenomenon after stent implantation. Table 5 shows a higher percentage of platelet-rich white thrombi in the plaque rupture group than in the plaque erosion group (64.2% vs 30.3%), and the difference was highly statistically significant. No significant differences were noted between both groups regarding the detection of postprocedural limiting edge dissection. Regarding the stent length, longer stents were encountered more frequently in the plaque rupture group, with no statistically significant difference with the plaque erosion group.

The 6-month Follow-up

The studied patients were followed up for 6 months. No major adverse cardiovascular events were detected in terms of death, MI, or target vessel revascularization apart from minor bleeding in a single patient. Additionally, 2 patients had readmission with decompensated heart failure.

Table 4: Comparison between demographic and clinical variables as regards plaque morphology

	Erosion		Rupture		*P* value
	No.	%	No.	%	
Sex male N=86 female N=14	28 5	32.6 35.7	58 9	67.4 64.3	0.8
Age (cutoff value=53.3 y) young N=50 old age N=50	15 18	30 36	35 32	70 64	0.5
Smoking N=79	25	31.6	54	68.4	0.5
Hypertension N=60	23	38.3	37	61.7	0.1
Diabetes N=34	15	44.1	19	55.9	0.09
Dyslipidemia N=48	14	29.2	34	70.8	0.4
Chest pain duration (h) mean±SD	12.3 8.6		8.4 7.8		0.02
STEMI (66) **Non-STEMI (33)**	11 (16.7) 22 (64.7)		55 (83.3) 12 (35.3)		0.00

STEMI, ST-segment-elevation myocardial infarction

Table 5: Comparison between plaque rupture and erosion regarding procedural outcomes

	Rupture N=67		Erosion N=33		*P* value
	No.	%	No.	%	
Prolapse	22	32.8	16	48.5	0.1
Dissection	4	6.0	2	6.1	0.9
No-reflow	11	16.4	0	0	0.002**
White thrombus	43	64.2	10	30.3	0.001**
Stent length (mm) mean±SD	30 8.8		28.4 11.8		0.4

DISCUSSION

The main outcome of the present study was the safety and feasibility of OCT-guided PCI in the setting of ACS. The majority of the study population had STEMI (66 patients), with the left anterior descending being the culprit vessel in 70% of the studied cases. The presence of acute pulmonary edema or even cardiogenic shock was not a barrier to the optimization of the outcome using OCT. Blood clearance using contrast definitely increased the total amount of the dye used; however, only 2 cases showed a postprocedural transient rise in serum creatinine, which normalized before hospital discharge.

Plaque rupture is the main cause of ACS, encountered in 77% of cases, especially in the setting of STEMI. Plaque rupture was responsible for 83% of STEMI cases in our study, while erosion was detected in 64% of non-STEMI patients. Necrotic-core atherosclerotic plaques were encountered in 64% of patients with ACS, followed by fibrotic and fibrocalcific plaques, respectively.

In this study, sex had no statistically significant influence on the etiology of ACS, which could be attributed to the fact that men comprised the vast majority of the studied subjects. Plaque rupture was more frequently encountered among the younger population, while plaque erosion had a numerically higher incidence rate of atherosclerotic risk factors such as diabetes mellitus, hypertension, and dyslipidemia and was, consequently, associated with a longer duration of symptom onset.

OCT pre-intervention was useful in identifying the nature of occlusive thrombi. White thrombi, which are rich in platelets, were detected in 64.2% of cases with plaque rupture, whereas red thrombi, which are fibrin-rich, were encountered in 69.7% of cases with plaque erosion. Less occlusive red thrombi were detected more frequently among cases of non-STEMI ACS, while more occlusive white thrombi were detected more frequently in the culprit vessel among patients with STEMI.

OCT study post-intervention was a perfect tool to optimize the procedural outcome and to decrease short and long-term adverse outcomes. The mean stent expansion rate was 93.2%, ranging between 86% and 114%, which is considered a near-optimal outcome. The mean minimum stent area achieved after final optimization was 8 mm^2, ranging from 3.7 mm^2 to 15.7 mm^2, provided that the stent diameter inserted ranged from 2.25 mm to 5 mm. Stent malapposition was detected in 56% of the studied patients, necessitating post-stent optimization with noncompliant high-pressure balloons. This finding may be overestimated in our study as all the studied subjects were in the setting of ACS with a heavy thrombus burden. Non–flow-limiting tissue or thrombus prolapse was encountered more frequently in the plaque erosion group (48.5%) than in the plaque rupture group (32.8%). No significant differences were observed between the 2 groups regarding the incidence of edge dissection. Only 6 cases were detected and properly managed by stenting. The no-reflow phenomenon developed exclusively among patients with plaque rupture. Eleven patients with plaque rupture and none of the patients with plaque erosion developed the no-reflow phenomenon, which was properly managed using intracoronary adenosine and calcium channel blockers. The higher incidence of the no-reflow phenomenon in the plaque rupture group could be attributed to the younger age of the patients, more occlusive white thrombi, and STEMI presentation. Measures to prevent the no-reflow phenomenon in terms of pharmacological preparation of the microvascular bed could be more beneficial once plaque rupture is detected as the phenomenon is highly anticipated.

CONCLUSIONS

The current study confirmed the feasibility and safety of frequency-domain OCT in optimizing procedural outcomes among patients with ACS. Significant stent malapposition could be angiographically missed in the setting of ACS without the aid of IVUS imaging. Plaque rupture was more frequently associated with negative angiographic outcomes vis-à-vis the no-reflow phenomenon.

Limitations

The salient limitation to the current investigation is its single-center retrospective design with a small cohort of patients. Nearly none of the studied patients had calcified nodules as the sole etiology of ACS. A multicenter randomized study with a long-term follow-up is highly recommended.

Ethical Approval and Consent to Participate

The Research Ethics Committee (REC) of the Faculty of Medicine, Ain Shams University, reviewed and approved the study. The Research Ethics Committee is organized and operated according to the guidelines of the International Council of Harmonization (ICH) Anesthesiology and the Islamic Organization of Medical Science

(IOMS), the United States Office of Human Research Protection, and the United States code of federal regulations. REC operates under federal wide assurance No FWA 000016385. REC does not declare the name of its members according to the university and REC standard operating procedures. The data of the patients were presented after they provided written informed consent following comprehensive explanations about the study stages and reassurances concerning the confidentiality of information.

Consent for Publication

Not applicable

Availability of Data and Material

All data, including angiograms and stored echocardiographic loops, are available with the authors, as well as in the Catheterization Laboratory and Echocardiography Unit of Ain Shams University.

Conflict of Interest

All the authors declare that there is no conflict of interest.

Funding

The present study was not funded. The studied cohort was recruited from a pool of patients presenting to the Catheterization Laboratory, Echocardiography Unit, and Cardiology Department of Ain Shams University.

Acknowledgments

Not applicable

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