JACC: CARDIOVASCULAR IMAGING
VOL. 6, NO. 3, 2013

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER INC.
http://dx.doi.org/10.1016/j.jcmg.2012.12.007

iCONCEPTS

CONCEPTS ON THE VERGE OF TRANSLATION

OCT-Based Diagnosis and Management of STEMI Associated With Intact Fibrous Cap

Francesco Prati, MD, PhD,*† Shiro Uemura, MD, PhD,‡ Geraud Souteyrand, MD, PhD,§ Renu Virmani, MD,‖ Pascal Motreff, MD, PhD,§ Luca Di Vito, MD, PhD,*† Giuseppe Biondi-Zoccai, MD, PhD,†¶ Jonathan Halperin, MD,# Valentin Fuster, MD, PhD,#** Yukio Ozaki, MD, PhD,†† Jagat Narula, MD, PhD#

Rome, Italy; Nara, Toyoake, Japan; Clermont-Ferrand, France; New York, New York; Gaithersburg, Maryland; and Madrid, Spain

In autopsy studies, at least 25% of thrombotic coronary occlusions are caused by plaque erosion in which thrombus often overlies atherosclerotic plaque without evident disruption of the fibrous cap. We performed optical coherence tomography imaging after aspiration thrombectomy and identified plaque erosion as the cause in 31 patients presenting with ST-segment elevation myocardial infarction. Plaque erosion was identified when the fibrous cap of the culprit lesion was intact. Based on clinical criteria, 40% of patients with subcritically occlusive plaque were treated with dual antiplatelet therapy without percutaneous revascularization (group 1), and the remaining 60% of patients underwent angioplasty and stenting (group 2). At a median follow-up of 753 days, all patients were asymptomatic, regardless of stent implantation. These observations support an alternative treatment strategy for patients with acute coronary events and optical coherence tomography–verified intact fibrous cap (or plaque erosion), where nonobstructive lesions might be managed without stenting. (J Am Coll Cardiol Img 2013;6:283–7)

Occlusive luminal thrombosis is the mechanism underlying most acute coronary syndromes (ACS). As many as 75% of autopsy studies after fatal ACS relate thrombotic occlusion to atherosclerotic plaque rupture; most of the remainder involve plaque erosion. Less common mechanisms involve thrombosis of a calcified nodule (1). Atherosclerotic lesions associated with plaque rupture may produce hemodynamically significant obstruction and typically contain a large necrotic core beneath a ruptured fibrous cap (RFC) that is attenuated

From the *Department of Interventional Cardiology, San Giovanni Hospital, Rome, Italy; †Centro per la Lotta contro l'Infarto (CLI) Foundation, Rome, Italy; ‡First Department of Medicine, Nara Medical University, Nara, Japan; §Department of Cardiology, Clermont-Ferrand University Hospital, Clermont-Ferrand, France; ‖Cardiovascular Institute Inc., Gaithersburg, Maryland; ¶Department of Medico-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Latina, Italy; #Zena and Michael A. Weiner Cardiovascular Institute, Icahn School of Medicine at Mount Sinai, New York, New York; **Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC), Madrid, Spain; and the ††Department of Cardiology, Fujita Health University Hospital, Toyoake, Japan. Dr. Motreff is a consultant to St. Jude Medical. Dr. Narula has a relationship with St. Jude Medical. Dr. Prati is a consultant to St. Jude Medical. Dr. Virmani has a relationship with Terumo. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. Drs. Prati, Uemura, Souteyrand, and Virmani contributed equally to this work. H. William Strauss, MD, served as Guest Editor for this article.

Manuscript received December 3, 2012; accepted December 14, 2012.

and inflamed (Fig. 1). Discontinuity of the fibrous cap brings circulating platelets into contact with the highly thrombogenic plaque core, leading to acute thrombus formation that occludes the arterial lumen. In contrast, erosion of plaque rich in proteoglycans and smooth muscle cells predisposes to thrombus formation over an intact fibrous cap (IFC). Because the pathogenesis of ACS in patients with an RFC differs from that in patients with an IFC, it is possible that clinical management of these 2 groups of patients may differ.

See page 288

Current treatment guidelines for patients with ACS rely heavily on catheter-based reperfusion of the infarct-related artery and intracoronary stent placement. The underlying plaque morphology is not routinely identified because of the limited resolution of conventional imaging modalities, such as intravascular ultrasound. Because stenosis of the arterial lumen might not always be significant in erosive pathology and the vessel wall not disrupted, it seems reasonable that reliable characterization of plaque morphology might justify an alternative approach that foregoes coronary stenting as the initial strategy for this subset of patients. Intracoronary optical coherence tomography (OCT) provides superior resolution (10 to 15 μm), allowing more detailed analysis of plaque morphology (2), including discriminating IFC from RFC in patients with ACS. Plaque rupture and plaque erosion in the culprit lesions of patients with ACS can be distinguished as discrete syndromes on the basis of an RFC (ACS-RFC) and IFC (ACS-IFC) (2).

ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndromes

IFC = intact fibrous cap

OCT = optical coherence tomography

RFC = ruptured fibrous cap

TIMI = Thrombolysis In Myocardial Infarction

We describe a series of patients in whom ACS was attributed to IFC after aspiration thrombectomy. A subset of these patients was treated with dual antiplatelet therapy, without angioplasty or stent placement. Considering the risks of in-stent thrombosis and restenosis and the need for prolonged dual antiplatelet therapy that entails an increased risk of bleeding, such an approach may improve long-term outcomes. From the OCT databases of 4 institutions, we identified 31 patients with ST-segment elevation myocardial infarction who underwent coronary angiography within 12 h after the onset of symptoms with the intent to perform a primary percutaneous coronary intervention with thrombus aspiration. Patients presenting in cardiogenic shock were excluded. Procedures were performed according to current clinical practice guidelines. The management decisions, including use of glycoprotein IIb/IIIa inhibitors or antiplatelet agents, and the decision to perform balloon angioplasty or stent implantation were made by the operator according to the local practice. Patients received unfractionated heparin (5,000 to 10,000 IU), aspirin (300 mg before the primary percutaneous coronary intervention, followed by 100 mg/day), and clopidogrel (300 to 600 mg initially followed by 75 mg/day) or prasugrel at the discretion of the treating physician (Table 1). After discharge, patients were followed at 1 to 3 months and at 6 months, in accordance with local practice. One year after the index ACS event, patients were evaluated again, either in the clinic or by telephone by experienced research nurses.

Because thrombus hampers the assessment of underlying plaque anatomy, erosion of the fibrous cap was documented by OCT after the thrombus was removed or reduced by aspiration, as previously described (2). Table 2 shows procedural and angiographic characteristics of lesions in 12 patients in the group managed with thrombectomy only (group 1) and 19 cases in those managed with aspiration plus stent implantation (group 2). Three patients in group 1 who were initially managed with systemic thrombolysis at community hospitals and transferred did not require aspiration (Fig. 2). Sixty-seven percent of patients in group 1 and 58% in group 2 presented with total coronary occlusions (Thrombolysis In Myocardial Infarction [TIMI] flow grades 0 to 1; p = NS). The median total ischemic times were 3.5 ± 3.0 h and 3.6 ± 2.3 h in groups 1 and 2, respectively (p = NS). There was only mild residual stenosis and no difference between groups in the final TIMI flow grade achieved (3 for each). After a median follow-up of 753 days, target lesion revascularization was performed in 1 patient in group 2, but no myocardial infarction, heart failure, or deaths occurred in either group.

Plaque erosion is an entity distinct from plaque rupture (1,2). Most erosive lesions are devoid of necrotic core, and, when present, the core does not communicate with the lumen because of a thick fibrous cap. Such lesions have been reported in younger individuals, including premenopausal women, with smoking as the most prevalent risk factor. Many of these lesions display relatively minor luminal narrowing, and thrombus removal without balloon dilation or stent implantation may be sufficient to restore vessel patency. The luminal thrombosis in plaque erosion has been attributed to apoptosis

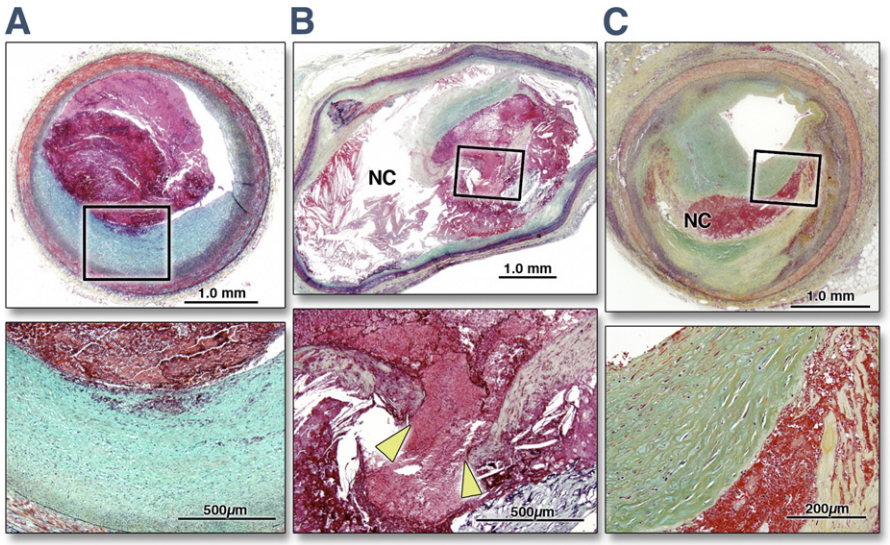

Figure 1. Histomorphological Characteristics of Plaque Erosion, Plaque Rupture, and a Stable Plaque

Cross-sectional images of 2 culprit coronary plaques obtained from the patients with acute coronary syndromes **(A,B)** and a stable unrelated plaque **(C)** from a nonculprit site in another patient with sudden death; the **boxed areas** in the **top panels** are magnified in the **bottom panels** for better histological characterization. The sections are stained with Movat's pentachrome. **(A)** The eroded plaque shows subcritical stenosis, an unremarkable necrotic core, and overlying thrombus on an intact fibrous cap. The cap is rich in smooth muscle cells and proteoglycans, and there is minimal inflammation at the base of the thrombus. The plaque does not show any positive remodeling. **(B)** Conversely, a positively remodeled, critically occlusive atherosclerotic plaque with a cholesterol crystal–rich large necrotic core (NC) covered by a very thin and inflamed fibrous cap, which is disrupted (area between the **yellow arrowheads**). Smooth muscle cells are visible in the medial layer and thin fibrous cap and minimally present at the base of the neointima. A large thrombogenic necrotic core is in communication with the vessel lumen with an occlusive thrombus. **(C)** A stable plaque shows smooth muscle and collagen-rich histology. The hemorrhagic necrotic core in the middle that separates the collagen of 2 separate ages represents a healed rupture site. The lesion is critically narrowed but does not show any positive remodeling or overlying thrombus.

or degradation of endothelial cells lining the plaque surface. Therefore, after thrombus removal, treatment with antiplatelet drugs may allow healing of the endothelial layer. The mechanisms involved may be similar to re-endothelialization after stent implantation. Avoiding stent deployment could potentially

Table 1. Patient Characteristics

	Group 1 (n = 12)	Group 2 (n = 19)	p Value
Male	10 (83)	16 (84)	
Age, yrs	52.2 ± 12.0	62.6 ± 10.8	0.019
Diabetes	1 (8)	7 (37)	0.18
Dyslipidemia	4 (33)	8 (42)	0.94
Hypertension	1 (8)	10 (53)	0.033
Smoking	7 (58)	13 (68)	0.85
Family history	5 (42)	3 (16)	0.23
Previous MI	2 (17)	2 (10)	0.95
Previous PCI	1 (8)	2 (10)	0.67
LVEF %	54.5 ± 13.2	53.8 ± 14.2	0.55
MVD	2 (17)	6 (32)	0.61
Location of culprit lesion			
LM	0	1 (5)	0.81
LAD	7 (58)	9 (47)	0.82
LCx	2 (17)	2 (10)	0.96
RCA	3 (25)	7 (37)	0.77

Values are n (%) or mean ± SD.
LAD = left anterior descending artery; LCx = left circumflex artery; LM = left main coronary artery; LVEF = left ventricular ejection fraction; MI = myocardial infarction; MVD = multivessel disease; PCI = percutaneous coronary intervention; RCA = right coronary artery.

Table 2. Procedural Characteristics

	Group 1 (n = 12)	Group 2 (n = 19)	p Value
Glycoprotein IIb/IIIa inhibitors	4 (33	4 (21)	0.73
ADP antagonists			0.042
Clopidogrel	7 (58)	18 (95)	
Prasugrel	5 (42)	1 (5)	
Angiographic analysis			
Pre-aspiration DS, %	79.4 ± 33.3	87.9 ± 17.3	0.95
Post-aspiration DS, %	27.1 ± 19.4	32.0 ± 35.2	0.48
Pre-aspiration TIMI flow grade ≤2	9 (75)	15 (79)	0.85
Post-aspiration TIMI flow grade ≤2	1 (8)	0	0.81
Total ischemic time, h	3.5 ± 3.0	3.6 ± 2.3	0.82

Values are n (%) or mean ± SD.
ADP = adenosine diphosphate; DS = diameter stenosis; TIMI = Thrombolysis In Myocardial Infarction.

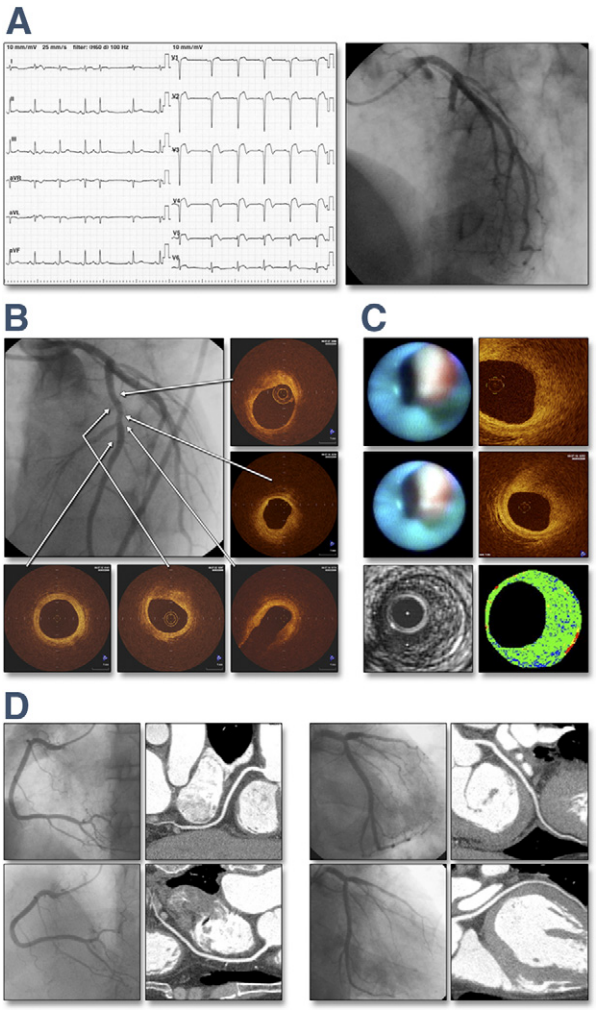

Figure 2. Management of a Patient Presenting With Acute Coronary Syndrome With an Intact Fibrous Cap

Severe chest discomfort and shortness of breath developed in a 66-year-old man after 12 h of intermittent and stuttering retrosternal discomfort. He presented to a local hospital; his blood pressure was 96/57 mm Hg, his heart rate was 84 beats/min, and an electrocardiogram revealed ST-segment elevation in precordial leads **(A)**. The coronary risk factors included dyslipidemia and 46-pack-year smoking history. An emergent coronary angiography was performed 4 h after the onset of chest pain, which revealed total occlusion of the proximal segment of left anterior descending coronary artery **(A)**. Then intravenous administration of heparin (10,000 IU) and half-dose alteplase was started, and he was transferred to a tertiary cardiovascular care center for a percutaneous coronary intervention. Repeat coronary angiography (8 h after the onset of chest pain) demonstrated no thrombus or stenosis at the original site of total occlusion. Optical coherence tomography (OCT), angioscopy, and gray-scale intravascular ultrasound, and integrated backscatter intravascular ultrasound **(B, C)** were performed. On arrival, CK-MB was 399 (normal: 0.6 to 3.5) ng/ml, and troponin I was 60.80 (normal: 0.00 to 0.06) ng/ml. Coronary angioscopy showed faint red thrombus formation through the blue coronary angioscopy guide catheter, whereas OCT did not show a typical red thrombus with a high backscattering protrusion mass with signal-free shadowing, but some signal reduction was observed from 12 to 3 o'clock positions **(C)**. Multiple slices of OCT images revealed an intact fibrous cap **(B)**. Intravascular ultrasound and integrated backscatter intravascular ultrasound demonstrated predominantly a fibrous plaque **(green)** and negligible lipid-rich component **(blue) (C)**. No intervention was undertaken. Pre-discharge curved multiplanar reconstruction computed tomography images confirmed the absence of positive remodeling and no significant stenosis at the site of the original occlusion **(D)** and mainly normal coronary arteries.

reduce the risks of both early (dissection, embolism, occlusive thrombosis) and late (restenosis, neoatherosclerosis, and thrombosis) complications.

These observations suggest that characterization of underlying plaque morphology by OCT may provide insight into the pathogenesis of some cases of ACS in which plaque erosion rather than rupture is an underlying cause. Reliable identification of these features may have practical implications for management, allowing selection of patients who can be treated using measures that reduce the burden of intravascular thrombus without intra-

coronary stenting. Because ACS-IFC appears to involve a mechanism of luminal obstruction distinct from that in ACS-RFC, a different interventional approach to management may be warranted in these cases. Perhaps the role of antithrombin agents may warrant reconsideration in ACS-IFC. Furthermore, because these lesions involve an IFC, the risk of intraplaque hemorrhage may be lower than in those with ACS-RFC, raising the possibility that specific strategies of catheter-directed lytic therapy (e.g., plasmin) may be relatively safe and efficacious. Definitive trials comparing the safety and efficacy of these alternative approaches will depend foremost on accurate imaging to exclude evidence of rupture or calcification of the offending coronary lesion.

Study limitations. The limitations of this observational study include its nonrandomized design, small sample size, and the lack of a comparison group of ACS-RFC patients managed either with or without stent implantation. Also, no conclusions can be drawn about various alternative methods of thrombus removal or adjunctive antithrombotic therapy, nor can we be certain about the subclinical events occurring at the plaque surface that promote thrombus formation in patients with ACS-IFC and predispose to the onset of the acute ischemic syndrome.

Conclusions

We demonstrate in a limited number of patients with ACS that characterization of plaque morphology by OCT could identify nonobstructive lesions amenable to treatment with an antiplatelet strategy alone, without angioplasty or coronary stent deployment, and result in satisfactory clinical outcomes. The PERADAM-OCT (Plaque Erosion in ACS: OCT-Based Diagnosis And Management, An International Registry) is beginning to gather additional data about the factors predisposing to plaque erosion and clinical presentation on ACS in patients with lesions of this type. Randomized trials will be needed, however, to clarify the role of aspiration thrombectomy and catheter-directed lytic therapy without stent implantation in cases of OCT-verified ACS-IFC and further evaluate the long-term outcomes of an alternative management strategy for this unique cause of ACS.

Reprint requests and correspondence: Dr. Jagat Narula, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place, Box 1030, New York, New York 10029. *E-mail: narula@mountsinai.org.*

REFERENCES

1. Burke AP, Farb A, Malcom GT, Liang YH, Smialek J, Virmani R. Coronary risk factors and plaque morphology in men with coronary disease who died suddenly. N Engl J Med 1997;336:1276–82.
2. Ozaki Y, Okumura M, Ismail TF, et al. Coronary CT angiographic characteristics of culprit lesions in acute coronary syndromes not related to plaque rupture as defined by optical coherence tomography and angioscopy. Eur Heart J 2011;32:2814–23.

Key Words: acute coronary syndrome ■ aspiration thrombectomy ■ optical coherence tomography ■ plaque erosion.