International Journal of Cardiology 220 (2016) 112–115

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Clinical and morphological presentations of acute coronary syndrome without coronary plaque rupture — An intravascular ultrasound study

Kenichi Tsujita [a,*], Kenshi Yamanaga [a], Naohiro Komura [a], Kenji Sakamoto [a], Takashi Miyazaki [a], Yu Oimatsu [a], Masanobu Ishii [a], Noriaki Tabata [a], Tomonori Akasaka [a], Daisuke Sueta [a], Eiichiro Yamamoto [a], Megumi Yamamuro [a], Yasuhiro Izumiya [a], Sunao Kojima [a], Sunao Nakamura [a], Koichi Kaikita [a], Seiji Hokimoto [a], Hisao Ogawa [a,b]

[a] Department of Cardiovascular Medicine, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan
[b] Department of Cardiovascular Medicine, National Cerebral and Cardiovascular Center Hospital, Suita, Japan

ARTICLE INFO

Article history:
Received 16 March 2016
Accepted 24 June 2016
Available online 25 June 2016

Keywords:
Imaging
Ultrasonics
Catheterization
Plaque
Myocardial infarction

ABSTRACT

Background: Although acute coronary syndrome (ACS) mainly arises from plaque ruptures (PR), precise mechanisms underlying ACS without PR are unknown. We sought to examine clinical, angiographic and intravascular ultrasound (IVUS) characteristics of ACS without PR.

Methods and results: Culprit lesions of 161 ACS patients were categorized by the presence or absence of PR (PR group: n = 57, Non-PR group: n = 104). Lower abdominal circumference (86 ± 10 cm vs 90 ± 9 cm, p = 0.02), lower prevalence of myocardial infarction (53% vs 82%, p = 0.0002), and higher prevalence of definite vasospasm (15% vs 2%, p = 0.006) were found in Non-PR group. Morphologically, Non-PR group was associated with simpler Ambrose classification (36% vs 14%, p = 0.004), less hypoechoic plaque (45% vs 65%, p = 0.04) and lower incidence of IVUS-detected thrombus (21% vs 54%, p < 0.0001), compared with PR group. On quantitative IVUS, although minimum lumen area (MLA) was similar between the groups, vessel (14.2 ± 5.4 mm^2 vs 17.5 ± 5.1 mm^2, p = 0.0002) and plaque (11.6 ± 5.0 mm^2 vs 14.9 ± 4.9 mm^2, p < 0.0001) areas were significantly smaller at MLA site in Non-PR group than in PR group. On multivariate analysis, average plaque area was only an independent IVUS-predictor of non-rupture ACS (odds ratio: 0.85, p = 0.01).

Conclusion: Compared to ACS with PR, non-rupture ACS arise from more hyperechoic (allegedly "stable") plaque with smaller vessel and plaque area, leading to lower incidence of thrombotic occlusion. Coronary vasospasm might be a possible pathogenic mechanism underlying non-rupture ACS.

1. Introduction

Pathological studies have indicated that representative lesions responsible for acute coronary syndrome (ACS) are ruptures of vulnerable plaques with a subsequent thrombosis [1]. On the other hand, Naghavi et al. demonstrated that various types of plaque could be ACS-prone coronary plaque, namely, ACS might occur from any stage of atherosclerosis [2]. We have also shown that coronary vasospasm could cause ACS by injuring endothelial cells and accelerating thrombogenic responses [3].

In terms of the association between the presence of plaque rupture and ischemic myocardial damage, Tanaka et al. showed that ST-segment elevation myocardial infarction (STEMI) caused by plaque rupture was associated with a large degree of myocardial damage and poor functional recovery as compared with STEMI of different etiologies, even after successful primary angioplasty [4]. However, precise mechanisms underlying ACS without plaque ruptures have not been well studied in vivo. We therefore sought to examine clinical, angiographic and intravascular ultrasound (IVUS) characteristics of ACS without plaque ruptures.

2. Methods

2.1. Study population

This study included patients with ACS who were admitted to Kumamoto University Hospital and underwent coronary angiography (CAG) between December 2008 and May 2012. ACS was defined as STEMI, non-STEMI (NSTEMI) and unstable angina pectoris (UAP). A consecutive series of 161 ACS patients whose culprit lesions were observed on preintervention IVUS were enrolled. These culprit lesions

* Corresponding author at: 1-1-1 Honjo, Chuo-ku, Kumamoto 860-8556, Japan.
E-mail address: tsujita@kumamoto-u.ac.jp (K. Tsujita).

http://dx.doi.org/10.1016/j.ijcard.2016.06.191
0167-5273/

were classified into two groups based on the presence or absence of plaque rupture (Rupture group: n = 57, Non-rupture group: n = 104). Clinical characteristics and lesion morphologies visualized by IVUS were compared between the two groups. Plaque rupture was defined as a plaque ulceration with a tear detected in a fibrous cap.

2.2. IVUS image acquisition & analysis

We identified the culprit lesion based on electrocardiogram and CAG and analyzed each plaque using IVUS. IVUS image acquisition was performed in the culprit lesion before balloon dilatation or just after 1.5–2.0 mm balloon dilatation with commercially available IVUS systems (Boston Scientific Corp., Natick, MA or Terumo Corp., Tokyo, Japan). The IVUS catheter was advanced beyond the culprit lesions and withdrawn at a pullback speed of 0.5 mm/s automatically.

2.3. Statistical analysis

SPSS version 10.0 software (SPSS Inc., Chicago, Illinois) was used to perform all statistical analysis. Continuous variables (mean ± SD) were compared with unpaired Student *t* test or Mann–Whitney *U* test. Categorical variables (frequencies) were compared with chi-square statistics or the Fisher exact test. Logistic regression analysis was employed to determine predictors of onset of non-rupture ACS. Significant variables ($p < 0.05$ in the univariate analysis), except for internally-correlated variables, were entered into multivariate analysis. A p value <0.05 was considered significant.

Table 1
Baseline patients characteristics and angiographic findings.

Characteristics	Rupture ACS (n = 57)	Non-Rupture ACS (n = 104)	p value
Clinical background			
Male gender	41 (72%)	72 (69%)	0.72
Age, years	67 ± 13	71 ± 12	0.13
Body mass index, kg/m2	24.4 ± 3.6	23.5 ± 3.4	0.10
Abdominal circumference, cm	89.8 ± 8.8	86.1 ± 9.5	0.02
Hypertension	35 (61%)	71 (68%)	0.38
Dyslipidemia	42 (74%)	67 (64%)	0.23
Diabetes mellitus	19 (33%)	34 (33%)	0.93
Current smoking	19 (33%)	27 (26%)	0.32
Comorbid VSA	1 (2%)	16 (15%)	0.006
ACS type			
UAP	10 (18%)	49 (47%)	0.0001
NSTMI	43 (75%)	16 (15%)	
STEMI	4 (7%)	39 (38%)	
TC, mg/dL	165 ± 32	163 ± 34	0.54
LDL-C, mg/dL	103 ± 30	101 ± 32	0.47
HDL-C, mg/dL	43 ± 11	45 ± 10	0.24
TG, mg/dL	111 ± 43	107 ± 47	0.33
HbA1c, %	6.1 ± 1.2	5.8 ± 1.0	0.16
Angiographic findings			
Ambrose class simple	8 (14%)	37 (36%)	0.004
Ambrose class complex	49 (86%)	67 (64%)	
SYNTAX score	9.2 ± 5.9	10.2 ± 6.6	0.43
Culprit lesion			
LAD	31 (54%)	69 (66%)	
LCX	6 (11%)	13 (13%)	0.16
RCA	20 (35%)	22 (21%)	
Thrombectomy	34 (60%)	20 (19%)	<0.0001
Angiographic stain	15 (26%)	8 (8%)	0.001
Angiographic thrombus	26 (46%)	18 (17%)	0.0001

Values are presented as n (%) or mean ± standard deviation. ACS indicates acute coronary syndrome; UAP, unstable angina pectoris; NSTEMI, non-ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride; HbA1c, hemoglobin A1c; LAD, left ascending artery; LCX, left circumflex; RCA, right coronary artery; VSA, vasospastic angina.

3. Results

3.1. Baseline patients characteristics

Among 161 ACS patients, plaque rupture was observed at the culprit lesion of 57 patients. The baseline clinical characteristics and angiographic findings of the study patients are shown in Table 1. There were no significant differences in clinical characteristics including traditional coronary risk factors between Rupture and Non-rupture group, except for higher rate of comorbid coronary vasospastic angina in Non-rupture group ($p = 0.006$). In terms of clinical presentation of ACS, plaque rupture was significantly associated with diagnosis of myocardial infarction (release of cardiac enzyme, $p = 0.0001$). Angiographic data showed in general more complex angiographic morphologies (Ambrose complex class, angiographic thrombus and angiographic stain) in Rupture group.

3.2. Comparison of IVUS findings of ACS culprit lesions

Gray-scale IVUS findings of culprit lesion morphology are listed in Table 2. Culprit plaque echodensity was more hypoechoic in Rupture ACS than in Non-Rupture ACS. Vulnerable features of culprit lesions such as echolucent plaque (95% vs 82%, $p = 0.03$) and microcalcification (79% vs 63%, $p = 0.04$) were more often seen in Rupture ACS compared with Non-Rupture ACS. Furthermore, regarding cross-sectional quantitative IVUS findings at minimum lumen area (MLA) site, although MLA was comparable between the groups, external elastic membrane (EEM, ≈vessel) area, plaque area, and plaque burden at MLA site were significantly larger in Rupture ACS group than in Non-Rupture ACS group. Volumetric IVUS analysis showed that EEM volume and

Table 2
IVUS Findings in patients with and without plaque rupture at culprit lesions.

Characteristics	Rupture ACS (n = 57)	Non-Rupture ACS (n = 104)	p value
Plaque vulnerability on IVUS			
Echodensity of culprit plaque			
Hypoechoic, %	37 (65%)	47 (45%)	0.04
Hyper/isoechoic, %	16 (28%)	39 (38%)	
Mixed, %	1 (2%)	13 (13%)	
Calcified, %	3 (5%)	5 (5%)	
Attenuated plaque, %	48 (84%)	76 (73%)	0.11
Ruptured plaque, %	57 (100%)	0 (0%)	<0.0001
Echolucent plaque, %	54 (95%)	85 (82%)	0.03
Microcalcification, %	45 (79%)	66 (63%)	0.04
Calcified plaque, %	44 (77%)	79 (76%)	0.86
Thrombus on IVUS	31 (54%)	22 (21%)	<0.0001
Quantitative parameters at MLA site			
MLA, mm^2	2.6 ± 0.8	2.7 ± 0.9	0.81
EEM, mm^2	17.5 ± 5.1	14.2 ± 5.4	0.0002
Plaque area, mm^2	14.9 ± 4.9	11.6 ± 5.0	<0.0001
Plaque burden, %	84 ± 6	79 ± 8	0.0004
Eccentricity	6.1 ± 8.6	7.3 ± 8.7	0.15
Prox. ref. EEM, mm^2	18.8 ± 5.5	16.2 ± 5.5	0.01
Dist. ref. EEM, mm^2	16.0 ± 5.6	13.2 ± 5.8	0.0001
Remodeling index	1.02 ± 0.19	0.98 ± 0.19	0.38
Volumetric analysis of culprit plaques			
Lumen volume, mm^3	88 ± 45	71 ± 47	0.004
EEM volume, mm^3	315 ± 164	236 ± 156	0.001
Plaque volume, mm^3	228 ± 125	165 ± 112	0.0007
Plaque length, mm	17.3 ± 6.8	16.2 ± 8.6	0.14
Mean lumen CSA, mm^3/mm	5.1 ± 1.7	4.4 ± 1.7	0.003
Mean EEM CSA, mm^3/mm	17.9 ± 5.1	14.5 ± 5.1	<0.0001
Mean plaque CSA, mm^3/mm	12.9 ± 3.9	10.1 ± 3.9	<0.0001

Values are presented as n (%) or mean ± standard deviation. IVUS indicates intravascular ultrasound; MLA, minimum lumen area; EEM, external elastic membrane; CSA, cross-sectional area.