Comparison of Virtual Histology to Intravascular Ultrasound of Culprit Coronary Lesions in Acute Coronary Syndrome and Target Coronary Lesions in Stable Angina Pectoris

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Coronary plaque composition cannot be assessed accurately using gray-scale intravascular ultrasound (IVUS). Using virtual histology IVUS (VH-IVUS), a comparison of coronary plaque composition between acute coronary syndromes (ACS) and stable angina pectoris (SAP) was performed. Preintervention IVUS of de novo culprit and target lesions was performed in 318 patients (123 with ACS and 195 with SAP). Using VH-IVUS, plaque was characterized as fibrotic, fibrofatty, dense calcium, and necrotic core. VH-IVUS-derived thin-cap fibroatheroma (VH-TCFA) was defined as necrotic core ≥10% of plaque area without overlying fibrous tissue in a plaque burden ≥40%. Lesions were classified into 3 groups: ruptured, VH-TCFA, and non–VH-TCFA plaque. Unstable lesions were defined as either VH-TCFA or ruptured plaque. Compared with patients with SAP, those with ACS had significantly more unstable lesions (89% vs 62%, p <0.001). Planar VH-IVUS analysis at the minimum luminal site and at the largest necrotic core site and volumetric analysis over a 10-mm-long segment centered at the minimum luminal site showed that the percentage of necrotic core was significantly greater and that the percentage of fibrofatty plaque was significantly smaller in patients with ACS. The percentages of fibrotic and fibrofatty plaque areas and volumes were smaller, and the percentages of necrotic core areas and volumes were larger in VH-TCFAs compared with non-TCFAs. Ruptured plaques in VH-IVUS analyses showed intermediate findings between VH-TCFAs and non–VH-TCFAs. In conclusion, culprit lesions in patients with ACS were more unstable and had greater amounts of necrotic core and smaller amounts of fibrofatty plaque compared with target lesions in patients with SAP. **(Am J Cardiol 2007;100:953–959)**

Clinical symptoms and presentations, not lesion morphology, define acute coronary syndromes (ACS) and differentiate ACS from stable angina pectoris (SAP). However, unstable clinical symptoms in patients with ACS are associated with unstable plaque characteristics.[1–4] Conventional gray-scale intravascular ultrasound (IVUS) has significant limitations in accurately assessing atheromatous plaque composition. These limitations have been partially addressed by virtual histology IVUS (VH-IVUS), which characterizes plaque as calcified, fibrotic, fibrofatty, or necrotic core.[5,6] The purpose of this study was to use VH-IVUS to compare coronary plaque composition between patients with ACS and patients with SAP.

Methods

Study population: From June 2005 to July 2006, 318 patients (123 with ACS and 195 with SAP) with de novo culprit and target lesions underwent preintervention VH-IVUS at Asan Medical Center. The ACS group included 41 patients with unstable angina, 28 patients with non–ST-segment elevation myocardial infarction, and 54 patients with ST-segment elevation myocardial infarction. Acute myocardial infarction was defined as continuous chest pain at rest with abnormal levels of cardiac enzymes (creatinine kinase-MB or troponin T). SAP was defined as no change in the frequency, duration, or intensity of symptoms within 6 weeks before the intervention.[7] The culprit lesion in ACS or the target lesion in SAP was identified by the combination of left ventricular wall motion abnormalities, electrocardiographic findings, angiographic lesion morphology, and scintigraphic defects. In patients with SAP who underwent multivessel intervention, the lesion with the worst diameter stenosis and more complex morphology in the territory of scintigraphic reversible defects was selected as the target

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Table 1
Baseline clinical characteristics

Variable	ACS (n = 123)	SAP (n = 195)	p Value
Age (yrs)	59 ± 11	60 ± 9	0.7
Men	104 (85%)	126 (65%)	<0.001
Hypertension	47 (38%)	97 (50%)	0.044
Diabetes mellitus	22 (18%)	49 (25%)	0.131
Cigarette smoker	65 (53%)	38 (20%)	<0.001
Lipid profiles at baseline (mg/dl)			
Total cholesterol	185 ± 42	168 ± 35	<0.001
HDL cholesterol	39 ± 11	44 ± 13	0.004
LDL cholesterol	117 ± 38	94 ± 27	<0.001
Triglycerides	176 ± 147	158 ± 93	0.25
C-reactive protein (mg/dl)	0.6 ± 0.9	0.3 ± 0.6	<0.001
Coronary intervention	121 (98%)	191 (98%)	0.6
No. of stents used	1.2 ± 0.4	1.2 ± 0.4	0.21
No. of narrowed coronary arteries			0.018
1	71 (58%)	139 (71%)	
2	35 (28%)	44 (23%)	
3	17 (14%)	12 (6%)	

HDL = high-density lipoprotein; LDL = low-density lipoprotein.

Table 2
Gray-scale intravascular ultrasound findings between acute coronary syndromes and stable angina pectoris

Variable	ACS (n = 123)	SAP (n = 195)	p Value
Minimum luminal area			
EEM area (mm^2)	17.1 ± 4.5	15.0 ± 4.5	<0.001
Luminal area (mm^2)	3.7 ± 1.0	3.8 ± 0.9	0.3
P&M area (mm^2)	13.4 ± 4.4	11.2 ± 4.4	<0.001
Remodeling index	1.07 ± 0.18	1.02 ± 0.19	0.038
Largest necrotic core			
EEM area (mm^2)	17.4 ± 4.4	15.7 ± 5.4	0.003
Luminal area (mm^2)	4.8 ± 1.7	5.0 ± 2.1	0.3
P&M area (mm^2)	12.6 ± 4.2	10.7 ± 4.4	<0.001
Volumetric analysis			
EEM volume (mm^3)	167.7 ± 43.8	149.2 ± 40.5	<0.001
Luminal volume (mm^3)	59.5 ± 15.6	60.1 ± 14.1	0.7
P&M volume (mm^3)	108.3 ± 36.7	89.1 ± 34.4	<0.001

lesion for VH-IVUS analysis.[8] Total occlusions, bifurcation lesions, lesions with severe angulations, and heavily calcified lesions (all because of technical difficulties in performing smooth, motorized catheter pullback) were excluded from this study.

IVUS imaging and analysis: VH-IVUS examination was performed before any intervention and after the intracoronary administration of nitroglycerin 0.2 mg using a motorized transducer pullback system (0.5 mm/s). A 2.9Fr IVUS imaging catheter (Eagle Eye; Volcano Corporation, Rancho Cordova, California) incorporated a 20-MHz phased-array transducer.

Conventional gray-scale quantitative IVUS analyses were performed according to criteria of the clinical expert consensus document on IVUS to include external elastic membrane (EEM), luminal, and plaque and media (P&M; defined as EEM minus luminal) areas.[9] Plaque burden was defined as P&M area divided by EEM area. A remodeling index was calculated as the lesion EEM divided by the mean reference EEM area. IVUS signs of plaque rupture were a cavity that communicated with the lumen with an overlying residual fibrous cap fragment.[7,8]

Table 3
Virtual histology intravascular ultrasound findings between acute coronary syndromes and stable angina pectoris

Variables	ACS (n = 123)	SAP (n = 195)	p Value
Minimum luminal area site			
Absolute areas (mm^2)			
Fibrotic (green)	5.3 ± 2.7	4.6 ± 3.0	0.030
Fibrofatty (yellow-green)	0.5 ± 0.6	0.5 ± 0.6	0.6
Dense calcium (white)	0.8 ± 0.7	0.6 ± 0.6	0.001
Necrotic core (red)	3.1 ± 1.9	2.1 ± 1.3	<0.001
Percentages			
Fibrotic	53 ± 15	56 ± 15	0.073
Fibrofatty	5 ± 5	7 ± 6	0.020
Dense calcium	9 ± 7	8 ± 8	0.4
Necrotic core	33 ± 14	29 ± 14	0.015
Largest necrotic core site			
Absolute areas (mm^2)			
Fibrotic	5.0 ± 4.3	4.0 ± 2.8	0.015
Fibrofatty	0.4 ± 0.4	0.4 ± 0.5	0.6
Dense calcium	0.9 ± 0.7	0.7 ± 0.7	0.003
Necrotic core	3.4 ± 2.0	2.3 ± 1.6	<0.001
Percentages			
Fibrotic	50 ± 15	53 ± 15	0.105
Fibrofatty	4 ± 4	5 ± 5	0.024
Dense calcium	10 ± 7	9 ± 8	0.5
Necrotic core	36 ± 13	33 ± 14	0.034
Volumetric analysis			
Absolute volumes (mm^3)			
Fibrotic	41.9 ± 22.4	32.3 ± 20.8	<0.001
Fibrofatty	4.7 ± 4.5	4.5 ± 4.7	0.7
Dense calcium	6.4 ± 5.1	4.4 ± 4.6	0.001
Necrotic core	20.3 ± 12.6	14.3 ± 9.5	<0.001
Percentages			
Fibrotic	56 ± 13	57 ± 13	0.3
Fibrofatty	6 ± 5	8 ± 5	0.045
Dense calcium	9 ± 7	9 ± 8	0.5
Necrotic core	29 ± 12	27 ± 11	0.081

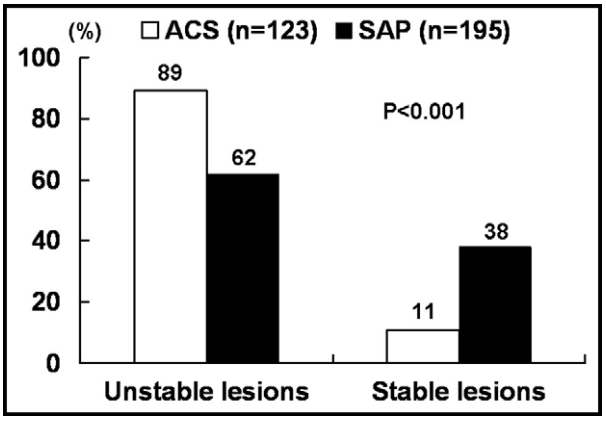

Figure 1. Incidence of unstable and stable plaques in patients with ACS compared with those with SAP. Unstable and stable lesions were defined as either VH-TCFA or ruptured plaque and non–VH-TCFA plaque, respectively.

Table 4
Gray-scale intravascular ultrasound findings comparing ruptured plaques with virtual histology intravascular ultrasound–derived thin-cap fibroatheromas and non–virtual histology intravascular ultrasound–derived thin-cap fibroatheromas

Variable	Plaque Rupture (n = 74)	Non–Plaque Rupture		p Value†
		VH-TCFA (n = 156)	Non-VH-TCFA (n = 88)	
Minimum luminal area site				
EEM area (mm^2)	18.7 ± 4.4	15.0 ± 4.4*	14.8 ± 4.3	<0.001
Luminal area (mm^2)	3.8 ± 0.8	3.7 ± 0.9	3.7 ± 0.9	1.0
P&M area (mm^2)	14.9 ± 4.4	11.3 ± 4.2*	11.1 ± 4.2	<0.001
Remodeling index	1.10 ± 0.20	1.03 ± 0.19*	1.00 ± 0.15	0.003
Largest necrotic core site				
EEM area (mm^2)	19.2 ± 5.8	15.7 ± 4.7*	15.0 ± 4.3	<0.001
Luminal area (mm^2)	5.1 ± 2.5	4.9 ± 1.9	4.6 ± 1.7	0.3
P&M area (mm^2)	14.1 ± 4.6	10.8 ± 4.0*	10.4 ± 4.0	<0.001
Volumetric analysis				
EEM volume (mm^3)	183.6 ± 40.9	150.0 ± 42.4*	144.5 ± 34.5	<0.001
Luminal volume (mm^3)	60.5 ± 16.4	59.1 ± 14.4	60.8 ± 13.6	0.6
P&M volume (mm^3)	122.9 ± 38.4	91.2 ± 33.8*	83.8 ± 27.8	<0.001

* p <0.05 comparing VH-TCFAs and ruptured plaques. There were no differences when VH-TCFAs were compared with non–VH-TCFAs.
† Analysis of variance.

Planar VH-IVUS analysis was performed at the site of the minimal luminal area and the site of the largest necrotic core. Volumetric VH-IVUS analysis was performed along a 10-mm segment centered on the minimal luminal area; calculations were made using Simpson's rule. VH-IVUS analysis classified and color-coded tissue as green (fibrotic), yellow-green (fibrofatty), white (dense calcium), and red (necrotic core).[5,6] VH-IVUS analyses are reported in absolute amounts and as percentages (relative amounts) of plaque area and volume. VH-IVUS-derived thin-cap fibroatheroma (VH-TCFA) was defined as a necrotic core ≥10% of plaque area at either the minimal luminal area site or the largest necrotic core site in ≥3 consecutive frames without evident overlying fibrous tissue in the presence of ≥40% plaque burden.[6]

Because plaque rupture is 1 of the final fates of TCFA, and the identification of TCFA before the rupture of plaque occurs is clinically significant, plaque rupture has different characteristics from TCFA. Differentiation between TCFA and non-TCFA is also clinically important because plaque rupture occurs mainly in TCFA lesions rather than non-TCFA lesions. Therefore, according to gray-scale and VH-IVUS findings, culprit and target lesions were classified into 3 groups: ruptured plaque, VH-TCFA, and non–VH-TCFA plaque. Unstable lesions contained either VH-TCFAs or ruptured plaques.

Statistical analysis: Statistical analysis was performed with SPSS (SPSS, Inc., Chicago, Illinois). Data are presented as frequencies or mean ± SD. Comparisons were performed with chi-square statistics or Fisher's exact test and the unpaired Student's *t* test, the Mann-Whitney U test, or analysis of variance. Multiple stepwise logistic regression analysis was performed to assess independent predictors for VH-TCFA. A p value <0.05 was considered statistically significant.

Results

Baseline clinical characteristics are listed in Table 1. Table 2 lists gray-scale IVUS findings of culprit and target lesions, comparing patients with ACS and those with SAP. Patients with ACS had significantly larger EEM and P&M areas and larger remodeling indexes than those with SAP.

Table 3 lists VH-IVUS analysis of culprit and target lesions, comparing patients with ACS and those with SAP. Planar VH-IVUS analysis at the minimum luminal site and at the largest necrotic core site showed that the percentage of necrotic core area was significantly greater (33% vs 29%, p = 0.015, and 36% vs 33%, p = 0.034, respectively) and that the percentage of fibrofatty plaque (5% vs 7%, p = 0.020, and 4% vs 5%, p = 0.024, respectively) was significantly smaller in patients with ACS. There was a tendency toward smaller percentages of fibrotic plaque (53% vs 56%, p = 0.073, and 50% vs 53%, p = 0.105, respectively) in patients with ACS. Volumetric VH-IVUS analysis over a 10-mm-long segment centered at the minimum luminal site supported these observations.

VH-TCFAs: Culprit lesions in the 123 patients with ACS contained 45 ruptured plaques (37%), 64 VH-TCFAs (52%), and 14 non–VH-TCFA (11%); conversely, target lesions in 195 patients with SAP contained 29 ruptured plaques (15%), 92 VH-TCFAs (47%), and 74 non–VH-TCFAs (38%) (p <0.001, patients with ACS vs patients with SAP). Therefore, compared with patients with SAP, those with ACS had significantly more unstable lesions (89% vs 62%, p <0.001; Figure 1).

There were no significant differences in gray-scale IVUS findings between nonruptured lesions with VH-TCFA and nonruptured lesions without VH-TCFA (Table 4). However, VH-TCFAs had smaller EEM and P&M areas and volumes compared with the ruptured plaques.

In the VH-IVUS analysis, there were smaller percentages of fibrotic and fibrofatty plaque areas and volumes and a

Table 5
Virtual histology intravascular ultrasound findings comparing ruptured plaques with virtual histology intravascular ultrasound–derived thin-cap fibroatheromas and non–virtual histology intravascular ultrasound–derived thin-cap fibroatheromas

Variable	Plaque Rupture (n = 74)	Non–Plaque Rupture		p Value‡
		VH-TCFA (n = 156)	Non–VH-TCFA (n = 88)	
Minimum luminal area site				
Absolute areas (mm^2)				
Fibrotic (green)	6.5 ± 2.9	4.0 ± 2.4*,†	5.0 ± 3.1	<0.001
Fibrofatty (yellow-green)	0.7 ± 0.7	0.4 ± 0.5*,†	0.7 ± 0.7	<0.001
Dense calcium (white)	0.8 ± 0.7	0.7 ± 0.6	0.6 ± 0.8	0.14
Necrotic core (red)	3.2 ± 1.9	2.8 ± 1.6*	1.4 ± 0.9	<0.001
Percentages				
Fibrotic	58 ± 15	50 ± 13*,†	64 ± 15	<0.001
Fibrofatty	7 ± 6	4 ± 4*,†	9 ± 7	<0.001
Dense calcium	7 ± 7	9 ± 8	8 ± 9	0.3
Necrotic core	28 ± 14	37 ± 12*,†	20 ± 10	<0.001
Largest necrotic core site				
Absolute areas (mm^2)				
Fibrotic (green)	6.2 ± 2.2	3.6 ± 2.2†	4.4 ± 2.9	<0.001
Fibrofatty (yellow-green)	0.6 ± 0.6	0.3 ± 0.3*,†	0.6 ± 0.6	<0.001
Dense calcium (white)	0.9 ± 0.8	0.7 ± 0.6	0.7 ± 0.8	0.09
Necrotic core (red)	3.5 ± 2.0	3.0 ± 1.7*	1.6 ± 1.2	<0.001
Percentages				
Fibrotic	53 ± 15	46 ± 12*,†	60 ± 15	<0.001
Fibrofatty	5 ± 5	3 ± 3*,†	7 ± 6	<0.001
Dense calcium	9 ± 7	10 ± 7	10 ± 10	0.5
Necrotic core	33 ± 14	41 ± 10*,†	23 ± 10	<0.001
Volumetric analysis				
Absolute volumes (mm^3)				
Fibrotic	52.2 ± 25.4	30.5 ± 18.2†	32.0 ± 18.4	<0.001
Fibrofatty	6.6 ± 5.7	3.3 ± 3.8*,†	5.2 ± 4.2	<0.001
Dense calcium	6.5 ± 5.4	5.5 ± 4.7*	3.4 ± 4.2	<0.001
Necrotic core	21.8 ± 11.9	17.8 ± 11.4*,†	10.1 ± 6.1	<0.001
Percentages				
Fibrotic	59 ± 12	53 ± 12*,†	62 ± 13	<0.001
Fibrofatty	7 ± 5	5 ± 4*,†	10 ± 5	<0.001
Dense calcium	8 ± 6	10 ± 7*,†	8 ± 9	0.009
Necrotic core	26 ± 11	32 ± 10*,†	21 ± 9	<0.001

* p <0.05 comparing TCFAs with non–VH-TCFAs.
† p <0.05 comparing TCFAs with ruptured plaques.
‡ Analysis of variance.

larger percentage of necrotic core areas and volumes in VH-TCFAs compared with non-TCFAs (Table 5). Ruptured plaques in VH-IVUS analyses showed intermediate findings between VH-TCFA and non-VH-TCFA plaques; the percentages of fibrotic and fibrofatty plaque areas and volumes were greater, and the percentage of necrotic core area and volume was smaller in ruptured plaques compared with VH-TCFAs (Table 5).

Clinical characteristics of subgroup patients without plaque rupture are listed in Table 6. Multiple stepwise logistic regression analysis including all clinical variables with p values <0.2 in univariate analysis (male gender, low-density lipoprotein and high-density lipoprotein cholesterol levels, and ACS) indicated that ACS was the only independent predictor of VH-TCFA (odds ratio 2.739, 95% confidence interval 1.252 to 5.993, p = 0.012) in patients without ruptured plaques.

Table 7 lists VH-IVUS analysis of culprit lesions, comparing patients with non–ST-segment-elevation myocardial infarction or unstable angina and those with ST-segment elevation myocardial infarction.

Discussion

The present preintervention gray-scale and VH-IVUS analysis of 318 patients showed distinctly different VH-IVUS morphologies between culprit lesions in patients with ACS and target lesions in patients with SAP. Necrotic cores were larger and fibrofatty plaque was less, and there were more unstable lesions (either plaque rupture or VH-TCFA) in patients with ACS compared with those with SAP.

The angiographic assessment of coronary luminal stenosis has been considered a surrogate marker of the severity of atherosclerosis. However, coronary angiography, a luminogram, has low predictive value to assess atherosclerotic plaque burden or to predict ACS events.[10–12] Although IVUS provides cross-sectional morphometric detail (e.g., identification of ruptured plaques, assessment of remodel-

Table 6
Baseline clinical characteristics of patients without plaque rupture comparing patients with virtual histology intravascular ultrasound–derived thin-cap fibroatheromas with patients without virtual histology intravascular ultrasound–derived thin-cap fibroatheromas

Variable	Lesions With VH-TCFA (n = 156)	Lesions Without VH-TCFA (n = 88)	p Value
Age (yrs)	61 ± 10	59 ± 10	0.2
Men	111 (73%)	53 (60%)	0.08
Hypertension	67 (43%)	44 (50%)	0.3
Diabetes mellitus	35 (22%)	21 (24%)	0.8
Cigarette smoker	45 (29%)	21 (24%)	0.4
Lipid profiles at baseline (mg/dl)			
Total cholesterol	172 ± 35	170 ± 39	0.7
HDL cholesterol	42 ± 11	45 ± 15	0.08
LDL cholesterol	104 ± 33	94 ± 29	0.07
Triglycerides	163 ± 130	156 ± 88	0.6
C-reactive protein (mg/dl)	0.4 ± 0.7	0.3 ± 0.5	0.5
ACS	64 (41%)	14 (16%)	<0.001
No. of narrowed coronary arteries			0.5
1	105 (67%)	64 (73%)	
2	36 (23%)	19 (22%)	
3	15 (10%)	5 (5%)	

Abbreviations as in Table 1.

Table 7
Virtual histology intravascular ultrasound findings between non–ST-segment elevation myocardial infarction or unstable angina pectoris and ST-segment-elevation myocardial infarction

Variable	Non–ST-Segment Elevation Myocardial Infarction/Unstable Angina Pectoris (n = 69)	ST-Segment Elevation Myocardial Infarction (n = 54)	p Value
Minimum luminal area site			
Absolute areas (mm^2)			
Fibrotic (green)	5.1 ± 2.7	5.6 ± 2.7	0.3
Fibrofatty (yellow-green)	0.5 ± 0.5	0.6 ± 0.6	0.3
Dense calcium (white)	0.9 ± 0.8	0.8 ± 0.6	0.5
Necrotic core (red)	3.1 ± 2.1	3.2 ± 1.8	0.8
Percentages			
Fibrotic	52 ± 17	55 ± 13	0.3
Fibrofatty	5 ± 5	6 ± 6	0.2
Dense calcium	10 ± 9	8 ± 5	0.102
Necrotic core	34 ± 15	32 ± 13	0.5
Largest necrotic core site			
Absolute areas (mm^2)			
Fibrotic	5.1 ± 5.3	4.9 ± 2.3	0.8
Fibrofatty	0.4 ± 0.4	0.4 ± 0.4	0.2
Dense calcium	1.0 ± 0.7	0.8 ± 0.7	0.192
Necrotic core	3.4 ± 2.2	3.3 ± 1.7	0.7
Percentages			
Fibrotic	49 ± 16	51 ± 13	0.3
Fibrofatty	4 ± 4	5 ± 5	0.186
Dense calcium	11 ± 8	8 ± 6	0.06
Necrotic core	37 ± 14	35 ± 12	0.6
Volumetric analysis			
Absolute volumes (mm^3)			
Fibrotic	38.0 ± 20.2	46.8 ± 24.3	0.03
Fibrofatty	3.9 ± 3.7	5.8 ± 5.2	0.025
Dense calcium	6.6 ± 5.2	6.0 ± 5.0	0.5
Necrotic core	20.5 ± 13.5	20.1 ± 11.6	0.9
Percentages			
Fibrotic	54 ± 14	58 ± 12	0.072
Fibrofatty	6 ± 5	7 ± 6	0.076
Dense calcium	10 ± 7	8 ± 6	0.136
Necrotic core	31 ± 12	26 ± 11	0.054

ing) and quantifies atherosclerotic plaque area and volume and plaque burden, more recent studies have suggested that gray-scale IVUS has limited value for the identification of specific plaque components.[4–6,13,14]

Spectral analysis (i.e., VH-IVUS) has the potential to provide detailed qualitative and quantitative information; the identification of 4 specific plaque components has been validated in explanted human coronary segments as well as in retrieved directional coronary atherectomy specimens.[5,15] We applied these histologically validated VH-IVUS findings to real clinical practice and compared coronary plaque composition between patients with ACS and those with SAP. The amounts of necrotic core were larger and the amounts of fibrotic and fibrofatty plaque were less in patients with ACS. The results of the present study are similar to those of a previous pathologic study showing larger necrotic cores in TCFAs compared with stable plaques (24% vs 12%, $p = 0.01$).[3]

The rupture of a vulnerable plaque and subsequent thrombus formation are the most important mechanisms leading to ACS.[1–3] Retrospective pathologic studies of patients with coronary artery disease who died suddenly showed culprit lesion plaque rupture in about 70% of patients.[1,2,16] IVUS studies have reported a 16% to 66% incidence of plaque rupture in the culprit lesions of patients with ACS.[8,17,18] Wide variation in the incidence of ruptured plaque might be partly related to different clinical presentations, different study populations, different lesion segments (culprit vs nonculprit lesions), and different resolution powers of IVUS catheters (a 20-MHz phased-array transducer vs a rotating 30- or 40-MHz transducer). In the present study, ruptured plaques detected with gray-scale IVUS were more common in patients with ACS than in those with SAP, and most patients with ACS had unstable lesion morphology. Several pathologic studies have suggested that TCFAs are particularly prone to rupture and result in acute coronary artery occlusions.[1–3] Using a VH-IVUS definition of TCFA similar to the one used in the present study, Rodriguez-Granillo et al[6] reported that 23 patients with ACS had a significantly higher prevalence of VH-TCFAs in secondary, nonobstructive lesions (diameter stenosis <50%) compared with 32 patients with SAP. In the present study, primary lesions (lesions targeted for intervention) were also more often unstable in patients with ACS than in those with SAP.

A previous pathologic study showed that the percentage of necrotic core was significantly larger in ruptured plaques than in TCFAs.[3] There are 2 explanations why this was not seen in the present study. VH-IVUS cannot identify the thrombus that commonly follows plaque rupture. It most often appears "green" and is classified as fibrotic plaque, reducing the calculated relative size of the necrotic core. In addition, we studied lesions after rupture, after the necrotic core may have embolized.

The present study also detected ruptured plaques in 15% of target lesions in patients with SAP (similar to previous studies[7,8]) and VH-TCFAs in 47% of target lesions in patients with SAP. VH-TCFAs may stabilize without plaque rupture or clinical presentation. Unstable clinical symptoms may depend on the severity of the original and/or coexisting stenosis or on thrombus formation, not just on plaque rupture.[19] The relatively higher incidence of VH-TCFAs in patients with SAP in the present study compared with histologic reports may be partly explained by the different definitions of TCFA used and the different patient populations studied. However, it is interesting to speculate that the presence of unstable lesion morphology (ruptured plaque or VH-TCFA) may have contributed to the clinical progression to intervention-requiring symptoms in many of the patients with SAP in the present study.

This study was a single-center, retrospective study. VH-IVUS cannot determine the presence of thrombus. Total occlusions, bifurcation lesions, lesions with severe angulations, and heavily calcified lesions were excluded from this study. Therefore, this study might not represent the whole spectrum of patients with ACS and patients with SAP.

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