VH-IVUS Study

Clinical Implications and Correlations with Other Diagnostic Techniques

Asan Medical Center Experience

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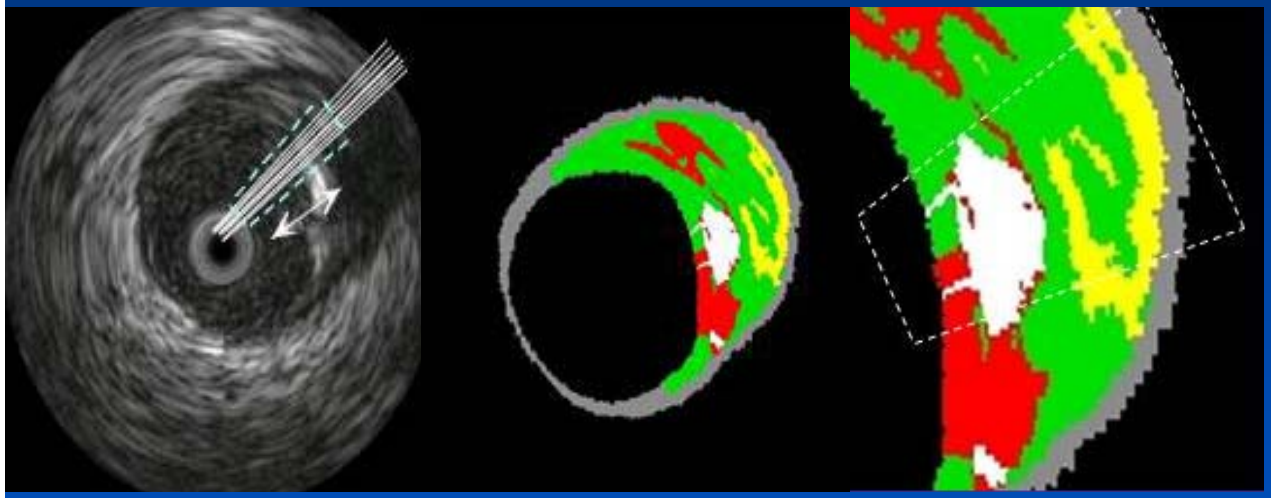
Background

- Accurate evaluation of plaque characteristics in the culprit or non-culprit lesions are the key determinant to predict the future clinical events.
- Gray-scale IVUS has several limitations in assessing plaque morphology and tissue compositions.
- VH analyses of the IVUS backscatter signals allows reliable plaque characterization into specific plaque types.

Virtual Histology -IVUS

In-vivo characterization of plaque composition via advanced spectral analysis



- Fibrous
- Fibro-fatty
- Necrotic
- Calcium

4 Major Components

VH-IVUS Study:
AMC Experience

- VH-IVUS & Clinical presentation
- Three-vessel VH-IVUS Study
- Distal Embolization
- VH Findings vs. Other Diagnostic Imaging

  : Comparison with OCT

VH-IVUS

Comparisons of Plaque Compositions Between SA and ACS: A VH-IVUS Analysis of Target/Culprit Lesions

In 318 patients.

(195 SAP and 123 ACS)

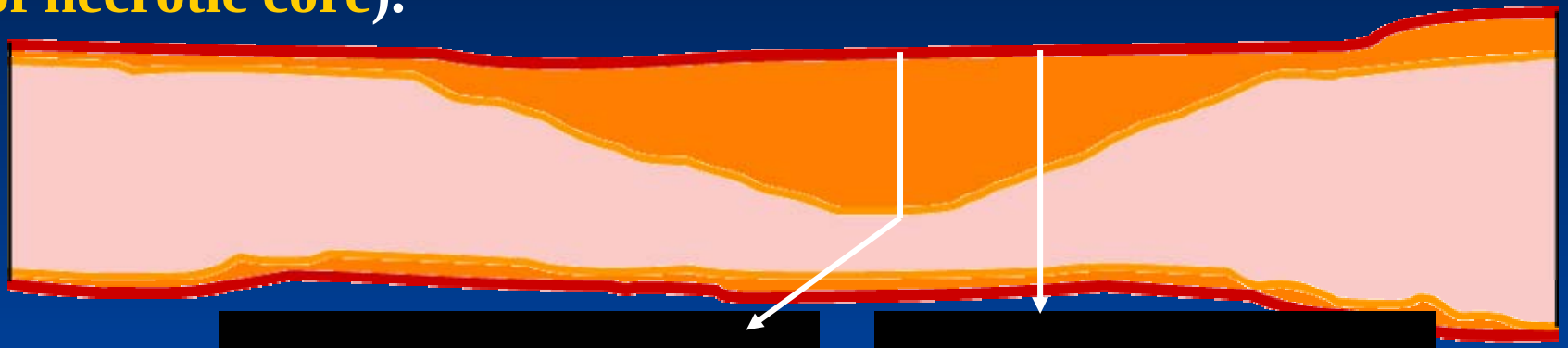
Hong et al. Am J Cardiol 2007;100:953-959

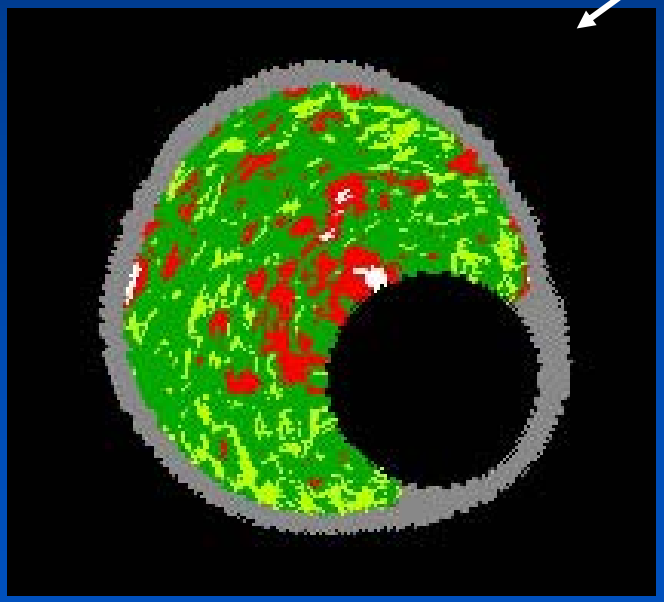
Exclusion criteria

- Long lesions (lesion length >30mm)
- Severely calcific lesions
- Totally occluded lesions
- Severely angulated lesions
- Bifurcation lesions
- In-stent restenosis lesion
- saphenous vein graft lesion

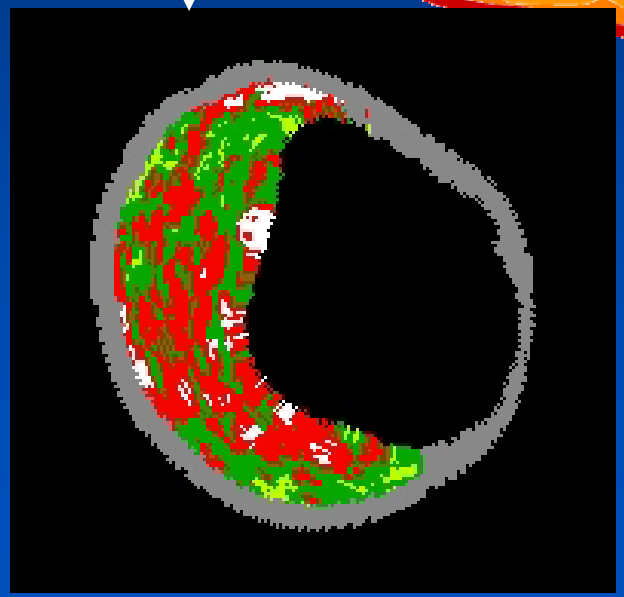
VH-IVUS Measurements

Planar VH-IVUS measurements were performed at 2 lesion segments (minimum lumen cross-sectional area and the largest of necrotic core).



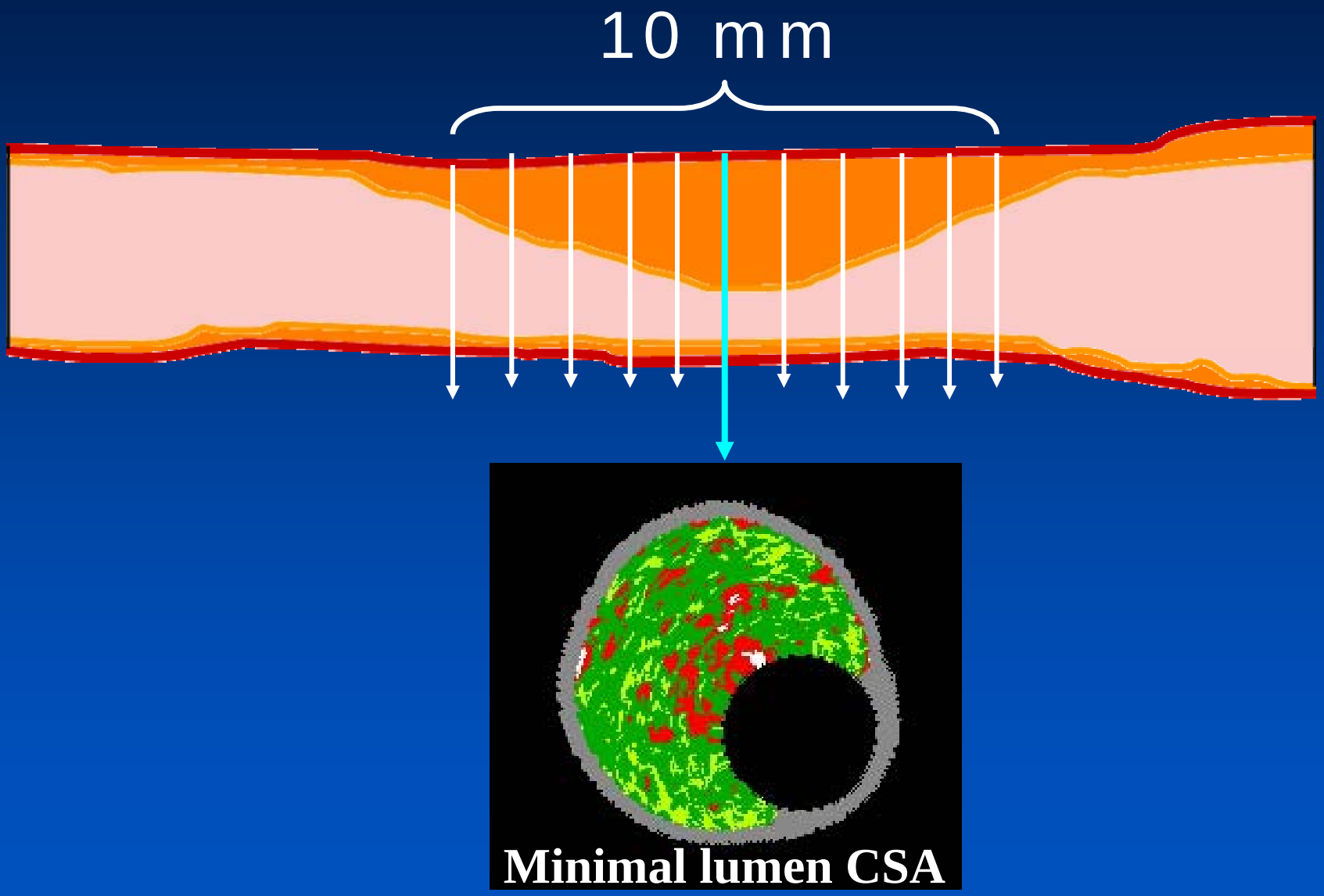


Minimal lumen CSA



Largest necrotic core burden

Volumetric VH-IVUS Analysis

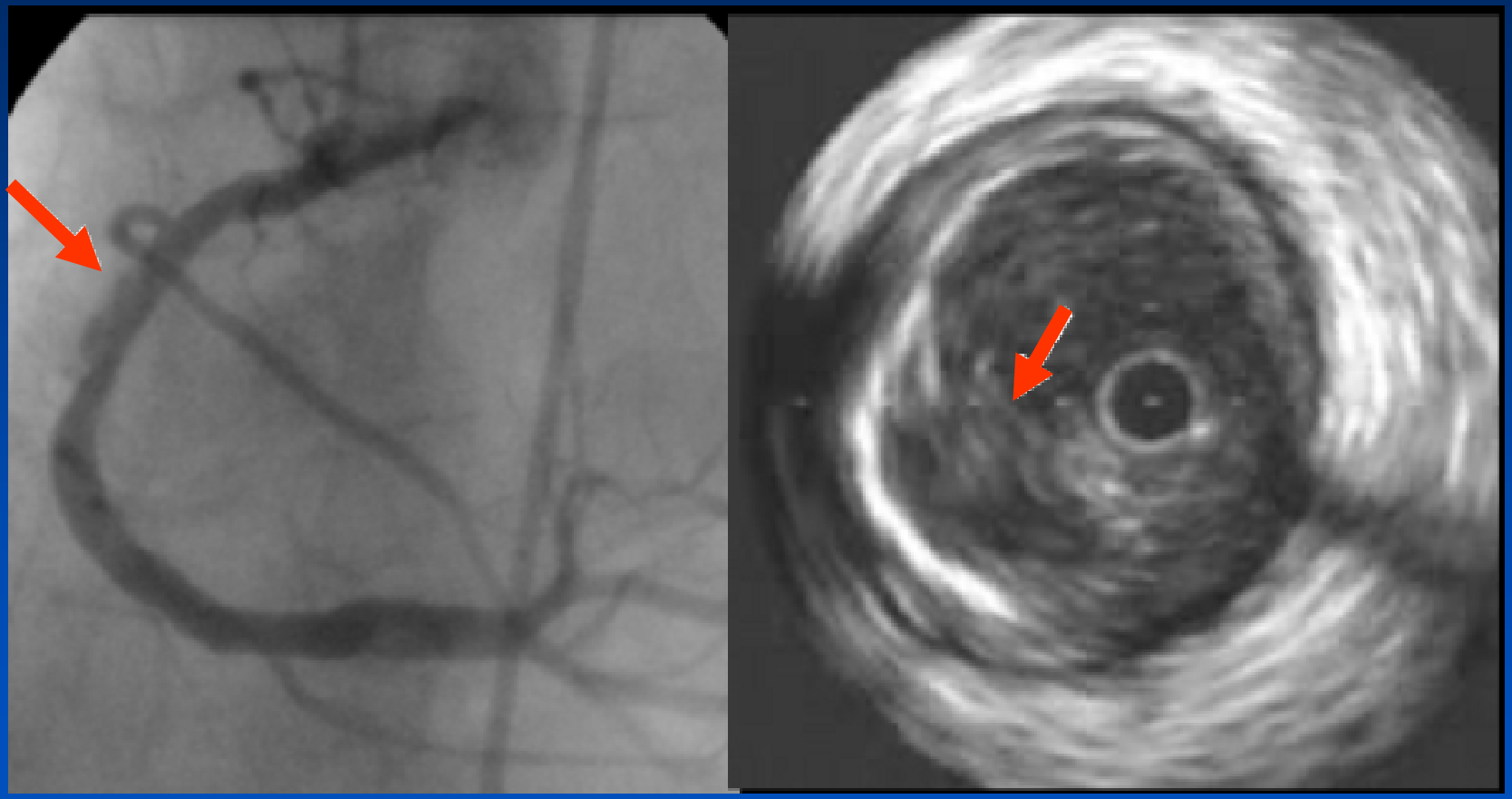


Plaque classification

- **Ruptured plaque**
- **Unruptured plaque**
  - **VH-TCFA plaque**
  - **Non-VH-TCFA plaque**

IVUS Definition of Plaque Rupture

A plaque with cavity that communicated with the lumen with an overlying residual fibrous cap fragment



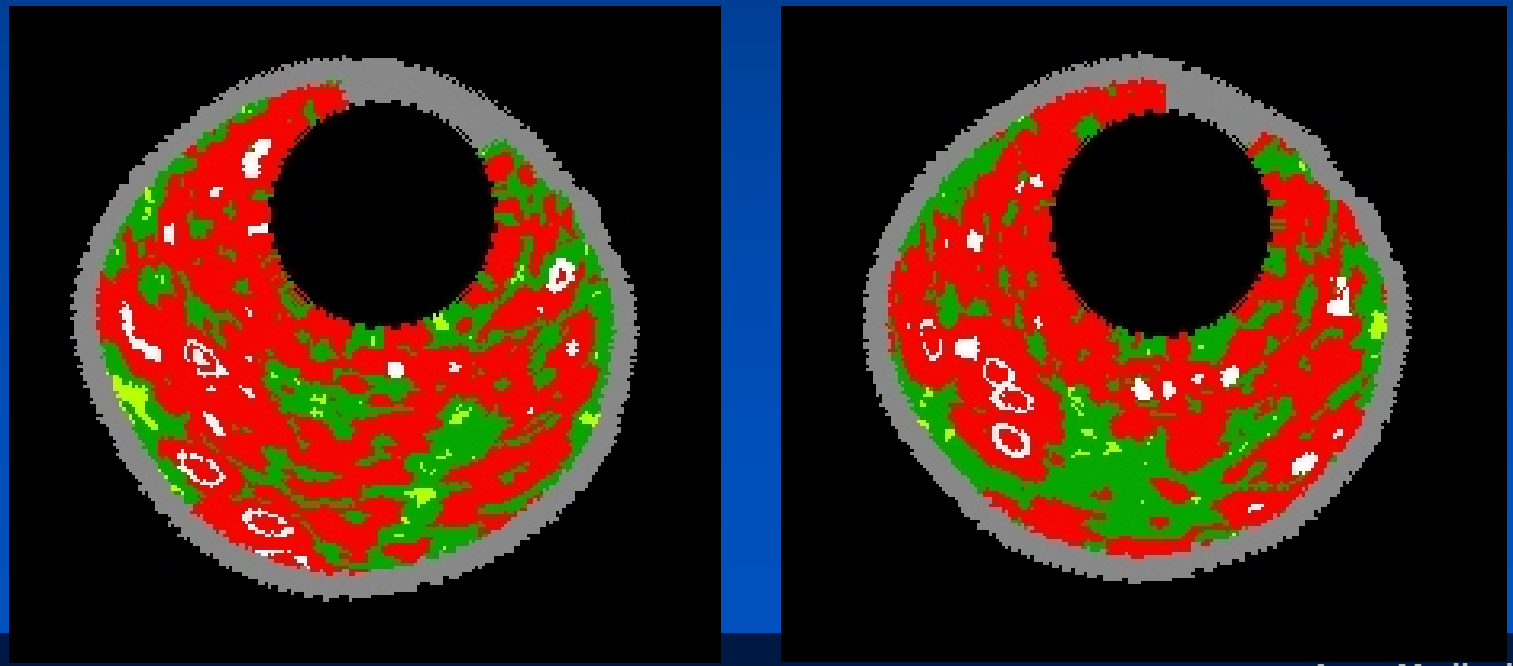
Thin-Cap FibroAtheroma (TCFA) by VH-IVUS

- In at least three consecutive frames:

1) necrotic core $\geq$ 10% without evident overlying fibrous tissue and

2) percent atheroma area $\geq$ 40%.

(Rodriguez-Granillo GA et al. *J Am Coll Cardiol* 2005;46:2038–42)



Baseline Characteristics

	ACS (n=123)	SAP (n=195)	*p*
Age (yrs)	59±11	60±9	0.7
Men	104 (85%)	126 (65%)	<0.001
Diabetes mellitus	22 (18%)	49 (25%)	0.131
Hypertension	47 (38%)	97 (50%)	0.044
Smoking	65 (53%)	38 (20%)	<0.001
No. of disease vessel			0.018
One vessel	71 (58%)	139 (71%)	
Two vessel	35 (28%)	44 (23%)	
Three vessel	17 (14%)	12 (6%)	

Baseline Characteristics

	ACS (n=123)	SAP (n=195)	*p*
Lipid profiles			
Total cholesterol (mg/dl)	185±42	168±35	<0.001
Triglyceride (mg/dl)	176±147	158±93	0.25
HDL-cholesterol (mg/dl)	39±11	44±13	0.004
LDL-cholesterol (mg/dl)	117±38	94±27	<0.001
hs-CRP level (mg/dl)	0.6±0.9	0.3±0.6	<0.001

Grey-scale IVUS

AMC-VH

	ACS (n=123)	SAP (n=195)	*p*
Minimum lumen area			
EEM CSA (mm^2)	17.1±4.5	15.0±4.5	<0.001
Lumen CSA (mm^2)	3.7±1.0	3.8±0.9	0.3
Plaque CSA (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 CSA (mm^2)	17.4±4.4	15.7±5.4	0.003
Lumen CSA (mm^2)	4.8±1.7	5.0±2.1	0.3
Plaque CSA (mm^2)	12.6±4.2	10.7±4.4	<0.001
Volumetric analysis			
EEM CSA (mm^3)	167.7±43.8	149.2±40.5	0.001
Lumen CSA (mm^3)	59.5±15.6	60.1±14.1	0.7
Plaque CSA (mm^3)	108.3±36.7	89.1±34.4	<0.001

VH-IVUS in minimum lumen area

	ACS (n=123)	SAP (n=195)	*p*
Absolute area (mm^2)			
Fibrotic	5.3±2.7	4.6±3.0	0.030
Fibrofatty	0.5±0.6	0.5±0.6	0.6
Dense calcium	0.8±0.7	0.6±0.6	0.001
Necrotic core	3.1±1.9	2.1±1.3	0.001
Percentage (%)			
Fibrotic	53±15	56±15	0.073
Fibrofatty	5±5	7±6	0.020
Calcific	9±7	8±8	0.4
Necrotic	33±14	29±14	0.015

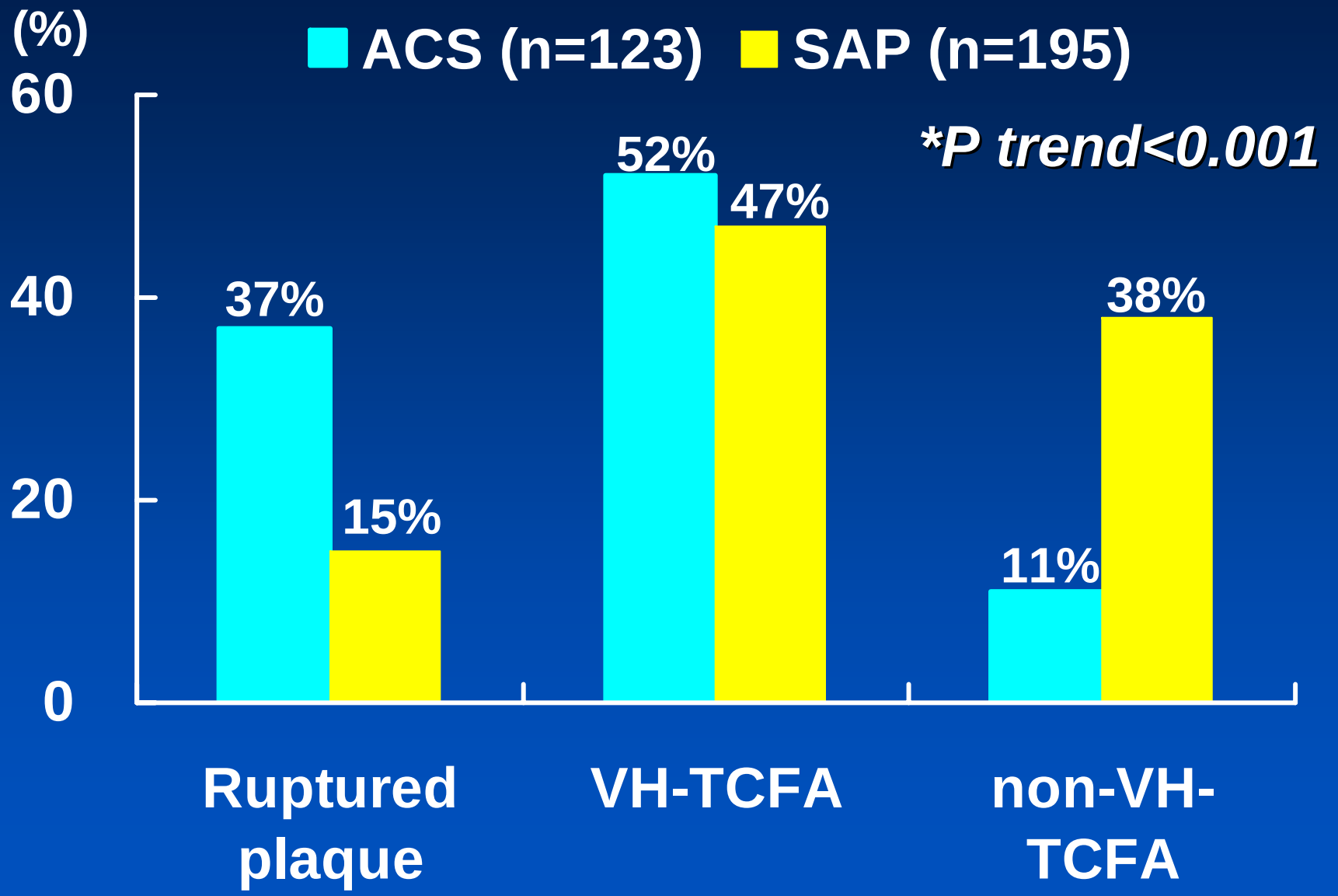
VH-IVUS in largest necrotic core

	ACS (n=123)	SAP (n=195)	*p*
Absolute area (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
Percentage (%)			
Fibrotic	50±15	53±15	0.105
Fibrofatty	4±4	5±5	0.024
Calcific	10±7	9±8	0.5
Necrotic	36±13	33±14	0.034

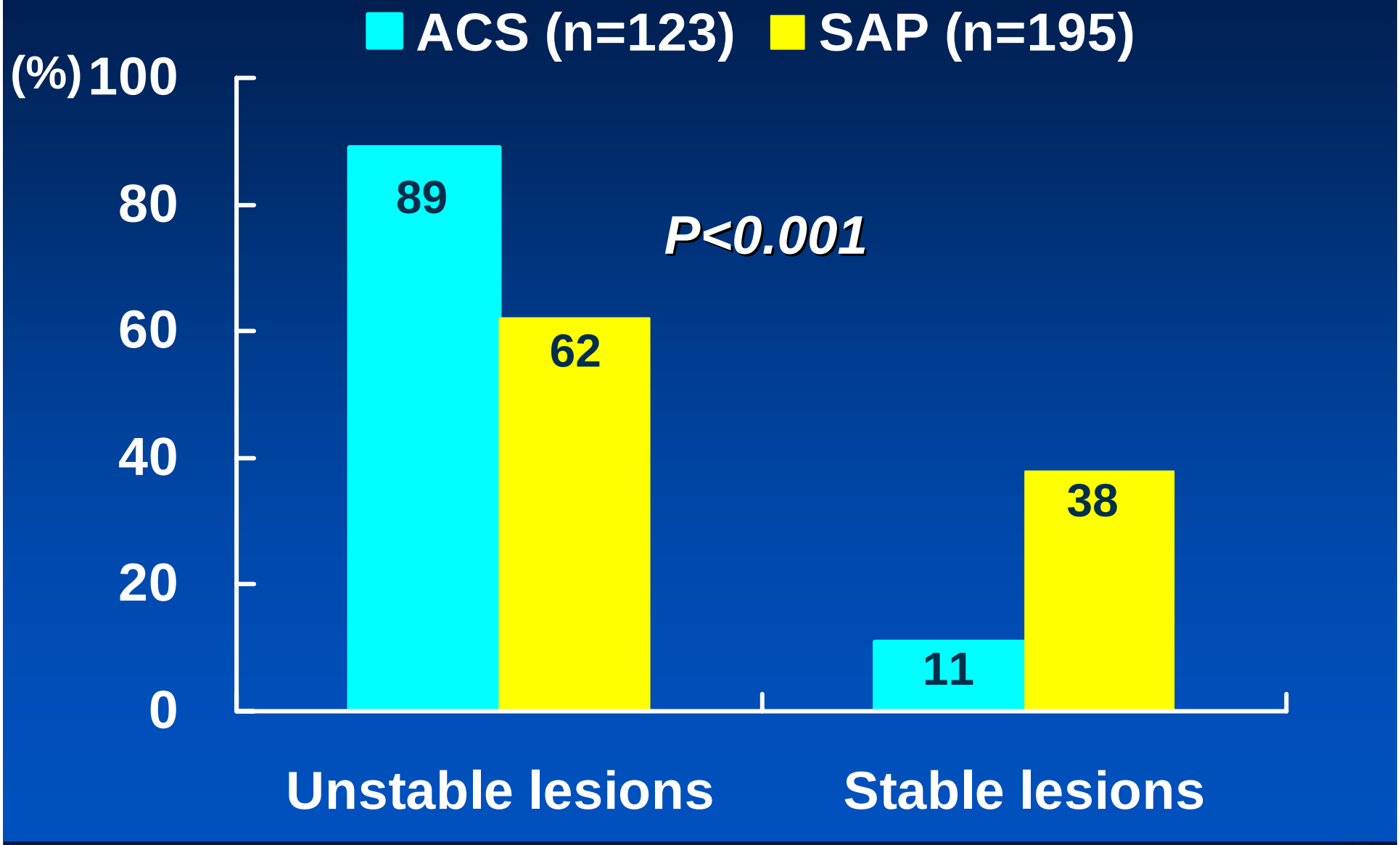
VH-IVUS in volumetric analysis

	ACS (n=123)	SAP (n=195)	*p*
Absolute area (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**
Percentage (%)			
Fibrotic	**56±13**	**57±13**	**0.3**
Fibrofatty	**6±5**	**8±5**	**0.045**
Calcific	**9±7**	**9±8**	**0.5**
Necrotic	**29±12**	**27±11**	**0.081**

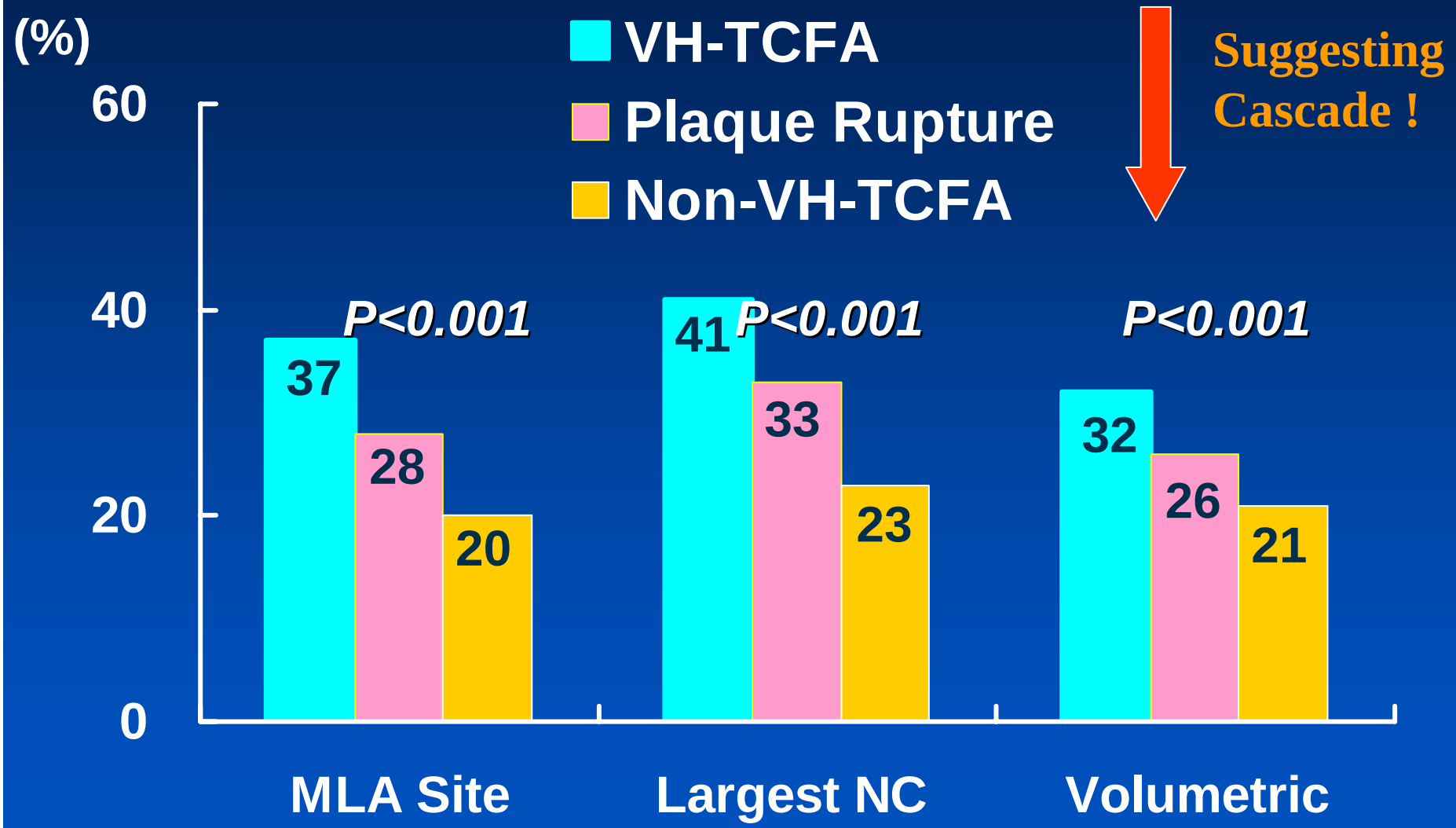
Percentages of VH-TCFAs



Unstable vs. Stable Plaques



Necrotic Component (%)



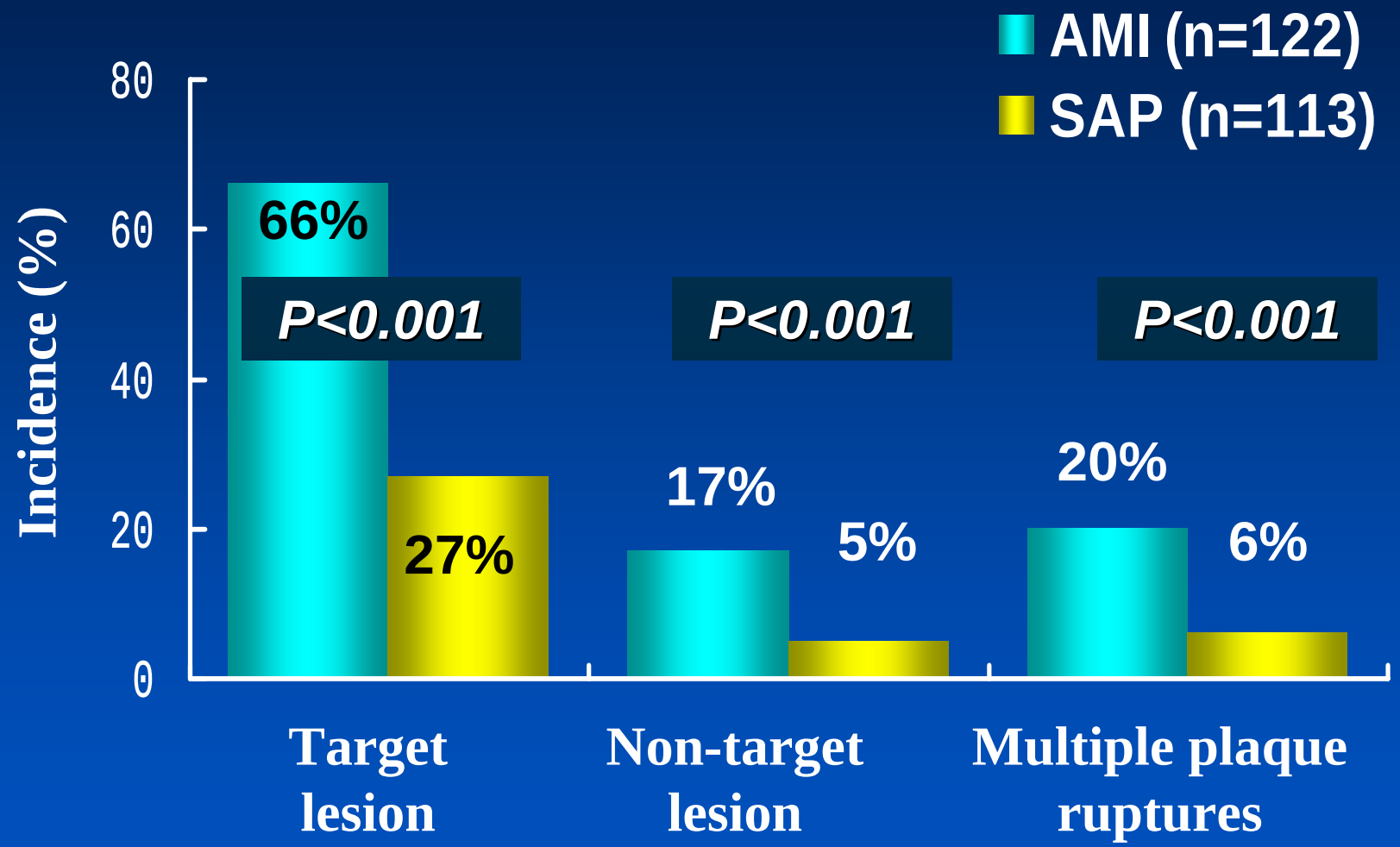
VH Study – SAP vs. ACS

- Larger area of necrotic core and smaller area of fibrotic and fibrofatty plaque were observed in the culprit lesions of ACS patients than in that of SAP patients.
- Unstable lesions (plaque rupture plus VH-TCFA lesions) were more frequently observed in ACS patients.
- The percentages of necrotic core areas and volumes were larger in VH-TCFAs compared with non-TCFAs. Ruptured plaques showed intermediate findings between VH-TCFAs and non–VH-TCFAs.

VH-TCFA

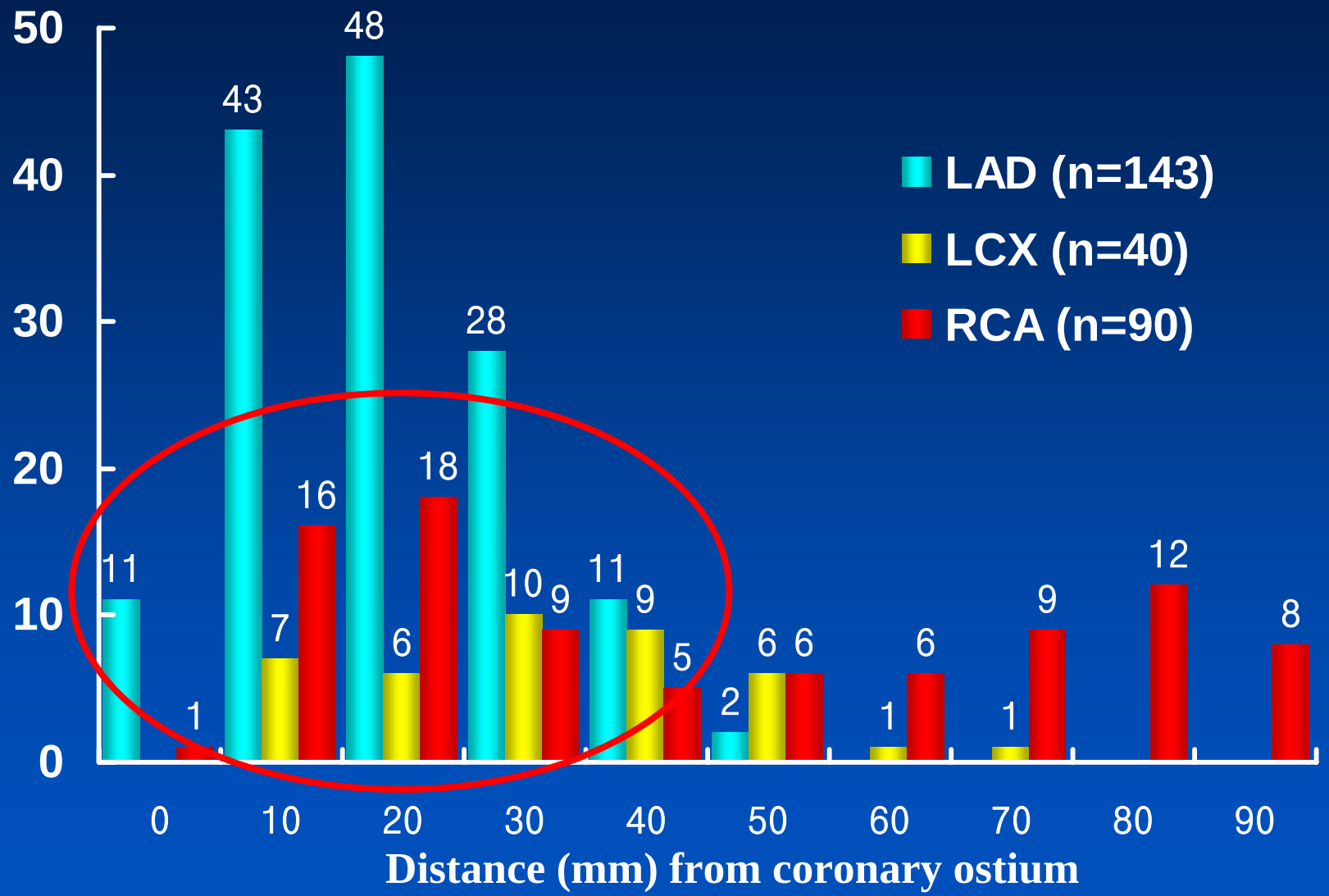
Three-vessel IVUS Study

Incidence of Plaque Rupture (3-Vessel IVUS Study)



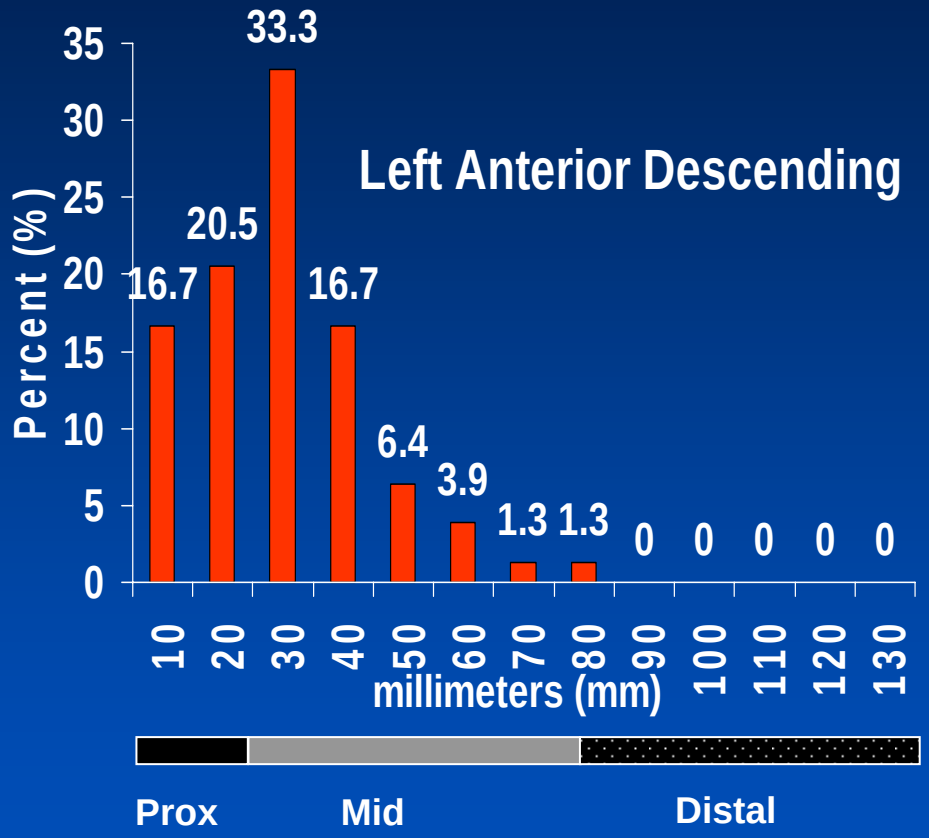
Hong MK, et al. Circulation 2004; 110: 928-933

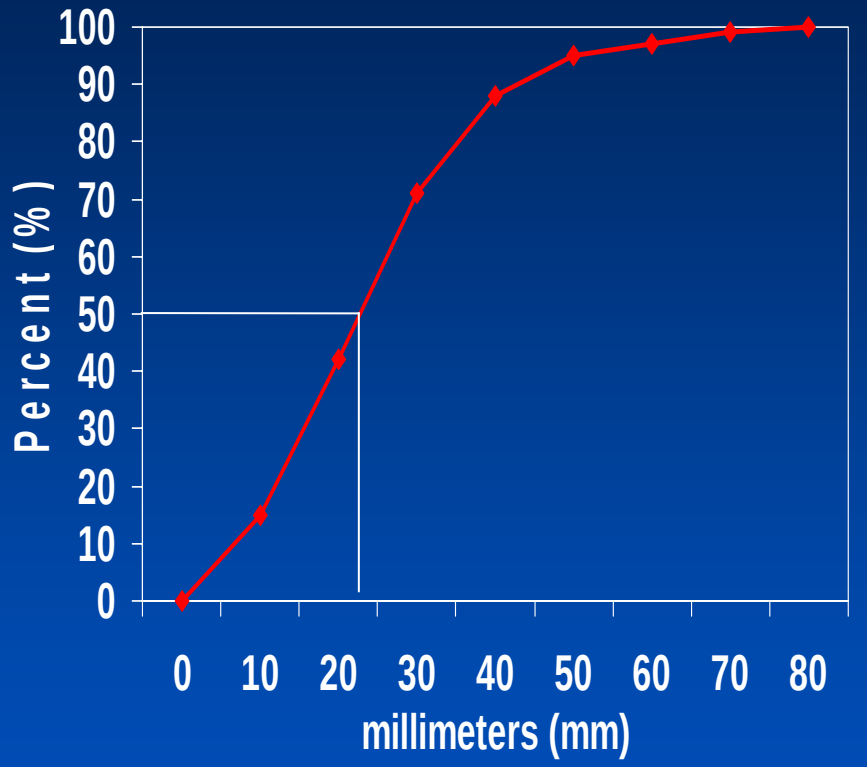
Location of 273 Plaque Rupture at Coronary Vessels in 158 ACS and 48 SA



MK Hong et al, J Am Coll Cardiol 2005; 46: 261-265

Anatomical Distribution of Lesions in 208 AMI patients





"Ruptured plaques tend to cluster in predictable "hot spots" within the proximal third of the arteries"

Wang, et al. *Circulation* 2004 Jul 20; 110(3)278-84

VH-TCFA

Three-vessel IVUS Study

Clustering of Ruptured Plaque and Thin-Cap Fibroatheroma: A 3-Vessel Virtual Histology Intravascular Ultrasound Analysis in 212 Patients

Hong et al. Am J Cardiol 2008;101:568-72

Study Populations

- From July 2005 to December 2006, 3-vessel pre-intervention VH-IVUS was attempted in 216 patients and was successful in 212 patients (105 with ACS and 107 with SAP) without any complications.

- The ACS group included 47 patients with unstable angina, 22 patients with NSTEMI, and 36 patients with STEMI.

Measured length by VH-IVUS

The total length of the coronary artery imaged by VH-IVUS was

72±16mm in the LAD,
54±12mm in the LCX, and
92±19mm in the RCA.

Baseline clinical characteristics

	ACS (n=105)	SAP (n=107)	p-value
Age (years)	60±11	60±10	0.9
Men, # (%)	90 (86)	80 (75)	0.046
Hypertension, # (%)	44 (42)	50 (47)	0.5
Diabetes mellitus, # (%)	20 (19)	24 (22)	0.5
Cigarette smoker, # (%)	54 (51)	27 (25)	<0.001
Number of narrowed coronary arteries, # (%)			0.11
1	66 (63)	80 (75)	
2	26 (25)	21 (20)	
3	13 (12)	6 (5)	

Baseline clinical characteristics

	ACS (n=105)	SAP (n=107)	p-value
Lipid profiles at baseline			
Total cholesterol (mg/dL)	182±38	170±34	0.024
HDL cholesterol (mg/dL)	41±13	46±15	0.015
LDL cholesterol (mg/dL)	112±36	94±28	<0.001
Triglycerides (mg/dL)	162±128	158±101	0.8
C-reactive protein (mg/dL)	0.6±1.0	0.2±0.2	0.001

Gray-scale IVUS findings of culprit/target lesions

	ACS (n=105)	SAP (n=107)	p-value
Minimum lumen area site			
EEM area (mm^2)	16.4 ± 4.2	14.9 ± 4.1	0.008
Lumen area (mm^2)	3.7 ± 0.7	3.8 ± 0.8	0.2
P&M area (mm^2)	12.8 ± 4.2	11.1 ± 3.9	0.003
Remodeling index	1.06 ± 0.17	0.99 ± 0.18	0.010
Largest necrotic core site			
EEM area (mm^2)	16.9 ± 4.2	15.5 ± 4.4	0.017
Lumen area (mm^2)	4.4 ± 1.2	4.7 ± 1.7	0.13
P&M area (mm^2)	12.5 ± 4.2	10.8 ± 3.8	0.002

VH-IVUS findings of culprit/target lesions at MLA site

	ACS (n=105)	SAP (n=107)	p-value
Absolute areas (mm^2)			
Fibrotic	4.9 ± 2.6	4.2 ± 2.5	0.059
Fibrofatty	0.4 ± 0.5	0.5 ± 0.5	0.133
Dense calcium	0.8 ± 0.7	0.6 ± 0.8	0.086
Necrotic core	3.1 ± 1.5	2.3 ± 1.2	<0.001
Percentages (%)			
Fibrotic	51 ± 15	53 ± 15	0.3
Fibrofatty	4 ± 4	6 ± 6	0.002
Dense calcium	9 ± 8	9 ± 8	0.8
Necrotic core	35 ± 12	32 ± 13	0.031

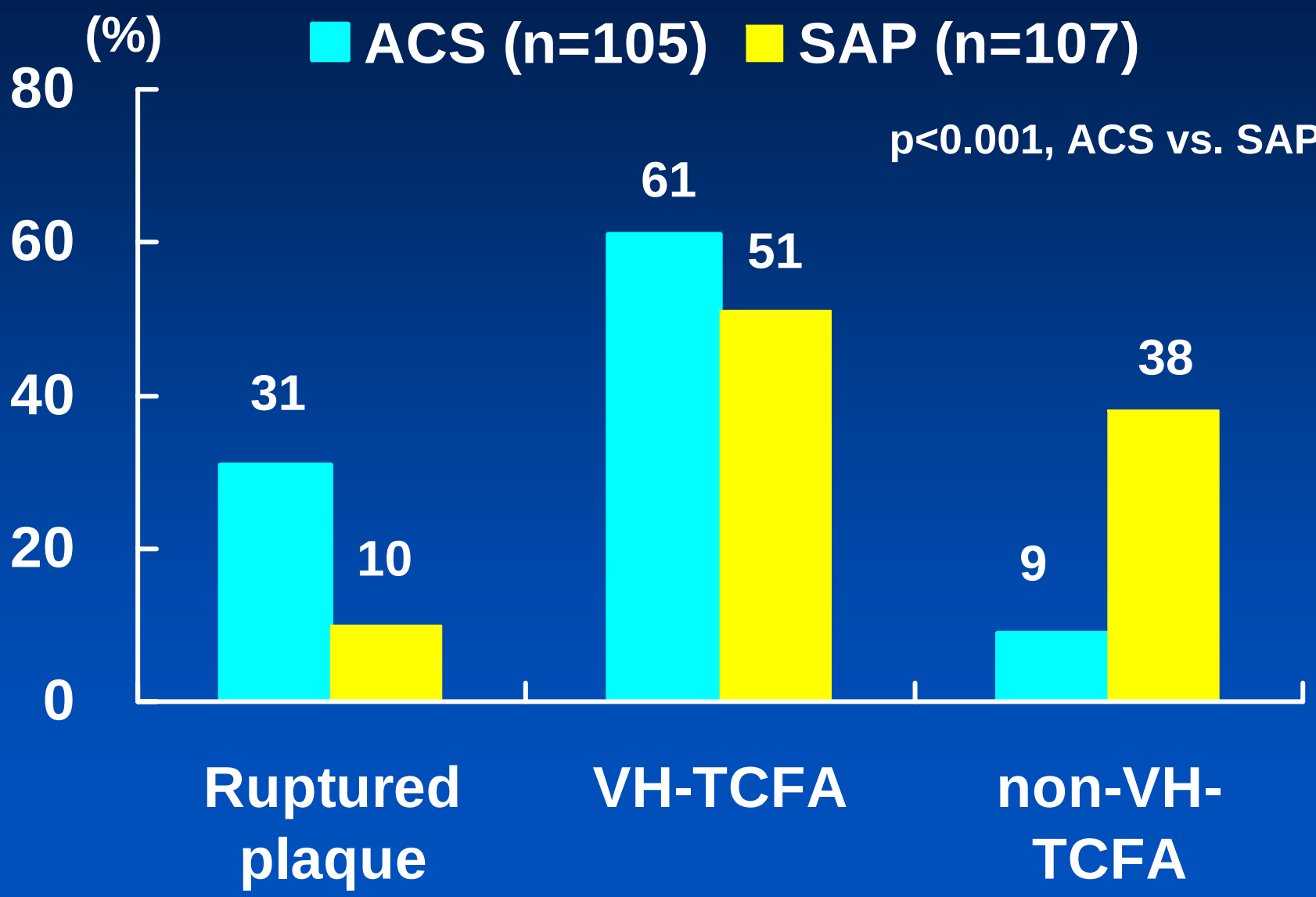
VH-IVUS findings of culprit/target lesions at Largest NC site

	ACS (n=105)	SAP (n=107)	p-value
Absolute areas (mm^2)			
Fibrotic	4.9 ± 4.6	4.0 ± 2.3	0.066
Fibrofatty	0.4 ± 0.4	0.5 ± 0.5	0.149
Dense calcium	0.9 ± 0.8	0.6 ± 0.6	0.004
Necrotic core	3.5 ± 1.7	2.5 ± 1.4	<0.001
Percentages (%)			
Fibrotic	48 ± 14	52 ± 14	0.067
Fibrofatty	4 ± 4	5 ± 6	0.005
Dense calcium	10 ± 8	9 ± 7	0.180
Necrotic core	38 ± 11	34 ± 13	0.018

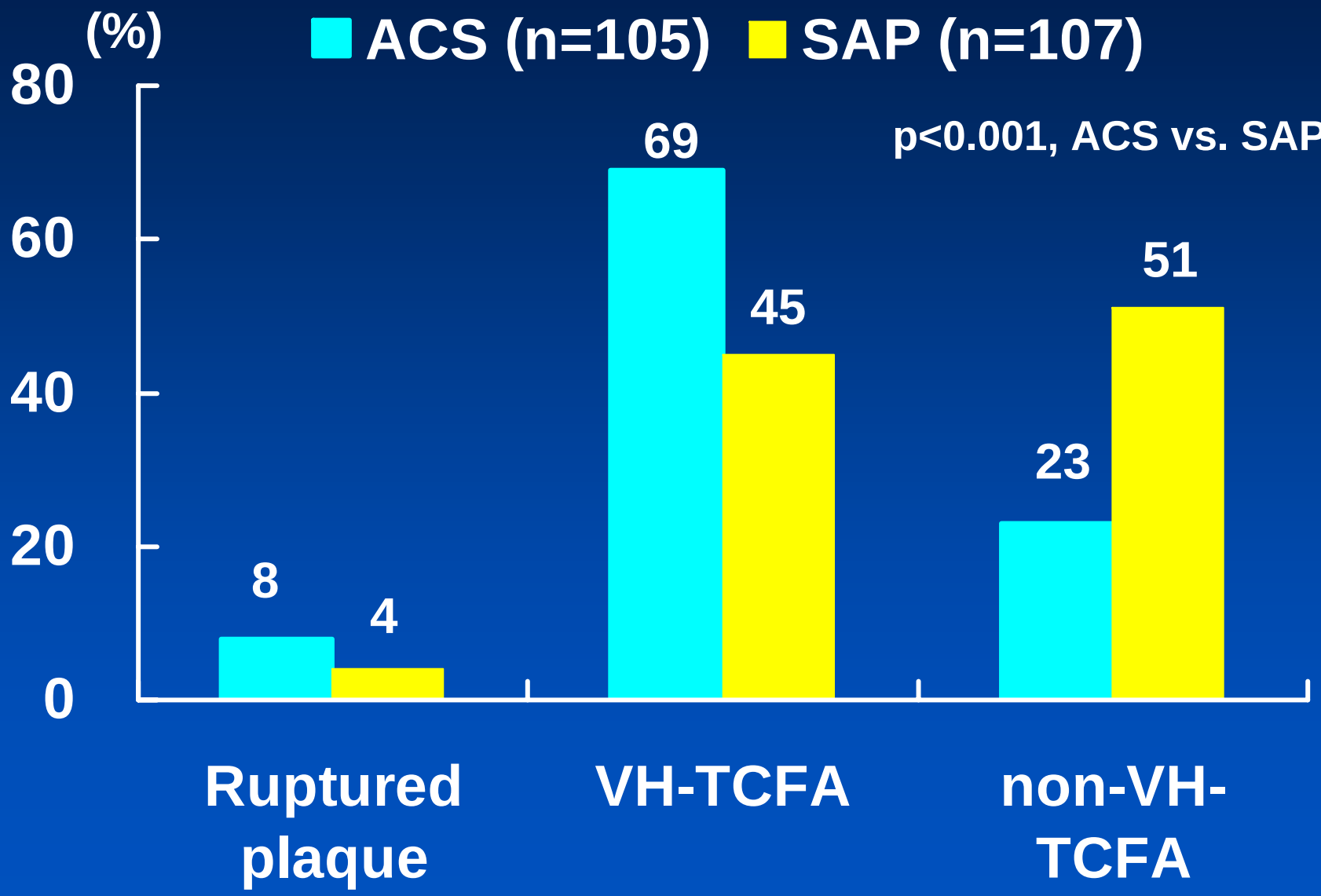
Total Number of Plaque

	Total (n=212)	ACS (n=105)	SAP (n=107)
Ruptured plaque	76	55	21
VH-TCFA	439	262	177
Non-VH-TCFA	252	75	177

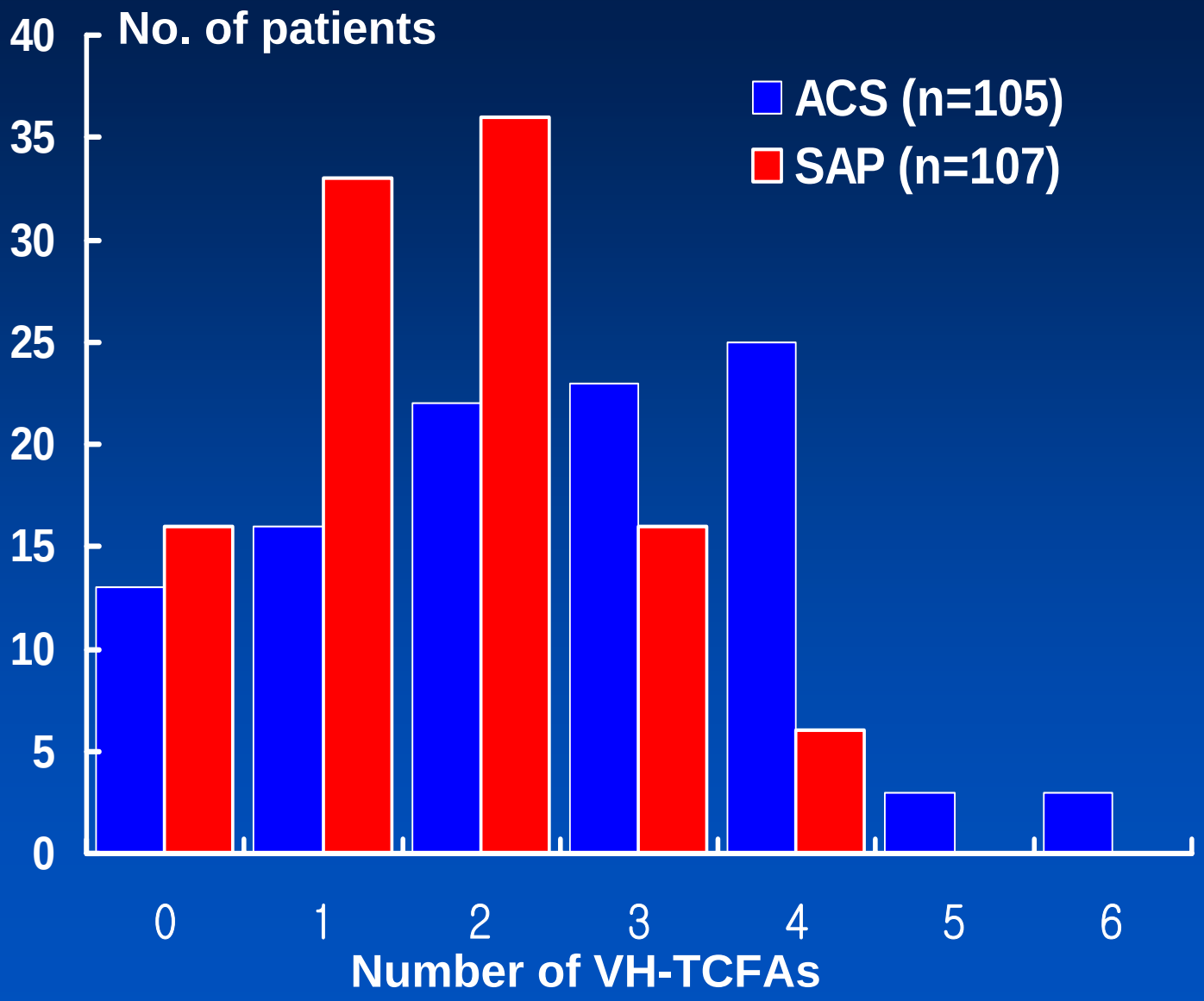
Culprit/target lesions



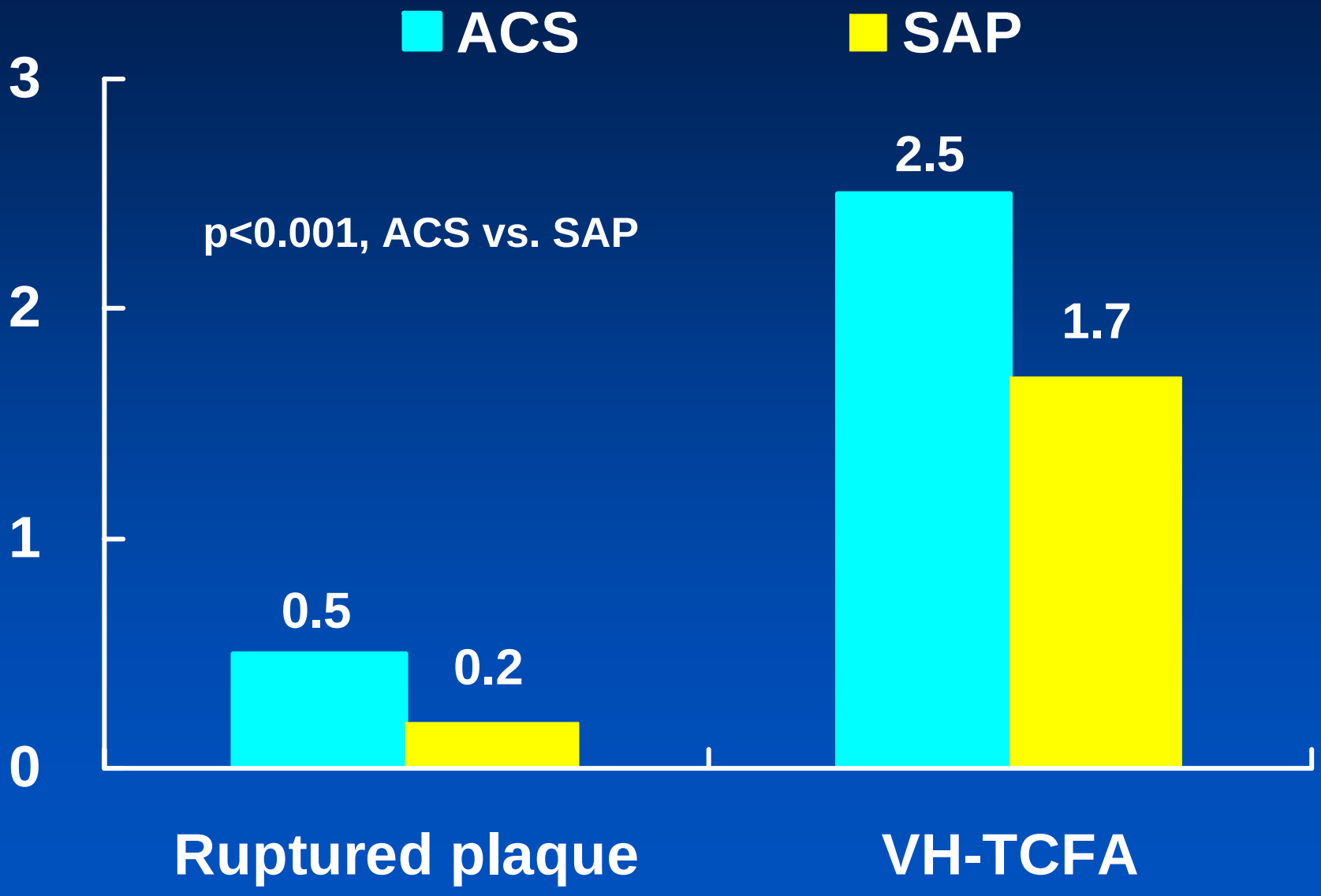
Non-culprit/non-target lesions



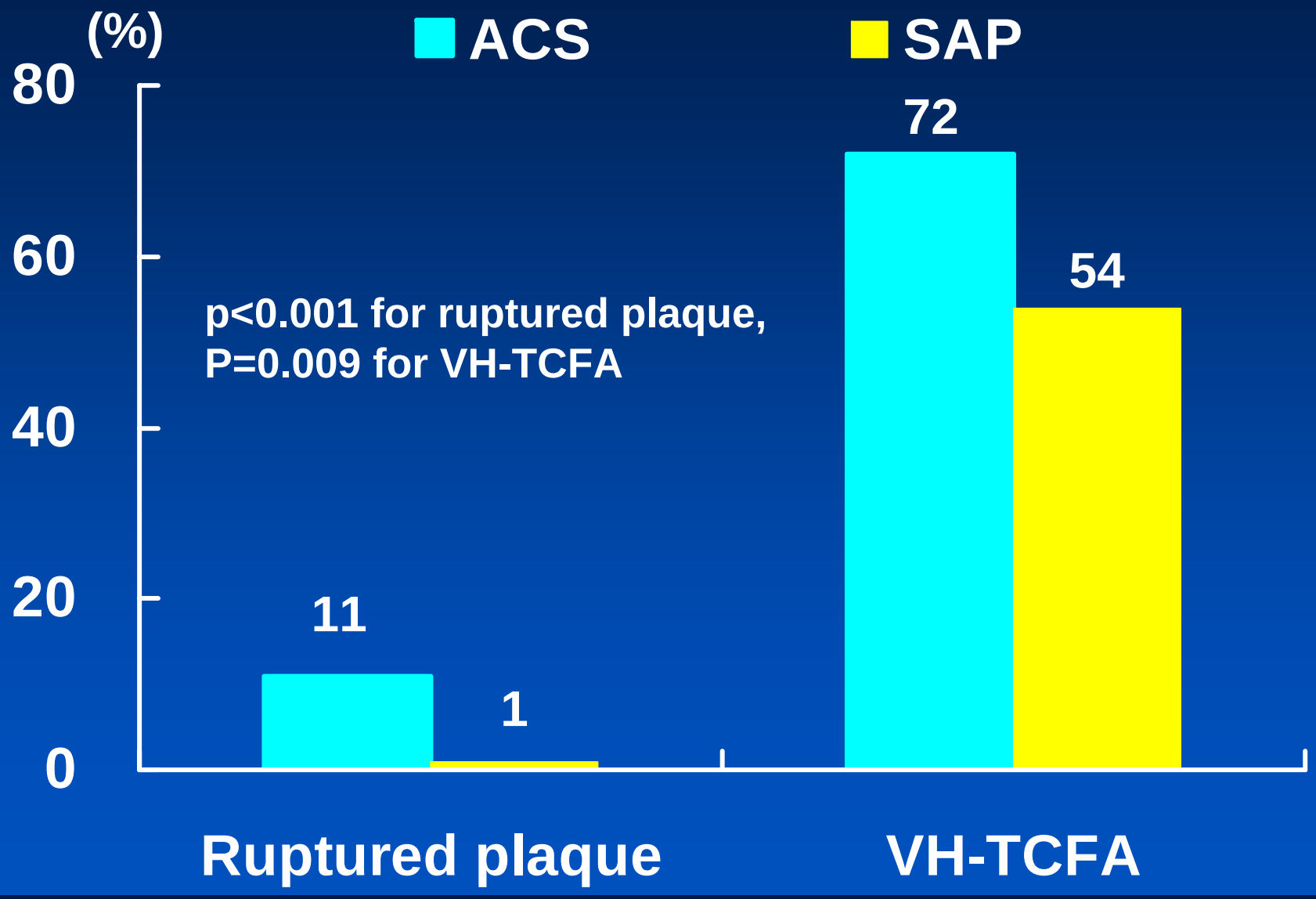
Frequency distribution of VH-TCFA



Average number of ruptured plaque and VH-TCFA



Multiple ruptured plaque and VH-TCFA

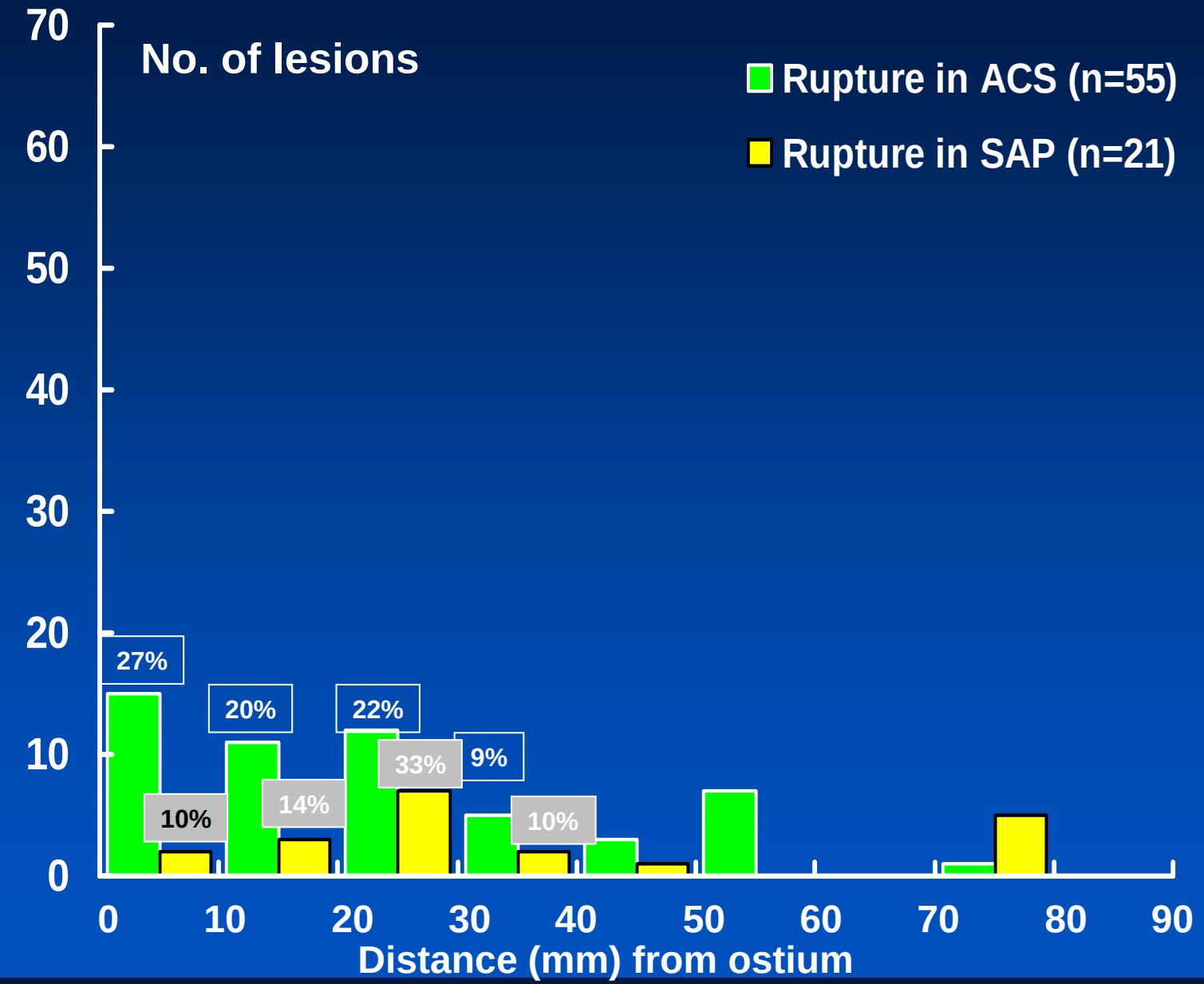


Independent clinical predictors

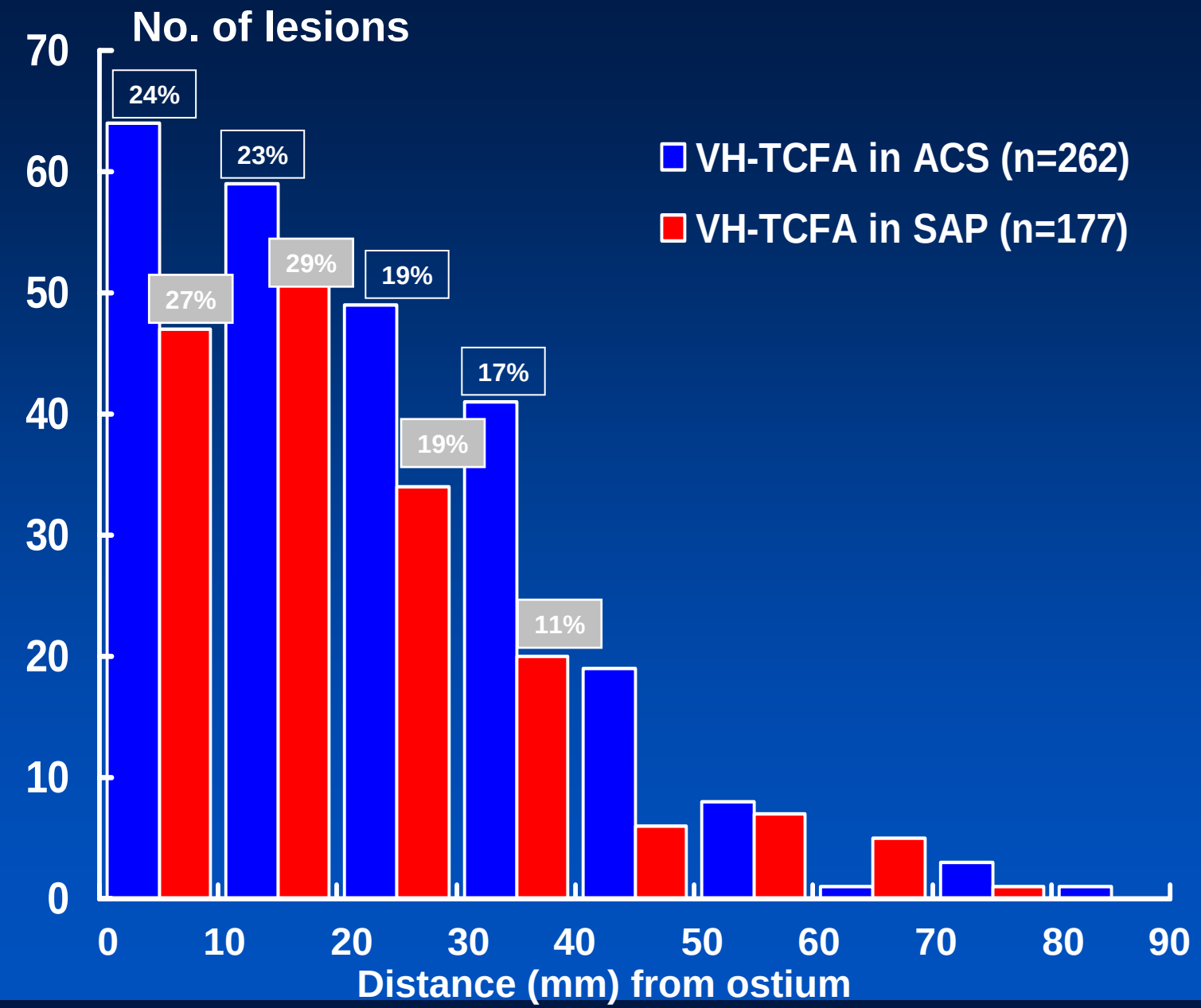
- **ACS presentation was the only independent clinical predictor for multiple ruptured plaques (p=0.013, OR=13.67, 95% CI=1.75 to 107.12).**

- **ACS was also the only independent clinical predictor for multiple VH-TCFAs (p=0.011, OR=2.18, 95% CI=1.20 to 3.97).**

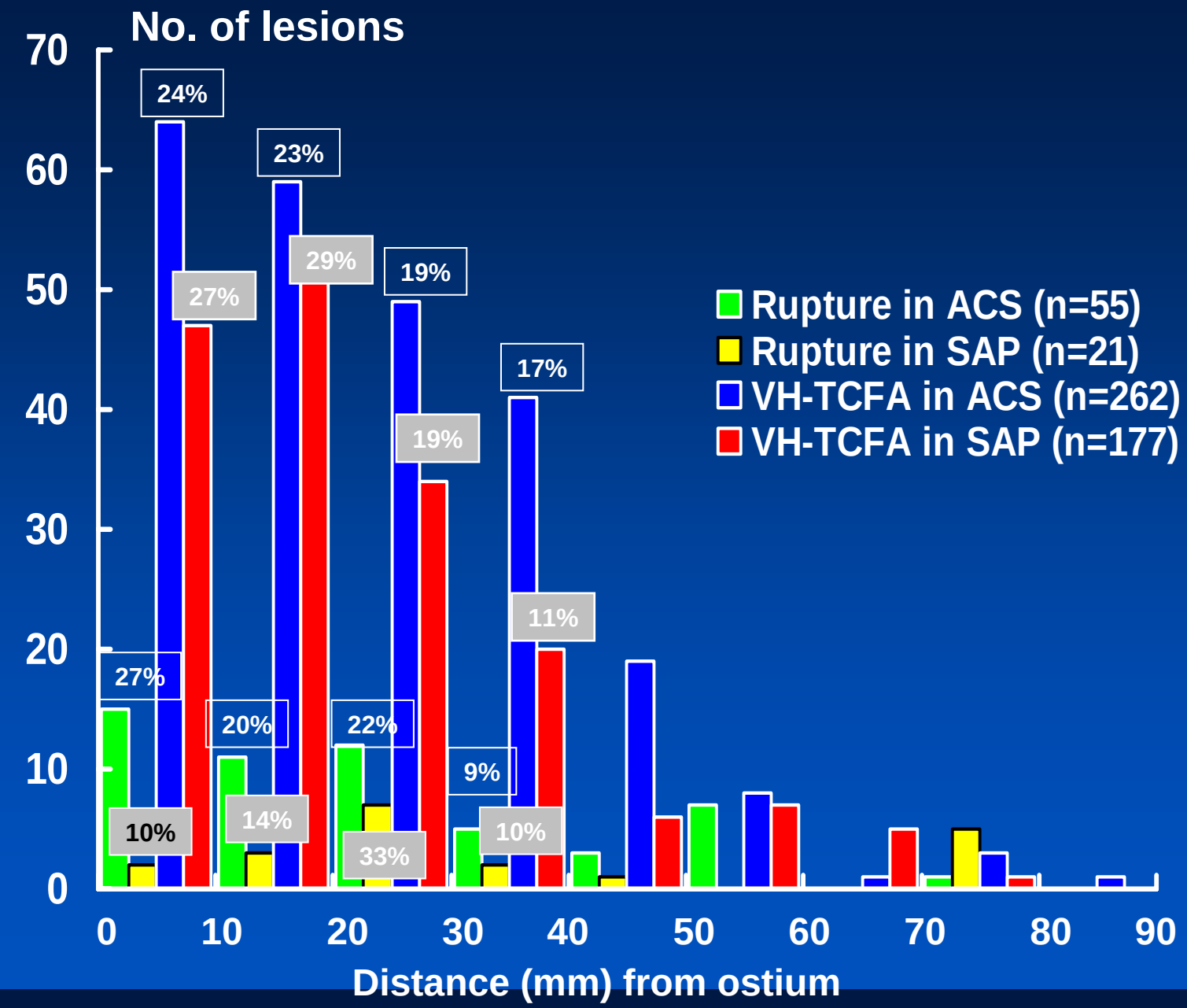
Axial distribution of ruptured plaque



Axial distribution of VH-TCFA



Axial distribution of VH-TCFA/ruptured plaque



Conclusions

The current 3-vessel VH-IVUS analysis of 212 patients (105 with ACS and 107 with SAP) showed a greater frequency of ruptured plaques, VH-TCFAs, multiple ruptured plaques, and multiple VH-TCFAs in ACS patients compared to SAP patients.

Ruptured plaques and VH-TCFAs were clustered in the first 40mm of each coronary artery in both ACS and SAP patients

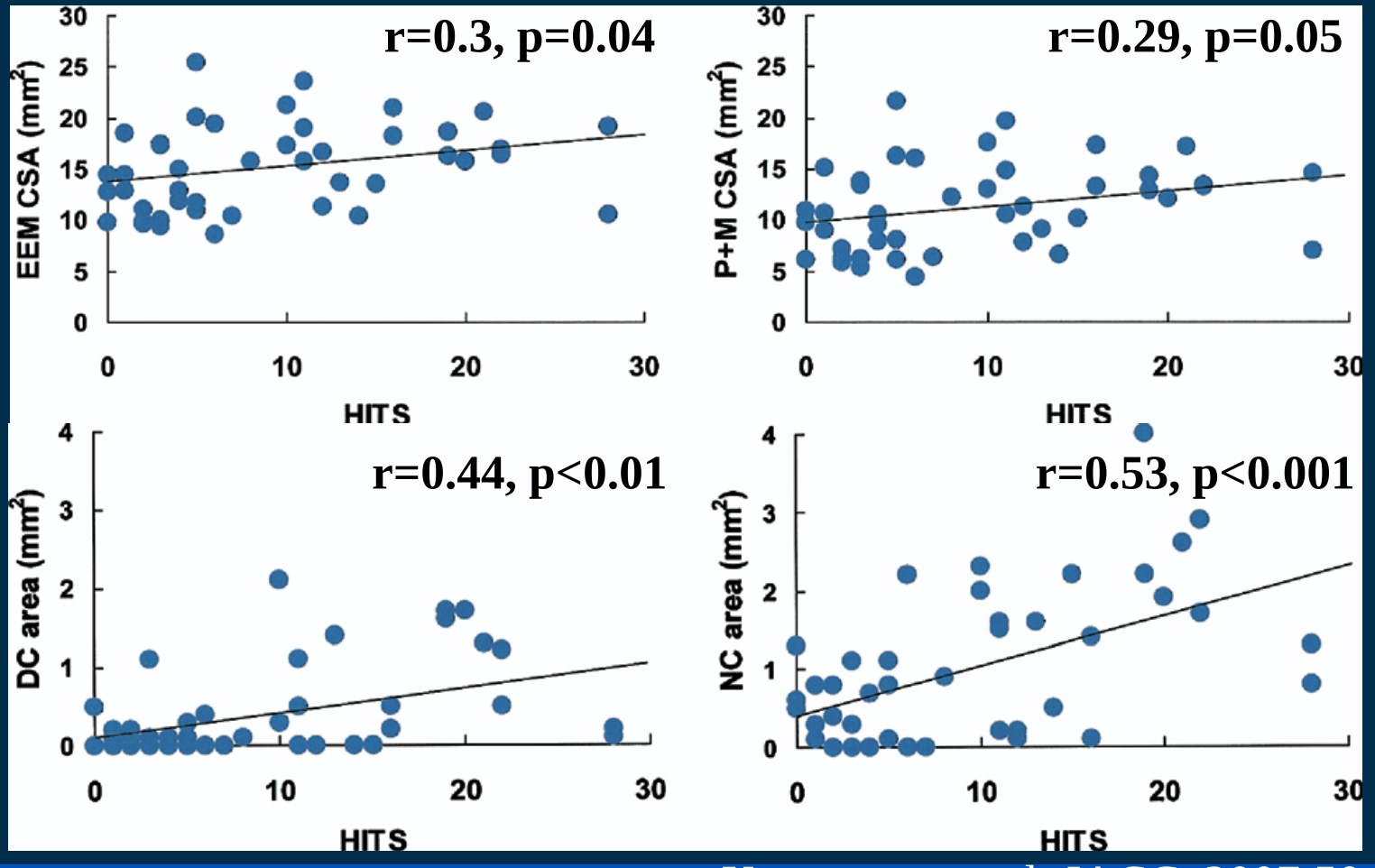
VH-IVUS

Relationship between Coronary Plaque Composition and Distal Embolization

Park et al. VH Summit 2007

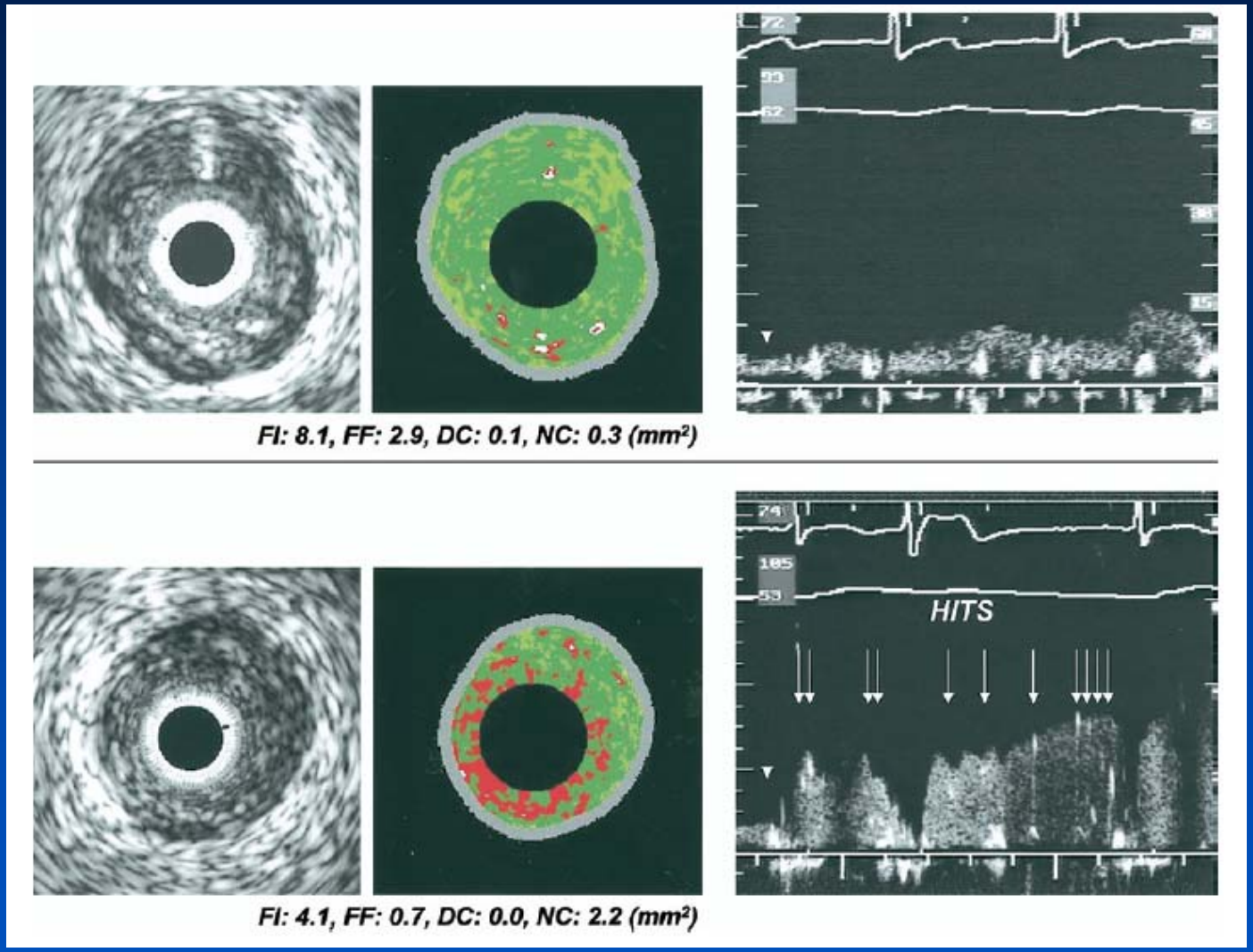
VH parameters & HITS with a Doppler wire

****HITS (high-intensity transient signals) represents small embolic particles**



Kawamoto, et al. JACC. 2007;50:1635-40

Representative Case



Non-HITS

HITS

Kawamoto, et al. JACC. 2007;50:1635-40

Independent predictors of the highest HITS count tertile by multivariate analysis

	OR	95% CI	p
EEM CSA, mm^2	1.21	0.25-5.73	0.813
P+M CSA, mm^2	0.81	0.17-3.90	0.788
Dense calcium, mm^2	1.25	0.22-7.21	0.804
Necrotic core, mm^2	4.41	1.03-18.81	0.045

Kawamoto, et al. JACC. 2007;50:1635-40

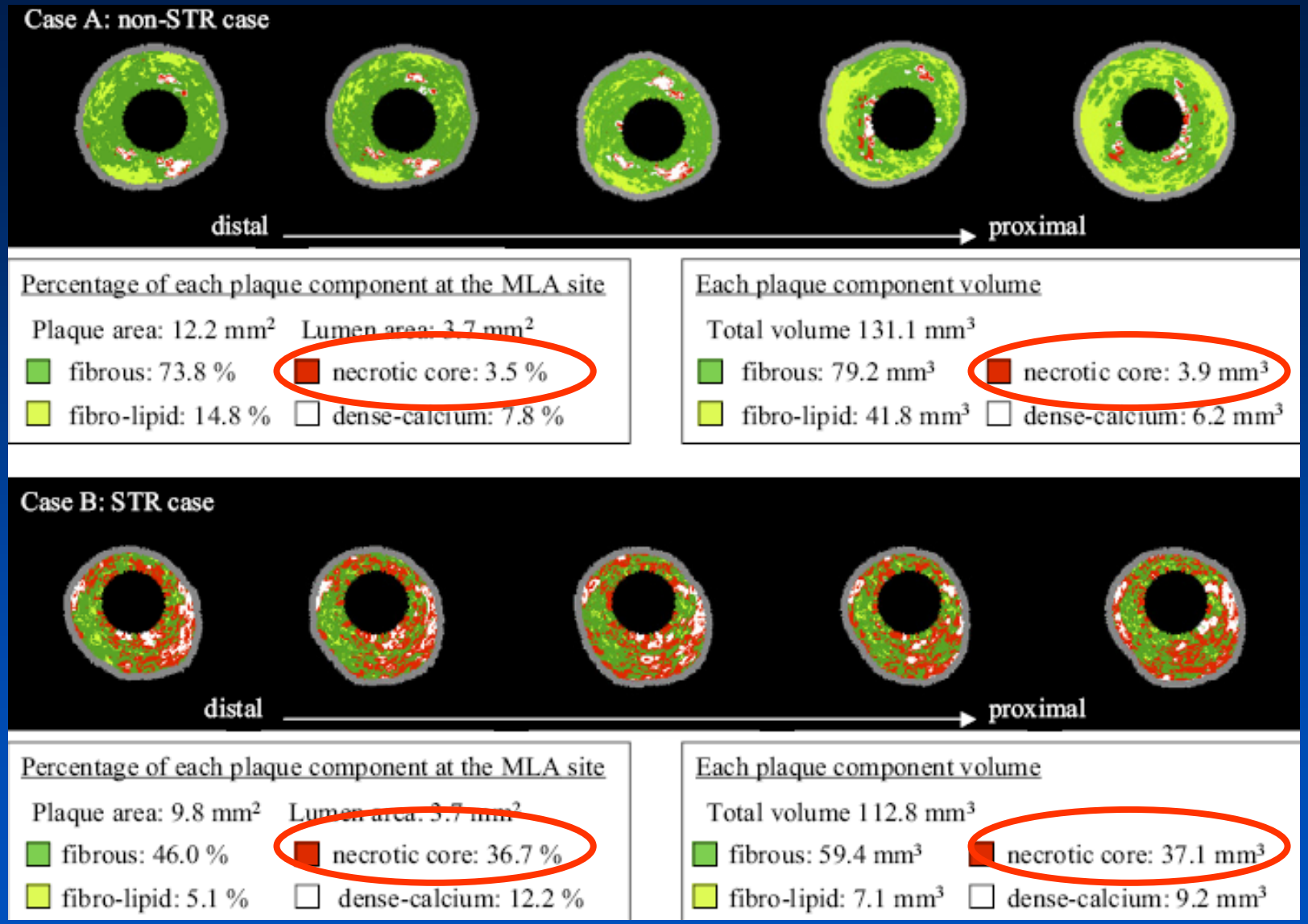
VH parameters & STR after Primary Stenting for STEMI

****STR (ST-segment Re-elevation) represents distal embolization**

Parameters (volume; mm^3)	STR (n=11)	Non-STR (n=60)	P
Total plaque volume	122.0 ± 57.5	111.4 ± 69.2	0.636
Fibrotic	67.1 ± 30.7	68.2 ± 35.3	0.920
Fibro-lipid	9.8 ± 10.4	13.2 ± 11.4	0.368
Dense calcium	12.2 ± 8.6	9.6 ± 13.9	0.559
Necrotic core	32.9 ± 14.1	20.4 ± 19.2	0.044

Kawaguchi, et al. JACC. 2007;50:1641-6

Representative Case



Kawaguchi, et al. JACC. 2007;50:1641-6

AMC Experience

Impact of Plaque Composition on Post-myocardial Necrosis in 283 Patients

(Stented Segment Analysis)

Park et al. VH Summit 2007

Exclusion criteria

- Acute myocardial infarction
- Elevated baseline CK-MB levels
- Saphenous vein graft intervention
- Long lesions >30mm
- Total occlusions
- Severe angulations
- Heavily calcified lesions

Baseline Characteristics

No. of patients	CK-MB Subgroups >3 times (n=13)	1-3 times (n=21)	Normal (n=249)	P
Age (yrs)	63.8±7.9	61.6±10.3	60.0±9.7	0.31
Male gender	9 (69%)	14 (67%)	168 (67%)	0.94
Diabetes	3 (23%)	5 (24%)	58 (23%)	0.99
Hypertension	8 (62%)	13 (62%)	118 (47%)	0.14
Hyperlipidemia	1 (8%)	4 (19%)	51 (21%)	0.30
Smoking	2 (15%)	5 (24%)	65 (26%)	0.40
Previous MI	0 (0%)	2 (10%)	12 (5%)	0.85
Unstable angina	6 (46%)	8 (38%)	79 (32%)	0.23

Lesion Characteristics

No. of lesions	CK-MB Subgroups >3 times (n=15)	1-3 times (n=28)	Normal (n=289)	P
Diseased artery				0.72
LAD	8 (53%)	15 (54%)	167 (58%)	
LCX	4 (27%)	7 (25%)	31 (11%)	
RCA	3 (20%)	3(11%)	78 (27%)	
LM	0 (0%)	3 (11%)	13 (5%)	
Direct stenting	3 (20%)	7 (25%)	79 (27%)	0.80
Balloon/artery ratio	1.30±0.21	1.26±0.23	1.24±0.23	0.03
No. of stents	1.3±0.7	1.2±0.6	1.3±0.8	0.78
Total stent length	33.8±7.9	31.6±10.3	30.0±9.7	0.22

IVUS analysis (pre-procedure stented segment analysis)

	>3 times (n=15)	1-3 times (n=28)	Normal (n=239)	P
MLA site (mm2)				
EEM	15.6±4.7	14.7±4.9	15.4±4.5	**0.78**
Lumen	3.9±1.4	4.3±1.4	4.1±1.9	**0.31**
Plaque	11.7±4.7	10.4±4.3	11.2±4.3	**0.59**
Largest NC site (mm3)				
EEM	16.7±5.3	15.1±5.4	15.9±5.0	**0.58**
Lumen	5.0±1.9	5.2±2.4	4.9±1.9	**0.83**
Plaque	11.7±4.5	9.9±4.0	11.0±4.2	**0.35**

VH-IVUS analysis (MLA site)

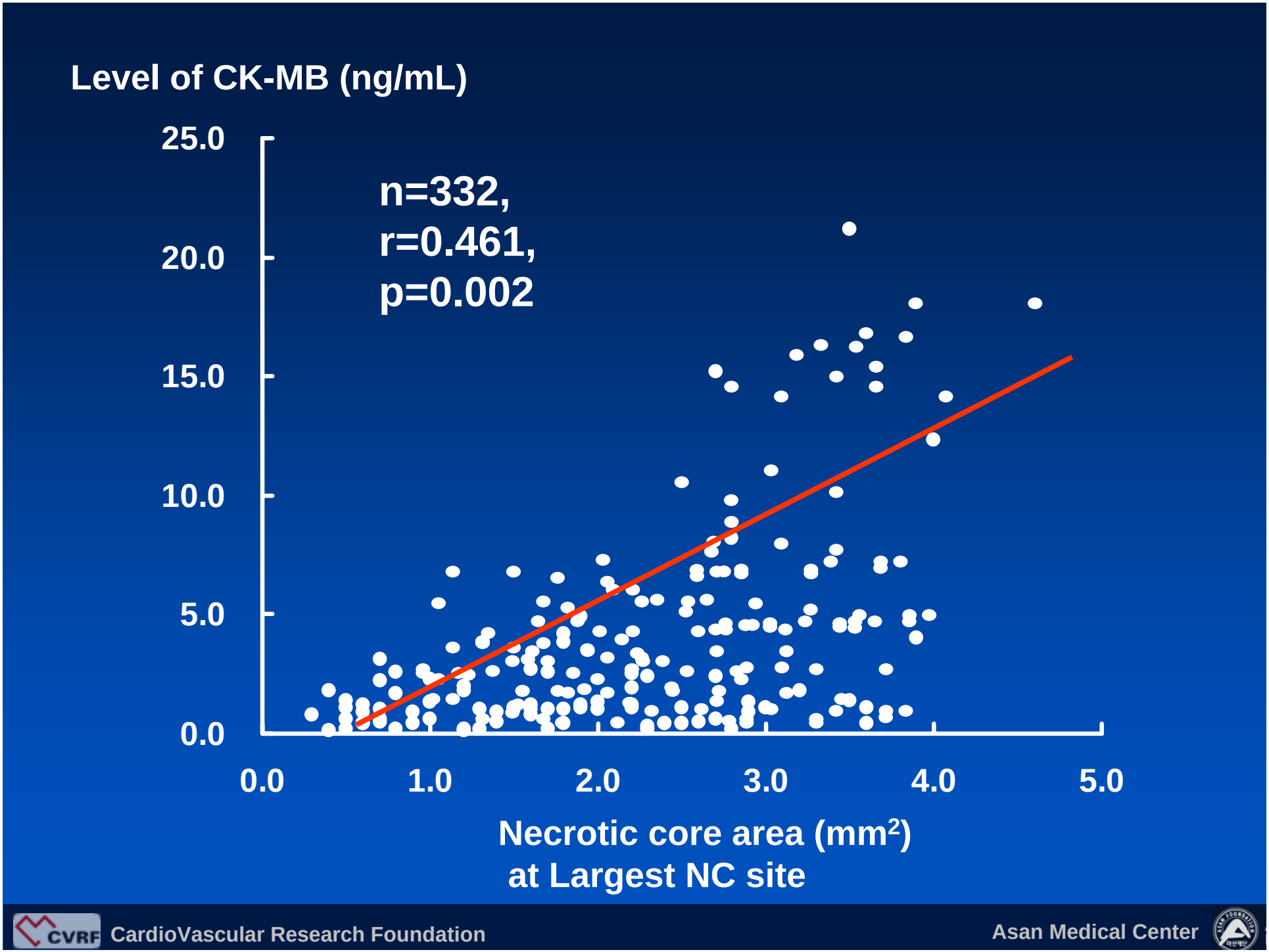
	>3 times (n=15)	1-3 times (n=28)	Normal (n=239)	P
Area (mm2)				
Fibrotic	4.1±2.6	4.3±2.7	4.4±2.9	**0.22**
Fibrofatty	0.3±0.4	0.5±0.7	0.5±0.6	**0.64**
Dense calcium	0.7±0.7	0.5±0.5	0.7±0.8	**0.37**
Necrotic core	2.5±1.4	2.3±1.6	2.0±1.2	**0.03**
Percent (%)				
Fibrotic	50±21	56±16	53±17	**0.12**
Fibrofatty	4±5	6±5	6±5	**0.49**
Dense calcium	9±9	8±7	10±10	**0.58**
Necrotic core	37±14	32±14	29±13	**0.06**

VH-IVUS analysis (Largest NC site)

	>3 times (n=15)	1-3 times (n=28)	Normal (n=239)	P
Area (mm2)				
Fibrotic	3.6±2.9	3.8±2.6	3.9±2.6	**0.21**
Fibrofatty	0.3±0.4	0.3±0.5	0.4±0.5	**0.64**
Dense calcium	0.7±0.7	0.6±0.6	0.8±0.7	**0.38**
Necrotic core	2.8±1.6	2.5±1.7	2.1±1.3	**0.001**
Percent (%)				
Fibrotic	49±20	52±17	54±16	**0.11**
Fibrofatty	3±5	5±4	5±5	**0.32**
Dense calcium	11±9	9±8	12±9	**0.43**
Necrotic core	37±14	34±14	29±13	**0.021**

Independent Correlates of post-PCI CK-MB elevation

	OR	95% CI	p
Balloon-to-artery ratio	1.01	1.01–1.02	0.04
Necrotic core area at the largest NC area site	1.14	1.06–1.72	0.022


Level of CK-MB (ng/mL)
25.0
20.0
15.0
10.0
5.0
0.0
n=332,
r=0.461,
p=0.002
0.0
1.0
2.0
3.0
4.0
5.0
Necrotic core area (mm²)
at Largest NC site

Conclusions

- Post-PCI CK-MB enzyme level correlated with a larger pre-PCI necrotic core area at the minimal lumen site as assessed by VH-IVUS analysis.

- More aggressive medical treatment (i.e. use of platelet glycoprotein IIb/IIIa inhibitors or a larger loading dose of clopidogrel or statin before PCI) and less aggressive procedures may be warranted to prevent higher CK-MB elevations in these lesion subsets.

VH-IVUS and OCT findings: AMC Experience

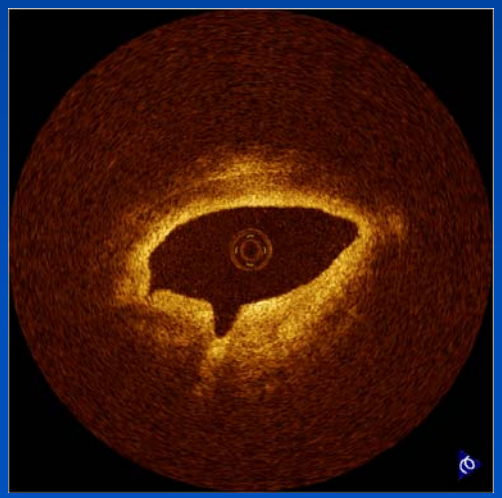
Relationship between Coronary Plaque Composition and OCT-TCFA

DW Park et al. ACC 2008

OCT Plaque Imaging

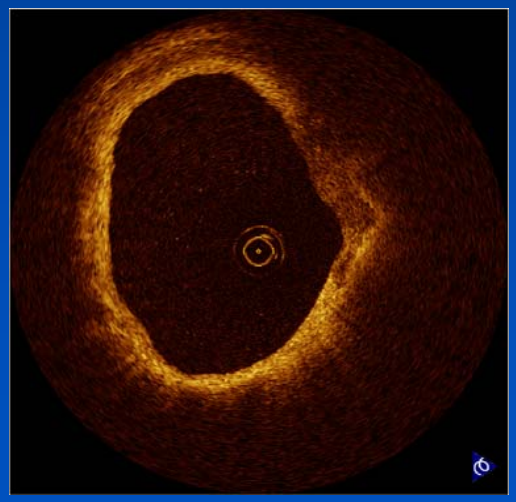
Fibrous

- High reflectivity
- Homogenous
- Finely textured



Lipid-rich

- Low reflectivity
- Homogenous
- Diffuse margins

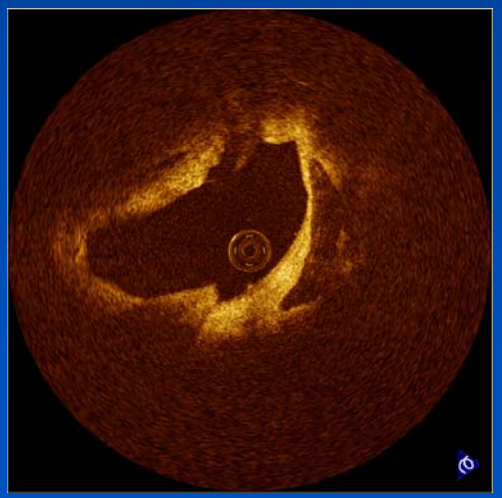


Calcified

- Low reflectivity
- Inhomogeneous
- Sharp margins

or

Isolated, strong reflections in dark background



Objective

- **To evaluate in vivo the relationship between coronary plaque tissue composition using VH-IVUS and morphologic characterization of vulnerable plaque assessed by OCT**

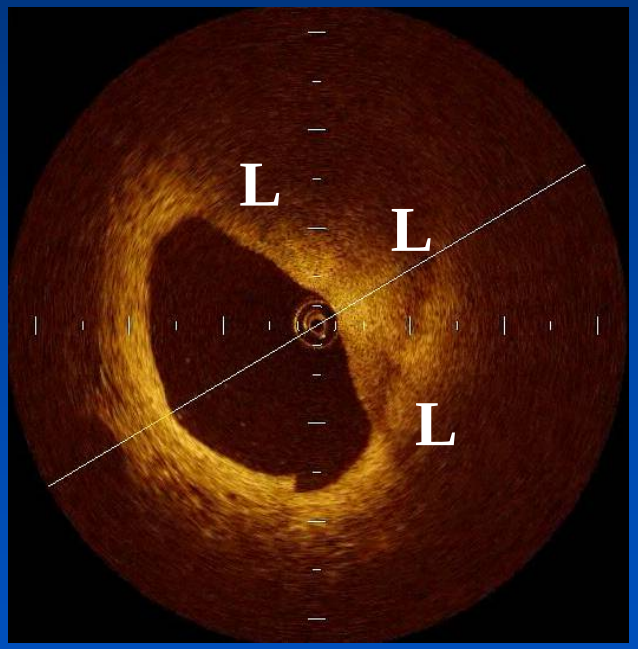
- Serial, pre-intervention, conventional IVUS, VH-IVUS and OCT was consecutively performed in the culprit lesions of **41 patients.**

DW Park et al. ACC 2008

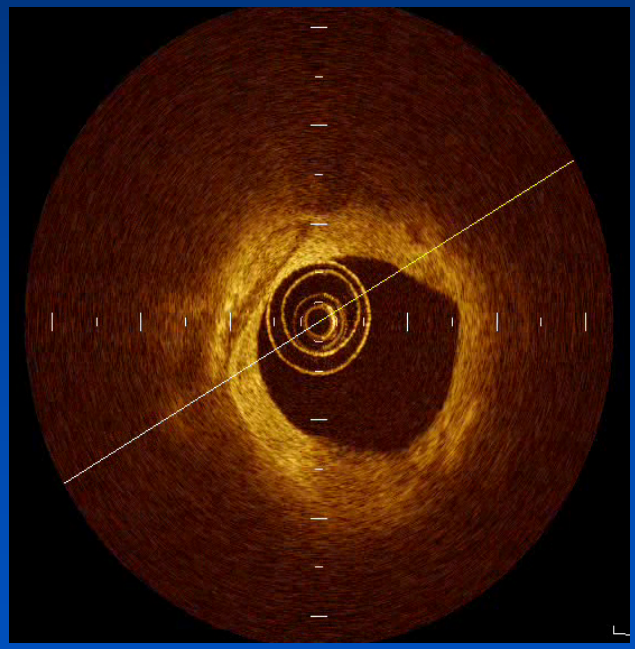
OCT-derived Thin-Cap FibroAtheroma (TCFA)

For all images with an OCT-determined lipid pool:

1) lipid-rich plaque (≥2 quadrants)
2) the thinnest part of a fibrous cap measuring ≤65 μm



TCFA

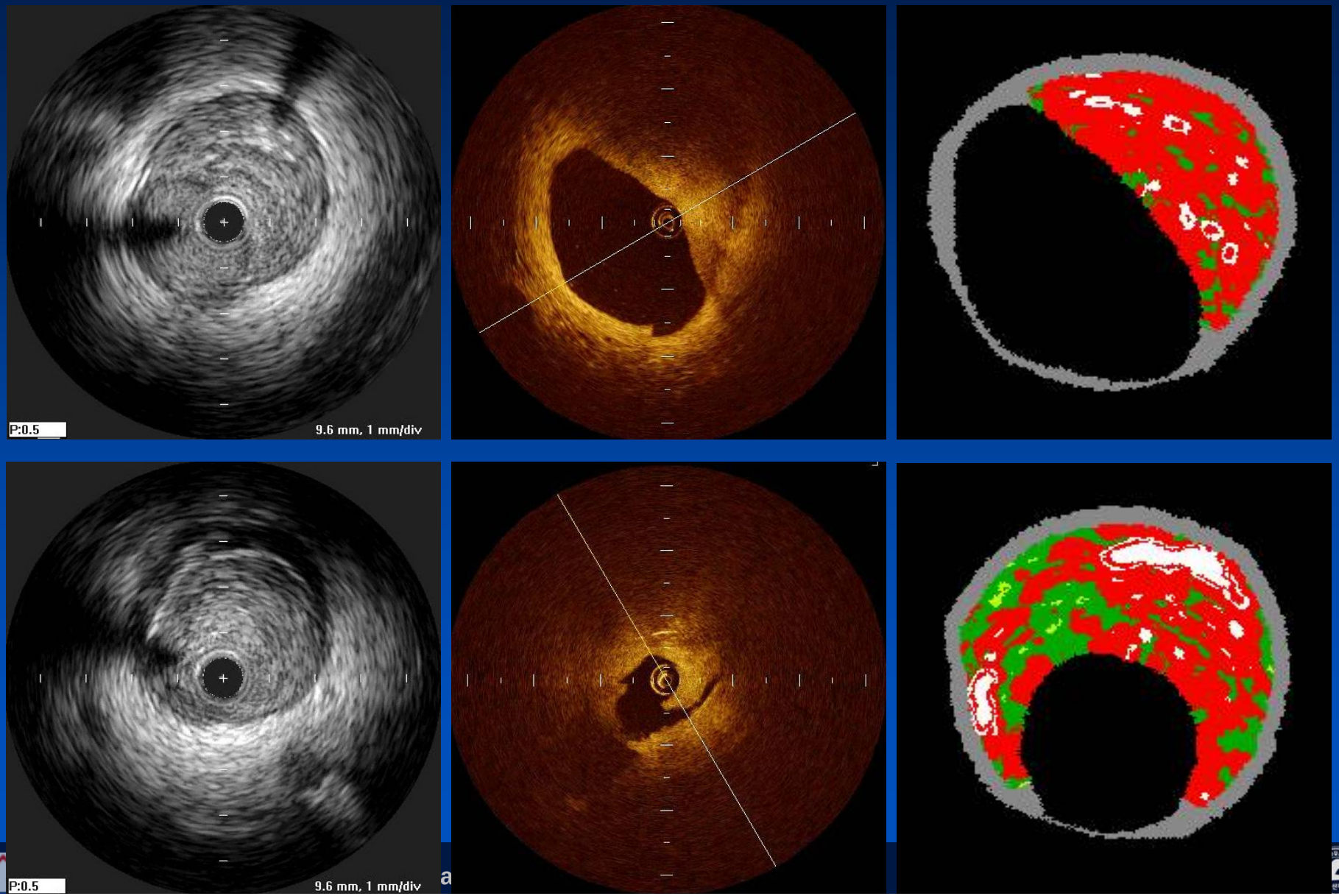


Non-TCFA

IK Jang et al. *Circulation* 2005;111:1551

Patients with Unstable Angina

Well matched with IVUS, OCT and clinical presentation



Baseline Characteristics

The frequency of OCT-derived TCFA: 23/41 (56%)

	OCT-TCFA (n=23)	No TCFA (n=18)	P
Age (yrs)	63.0±8.1	61.9±10.5	0.72
Male gender	15 (65%)	9 (50%)	0.33
Diabetes	9 (39%)	7 (39%)	0.99
Hypertension	11 (48%)	12 (67%)	0.29
Hypercholesterolemia	7 (30%)	3 (17%)	0.47
Smoking	12 (52%)	8 (44%)	0.62
Previous MI	1 (4%)	1 (6%)	1.00
Previous PCI	1 (4%)	2 (11%)	0.57
LV EF (%)	58.7±6.8	62.3±3.5	0.034

Baseline Characteristics

	OCT-TCFA (n=23)	No TCFA (n=18)	P
Clinical presentation			0.036
Stable angina	7 (30%)	13 (72%)	
Unstable angina	12 (52%)	4 (22%)	
MI	4 (17%)	1 (5%)	
Target site			0.65
LAD	10 (44%)	8 (44%)	
LCX	5 (22%)	2 (11%)	
RCA	8 (35%)	8 (44%)	
Multivessel disease	13 (57%)	8 (44%)	0.44

Baseline Characteristics

	OCT-TCFA (n=23)	No TCFA (n=18)	P
Lipid profiles (mg/dl)			
Total cholesterol	184±40	176±28	0.51
TG	149±87	155±90	0.83
HDL	45±15	47±12	0.51
LDL	120±36	113±27	0.50
hs-CRP (mg/dl)	0.6±0.9	0.9±1.8	0.49
Lipoprotein (a) (mg/dl)	24.5±18.3	22.1±20.2	0.70
Homocystein (mg/dl)	11.7±2.5	12.8±3.7	0.28

Lesion Characteristics
: OCT morphological measurements

	OCT-TCFA (n=23)	No TCFA (n=18)	P
Plaque disruption	14 (61%)	3 (17%)	0.004
Calcium	14 (61%)	9 (50%)	0.49
Thrombus	9 (39%)	1 (6%)	0.025
Fibrous cap thickness (μm)	51.3±8.7	103.5±33.9	<0.001

Lesion Characteristics
: Conventional IVUS and VH-IVHS

	OCT-TCFA (n=23)	No TCFA (n=18)	P
Remodeling type			0.73
Positive (>1.05)	9 (43%)	5 (33%)	
Intermediate (0.95-1.05)	2 (10%)	3 (20%)	
Negative (<0.95)	10 (48%)	7 (47%)	
Lipid-core	10 (46%)	9 (56%)	0.51
Plaque disruption	7 (32%)	2 (13%)	0.25
Thrombus	2 (9%)	0 (0%)	0.49
Calcium	15 (65%)	9 (56%)	0.52
VH-TCFA	10 (43%)	2 (13%)	0.03

Grey-scale IVUS Measurement

The frequency of OCT-derived TCFA: 23/41 (56%)

	OCT-TCFA (n=23)	No TCFA (n=18)	P
Minimum lumen area			
EEM CSA (mm^2)	16.1±3.9	14.6±4.5	0.28
Lumen CSA (mm^2)	4.2±1.4	4.1±1.2	0.91
Plaque CSA (mm^2)	11.9±3.5	10.5±3.9	0.24
Remodeling index	1.02±0.31	0.95±0.15	0.44
Largest necrotic core			
EEM CSA (mm^2)	15.7±3.5	13.6±3.1	0.08
Lumen CSA (mm^2)	5.4±2.2	5.3±1.7	0.83
Plaque CSA (mm^2)	10.3±2.6	8.4±2.3	0.024

VH-IVUS Measurement

	OCT-TCFA (n=23)	No TCFA (n=18)	P
Minimum lumen area site			
Absolute area (mm^2)			
Fibrotic	4.9±3.2	4.6±3.6	0.75
Fibrofatty	0.5±0.6	0.6±0.7	0.75
Dense calcium	0.9±0.5	1.0±0.9	0.88
Necrotic core	2.5±1.6	1.6±1.5	0.04
Percentages (%)			
Fibrotic	51±21	54±29	0.72
Fibrofatty	6±6	8±8	0.32
Dense calcium	13±7	15±14	0.60
Necrotic core	31±21	23±23	0.07

VH-IVUS Measurement

	OCT-TCFA (n=23)	No TCFA (n=18)	P
Largest necrotic core site			
Absolute area (mm^2)			
Fibrotic	3.2±2.1	3.0±2.2	0.75
Fibrofatty	0.3±0.4	0.4±0.5	0.75
Dense calcium	1.0±0.6	0.8±0.6	0.88
Necrotic core	2.8±1.5	1.6±1.0	0.003
Percentages (%)			
Fibrotic	39±20	48±24	0.42
Fibrofatty	4±5	6±7	0.27
Dense calcium	14±7	15±11	0.73
Necrotic core	44±20	31±22	0.03

Independent correlates of OCT-TCFA

	OR	95% CI	*p*-value
Acute coronary syndrome	8.42	1.47-48.14	0.017
Necrotic core area at the largest necrotic core site (mm^2)	2.81	1.27-6.20	0.011

Conclusion

- Morphological plaque vulnerability assessed by OCT was well correlated with vulnerable plaque tissue composition assessed by VH-IVUS.

- Largest necrotic core area determined by VH-IVUS was most strongly associated with the incidence of OCT-derived TCFA.

Terminology:

- **Culprit Plaque:**
  a Retrospective Terminology
- **Vulnerable Plaque:**
  a Prospective Terminology

Vulnerable Plaque : Major limitations

- **Everything that we know about vulnerable plaque mainly come from in vivo detection of plaque rupture in patients presented with ACS**
- ***NOT from prospective identification of vulnerable plaques before they rupture and/or thrombus formation***

BIOCHEMICAL AND BIOIMAGING MARKERS

* **Major risk factors**

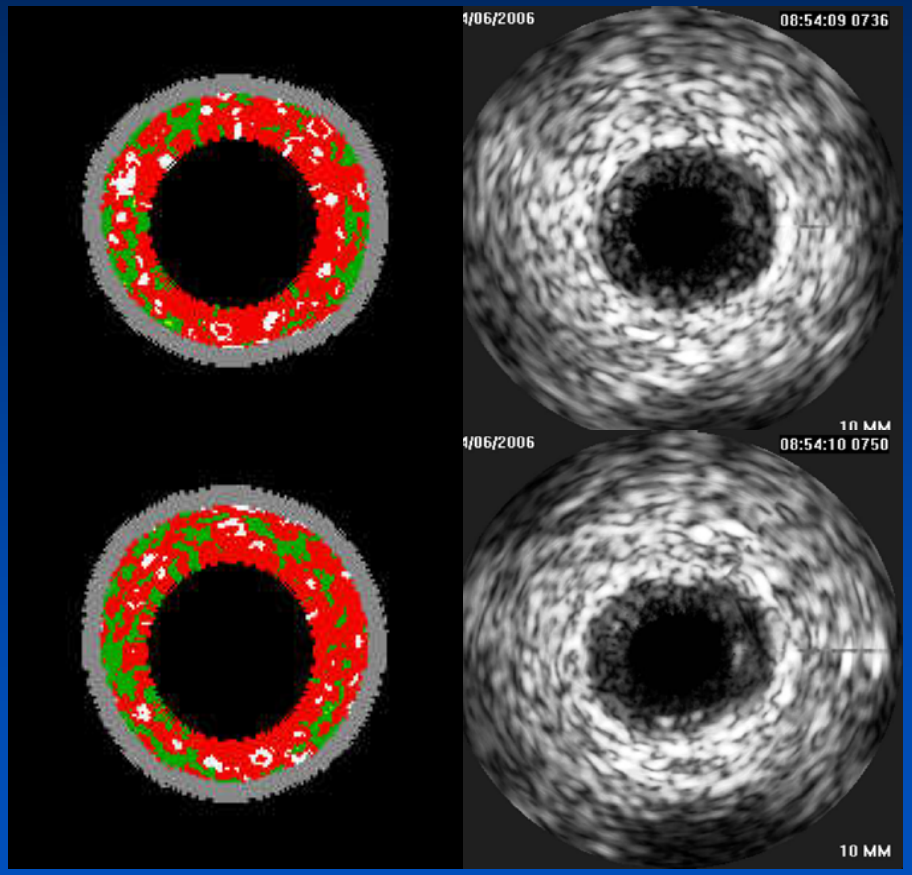
Genetic & Progenitor Cell Markers

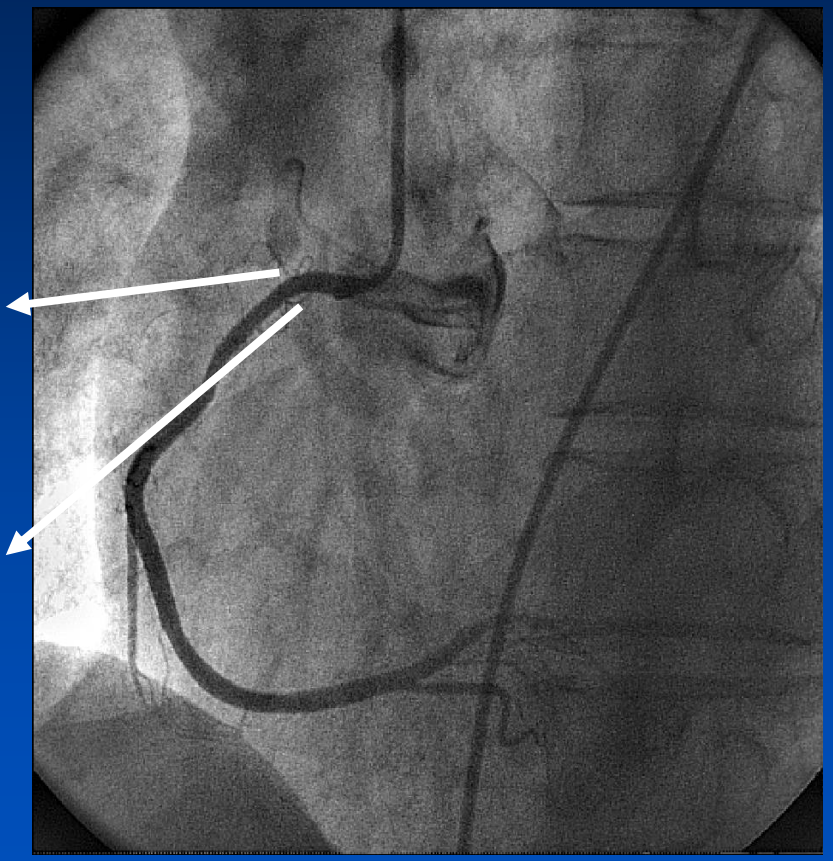
Serum Markers

Imaging Markers
: Early Detection
: Risk Stratification

* **Atherothrombotic disease**
Cardiovascular events

Detection of vulnerable plaque is important to identify high risk patients.





How can we detect and treat this ?

Effect of High-Dose and Low-Dose Statin on Coronary Plaque Modification

The **STABLE** trial

(***ST***atin and ***A***theroma Vulnera***B***i***L***ity ***E***valuation)

Statin-naïve patients with angiographically documented mild to moderate coronary disease
(Total 312 patients needed)

2:1 randomization

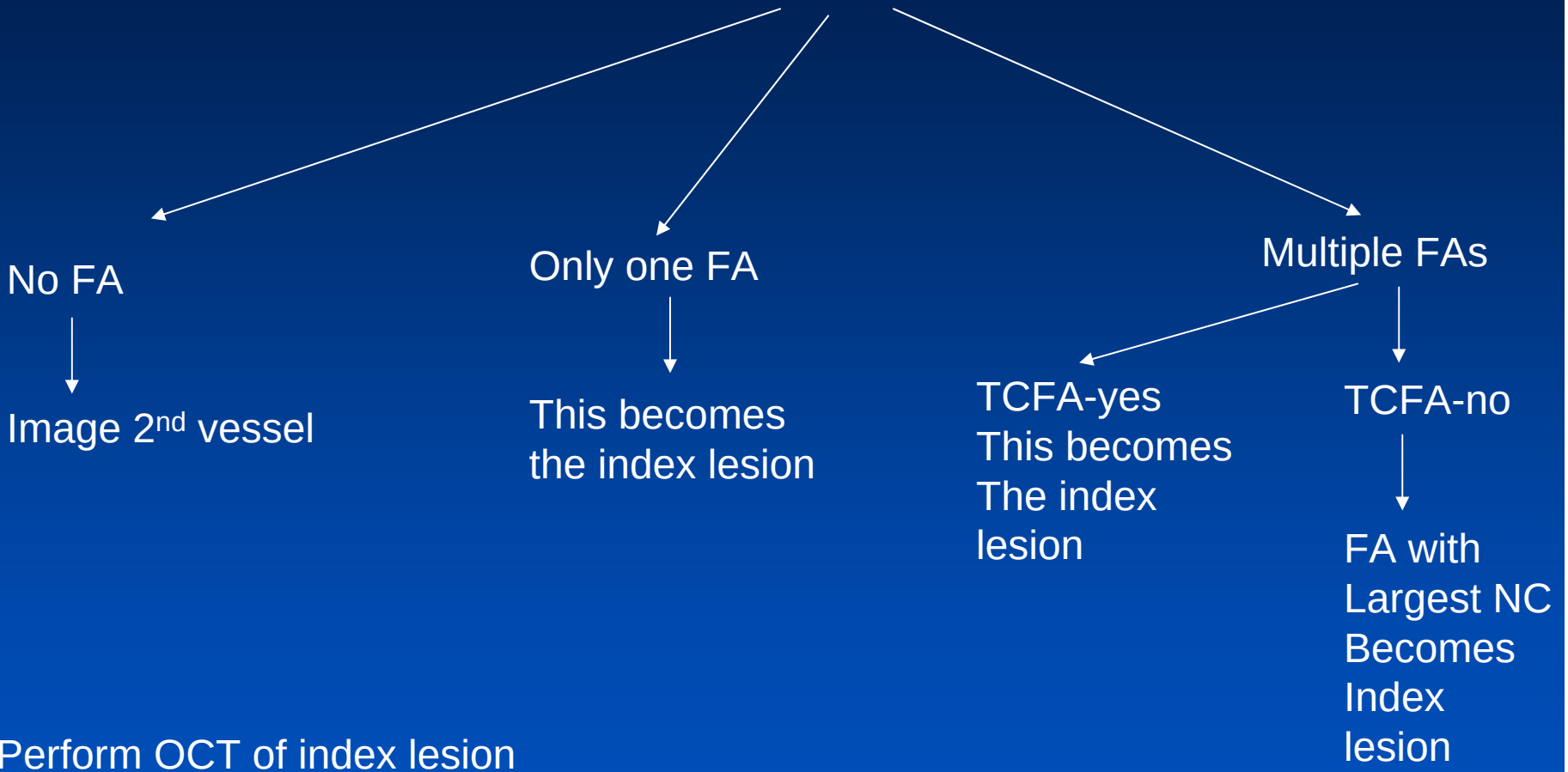
Rosuvastatin 40mg (n=208)

Rosuvastatin 10mg (n=104)

VH-IVUS, Conventional IVUS, and OCT follow-up at 12 months
Clinical follow-up at 12 months

****Primary end point:** % compositional change of coronary plaque from baseline to 12-months follow-up.

1. Perform IVUS with VH of “index” vessel - at least prox 50 mm
2. Perform on-site VH IVUS analysis of “index” vessel
3. Identify all Fibroatheromas



4. Perform OCT of index lesion
5. VH IVUS study sent to core lab to see if index lesion meets enrollment criteria (FA)
   a. If yes, patient is followed for 12 mos and imaging repeated
   b. if no, patient is de-enrolled and a replacement patient sought