What Can 2D IVUS Teach Us About Vulnerable Plaque

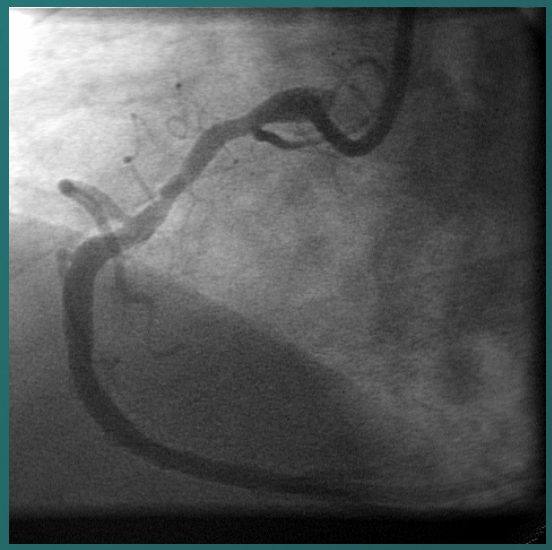
Gary S. Mintz, MD

Cardiovascular Research Foundation
New York City, NY

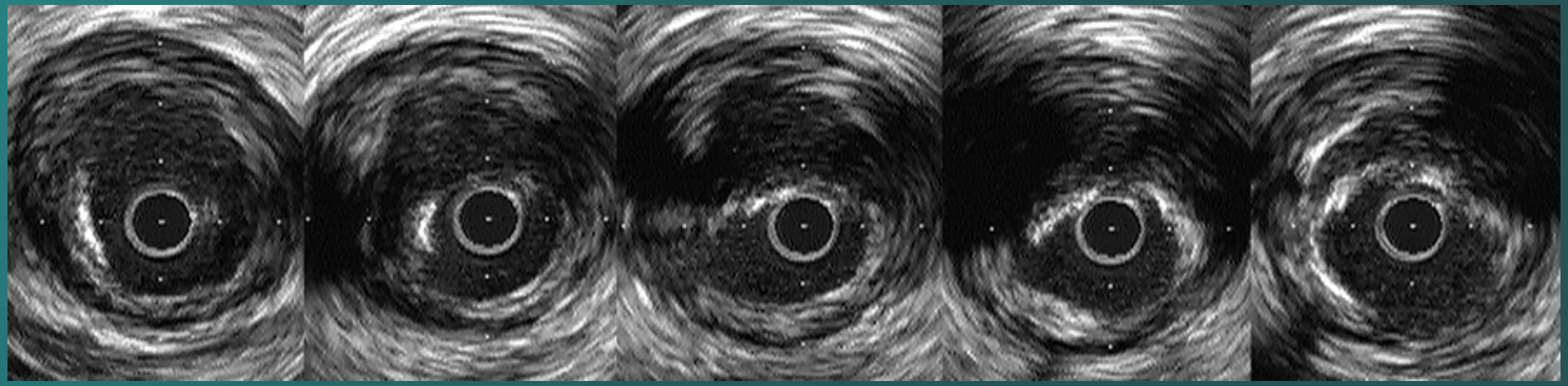
Disclosure

- BostonScientific
- Volcano

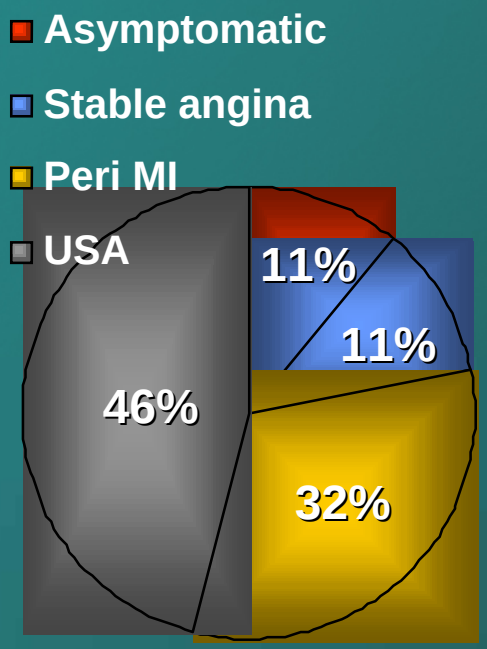
- **Today, in reality, almost everything that we *currently* know about vulnerable plaque has come either from histopathology or from in vivo detection of plaque rupture or study of patients who present with acute coronary syndromes - *NOT from prospective correlative studies or prospective identification of vulnerable plaques before they rupture, rapidly progress, or thrombose.***



0 → 1mm → 4mm



300 plaque ruptures in 257 arteries of 254 pts

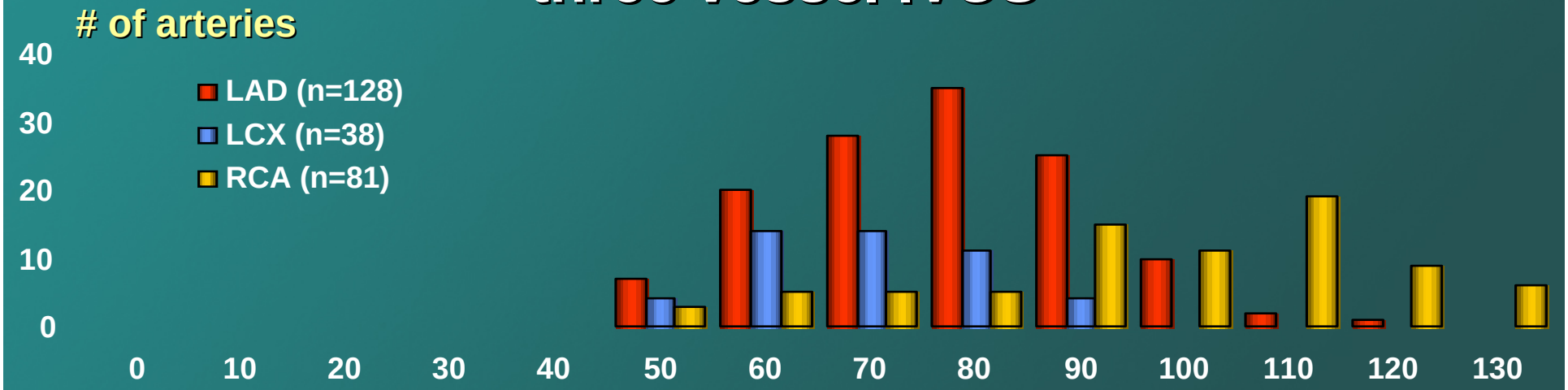


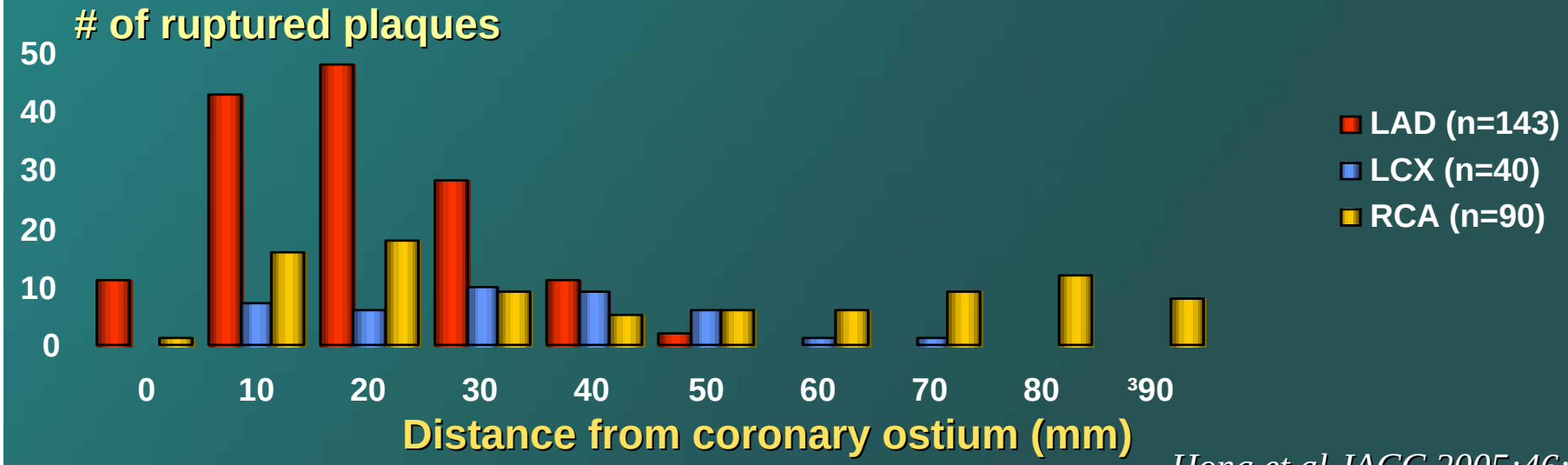
Tear in fibrous cap identified in 59%: at shoulder of plaque in 68% in center of plaque in 32%

The frequency of stable angina or no symptoms in patients with plaque rupture suggests that asymptomatic rupture and healing are common and may be one of the mechanisms of progression of CAD

Maehara et al J Am Coll Cardiol 2002;40:904-10

Location of 273 ruptured plaques in 158 patients with ACS and 48 patients with stable angina and three vessel IVUS

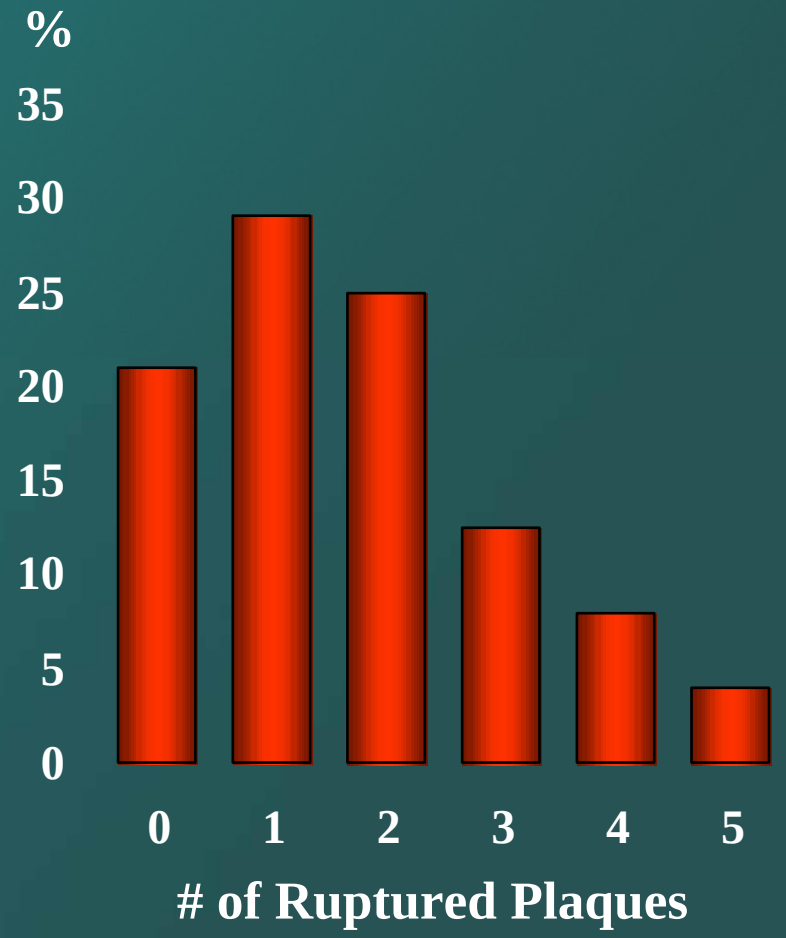




Hong et al JACC 2005;46:261-5

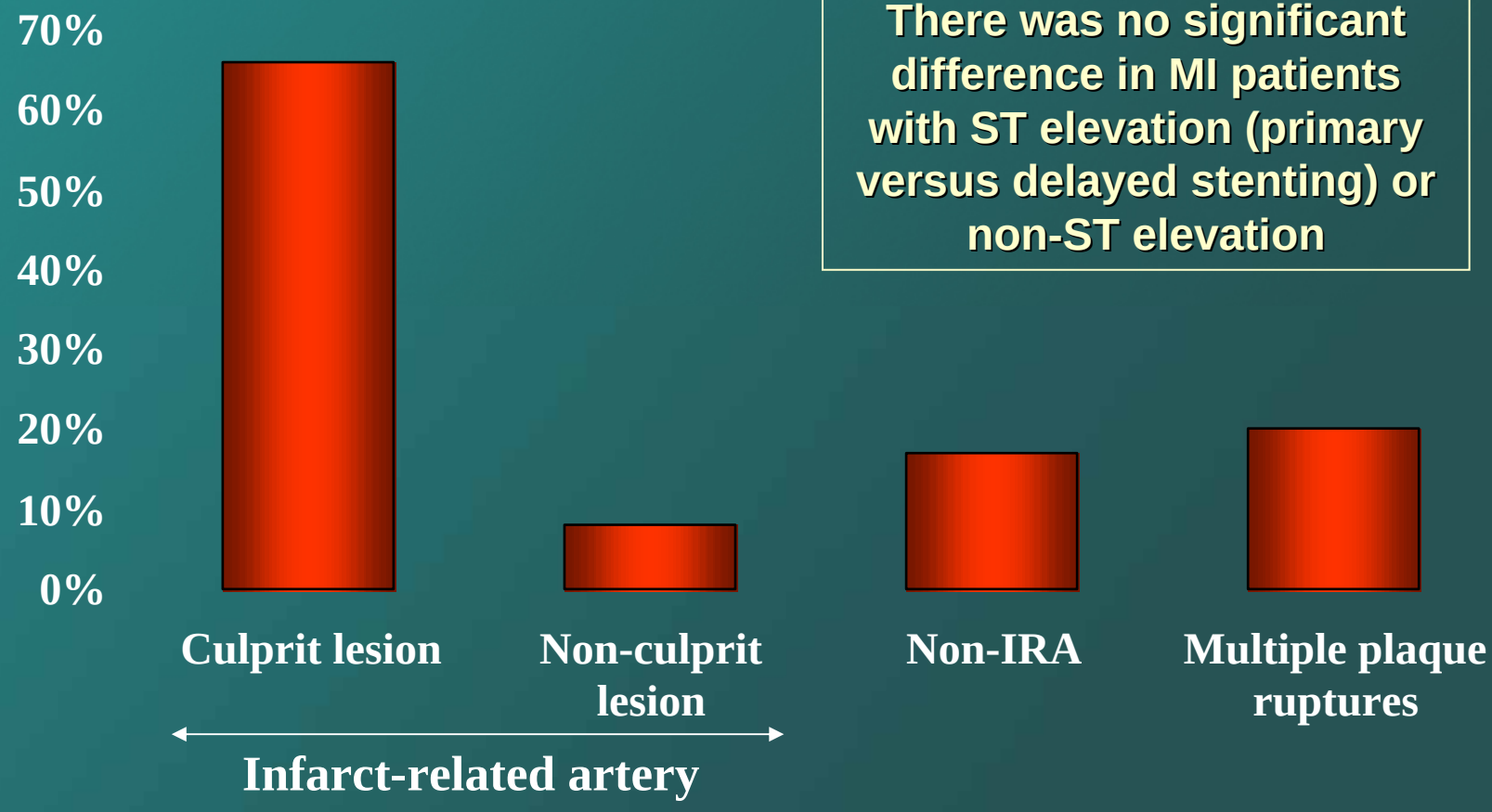
Three Vessel IVUS Imaging in 24 Pts with ACS and Positive Tn

- 50 ruptured plaques
  - 9 culprit lesion
  - 41 nonculprit lesion
- 19 pts had at least 1 nonculprit plaque rupture (79%)
  - 17 pts had 1 plaque rupture in a second artery
  - 3 pts had plaque ruptures in all 3 arteries



Rioufol et al Circulation 2002;106:804-808

Frequency of ruptured plaques in 122 patients with MI and 3-vessel IVUS

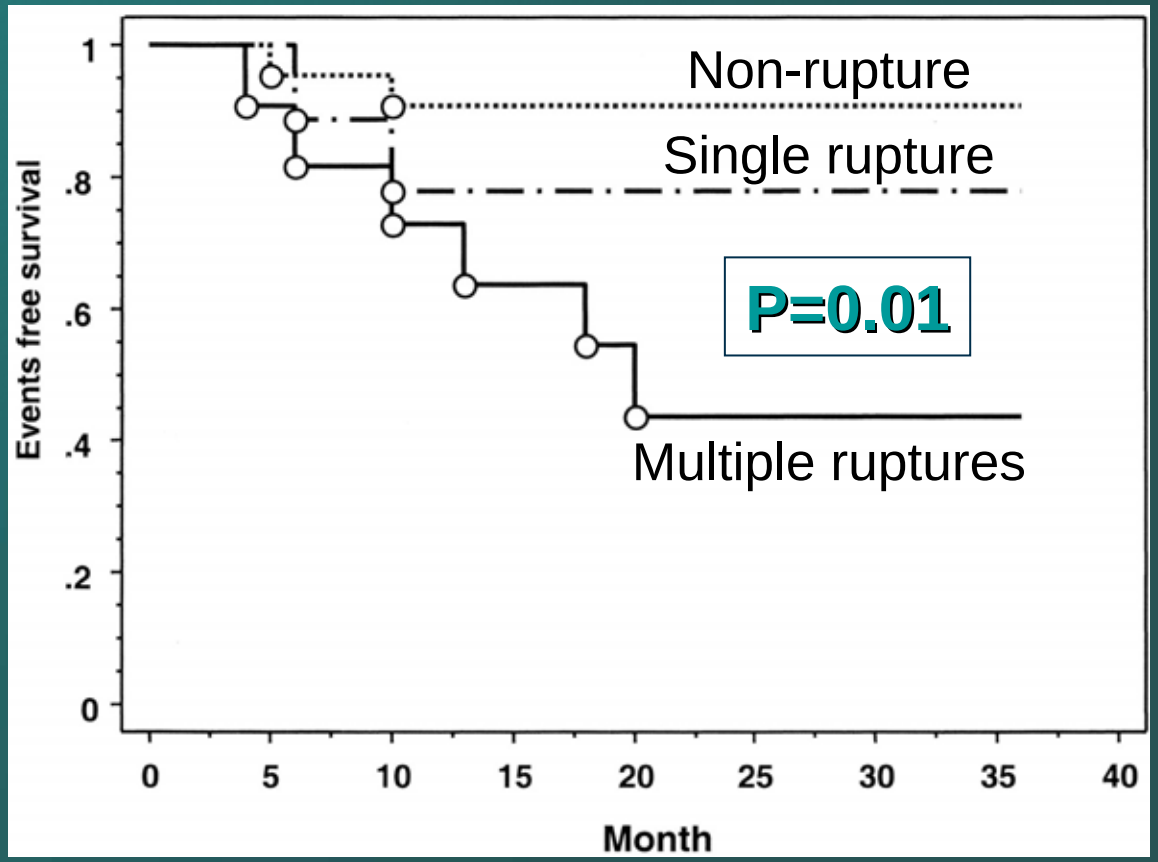


There was no significant difference in MI patients with ST elevation (primary versus delayed stenting) or non-ST elevation

Hong et al Circulation 2004;110:928-337

IVUS in 129 arteries of 45 1st MI patients

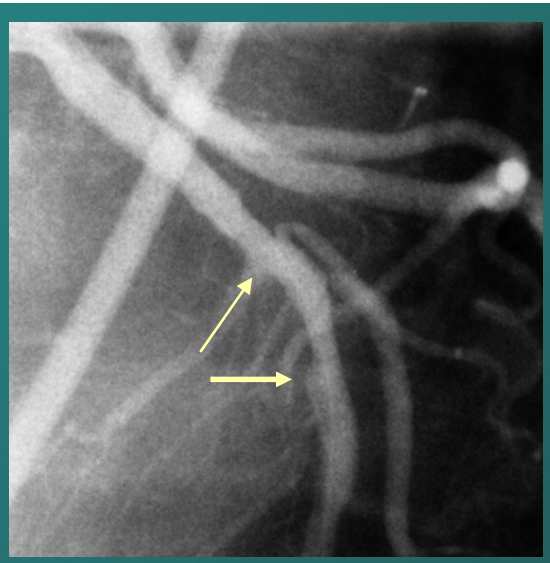
- Culprit plaque rupture in 21 pts (47%)
- Secondary plaque rupture in 11 pts (24%)
- hs-CRP correlated with # of plaque ruptures (p<0.01)



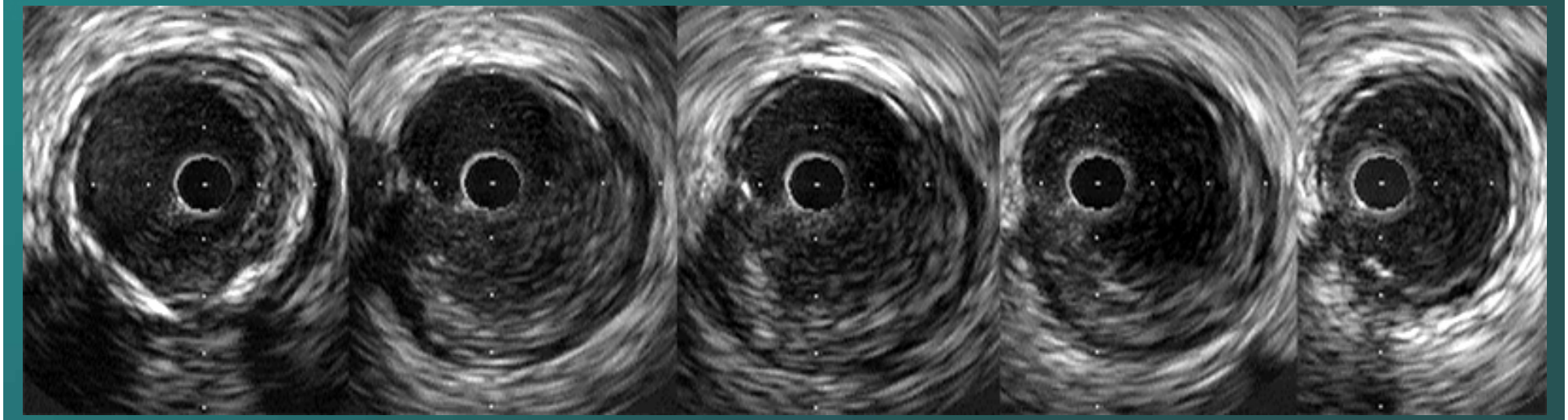
Tanaka et al. J Am Coll Cardiol 2005;45:1594-9

What is the fate of non-flow-limiting ruptured plaques

- 14 pts with 28 plaque ruptures with MLA >4.0mm^2 treated with statins and dual antiplatelet therapy
  - At 22±13 months, half had healed with no clincal events
  - (Rioful et al. Circulation 2004;110:2875-80)
- 28 pts with non-culprit plaque ruptures (only half treated with statins) were followed for 11.9±1.3 months
  - Statin-treated patients had a decrease in plaque area of 0.6±0.8mm^2 (vs an increase of 0.3±0.7mm^2 in controls, p=0.005).
  - Complete healing was observed in 4 (29%) statin-treated vs no control patients (p=0.049).
  - Target lesion revascularization was performed in 3 control (21%) vs no statin-treated patient (p=0.11).
  - Lesions requiring revascularization had a decrease in lumen area (-1.7±1.4mm^2 vs 0.1±0.8mm^2, p=0.001) as well as an increase in plaque area (1.1±1.0mm^2 vs -0.3±0.7mm^2, p=0.04).
  - (Hong et al. Unpublished results)



Proximal 0 → 3mm → 12mm

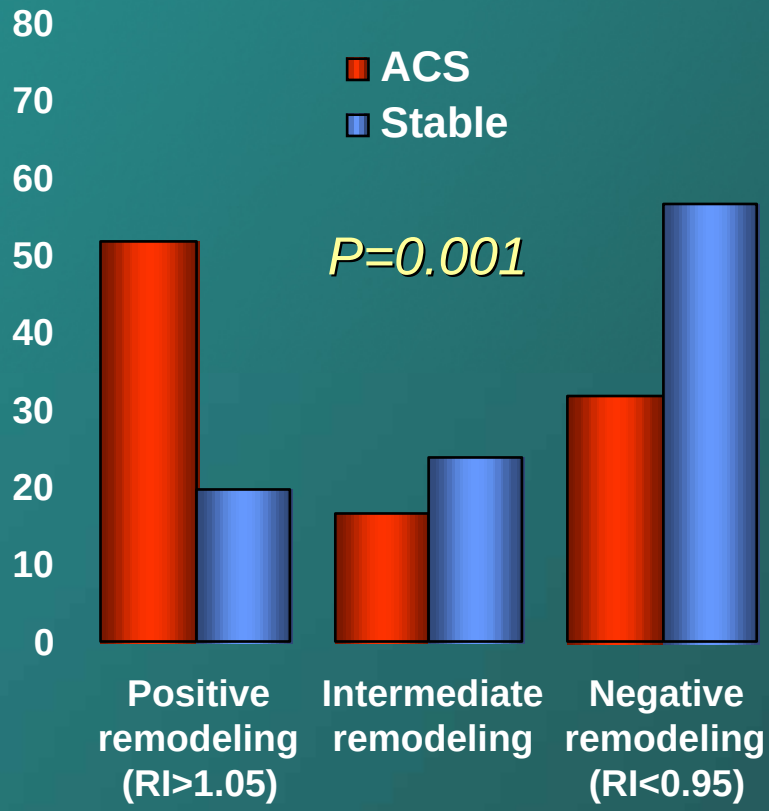


EEM CSA = 21.0mm^2
Lumen CSA = 9.5mm^2
P+M CSA = 11.5mm^2

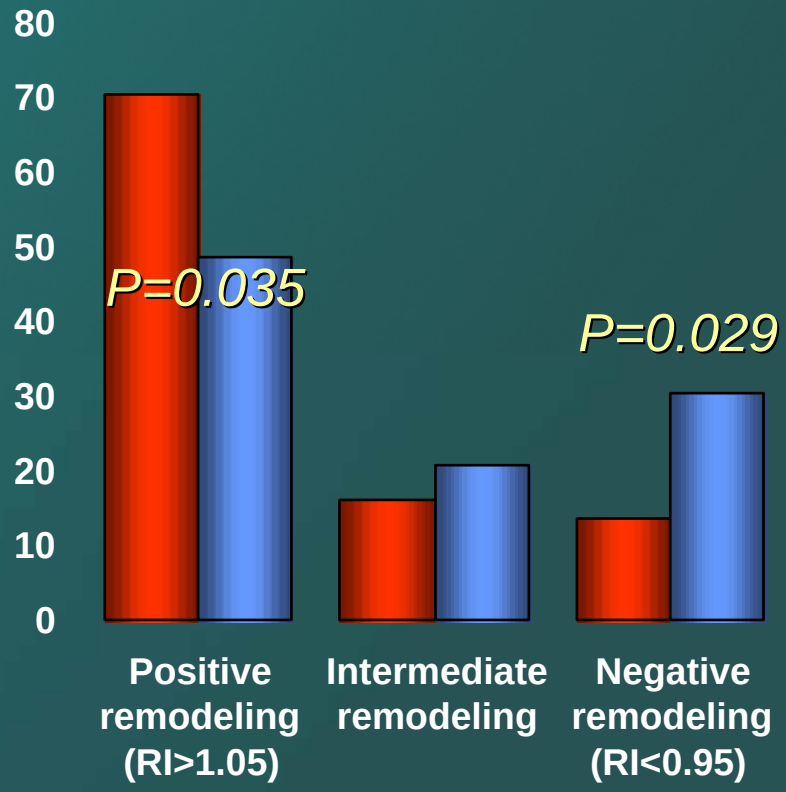
EEM CSA = 23.5mm^2
Lumen CSA = 5.5mm^2
P+M CSA = 18.0mm^2

EEM CSA = 13.7mm^2
Lumen CSA = 9.3mm^2
P+M CSA = 4.4mm^2

Association of positive remodeling and ACS

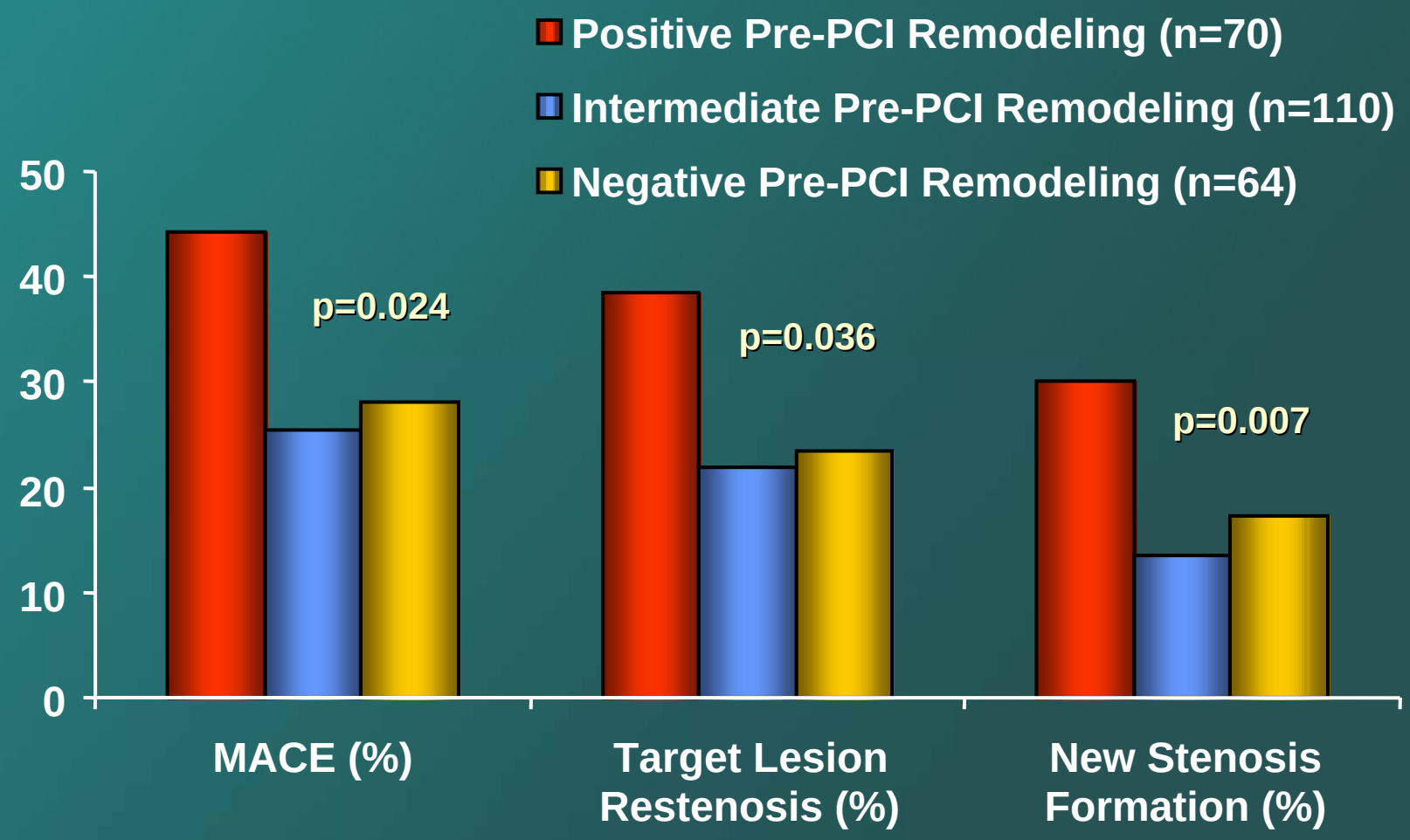


Schoenhagen et al. Circulation 2000;101:598-603



Prati et al. Circulation 2003;107:2320-5

244 Patients with Stable Angina and Single Vessel Intervention



Wexberg et al. J Am Coll Cardiol 2000;36:1860-9

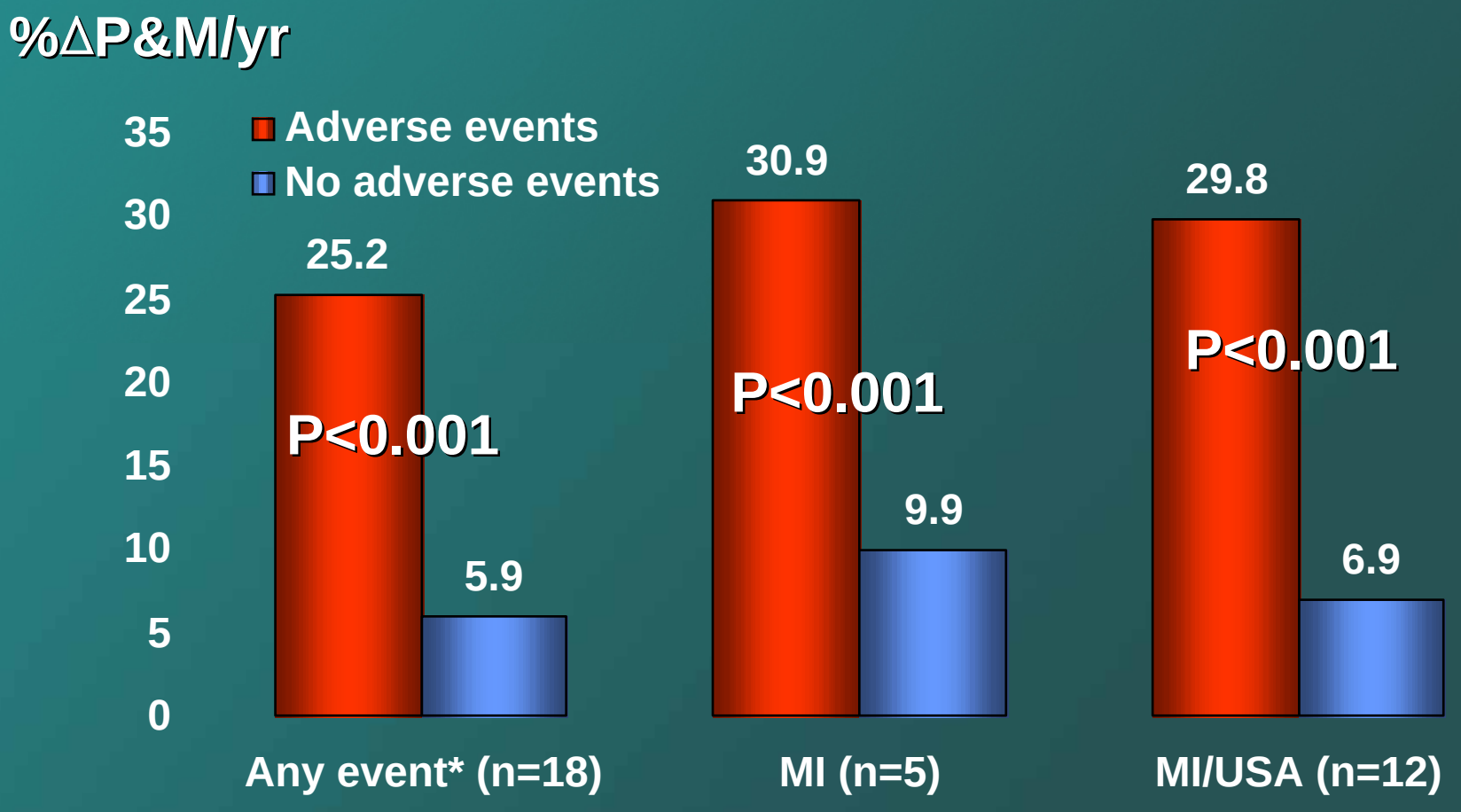
Predictors of recurrent ischemia w/i 1 mo in 64 pts with acute MI treated with thrombolysis

	Recurrent sxs (n=19)	No recurrent sxs (n=45)	Univariate p	Multivariate p
Multivessel ds	42%	24%	0.0236	NS
*+Remodeling**	*63%*	*24%*	*0.0032*	*0.0145*
Lesion EEM	17.5±4.0 mm^2	14.9±6.1 mm^2	0.0056	NS

**Lesion EEM CSA>mean reference EEM CSA*

Gyongyosi et al. Coronary Artery Disease 2001;12:167-72

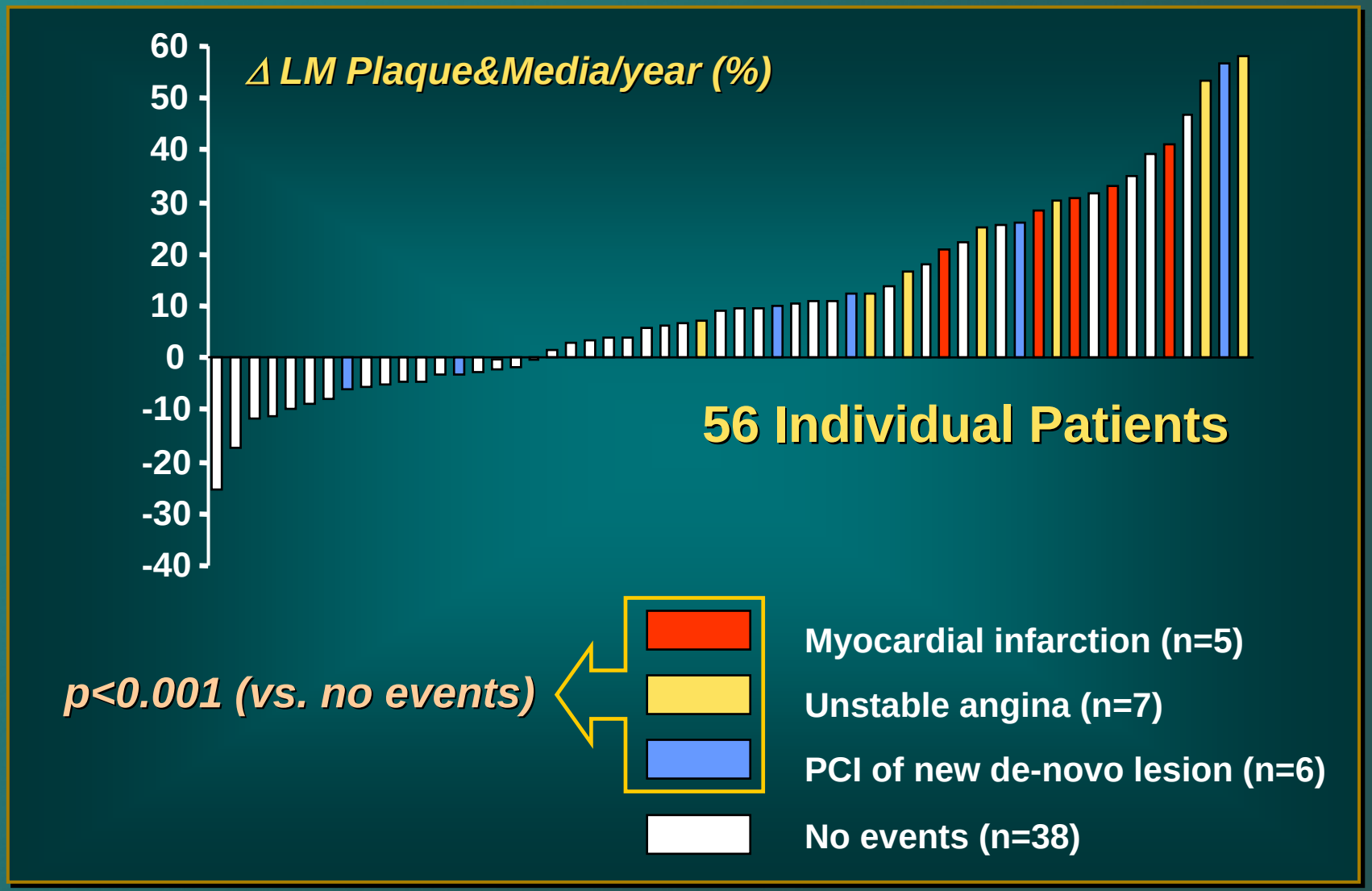
Relationship Between LM Plaque Progression and Non-LM Events



*Death, MI, USA, or PCI or another lesion

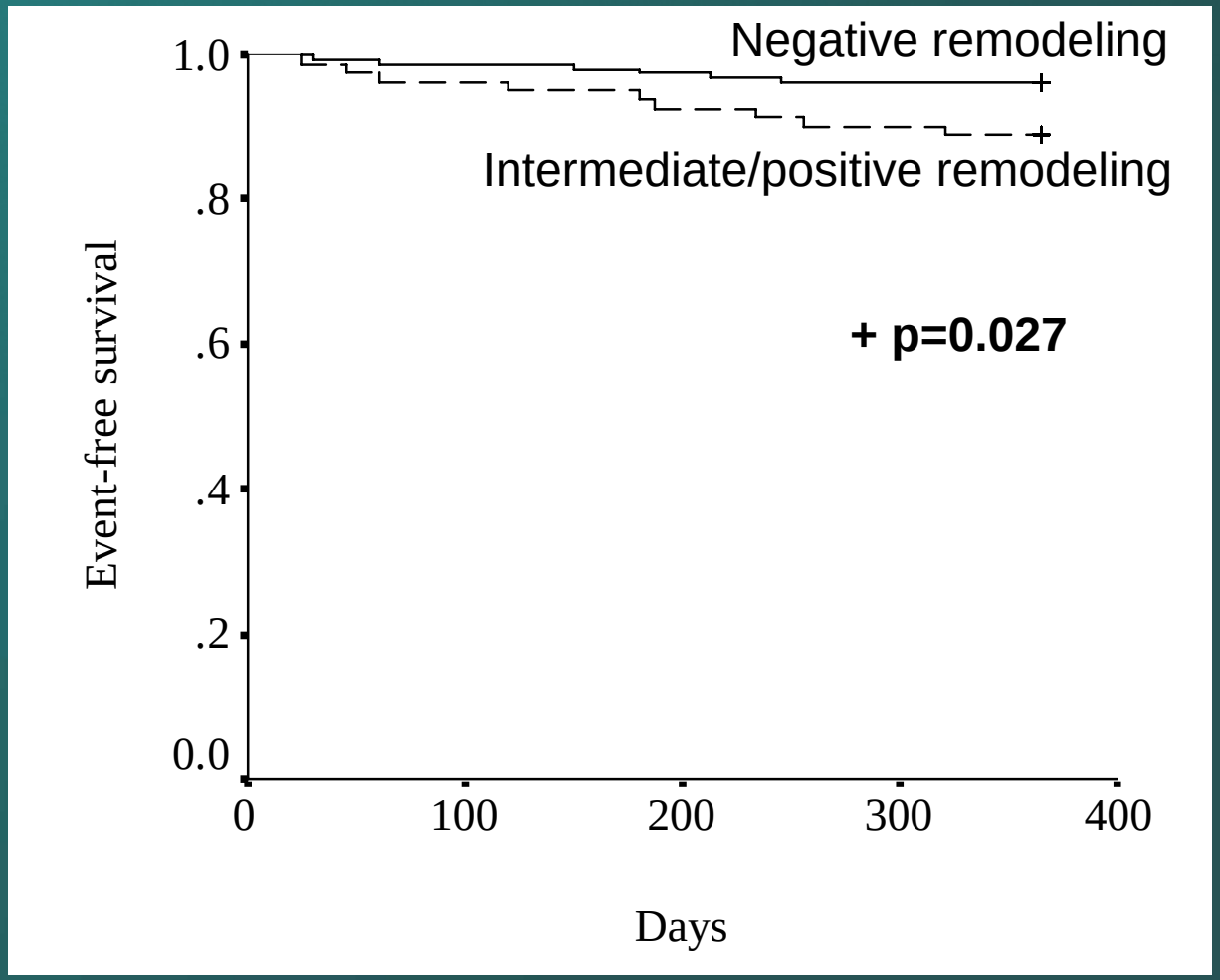
von Birgelen et al. Circulation 2004; 110:1579-85

LM Plaque Progression As a Predictor of Cardiovascular Events in Individual Patients



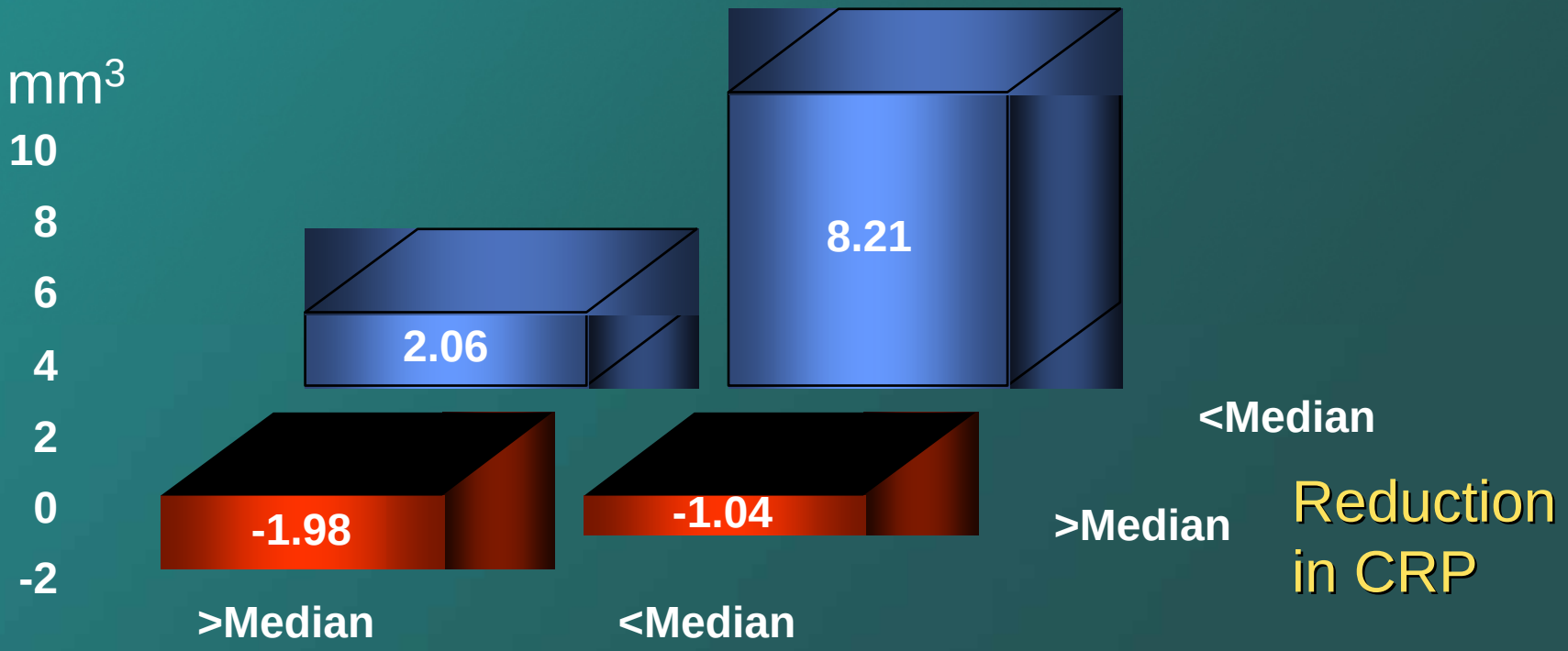
von Birgelen et al. Circulation 2004; 110:1579-85

Impact of Remodeling on Cardiac Events in 236 Patients with Angiographically Mild Left Main Coronary Artery Disease



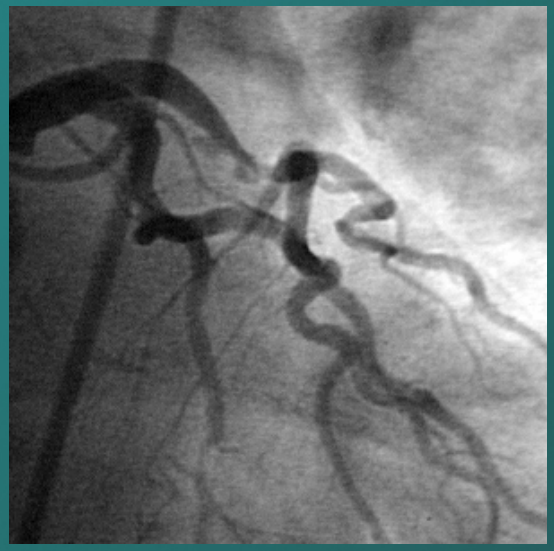
Hong et al. Unpublished

Change in total atheroma volume versus changes in LDL-C and CRP

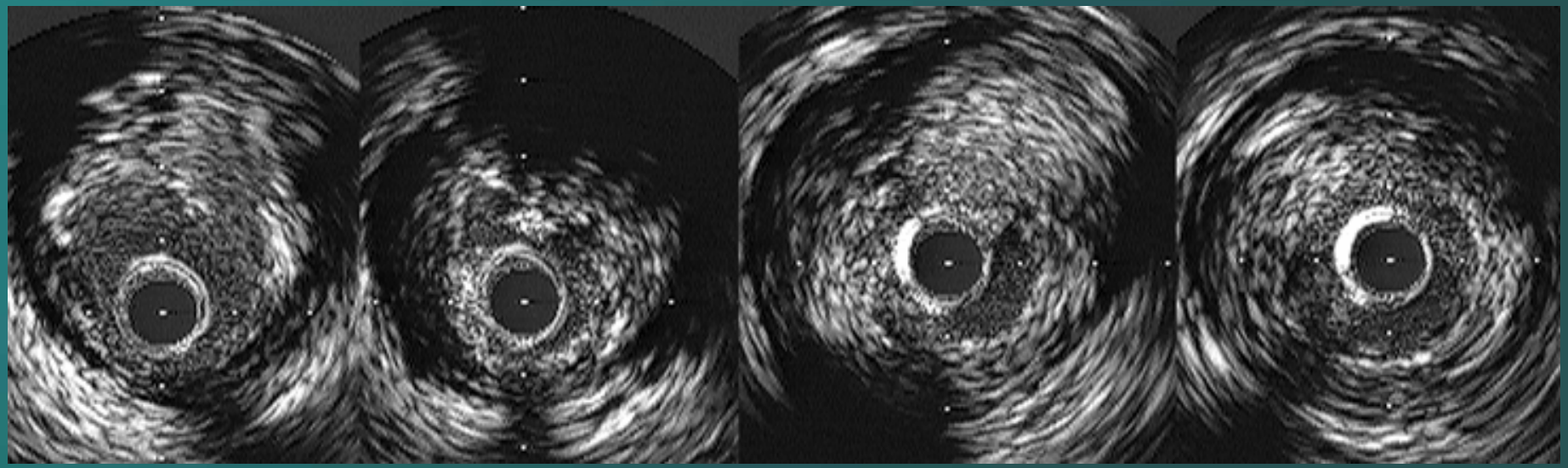


Median change in LDL-C= -37.1%
Median change in CRP= -24.1%

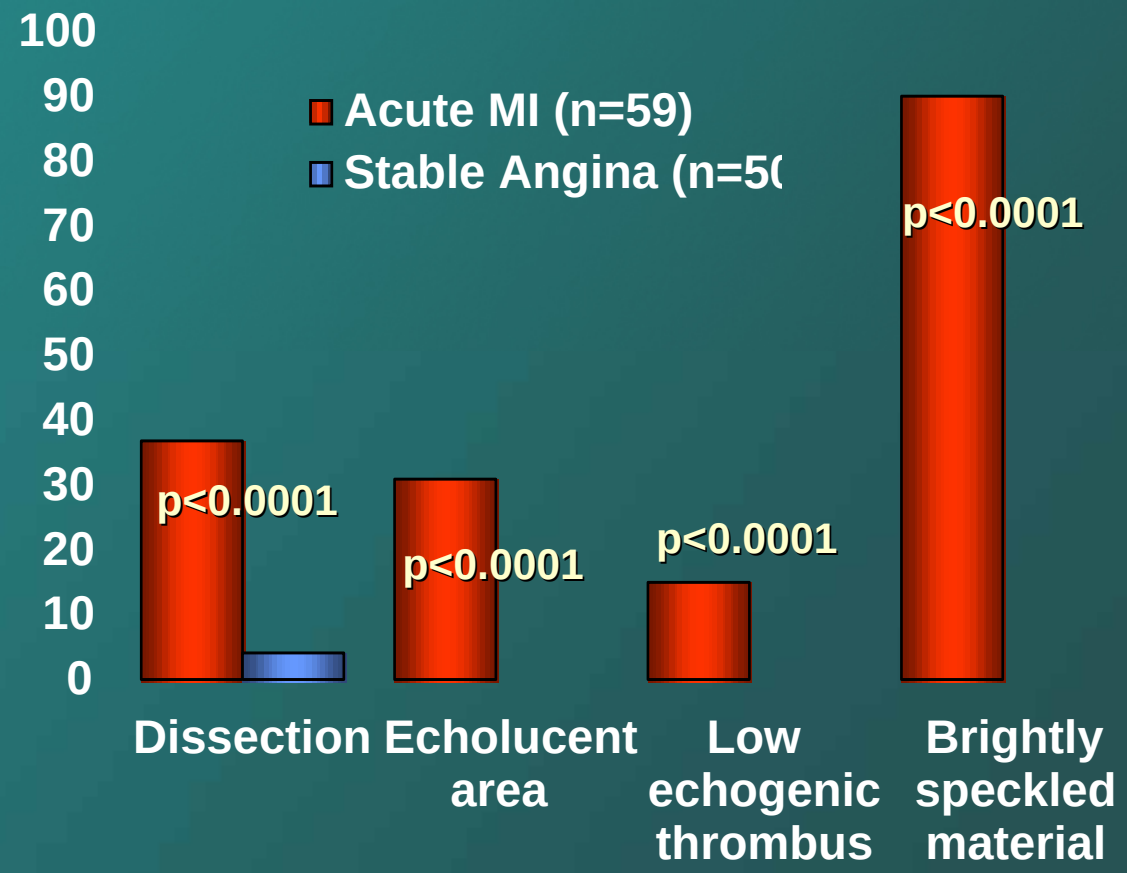
Nissen, et al. N Engl J Med 2005;352:29-38



0 → 2mm → 6mm

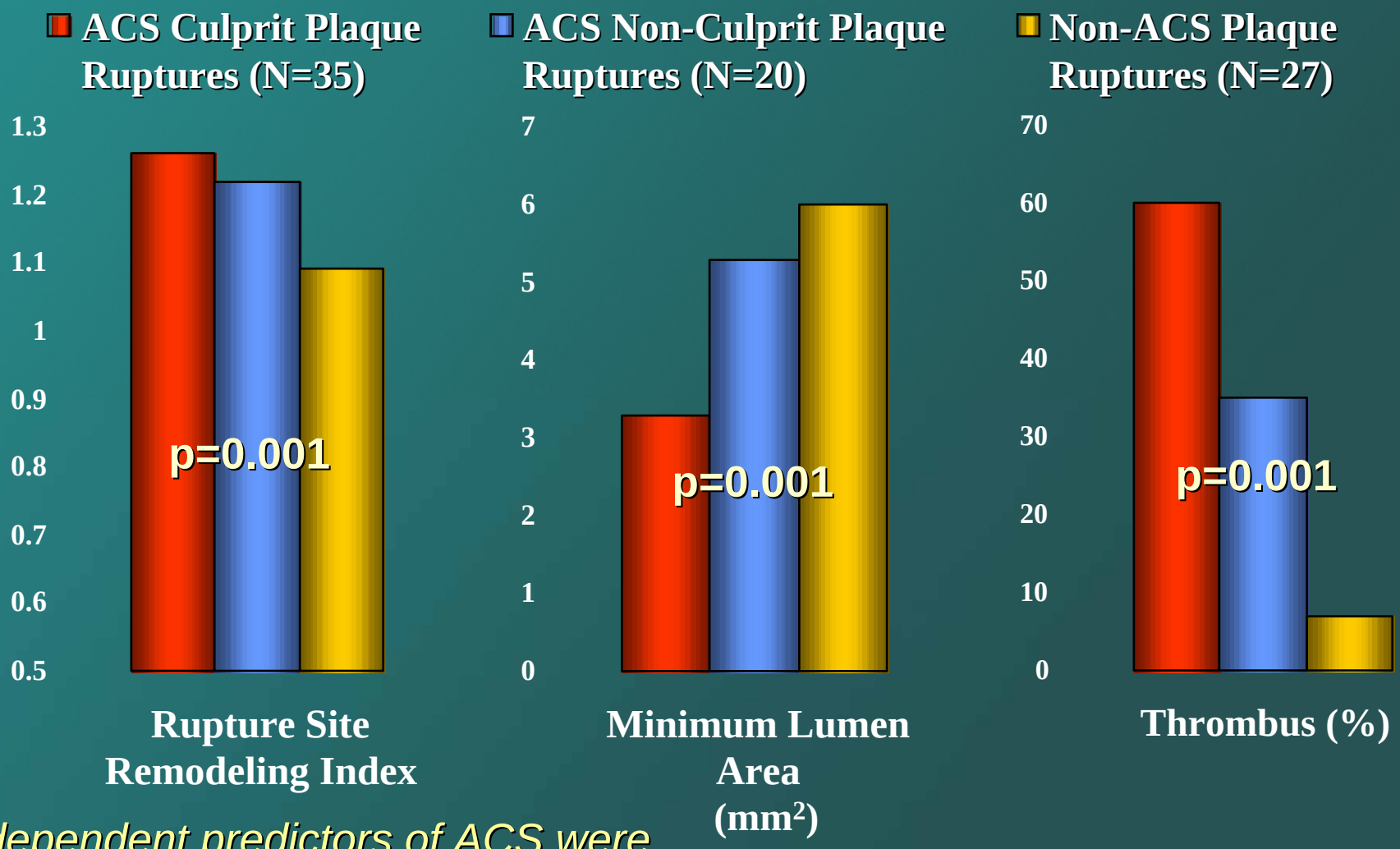


Lesion Characteristics in 59 Pts with AMI



Fukuda et al. Heart 2001;85:402-6

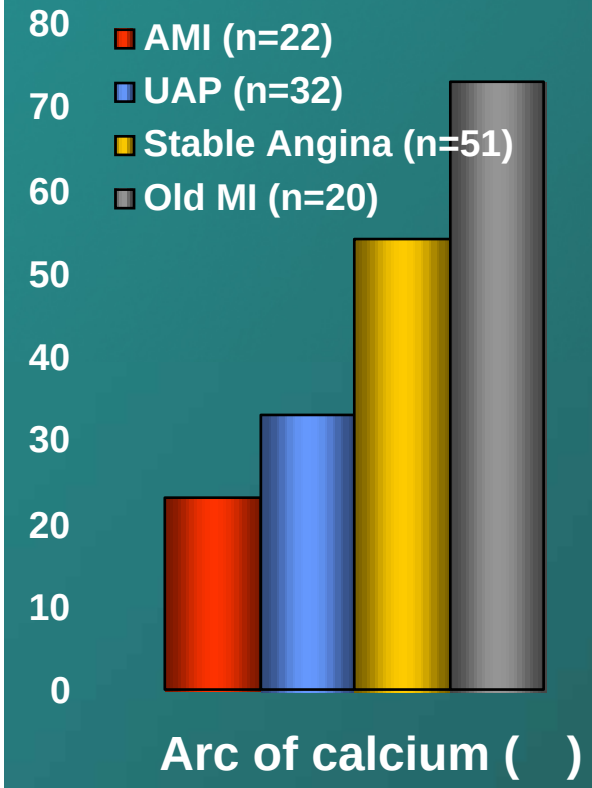
Comparison of Culprit & Non-Culprit Rupture Sites in ACS Patients and Rupture Sites in Non-ACS Patients



Independent predictors of ACS were MLA and thrombus (both p=0.01)

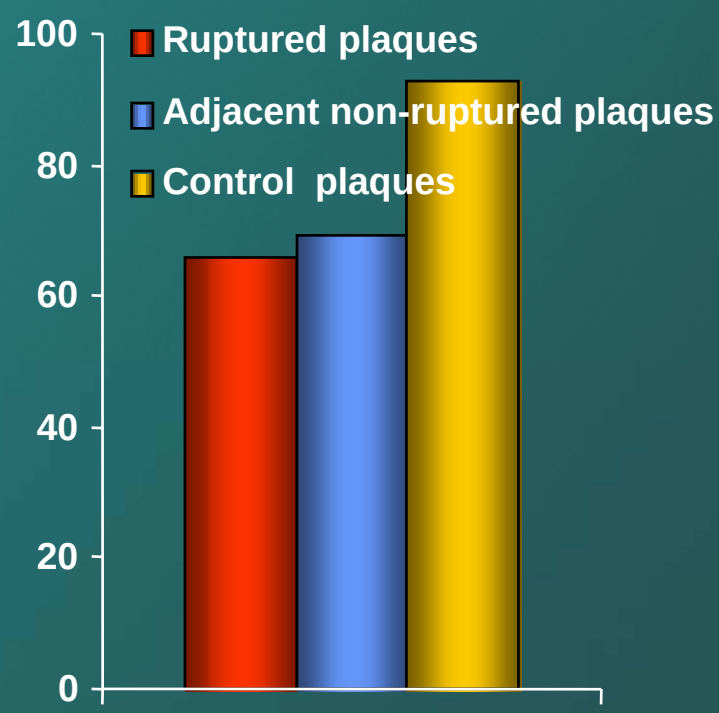
Fuji et al. Circulation 2003;108:2473-8

Calcium is less severe in unstable lesions



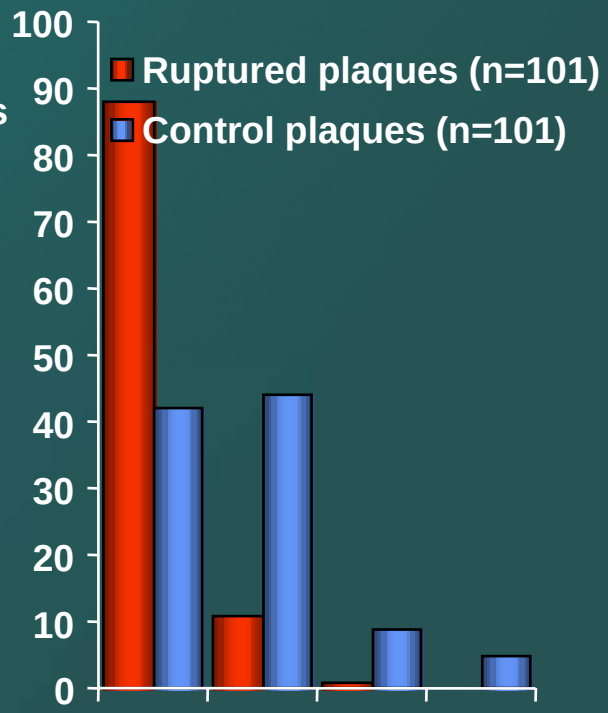
Arc of calcium ( )

Nakamura et al
JACC. 2001;37:63-9



29 fibrotic or fibrocalcific plaques

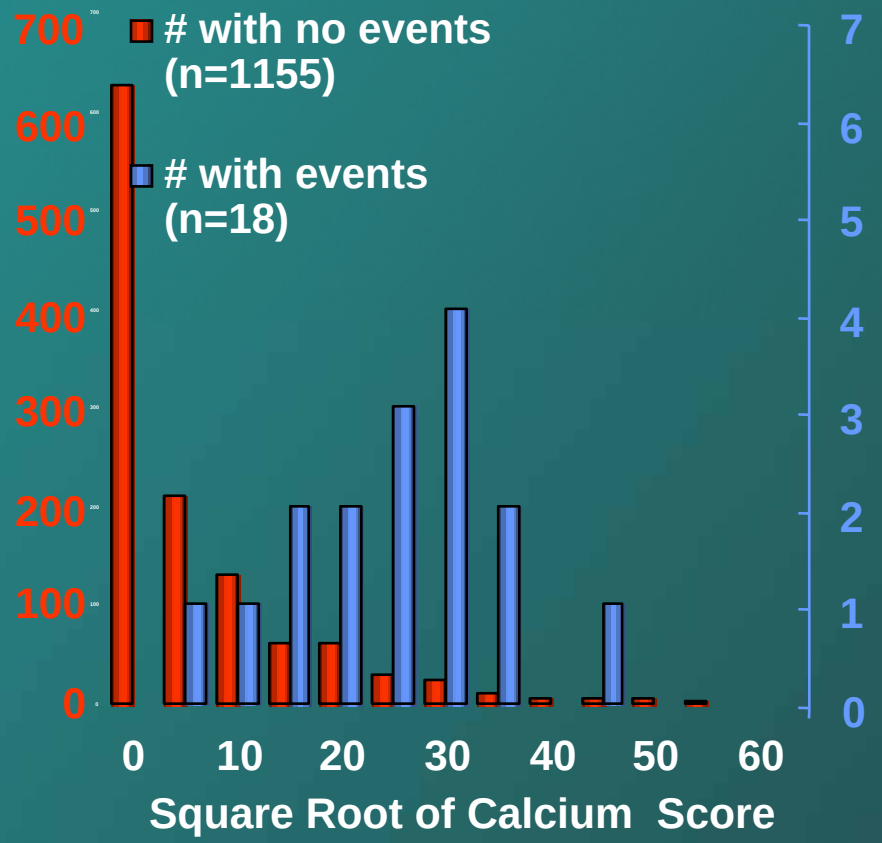
Von Birgelen et al
JACC 2001;37:1864-70



Quadrants Ca^{++}

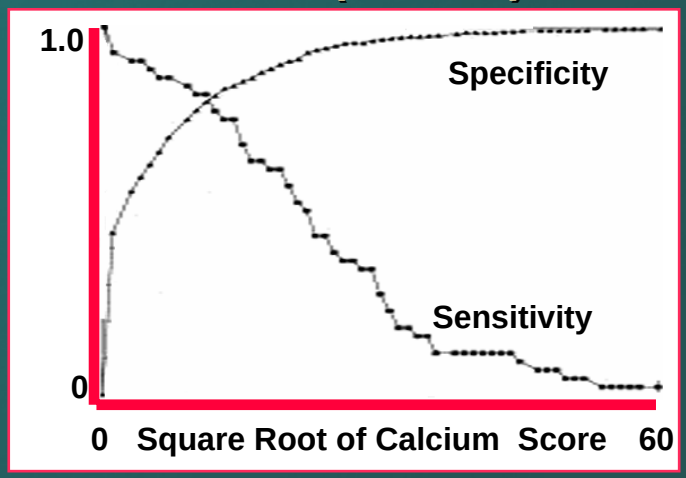
Fujii et al
Am J Cardiol 2005;96:352-7

EBCT calcium score predicts acute coronary events at 1 year follow-up

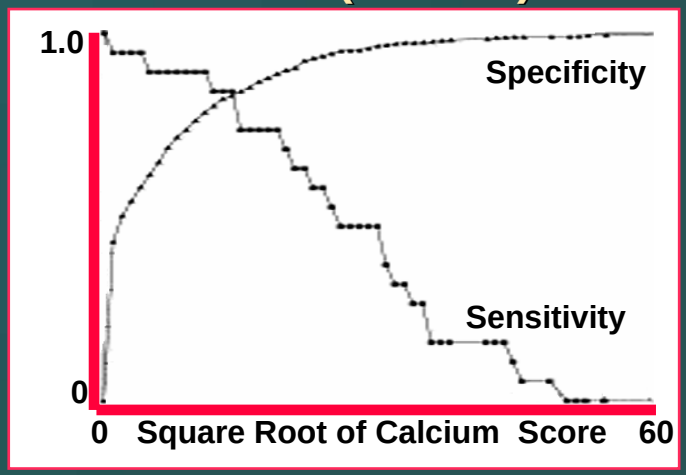


Arad et al. Circulation 1996;93:1951-3

MACE (n=1172)

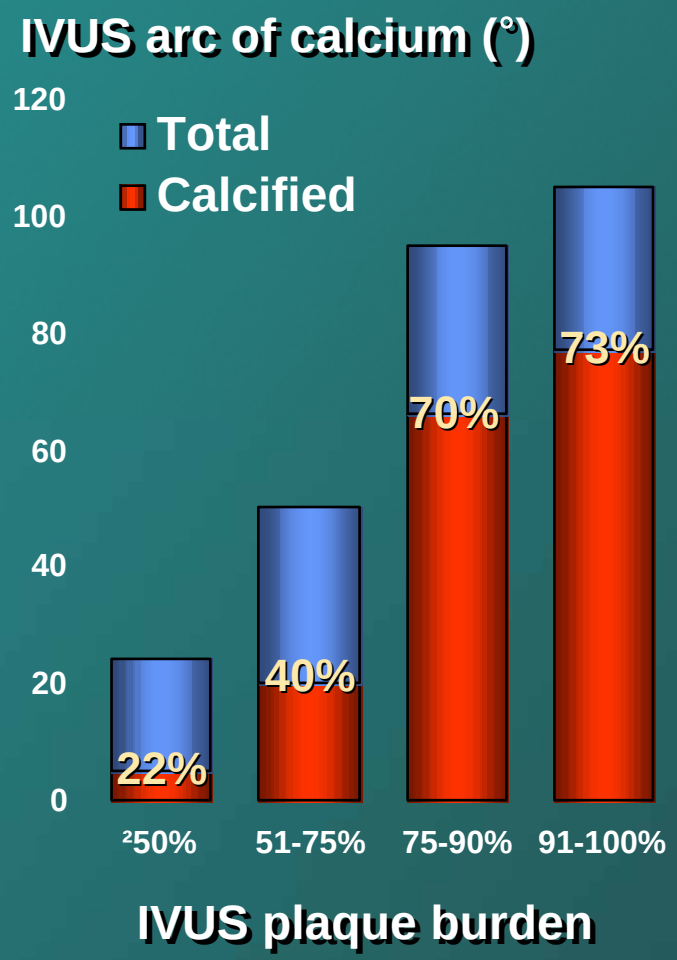


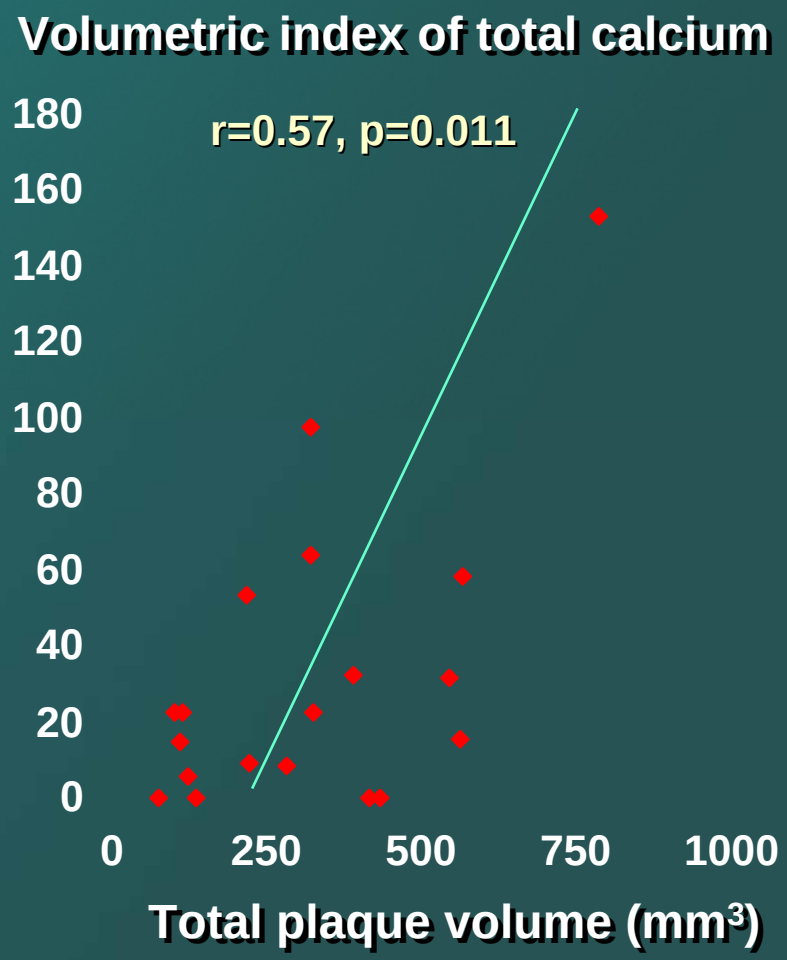
Death/MI (n=1172)



Arad et al. J Am Coll Cardiol 2000;36:1253-60

Calcium is an index of plaque volume





Mintz et al. J Am Coll Cardiol 1997;29:268-74

Tinana et al. Am J Cardiol 2002;89:757-60

72±12% of plaque volume (range 46-86%) is in non-stenotic segments

	Lesion	Non- Stenotic Segment	p
EEM vol (mm^3)	119 ±111	459 ±283	<0.0001
Lumen vol (mm^3)	29 ±30	228 ±156	<0.0001
P&M vol (mm^3)	90 ±86	231 ±140	<0.0001
Length (mm)	9.4 ±7.6	33.4 ±13.5	<0.0001

- The likelihood of developing acute coronary syndromes correlates with coronary plaque burden
- Vulnerable and ruptured plaques arise from non-stenotic segments where most of the plaque burden resides
- Measures of plaque burden - such as calcium - may, therefore, be indirect indices of vulnerable plaques.

Tinana et al. Am J Cardiol 2002;89:757-60

Patterns of Calcification

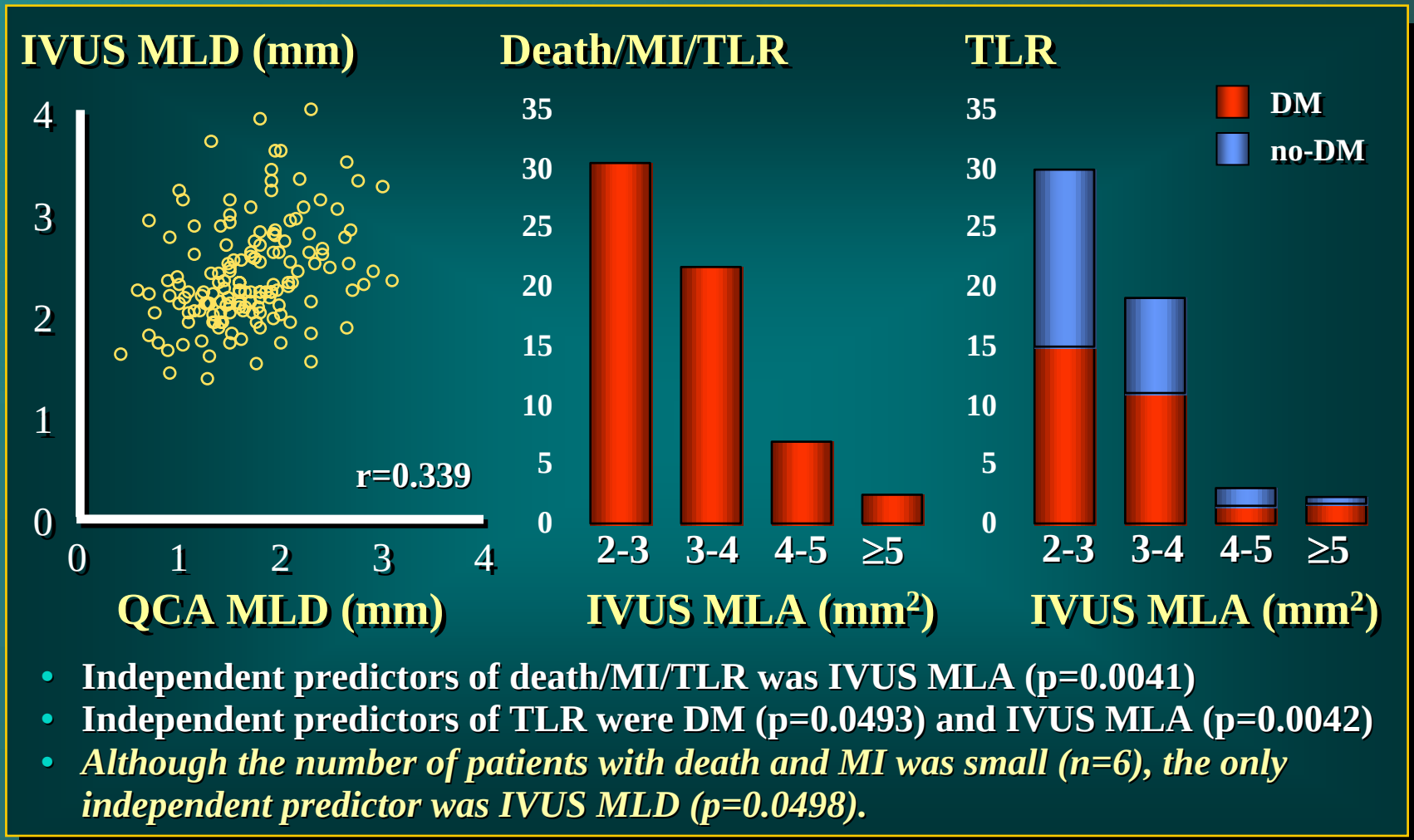
	MI (n=61)	Unstable angina (n=70)	Stable angina (n=47)
No calcification	26%	41%	21%
Spotty calcification	51%	40%	30%
Intermediate calcification	15%	16%	11%
Extensive calcification	8%	3%	38%

p<0.0001

- Spotty calcification=lesion with only small calcium deposits <90˚
- Intermediate calcification=arc of calcium of 90-180˚ in at least one cross-section
- Extensive calcificaiton=arc >180˚ in at least one cross-section

Ehara. Circulation 2004;110:3424-9

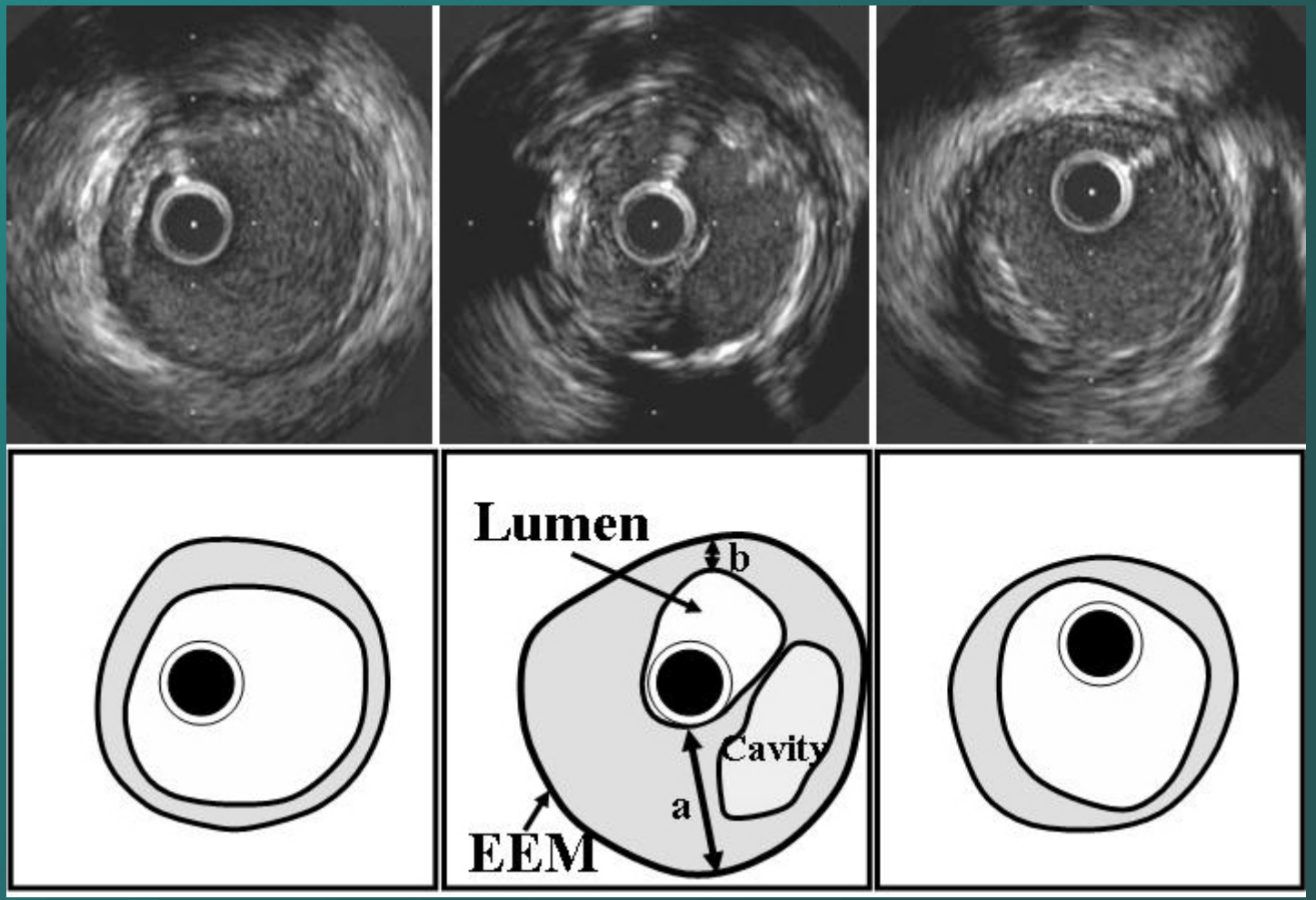
Clinical Follow up in 357 intermediate lesions in 300 pts deferred intervention after IVUS imaging



- Independent predictors of death/MI/TLR was IVUS MLA (p=0.0041)
- Independent predictors of TLR were DM (p=0.0493) and IVUS MLA (p=0.0042)
- *Although the number of patients with death and MI was small (n=6), the only independent predictor was IVUS MLD (p=0.0498).*

Abizaid et al. Circulation 1999;100:256-61

IVUS profile of ruptured plaques: Insights into pre-rupture morphology



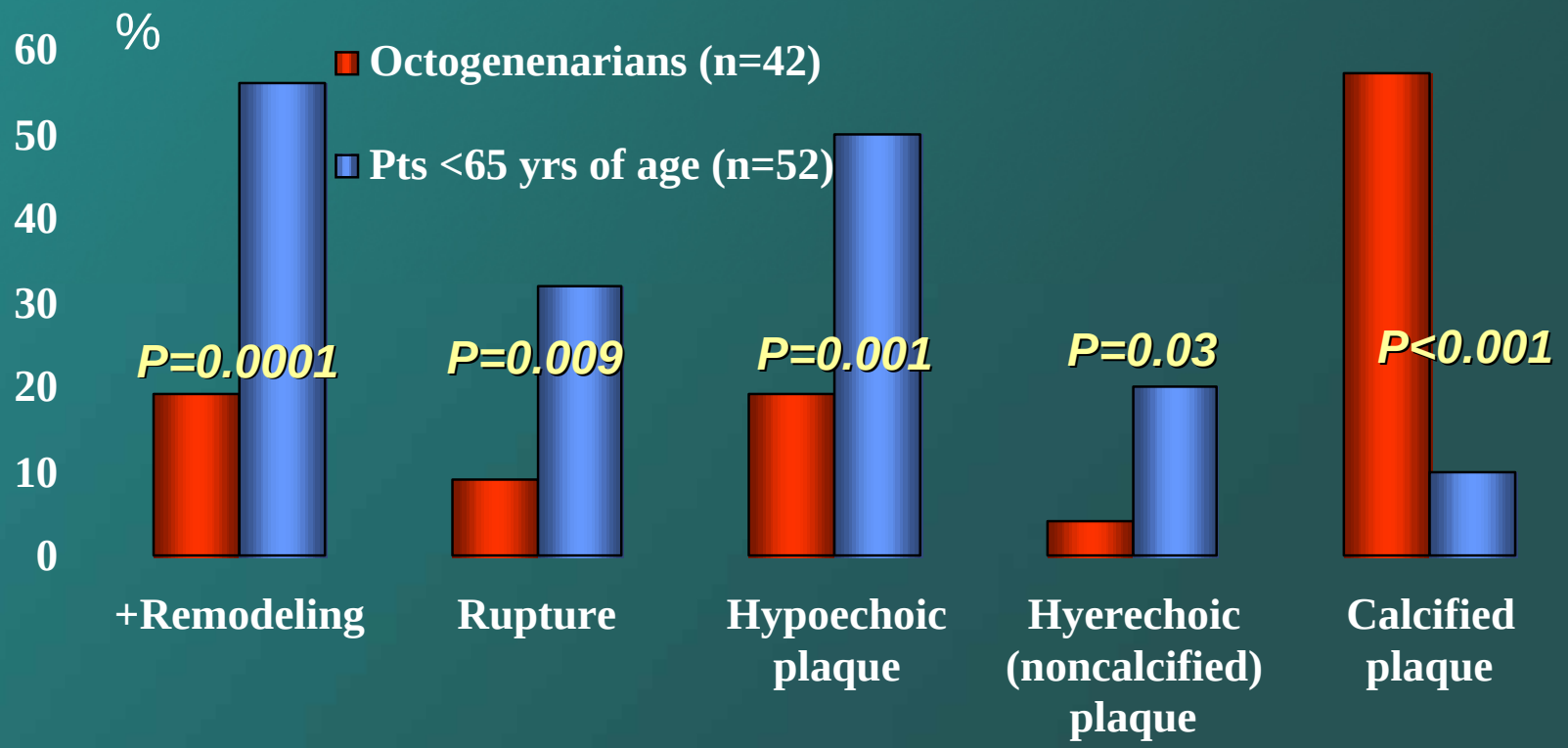
	Mean±1SD	CoV	10th Percentile	90th Percentile
Reference				
Lumen CSA	11.7±3.5	0.29	8.1	15.3
EEM CSA	20.2±5.6	0.27	14.2	26.7
P&M CSA	8.5±3.0	0.35	4.9	12.4
Plaque Burden	0.42±0.75	0.18	0.31	0.49
Lesion				
Lumen CSA	4.9±2.7	0.55	2.1	8.6
EEM CSA	20.8±6.0	0.29	14.3	28.5
P&M CSA	15.9±4.9	0.31	9.8	22.4
Min P&M Th	0.5±0.3	0.58	0.2	1.0
Max P&M Th	2.3±0.6	0.25	1.6	3.0
Eccentricity	0.32±0.23	0.71	0.09	0.66
Plaque Burden	0.76±0.10	0.12	0.63	0.88
AS	0.57±0.19	0.34	0.28	0.80
RI	1.10±0.20	0.18	0.87	1.38
Arc of Ca^{++}	46.9±51.2	1.09	0	106.7

- **Using the five variables with the narrowest coefficient of variance, 67% of 112 ruptured plaques fit *all* of following 10th or 90th percentile parameters**
  - **>14.3mm^2 lesion EEM area**
  - **>8.1mm^2 reference lumen area**
  - **>1.6mm maximum lesion plaque thickness**
  - **>0.63 lesion plaque burden**
  - **>0.87 remodeling index).**
- **89% fit 4 of these 5 parameters**
- **96% fit 3 of these 5 parameters.**

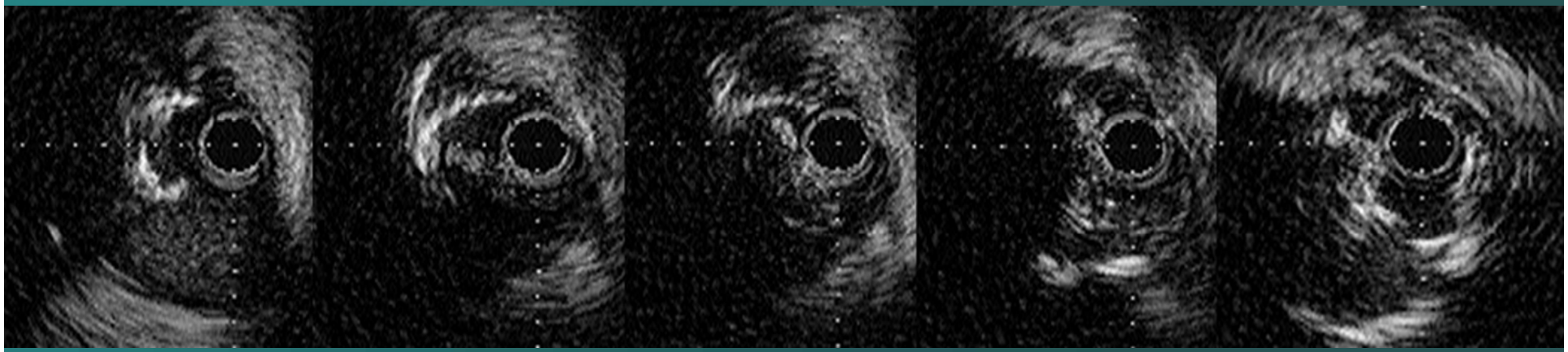
Fujii et al (unpublished)

Not all vulnerable plaques fit the standard definition of a thin-cap fibroatheroma (TCFA)

Negative remodeling and calcified plaque are more common in octogenarians with acute myocardial infarction



Hassani et al. J Am Coll Cardiol (in press)



0 → 1.5 → 6.0mm