Perspectives in Vulnerable Plaque Imaging

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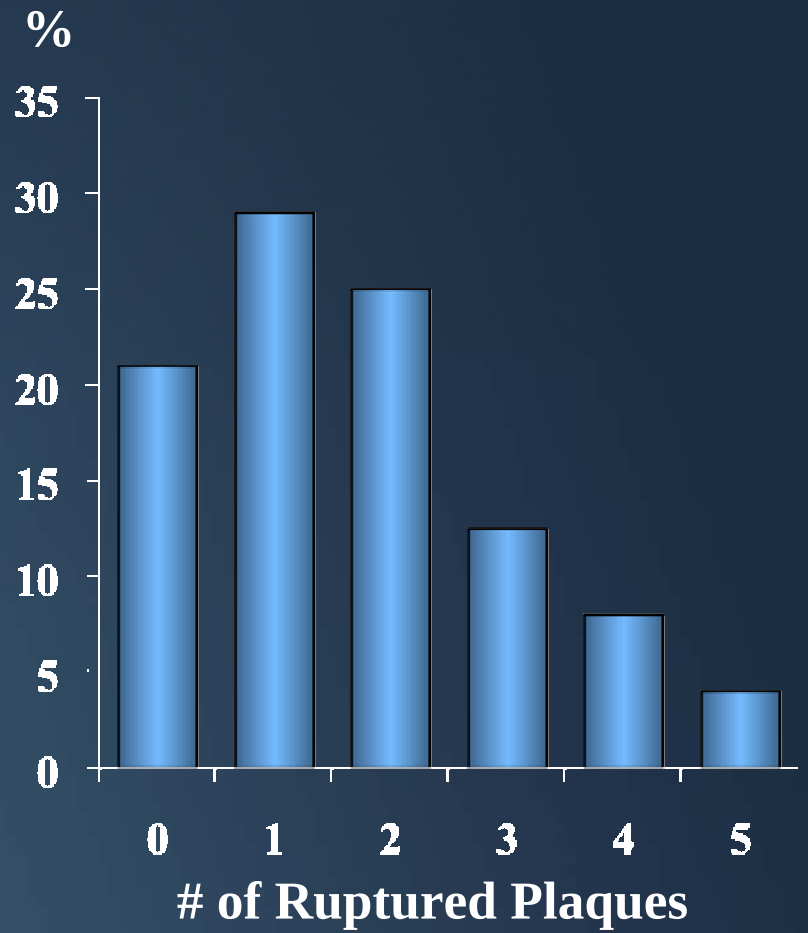
The Limits of Opening Arteries

NYTimes March 28, 2004

- A changing notion of how heart attacks occur ought to lower expectations for the traditional methods used to prevent arteries from clogging shut. It has long been customary for cardiologists to treat narrowing arteries by either enlarging and holding open the restricted channel or performing bypass surgery to carry blood around the narrowed section. The problem is, the vast majority of heart attacks are now known to originate in sections of artery that have not yet narrowed.
- As described in an article by Gina Kolata in last Sunday's Times, the old view of the progression of cardiovascular disease held that fatty deposits, or plaques, accumulate in the arteries slowly over decades, much as sludge builds up in a pipe, until one day the opening becomes so narrow that no blood can get through, and the patient suffers a heart attack. The newer view, which has taken hold in recent years but is little known to the public, is that heart attacks occur when an area of plaque ruptures and causes a blood clot to form, abruptly blocking the flow. In perhaps 75 to 80 percent of these cases, the plaque was not obstructing an artery, would not have been treated or bypassed and produced no symptoms.
- Experts agree that artery-opening methods -- like bypass surgery, or insertion of a balloon to mash down plaque and a wire-cage stent to keep the channel open -- can alleviate crushing chest pain and save some lives. But patients should not assume that their cardiovascular problems are "fixed" by such procedures, and patients without symptoms whose arteries are narrowing should be wary about undergoing these procedures to ward off a potential heart attack. **They may have hundreds of vulnerable plaques elsewhere that are more apt to burst and trigger a heart attack than are the more stable plaques in the narrow section. Most such patients might better be treated with drugs to lower their cholesterol levels, control their blood pressure and prevent blood clots, or should adopt a healthier life style by giving up smoking, eating heart-healthy foods and exercising.**
- This profound change in thinking about cardiovascular problems makes us yearn for the day when there can be much wider testing of one therapy against another to identify those that work best from those that may be oversold.

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



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Rioufol et al Circulation 2002;106:804-808

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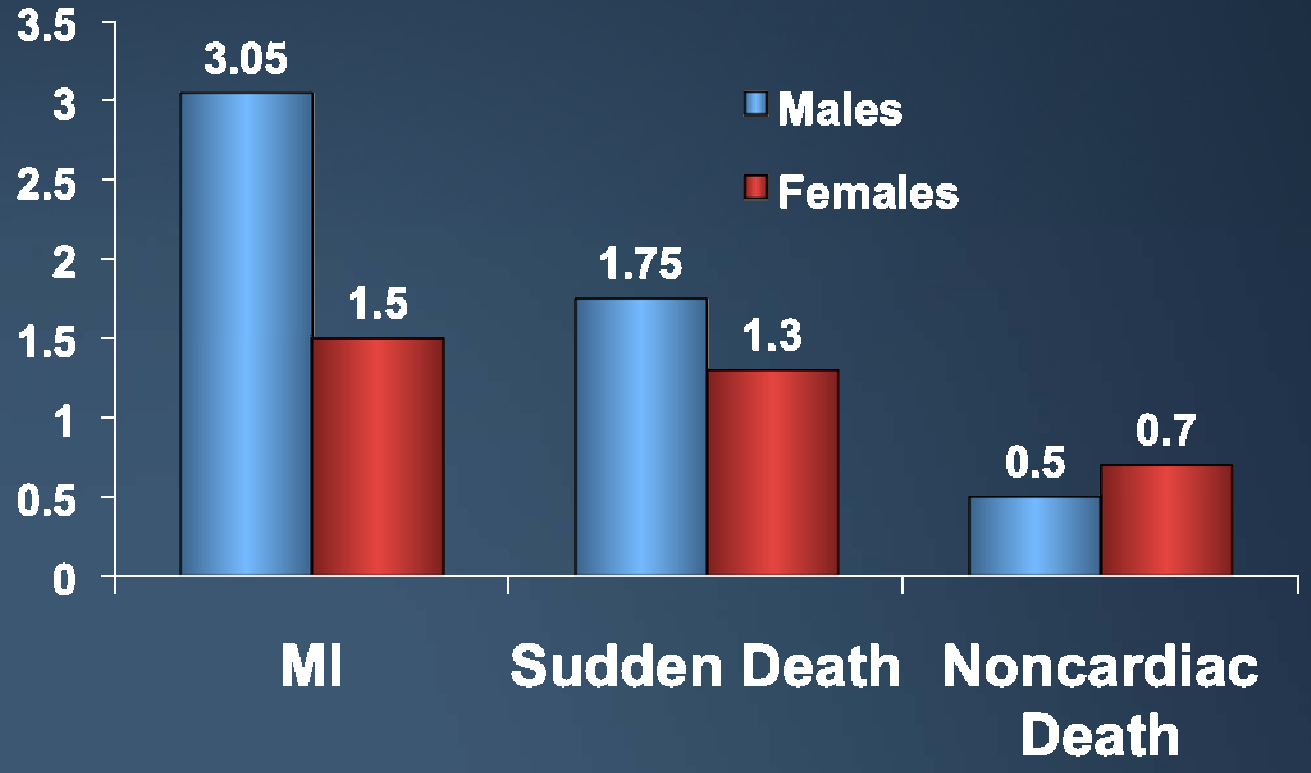
How common are vulnerable plaques?

Number of thin-cap fibroatheromas in patients dying with MI, sudden death, or noncardiac causes and studied at necropsy using *cross-sectional analysis*



(Burke et al. J Am Coll Cardiol 2003;41:1874-86-)

Number of thin-cap fibroatheromas in 50 patients studied at necropsy using *longitudinal analysis*

	All pts	Pts with ≥1 ruptured plaque	Pts with ≥1 TCFA or ruptured plaque	Pts with CV death
# of patients	50	14	20	33
# of ruptured plaques	19 (0.38/pt)		19 (0.95/pt)	15 (0.45/pt)
# fibroatheromas	193			
# TCFAs	23 (0.46/pt)	15 (1.21/pt)	23 (1.15/pt)	18 (0.55/pt)

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(Cheruvu et al. J Am Coll Cardiol 2007;50:940-9)

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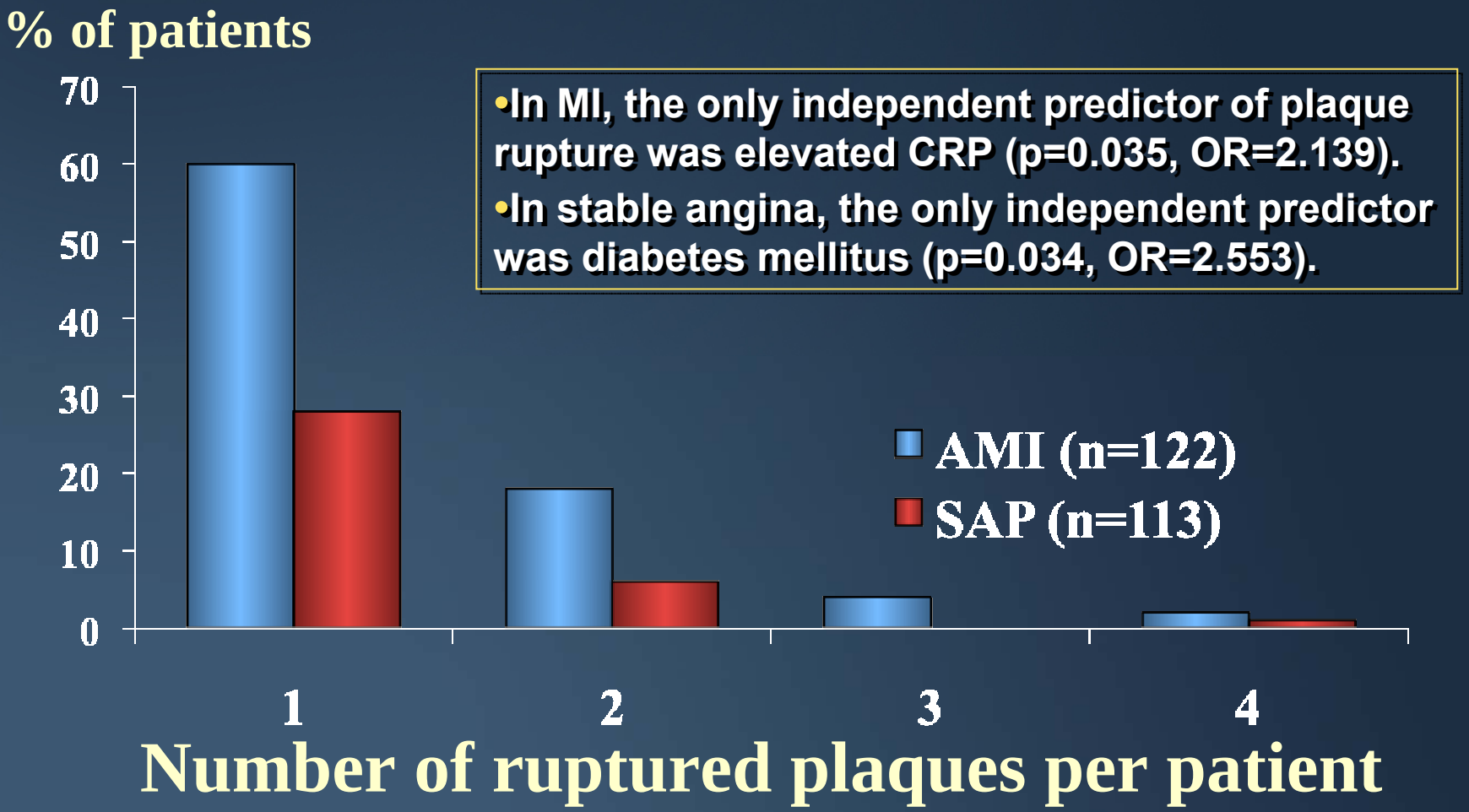
Ruptured plaques in patients with MI and stable angina



- In MI, the only independent predictor of plaque rupture was elevated CRP (p=0.035, OR=2.139).
- In stable angina, the only independent predictor was diabetes mellitus (p=0.034, OR=2.553).

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(Hong et al Circulation 2004;110:928-33)

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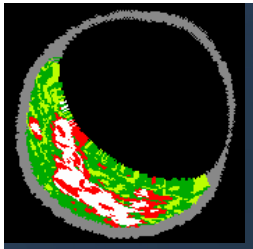
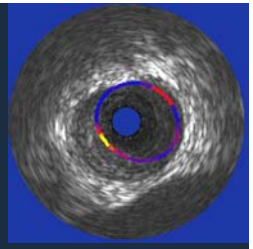


The PROSPECT Trial



700 pts with ACS undergoing 1 or 2-vessel PCI followed by 3-vessel imaging

QCA of entire coronary tree

IVUS

Virtual histology

Palpography (n=~350)

Proximal 6-8 cm of each coronary artery

Meds rec
Aspirin
Plavix 1yr
Statin
Repeat biomarkers
@ 30 days, 6 months

F/U: Until there are 100 VP events

MSCT Substudy
N=50-100

Repeat imaging in pts with events

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PI: Gregg W. Stone
Sponsor: Abbott Vascular (Partner: Volcano)

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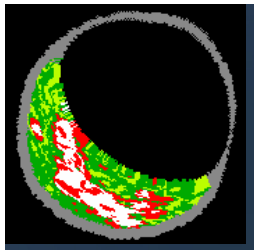


PROSPECT: Imaging Summary

Per patient incidence of VH-TCFAs/ThCFAs

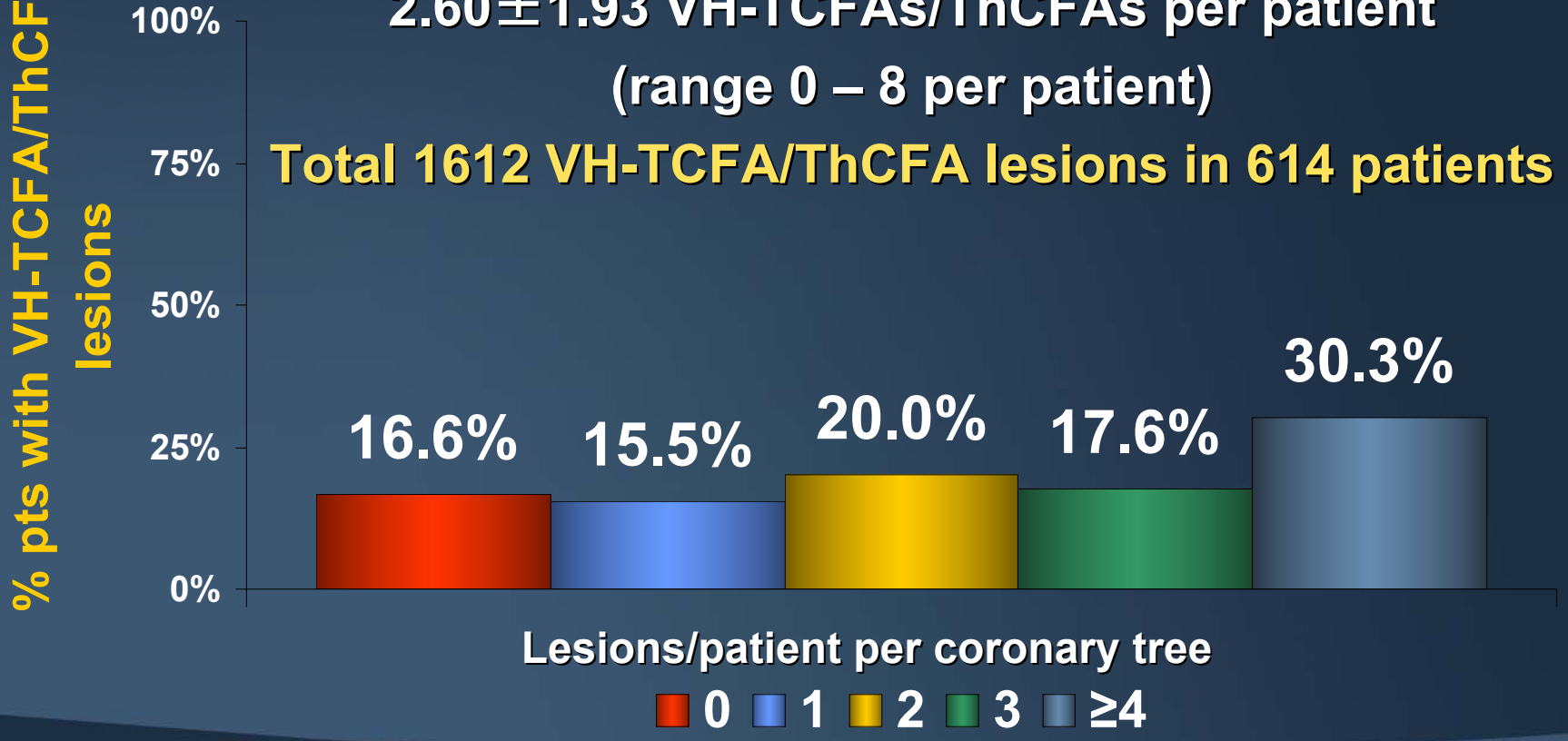
49.8% of patients have ≥1 VH-TCFA

71.8% of patients have ≥1 VH-ThCFA

2.60±1.93 VH-TCFAs/ThCFAs per patient

(range 0 – 8 per patient)

Total 1612 VH-TCFA/ThCFA lesions in 614 patients



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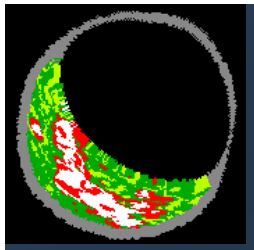


PROSPECT: Imaging Summary

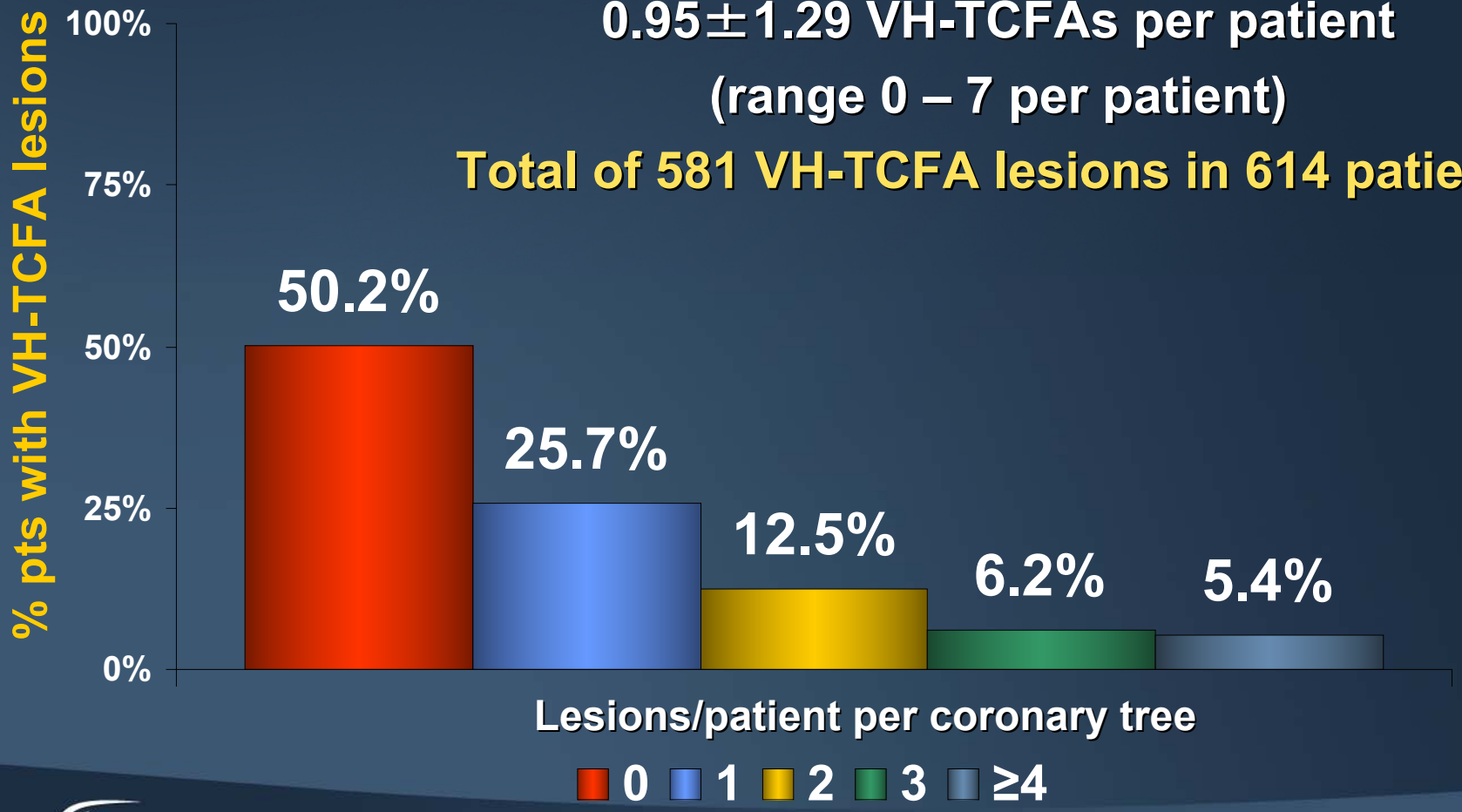
Per patient incidence of VH-TCFAs

49.8% of patients have ≥1 VH-TCFA

0.95±1.29 VH-TCFAs per patient

(range 0 – 7 per patient)

Total of 581 VH-TCFA lesions in 614 patients



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Location of 82 TCFAs in 34 patients with AMI and 17 patients with stable angina and three vessel OCT

In 34 AMI patients, there were 50 TCFAs (1.5/patient), 16 in the infarct related artery and 34 in the non-infarct related artery

Length of artery imaged beginning at the coronary ostium (mm)	
LAD	72±24mm
LCX	56±30mm
RCA	97±31mm

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(Fujii et al AHA 2007)

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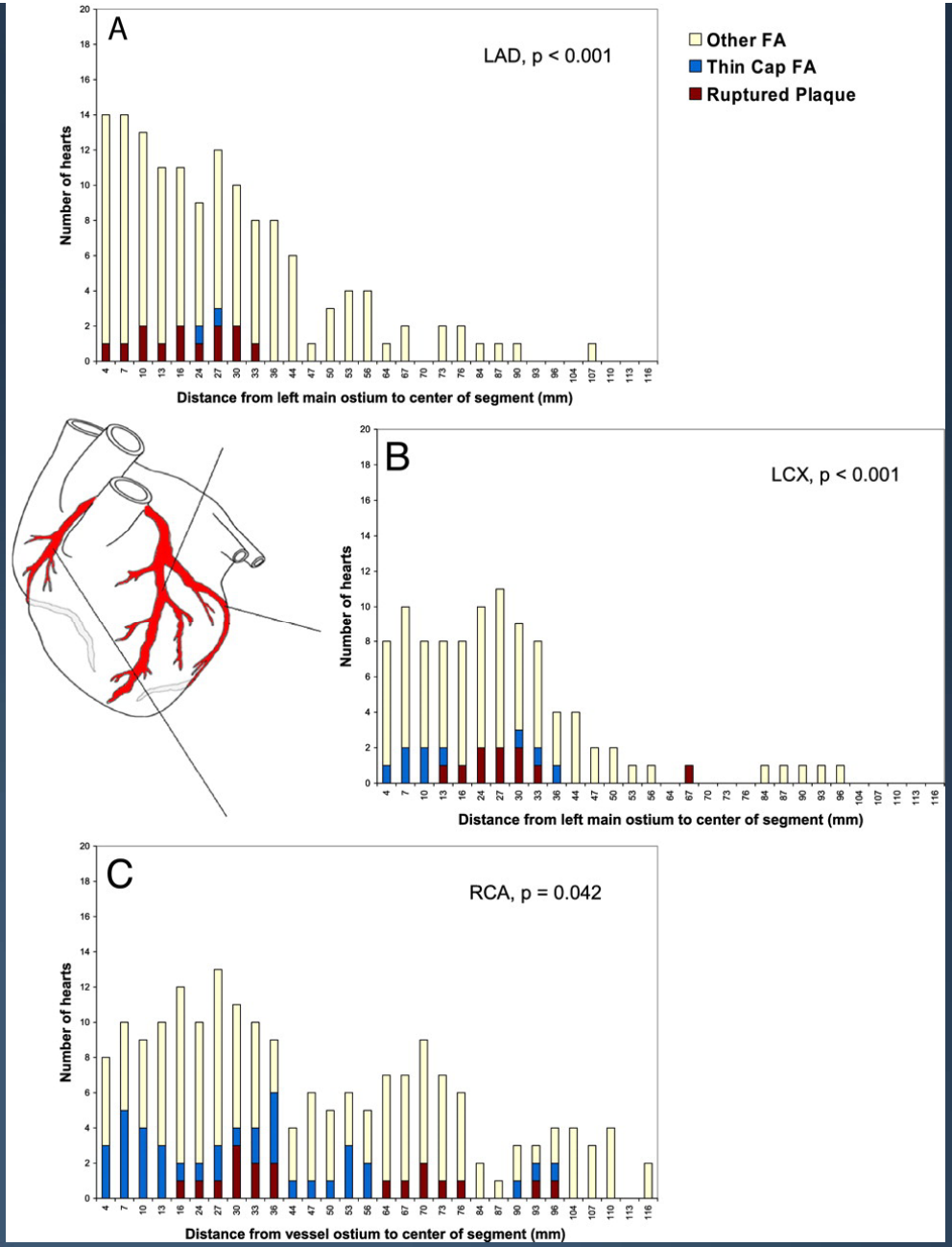
Are vulnerable plaque locations predictable?



Spatial Distribution of Advanced Coronary Lesions

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(Cheruvu et al. J Am Coll Cardiol 2007;50:940-9)

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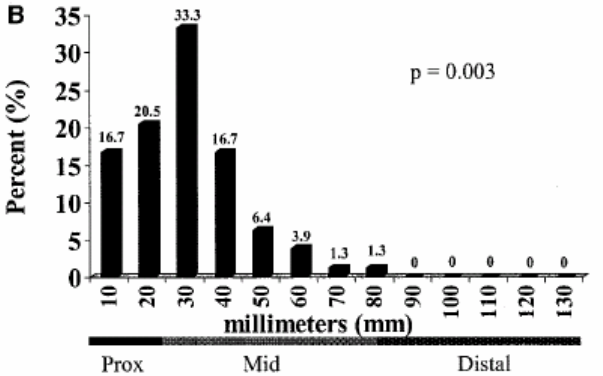
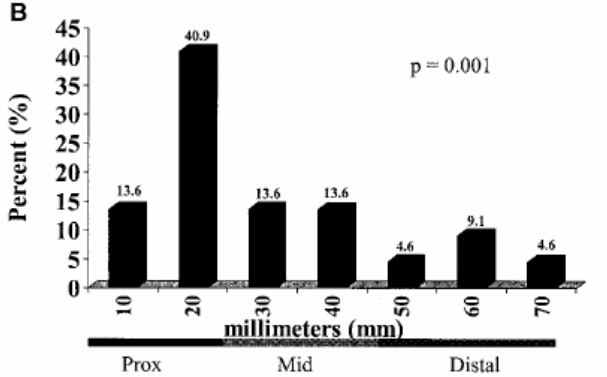
Angiographic location of acute coronary occlusions

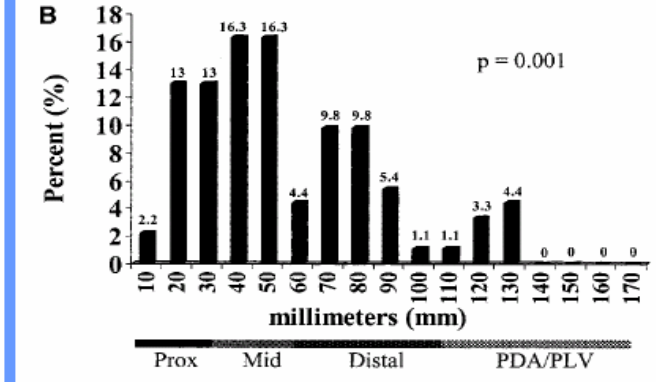
LAD



LCX



RCA



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(Wang et al. Circulation 2004;110:278-84)

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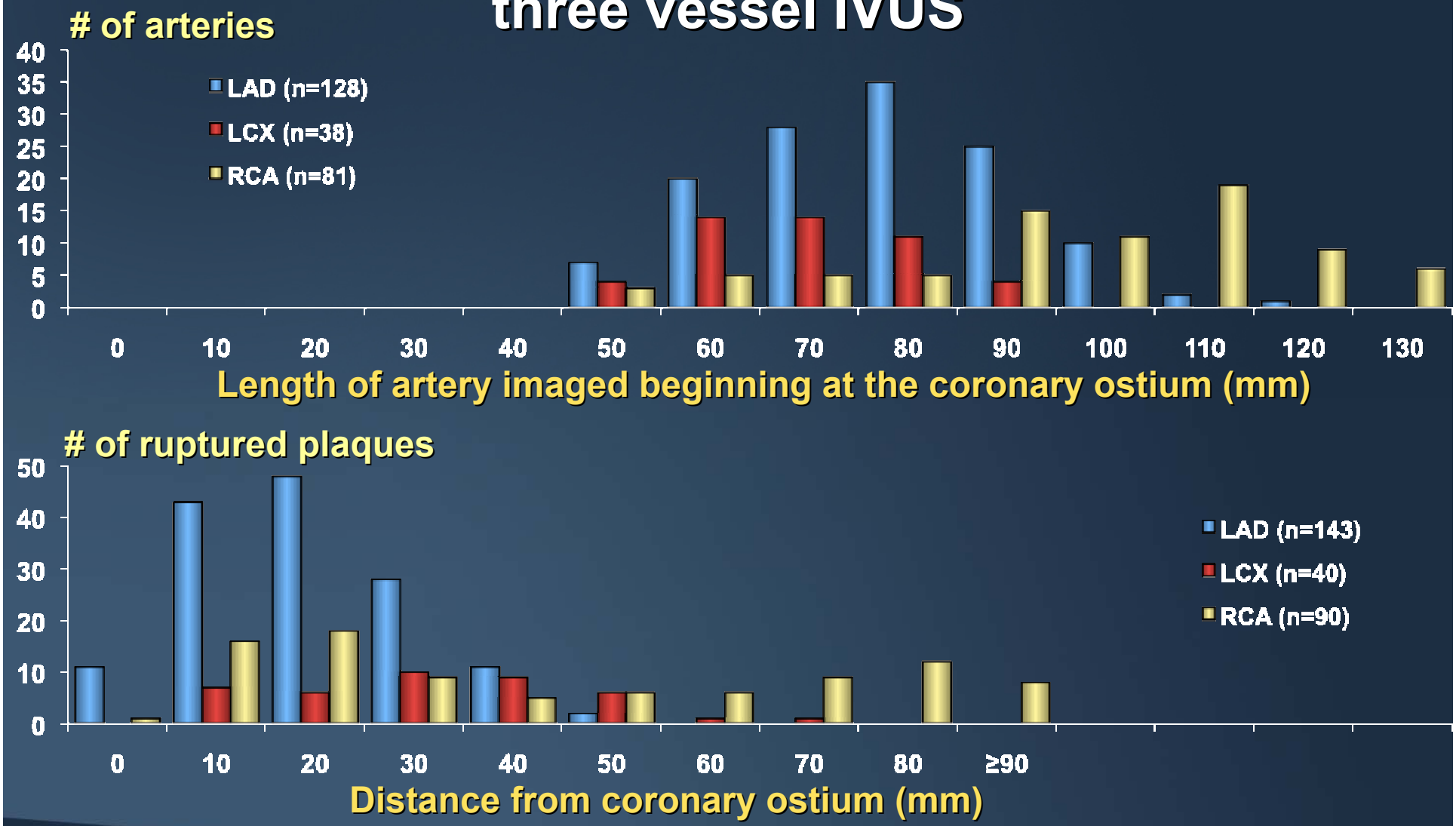
Location of 273 ruptured plaques in 158 patients with ACS and 48 patients with stable angina and three vessel IVUS



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(Hong et al J Am Coll Card 2005;46:261-5)

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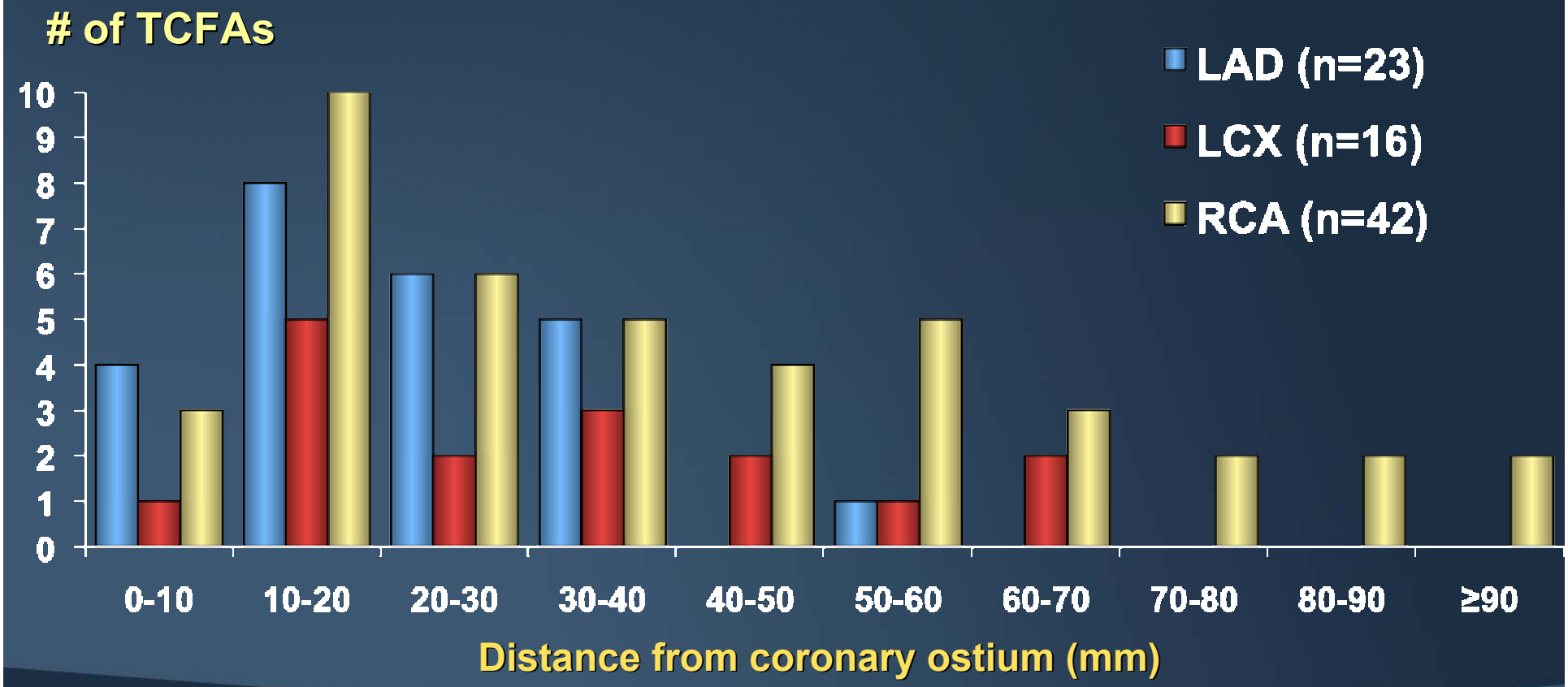
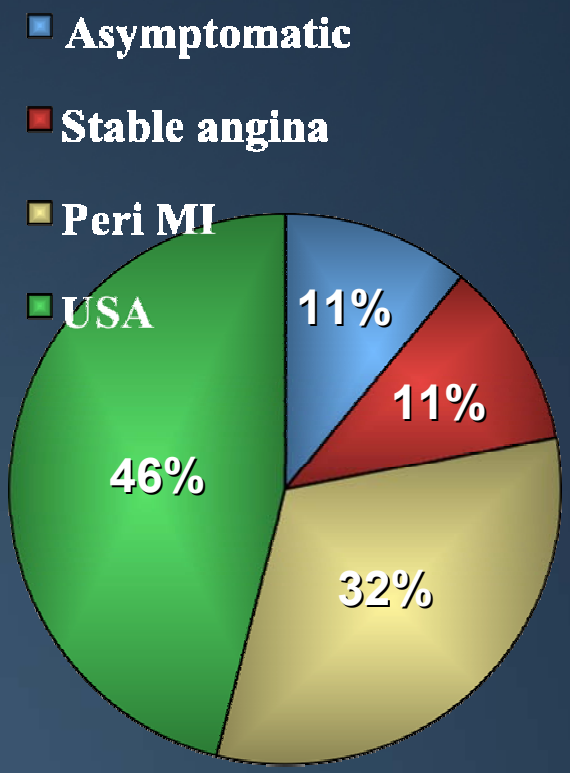
Location of 82 TCFAs in 34 patients with AMI and 17 patients with stable angina and three vessel OCT: Vulnerable plaques tend to cluster in predictable "hot spots" within the proximal segments of the LAD and LCX and the entire length of the RCA



(Fujii et al AHA 2007)

When vulnerable plaques rupture, do they always cause events?

Symptoms in 254 patients with 300 plaque ruptures in 257 arteries



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

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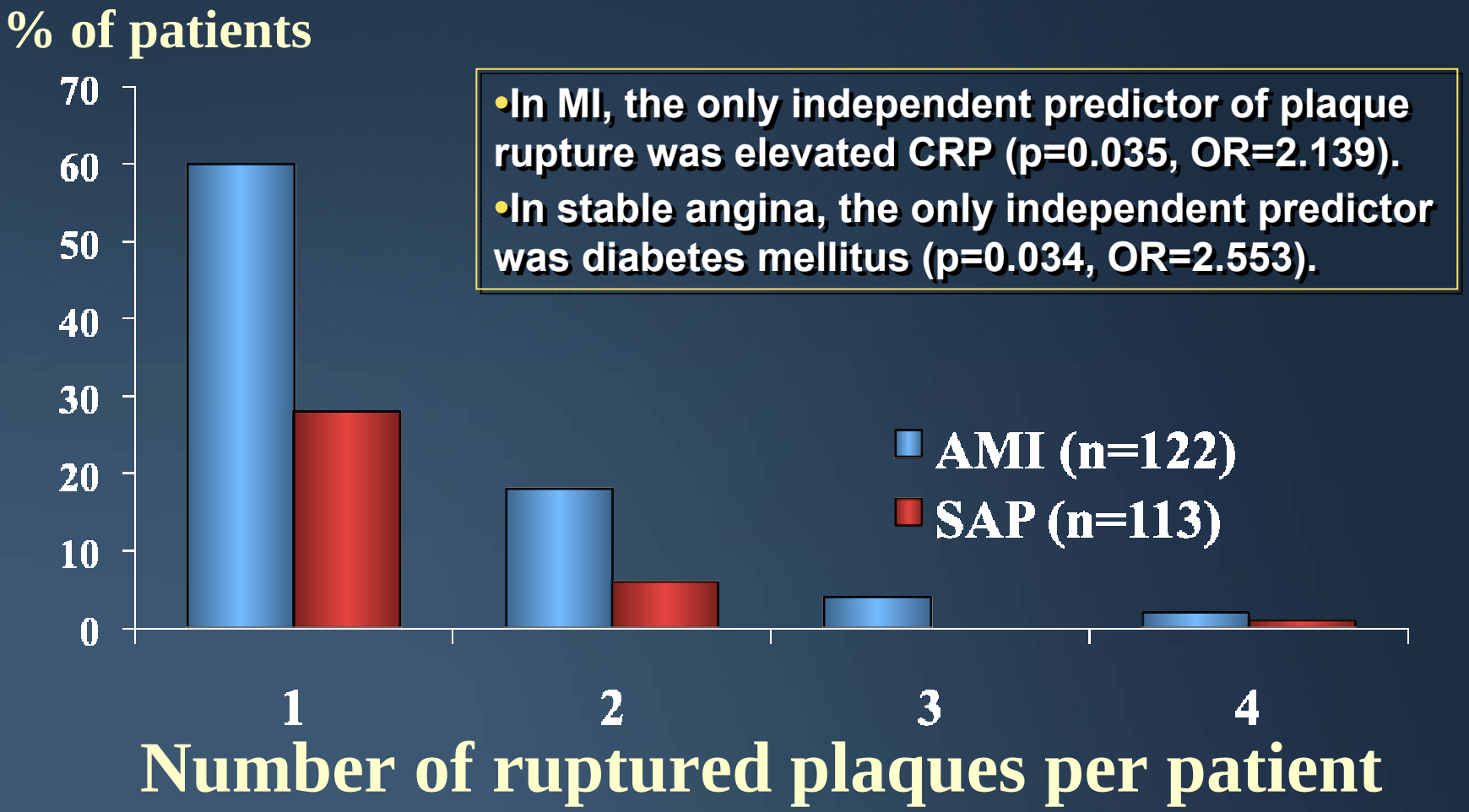
Ruptured plaques in patients with MI and stable angina



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(Hong et al Circulation 2004;110:928-33)

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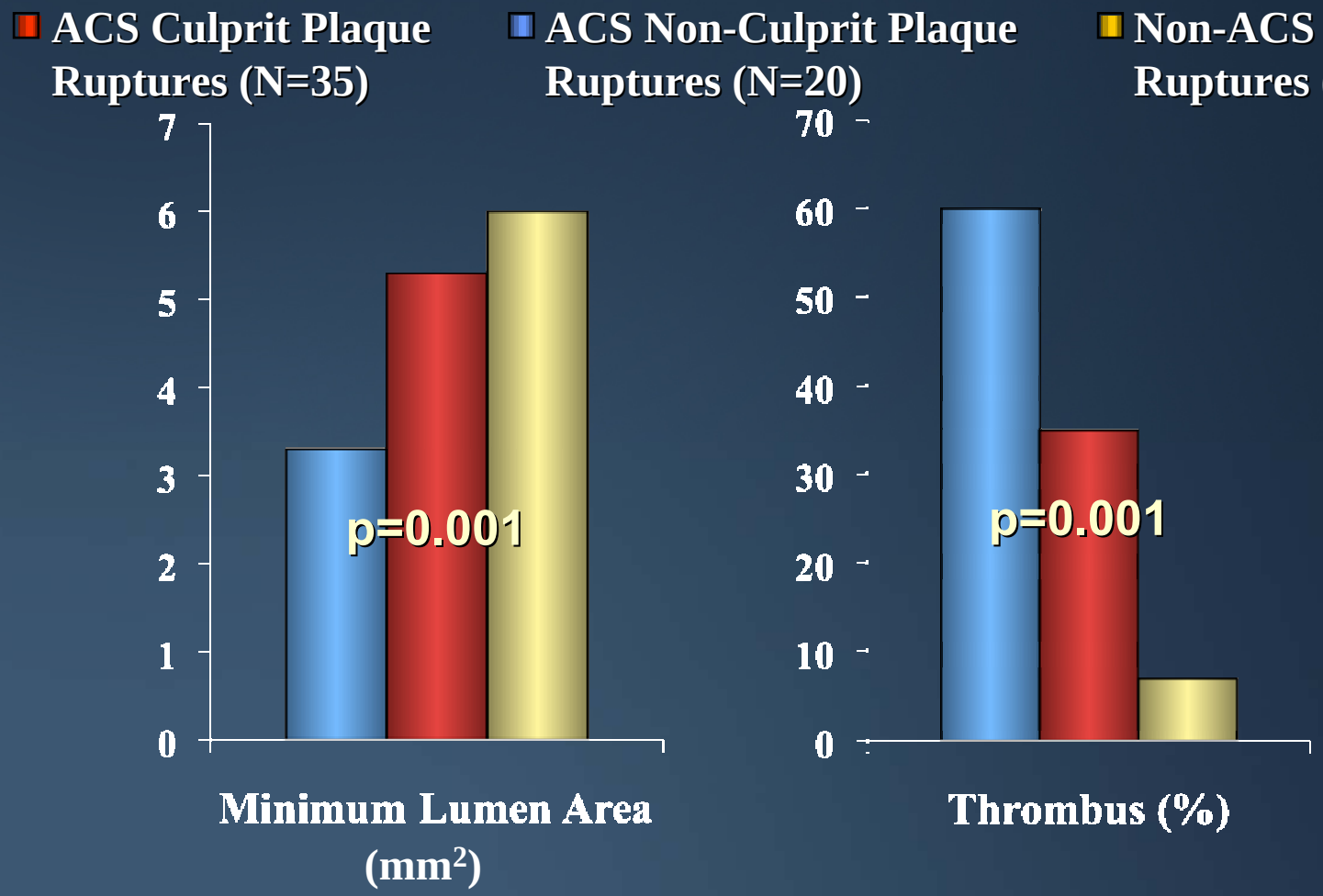
Comparison of Culprit & Non-Culprit Rupture Sites in ACS Patients and Rupture Sites in Non-ACS Patients



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

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

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Are all non-culprit events in the first year post-PCI related to vulnerable plaques? Or are some related to incomplete revascularization at the time of initial PCI?

Angiographic Occult Stenoses

- On pre-intervention IVUS, 404 patients with 436 arteries had 500 lesions with an IVUS minimum lumen area <4.0mm^2
- 28% (140/500) had an angiographic DS<50%

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(Maehara et al. Am J Cardio 2003;91:1335-8)

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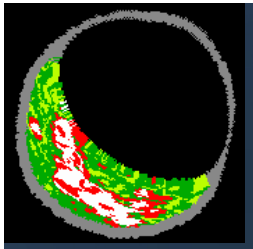
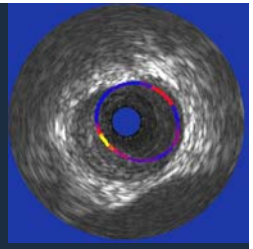
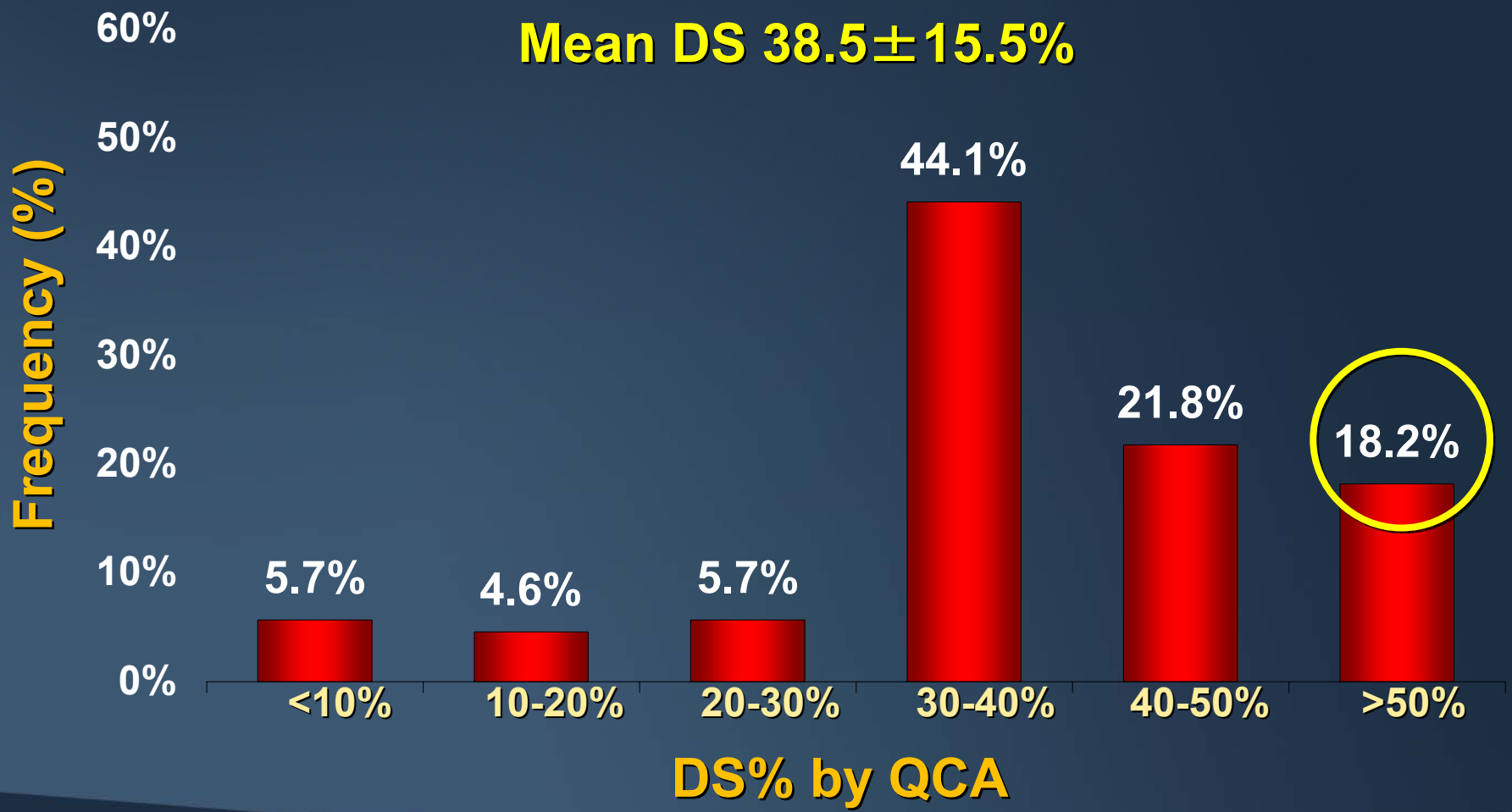


PROSPECT: Imaging Summary



QCA DS% in 1798 angiographically visible lesions

Mean DS 38.5±15.5%



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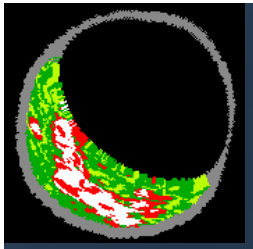
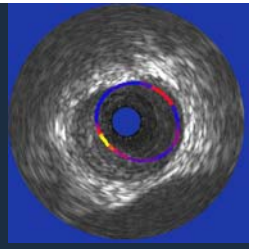


PROSPECT: Imaging Summary

IVUS of angiographic non-culprit lesions



By IVUS (in 786 of the 1798 total angiographic lesions)

EEM area, mm²	16.72 ± 6.36	MLD, mm	2.82 ± 0.64
Lumen area, mm²	8.89 ± 4.12	Mean LD, mm	3.26 ± 0.72
Plaque a			4.04 ± 0.88
Plaque burden %	47 ± 11	Mean VD, mm	4.45 ± 0.87
MLA, mm²	6.36 ± 3.75	Max VD, mm	4.90 ± 1.02
Remodeling index	0.94 ± 0.16	Lumen ecc.	0.93 ± 0.70

210 (26.7%) angiographically mild lesions had an MLA <4.0 mm²

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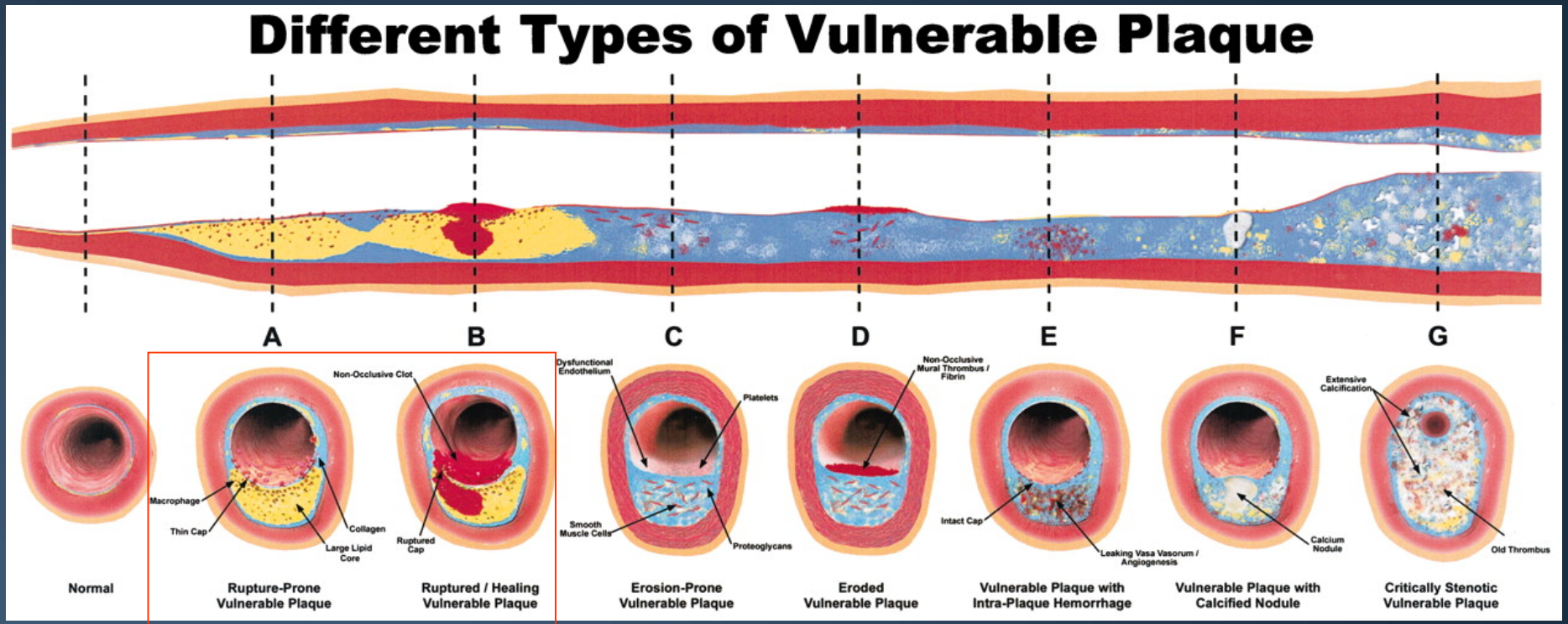
Are all vulnerable plaques thin-cap fibroatheromas?



70% of ACS culprit lesions

(Naghavi et al. Circulation 2003;108:1664-72)

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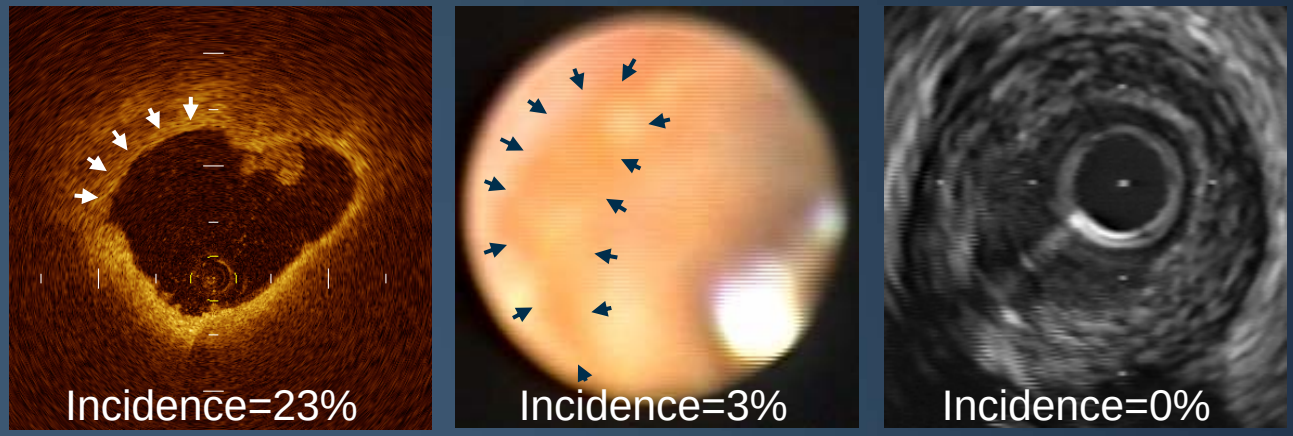
In vivo comparison of OCT and angioscopy in assessing culprit lesions in 30 AMI patients

Plaque rupture

Plaque erosion



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(Kubo et al. J Am Coll Cardiol 2007;50:933-9)

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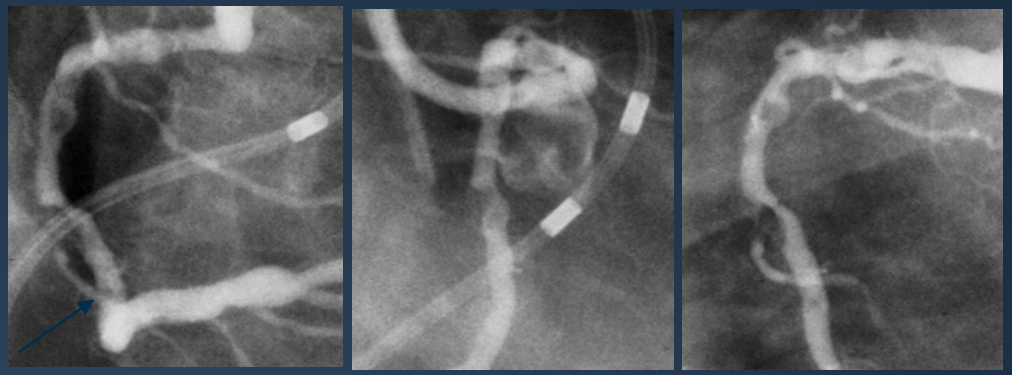

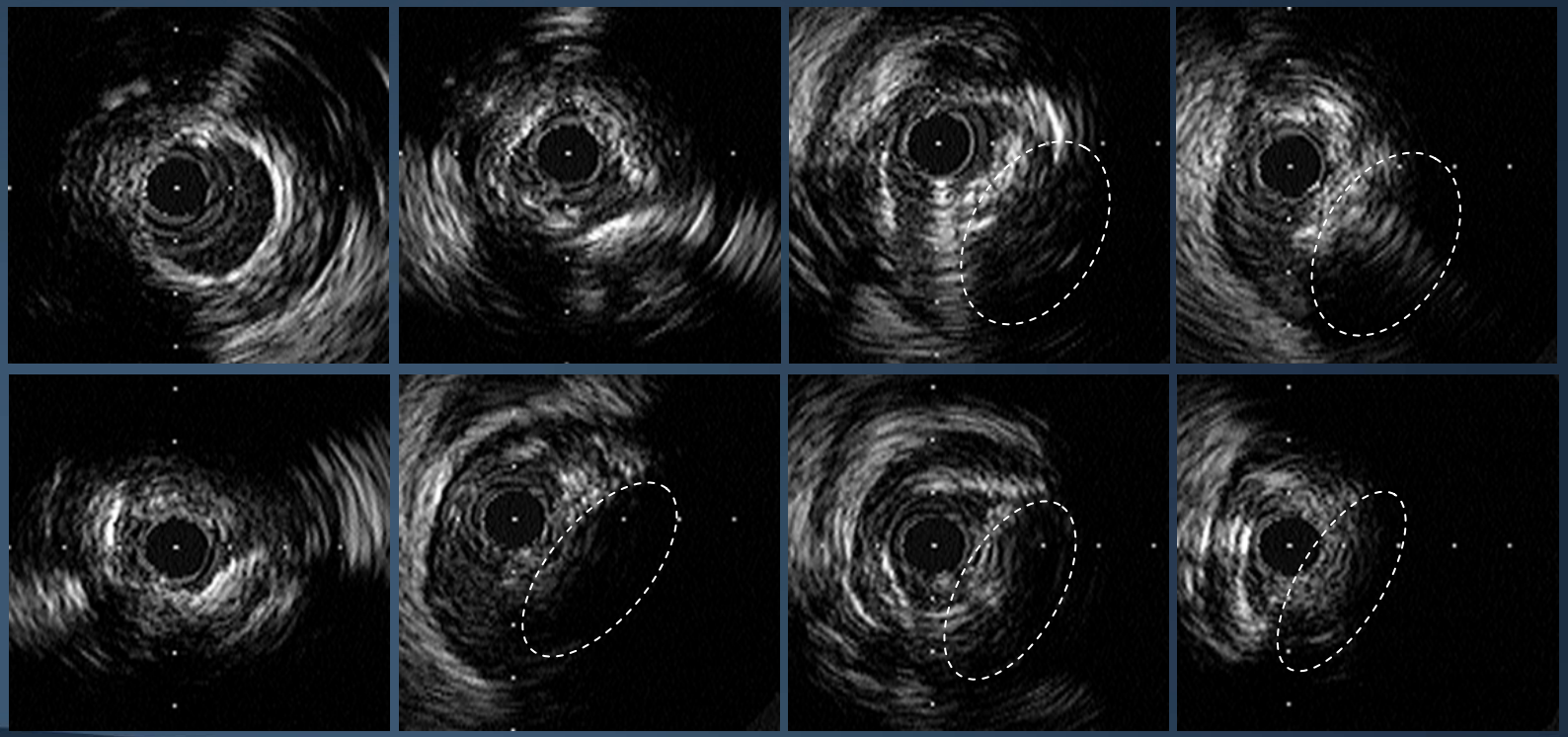

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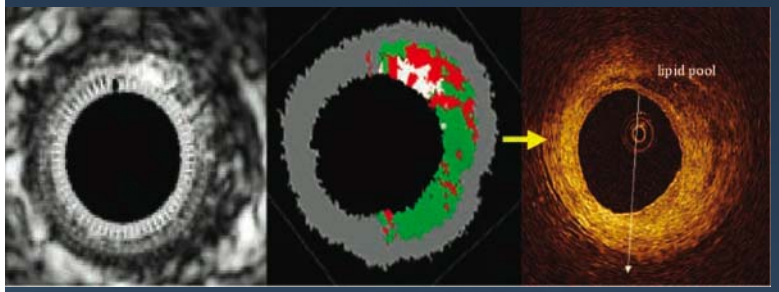
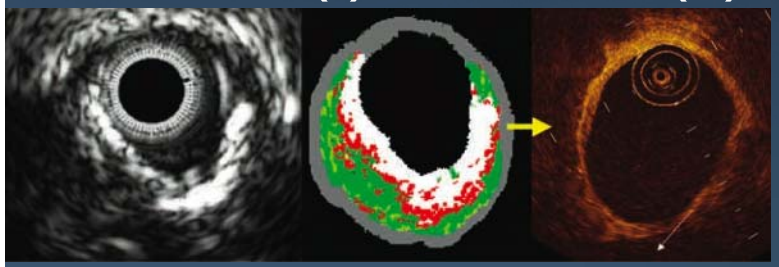
Do all of the new intravascular imaging modalities agree well diagnosing a TCFA?

OCT vs VH-IVUS TCFA diagnosis in 126 lesions in 56 pts

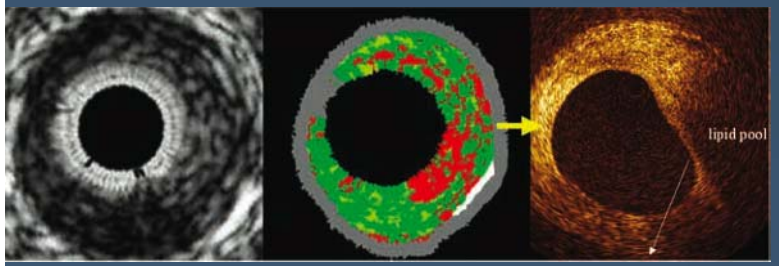
VH-IVUS (+) and OCT (-)



VH-IVUS (-) and OCT (+)



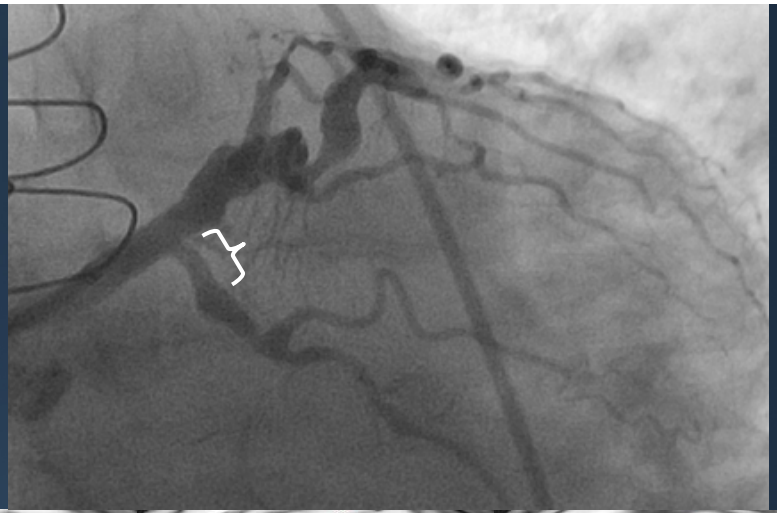
VH-IVUS (+) and OCT (+)

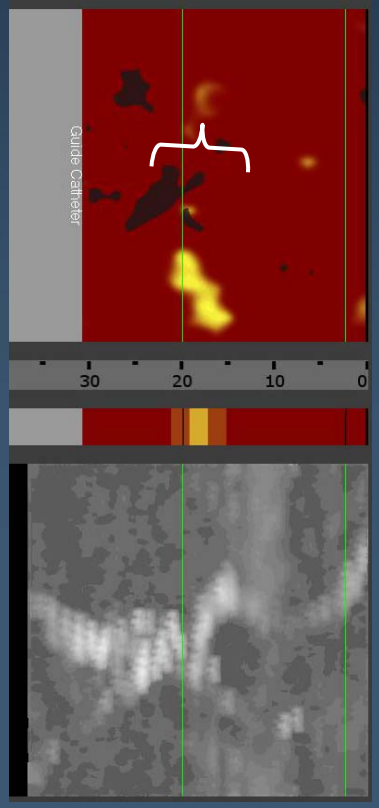


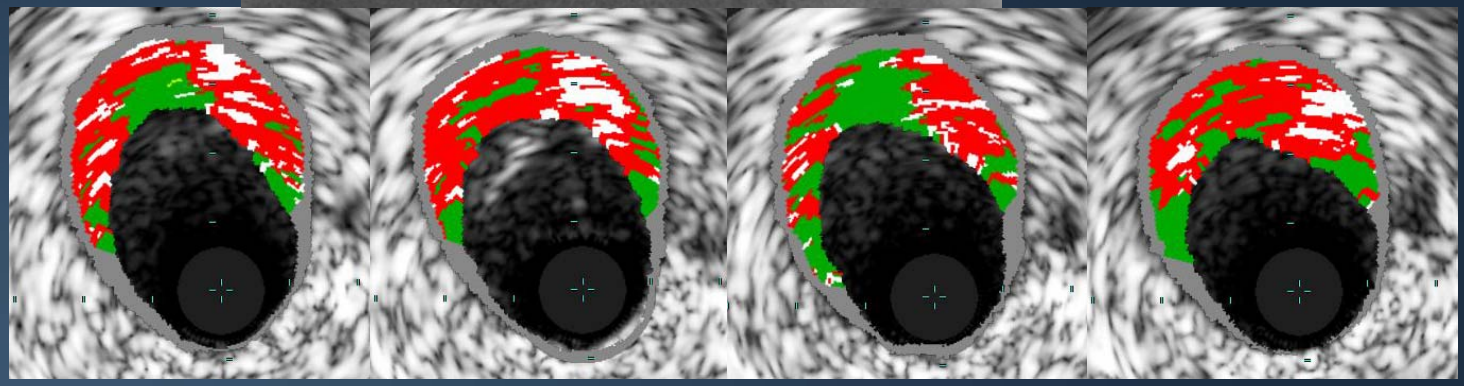
VH-IVUS	OCT +	OCT -
+	28 (22%)	33 (26%)
-	8 (6.3%)	

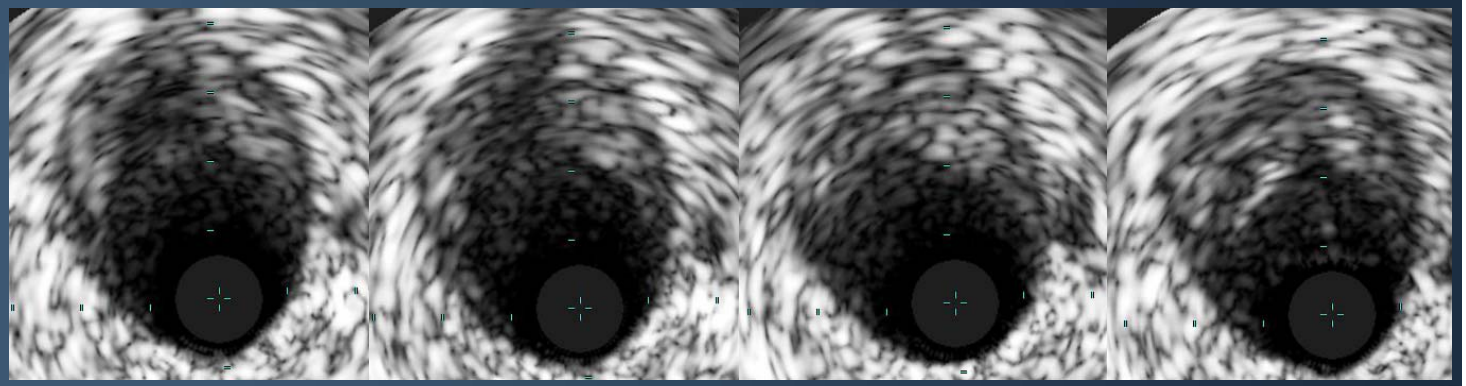
(Sawada et al. Eur Heart J, in press)

proximal distal









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Who should be studied?

- Primary preventions
  - All patients?
  - High risk patients?
  - Invasive vs non-invasive diagnosis?
- Secondary prevention
  - Just the PCI artery?
  - All arteries?
- How often should a patient be restudied?
- What is the risk of multivessel invasive imaging?
- What is the cost?

What is the temporal stability of vulnerable plaques?

- How quickly do they form?
- How often do they heal spontaneously?
- How often do they rupture without causing events?
- What is the impact of modern medical therapy: ASA, clopidogrel, statin?

Conclusion

- I make the assumption that we will be able to detect TCFAs. After all, we are smart people, and a lot of money and time is being spent on this problem.
- However, that does not mean that this makes sense and will become a clinical reality.