Then, How to Define Vulnerable Plaque?

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Disclosure Statement of Financial Interest

I, Soo-Jin Kang DO NOT have a financial interest /arrangement or affiliation with organizations that could be perceived as a conflict of interest in the context of the subject of this presentation

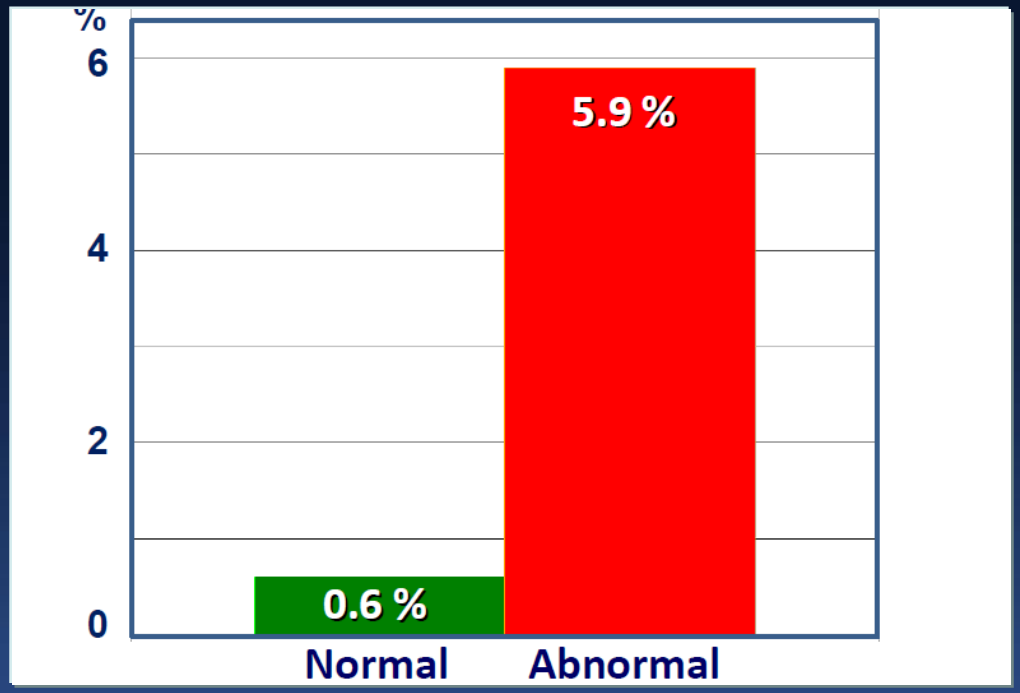
Definition of Vulnerable Plaque

- Vulnerable = “Susceptible to injury or attack”
- Thrombosis-prone plaque and plaque with a high probability of undergoing rapid progression

Burke, Virmani et al. NEJM 1997; 336:1276-82

Prognosis of Low-risk SPECT

Annual risk of cardiac death / MI

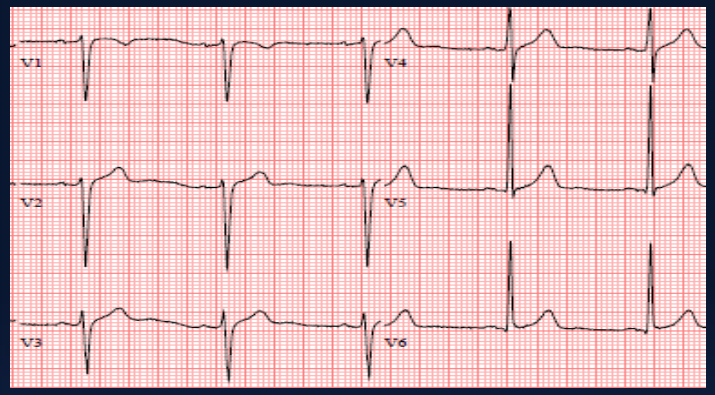


Ischemia is the predictor of cardiac death and MI
However, we need more beyond ischemia

Shaw et al. J Nucl Cardiol 2004;11:171-85

51-year old male

2014,3,9



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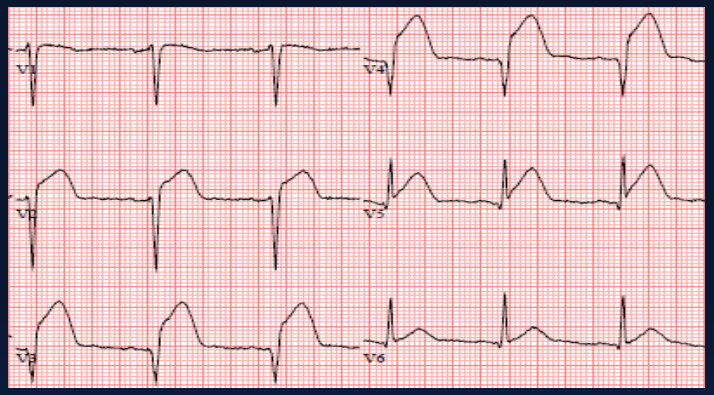
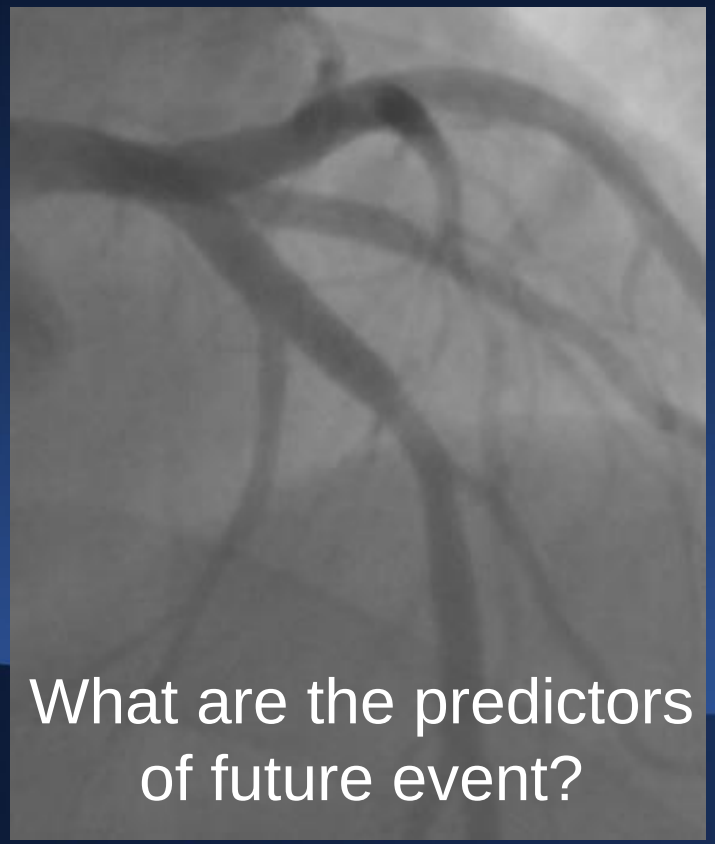
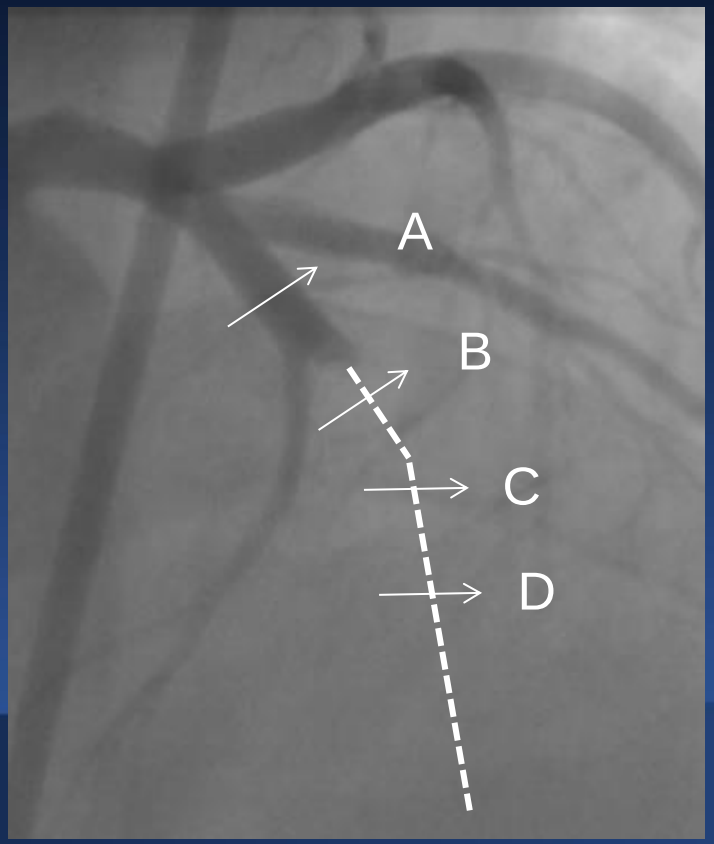
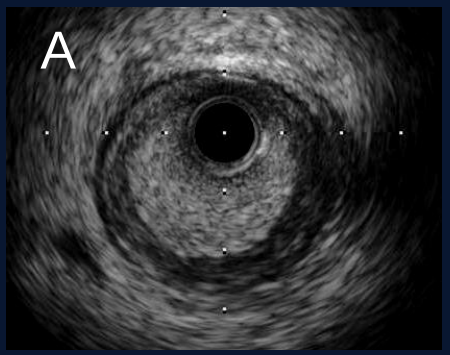
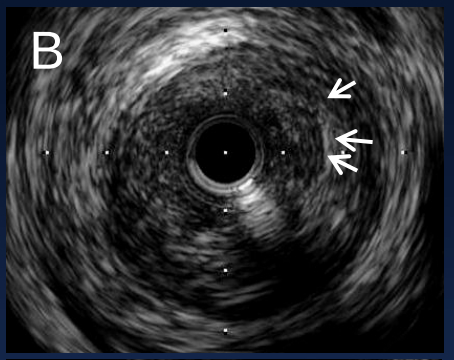
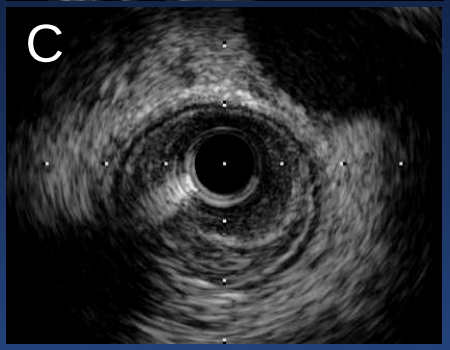


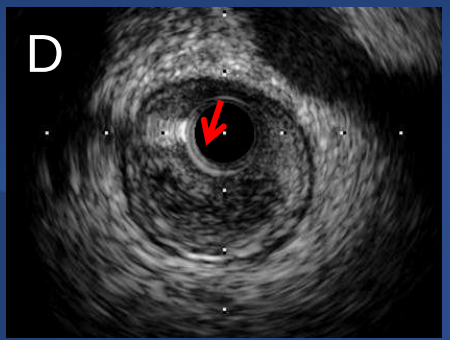






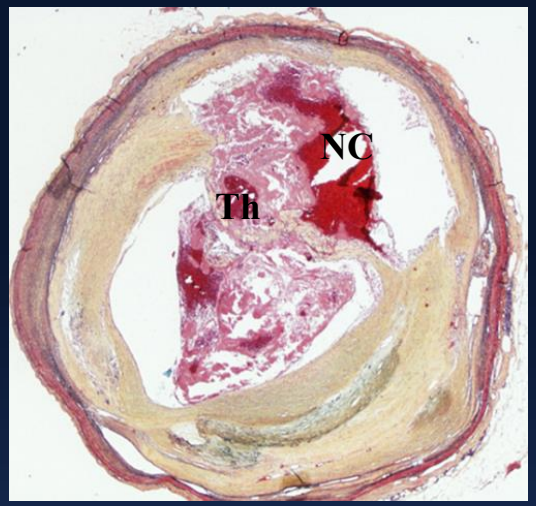




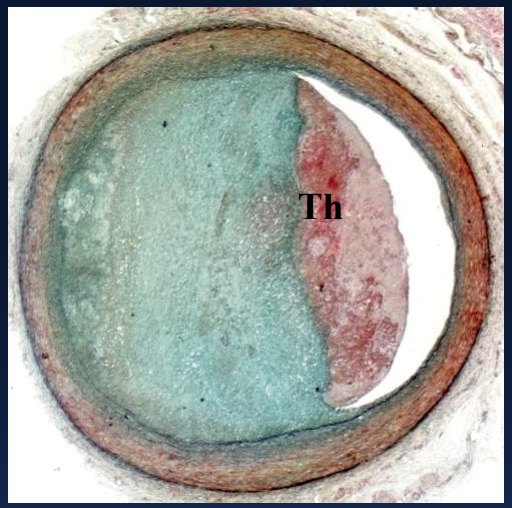


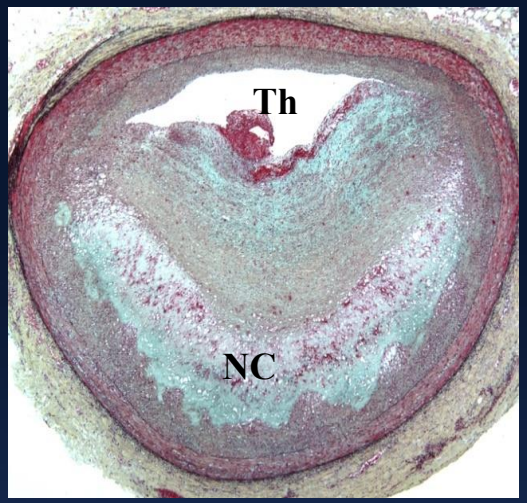
Causes of Coronary Thrombosis

Rupture 60-75%

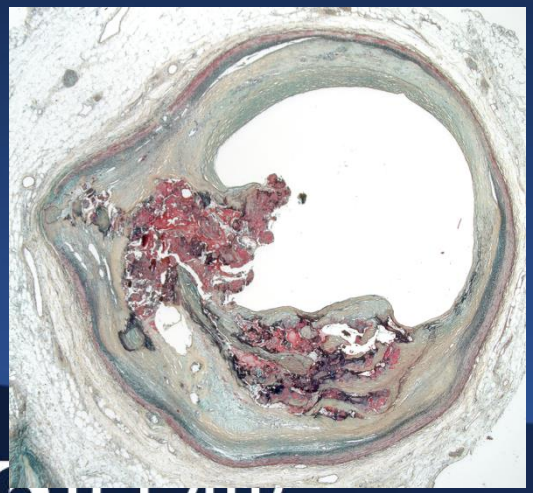


Erosion 30-35%

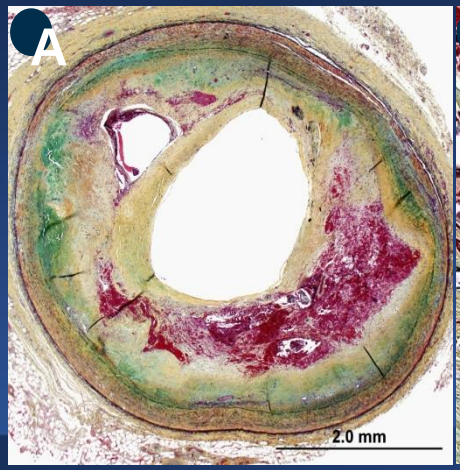


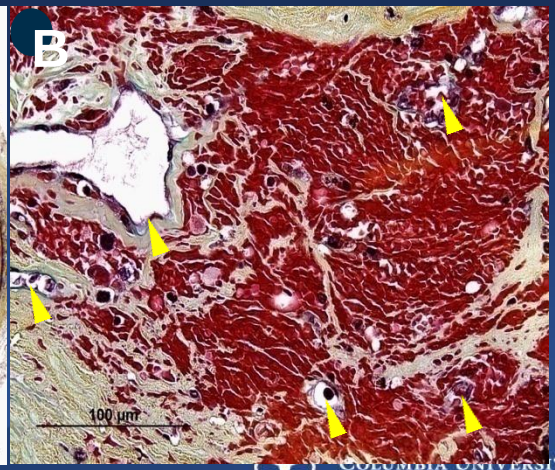


Calcified nodule (2-7%)



Intra-plaque hemorrhage





Virmani R et al. Arterioscler Thromb Vasc Biol 2000;20:1262

Criteria for Defining Vulnerable Plaque

Based on the Study of Culprit Plaques

Major Criteria

- Thin cap with large lipid core
- Active inflammation (macrophage, T-cell)
- Endothelial denudation with superficial platelet aggregation
- Fissured plaque
- Stenosis 90%

Minor Criteria

- Superficial calcified nodule
- Intraplaque hemorrhage
- Positive remodeling
- Endothelial dysfunction
- Glistening yellow

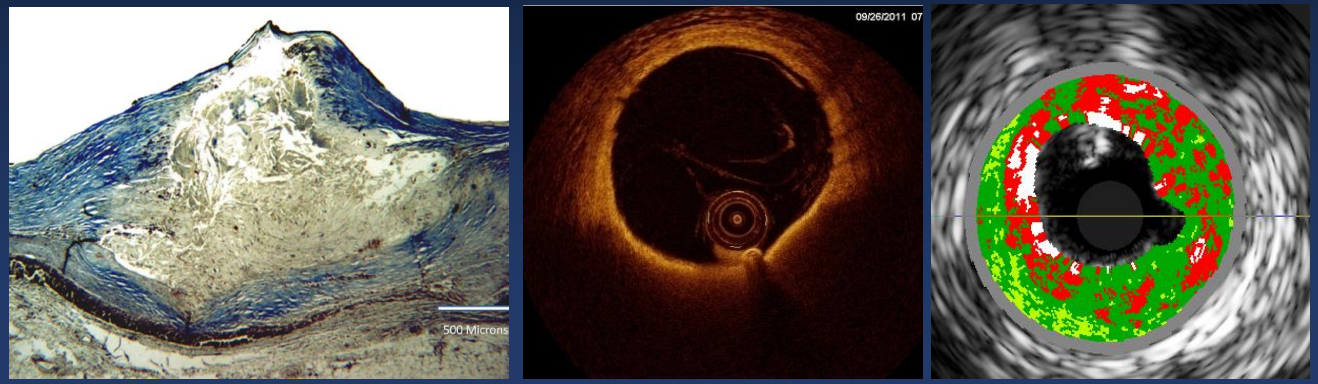
Naghavi et al. Circulation 2003;108:1664-72

Morphological Predictors of Plaque Rupture			
	p	Odds Ratio	95% CI
%Necrotic core	0.02	2.0	1.1 – 3.7
Cap thickness (<65 μm)	0.005	0.35	0.2 – 0.7
%Macrophage	0.052	1.8	1.0 – 3.2

Thin-cap Fibroatheroma (TCFA)

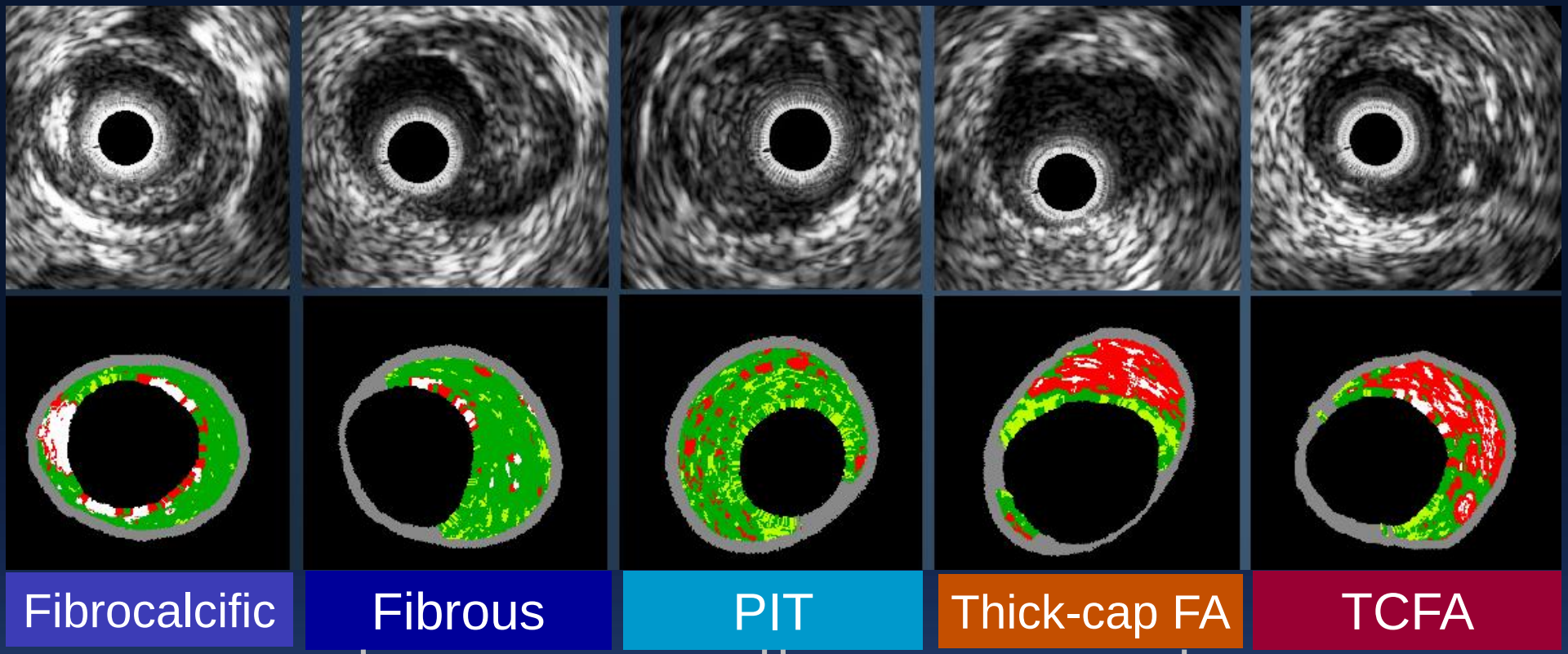
a Precursor of Plaque Rupture

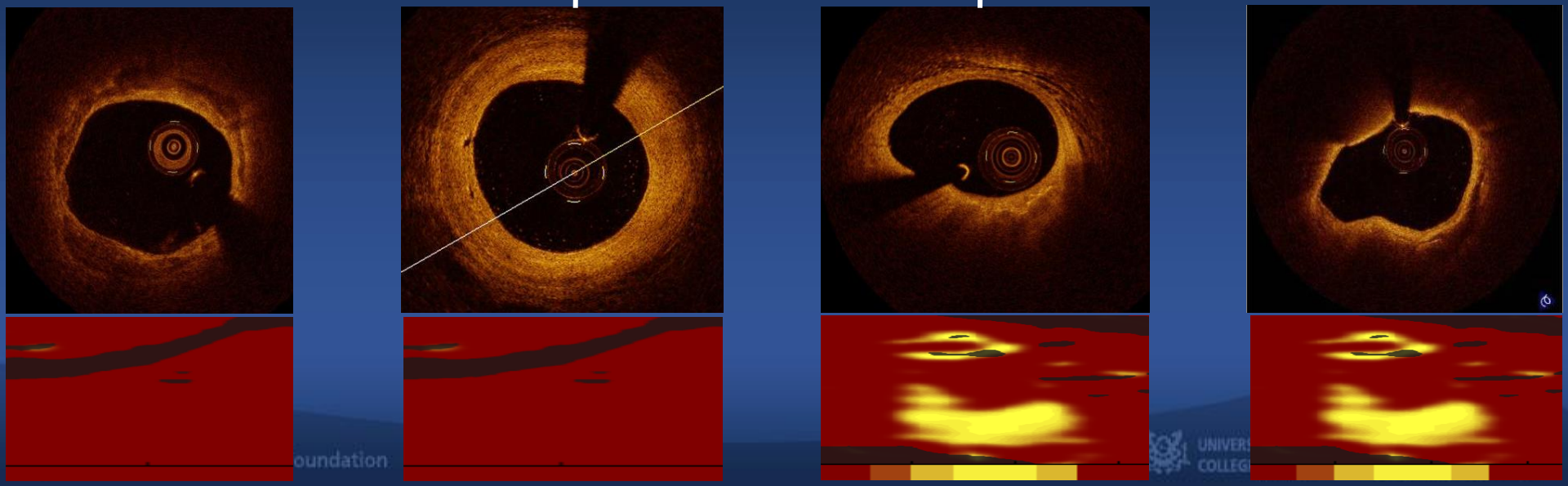
a Prototype of Vulnerable Plaque



Rodriguez-Granillo et al. JACC 2005;46:2038-42

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


Fibrocalcific
Fibrous
PIT
Thick-cap FA
TCFA



Natural History Studies of Non-culprit

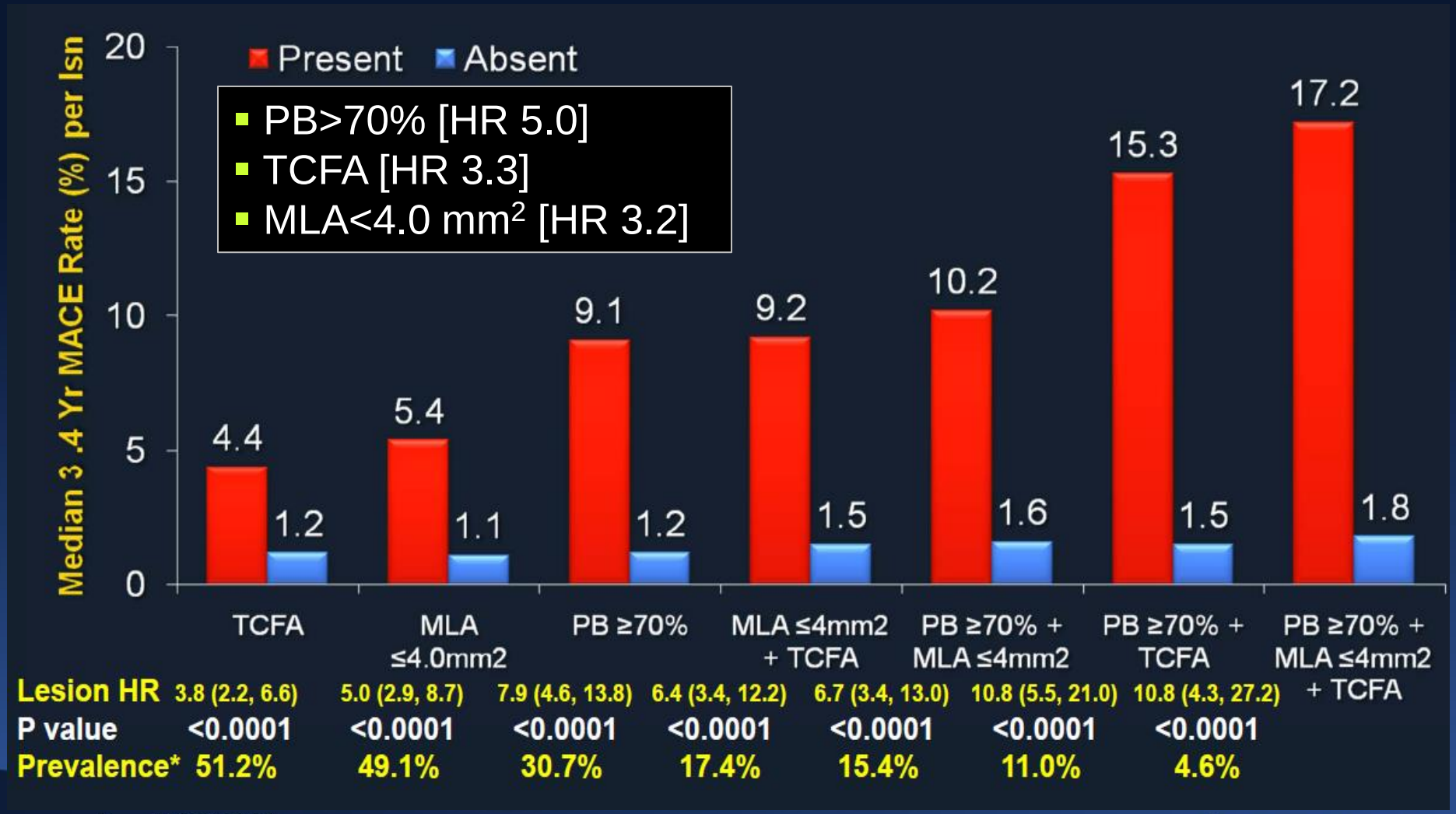
Prospective Validation of Morphological Predictors

	PROSPECT[1]	ATHEROREMO[2]	VIVA[3]
Population	697 ACS patients	581 patients (318 ACS, 263 SA)	170 patients (70 ACS, 100 SA)
Imaging	3 vessel VH-IVUS	1 vessel VH-IVUS	3 vessel VH-IVUS
Median f/u	3.4 years	1 year	1.7 years
NCL-TCFA	22% (>30° of NC abutted the lumen)	37%	60%
Death/ MI	NCL-related 1%	NCL-related 3.8%	Total 2.4%
MACE Def.	CV death, MI, hospitalization from progressive angina	Death, ACS, unplanned revasc	Death, MI, unplanned revasc
MACE	NCL-related 11.6%	NCL-related 7.7%	Total 9.4%

1. Stone G et al. NEJM 2011;364:226-35, 2. Calvert et al. JACC 2011;4:894–901, 3. Cheng et al. EHJ 2014;35:639-47

Predictors of Non-Culprit MACE

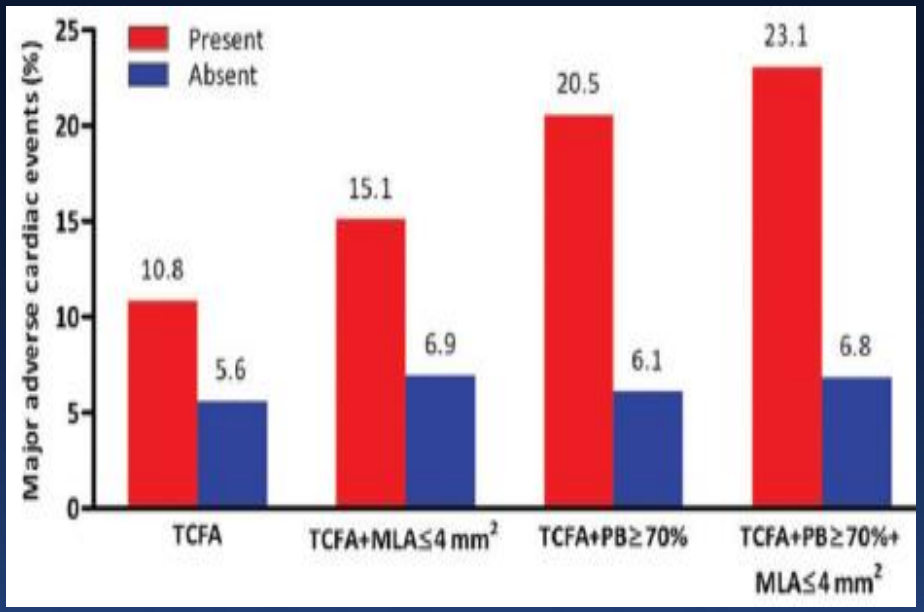
PROSPECT

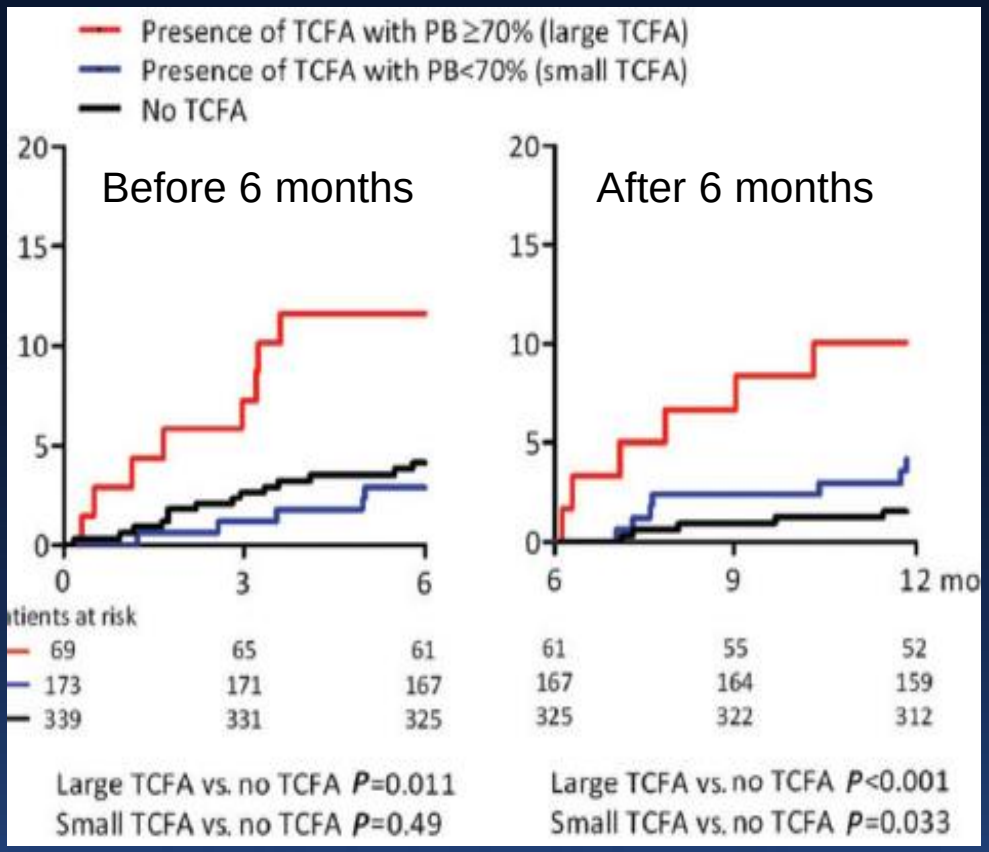


Stone G et al. NEJM 2011;364:226-35

Predictors of Non-Culprit MACE

ATHEROREMO



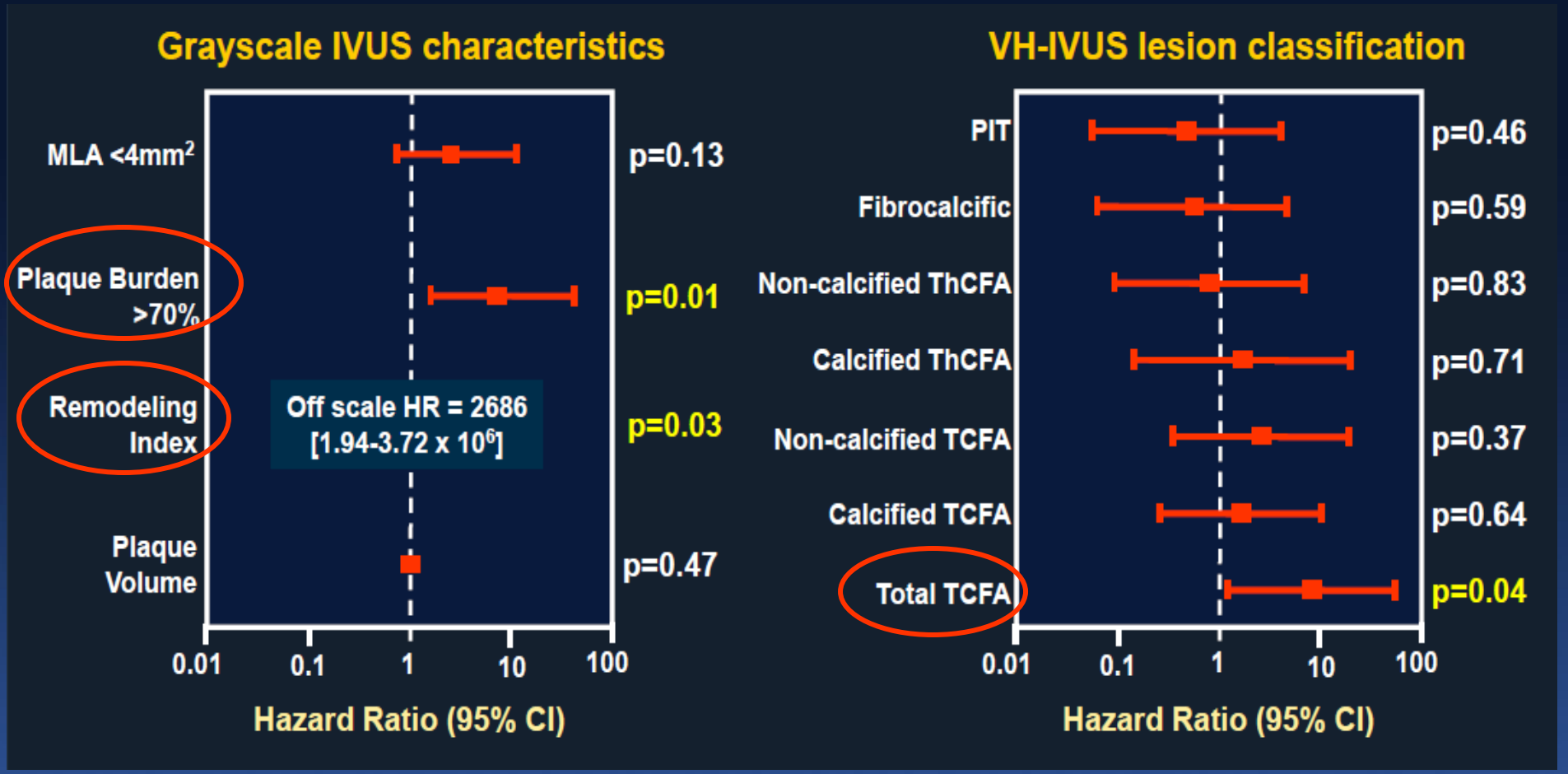


- PB>70% [HR 2.9]
- TCFA [HR 1.9]

Cheng et al. EHJ 2014;35:639-47

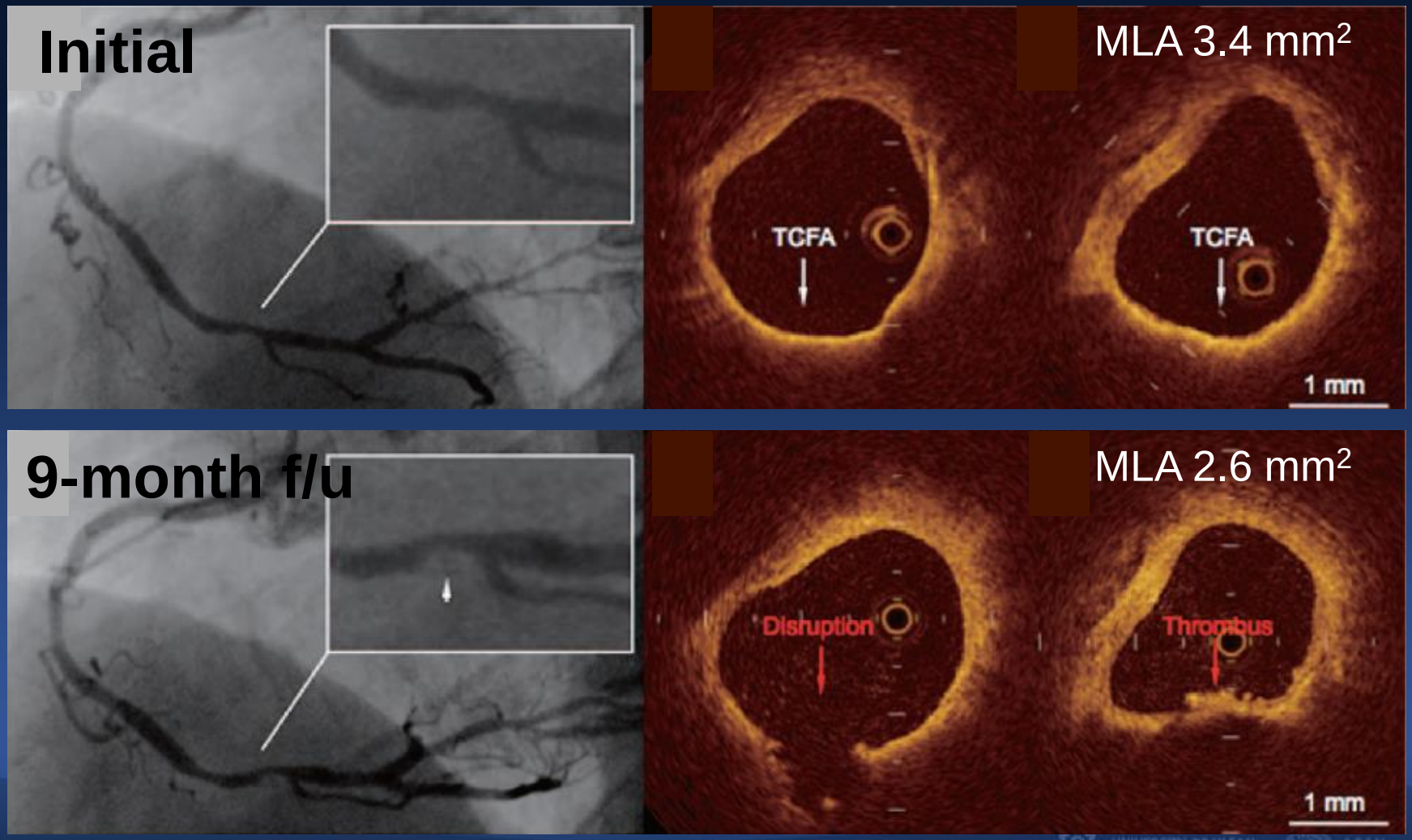
Predictors of Non-Culprit MACE

VIVA

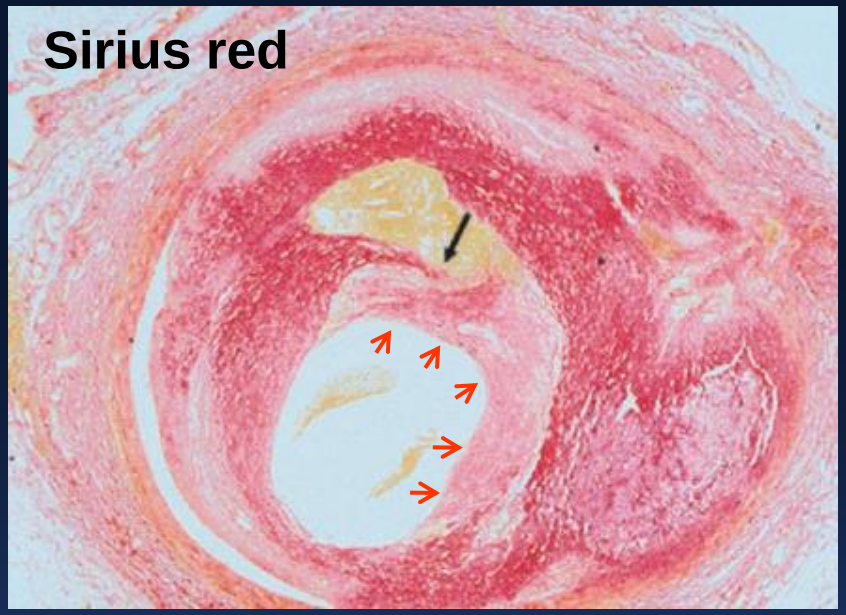


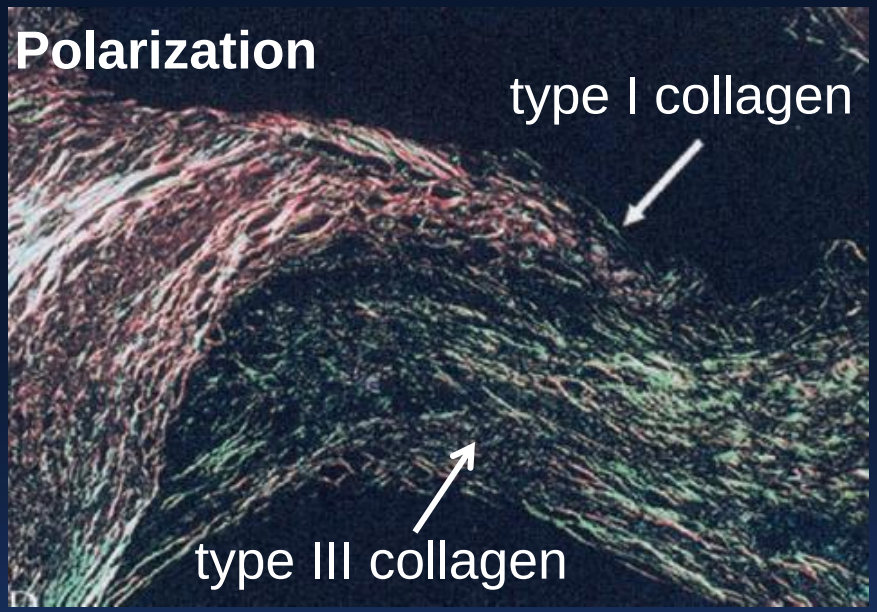
Calvert et al. JACC Cardiovasc Imaging 2011;4:894–901

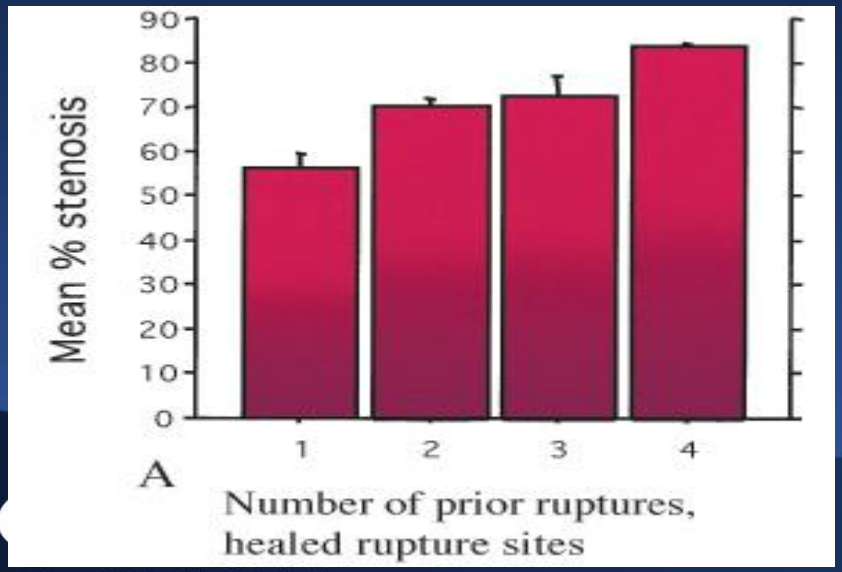
69-year old male, stable angina
PCI for LAD (culprit) and 9-month follow-up



Healed Plaque Ruptures
: A Role in Lesion Progression







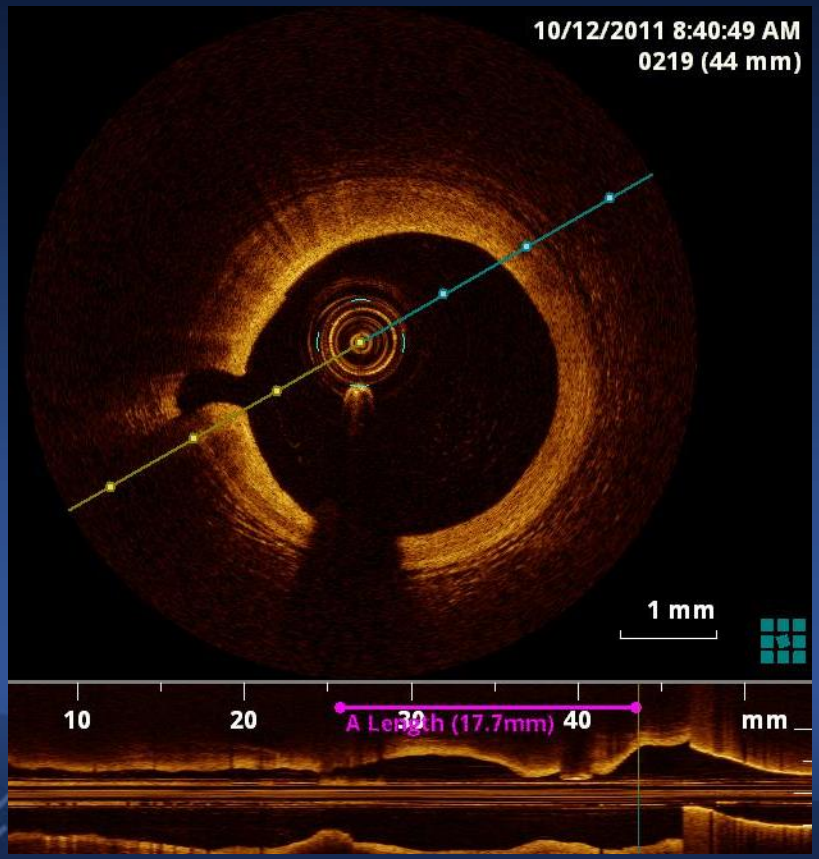
Inner layer, newly formed neointima composed of type III collagen, loose-SMC and proteoglycan-rich ECM

Burke et al. Circulation 2001;103:934–40

60/M

Baseline

FFR 0.88

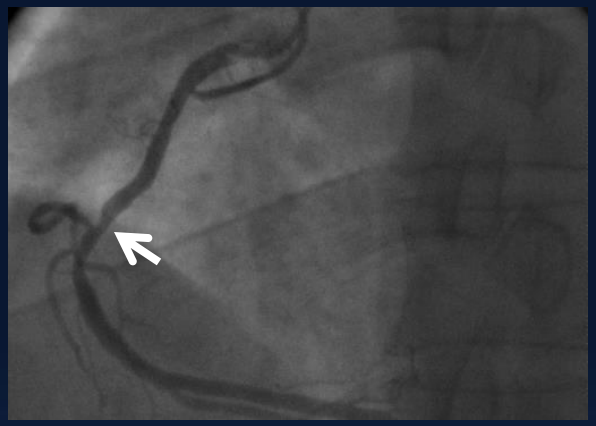


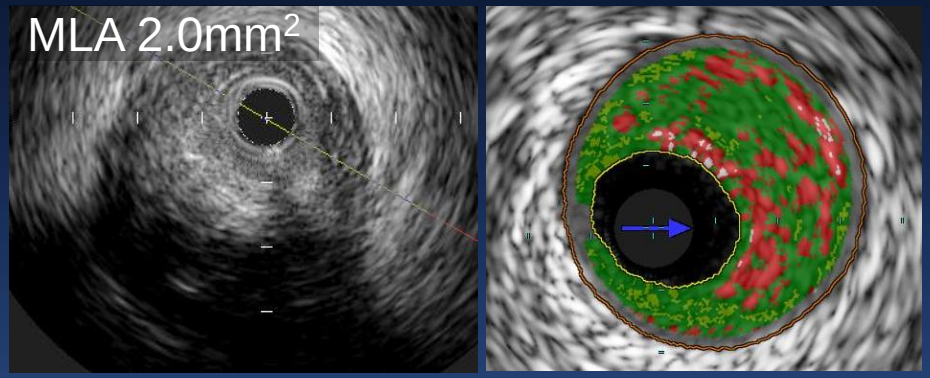
1-year F/U

FFR 0.75

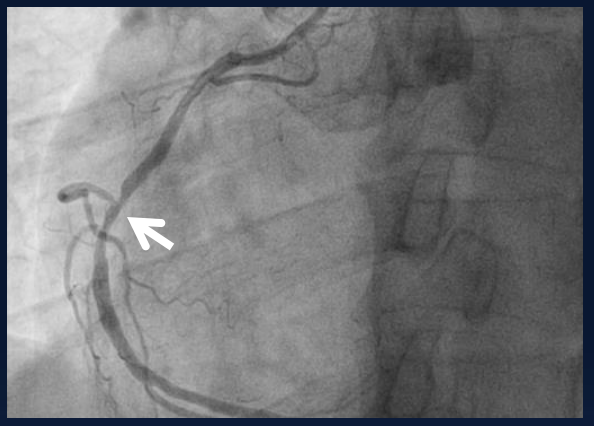
42/M

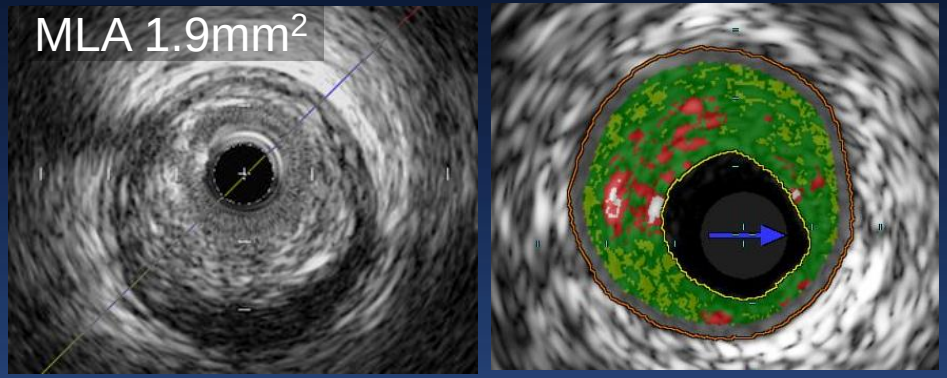
Baseline

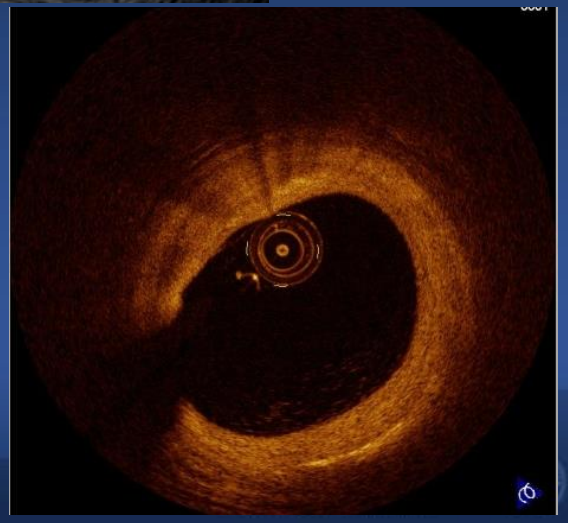




1-year F/U

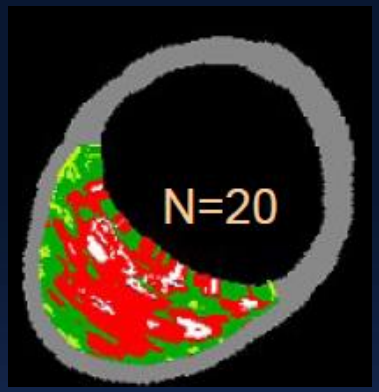






Dynamic Change in TCFA

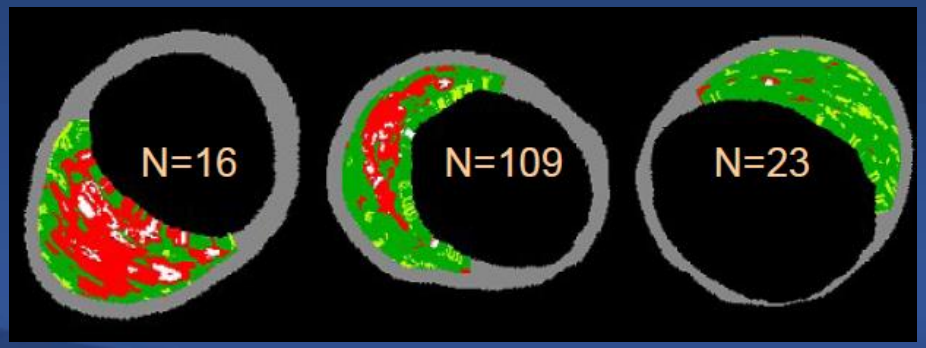
PROSPECT



25%

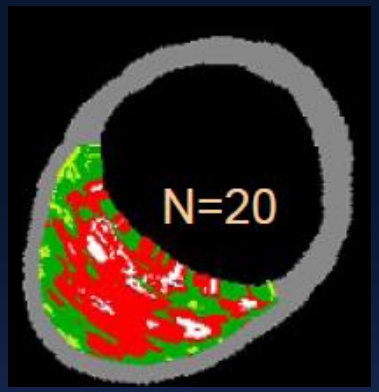
65%

10%



Kubo et al. J Am Coll Cardiol 2010;55:1590-7

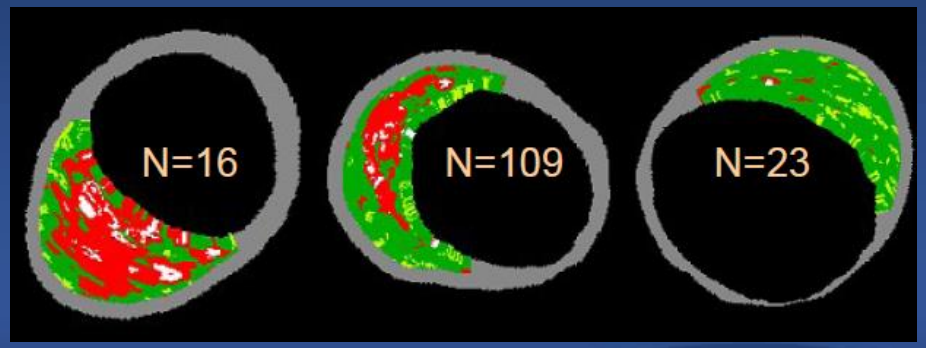
HORIZON-AMI



76%

14%

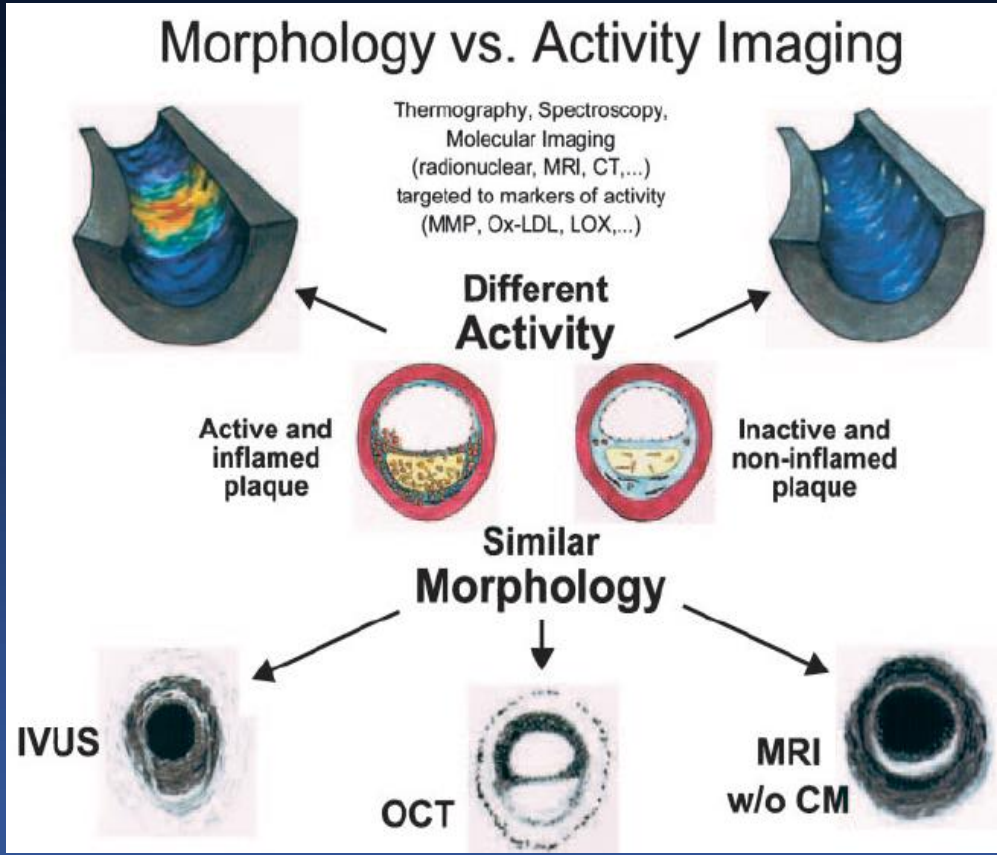
5%



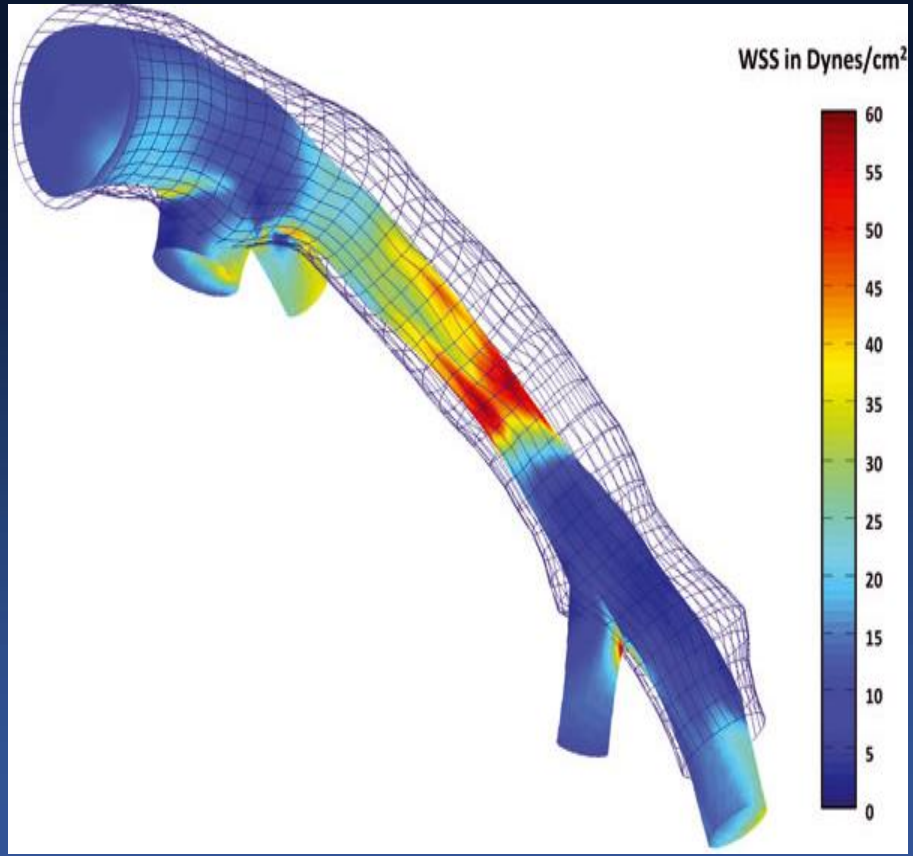
Zhao et al. JACC Imaging in press

What Affect Dynamic Change of Vulnerable Plaque?

Biological Activity



Wall Shear Stress



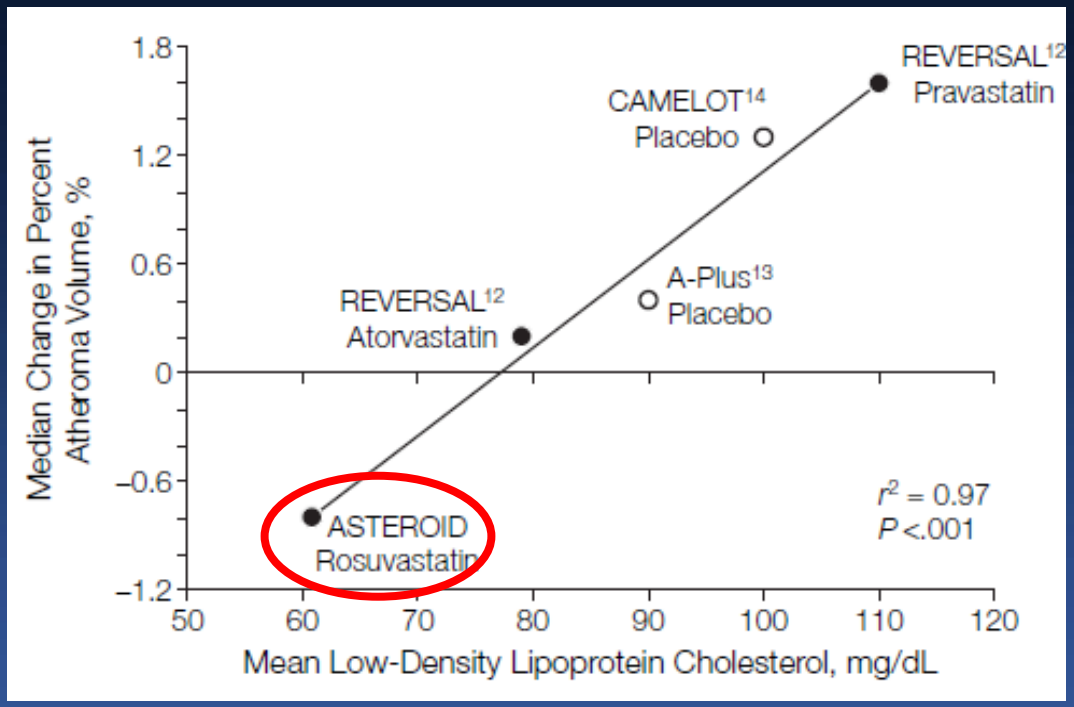
Circulation 2003;108:1664-72

Eshtehardi et al. J Am Heart Assoc 2012;1:e002543

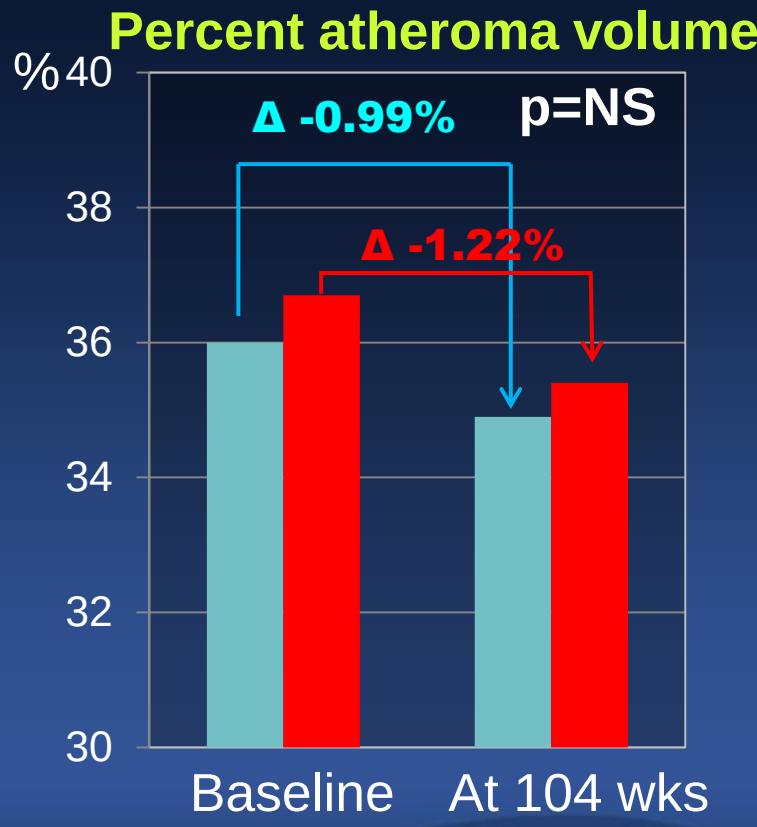
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of Two Intensive Statin Regimens on Progression of Coronary Disease



Nissen et al. JAMA 2006;295:1556-65

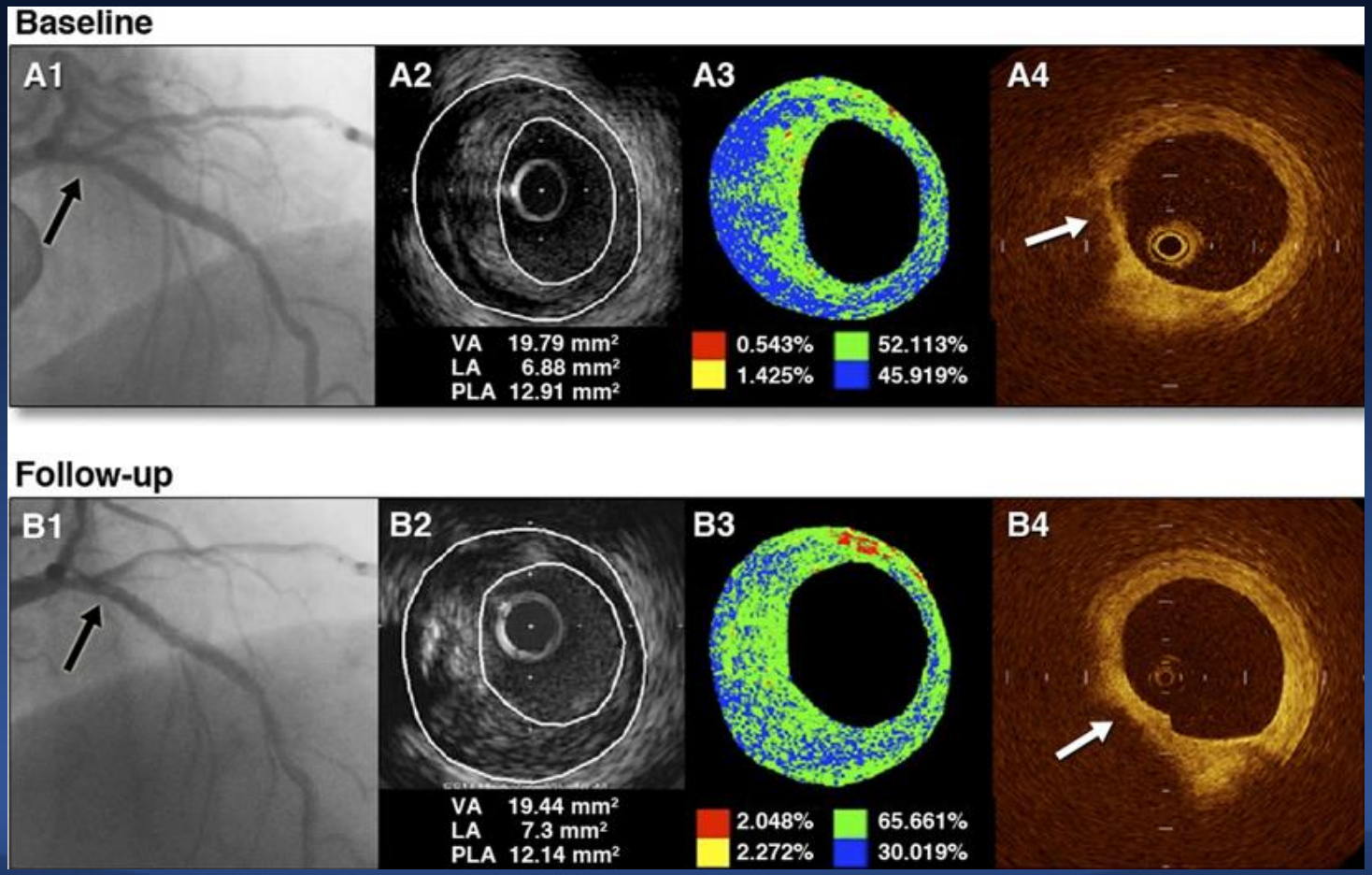


Stephen et al. N Engl J Med 2011;365:2078-87

Impact of Statin on Plaque Volume and Composition

Pitavastatin 4 mg vs. Dietary

Stable angina, 9-month follow-up



Hattori et al. J Am Coll Cardiol Img 2012;5:169–77

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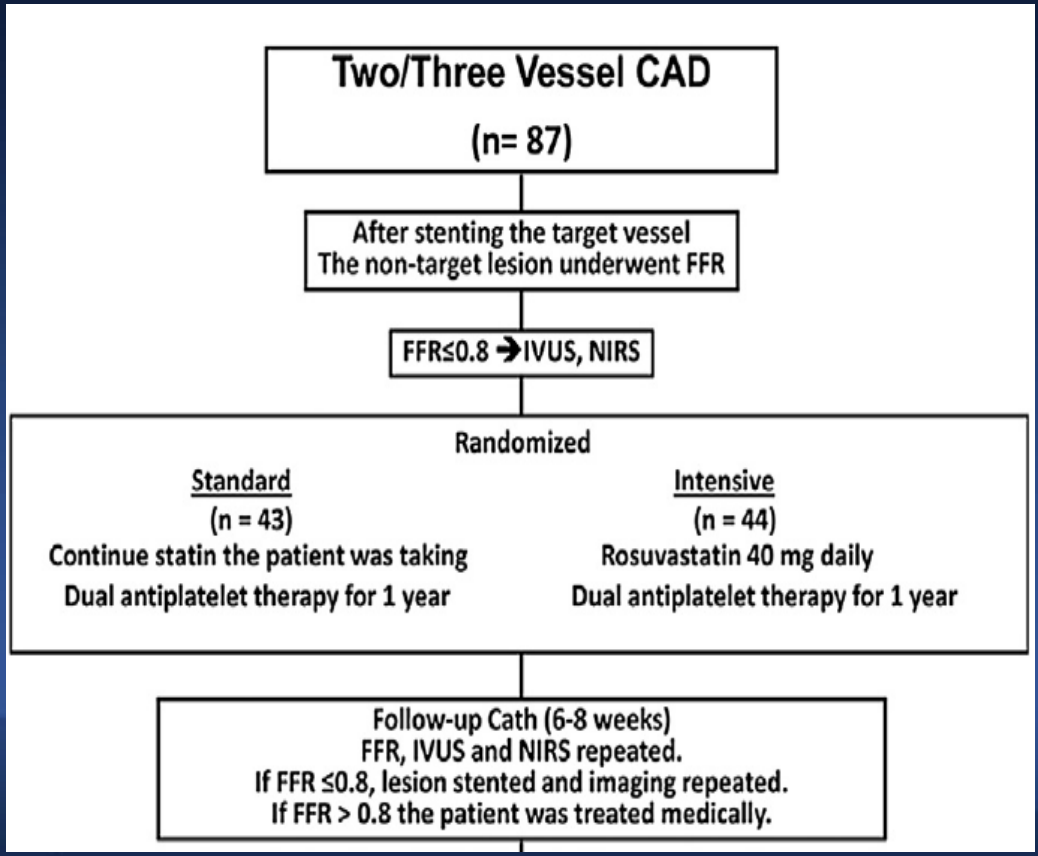
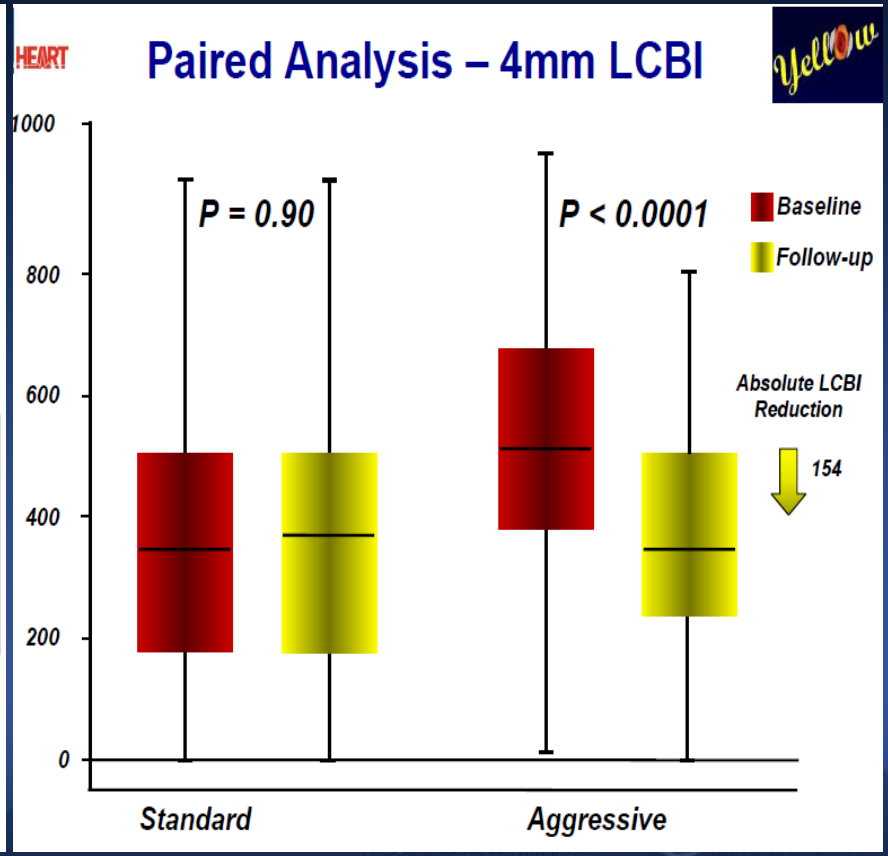
CLINICAL RESEARCH **Clinical Trials**

Changes in Plaque Lipid Content After Short-Term Intensive Versus Standard Statin Therapy

The YELLOW Trial (Reduction in Yellow Plaque by Aggressive Lipid-Lowering Therapy)





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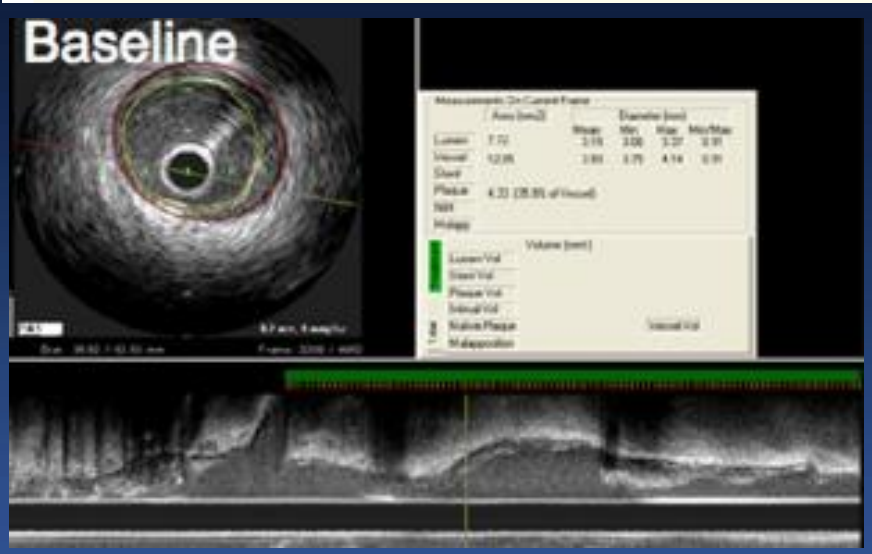
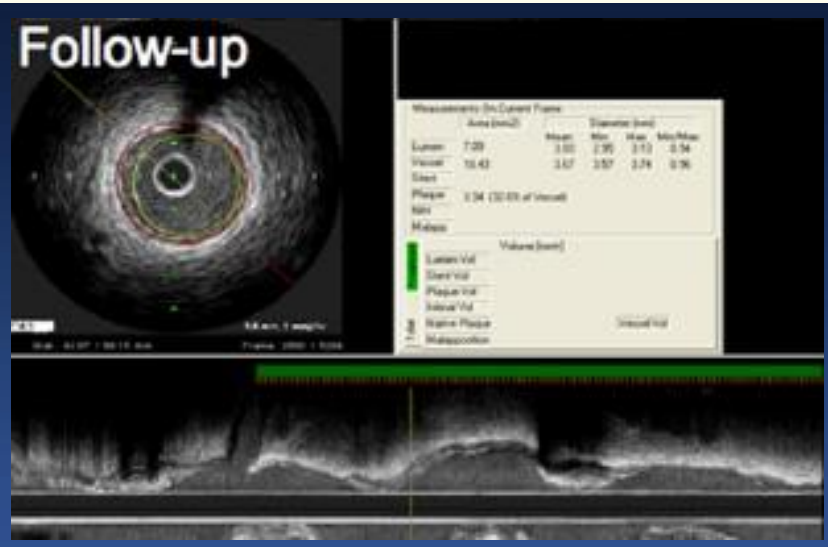
doi:10.1016/j.jacc.2009.09.062

CLINICAL RESEARCH — **Coronary Artery Disease**

Impact of Olmesartan on Progression of Coronary Atherosclerosis

A Serial Volumetric Intravascular Ultrasound Analysis From the OLIVUS (Impact of OLmesarten on progression of coronary atherosclerosis: evaluation by IntraVascular UltraSound) Trial





ΔPAV at 14 months

Olmesartan -0.7% *vs*. Control +3.1%

Hirohata et al. J Am Coll Cardiol 2010;55:976–82

SUMMARY

As a substrate of plaque progression and rupture, TCFA predicted NC-MACE. However, dynamic changes vary over time

- Plaque morphology
- Clinical factors
- Inducible ischemia
- Biological activities
- Mechanical shear stress
- Responsiveness to Rx