Vulnerable Plaque Today: Concept & Controversy
Imaging Approach: We Can Find It, Treat It Locally.

E. Regar
Prepared with J. van der Sijde & A. Karanasos
Thoraxcenter
Erasmus Medical Center
Rotterdam, NL

Atherosclerosis
A systemic disease to be treated systemically

Is atherosclerosis really a systemic disease?

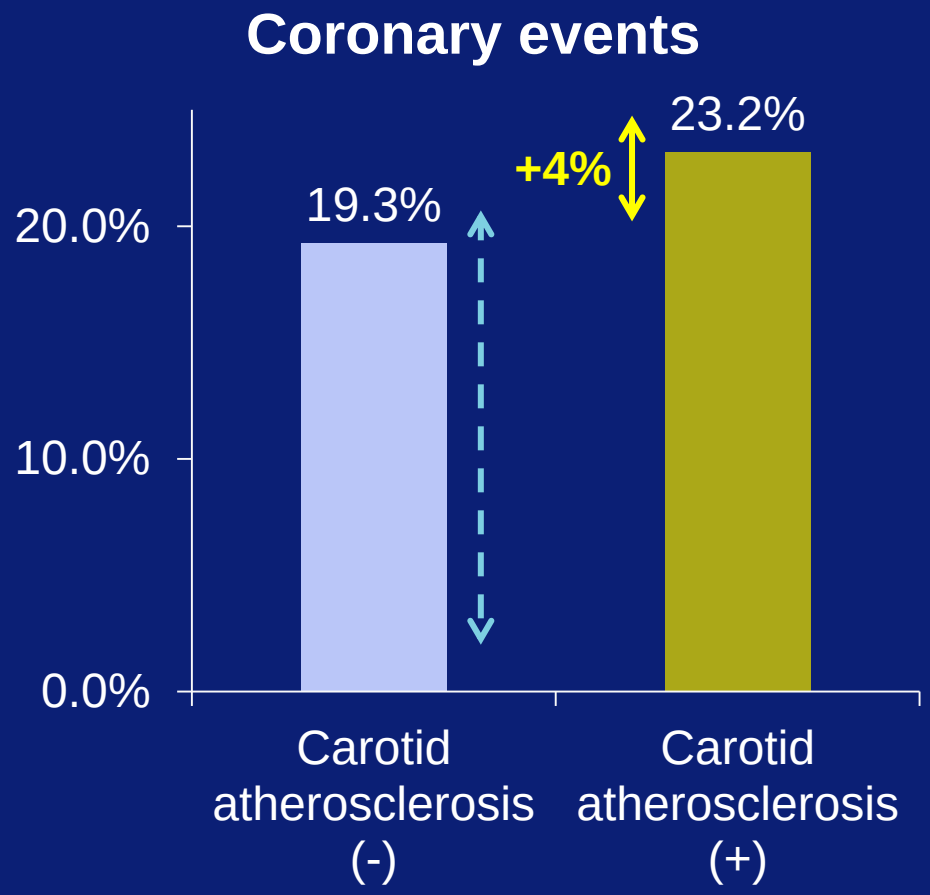
Chris Hodgson
Hodge's Cleveland
2013 People's Best New Chef nominee

Systemic nature of atherosclerosis

REACH registry

- Presence of carotid atherosclerosis increases the chance any coronary event.
- However, 19.3% of patients w/o carotid atherosclerosis had a coronary event.
- So, coronary events are also high in pts w/o systemic manifestations!
- But can we treat systemically?

Is atherosclerosis really a systemic disease?



Sirimarco G et al. Stroke. 2013.

Systemic therapy

Is atherosclerosis really a systemic disease?

A systemic disease would respond to systemic medication

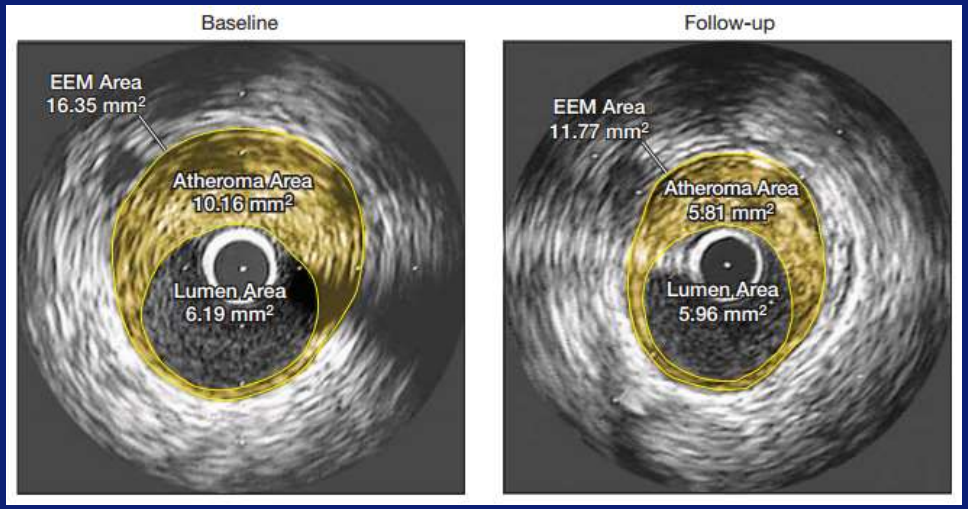
Systemic therapy → plaque regression
ASTEROID trial

Is atherosclerosis really a systemic disease?

24 months of rosuvastatin 40mg/d treatment

53.2% reduction of LDL-C level

14.7% increase of HDL-C level



↓ atheroma volume 0.98%

↓ atheroma volume in most diseased subsegment 6.1%

Nissen S et al. JAMA. 2006.

Systemic therapy → plaque regression

ASTEROID trial

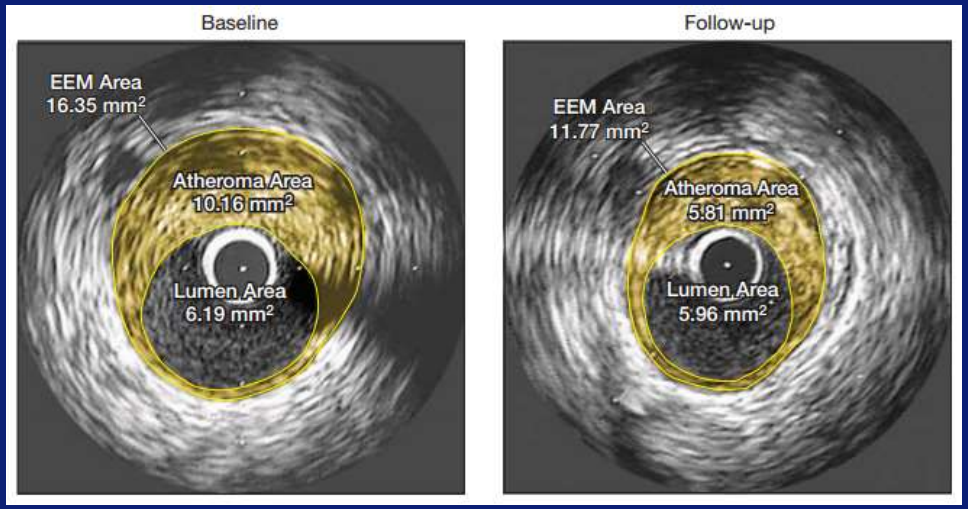
Is atherosclerosis really a systemic disease?

HOWEVER:

0.8% Death

2.0% MI

0.6% Stroke



↓ atheroma volume 0.98%

↓ atheroma volume in most diseased subsegment 6.1%

Nissen S et al. JAMA. 2006.

Systemic therapy

Is atherosclerosis really a systemic disease?

YES

Atherosclerosis is a systemic disease

BUT with local manifestations

Systemic therapy
Side-effects

Nitrates
Headache
Hypotension
Syncope
Relfex tachycardia

B-blockers
Fatigue, depression
Bradycardia
Heart block
Bronchospasm
Peripheral vasoconstriction

Aspirin
GI pain, ulceration, bleeding
Rash
Renal damage

Statins
Muscle ache
Hepatotoxicity
Myopathy
Constipation

ACEi
Hypotension
Headache
Cough
Renal damage

CCBs (HR lowering)
Bradycardia
Heart conduction defect
Low ejection fraction
Constipation

CCBs (DHP)
Headache
Ankle swelling
Fatigue
Flushing
Reflex tachycardia

Systemic therapy
Adherence

- Poor adherence
- Adherence is not greatly influenced by the class of drug prescribed

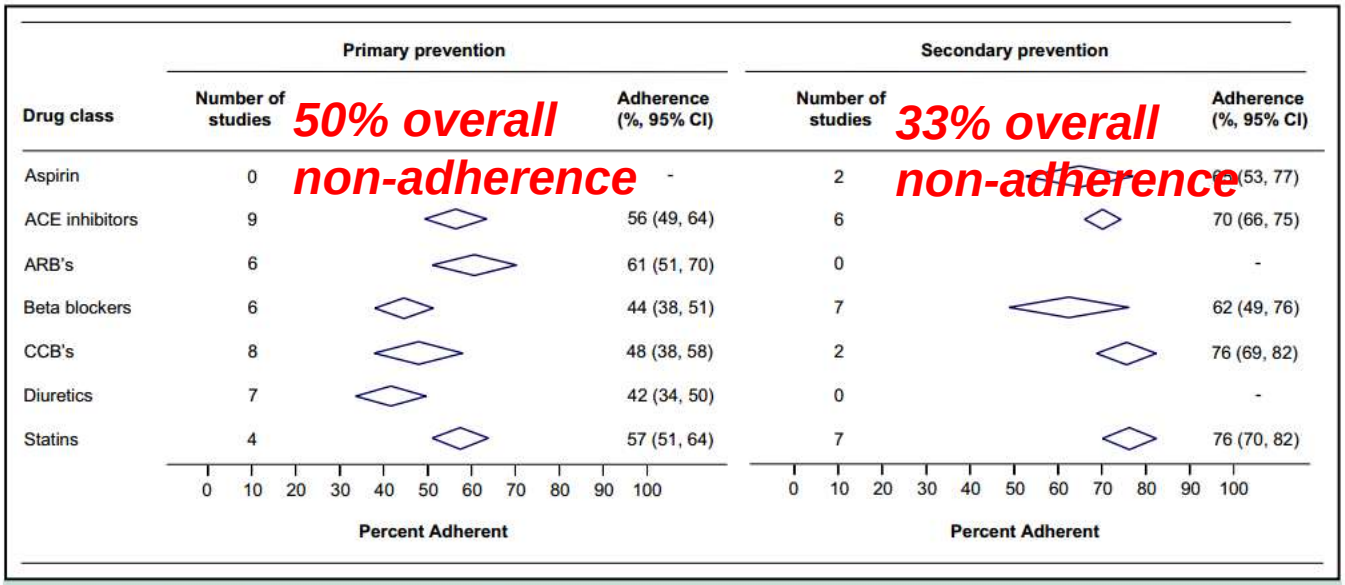


Figure 2 Percent adherence according to drug class and use in primary and secondary prevention. CI = confidence interval; ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; CCB = calcium channel blocker.

Naderi SH et al. Am J Med. 2012.

Systemic therapy

How many pills?

- 40 year old man stable angina
- Life expectancy of 80 years:

  5 pills a day

  x 365 days a year

  x 40 years

  = 73,000 pills.

73,000 pills x 1 gram = 73 kg of pills

Systemic therapy

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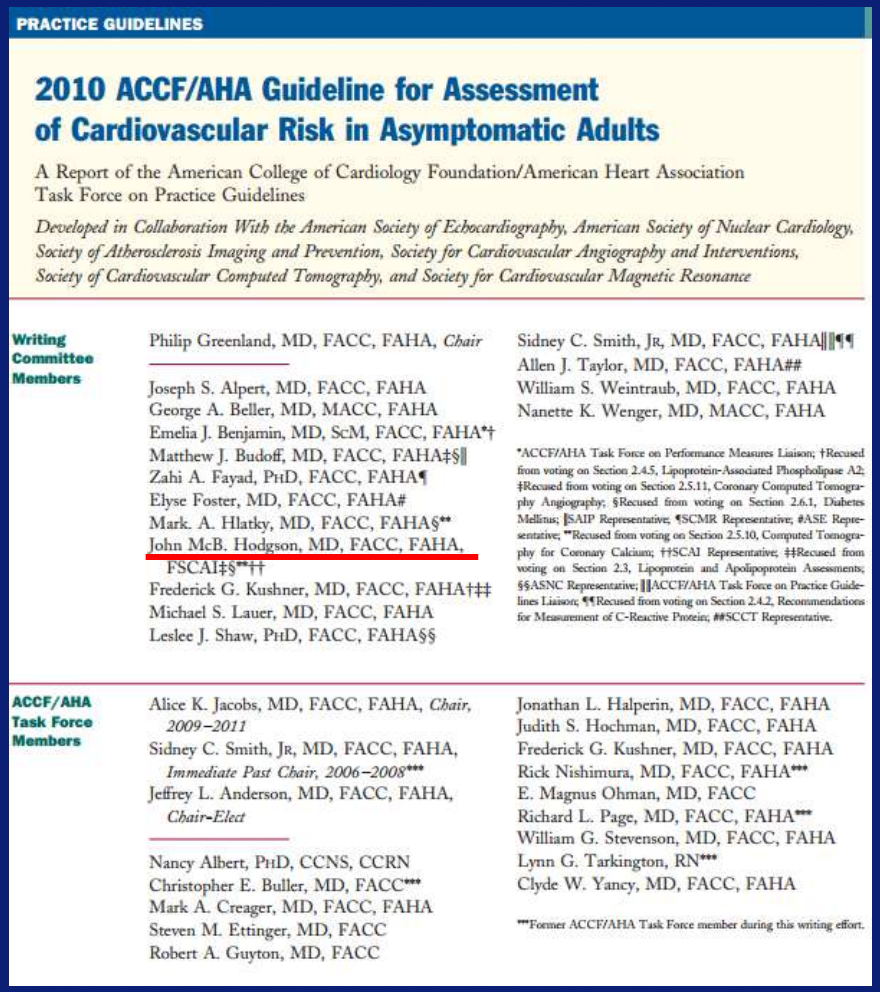
73,000 pills x 1 gram = 73 kg of pills

TO PREVENT THIS ???

Courtesy ms. ASA Autar, Dr. HMM van Beusekom

Systemic therapy
For whom?



PRACTICE GUIDELINES

2010 ACCF/AHA Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults

A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the American Society of Echocardiography, American Society of Nuclear Cardiology, Society of Atherosclerosis Imaging and Prevention, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance

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*ACCF/AHA Task Force on Performance Measures Liaison; †Recused from voting on Section 2.4.5, Lipoprotein-Associated Phospholipase A2; ‡Recused from voting on Section 2.5.11, Coronary Computed Tomography Angiography; §Recused from voting on Section 2.6.1, Diabetes Mellitus; ‖SAIP Representative; ¶SCMR Representative; #ASE Representative; **Recused from voting on Section 2.5.10, Computed Tomography for Coronary Calcium; ††SCAI Representative; ‡‡Recused from voting on Section 2.3, Lipoprotein and Apolipoprotein Assessments; §§ASNC Representative; ‖‖ACCF/AHA Task Force on Practice Guidelines Liaison; ¶¶Recused from voting on Section 2.4.2, Recommendations for Measurement of C-Reactive Protein; ##SCCT Representative.

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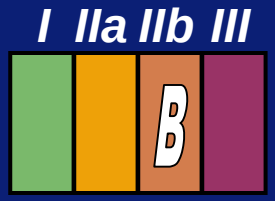
***Former ACCF/AHA Task Force member during this writing effort.

Systemic therapy

For whom?

Measurement of CAC is reasonable for cardiovascular risk assessment in asymptomatic patients at intermediate risk (10% to 20% 10-year risk)

Measurement of CAC may be reasonable for cardiovascular risk assessment in persons at low to intermediate risk (6% to 10% 10-year risk)



ACCF/AHA Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults. J Am Coll Cardiol. 2010.

However:

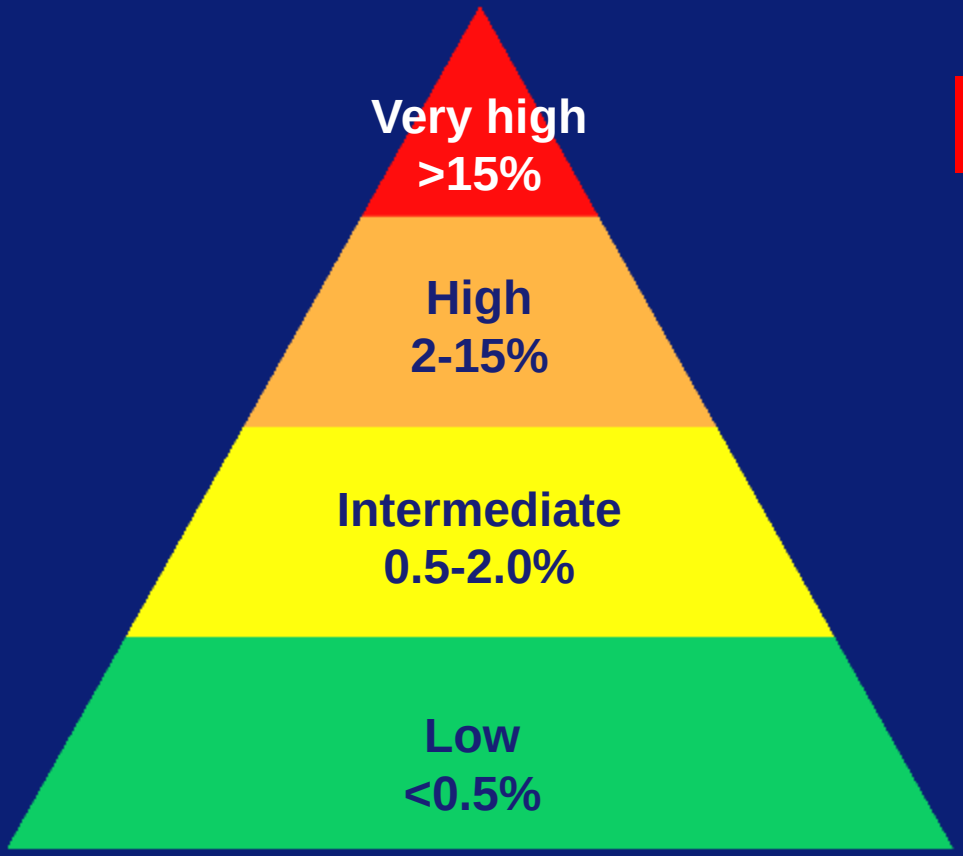
Calcification does not correlate with the presence of VP.

CAC score identifies the vulnerable patient rather than the VP.

Mariello A et al. Atherosclerosis. 2013.

Systemic therapy

Time for a different approach?



Need for VP detection???

Braunwald E. J Am Col Cardiol. 2006.

Systemic therapy or… personalized medicine?

Personalized Medicine: Hope or Hype?

By: Leslie Pray, Ph.D. © 2008 Nature Education
Citation: Pray, L. (2008) Personalized medicine: Hope or hype? *Nature Education* 1(1):72

Hippocrates used a person's physique and the seasons to personalize treatments for his patients. The modern scientific industry hopes to use your DNA.

Aa Aa Aa

European Heart Journal (2012) 33, 1564–1570
doi:10.1093/eurheartj/ehs112

REVIEW

Frontiers in cardiovascular medicine

Personalized medicine: hope or hype?

Keyan Salari[1], Hugh Watkins[2], and Euan A. Ashley[3]*

[1]Department of Genetics, Stanford University School of Medicine, Stanford, CA, USA; [2]Department of Cardiovascular Medicine, University of Oxford, Oxford, UK; and [3]Center for Inherited Cardiovascular Disease, Division of Cardiovascular Medicine, Stanford University School of Medicine, Falk Cardiovascular Research Building, 300 Pasteur Drive, Stanford, CA 94305, USA

Received 21 April 2011; revised 21 March 2012; accepted 3 April 2012; online publish-ahead-of-print 1 June 2012

Perspectives

Gray JA. The Lancet 2013

The Art of Medicine

The shift to personalised and population medicine

VP identification and treatment is personalized medicine

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Hippocrates used a person's physique and the seasons to personalize treatments for his patients. The modern scientific industry hopes to use your DNA.

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VP identification and treatment

Pre-requisites

- "Vulnerable plaque" caused by a thin-capped fibroatheroma can be identified with modern technology.

Ambrose JA et al. J Am Coll Cardiol 2008

VP identification

In vivo VP imaging

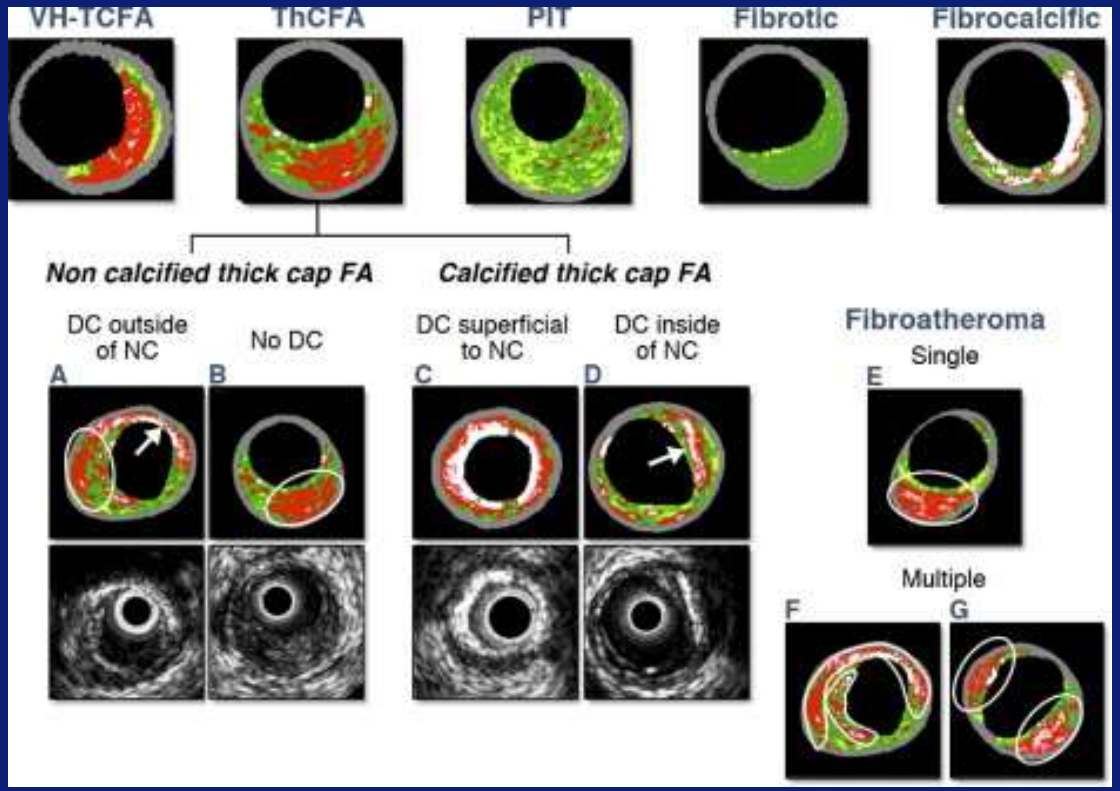
Vulnerable plaque can be identified in vivo by:

VP identification

In vivo VP imaging

Vulnerable plaque can be identified in vivo by:

VH-IVUS



Maehara et al. JACC Img 2012

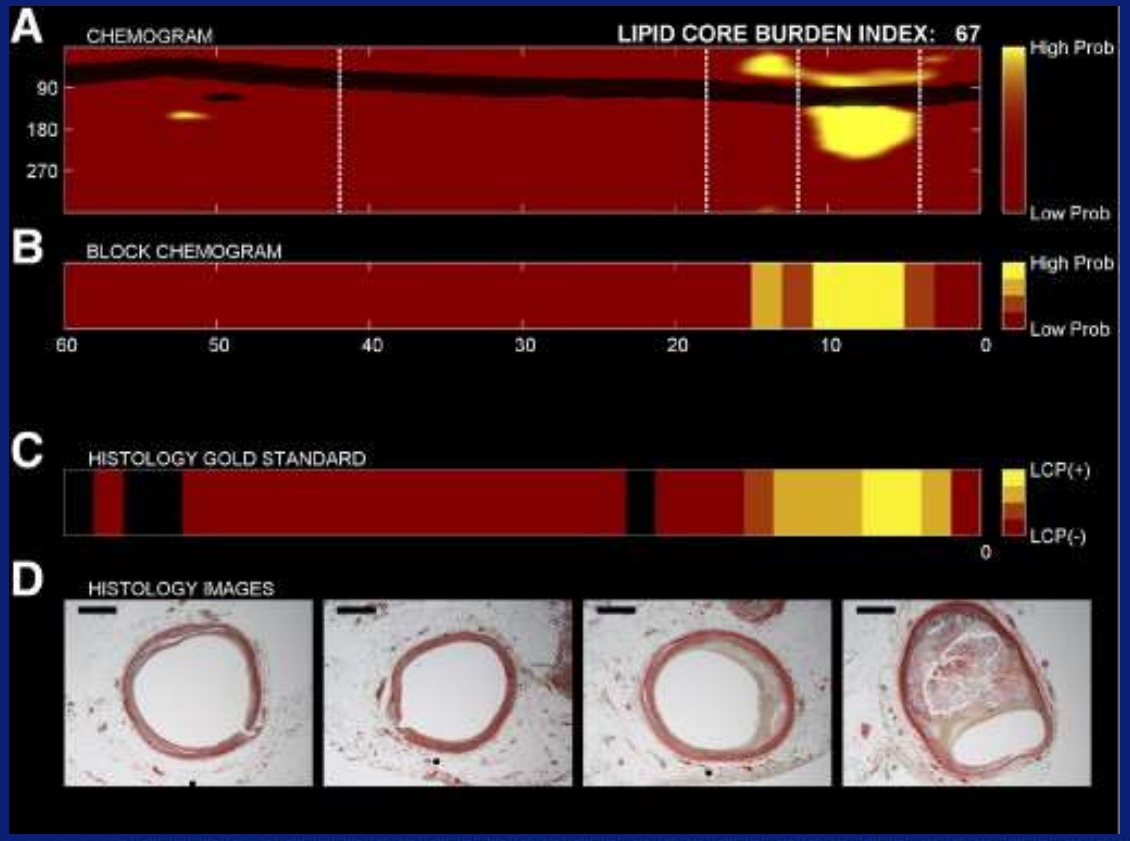
VP identification

In vivo VP imaging

Vulnerable plaque can be identified in vivo by:

VH-IVUS

NIRS



Gardner et al. JACC Img 2008

VP identification

In vivo VP imaging

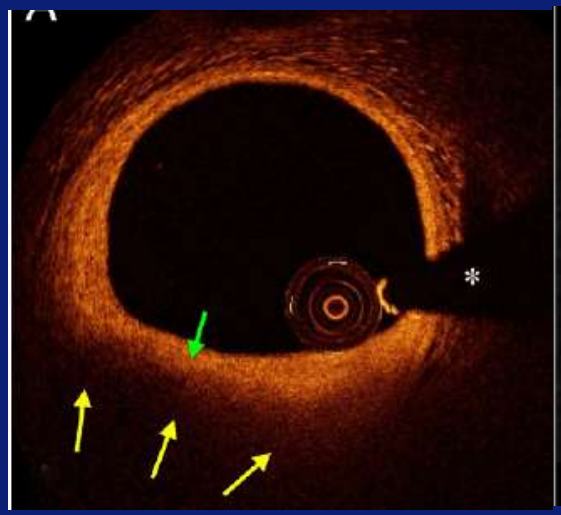
Evidence level: High

Vulnerable plaque can be identified in vivo by:

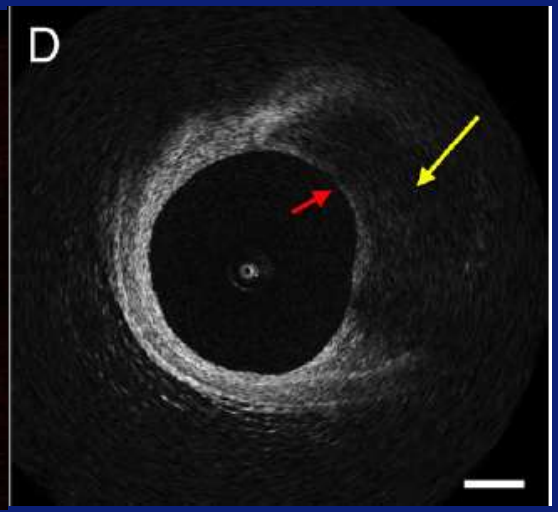
VH-IVUS

NIRS

OCT



Fibroatheroma with poorly defined borders and a cap



Fibroatheroma with thin fibrous cap

The International Working Group
For Intracoronary OCT Standardization And Validation

Tearney, Regar, Akasaka et al. JACC 2006

VP identification and treatment

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VP identification

Number of vulnerable plaques

ATHEROREMO study

Study of one non-culprit artery

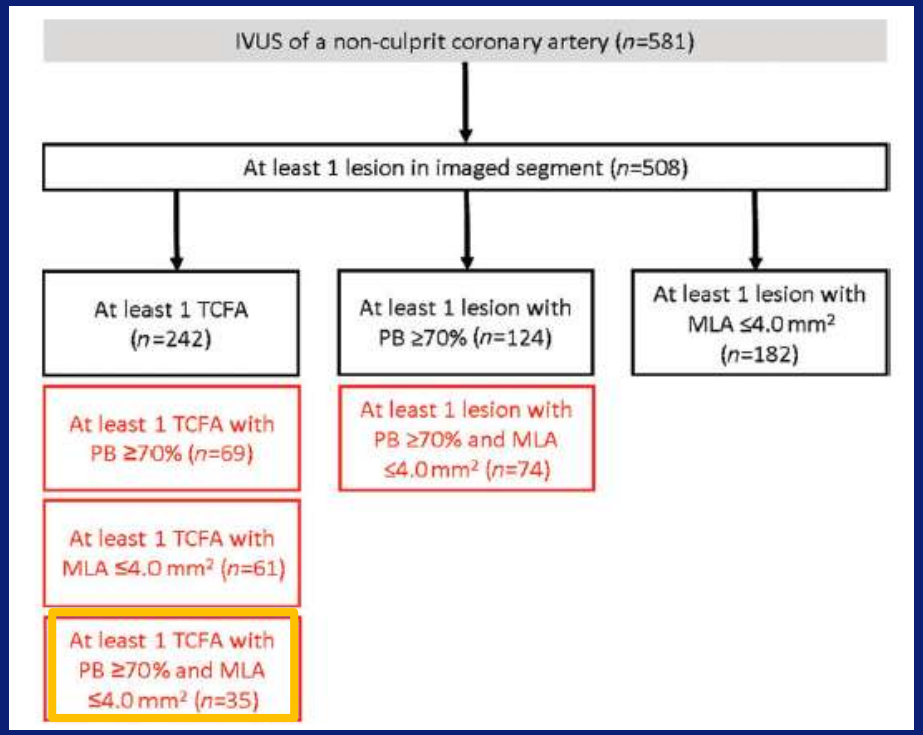
by VH-IVUS:

41.6% prevalence of VH-TCFA

11.8% prevalence of VH-TCFA with high plaque burden per artery

In PROSPECT study,

0.96 VH-TCFA per patient

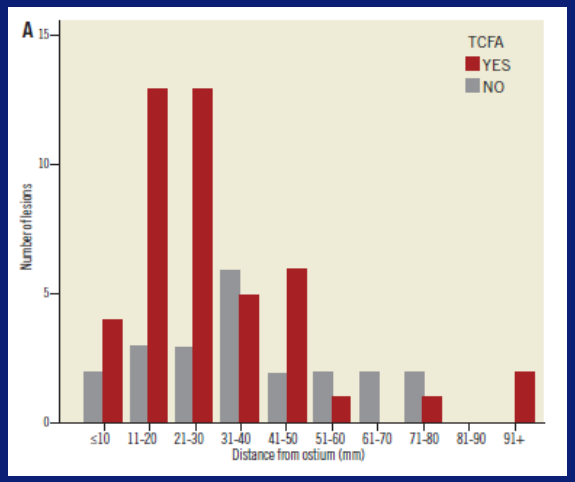


Cheng et al. Eur Heart J 2014

VP identification

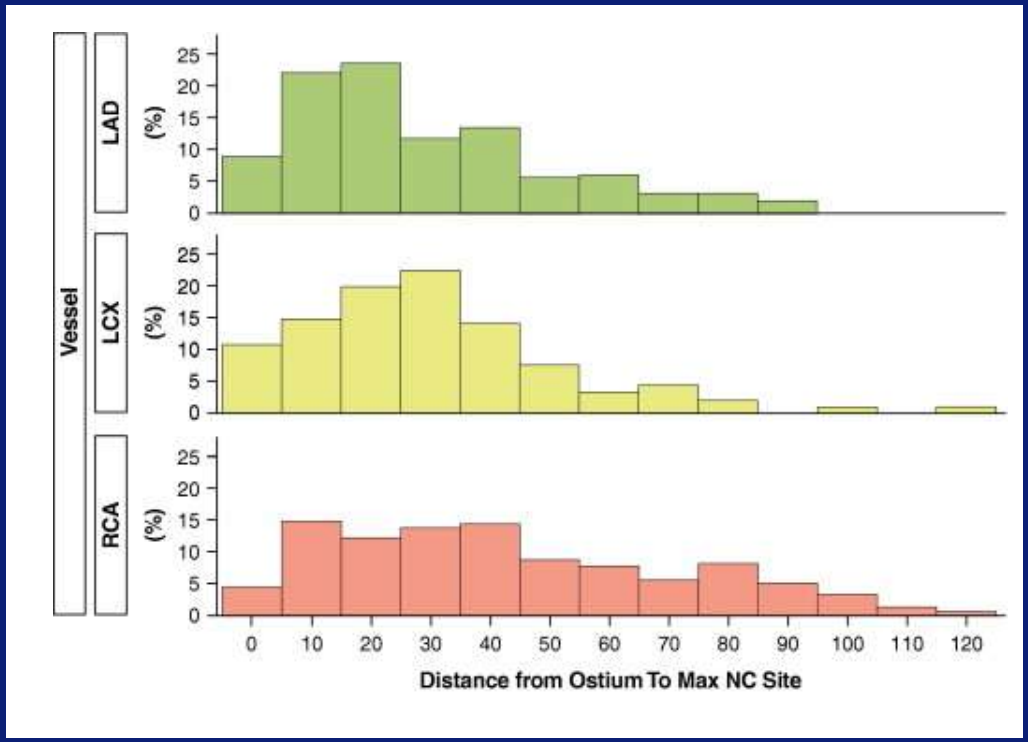
Location of vulnerable plaques

OCT



Clustering of vulnerable plaques in the proximal segments of coronary arteries

VH-IVUS



Toutouzas et al. Eurointervention 2012
Wykrzykowska et al. JACC Img 2012

VP identification and treatment

Pre-requisites

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- The number of "vulnerable plaques" is known, and the number is limited.
- The natural history of a "vulnerable plaque" has been identified in patients treated with optimal systemic therapies.

Ambrose JA et al. J Am Coll Cardiol 2008

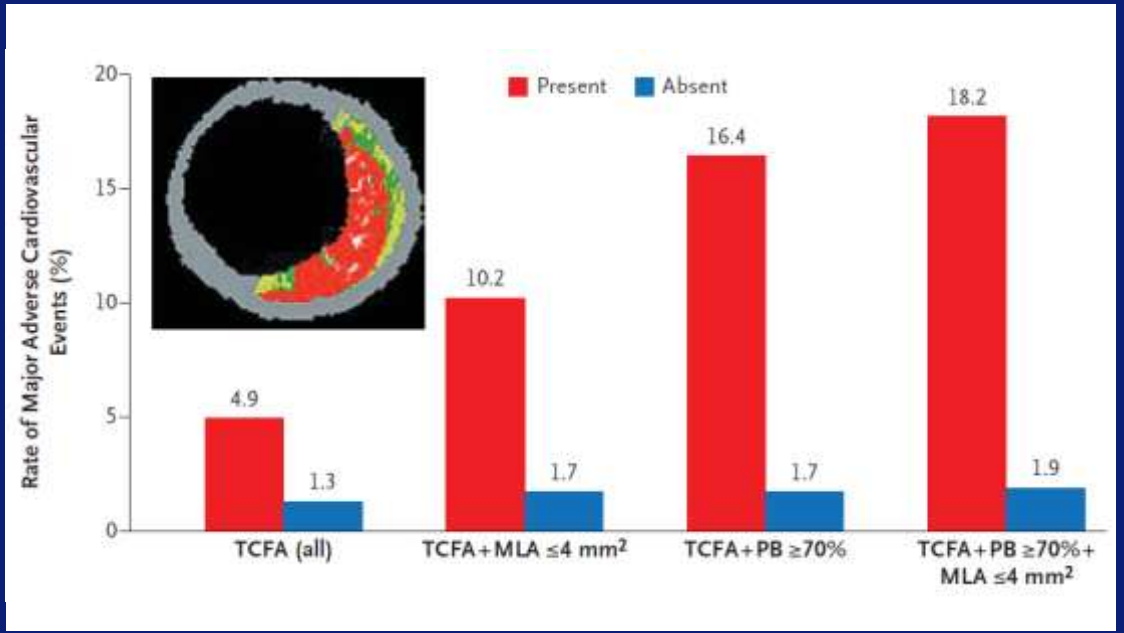
VP identification

Outcome of vulnerable plaques

PROSPECT study

Non-culprit lesions in pts with ACS have an increased risk of events despite optimal medical therapy:

- **VH-TCFA morphology**
- **Plaque burden > 70%**
- **MLA < 4.0mm**



Stone et al. N Eng J Med 2011

VP identification

Outcome of vulnerable plaques

ATHEROREMO study

Non-culprit lesions in pts with ACS and stable angina have an increased risk of events despite optimal medical therapy:

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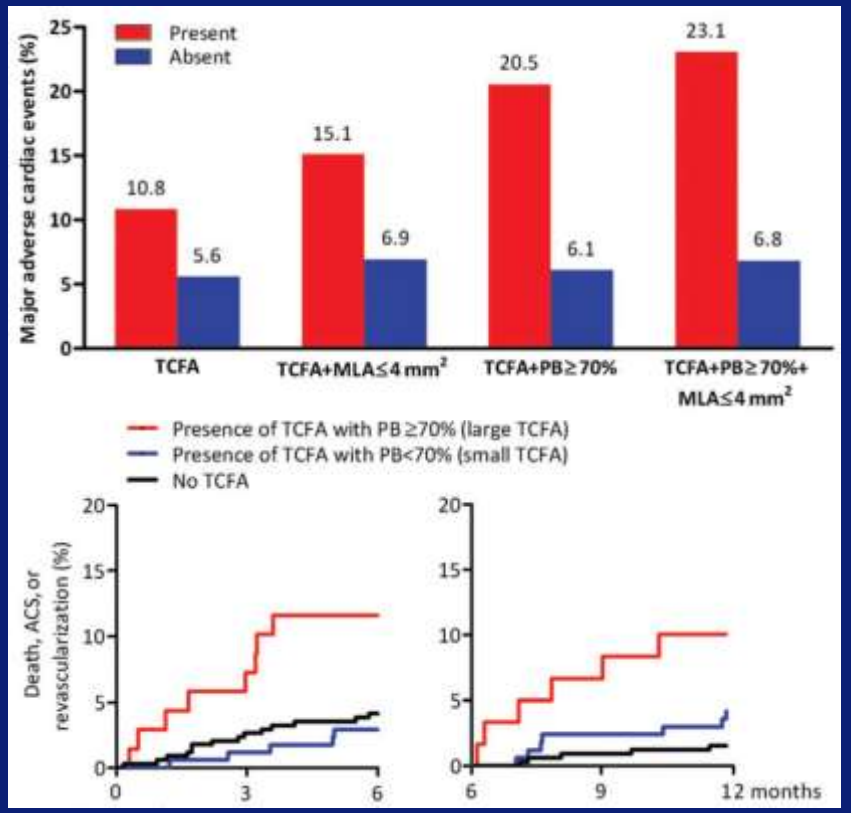
- Plaque burden > 70%
- MLA < 4.0mm



Cheng et al. Eur Heart J 2014

VP identification and treatment

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- The number of "vulnerable plaques" is known, and the number is limited.
- The natural history of a "vulnerable plaque" has been identified in patients treated with optimal systemic therapies.
- An interventional approach applied locally or regionally to an asymptomatic "vulnerable plaque" is proven to reduce future events relative to the best systemic medical therapy.

Ambrose JA et al. J Am Coll Cardiol 2008

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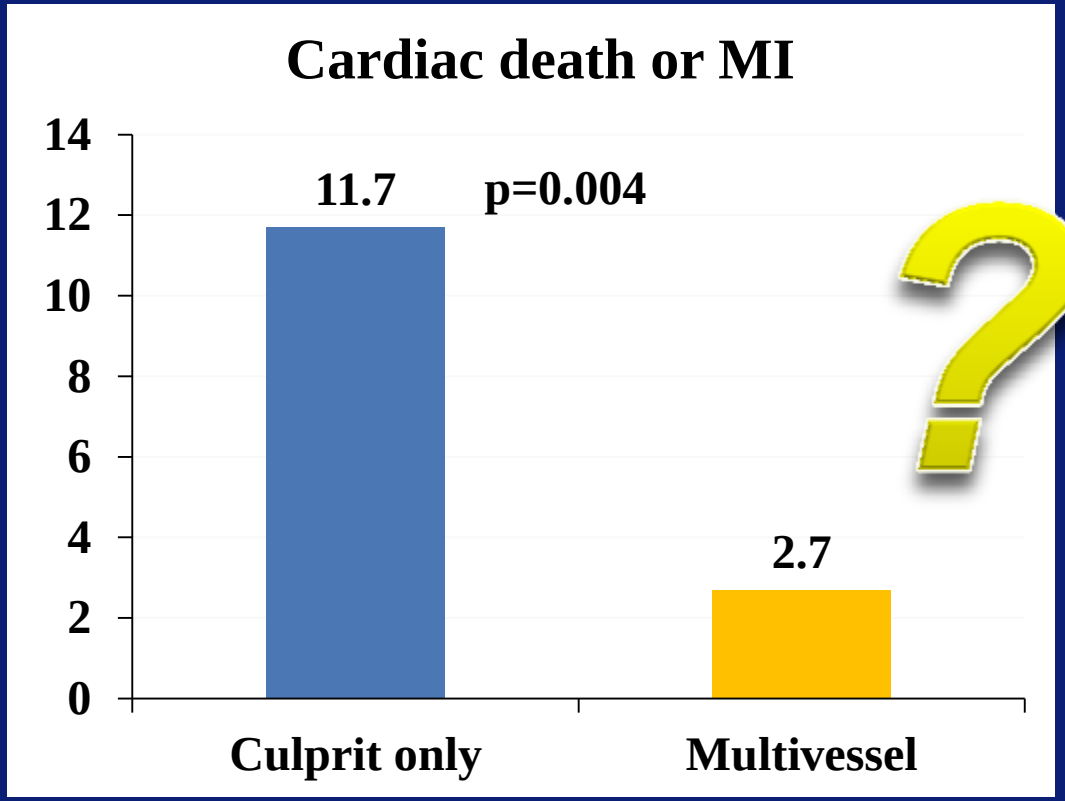
Ambrose JA et al. J Am Coll Cardiol 2008

VP treatment ?

DES

In patients with STEMI and multivessel coronary disease,
PCI of non-culprit reduced primary outcome, but also hard events



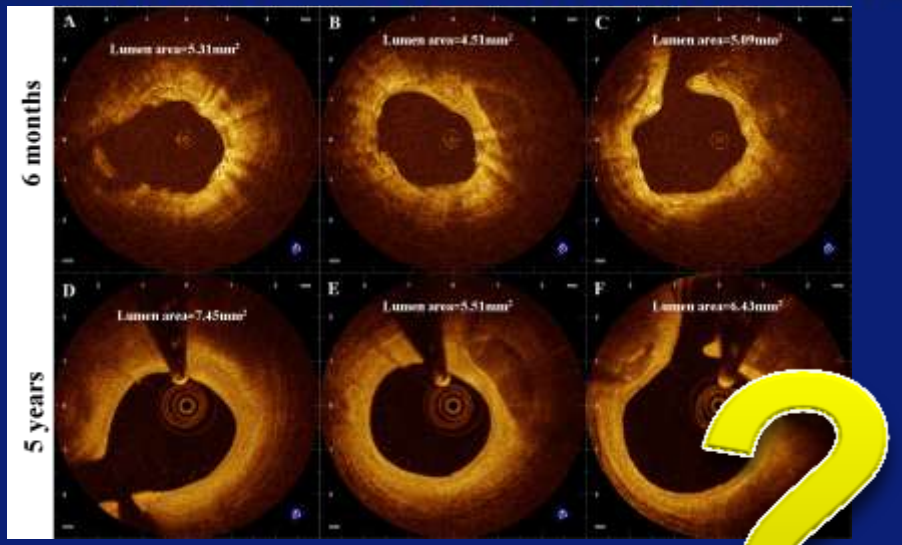
Wald et al. N Eng J Med 2013

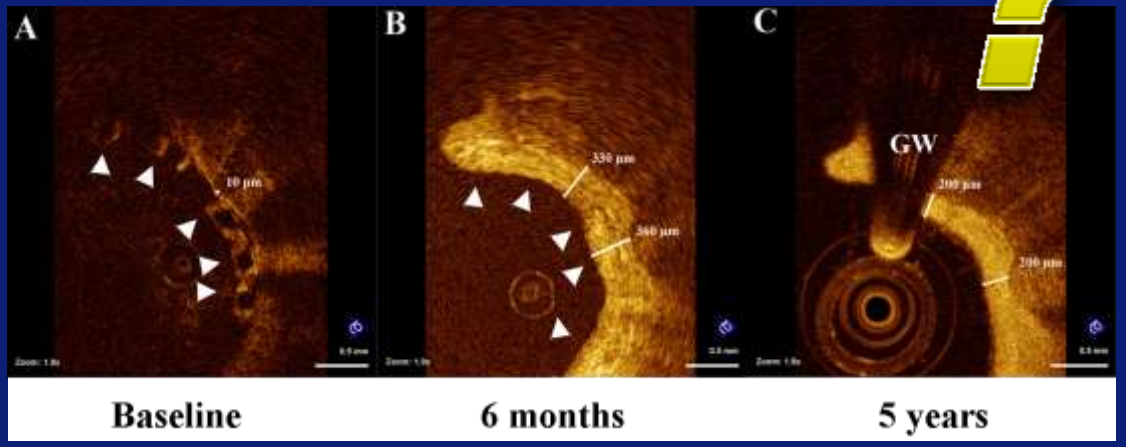
VP treatment ?

Bioresorbable scaffolds

BVS 5-year morphology

- Late lumen enlargement
- Development of signal-rich layer
- Separation of thrombogenic plaque and lumen





Karanasos et al. Circulation 2012

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London Marathon 2014: Man dies in hospital after collapse

The London Marathon 2014 saw about 36,000 people take part, many running for charity

A man who collapsed at the finish line of the London Marathon has died, organisers say.

The 42-year-old received medical attention immediately after completing Sunday's race but died in hospital.

Erasmus MC

Vulnerable Plaque
We Can Find It, Treat It Locally!

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Thank you for your attention!