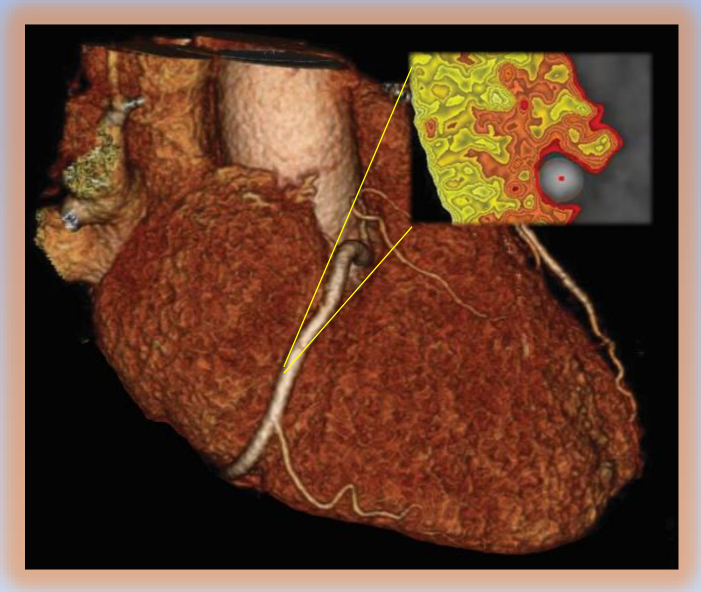


Cardiovascular risk stratification by CCTA imaging

Dr. Alexios Antonopoulos MD PhD
Imaging Specialist CCT/CMR, EACVI Ambassador in CT/CMR
Hon. Postdoc Scientist, Oxford Academic CT programme,
RDM Cardiovascular Medicine, Oxford, UK

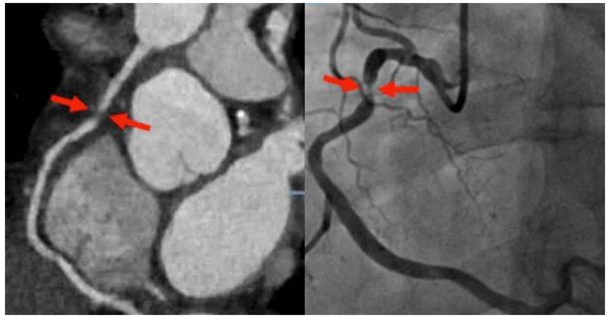
Current concepts in the prevention of CHD

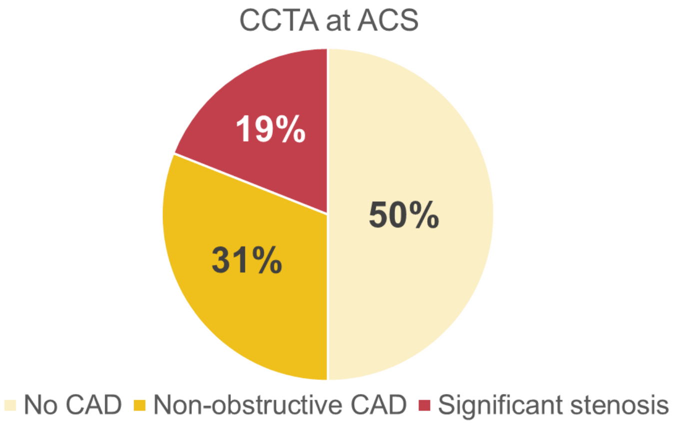
Coronary Artery Disease (CAD) Testing

- Cardiovascular disease is the world's biggest killer

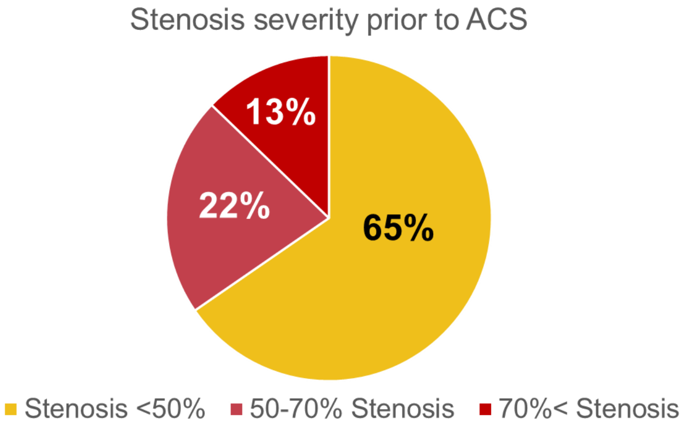
THE ASSUMPTION

Heart attacks are more likely to occur in patients with significant coronary artery stenoses





Hoffmann et al, *JACC* 2009

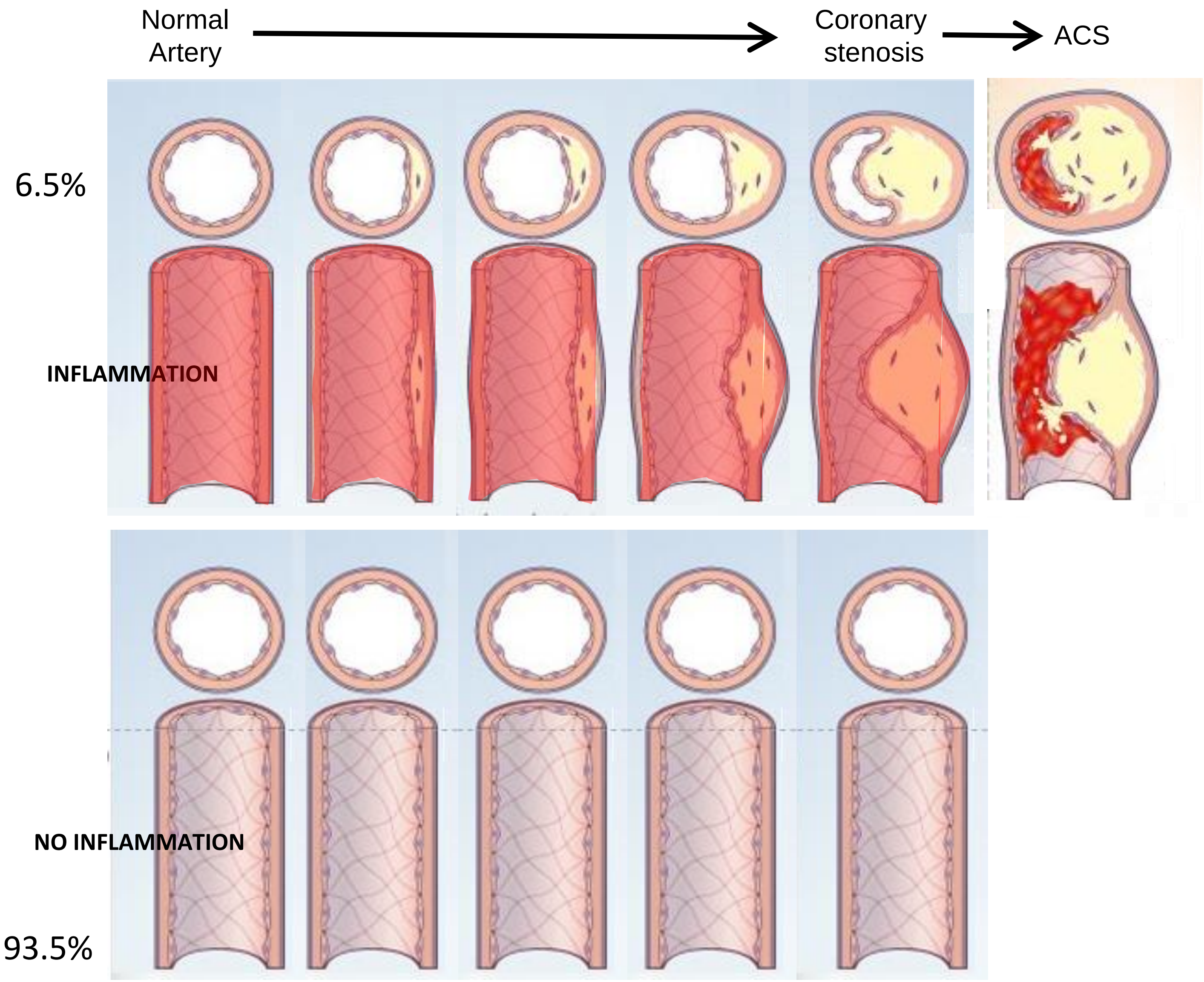


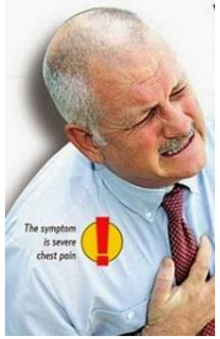
Chang et al, *JACC* 2018

THE REALITY

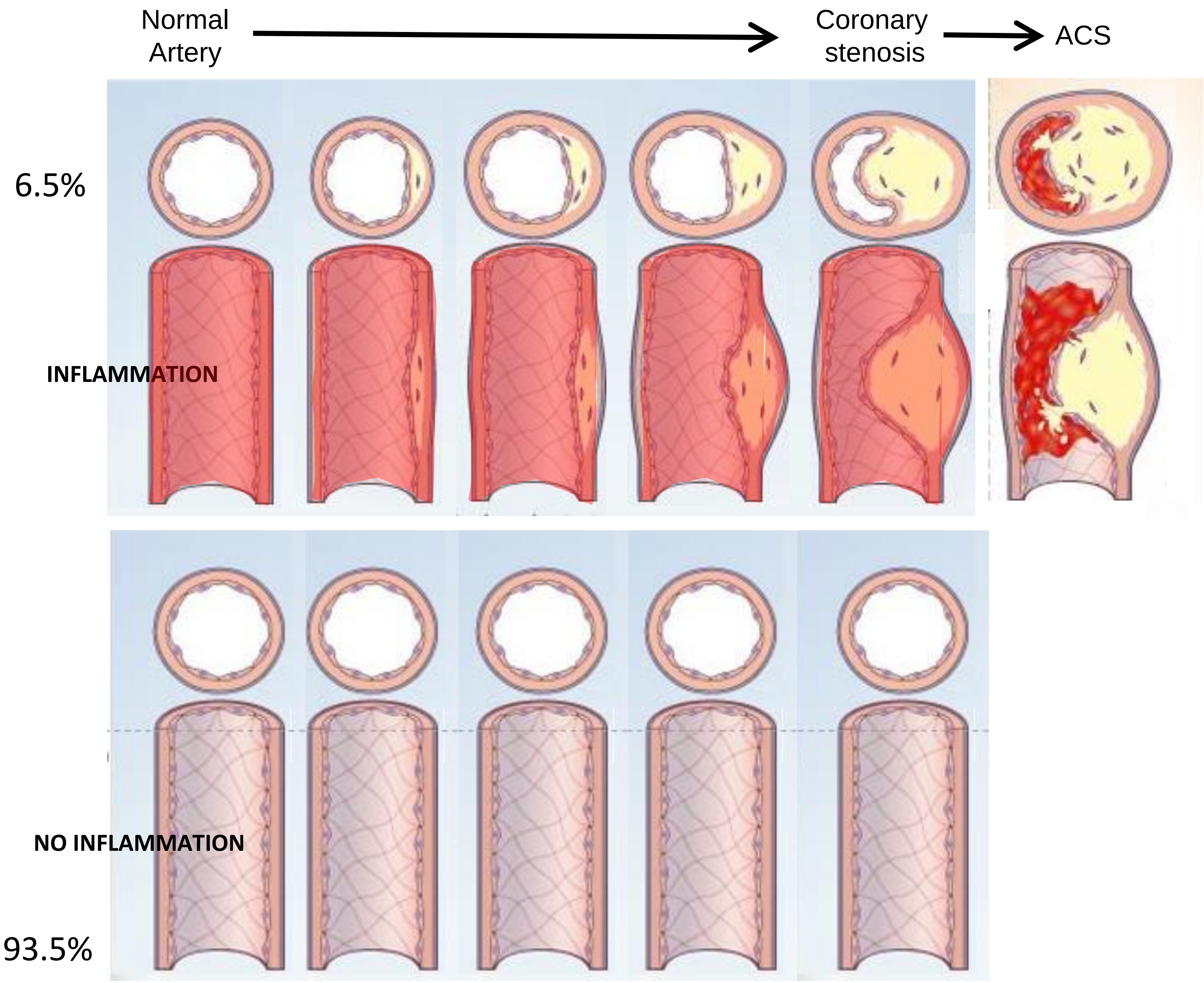
- **>50% of heart attacks occur in people with minor coronary artery stenoses**
- **Many patients at risk missed by current tests that rely on detecting luminal stenosis**
- **First presentation is often MI or death**

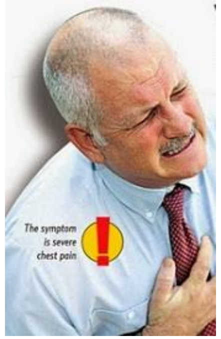
Inflammation in atherogenesis and plaque rupture





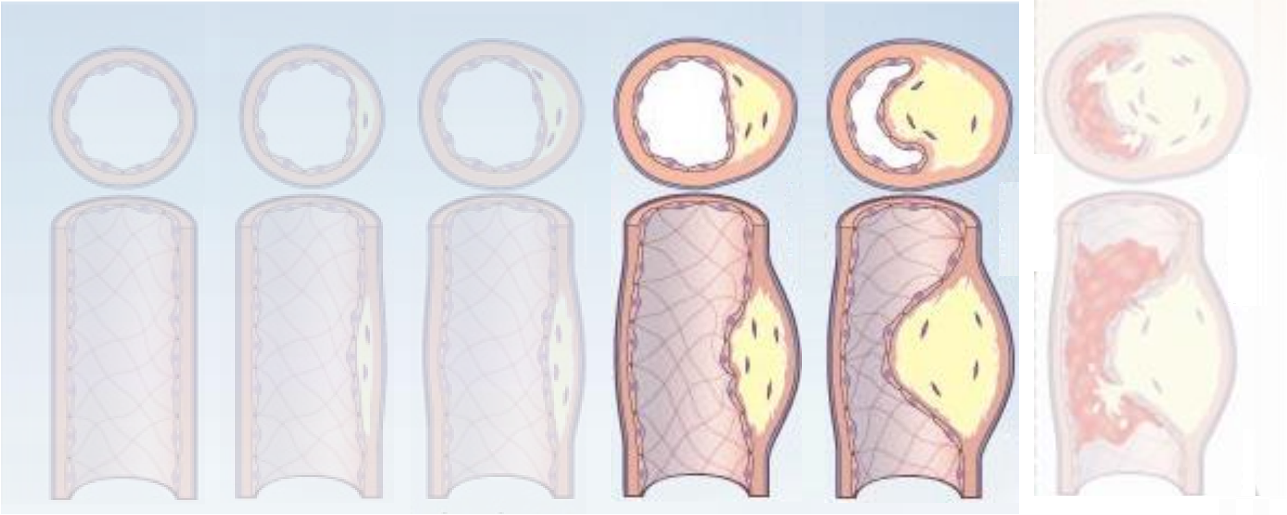
Inflammation in atherogenesis and plaque rupture

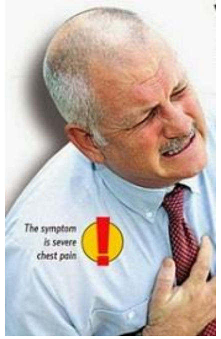




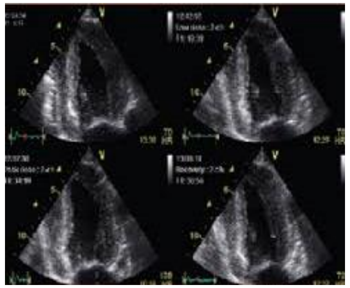
Discrepancies in cardiovascular diagnostics: The elephant in the room

Normal Artery → Narrowed Artery → Blocked Artery

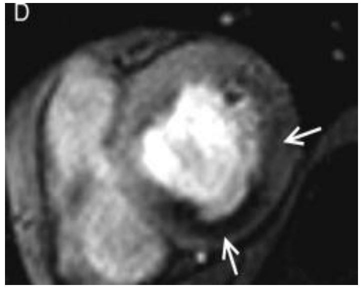




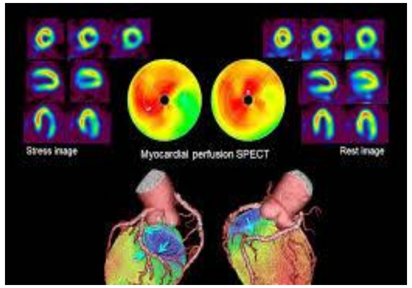
All current imaging tests



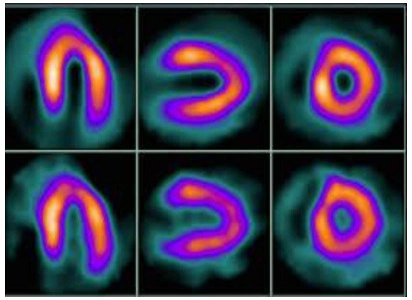
Stress echo



Stress CMR

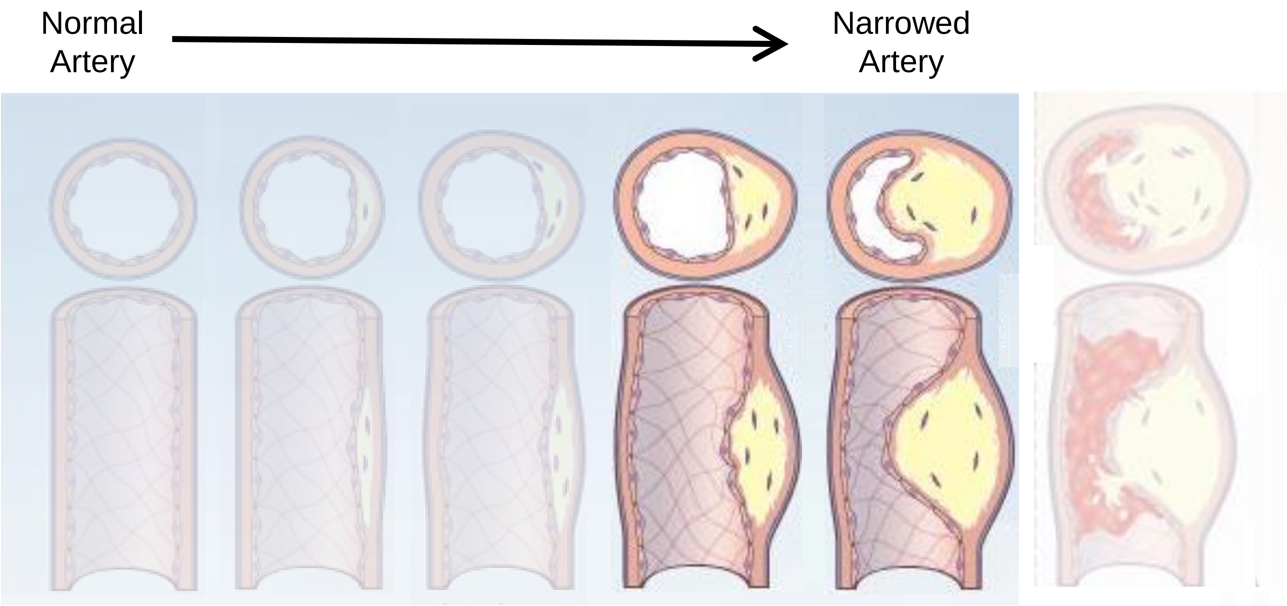


SPECT/CT



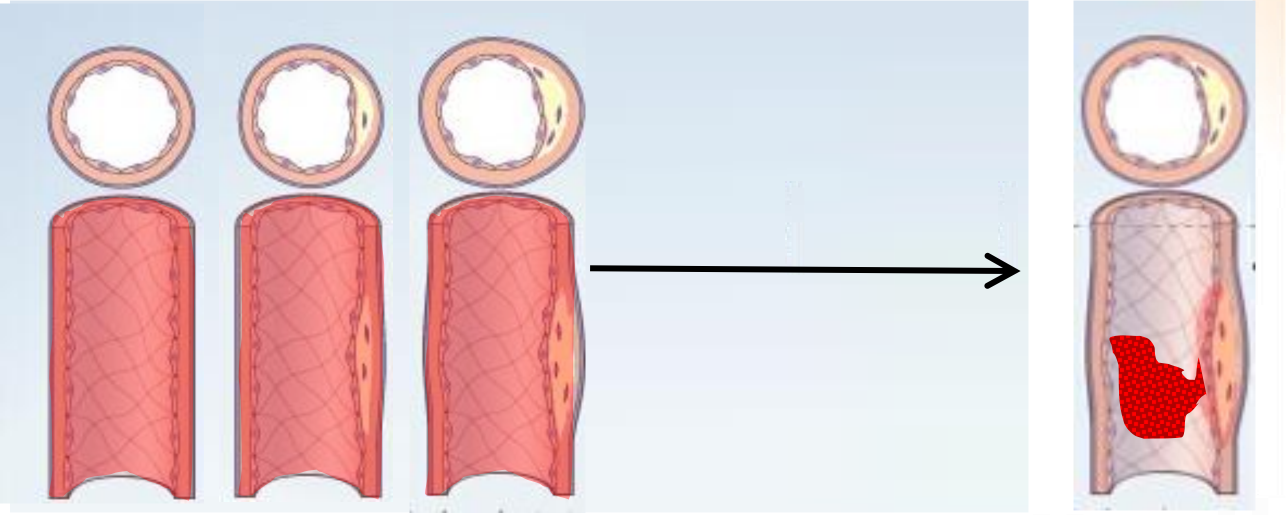
MPS

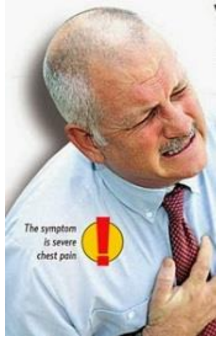
Most Coronary plaques don't cause heart attacks



“Minor” plaques cause many heart attacks

Blocked
Artery





Severity of Coronary Angiographic Lesions Before Myocardial Infarction

Study	No. of Patients	Interval Between First and Second Angiograms, mo	% Diameter Stenosis of Lesion Before MI, No. of Patients <50%	50%-75%	>75%
Ambrose et al[8]	23	18	12	6	5
Giroud et al[12]	92	24	72	8	12
Hackett et al[9]	10	21	9	1	0
Little et al[11]	58	24	36	15	7
Moise et al[14]*	116	39	17	66	33
Webster et al[13]	30	55	16	10	4
Total	329	30.2	162 (49%)	106 (32%)	61 (19%)

*Refers to progression to total occlusion with or without myocardial infarction (MI).

alled vascular inflammation!

ion in the coronaries, we would:

rmation

cks

al therapy!

Fishbein et al. Circulation. 1996;94:2662-2666

Detecting the vulnerable plaques could help prevent heart attacks

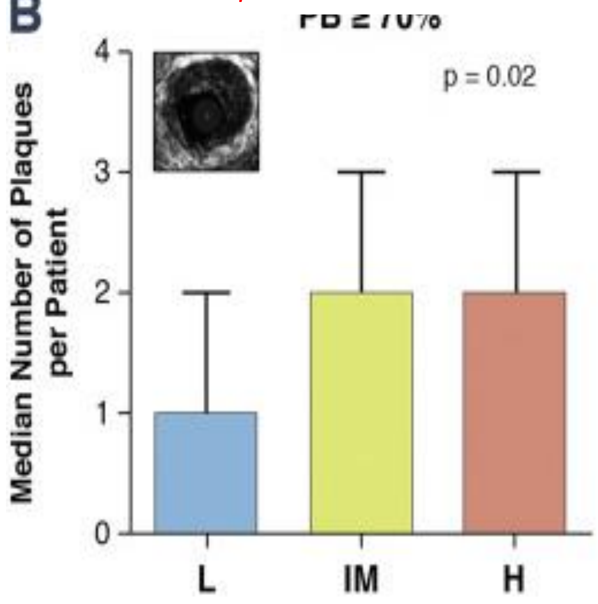
The challenge:
to detect the unstable plaques → unstable patient

Strategy #1
Detecting downstream myocardial damage

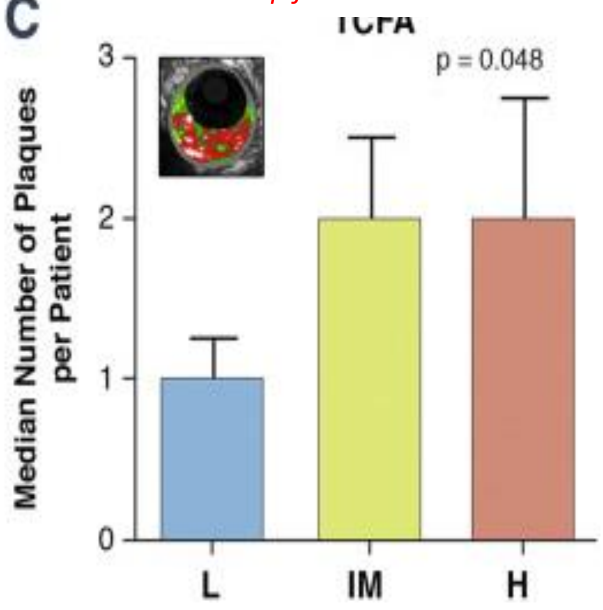
Unstable plaques cause minor downstream myocardial damage, even at rest!

(High-sensitivity troponin I)

Plaque burden >70%



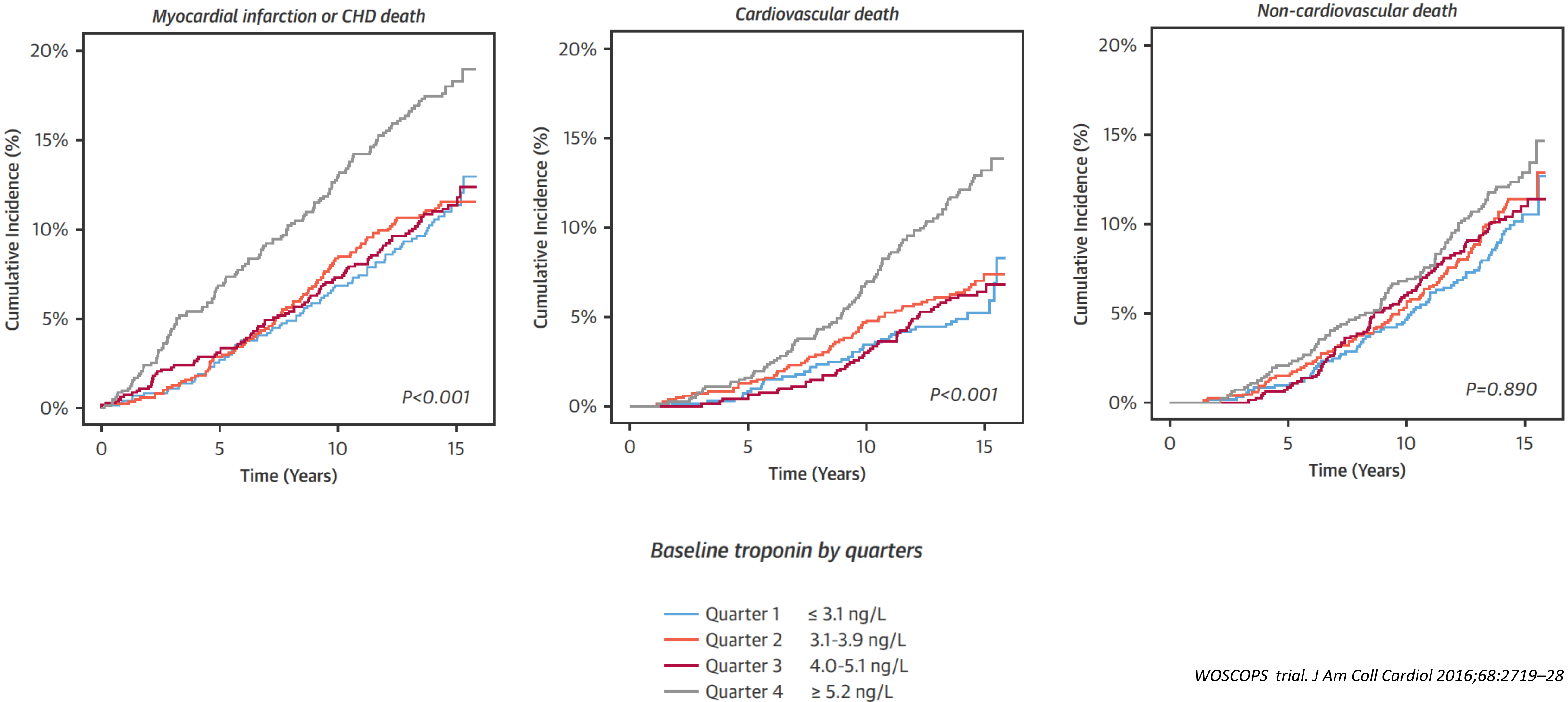
thin-cap fibroatheroma



Patients (n = 99) with stable CAD undergoing PCI + IVUS-VH

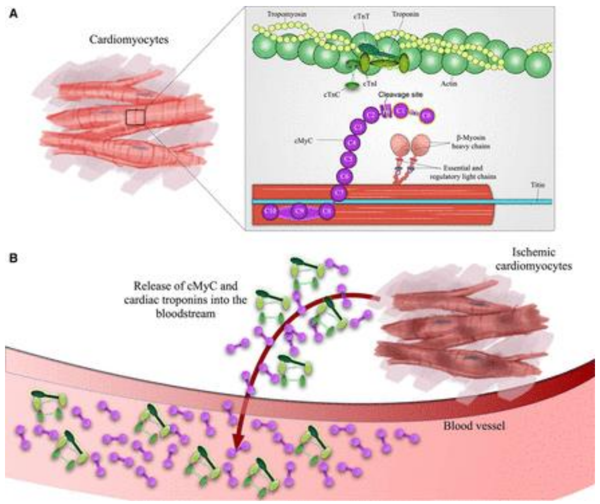
Brown AJ et al. JACC Cardiovasc Imaging. 2017;10(10)

Predictive value of baseline hs-cTnI for future events



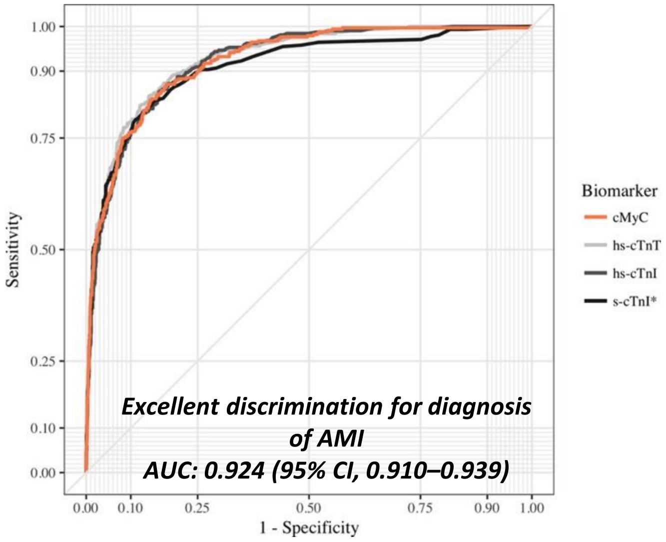
WOSCOPS trial. J Am Coll Cardiol 2016;68:2719–28

Beyond troponin: Cardiac myosin-binding protein C (cMyC)



✓novel biomarker of cardiac injury

✓serum concentration rises and falls more rapidly than TnT and TnI



Excellent discrimination for diagnosis of AMI
AUC: 0.924 (95% CI, 0.910–0.939)

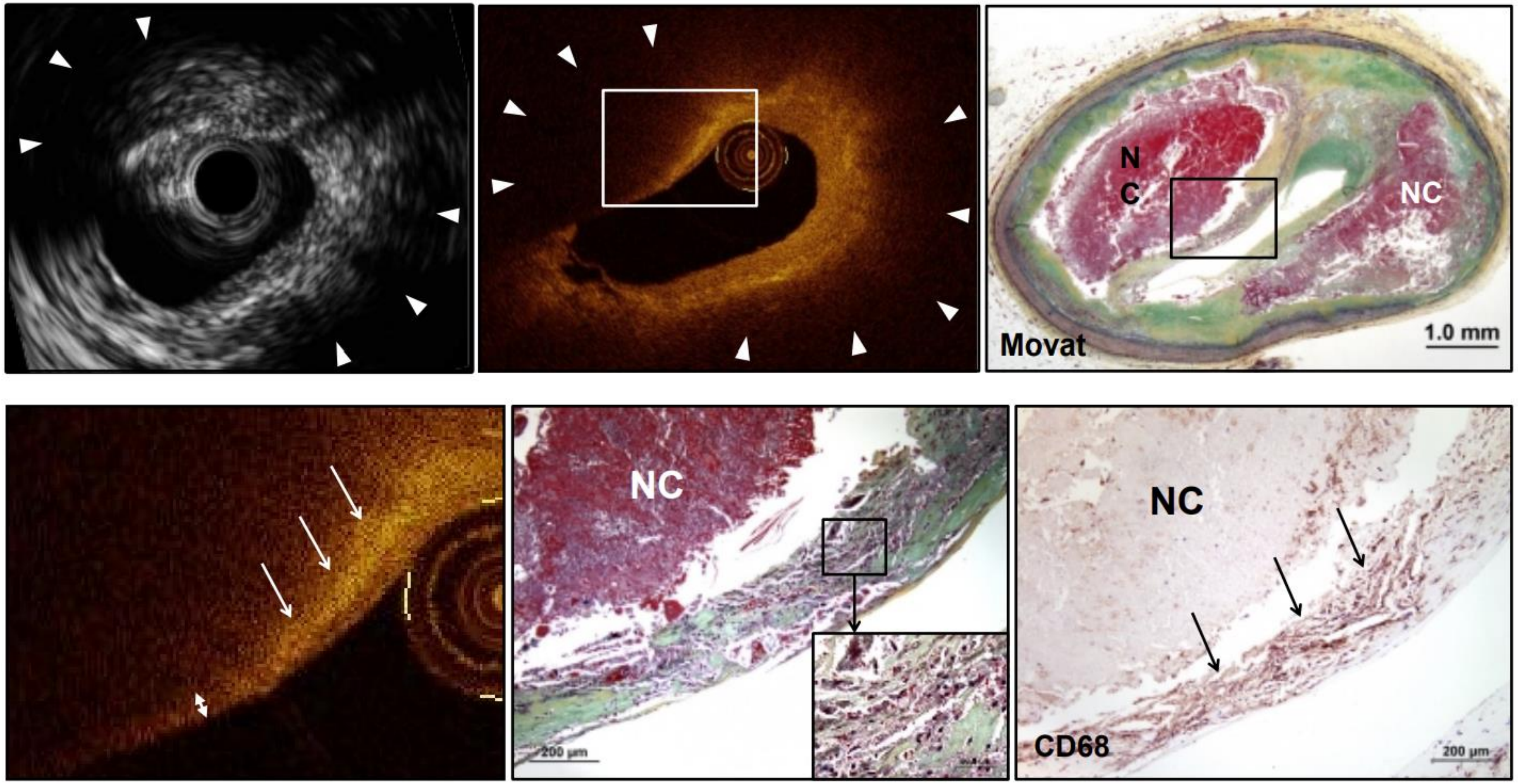
- *cMyC at presentation provides discriminatory power comparable to hs-cTnT and hs-cTnI in the diagnosis of AMI*
- *may perform favourably in patients presenting early after symptom onset*

Kaier TE et al. *Circulation.* 2017;136.

Strategy #2

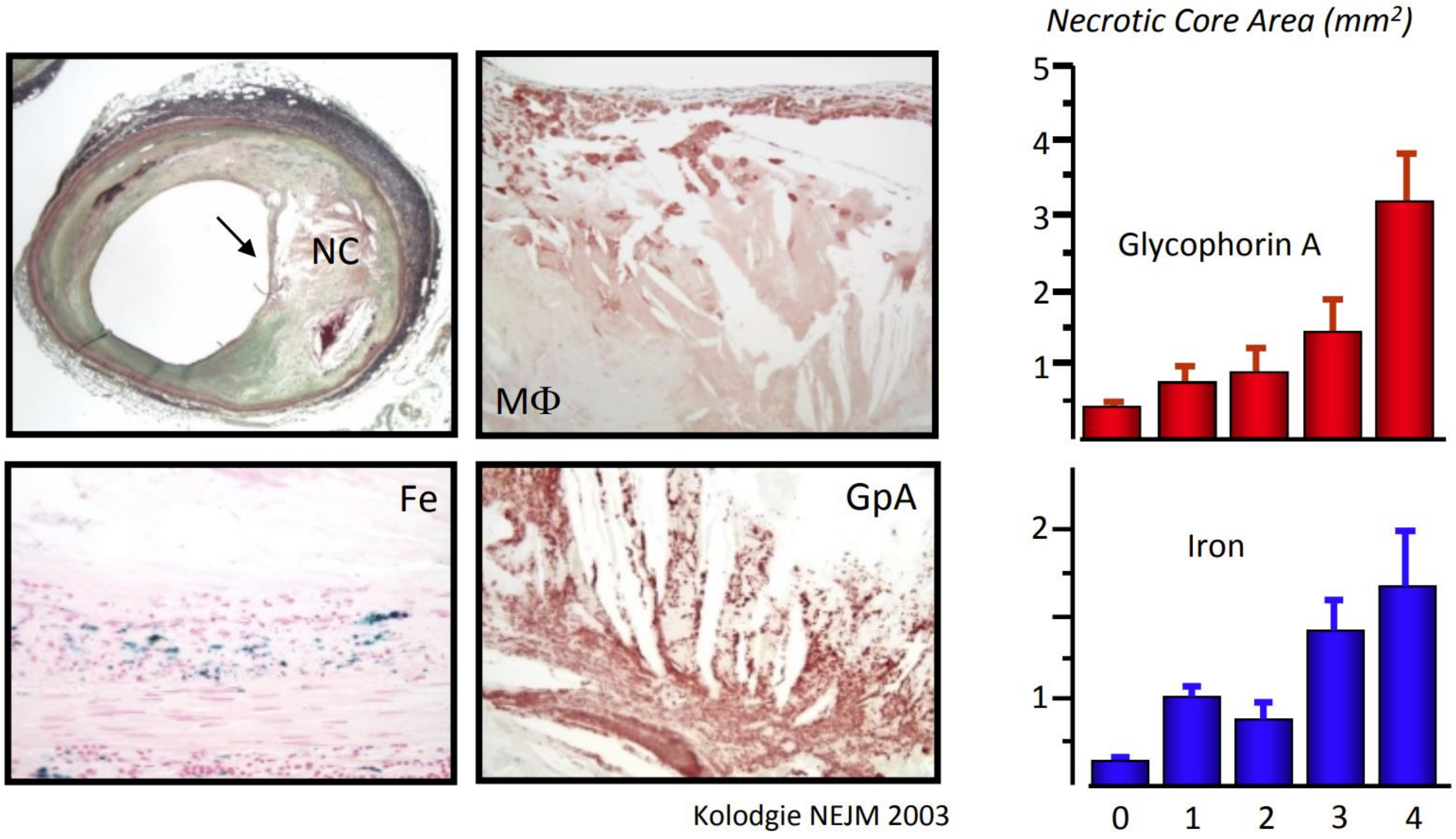
Detecting the vulnerable patient by studying coronary plaque characteristics

Vulnerable plaques have distinct histopathological characteristics



Narula, Virmani et al. Nature Rev. Cardiology 2013

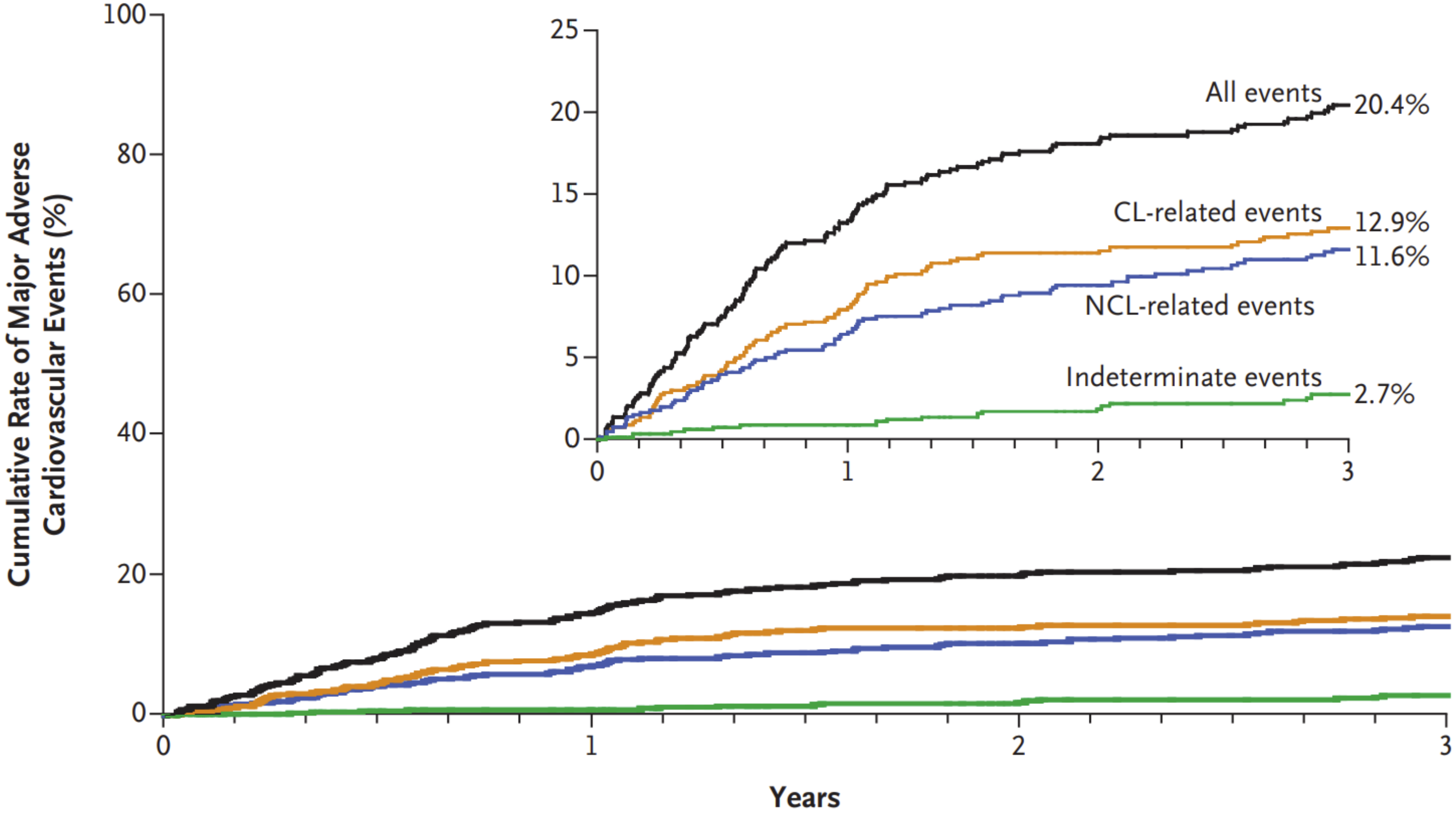
Intra-plaque hemorrhage and plaque vulnerability



Kolodgie NEJM 2003

Natural-History Study of Coronary Atherosclerosis

After ACS and stenting (PCI) major adverse cardiovascular events are equally attributable to recurrence at the site of culprit lesions (CL) and to nonculprit lesions (NCL).

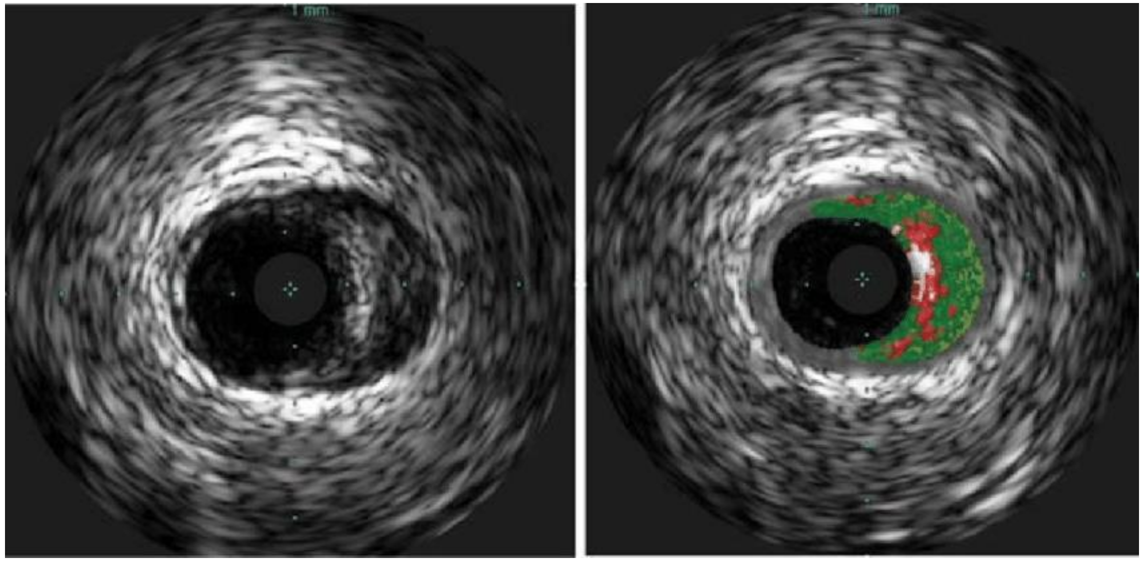


No. at Risk				
All patients	697	557	506	480
Patients with CL-related events	697	590	543	518
Patients with NCL-related events	697	595	553	521
Patients with indeterminate events	697	634	604	583

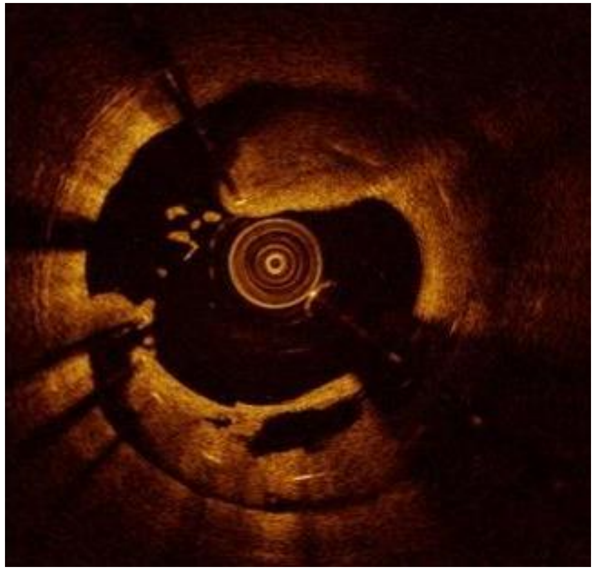
Stone P et al NEJM 2011

Studying plaque characteristics by invasive intracoronary imaging

Intravascular ultrasound (IVUS)

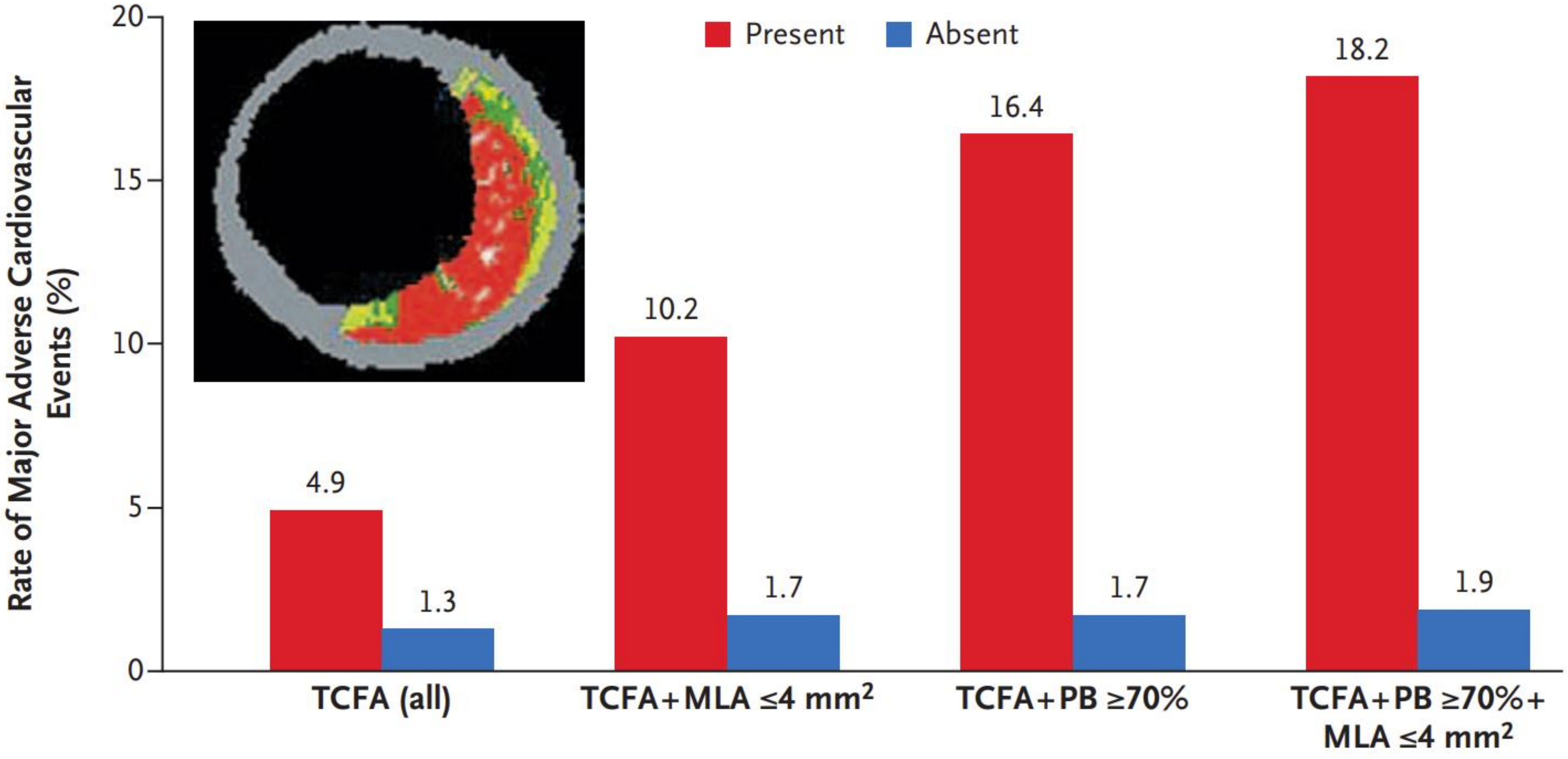


Optical coherence tomography (OCT)



Stone P et al NEJM 2011

Studying plaque characteristics by invasive intracoronary imaging

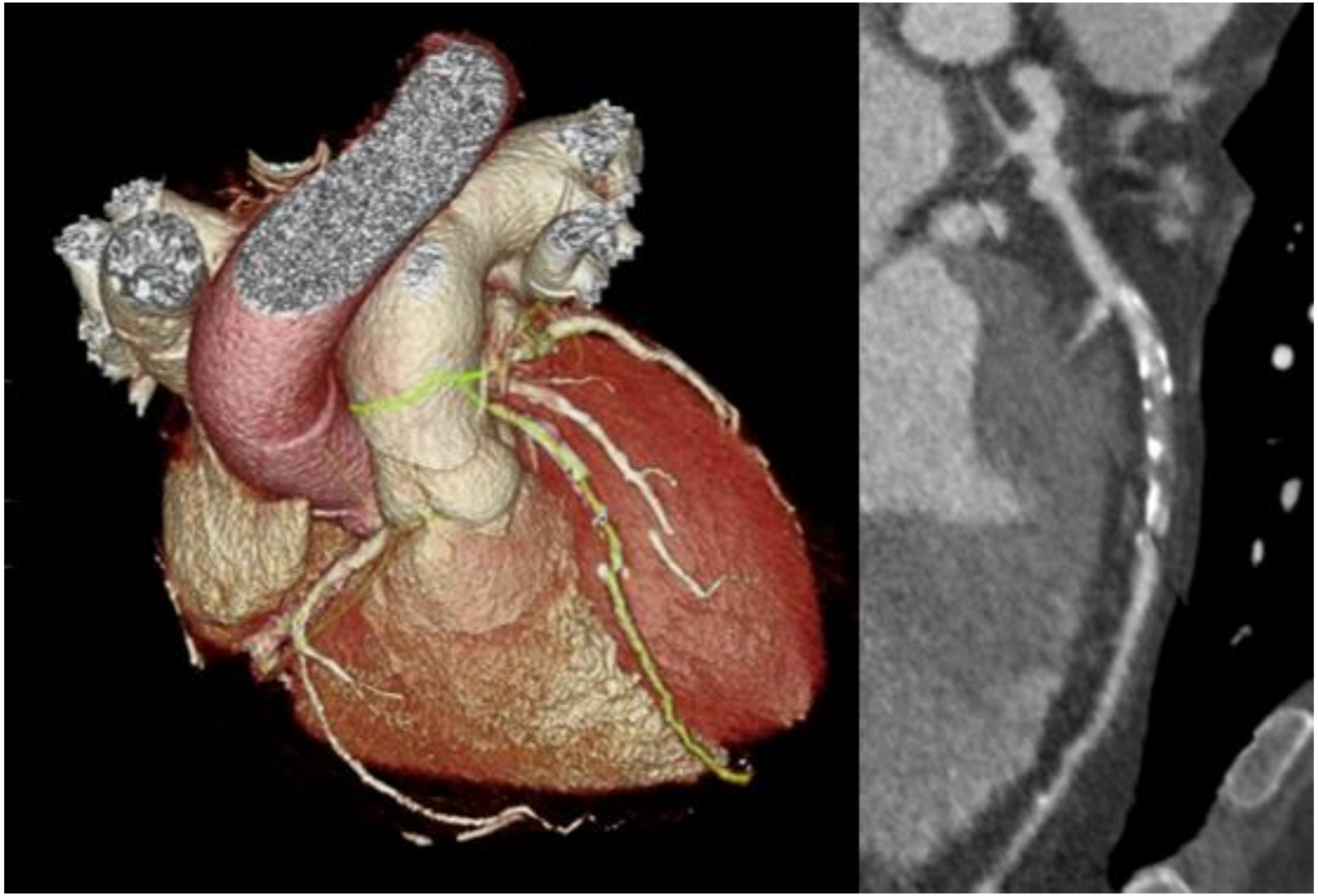


	TCFA (all)	TCFA+MLA ≤4 mm²	TCFA+PB ≥70%	TCFA+PB ≥70%+ MLA ≤4 mm²
Lesion hazard ratio (95% CI)	3.90 (2.25–6.76)	6.55 (3.43–12.51)	10.83 (5.55–21.10)	11.05 (4.39–27.82)
P value	<0.001	<0.001	<0.001	<0.001
Prevalence (%)	46.7	15.9	10.1	4.2

But invasive imaging in not suitable as a screening strategy to detect patients at risk

Stone G et al NEJM 2011

Studying plaque characteristics by computed tomography



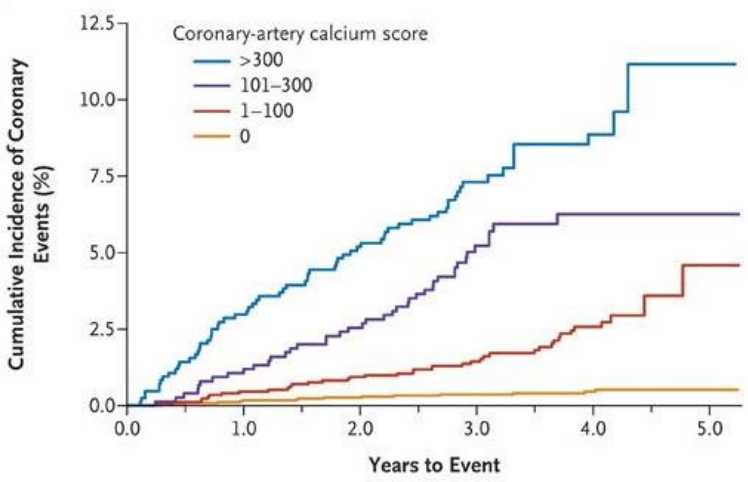
The prognostic value of coronary calcium on cardiovascular CT

The Multiethnic Study of Atherosclerosis (MESA) study (6000 + subjects)

Risk of Coronary Heart Disease

Risk factor	HR for model without CACS (95% CI)	P value	HR for model with CACS (95% CI)	P value
Age[*]	1.30 (1.21-1.41)	<0.001	1.08 (0.99-1.17)	0.09
Male sex	2.21 (1.60-3.06)	<0.001	1.48 (1.06-2.05)	0.02
Systolic blood pressure (mmHg)[†]	1.10 (1.03-1.18)	0.003	1.08 (1.01-1.15)	0.03
Use of blood pressure lowering medication	1.61 (1.21-2.15)	0.001	1.37 (1.03-1.82)	0.03
Total cholesterol (mg/dl)[‡]	1.07 (1.03-1.11)	0.001	1.05 (1.01-1.10)	0.01
High-density lipoprotein cholesterol (mg/dl)[‡]	0.81 (0.72-0.91)	<0.001	0.84 (0.75-0.94)	0.002
Current smoker	1.91 (1.25-2.91)	0.003	1.54 (1.00-2.35)	0.05
CACS (lnCAC + 1)			1.41 (1.31-1.51)	<0.001

HR denotes hazard ratio, CACS coronary artery calcium score, and CI confidence interval



Polonsky et al. JAMA. 2010 303(16): 1610–1616

Detrano et al. NEJM. 2008; 358:1336-1345

But…….. calcium is a sign of stable plaques!

Reflects irreversible changes in the anatomy of vascular wall

Cannot regress with treatment that lowers inflammation

Structural characteristics of the vulnerable plaque in CTA

The *vulnerable* plaque

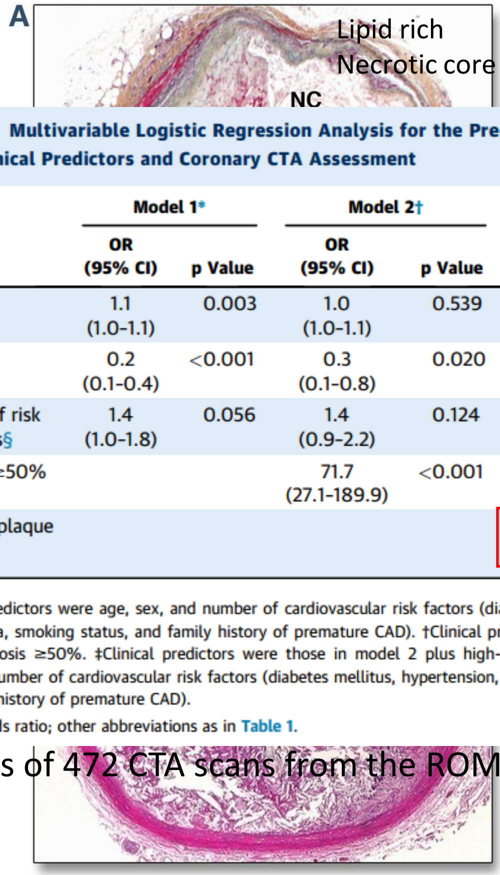


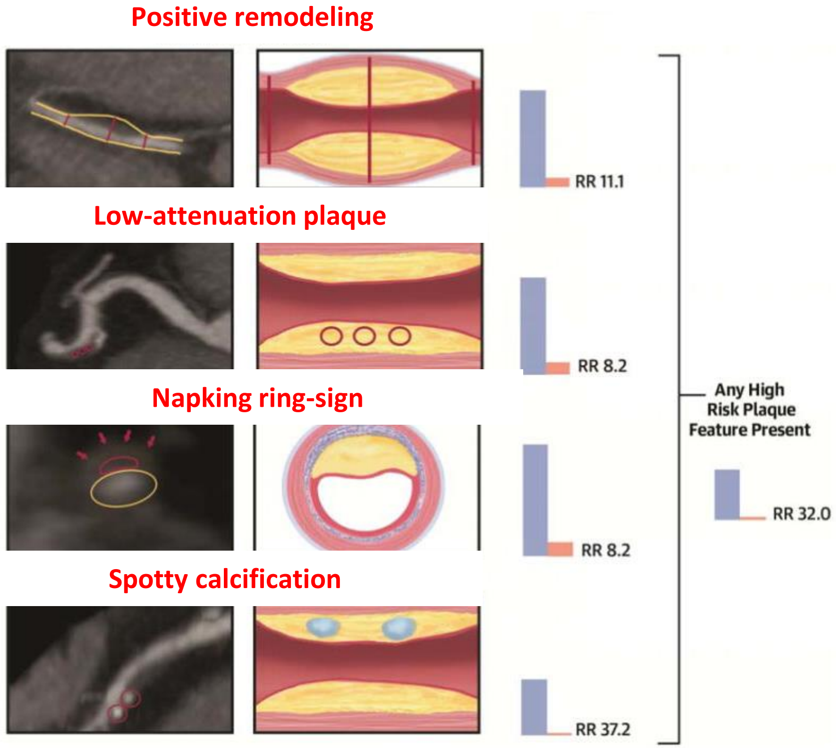
TABLE 3 Multivariable Logistic Regression Analysis for the Prediction of ACS Using Clinical Predictors and Coronary CTA Assessment

	Model 1*		Model 2†		Model 3‡	
	OR (95% CI)	p Value	OR (95% CI)	p Value	OR (95% CI)	p Value
Age	1.1 (1.0-1.1)	0.003	1.0 (1.0-1.1)	0.539	1.0 (0.9-1.1)	0.870
Female	0.2 (0.1-0.4)	<0.001	0.3 (0.1-0.8)	0.020	0.4 (0.1-1.2)	0.104
Number of risk factors§	1.4 (1.0-1.8)	0.056	1.4 (0.9-2.2)	0.124	1.3 (0.8-2.0)	0.278
Stenosis ≥50%			71.7 (27.1-189.9)	<0.001	38.6 (14.2-104.7)	<0.001
High-risk plaque					8.9 (1.8-43.3)	0.006

*Clinical predictors were age, sex, and number of cardiovascular risk factors (diabetes mellitus, hypertension, dyslipidemia, smoking status, and family history of premature CAD). †Clinical predictors were those in model 1 plus stenosis ≥50%. ‡Clinical predictors were those in model 2 plus high-risk plaque. §Number of risk factors = number of cardiovascular risk factors (diabetes mellitus, hypertension, dyslipidemia, smoking status, and family history of premature CAD).

OR = odds ratio; other abbreviations as in Table 1.

Analysis of 472 CTA scans from the ROMICAT-II trial



Van Velzen et al. J Nucl Cardiol. 2011;18(5): 893–903
Hecht et al. JACC Cardiovasc Imaging. 2015;8(11)
Puchner et al. JACC. 2014;64(7):684–692.

CTA plaque characteristics and risk of subsequent ACS events

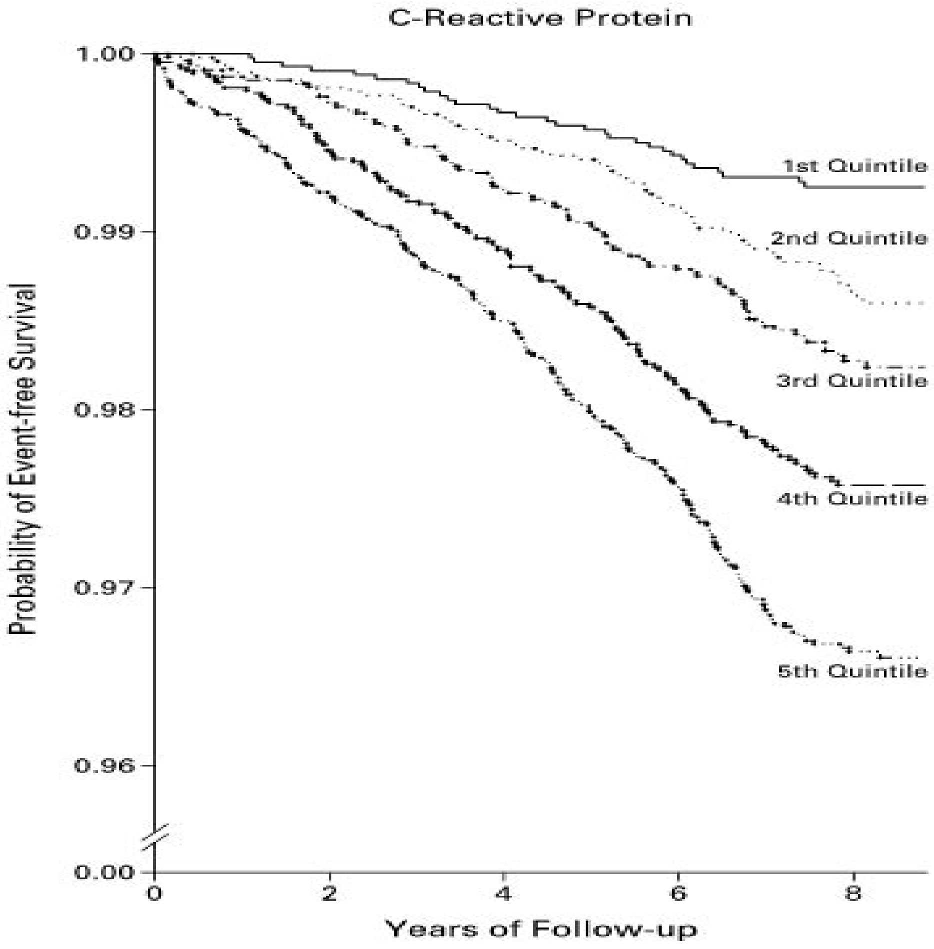
	ACS 0-12 mo	ACS 13-24 mo	No ACS in 24mo	*p*
Remodeling Index (percent)	131.2±5.1 (120.9–141.4)	120.8±5.9 (109.1–132.6)	113.4±1.6 (110.3–116.6)	.005
Total plaque volume (mm^3)	166.5±17.8 (131.1–201.9)	92.8±20.4 (52.1–133.6)	58.1±5.5 (47.1–69.1)	<.001
LAP volume (mm^3)	30.5±4.1 (22.3–38.8)	6.9±4.8 (-2.6–16.4)	1.2±1.3 (-1.3–3.8)	<.001
LAP area (mm^2)	4.7±0.5 (3.6–5.7)	1.2±0.6 (-6.6–2.4)	0.5±0.2 (0.2–0.9)	<.001
LAP/plaque area (percent)	31.5±4.5 (22.5–40.4)	8.1±5.2 (-2.2–18.4)	7.8±1.4 (5.0–10.5)	<.001

Motoyama, Narula et al. JACC 2009

Strategy #3

Detecting the vulnerable patient by quantifying systemic inflammation:
how specific can we be?

Detecting systemic inflammation to identify the high-risk patient

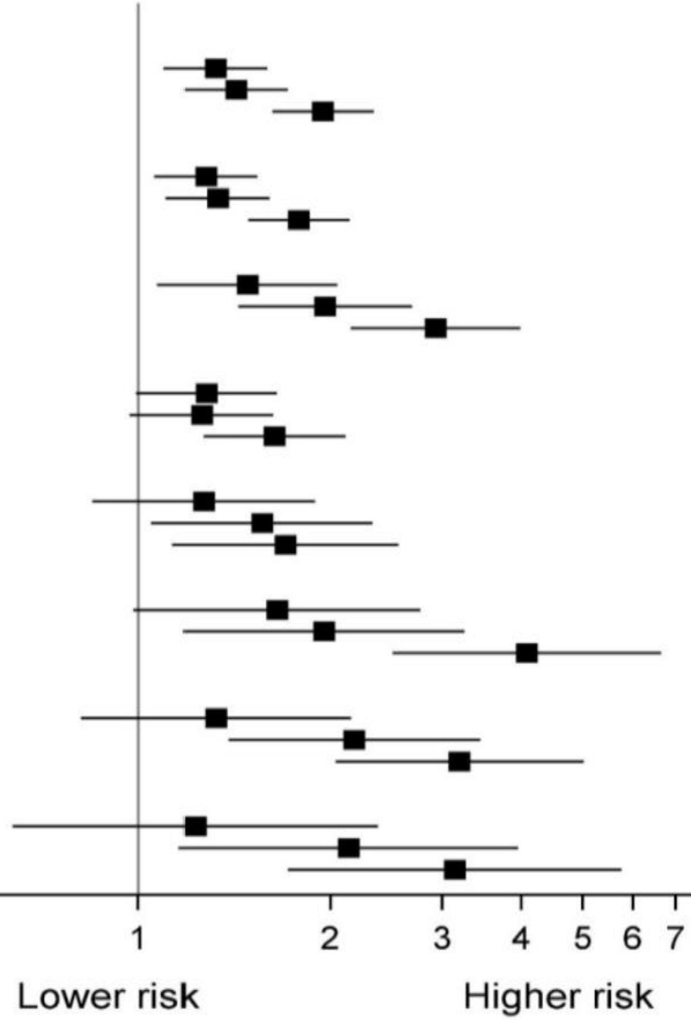


CRP *as a* ***risk factor*** *for adverse cardiovascular events*

Ridker PM et al. NEJM. 2002;347.

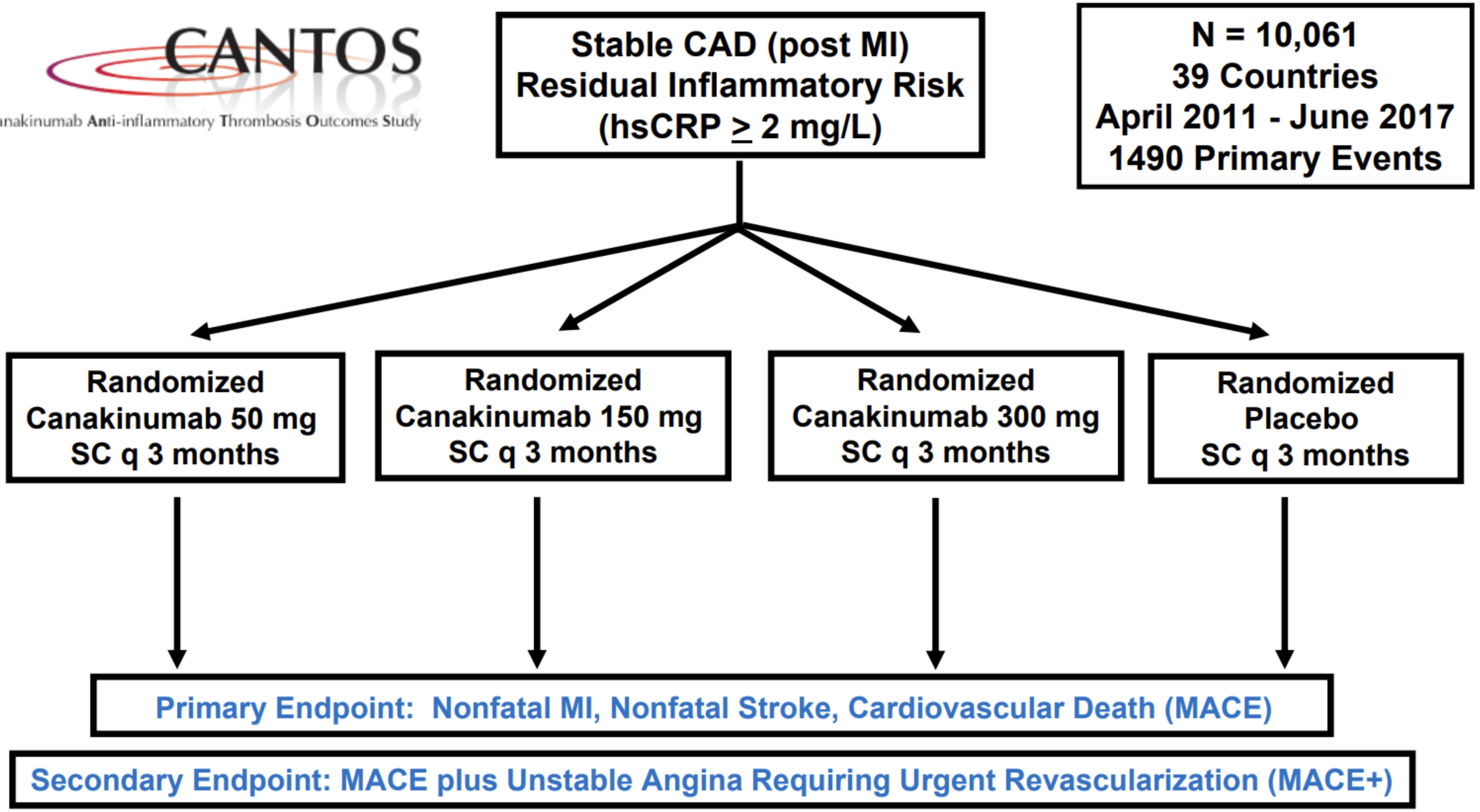
IL-6 as a predictor of CV events

Outcome IL6 (ng/L)	Number of patients	Events (%/3 yr)	HR (95%CI) Q1 as reference	P-value effect of biomarker level
MACE = CV death, MI or stroke				
<1.4	3048	175 (4.85)		
1.4-2.1	3824	323 (7.29)	1.32 (1.10-1.59)	
2.1-3.2	3619	363 (8.77)	1.42 (1.18-1.71)	
≥3.2	3600	544 (14.00)	1.95 (1.62-2.34)	<0.0001
MCE				
<1.4	3048	180 (5.00)		
1.4-2.1	3824	323 (7.30)	1.27 (1.06-1.53)	
2.1-3.2	3619	350 (8.47)	1.33 (1.11-1.60)	
≥3.2	3600	510 (13.14)	1.78 (1.48-2.15)	<0.0001
CV death				
<1.4	3048	54 (1.46)		
1.4-2.1	3824	117 (2.56)	1.48 (1.07-2.05)	
2.1-3.2	3619	166 (3.90)	1.96 (1.43-2.69)	
≥3.2	3600	298 (7.35)	2.93 (2.15-3.99)	<0.0001
MI				
<1.4	3048	96 (2.64)		
1.4-2.1	3824	172 (3.85)	1.28 (0.99-1.65)	
2.1-3.2	3619	176 (4.22)	1.26 (0.97-1.63)	
≥3.2	3600	242 (6.17)	1.63 (1.26-2.11)	0.0013
Stroke				
<1.4	3048	39 (1.06)		
1.4-2.1	3824	66 (1.46)	1.27 (0.85-1.89)	
2.1-3.2	3619	80 (1.90)	1.56 (1.05-2.33)	
≥3.2	3600	89 (2.22)	1.70 (1.13-2.56)	0.0527
Heart failure				
<1.4	3048	20 (0.54)		
1.4-2.1	3824	53 (1.17)	1.65 (0.98-2.77)	
2.1-3.2	3619	69 (1.64)	1.96 (1.18-3.25)	
≥3.2	3600	171 (4.31)	4.08 (2.50-6.64)	<0.0001
Non-CV death				
<1.4	3048	25 (0.68)		
1.4-2.1	3824	48 (1.05)	1.32 (0.81-2.15)	
2.1-3.2	3619	88 (2.07)	2.18 (1.38-3.45)	
≥3.2	3600	147 (3.62)	3.19 (2.04-5.01)	<0.0001
Cancer death				
<1.4	3048	14 (0.38)		
1.4-2.1	3824	25 (0.55)	1.23 (0.63-2.37)	
2.1-3.2	3619	47 (1.11)	2.14 (1.16-3.95)	
≥3.2	3600	75 (1.85)	3.14 (1.71-5.75)	<0.0001



Inhibition of IL-1b to prevent CV events

CANTOS
Canakinumab Anti-inflammatory Thrombosis Outcomes Study



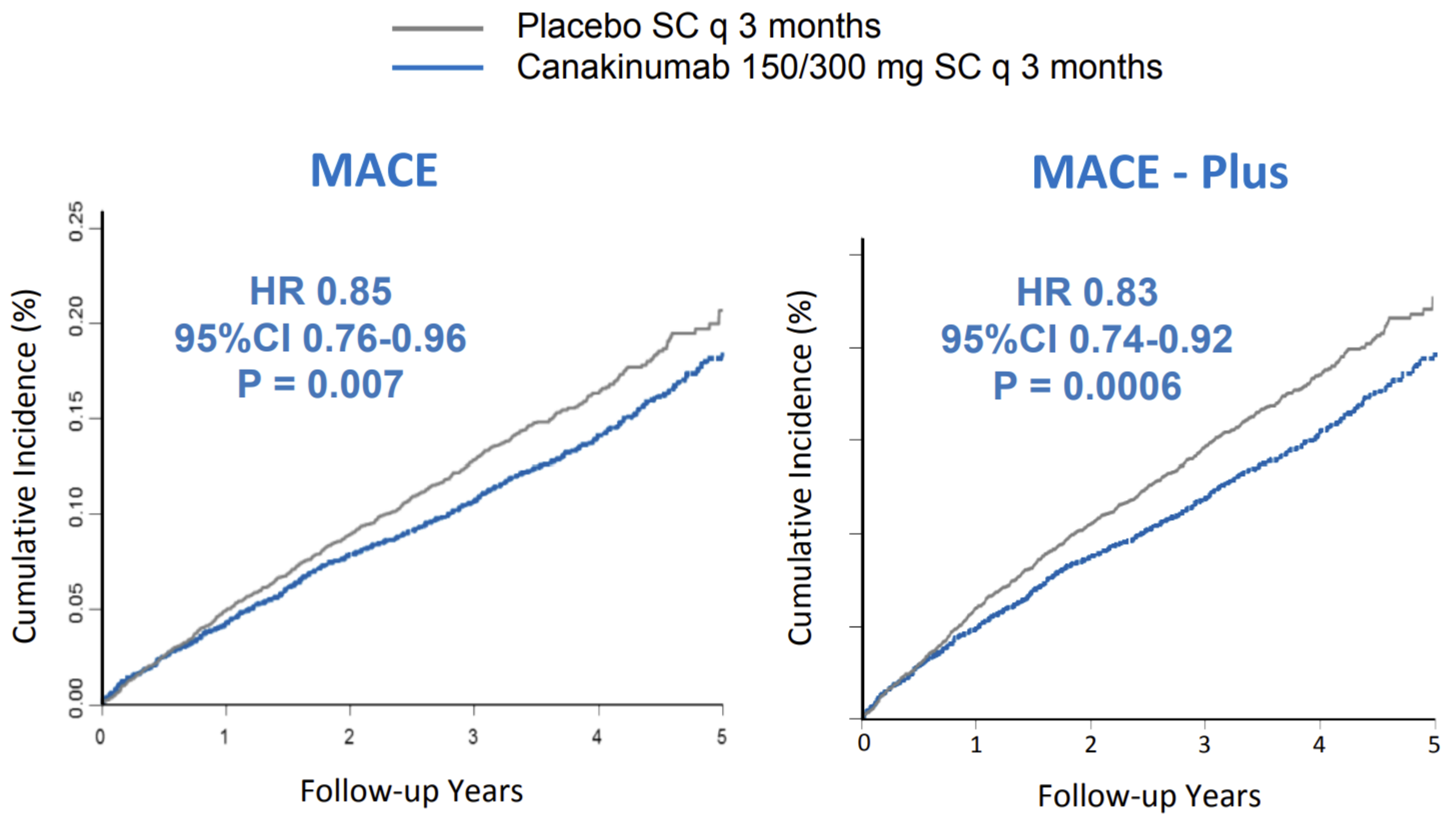
"Residual Inflammatory Risk"

Baseline LDLC 82mg/dL (2.1mmol/L) but hsCRP 4.1 mg/L

Ridker PM et al. N Engl J Med. 2017;377:1119-31

Inhibition of IL-1b to prevent CV events

CANTOS: Primary Cardiovascular Endpoints

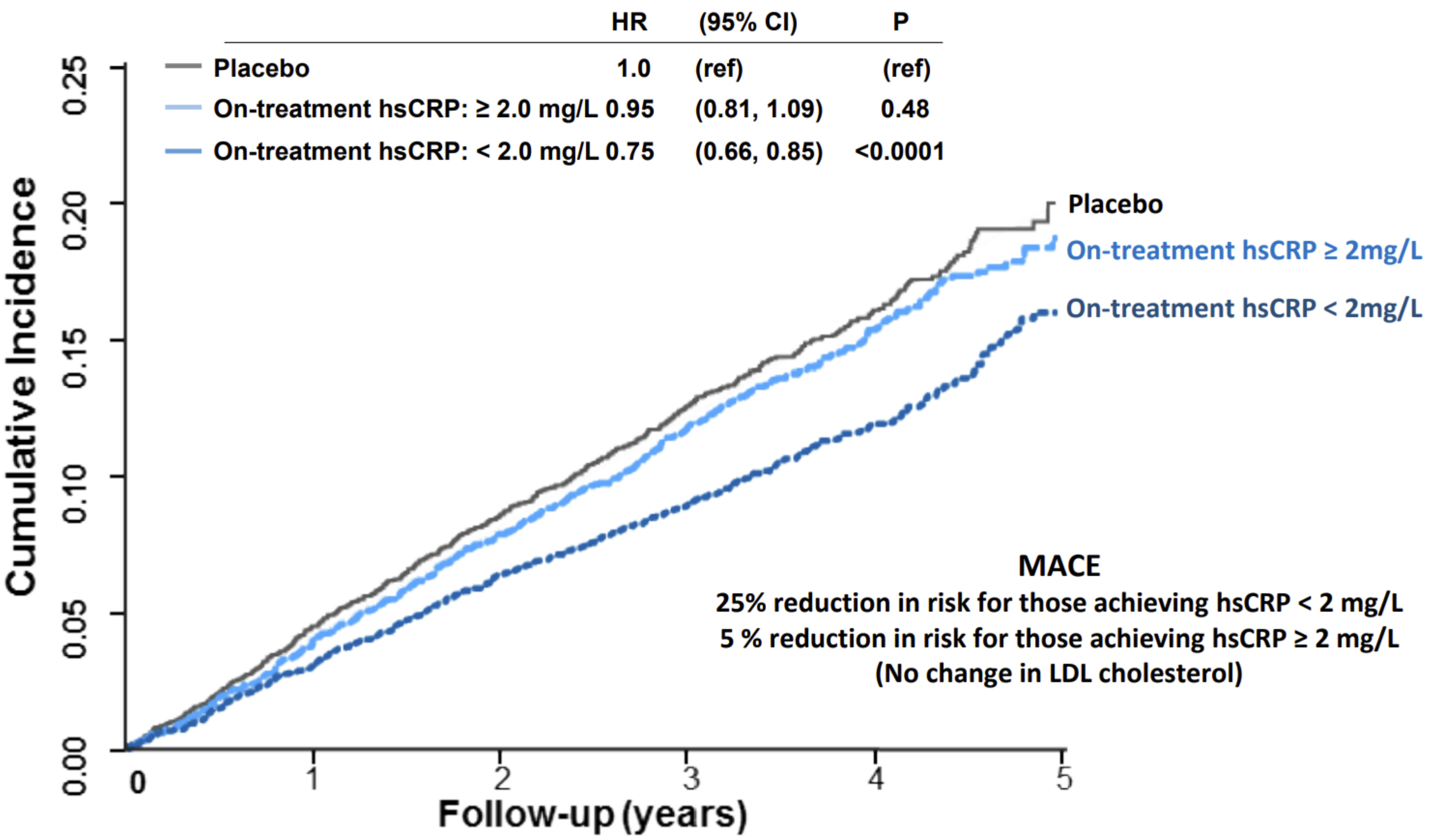


35 - 40% reductions in hsCRP and IL-6
No change in LDLC

Ridker PM et al. N Engl J Med. 2017;377:1119-31

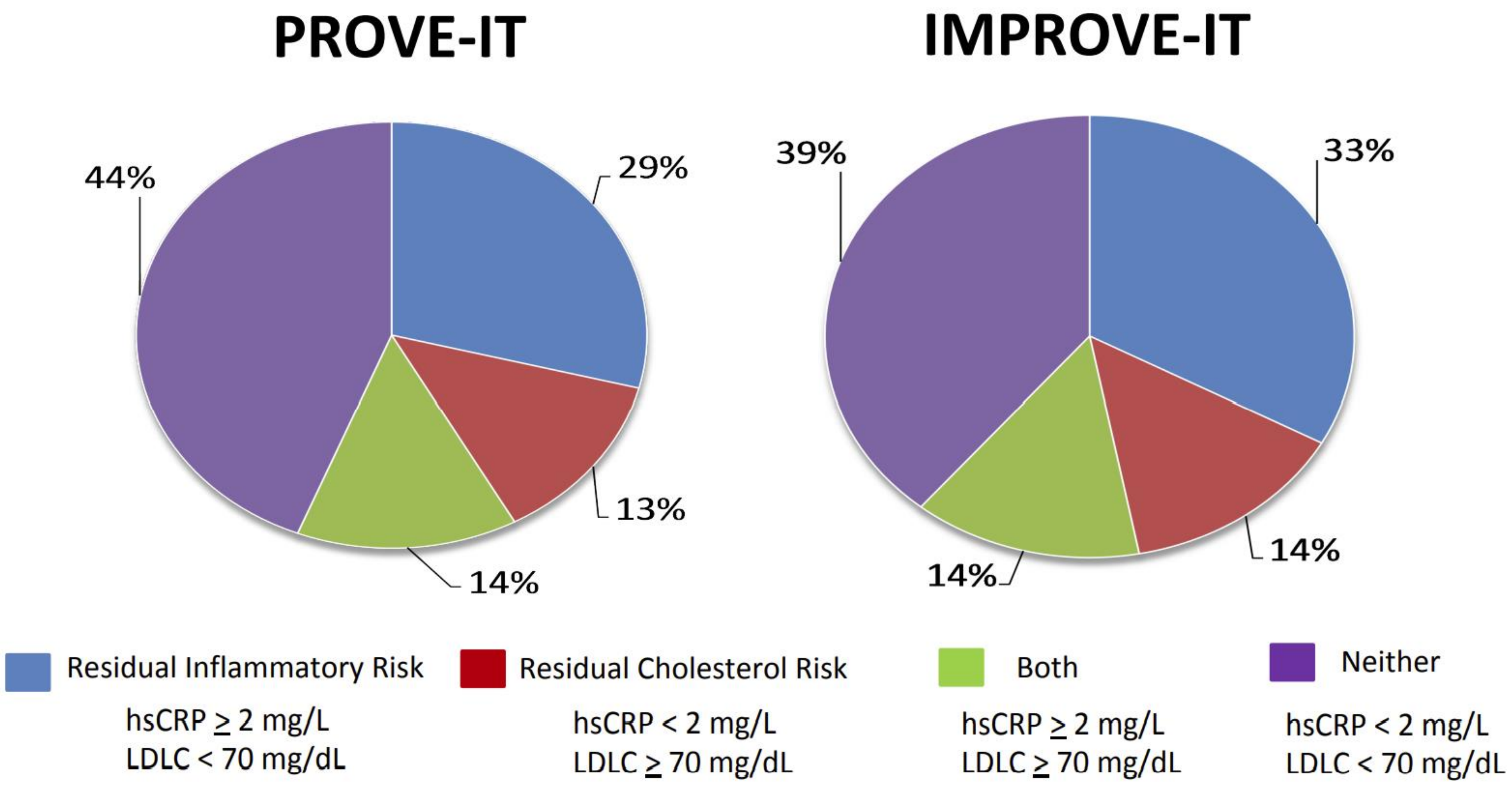
Inhibition of IL-1b to prevent CV events

CANTOS: Greater Risk Reduction Among Those With Greater hsCRP Reduction (MACE)



Ridker et al Lancet 2018;391:319-328

The problem with plasma biomarkers of inflammation



Ridker. Circulation Res 2017;120:617-9

Strategy #4

Detecting the vulnerable patient by quantifying coronary inflammation

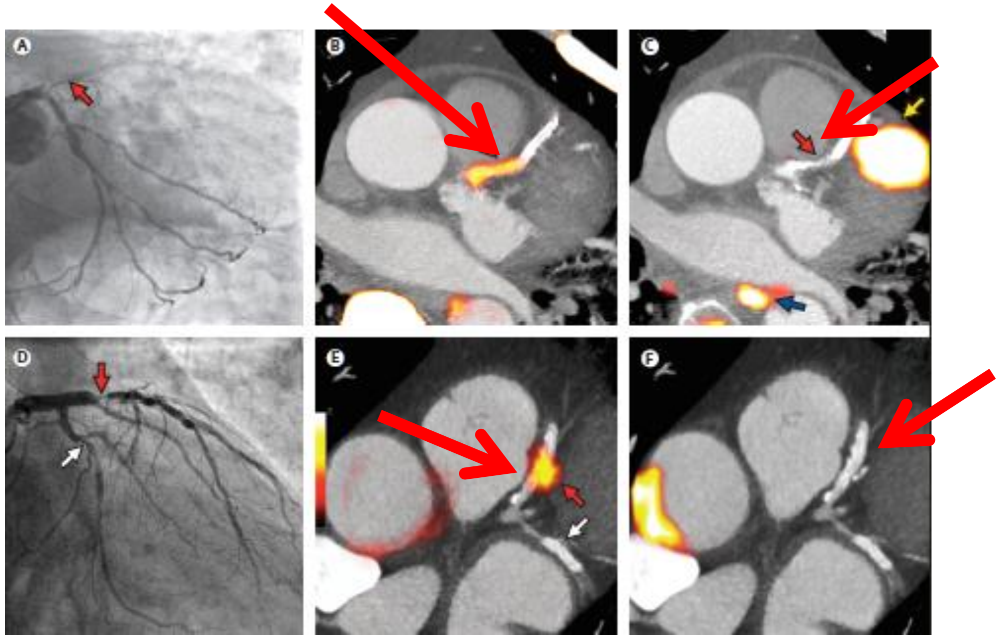
Using novel PET-CT radiotracers to detect unstable plaques

TABLE 1 A Summary of Agents and Their Potential Mechanisms of Uptake Applicable to Vascular Inflammation Imaging

Agent (Ref. #)	Potential Mechanism of Uptake
^{18}F-FLT (62)	Structural analogue of thymidine, images DNA synthesis within atheroma
^{11}C-PK11195 (63)	Affinity for translocator protein, upregulated on inflammatory cells
^{18}F-A85380 (64)	Binds arterial nicotinic acetylcholine receptors, possibly related to vascular damage
^{18}F-choline (65)	Images increased cell wall synthesis within atheroma
^{68}Ga-DOTA-octreotate (60)	Affinity for somatostatin receptors, which are highly expressed on macrophages
^{64}Cu-ATSM (66)	Trapped within cells in hypoxic state
^{18}F-MISO (67)	Trapped within cells in hypoxic state
^{68}Ga-NOTA-RGD (68)	Images neoangiogenesis as a result of hypoxia or chronic inflammation
^{64}Cu-DOTA-CANF (69)	Images neoangiogenesis via natriuretic peptide receptor affinity
^{18}F-FDG	A glucose analogue imaging increased metabolic rate in the presence of inflammation and hypoxia
^{18}F-sodium fluoride (59)	Images active calcification as a result of necrosis or inflammation
^{68}Ga-CXCR4 (70)	Images CXCR4 receptor expressed by inflammatory cells
^{18}F-florbetapen (61)	Imaging β-amyloid plaque as a component of inflammation

^{11}C-PK11195 = ^{11}C-(2-chlorophenyl)-N-methyl-N-(1-methylpropyl)-3-isoquinolinecarboxamide; A85380 = 3-([2S]-azetidinylmethoxy)pyridine dihydrochloride; ATSM = diacetyl-bis(N-methylthiosemicarbazone; CXCR4 = C-X-C chemokine receptor type 4; DOTA-CANF = 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid atrial natriuretic factor; FDG = fluorodeoxyglucose; FLT = fluorothymidine; MISO = fluoromisonidazole; NOTA-RGD = 1,4,7-triazacyclononane-N,N′,N″-triacetic acid arginine-glycine-aspartate.

^{18}F-NaF ^{18}FDG

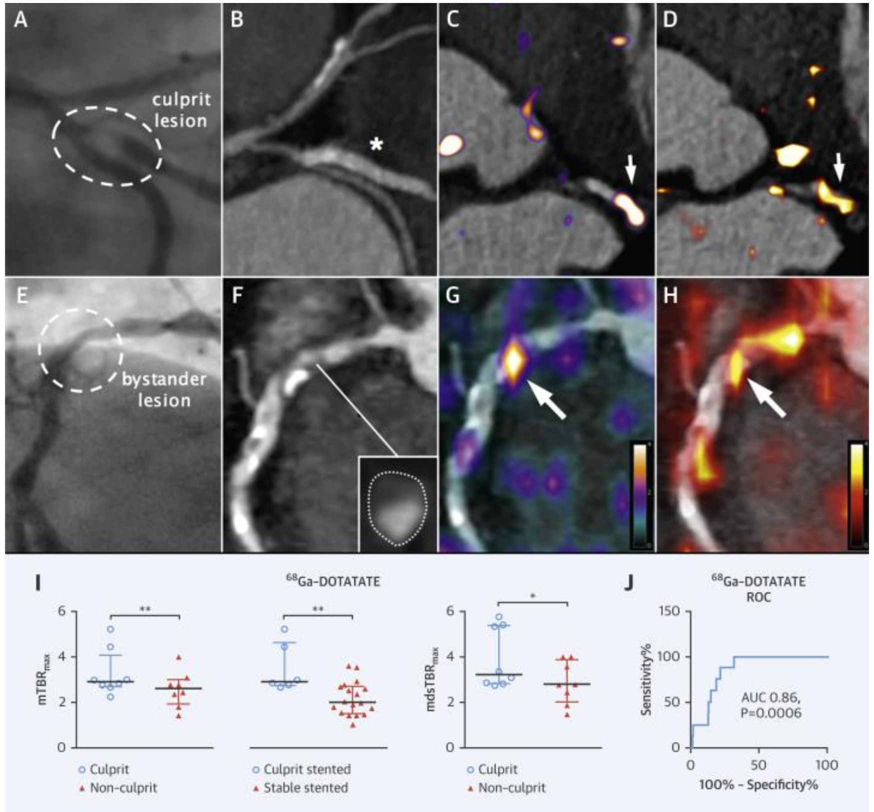


Joshi et al. *Lancet 2014; 383: 705-13*

Using novel PET-CT radiotracers to detect unstable plaques

68Ga-DOTATATE: somatostatin receptor subtype-2 (SST2)-binding PET tracer

68Ga-DOTATATE detects culprit coronary lesions



But PET-CT → high costs, limited availability, high radiation

Tarkin JM et al. *JACC 2017;69(14).*

The challenge remains

How to identify:

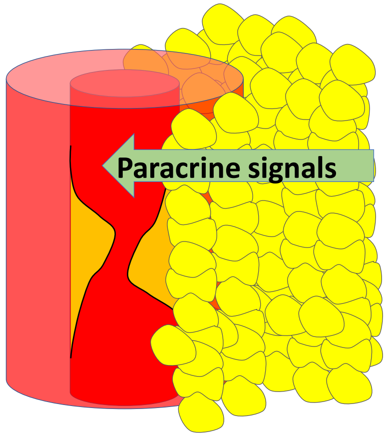
a) The **vulnerable "healthy"** individual who will develop atheroma

b) The **vulnerable "healthy"** individual who has minor atheroma **at risk for ACS**

c) The **vulnerable patient** with advanced disease, who despite optimum treatment remains **at risk for ACS** (due to rupture of either significant or "minor" plaques)

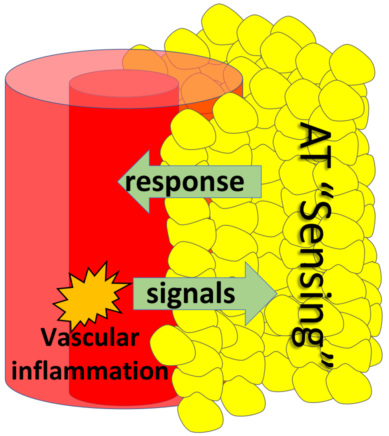
Perivascular fat and the vascular wall: The concept of "inside to outside" signalling

Classic approach (outside to inside signals)



Antonopoulos A et al; Obes Rev. 2009;10:269-79

New approach (inside to outside signals)

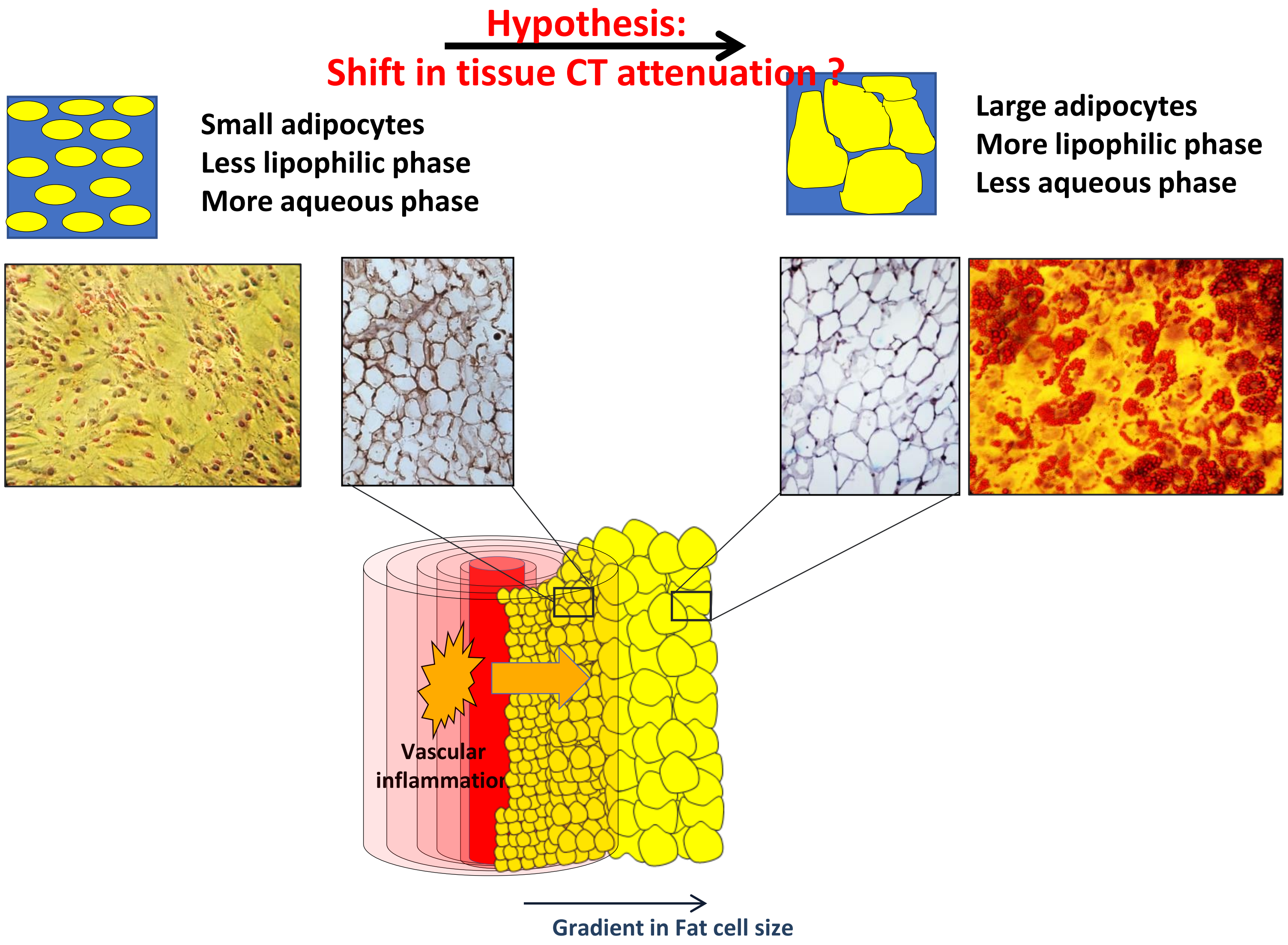


Margaritis et al; Circulation 2013;127:2209-21

<u>AT sensing</u>: includes processes that could affect adipogenesis!

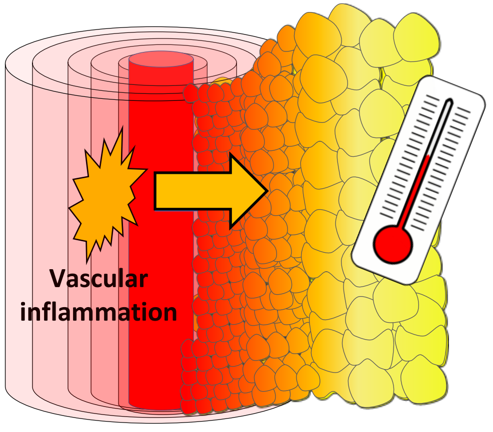
Antonopoulos A et al Diabetes 2015 64:2207-19

How can vascular inflammation affect PVAT adipogenesis?

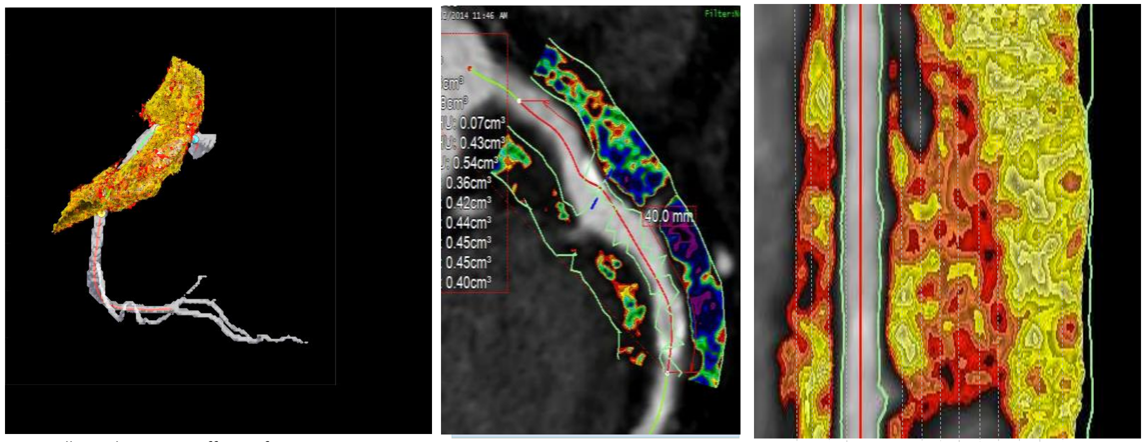


Antonopoulos A et al. *Science Translational Medicine 2017*

Perivascular fat: sensor of coronary inflammation
A new CT imaging analysis technology

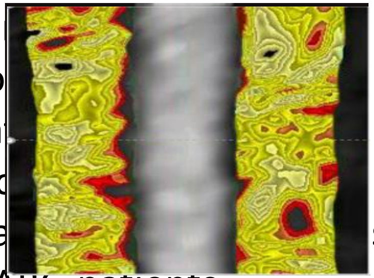


Perivascular Fat Attenuation Index (FAIPVAT)

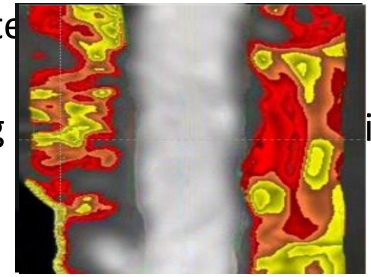


UK Intellectual Property Office, ref. 1414496.8, August 2014

Low FAI

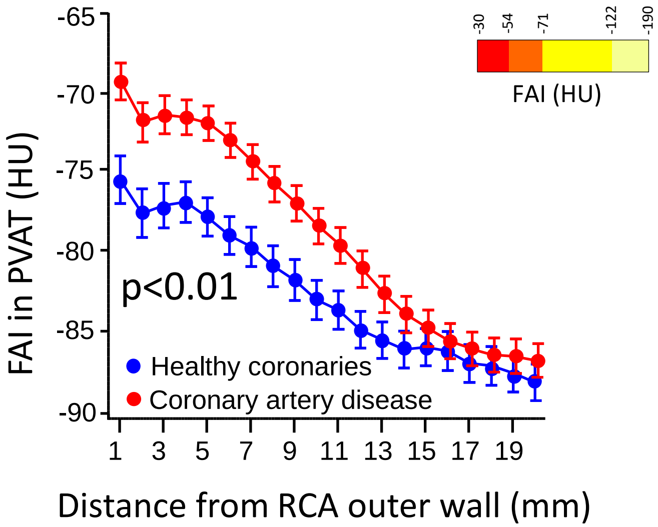


High FAI

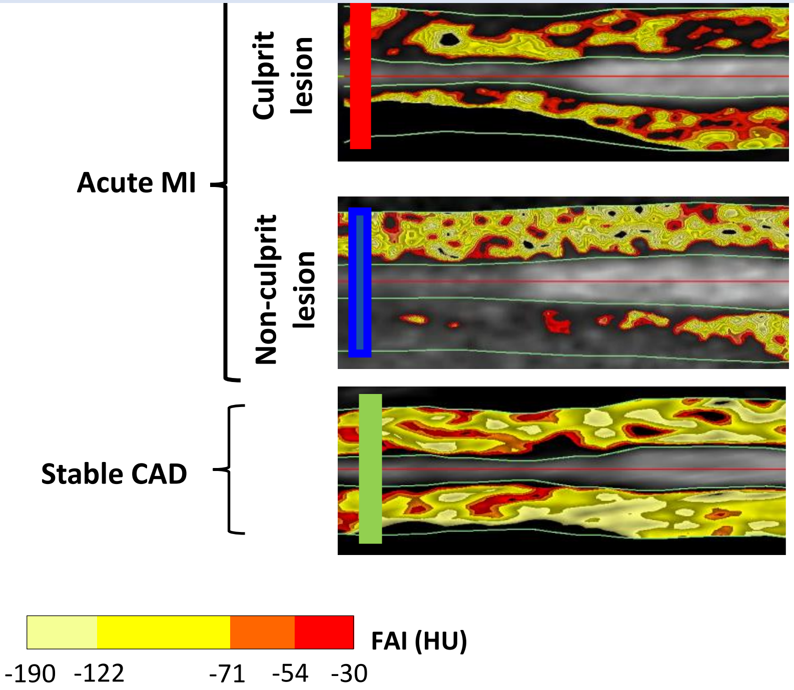


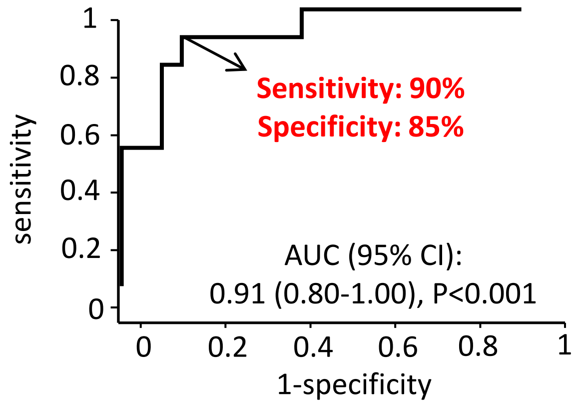
3D mappi inte d the
human co
Mathema ing ing with
Images fr
- ✓ 1400 a s
- ✓ 902 CABG patients
- ✓ 4273 CTAs (CAD, ACS, "healthy" coronaries)

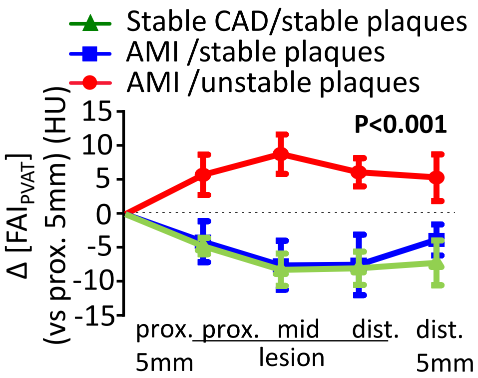
Antonopoulos A, Sanna F et al. *Science Translational Medicine 2017*

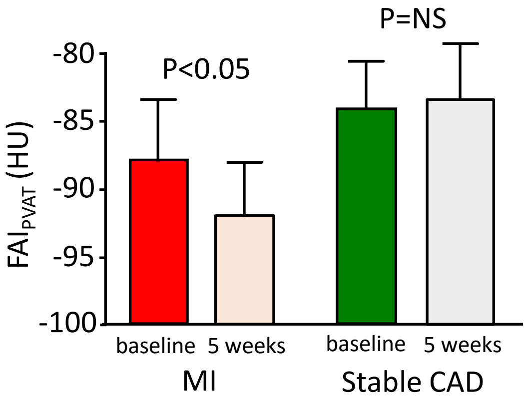


Can FAI_{PVAT} track coronary inflammation and its resolution post AMI



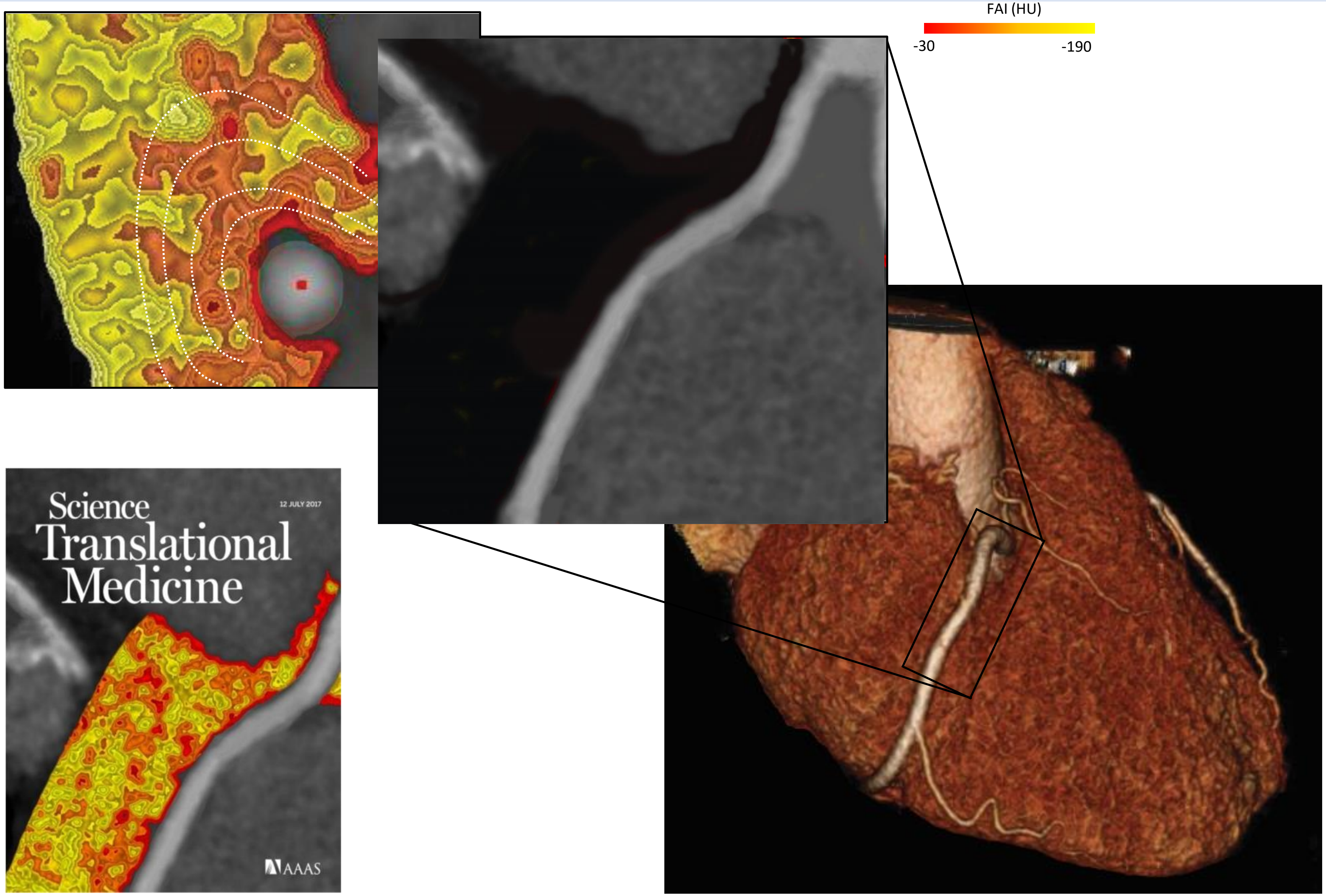






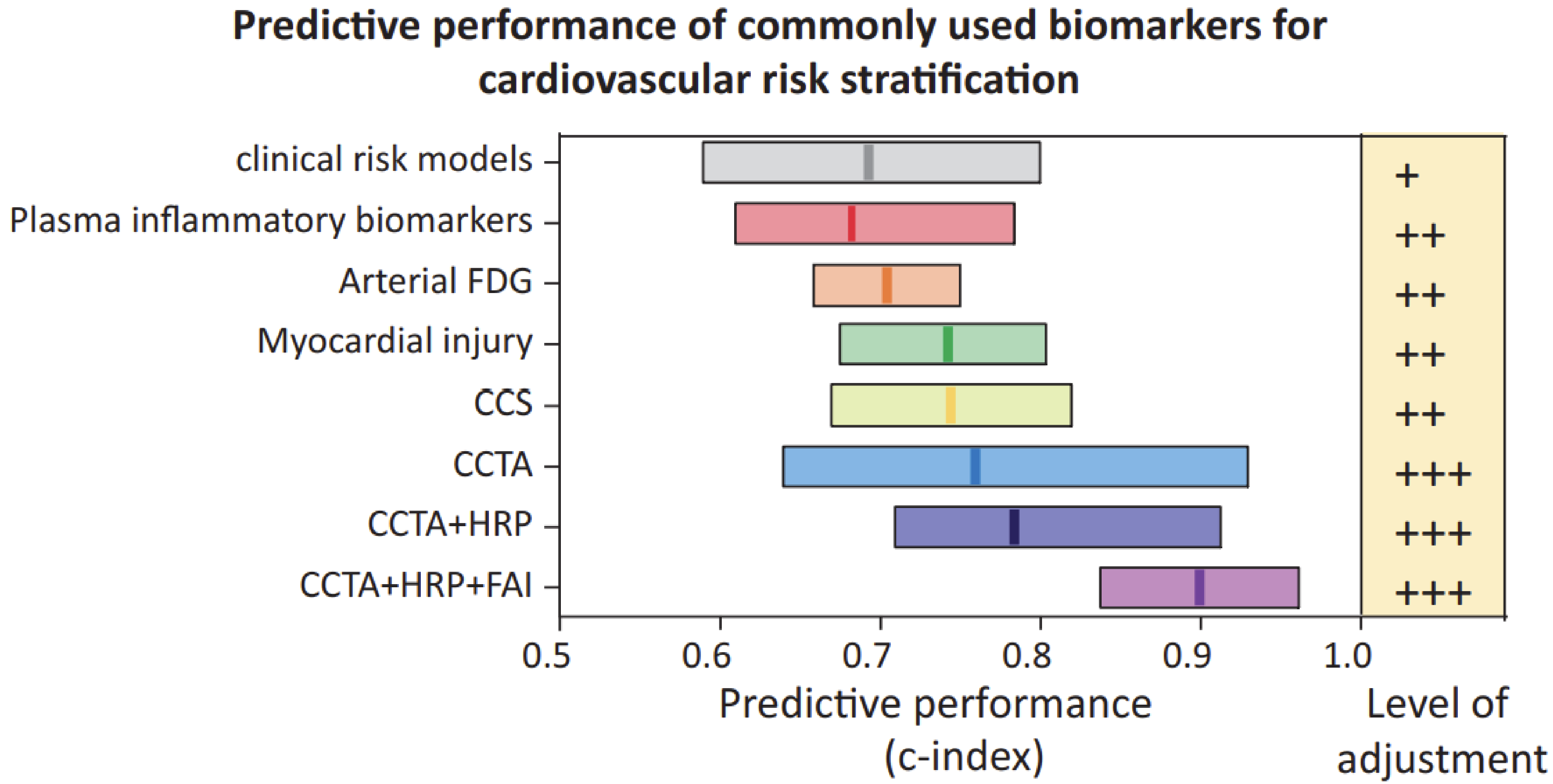
Antonopoulos A, Sanna F et al. *Science Tansl Med 2017*

Applying FAI Analysis as a new dimension of routine CTA



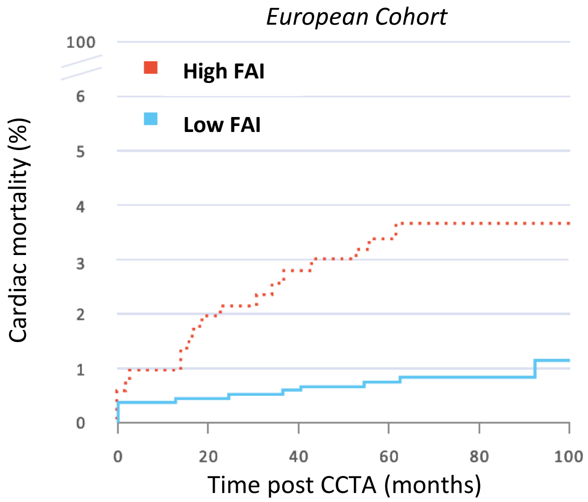
Antonopoulos A, Sanna F et al. *Science Translational Medicine 2017*

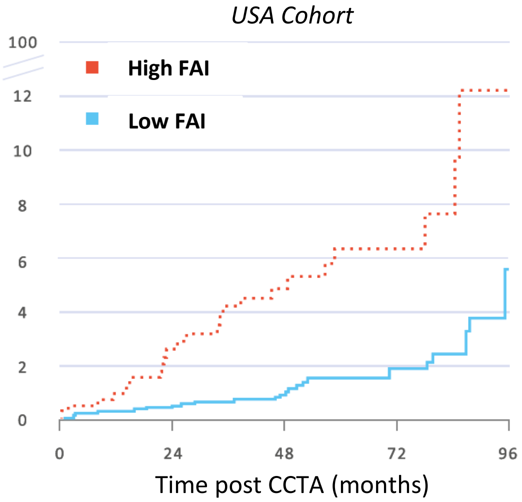
Comparative performance of

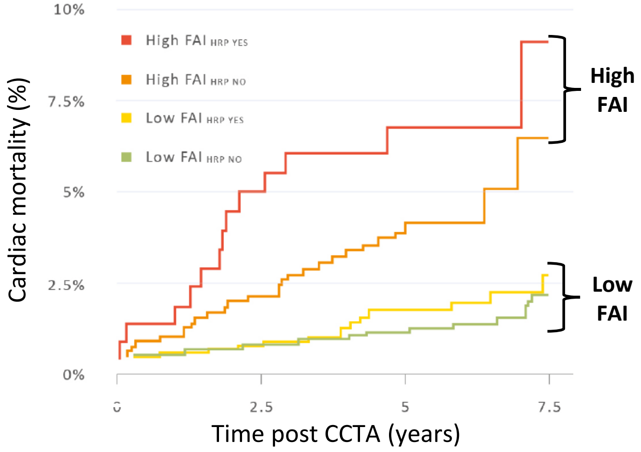


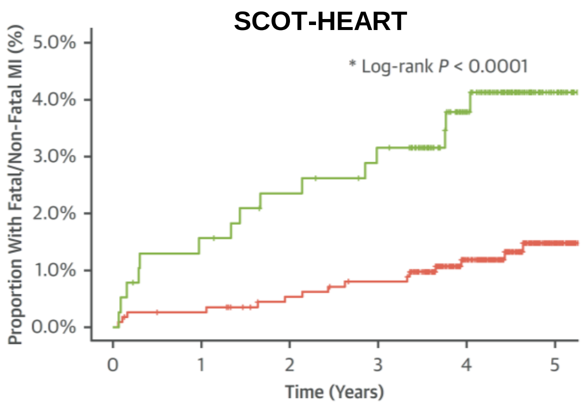
Antoniades C, Antonopoulos A, Deanfield J EHJ 2019

FAI Accurately Predicts Future Heart Attack Risk









CRISP-CT Study Design [1]

- 4000 participants from Europe and US
- Up to 10 years follow up

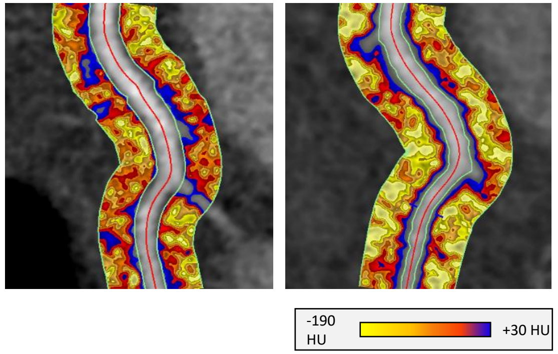
CRISP-CT Findings

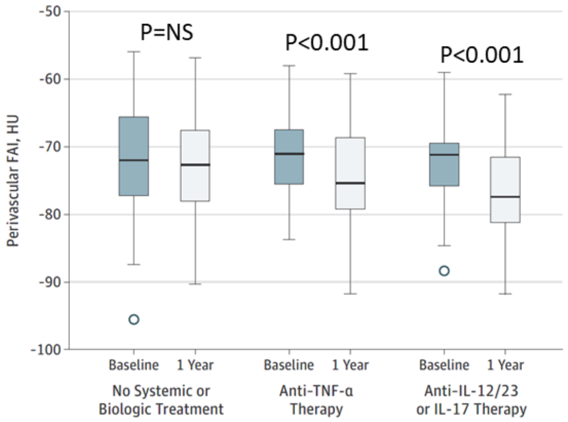
- Abnormal FAI associated with a
  - **6-9x** higher risk for **fatal heart attacks**
  - **5x** higher risk for **non-fatal heart attacks**
- After adjusting for all conventional risk factors (e.g., smoking, age, diabetes, high cholesterol)
- FAI is more predictive of future heart attacks than high-risk plaque (HRP) features [2]
- Findings confirmed in SCOT-HEART using uncorrected perivascular attenuation (PCAT) [3]

1. *Lancet* 2018; 392: 929–39
2. *J Am Coll Cardiol* 2020; 76 (6) 755–757
3. *J Am Coll Cardiol Img*. 2022, 15 (6) 1078–1088

FAI tracks Dynamic Changes in Response to Treatments

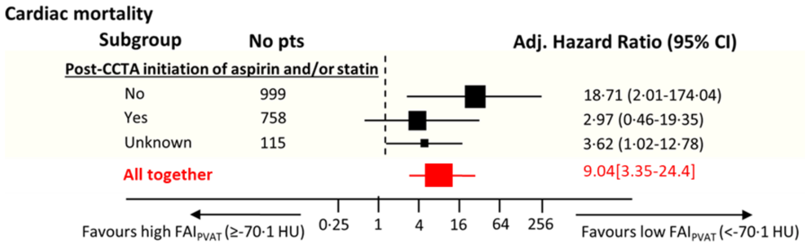
Changes of FAI in psoriasis patients after treatment with biologics



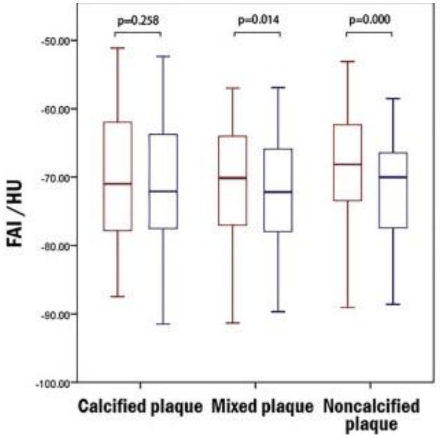


Elnabawi Y ….Mehta N; JAMA Cardiol 2019

Changes of FAI with **Statin** Treatment



Oikonomou et al. *Lancet* 2018

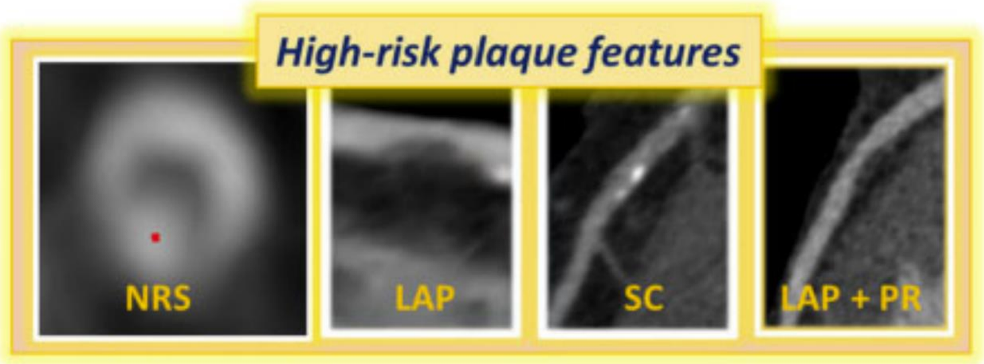


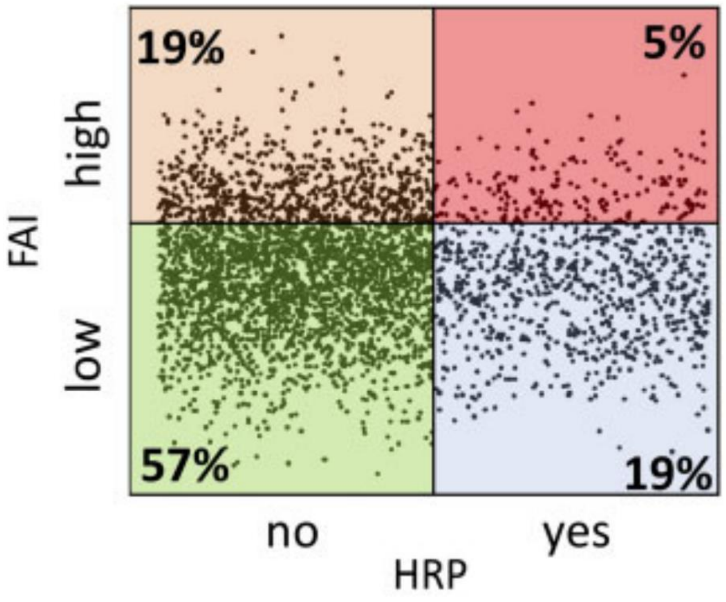
Dai et al et al. *Int J Cardiol* 2020

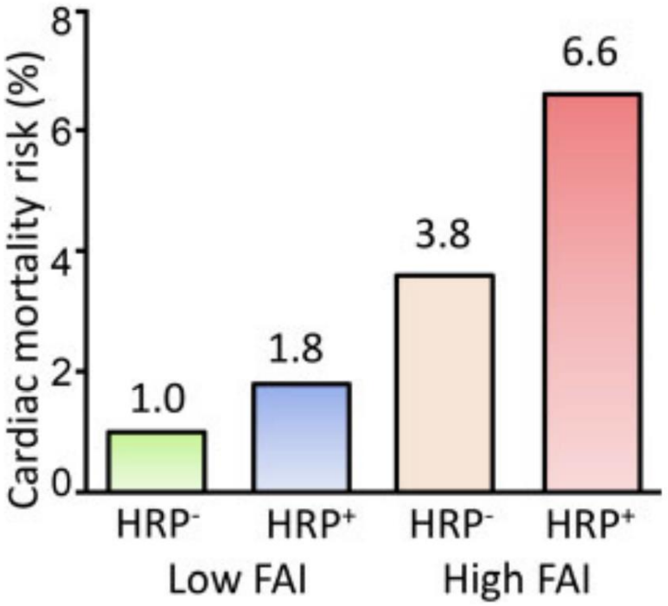
With treatment decision based on CCTA alone:

18x greater risk for patients with high FAI left untreated

Combination of HRP and PVAT imaging by CT for enhanced risk stratification





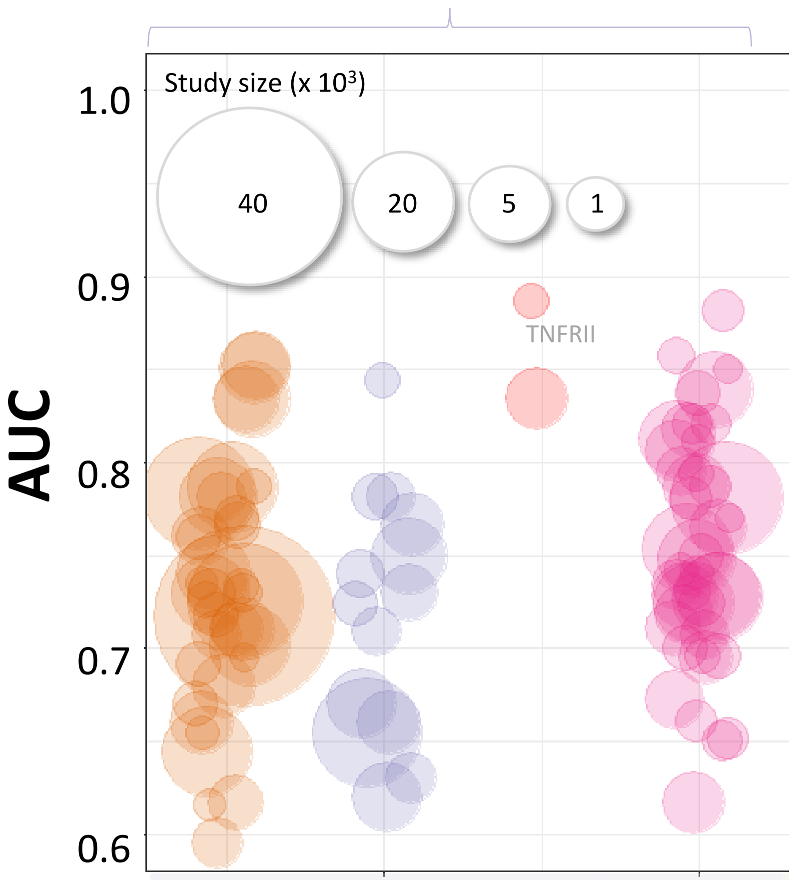


Antoniades C, Antonopoulos A, Deanfield J EHJ 2019

What does FAI add beyond the current state of the art?

- 94,821 relevant studies screened - 93 studies eligible (n=351,628 individuals)

Plasma biomarkers

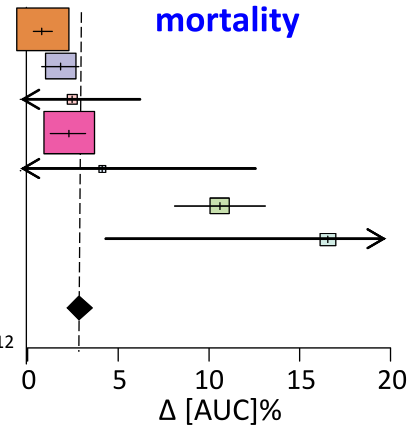


Biomarker	CRP	IL-6	TNF-α	cTnI/T
Studies, n	39	14	2	44
Population, n	170,674	45,549	3,354	112,288
AUC	**0.726**	**0.727**	**0.861**	**0.748**

MACEs + all-cause mortality

Biomarker	Size	Δ(AUC%)	[95%CI]
CRP	170,214	**0.8**	[0.3; 1.3]
IL6	45,549	**1.7**	[0.7; 2.7]
TNF-a	3,354	**2.3**	[-1.3; 5.9]
cTnI/T	112,288	**2.3**	[1.3; 3.3]
PET/CT	545	**4.0**	[-4.4; 12.4]
CT-HRP	14,191	**10.5**	[8.0; 13.0]
CT-HRP+PVAT	5,487	**16.5**	[3.9; 29.2]
Overall	**351,628**	**2.9**	**[2.1; 3.6]**

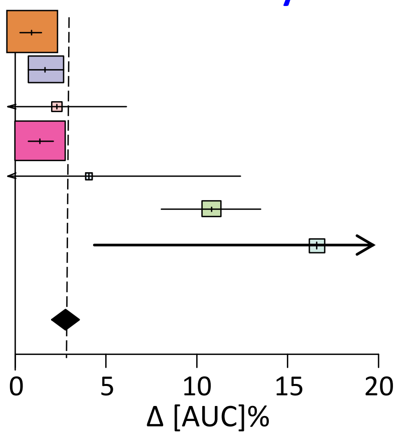
Q=67.7, p=1.18 x 10^{-12}



MACEs only

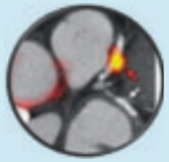
Biomarker	Size	Δ(AUC%)	[95%CI]
CRP	141,348	**0.9**	[0.3; 1.5]
IL6	39,322	**1.7**	[0.7; 2.7]
TNF-a	3,035	**2.3**	[-1.3; 5.9]
cTnI/T	80,770	**1.4**	[0.7; 2.1]
PET/CT	545	**4.0**	[-4.4; 12.4]
CT-HRP	10,933	**10.8**	[8.1; 13.5]
CT-HRP+PVAT	5,487	**16.5**	[3.9; 29.2]
Overall	**281,440**	**2.9**	**[2.1; 3.8]**

Q=54.8, p=4.9 x 10^{-10}



Antonopoulos AS et al. JACC Imaging 2021

Clinical approaches to the non-invasive detection of vascular inflammation

	Plasma markers of Inflammation	*Myocardial Injury biomarkers*	*miRNA profiling*	*CTA plaque phenotyping*	*Hybrid PET imaging*	*Perivascular FAI mapping*
						
Diagnosis*	-Poorly associated with vascular inflammation	-Index of plaque Instability, measuring downstream effects of rupture	-More studies needed	-Indirect, anatomical markers of plaque Inflammation	-High sensitivity for vascular inflammation	-Fat senses vascular inflammation
Prognosis#	-Independently predict CV events	-Independently predict CV events	-More studies needed	-High specificity -Independently predict CV events	-Studies needed	-Predictive of cardiac mortality
Limitations	-Poor specificity for vascular inflammation	-Measuring plaque rupture events	-Poor specificity -Analytical issues -Cost-effectiveness	-Operator dependent -Anatomy assessment	-Limited availability -Radiation exposure -Expensive	-Standardization -Complex analysis -Not widely available
Strengths	-Easy to measure -Population screening -Inexpensive	-Easy to measure -Population screening -Inexpensive	-Highly sensitive -Population screening -Wide screening	-Wide availability -Prognostic value -Risk reclassification	-Disease activity -High sensitivity -Good specificity	-Specific for vascular inflammation -Hardware agnostic -Prognostic value -Risk reclassification

Antoniades C, Antonopoulos A, Deanfield J EHJ 2019

Non-invasive detection of the vulnerable patient

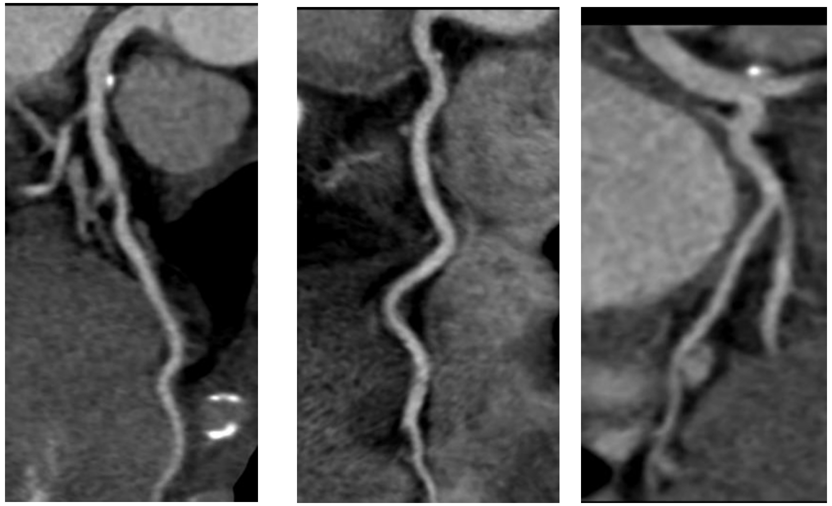
- Need to dissociate the degree of stenosis from the risk of future events
- The unstable plaque is the inflamed one, and it is not necessarily large!
- Search for the vulnerable patients includes:
  - -Plasma biomarkers of
    - myocardial injury (cTnI, cMyC)
    - inflammation (e.g. hsCRP, ….)
    - } Specificity issues
  - -Imaging biomarkers
    - PET-CT (NaF, …)
    - CTA (Plaque morphology)
    - CTA-FAI (vascular inflammation, +/- plaque)

Quantification of **coronary** inflammation by newer imaging methods such as PET, CTA and CT imaging of PVAT may help detect the vulnerable patients at risk for plaque rupture events

How Do We Identify High Risk Patients?

LAD RCA LCX

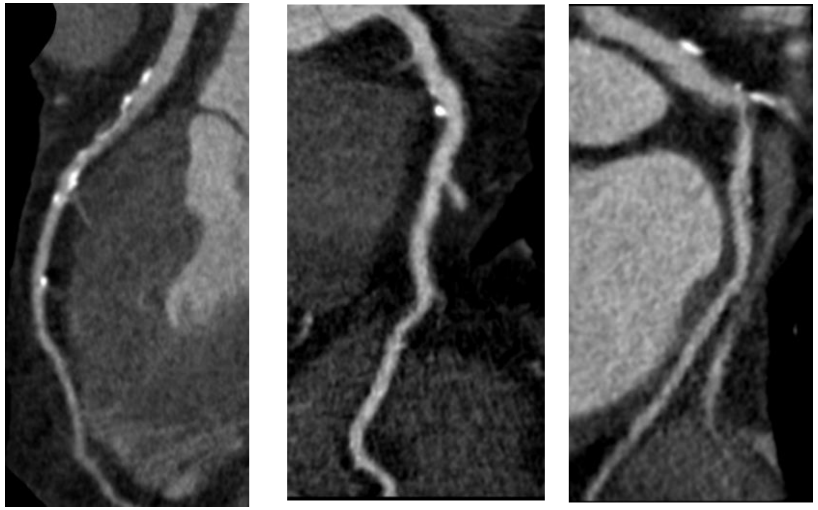
CASE A



- Male (age 52y old) with typical chest pain
- LDL=1.12mmol/L (atorvastatin 10mg OD)
- Hypertensive (candesartan, amlodipine)
- Ex smoker (stopped 2 years ago)
- Overweight BMI 26.5Kg/m^2
- No ischaemia, no stenosis, minor calcification

- *The patient died from a fatal heart attack (proximal LAD) 35 months later….*

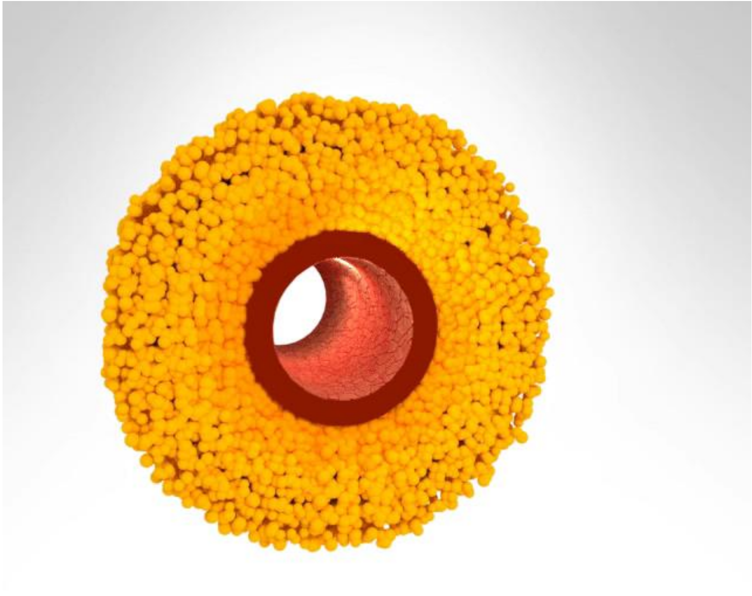
CASE B



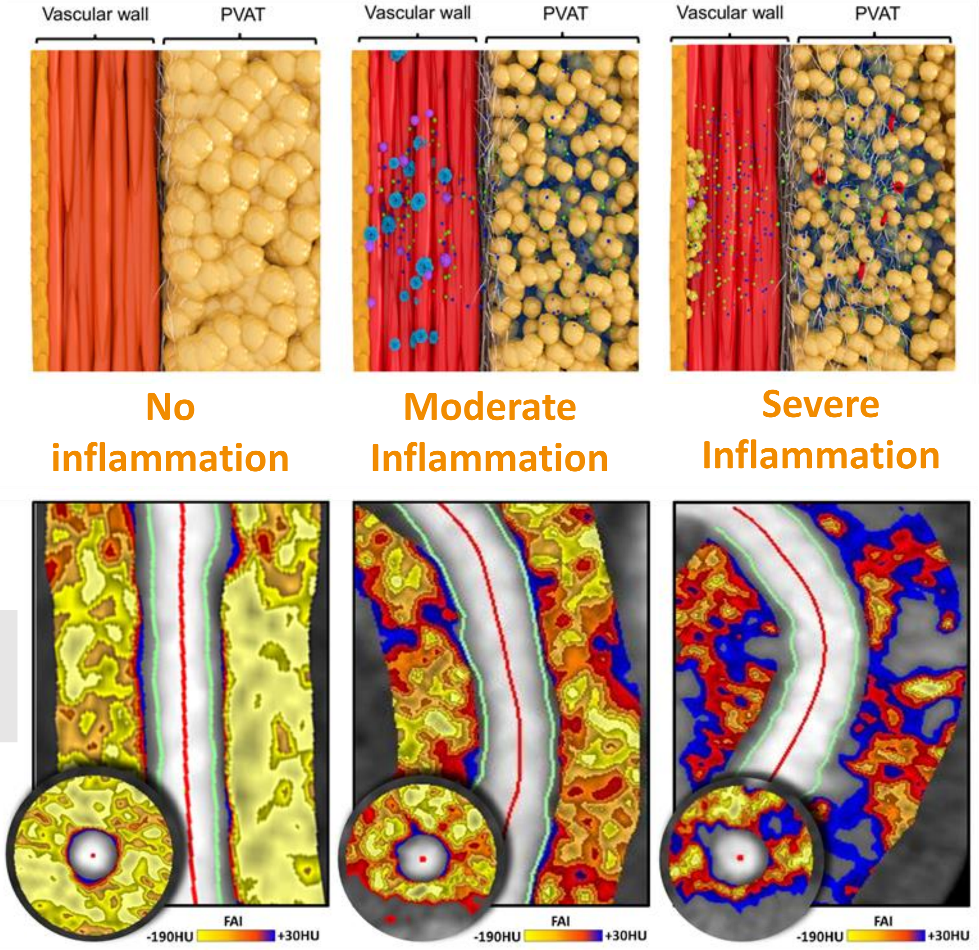
- Male (age 63y old) with typical chest pain
- LDL=2.2mmol/L (atorvastatin 40mg OD)
- Hypertensive (amlodipine, indapamide)
- Ex smoker (stopped 9 years ago)
- Obese BMI 31.5Kg/m^2
- DM on metformin HbA1c=6.7%
- No ischaemia, no stenosis, extensive plaque,incl low attenuation plaque

- *Follow up 11 years, no event throughout*

Perivascular FAI: a “Sensor” of Vascular Inflammation



Margaritis & Antonopoulos et al; Circulation 2013;127:2209-21
Antonopoulos et al; Diabetes 2015; 112:213-222
Antonopoulos et al; Circ Res 2016;118(5):842-55
Antonopoulos et al., Science Translational Medicine *2017*
Oikonomou & Antoniades. Nature Rev Cardiol 2018

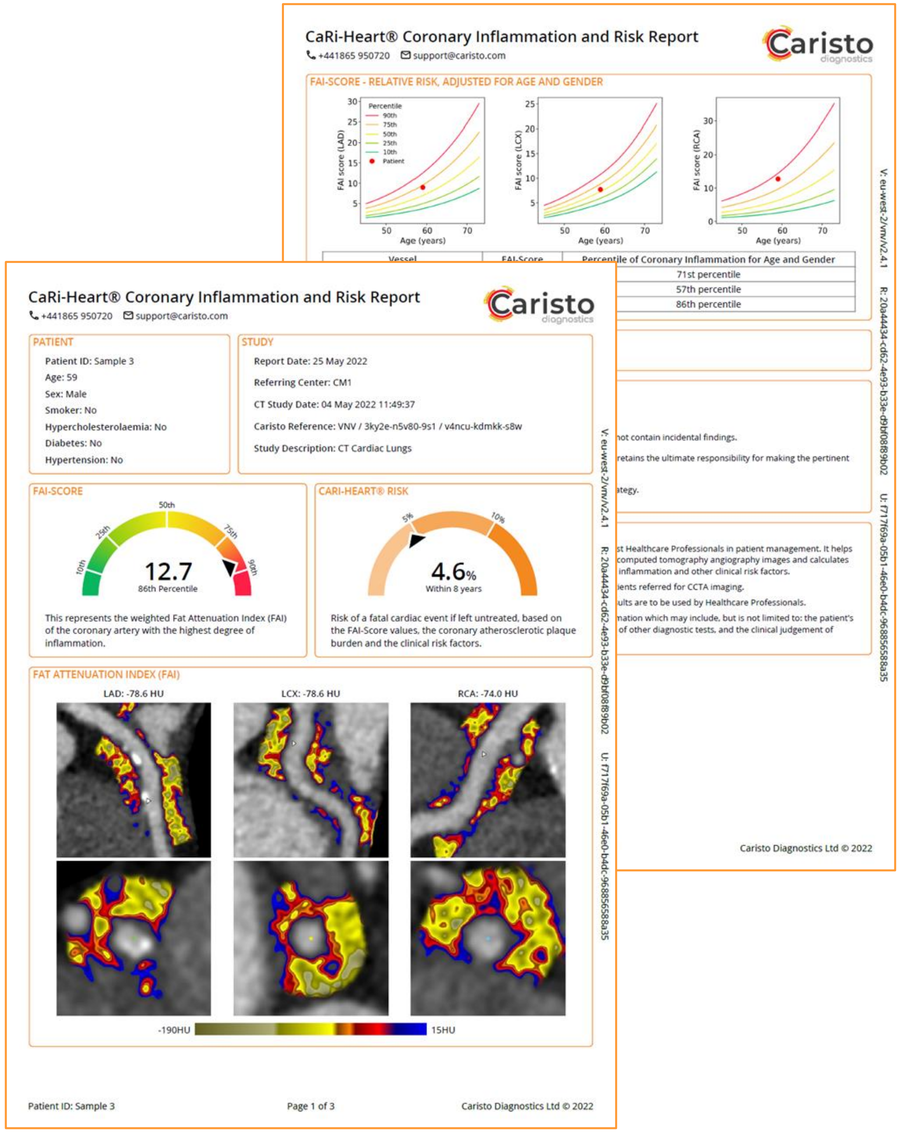


Braunwald’s Heart Disease 12th Edition© Elsevier Publishing 2021

Analysis performed on routine CTCA, as part of clinical practice

CaRi-Heart®

A CE-Marked Medical Device for Evaluation of Coronary Inflammation and Prediction of Future Cardiac Events



Fat Attenuation Index

- ➢ **Unadjusted, visual representation** of the extent of coronary inflammation in the 3 main epicardial coronary arteries

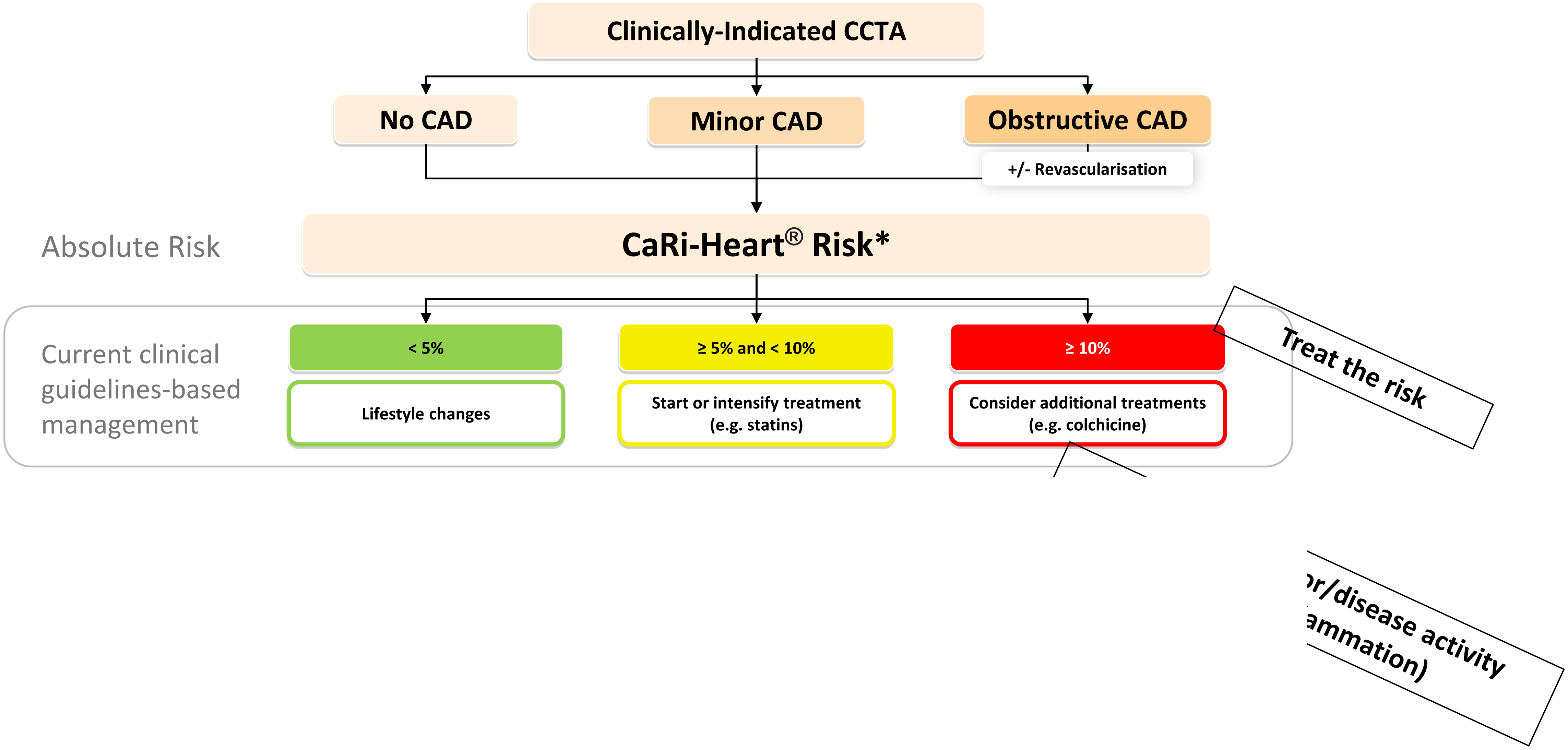
FAI-Score

- ➢ **Individualised quantification** of coronary inflammation in the 3 main epicardial coronary arteries, adjusted for age and gender
  - Percentile value represents the patient's relative risk
  - Can be viewed as a measure of disease activity

CaRi-Heart® Risk

- ➢ The **absolute risk** of a fatal cardiac event within the next 8 years, based on the personalised FAI-Score values, coronary atherosclerotic plaque burden and clinical risk factors

Use of pericoronary FAI in clinical practice

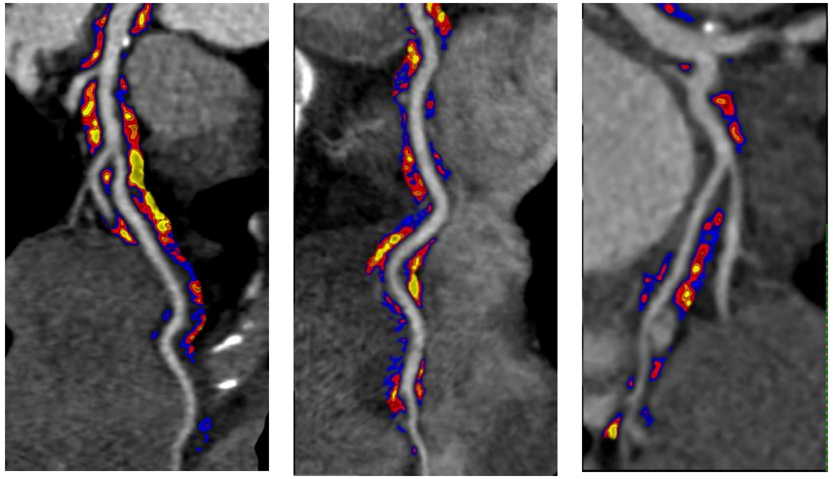


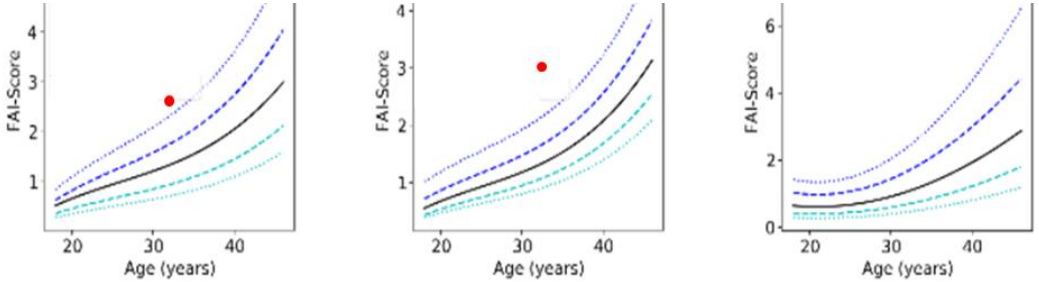
* 8-year risk of cardiac death : incorporates personalised FAI-Score with clinical risk factors, demographics, and plaque burden

Oikonomou EK & Antonopoulos AS et al. Cardiovasc Res 2021

Measuring FAI-Score Identifies High Risk Patients

CASE A

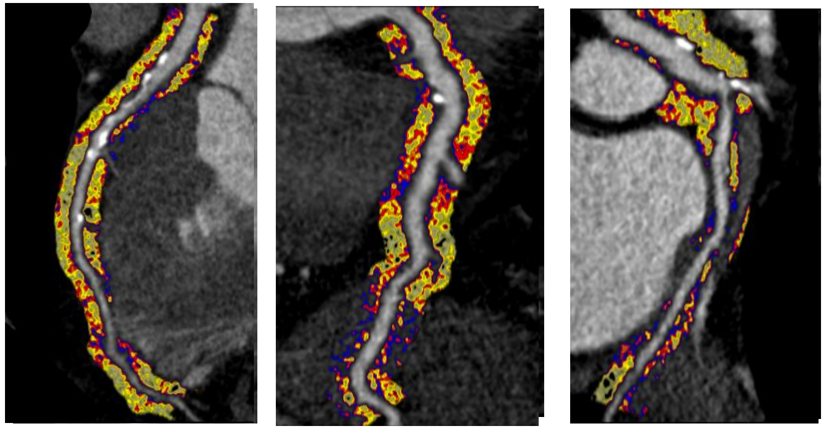


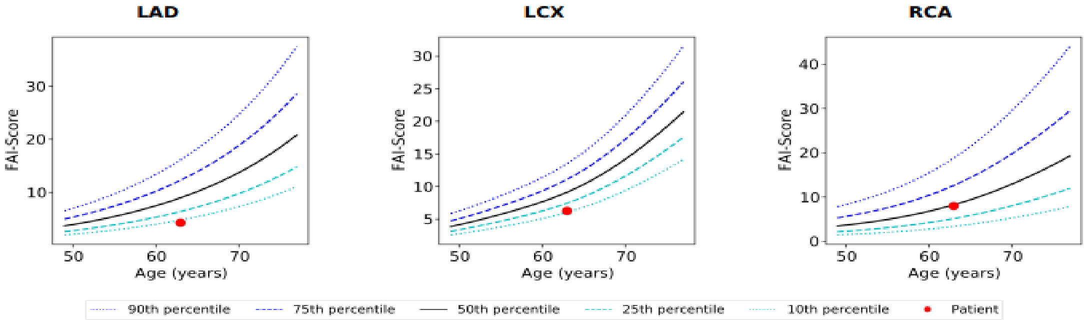


Vessel	FAI-Score	Percentile of Coronary Inflammation for Age and Gender
Left Anterior Descending Artery	2.7	93rd percentile
Left Circumflex Artery	3.0	99th percentile
Right Coronary Artery	7.7	99th percentile

CaRi-Heart® Risk (8y risk for cardiac death: 31.2%

CASE B





Vessel	FAI-Score	Percentile of Coronary Inflammation for Age and Gender
Left Anterior Descending Artery	4.2	6th percentile
Left Circumflex Artery	6.3	12th percentile
Right Coronary Artery	7.9	48th percentile

CaRi-Heart® Risk (8y risk for cardiac death: 9.8%

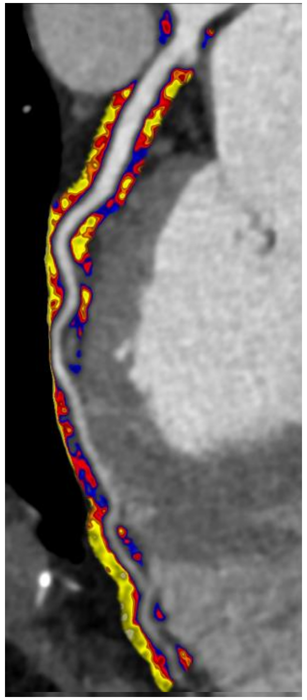
“Normal” Coronary Arteries but at high-Risk

History
- 56-year-old female
- Non-diabetic, normotensive
- LDL 66 mg/dL
- Pooled Cohort Equation: 2.3%

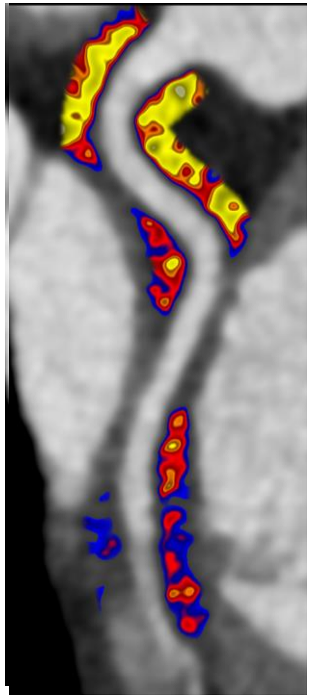
Management based on Conventional CCTA
- Lifestyle measures

Management after CaRi-Heart® Report
- Atorvastatin 40mg daily

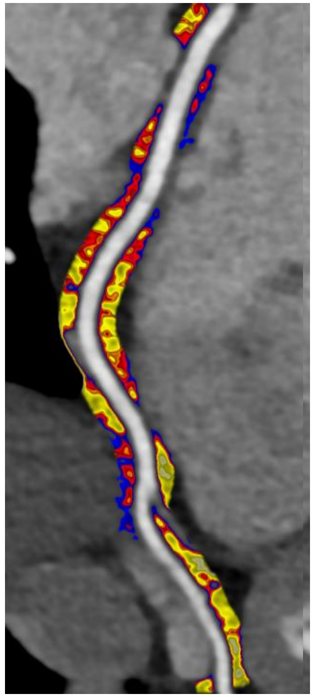
LAD

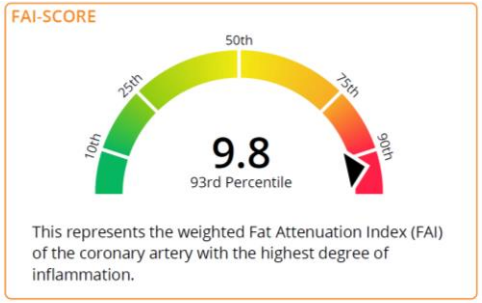


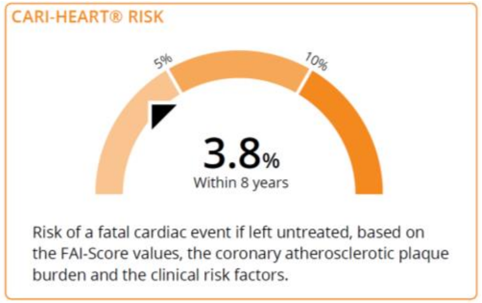
LCx

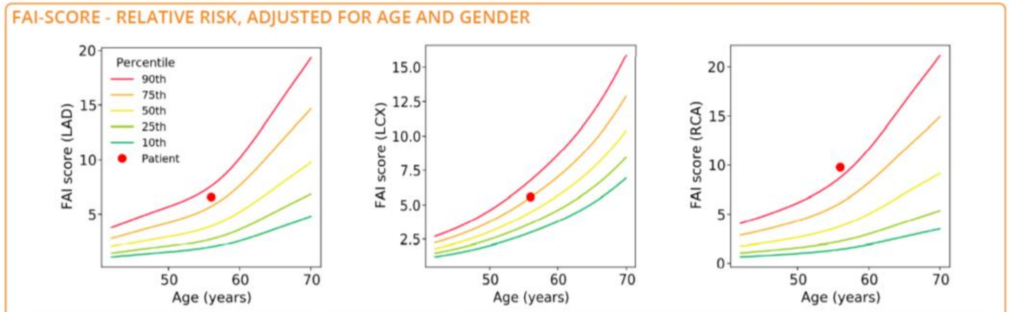


RCA







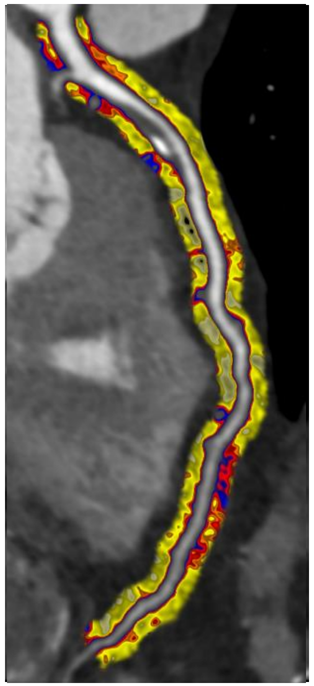


Vessel	FAI-Score	Percentile of Coronary Inflammation for Age and Gender
Left Anterior Descending Artery	6.6	83rd percentile
Left Circumflex Artery	5.6	76th percentile
Right Coronary Artery	9.8	93rd percentile

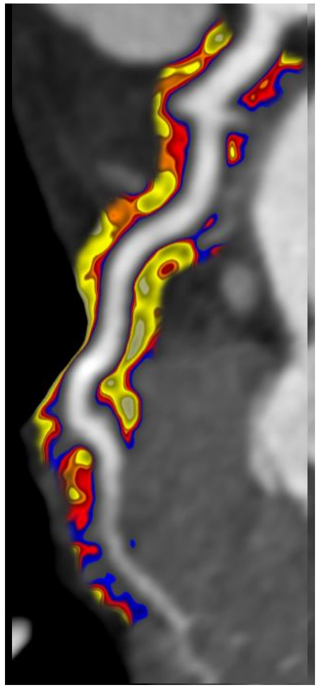
“High-Risk” Plaque But Low Risk Patient

History
- 71-year-old female
- Non-diabetic, normotensive
- LDL 64 mg/dL
- Pooled Cohort Equation: 15.9%
- Atorvastatin 20mg daily

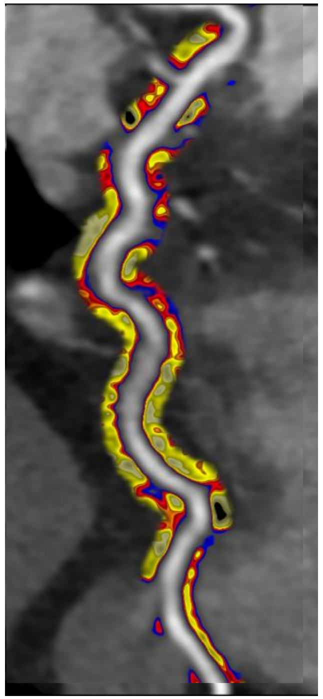
LAD



LCx

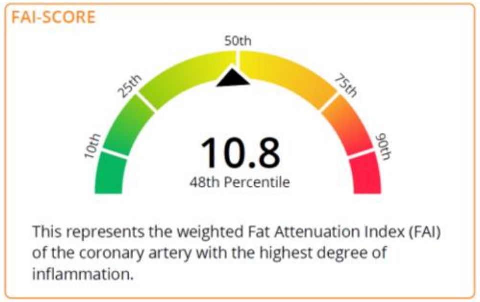


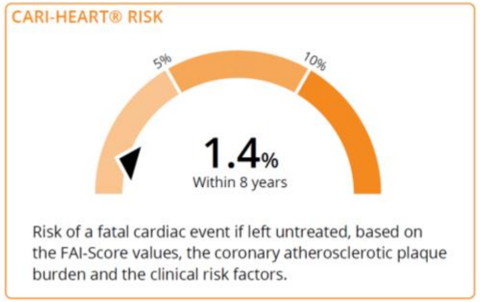
RCA



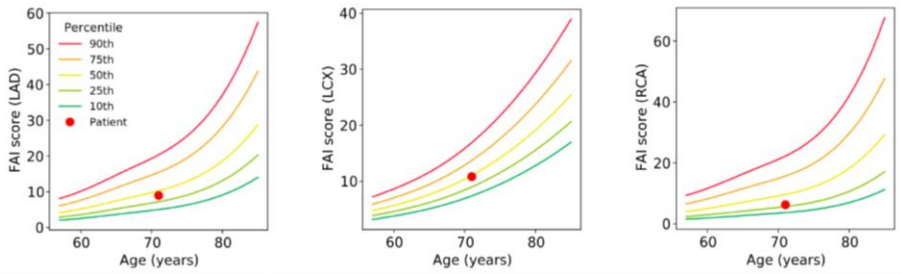
Management based on Conventional CCTA
- ?Increase atorvastatin dose

Management after CaRi-Heart® Report
- Atorvastatin dose unchanged





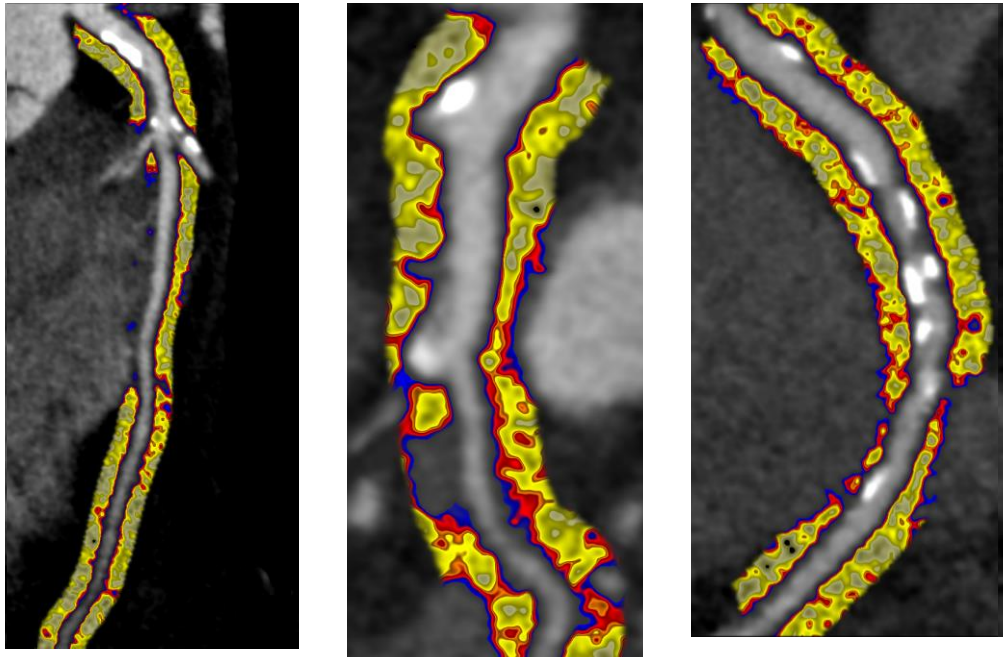
FAI-SCORE - RELATIVE RISK, ADJUSTED FOR AGE AND GENDER



Vessel	FAI-Score	Percentile of Coronary Inflammation for Age and Gender
Left Anterior Descending Artery	9.0	37th percentile
Left Circumflex Artery	10.8	48th percentile
Right Coronary Artery	6.3	30th percentile

Low Risk Patients Despite Extensive Disease

- 76-year-old male
- Hypertensive, non-diabetic
- LDL 73 mg/dL
- Pooled Cohort Equation: 14.7%
- Atorvastatin 10mg daily
- CCS = 768



Management based on Conventional CCTA
- ?Increase atorvastatin dose

Management after CaRi-Heart® Report
- Atorvastatin dose unchanged

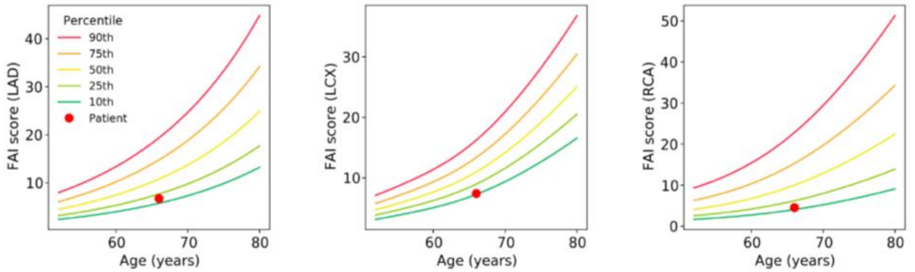
FAI-SCORE

This represents the weighted Fat Attenuation Index (FAI) of the coronary artery with the highest degree of inflammation.

CARI-HEART® RISK

Risk of a fatal cardiac event if left untreated, based on the FAI-Score values, the coronary atherosclerotic plaque burden and the clinical risk factors.

FAI-SCORE - RELATIVE RISK, ADJUSTED FOR AGE AND GENDER



Vessel	FAI-Score	Percentile of Coronary Inflammation for Age and Gender
Left Anterior Descending Artery	6.7	17th percentile
Left Circumflex Artery	7.4	11th percentile
Right Coronary Artery	4.5	12th percentile

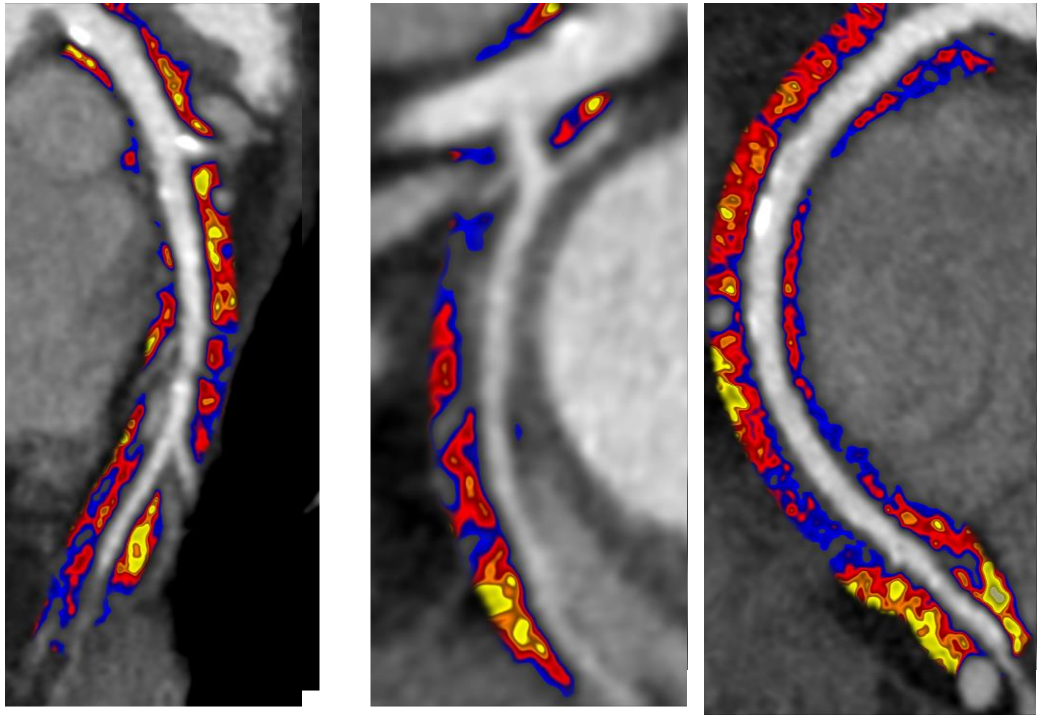
Identifying High Risk Patients Despite Minor Disease

- 56-year-old female
- Non-diabetic, normotensive
- LDL 68 mg/dL
- Pooled Cohort Equation: 7.9%
- Atorvastatin 10mg daily

Management based on Conventional CCTA
- No change in current treatment

Outcome
- Patient died from anterior MI 33 months after CCTA

LAD **LCx** **RCA**



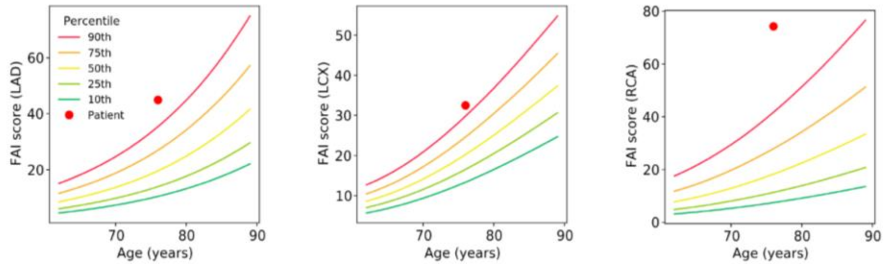
FAI-SCORE

This represents the weighted Fat Attenuation Index (FAI) of the coronary artery with the highest degree of inflammation.

CARI-DEVEL® RISK

Risk of a fatal cardiac event if left untreated, based on the FAI-Score values, the coronary atherosclerotic plaque burden and the clinical risk factors.

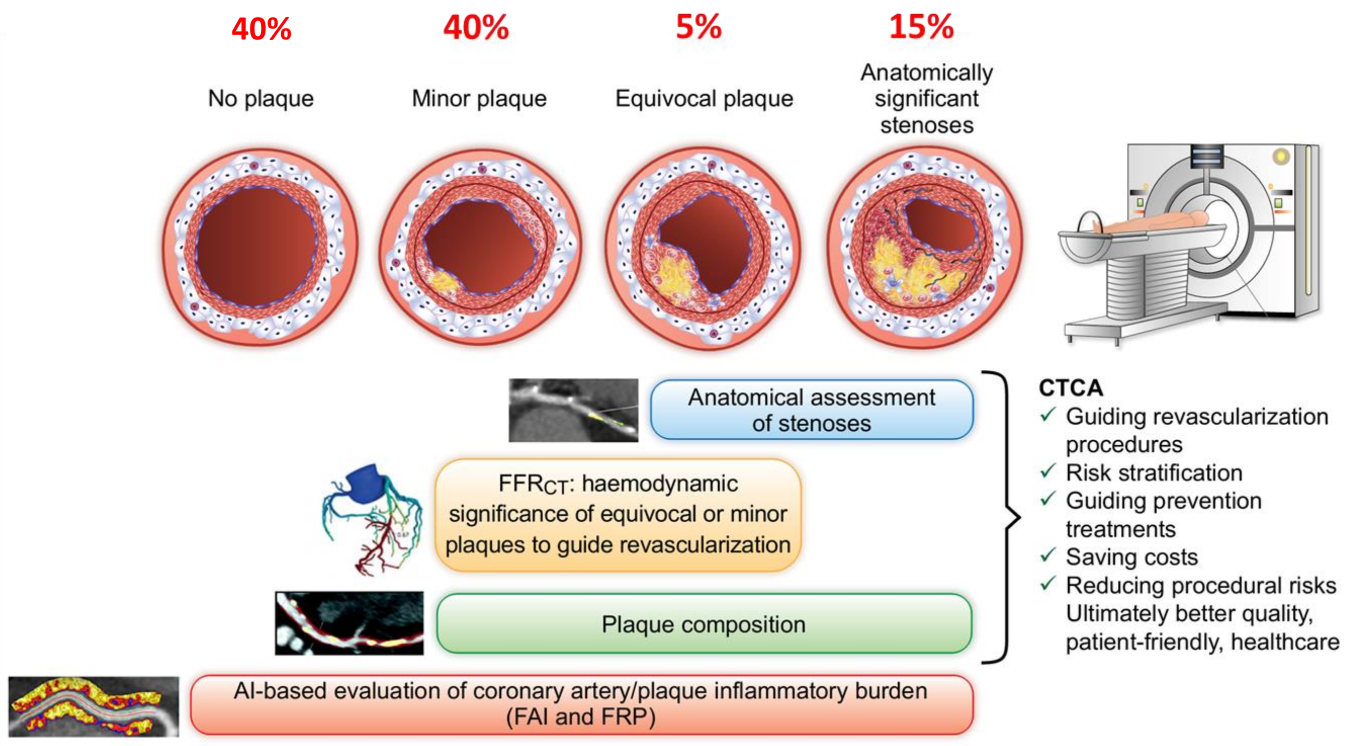
FAI-SCORE - RELATIVE RISK, ADJUSTED FOR AGE AND GENDER



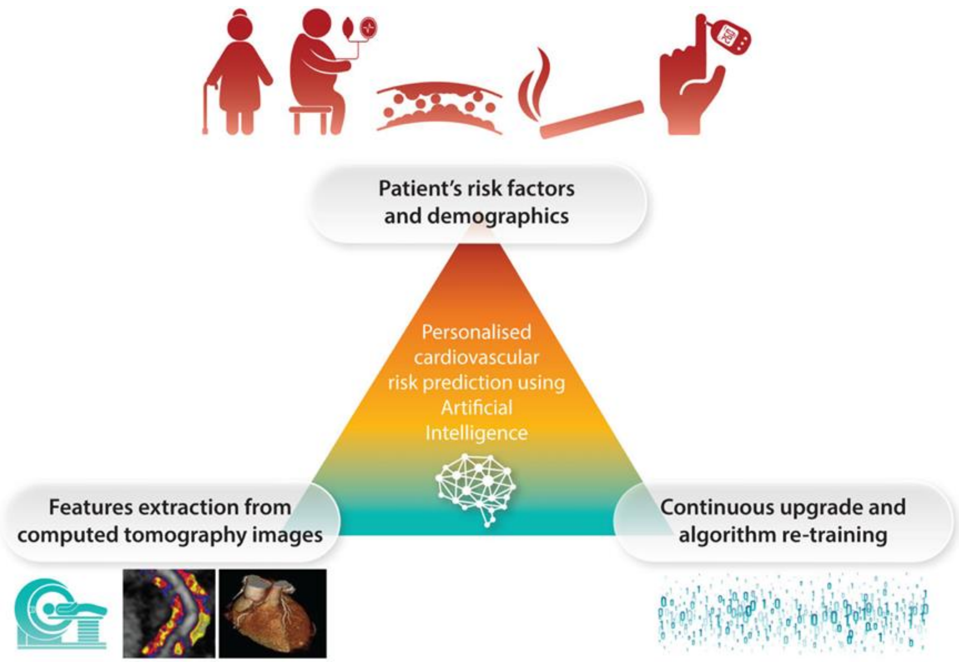
Vessel	FAI-Score	Percentile of Coronary Inflammation for Age and Gender
Left Anterior Descending Artery	44.9	97th percentile
Left Circumflex Artery	32.5	94th percentile
Right Coronary Artery	74.3	99th percentile

CTCA: an One-Stop-Shop for Coronary Diagnostics

Enhanced Diagnostics



Improved Risk Stratification



Antonopoulos AS et al. Eur J Prev Cardiology 2021
Antoniades & West; Eur Heart J 2021

Questions ?