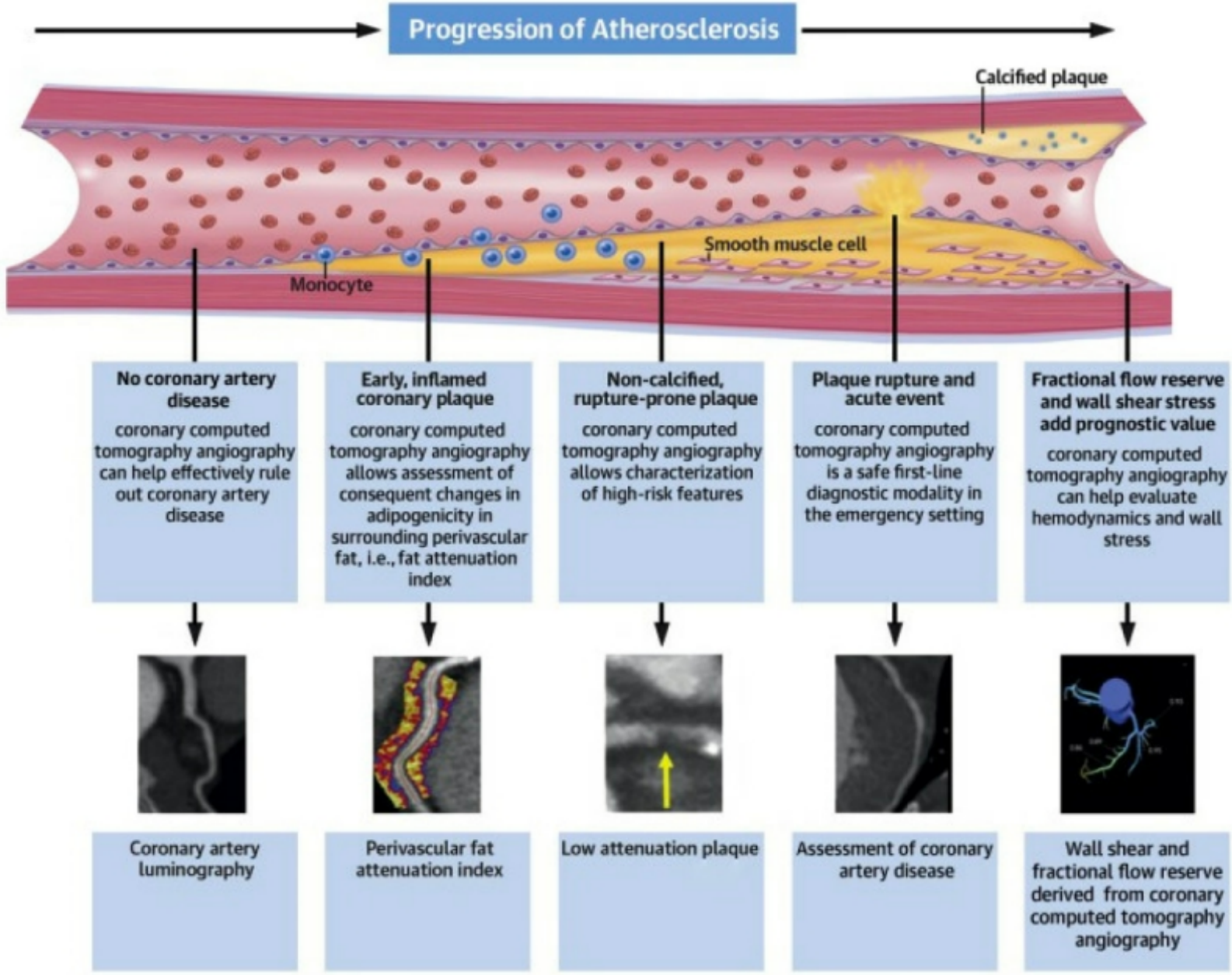
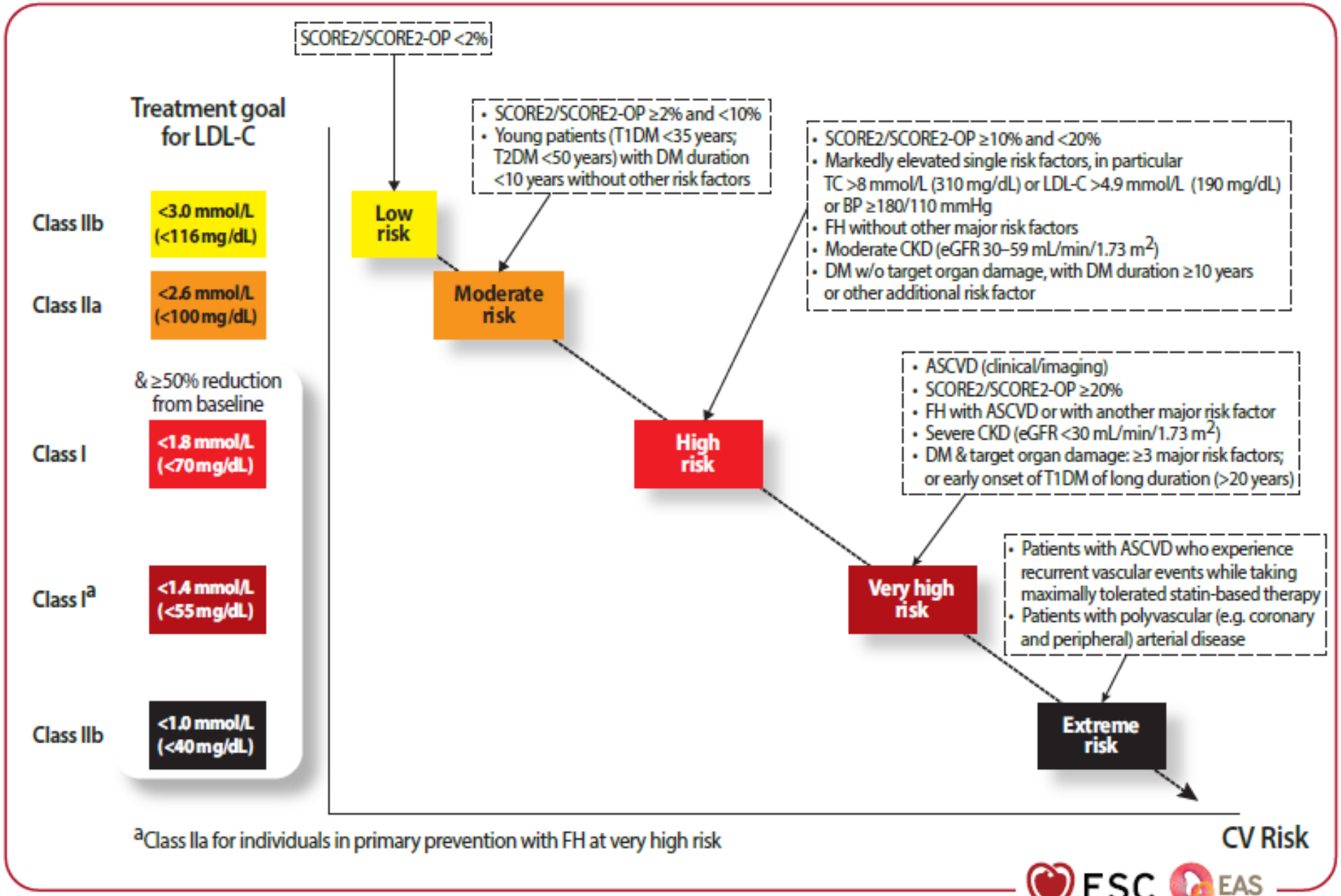
Aterosclerosi coronarica a rischio di eventi

Roma, Giugno 2026

Francesco Prati MD
San Giovanni Hosp. Rome
CLI Foundation



Abdelrahman KM et al. J Am Coll Cardiol. 2020


SCORE2/SCORE2-OP <2%
Treatment goal for LDL-C
Class IIb
<3.0 mmol/L (<116 mg/dL)
Class IIa
<2.6 mmol/L (<100 mg/dL)
& ≥50% reduction from baseline
Class I
<1.8 mmol/L (<70 mg/dL)
Class I[a]
<1.4 mmol/L (<55 mg/dL)
Class IIb
<1.0 mmol/L (<40 mg/dL)
Low risk
• SCORE2/SCORE2-OP ≥2% and <10%
• Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years without other risk factors
Moderate risk
• SCORE2/SCORE2-OP ≥10% and <20%
• Markedly elevated single risk factors, in particular TC >8 mmol/L (310 mg/dL) or LDL-C >4.9 mmol/L (190 mg/dL) or BP ≥180/110 mmHg
• FH without other major risk factors
• Moderate CKD (eGFR 30–59 mL/min/1.73 m2)
• DM w/o target organ damage, with DM duration ≥10 years or other additional risk factor
High risk
• ASCVD (clinical/imaging)
• SCORE2/SCORE2-OP ≥20%
• FH with ASCVD or with another major risk factor
• Severe CKD (eGFR <30 mL/min/1.73 m2)
• DM & target organ damage: ≥3 major risk factors; or early onset of T1DM of long duration (>20 years)
Very high risk
• Patients with ASCVD who experience recurrent vascular events while taking maximally tolerated statin-based therapy
• Patients with polyvascular (e.g. coronary and peripheral) arterial disease
Extreme risk
CV Risk
[a]Class IIa for individuals in primary prevention with FH at very high risk
ESC
EAS

HIGH RISK PLAQUES

- High Clinical Risk Score (Score 2)
- Diabetes
- Renal Insufficiency
- Diffuse atherosclerosis

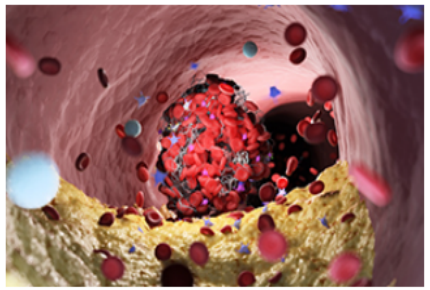
COMMISSIONS

The *Lancet* Commission on rethinking coronary artery disease: moving from ischaemia to atheroma

Published: March 31, 2025

Executive summary

For decades, the management of coronary artery disease has focused on epicardial obstruction and ischaemia, which is often recognised too late for long-term intervention. This approach limits the potential for effective intervention, which particularly concerning because coronary artery disease remains a leading cause of global morbidity and mortality. Current cardiovascular care emphasises restoration of blood flow rather than prevention of disease progression. Despite significant health-care spending on ischaemia, the primary mechanisms of myocardial infarction—atherosclerotic plaque rupture and erosion—often occur earlier in the disease process. The *Lancet* Commission aims to redefine coronary artery disease by shifting the focus from ischaemic heart disease to atherosclerotic coronary artery disease, emphasising early detection, management of risk factors, and a comprehensive approach to prevention throughout the life course.

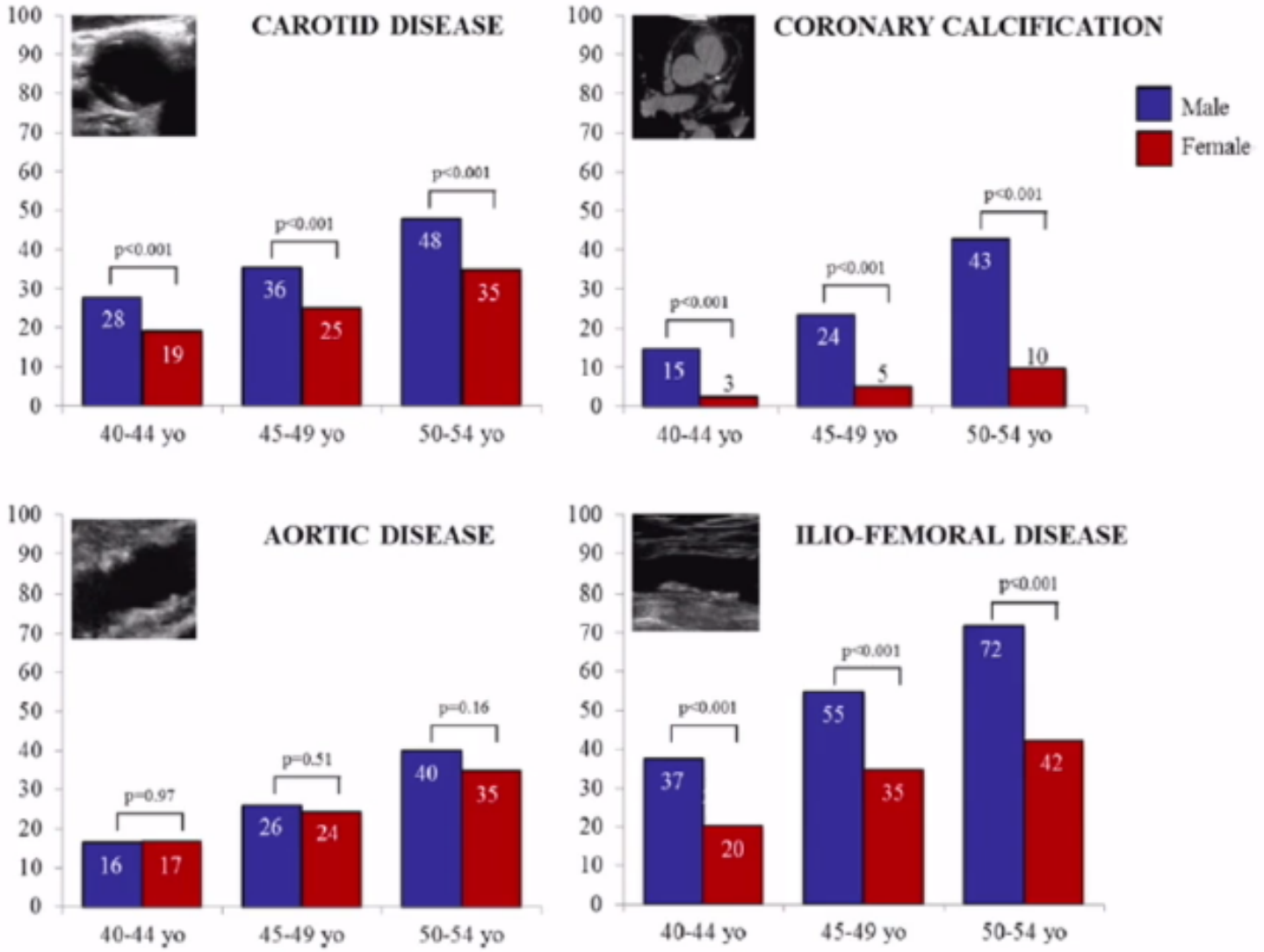


Related links

Lancet Cardiology & Vascular Medicine Specialty Collection

Prevalence of Subclinical Atherosclerosis: the PESA study

- **4184** asymptomatic participants, mean age, 45.8 years; 63% male
- Followed for 6 years
- Atheroscleoris classified as:
  - disease **free** (0 site affected)
  - **focal** (1 site affected)
  - **intermediate** (2-3 sites)
  - **generalized** (4-6 sites)
- Overall prevalence: **63%**
- Intermediate and generalized disease: 41%
- Plaques were most common in the **iliofemorals** arteries (44%)
- **M**>>W
- Prevalence increases with **age**

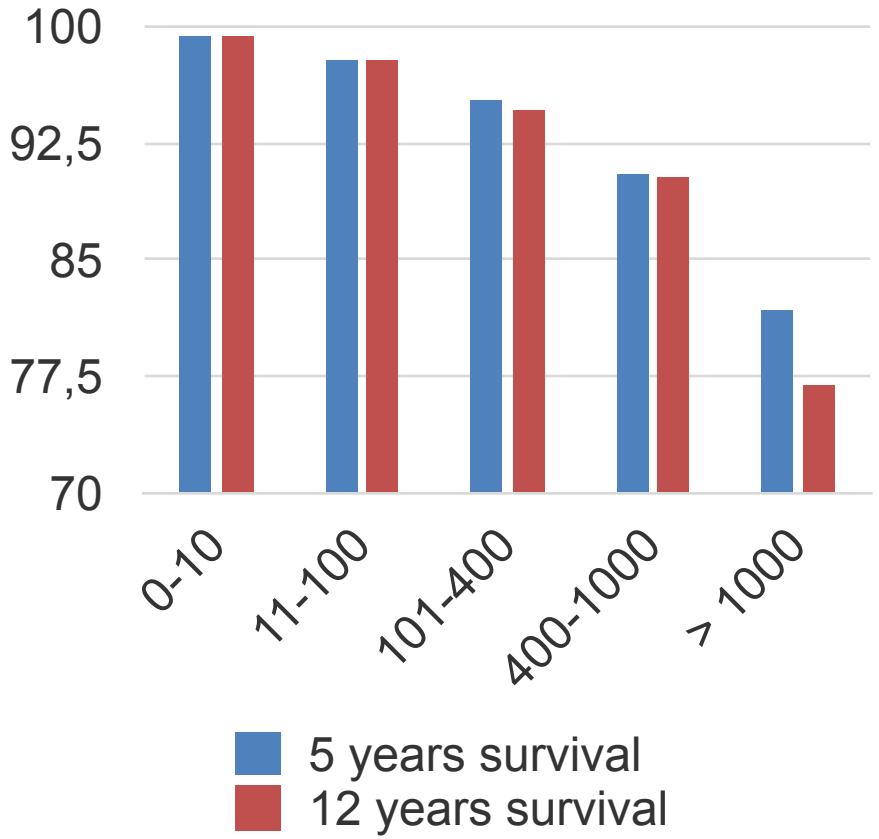


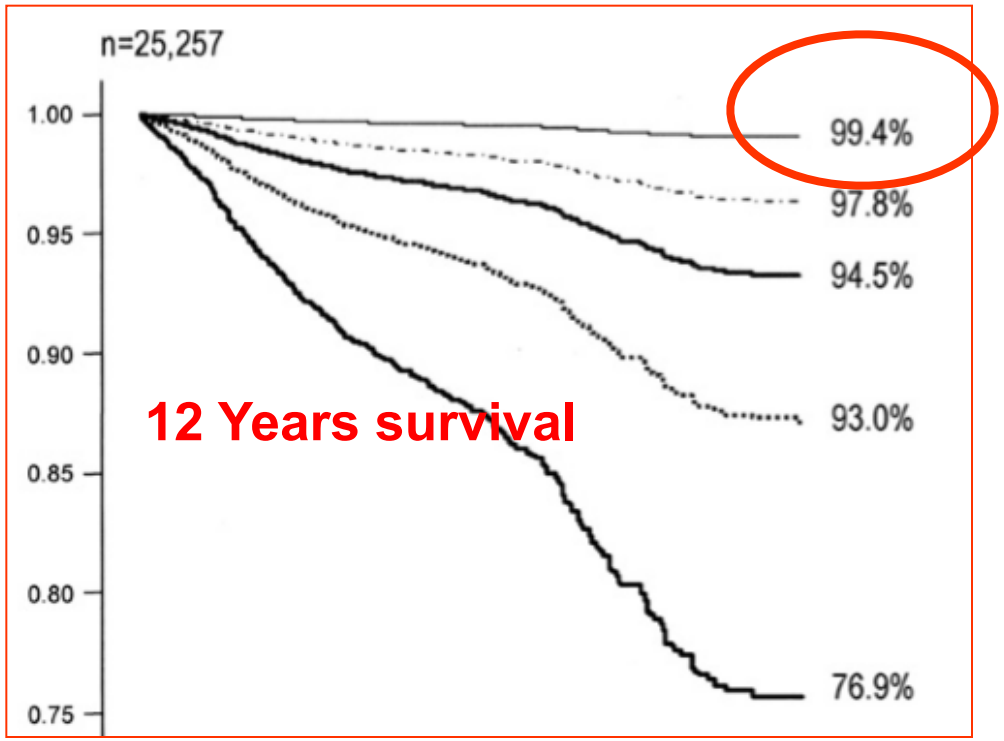
ESC Preventive Cardiology 2021

Fernandez-Friera L et al, Circulation 2015;131: 2104-2113

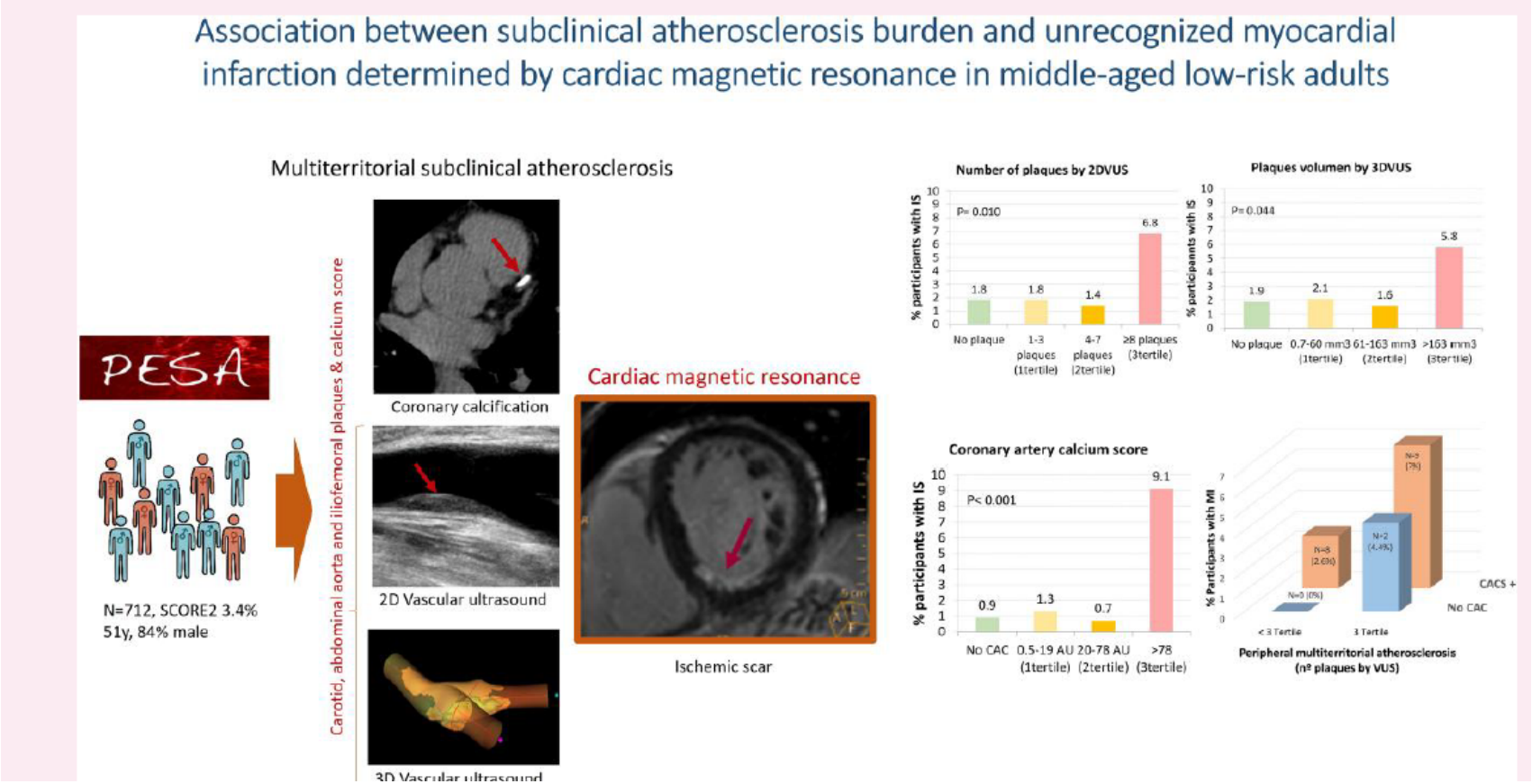
Hecht et al. JACC 2010

Survival according to calcium score





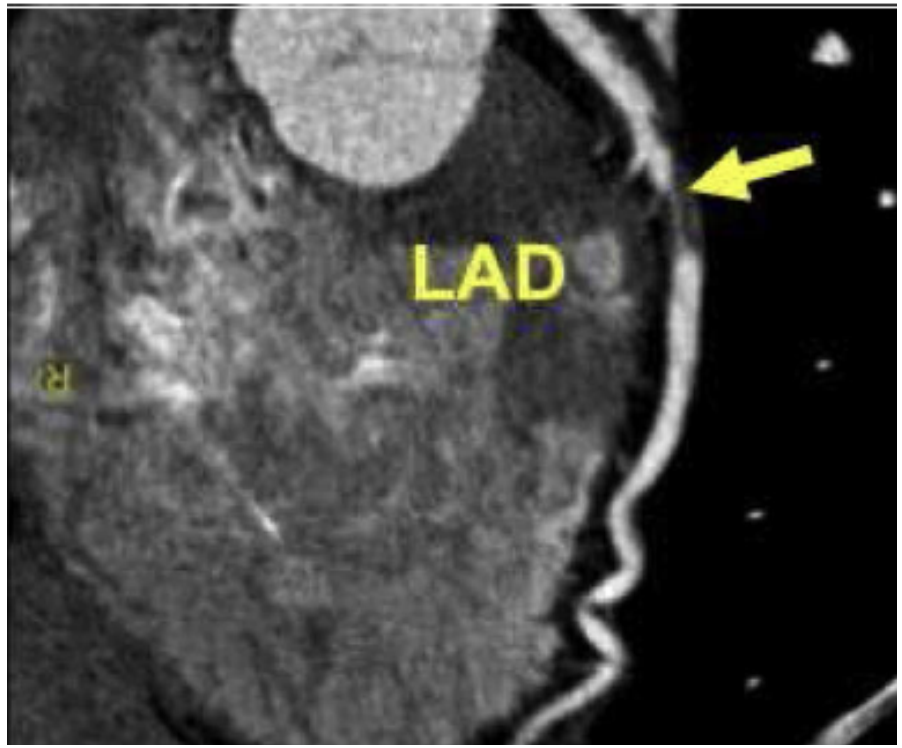
Association between subclinical atherosclerosis burden and unrecognized myocardial infarction detected by cardiac magnetic resonance in middle-aged low-risk adults



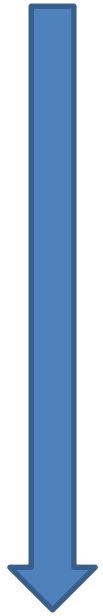
Eur Heart J Cardiov Imag 2024

A Correct Approach?

- Primary prevention Program
- Coronary CT Scan Narrowings
- Referral to an interventional cardiologist

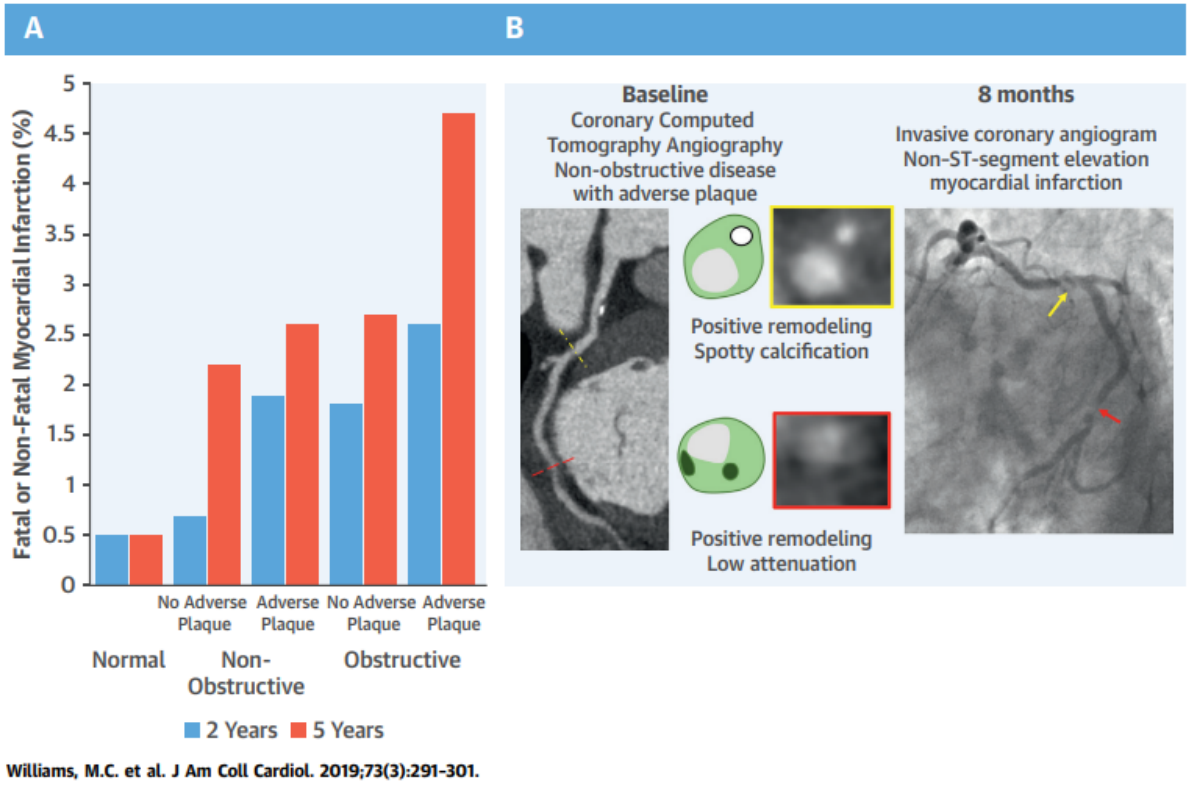


- Atherosclerosis detection (yes or no)
- Extension of atherosclerosis
  - Multiple sites and Quantification
- Qualitative assessment
- Functional assessment (Active plaques)



Coronary Artery Plaque Characteristics Associated With Adverse Outcomes in the SCOT-HEART Study

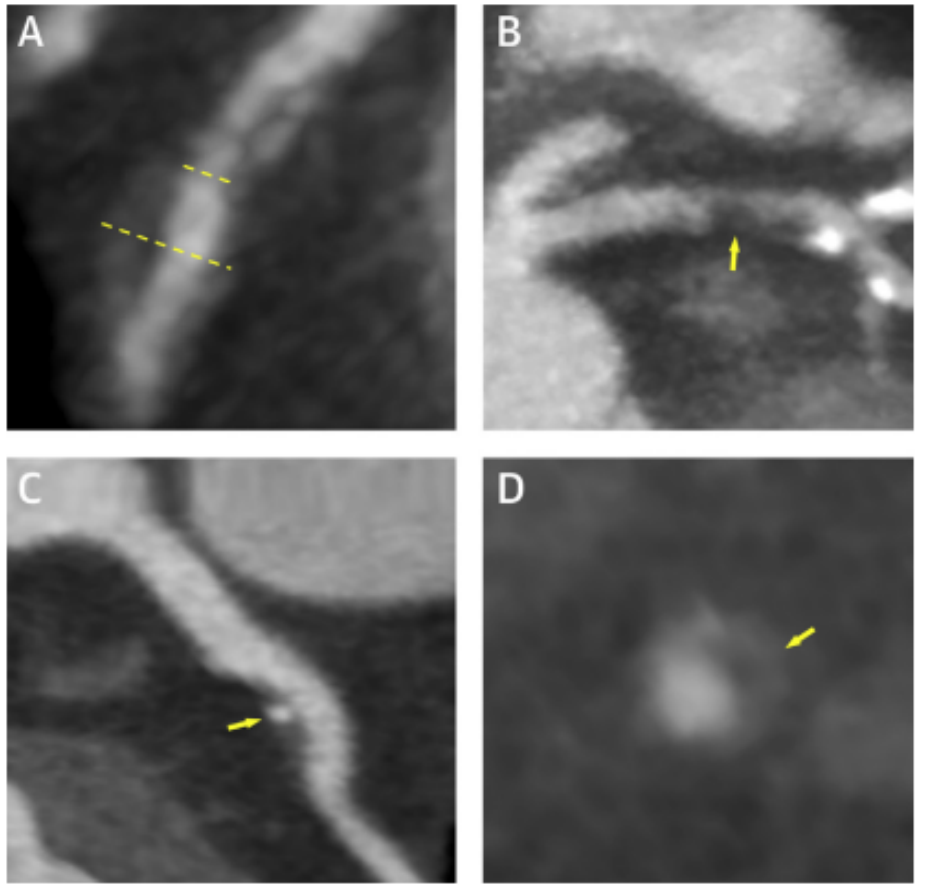
CENTRAL ILLUSTRATION Adverse Plaque on Computed Tomography Coronary Angiography Identifies Patients at an Increased Risk of Subsequent Events



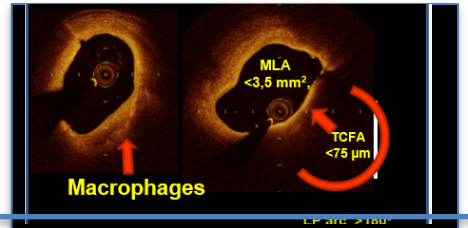
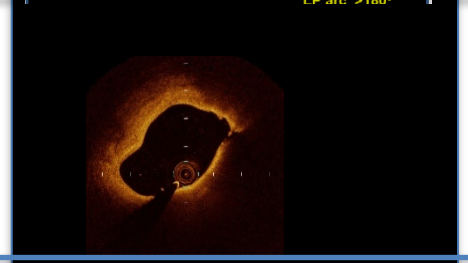
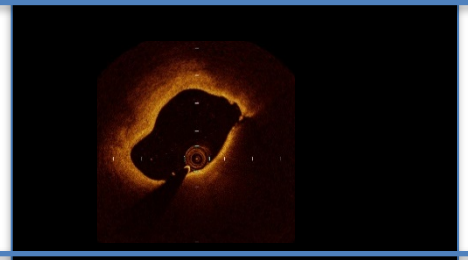
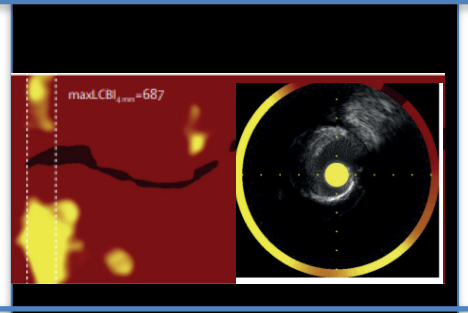
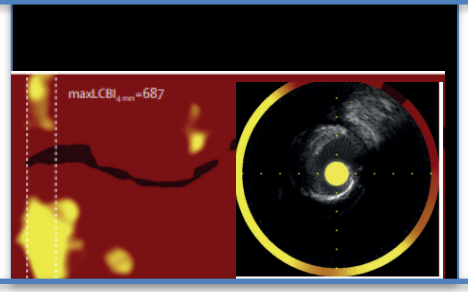
Williams, M.C. et al. J Am Coll Cardiol. 2019;73(3):291-301.

(A) Bar graph of the frequency of coronary heart disease death or nonfatal myocardial infarction at 2 and 5 years for patients with normal coronary arteries and nonobstructive or obstructive disease with and without adverse plaque. **(B)** Coronary computed tomography angiography and invasive coronary angiography images from a patient with nonobstructive coronary artery disease who had a subsequent non-ST-segment elevation myocardial infarction. The **red/yellow dotted lines** and **arrows** correspond to the location of the plaques in the **red/yellow boxes**.

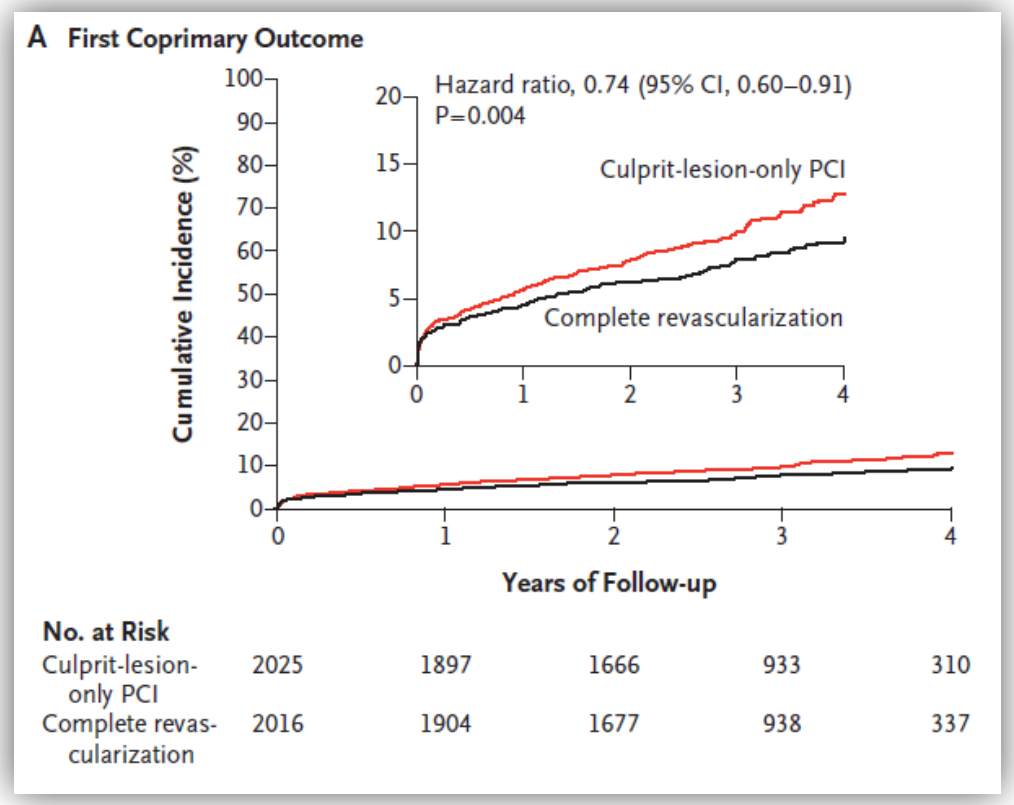
FIGURE 1 Coronary Plaque Characteristics Identified on Computed Tomography Coronary Angiography



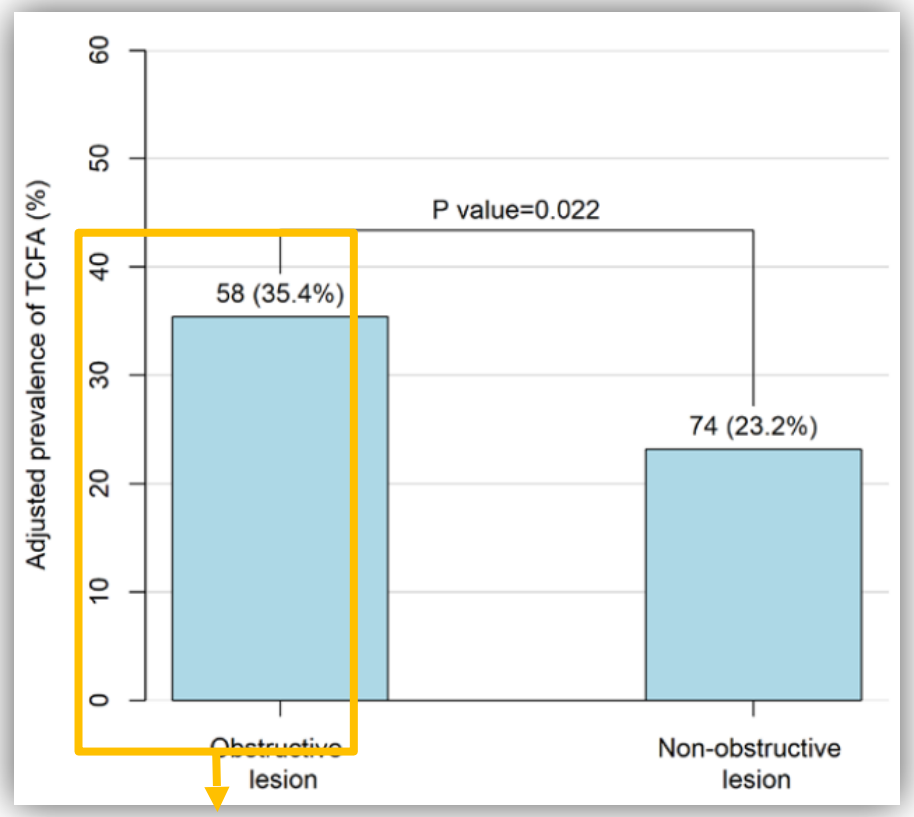
Williams C et al. JACC 2015

CLIMA	Eur. Heart J. 2021		No FFR	4 OCT Features	CCS + ACS
COMBINE	Eur. Heart J. 2021		FFR Pos.	TFC	CCS + ACS Diabetics
PECTUS	JAMA 2023		FFR Pos.	2 OCT Features	ACS
LRP	Lancet 2019		No FFR.	$LCBI_{4mm}$ > 250	CCS + ACS
PROSPECT II	Lancet 2021		FFR Pos.	$LCBI_{4mm}$ ➢ 324.7 ➢ PB≥ 70%	CCS + ACS

PREVALENCE OF Plaque Vulnerability
COMPLETE Trial *1 out of 3 non-culprit lesions were TCFAs*



PCI of nonculprit lesions → ↓ CV death or MI



Nonculprit lesions were TCFAs in 35.4% of cases

Mehta et al. N Engl J Med. 2019 Oct 10;381(15):1411-1421

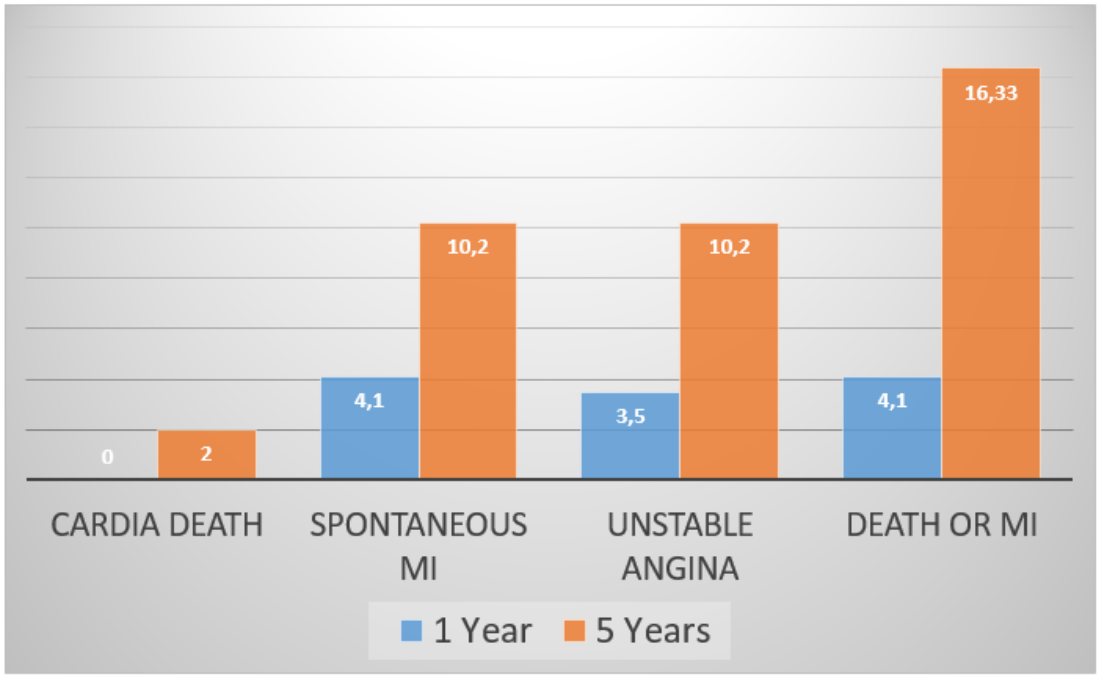
Pinilla-Echeverri et al. Circ Cardiovasc Interv. 2020;13:e008768.

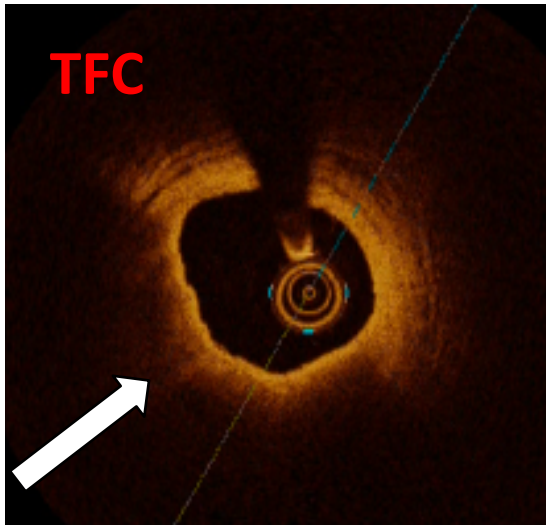
COMBINE OCT-FFR. Prospective natural history study in pts with DM and with ≥1 FFR-negative lesion

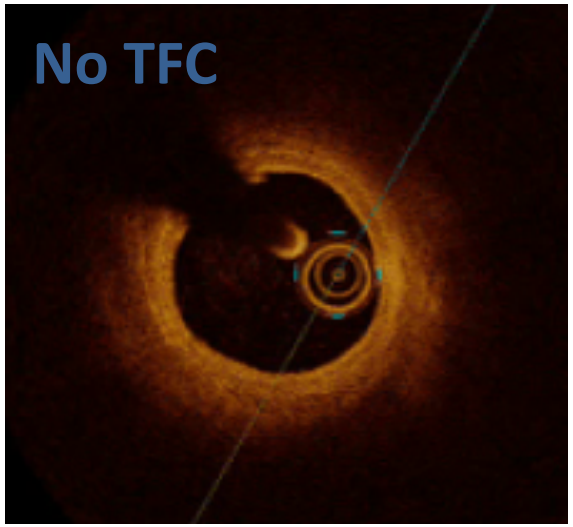
- 2 groups identified based on the presence of ≥1 TCFA lesion.

TCFA <65µm

N=390





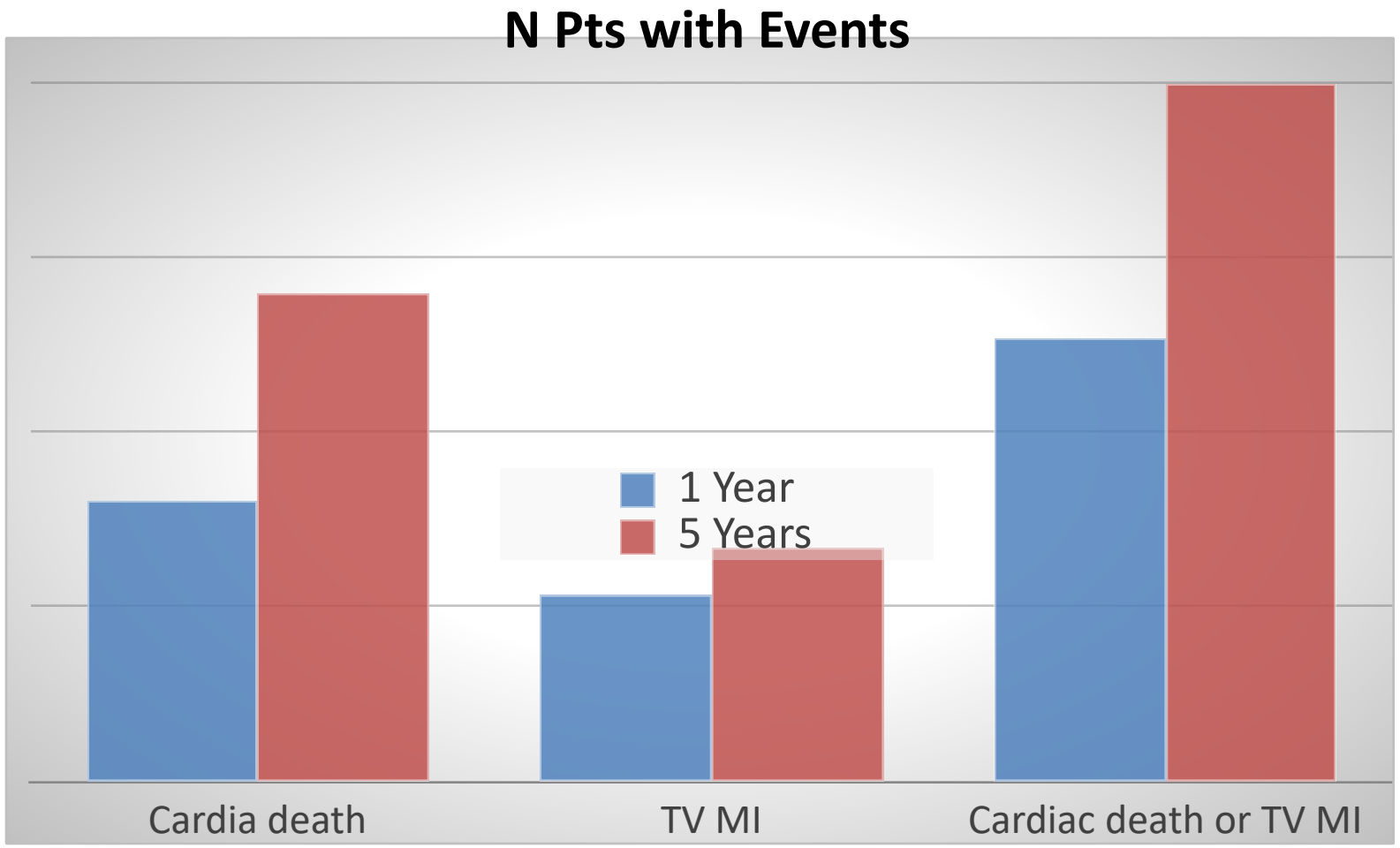


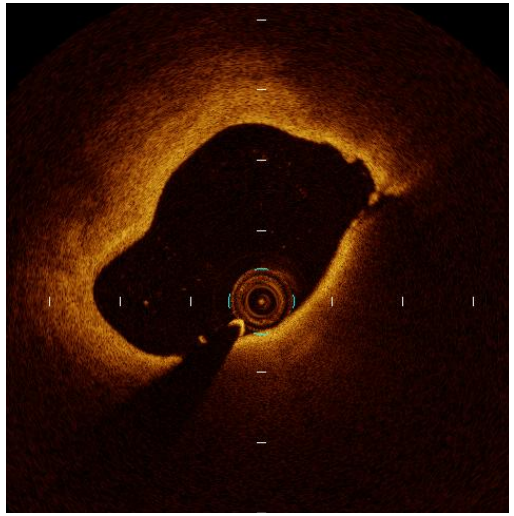
Fabris et al. Eurointervention 2023

CLIMA Study. Cardiac Death and or Target MI

In total 73 pts with main events out of 1003

TCFA <75µm





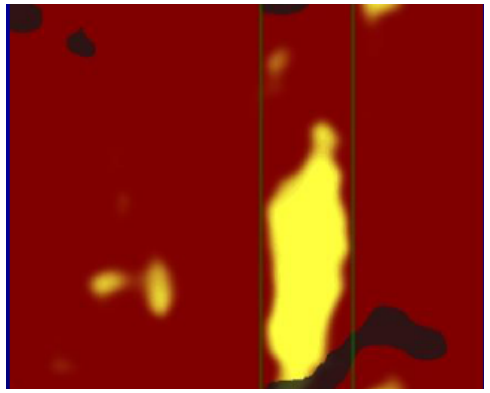
OCT Detected

N 1. FC Thickness:

Study	Def.	HR	p	Imag. Mod.
CLIMA 1 Y	<0.75	4.65 (2.4-9.0)	< 0.001	OCT
COMBINE	<0.65	4.65 (2.0-10.9)	< 0.001	OCT
Kubo EHJ. CVI 2021	<0.65	10.4 (6.5-16.7)	< 0.001	OCT
Jiang JACC 2023 4Y	<0.65	3.15 (1,7-5.6)	<0.001	OCT
CLIMA 5 Y	<0.75	3.46 (2.2-5.6)	<0.001	OCT

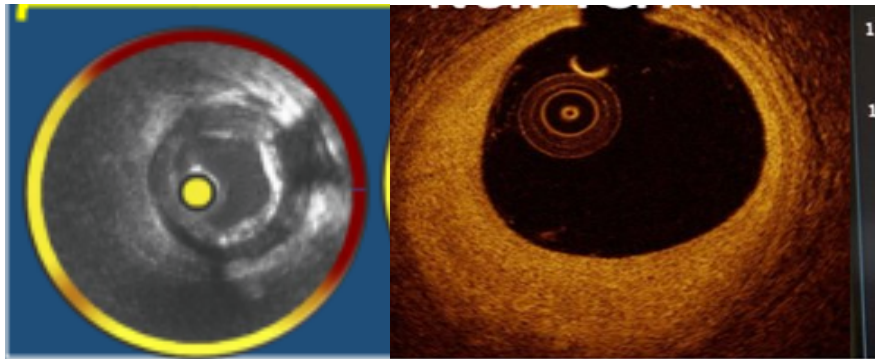
N 2. The lipid plaque

Predictive value of Lipid Plaque criteria for MACEs at patient level analysis



Best Detected with NIRS-IVUS

	Def.	HR	p	Imaging Mod.
CLIMA 1Y	Lipid Arc > 180⁰	2.40 (1.2-4,8)	p<0.013	OCT
Xing 2017 4Y	Lipid Arc > 193⁰	2.8 (1.1-5.6)	p=0.024	OCT
LRP 2 Y	Max LCBI > 400 4 mm	2.18 (1.5-3.2)	p<0·0001	NIRS-IVUS
PROSPECT II 3.7 Y	Max LCBI > 324 4 mm	2.1 (1.2-3.7)	p=0·0071	NIRS-IVUS
PROSPECT II 3.7 Y	Plaque burden > 70%	3.1 (1.6-5.8)	p<0·0001	NIRS-IVUS
PROSPECT I 3.4 Y	Plaque burden > 70%	5.03 (2.5-10.1)	p< 0.001	VH-IVUS
Kubo EHJ. CVI 2021	Lipid Arc > 180⁰	2.20 (8.8-23.6)	p<0.001	OCT
CLIMA 5Y	Lipid Arc > 180⁰	2.20 (1.37-3.52)	p<0.001	OCT

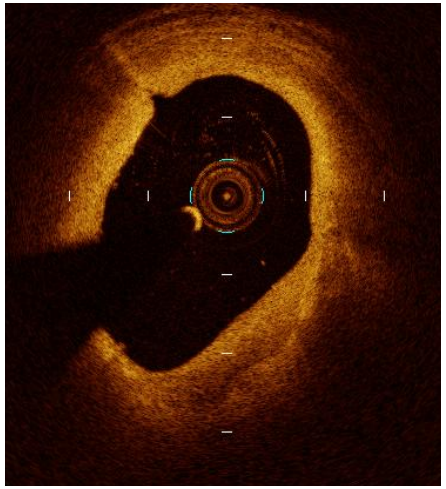


OCT and IVUS Detected

N 3. The Small Area

Predictive value of LA for MACEs at patient level analysis

	Def.	HR	p	Imaging Mod.
CLIMA 1Y	MLA <3.5 mm^2	2.07 (1.1-4.0)	p=0.032	OCT
PROSPECT I 3.4 Y	MLA < 4.0 mm^3	3.21 (1.6–6.4)	p< 0.001	NIRS-IVUS
PROSPECT II 3.7 Y	MLA < 4.0 mm^2	5.49(2.0-15.3)	p=0·0007	NIRS-IVUS
Jiang JACC 2023 4Y	MLA<3.5 mm^2	3.57 (1.42-8.99)	p<0.007	OCT
CLIMA 5Y	MLA <3.5 mm^2	1.77 (1.1-2.8)	p=0.016	OCT



OCT Detected

N 4. The Inflammation

Predictive value of inflammarory cells for MACEs at patient level analysis

	Def.	HR	p	Imaging Mod.
CLIMA 1 Y	Macrophages (yes/ no)	2.66 (1.2-6.1)	p=0.021	OCT
CLIMA 1 Y	Marcophages (arc > 67^0)	5.3	p< 0.001	OCT
CLIMA 5 Y	Macrophages (yes/ no)	1.81 (1.1-3.0)	p=0.021	OCT

Lancet
April 2024

Articles

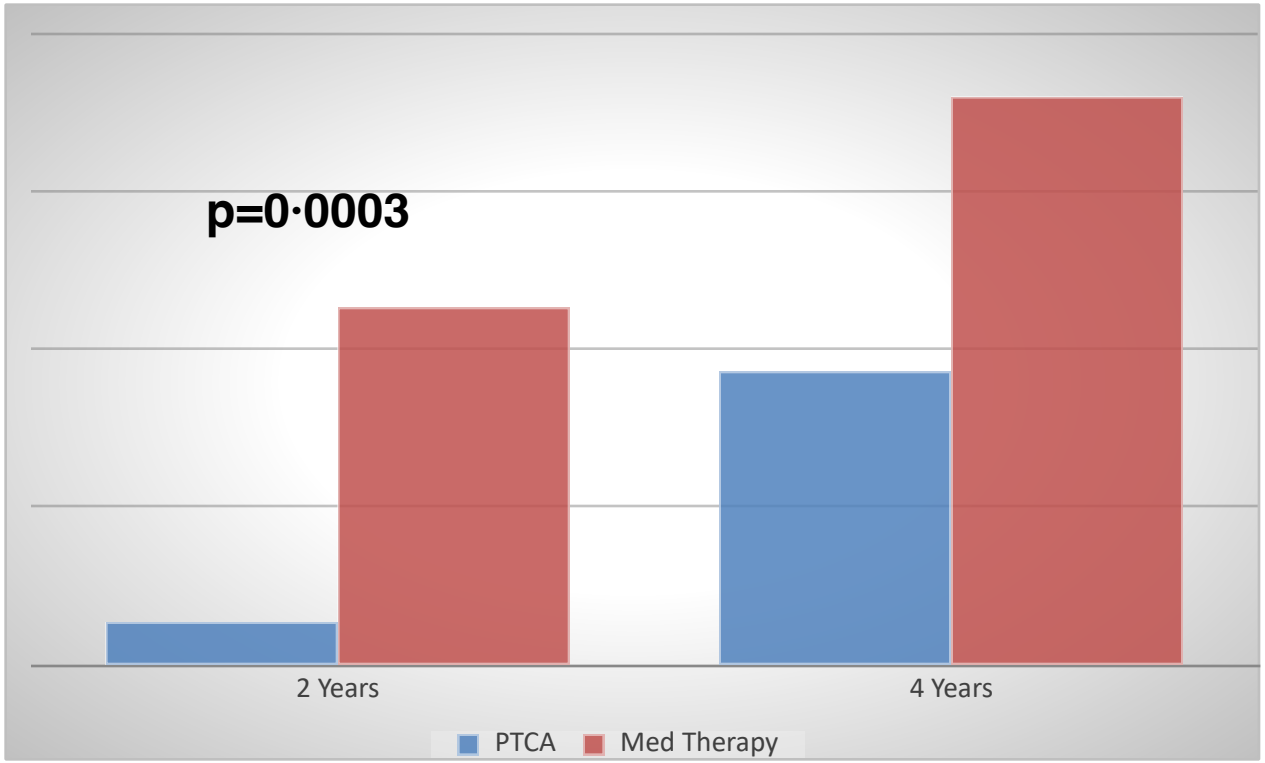
Preventive percutaneous coronary intervention versus optimal medical therapy alone for the treatment of vulnerable atherosclerotic coronary plaques (PREVENT): a multicentre, open-label, randomised controlled trial

Seung-Jung Park, Jung-Min Ahn*, Do-Yoon Kang, Sung-Cheol Yun, Young-Keun Ahn, Won-Jang Kim, Chang-Wook Nam, Jin-Ok Jeong, In-Ho Chae, Hiroki Shiomi, Hsien-Li Kao, Joo-Yong Hahn, Sung-Ho Her, Bong-Ki Lee, Tae Hoon Ahn, Ki-Yuk Chang, Jei Keon Chae, David Smyth, Gary S Mintz, Gregg W Stone, Duk-Woo Park, for the PREVENT Investigators†*

- **1606 pts with FFR negative, vulnerable plaques**
- **Randomly assigned to percutaneous coronary intervention (n=803) or optimal medical therapy alone (n=803).**
- **2-year follow-up**
- **Primary end-point: composite of death from cardiac causes, target-vessel myocardial infarction, ischaemia-driven target-vessel revascularisation, or hospitalisation for unstable or progressive angina,**

Incidence of composite primary end-point

Absolute difference –3·0 percentage points [95% CI –4·4 to –1·8]; p=0·0003).



PREVENT Study
Lancet, April 2024

The primary outcome: composite of death from cardiac causes, target-vessel myocardial infarction, ischaemia-driven target-vessel revascularisation, or hospitalisation for unstable or progressive angina, assessed in the intention-to-treat population at 2 years

Ongoing studies

JACC: CARDIOVASCULAR IMAGING VOL. 17, NO. 9, 2024

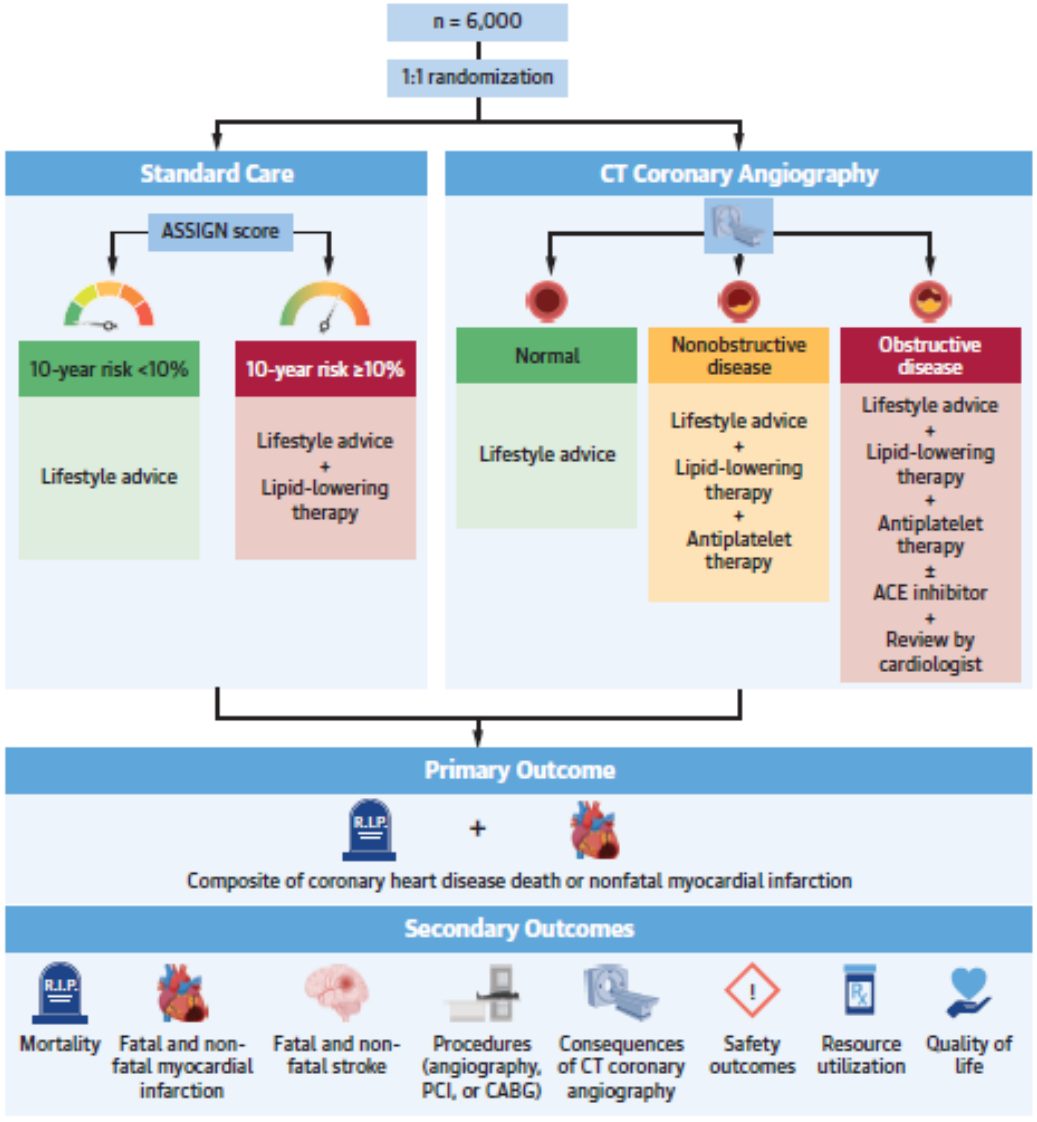
STATE-OF-THE-ART REVIEW

Rationale and Design of SCOT-HEART 2 Trial

CT Angiography for the Prevention of Myocardial Infarction

Michael McDermott, MBChB,[a] Mohammed N. Meah, MBChB, PhD,[a,b] Phyo Khaing, MBChB,[a] Kang-Ling Wang, MD,[a] Jennifer Ramsay, MBChB,[c] Gillian Scott, PhD,[d] Hannah Rickman, MPH,[d] Tom Burt, Ian McGowan, Timothy Fairbairn, MBChB, PhD,[b] Marise Bucukoglu,[d] Russell Bull, MBBChir,[e] Adam Timmis, MBChB, PhD,[f] Edwin J.R. van Beek, MD, PhD,[g] Giles Roditi, MBChB,[c,h] Philip D. Adamson, MBChB, PhD, MPH,[a,i] Steff Lewis, MSC, PhD,[d] John Norrie, MSc,[d] Brian McKinstry, MBChB, MD,[d] Bruce Guthrie, MBChB, PhD,[j] Lewis Ritchie, OBE, FRSE, MD,[k] Nicholas L. Mills, MBChB, PhD,[a,d] Marc R. Dweck, MBChB, PhD,[a] Michelle C. Williams, MBChB, PhD,[a] David E. Newby, MBChB, PhD[a]

CENTRAL ILLUSTRATION The SCOT-HEART 2 Trial Design



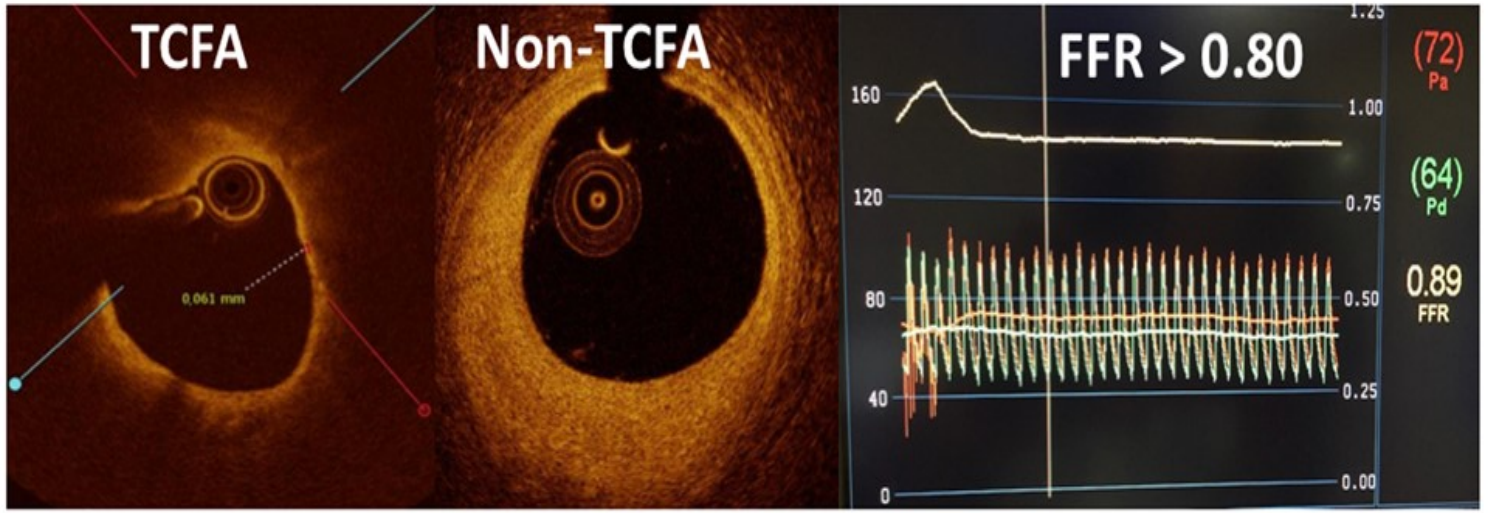
McDermott M, et al. JACC Cardiovasc Imaging. 2024;17(9):1101-1112.

ACE = angiotensin-converting enzyme; CABG = coronary artery bypass graft; CT = computed tomography; PCI = percutaneous coronary intervention; SCOT-HEART 2 = Scottish Computed Tomography of the Heart 2.

COMBINE-INTERVENE

Combine Intervene

Combine Intervene stands for: *COMBINE*d Ischemia and Vulnerable Plaque Percutaneous *INTERVEN*tion to Reduce



The COMBINE-INTERVENE Trial will investigate whether a PCI revascularization strategy based on combined FFR and OCT assessment is superior to a PCI revascularization strategy based on FFR-alone in patients with MVD with any presentation. The COMBINE-INTERVENE Trial is the first in line trial that will test focal percutaneous stenting for vulnerable plaque lesions independently from ischemia.

Study Design

Go to

Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	1222 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	Single (Participant)
Masking Description:	single blind
Primary Purpose:	Treatment
Official Title:	COMBINEd Ischemia and Vulnerable Plaque Percutaneous INTERVENtion to Reduce Cardiovascular Events
Actual Study Start Date :	March 16, 2022
Estimated Primary Completion Date :	March 16, 2026
Estimated Study Completion Date :	December 31, 2026

Centro per la Lotta contro l'Infarto - Fondazione Onlus

INTERCLIMA

CLI Foundation

study flow chart

Inclusion criteria:
- Single intermediate lesion in non culprit vessels of patients with acute coronary syndrome diagnosis
- Life expectancy >3 years
- Age>18 years

Intermediate lesion in a naïve major coronary segment (Ø ≥2.5 mm) determining stenosis between 40-70%

Exclusion criteria:
- incomplete imaging of the segment of interest (including at least 5 mm at both stenosis edges);
- diffusely segment diseased with more than one lesion (preventing correct adverse event attribution) or significant (>70%) lesion in the same coronary vessel;
- ostial left main or graft conduits involvement;
- prior myocardial infarction or revascularization in the same coronary vessel;
- non-cardiac co-morbid conditions that may result in protocol noncompliance.

QCA validation and randomization to
(stratified by LAD localization and center)

Randomization 1:1

iFR/FFR guidance (770)

55% DEFER

Non significant intermediate plaque
iFR >0.89/FFR >0.80

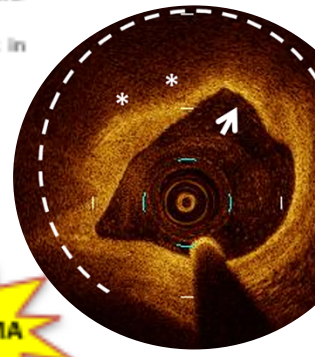
Significant intermediate plaque
iFR <0.89/FFR <0.80

OCT guidance (770)

12.3% CLIMA

Not vulnerable plaque
(Presence of less than 3 CT-defined vulnerability criteria* including fibrous cap thickness <75 µm)

Vulnerable plaque
(Presence of at least 3 out the 4 OCT-defined vulnerability criteria* including fibrous cap thickness <75 µm)



Deferred group

Interventional group

Target vessel failure[§] with intention-to-treat analyses

112 events expected

[§]composite of cardiac death, target vessel myocardial infarction

*simultaneous presence of:
MLA <3.5 mm^2,
fibrous cap thickness <75 µm,
circumferential lipid arc extension >180°,
and macrophage infiltration

Final Remarks

- Vulnerable plaques identify patients at high risk of events even in a long time span
- There is stil no general consensus on the morhpology criteria to be adopted (particularly single vs multiple) for identifying vulnerable plaques

Take Home Message

- **Subclinical atherosclerosis is common.**
- **Can be detected in the coronary tree with CT**
- **The SCOT Heart program is defining the prognostic role of CT in identifying (and treating) patients with (non obstructive and obstructive) coronary plaques**
- **Obstructive coronary plaques identify patients at higher risk of coronary events**
- **The SCOT Heart 2 will address the impact of coronary interventions of obstructive plaques**
- **Photocounting CT improves the identification of high risk plaques**