

Identifying vulnerable plaque features that predict cardiovascular events in patients with acute coronary syndromes and multivessel disease: the COMPLETE-2 OCT study

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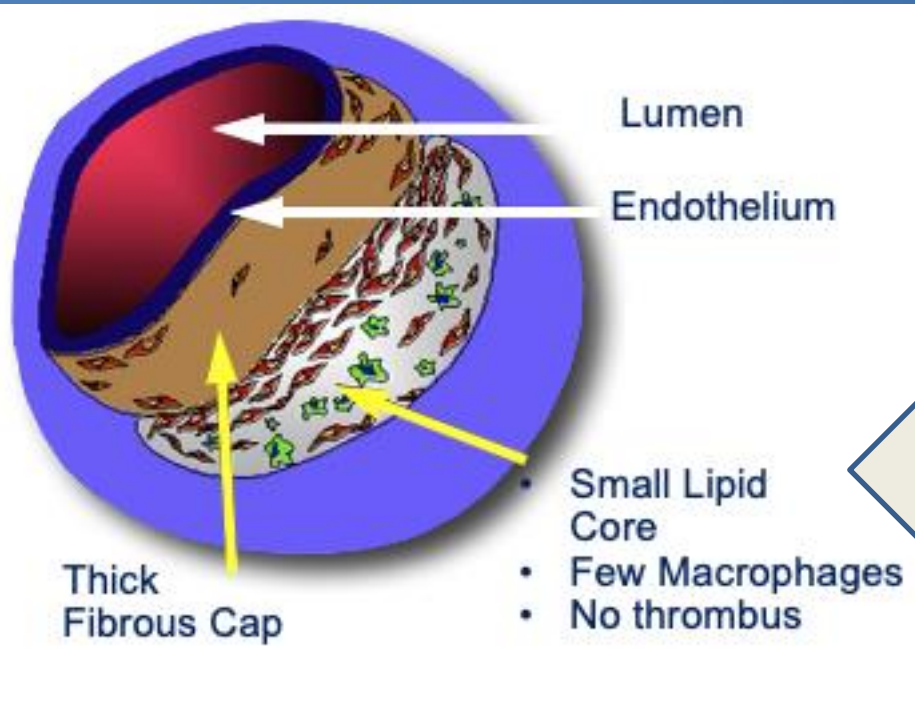
Hamilton Health Sciences



Understanding plaque morphology of non-culprit lesions in relation to physiology/angiography/image-guided revasc

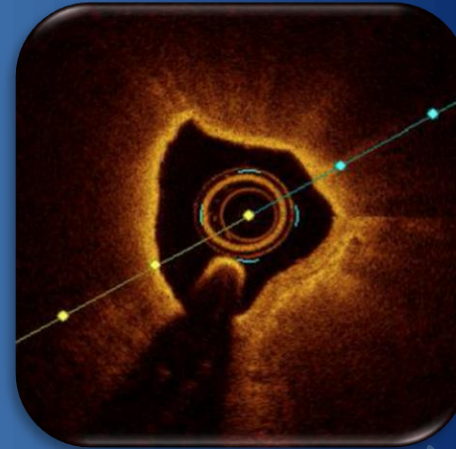
Stable CAD

Fibro-calcific plaques
Low Risk of Rupture



Physiology-Guided Strategy Standard

ACS Non-culprit

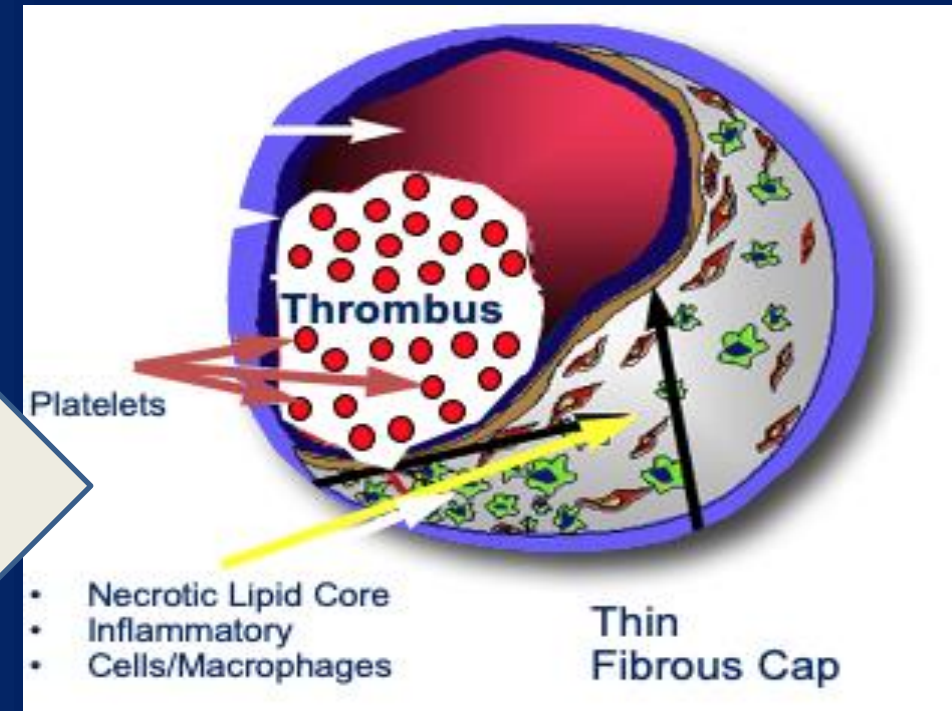


50% are TCFA
50% are stable plaques

Physiology vs Angiography Guided Strategy?

STEMI culprit

Plaque Rupture
Medical Emergency

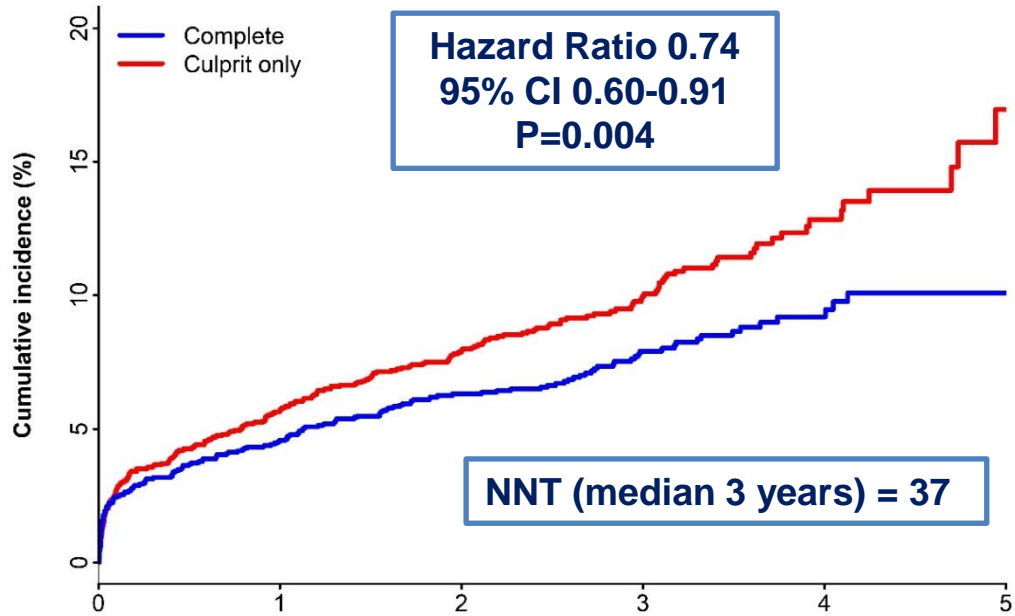


Angiography-Guided Revas Standard (PPCI)

COMPLETE Trial: Primary Outcomes

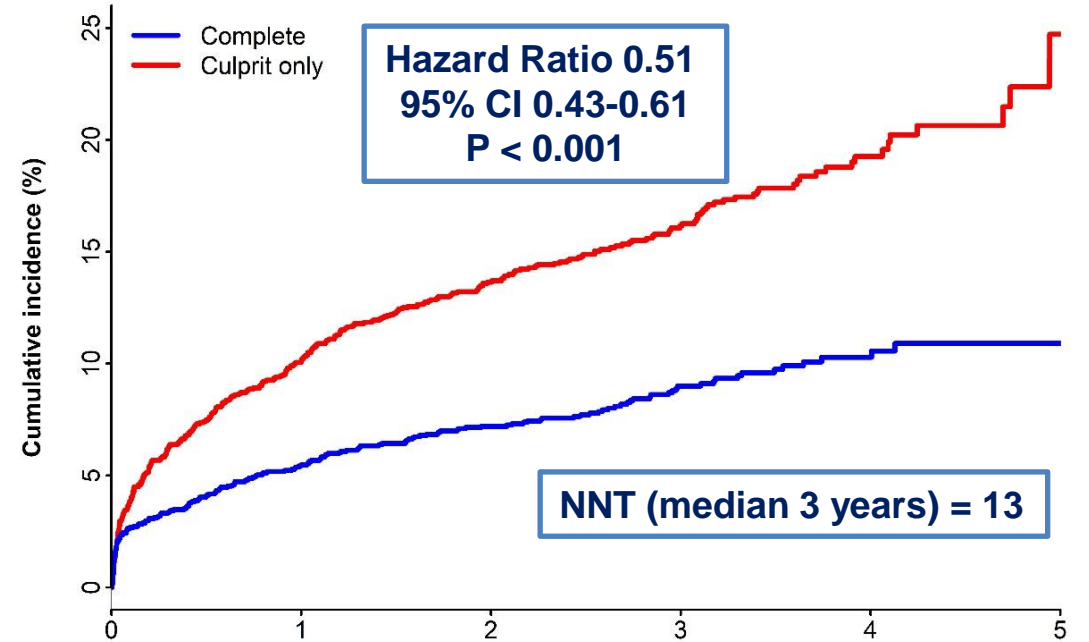
Multivessel vs Culprit Lesion-only PCI for STEMI and multi-vessel CAD

CV Death or New MI



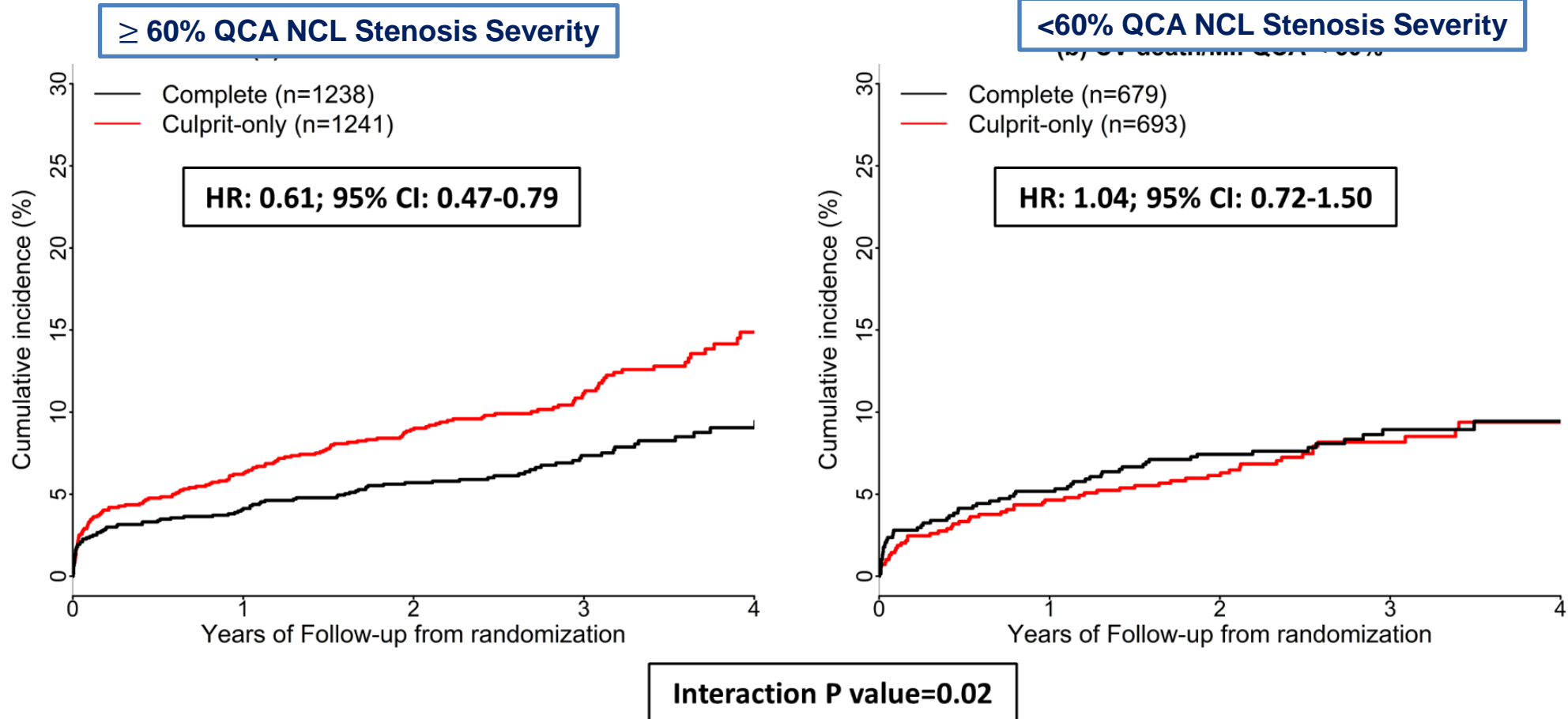
No. at Risk	Years of Follow-up					
	0	1	2	3	4	5
Complete	2016	1904	1677	938	337	70
Culprit only	2025	1897	1666	933	310	59

CV Death, New MI, or IDR



No. at Risk	Years of Follow-up					
	0	1	2	3	4	5
Complete	2016	1886	1659	925	329	66
Culprit only	2025	1808	1559	865	294	57

Outcomes by NCL Stenosis QCA Severity: Greater Benefit if Tighter NCL's CV Death and New MI

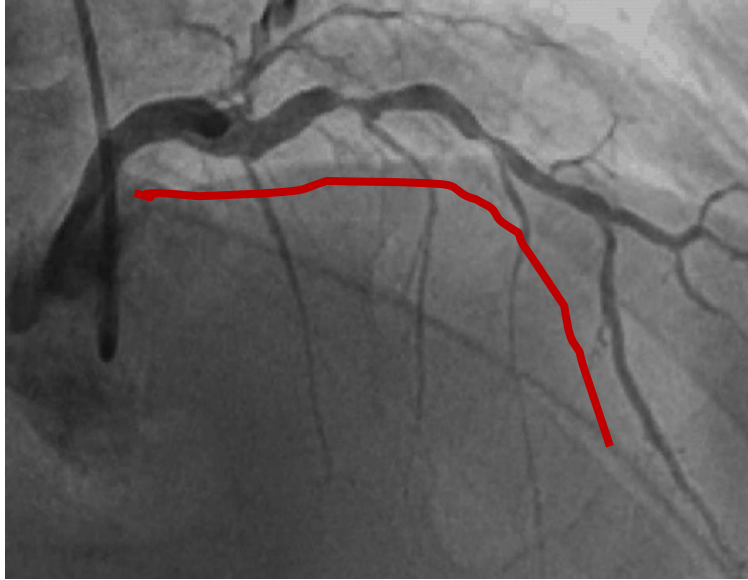




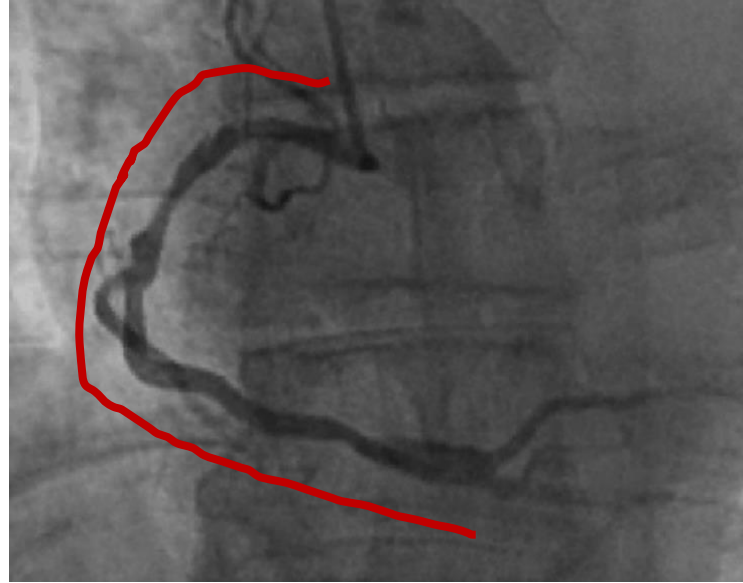
COMPLETE TRIAL

OCT COMPLETE: Imaging Protocol

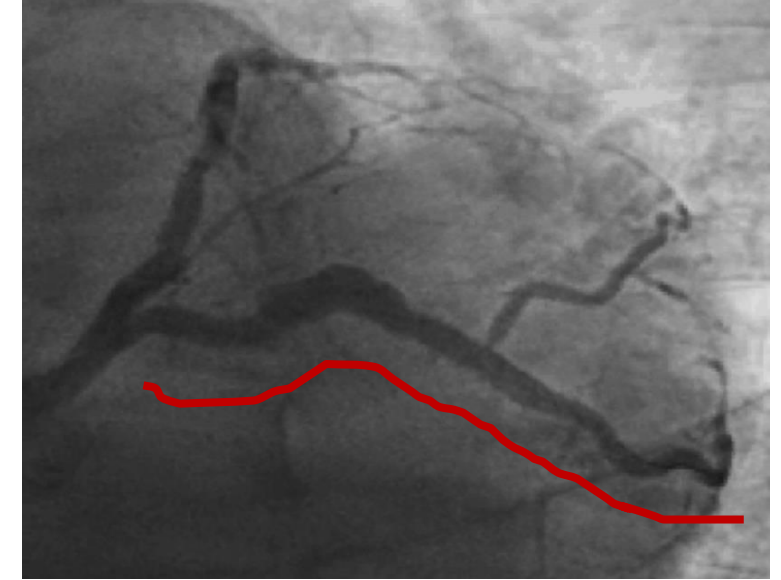
— OCT imaged segment (staged non-culprit PCI procedure)



Target 1 (LAD)
Obstructive NCL



Target 2 (RCA)
Additional vessel
Obstructive or Non-obstructive lesions



Target 3 (LCX)
STEMI vessel
If ≥ 50 mm unstented segment

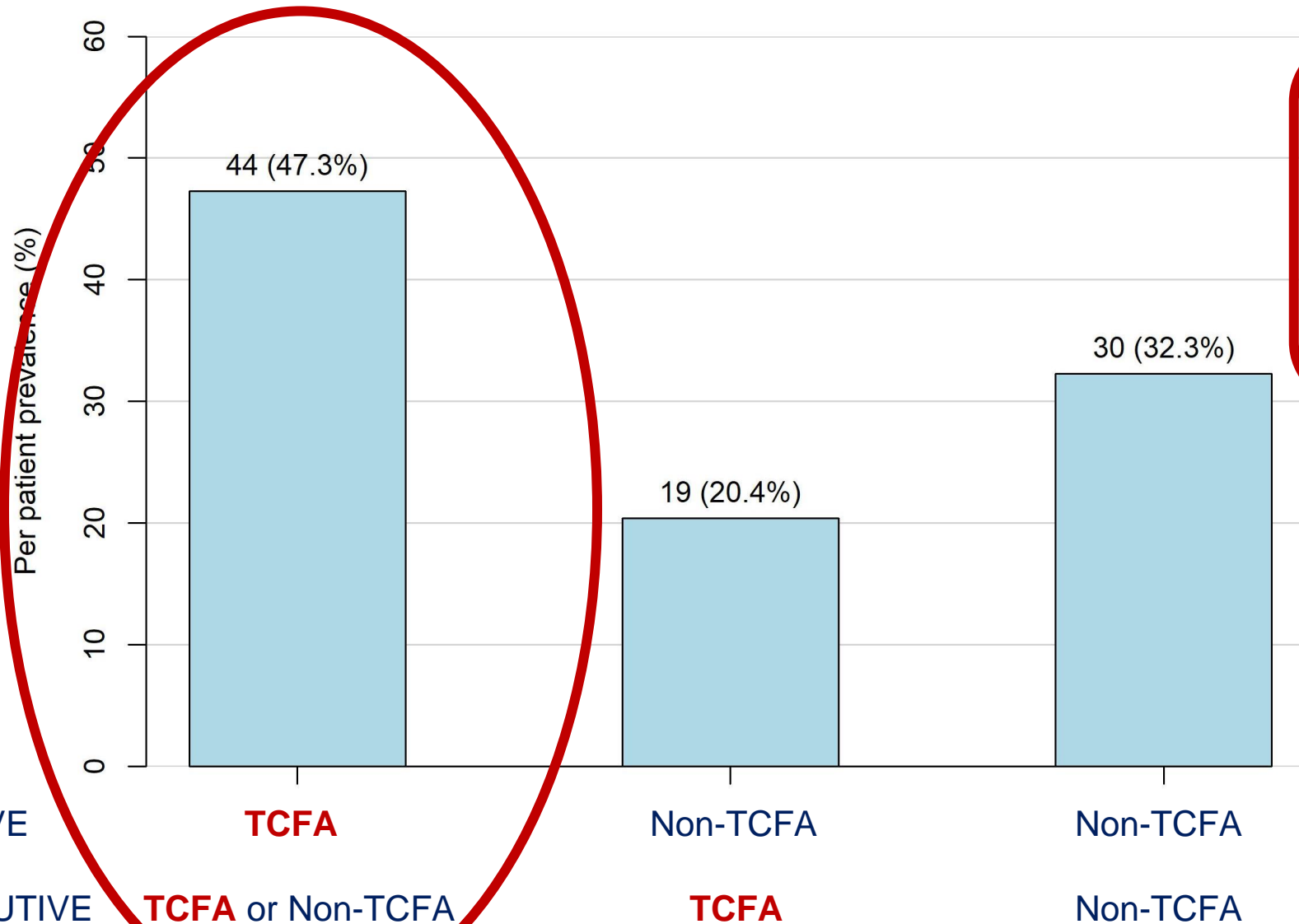
- Number of pullbacks / patient (mean): 2.82
- Imaged length / patient (mean): 152.5 mm

Example: Inferior STEMI
Culprit lesion LCX, Non-culprit lesion LAD



COMPLETE TRIAL

Results: Prevalence of TCFA (per patient)



Half of patients had an obstructive non-culprit lesion containing vulnerable plaque

OBSTRUCTIVE

TCFA

Non-TCFA

Non-TCFA

NON-OBSTRUCTIVE

TCFA or Non-TCFA

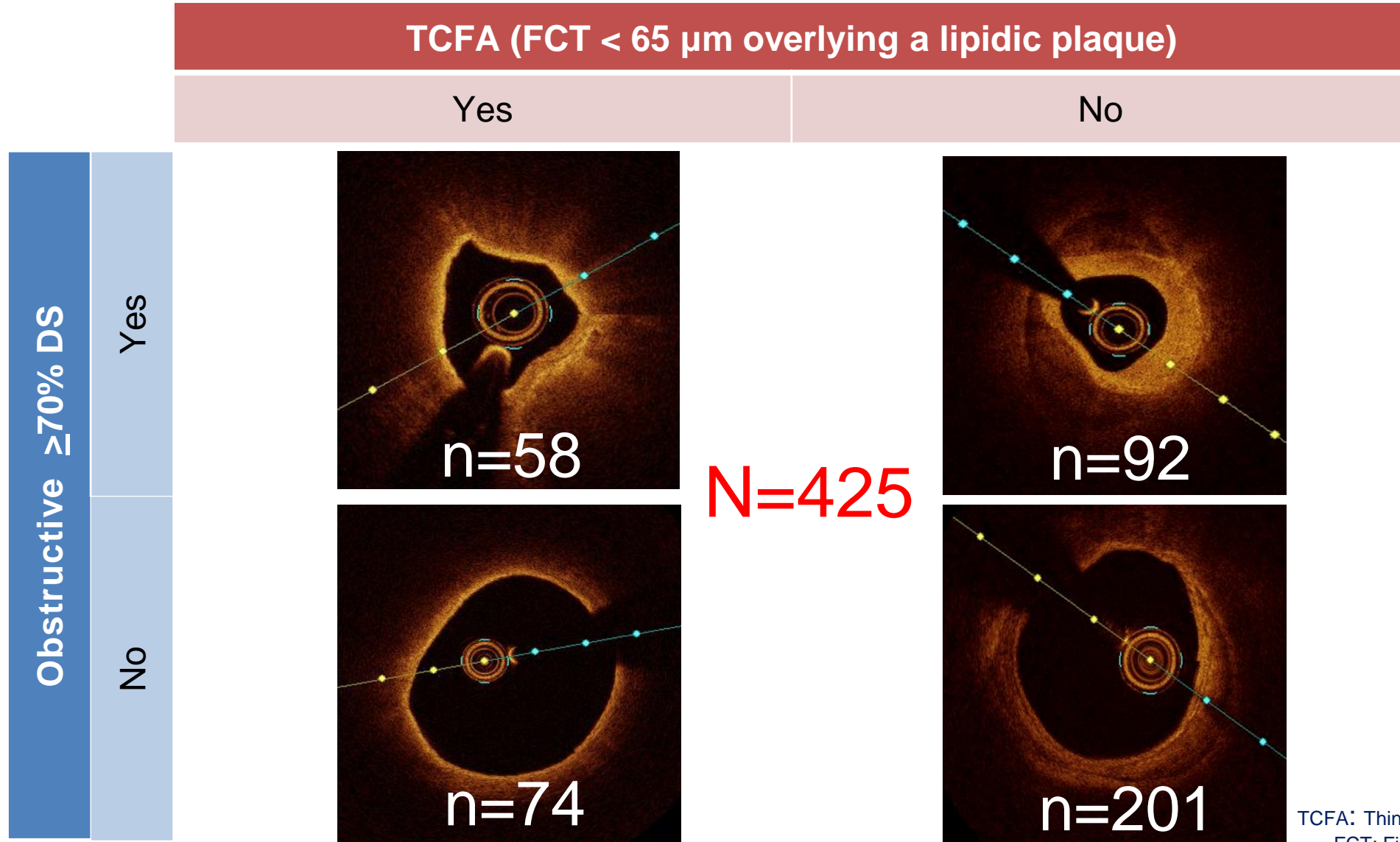
TCFA

Non-TCFA

Classification of non-culprit lesions



COMPLETE TRIAL



TCFA: Thin Cap Fibro Atheroma
FCT: Fibrous Cap Thickness

Results: Features of TCFA vs Non-TCFA in Obstructive lesions ($\geq 70\%$ diameter stenosis)



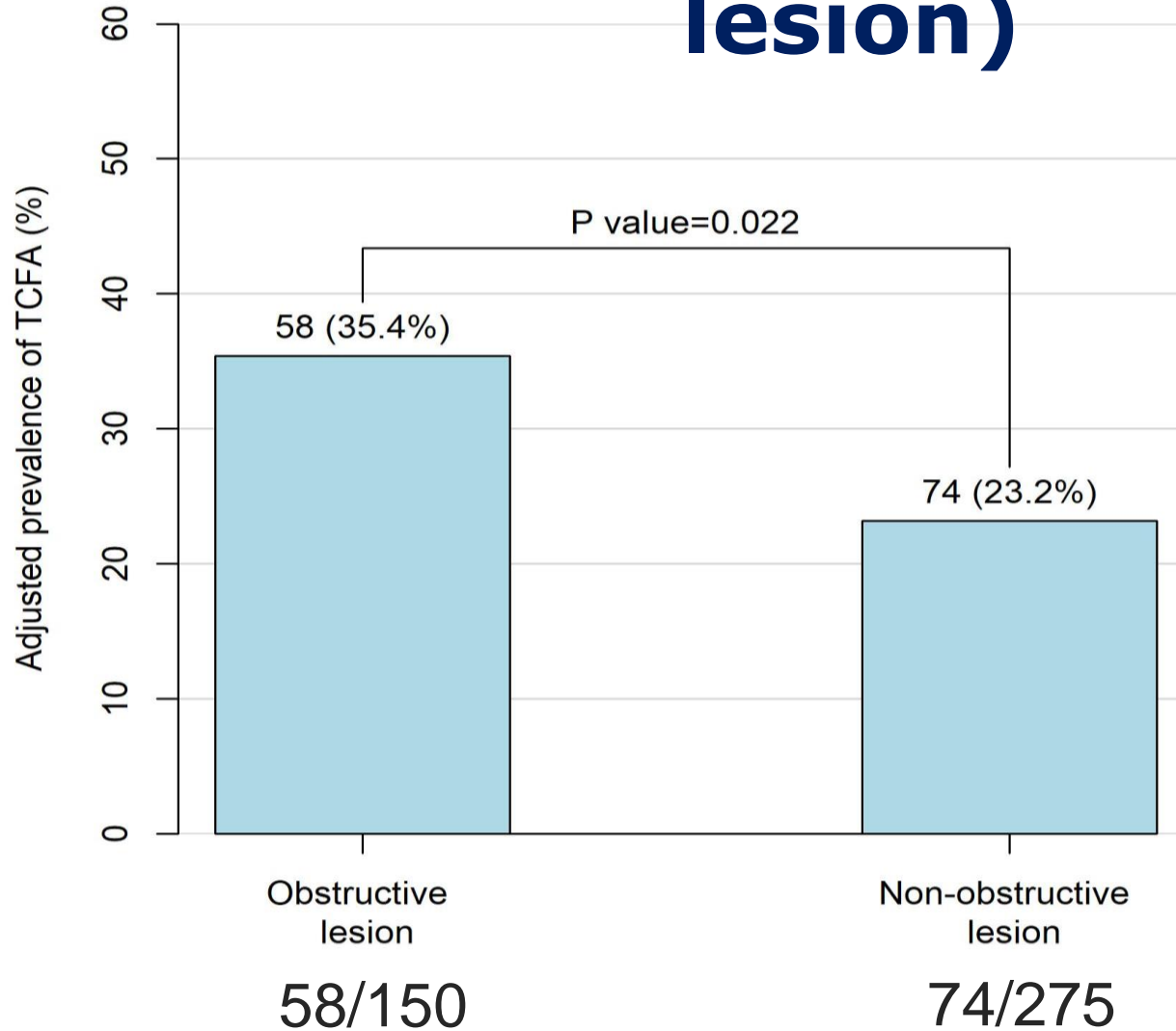
COMPLETE TRIAL

	TCFA (N=58)	Non-TCFA (N=92)	P value
Lesion Length (mm)	23.1	20.8	0.16
Number of LIPID quadrants	55.2	19.2	<0.001
% of LIPID quadrants	78.4	36.5	<0.001
Number of Fibrous quadrants	9.4	21.2	<0.001
% of Fibrous quadrants	16.9	43.7	<0.001
Number of Calcified quadrants	2.5	9.8	<0.001
% of Calcified quadrants	4.1	20.1	<0.001
Maximum Lipid Arc	342.2	212.5	<0.001
Mean Lipid Arc	203.8	84.5	<0.001
Mean FCT (μm)	54.5	152.2	<0.001
Minimum Lumen Area	1.9	1.7	0.52
Macrophages	55	48	<0.001
Microvessels	19	28	0.77
Cholesterol Crystals	48	42	<0.001

Obstructive TCFA lesions had significantly more lipid and more features of plaque vulnerability compared with non-obstructive TCFA lesions

TCFA: Thin Cap Fibro Atheroma

Primary Outcome: Prevalence of TCFA (per lesion)

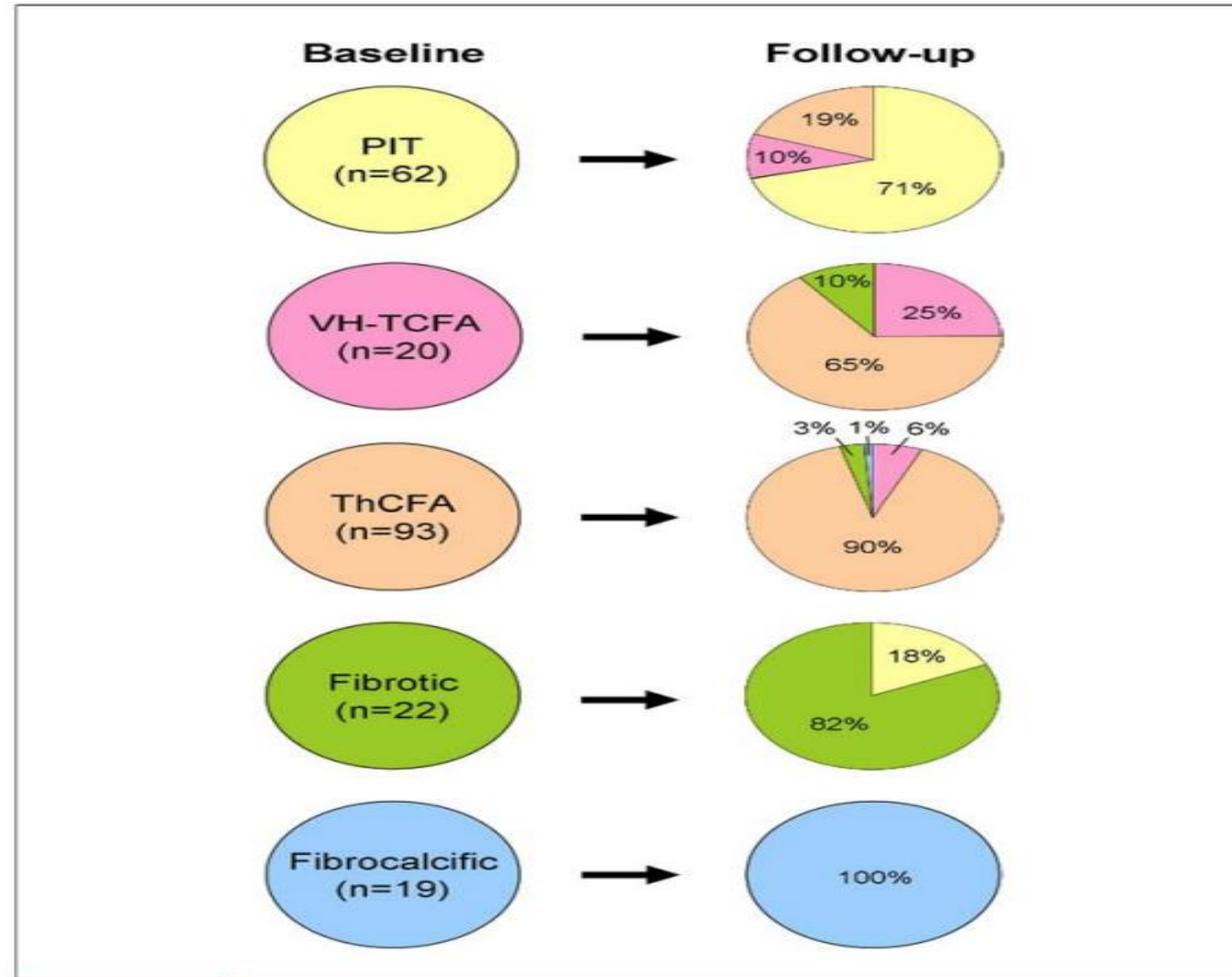


Obstructive non-culprit lesions are most likely to be vulnerable

TCFA: Thin Cap Fibro Atheroma

Non-Culprit Lesions are Dynamic: Retrospective VH-IVUS Study

Serial (baseline and 12-month follow-up) VH-IVUS examined 216 nonculprit lesions (plaque burden 40%) in 99 patients

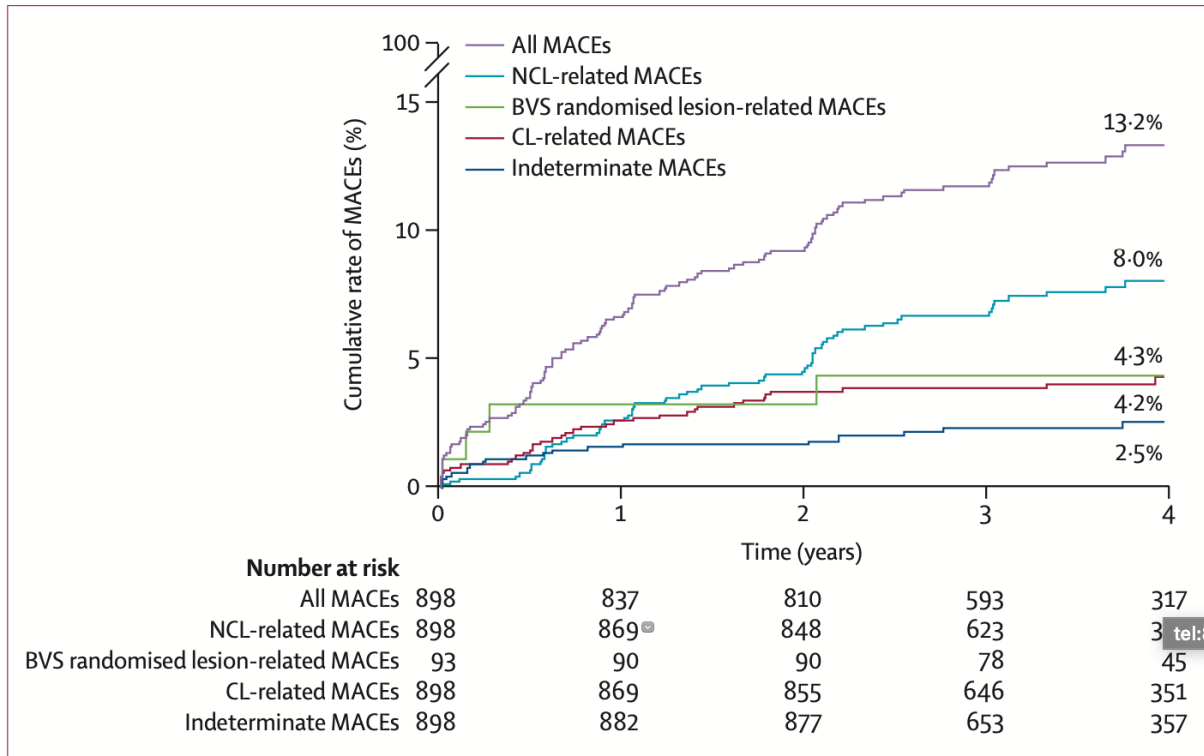




COMPLETE-2

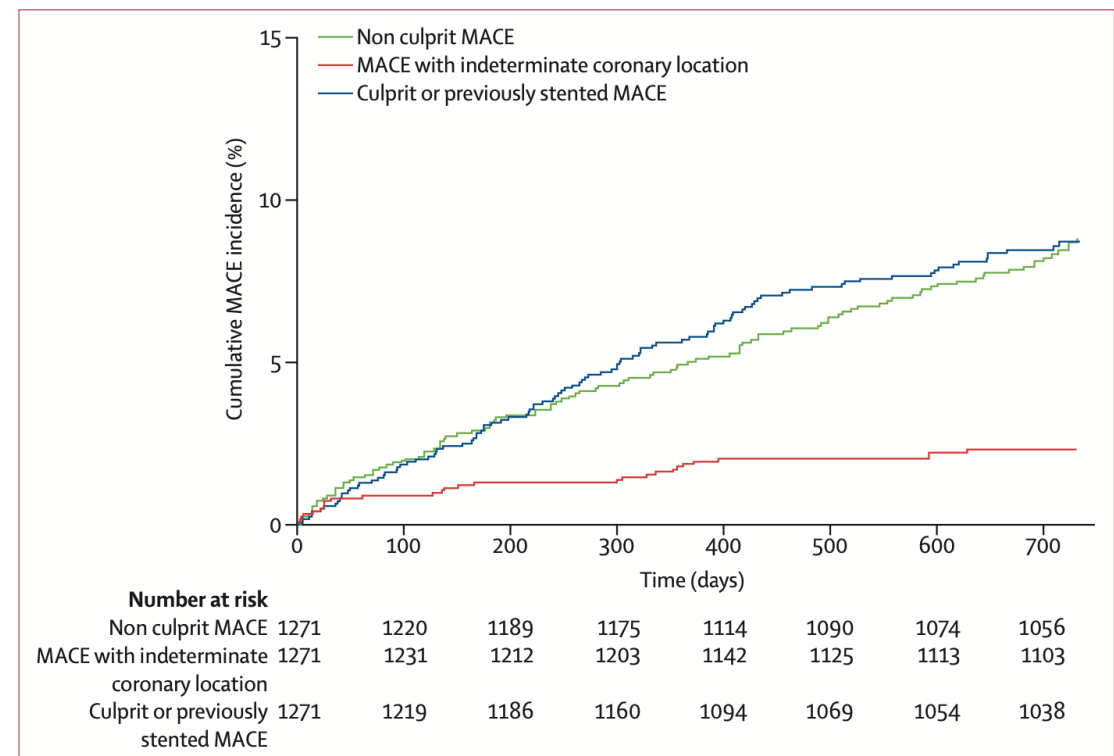
Prospective multivessel imaging studies needed to evaluate Culprit vs Non-culprit vs indeterminate MACE

Prospect 2 N=898



Erlinge et al. Lancet. 2021;397:985

Lipid Rich Plaque Study N=1271



Waksman et al. Lancet. 2019;394:1629-37.

No similar study conducted with OCT



COMPLETE-2 Study Design

STEMI or NSTEMI with Multivessel Coronary Artery Disease

At least one additional non-culprit lesion ≥ 2.5 mm diameter and $\geq 50\%$ stenosis

$N=5100$

Randomization

Stratified by STEMI or NSTEMI, single sitting or staged NCL PCI

Physiology-Guided NCL PCI

Routine PCI of all physiological positive lesions with the goal of complete revascularization

$n=2550$

Angiography-Guided NCL PCI

Routine PCI of all angiographical suitable lesions with the goal of complete revascularization

$n=2550$

OCT Substudy (Optional)

Primary Objective: Whether vulnerable plaque (lipid-rich plaque and thin cap fibroatheroma) as identified by OCT imaging predicts CV death, new MI, TLR, or unstable angina (related to a non-stented lesion)

$N=1510$

**Follow-up twice yearly
Median approx. 3.5 Years**



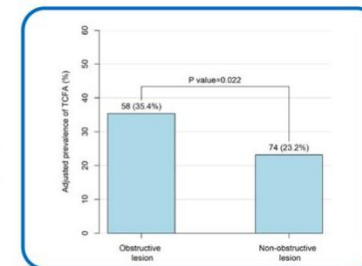
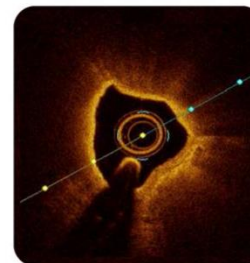
COMPLETE-2 OCT: A large-scale intracoronary imaging study

Primary Objective: To determine, in patients with STEMI or NSTEMI and multivessel CAD, whether vulnerable plaque, as identified by OCT imaging, predicts major cardiovascular events

Design: *Large-scale, prospective, observational, multicentre, imaging study of patients with STEMI or NSTEMI and multivessel CAD*

Sample Size: 1510 patients

Primary Outcome: Composite of CV death, new MI, unstable angina, or target lesion revascularization (TLR) related to a non-stented lesion at the *patient* level





COMPLETE-2

Recommended workflow for stent placement for OCT substudy patients

Pre-PCI OCT | Strategize



Post-PCI OCT | Optimize



M

Morphology

Search for High Calcium¹

Criteria:
>180 degrees, and
>0.5 mm thickness, and
>5 mm in length

L

Length

Select Landing Zones
Based on Healthy Tissue/
EEL Visualization²

Place landing zones in
healthy tissue (i.e. EEL
visualization)

Note: In the absence of EEL to
represent healthy tissue find
the largest lumen to avoid
areas of T CFA or lipid pools so
as to not land our stent edge
in these high-risk areas³

D

Diameter

Measure Vessel, Stent,
Balloon Diameters⁴

Use distal reference
measurements to select
stent diameter

Use distal reference
measurement for distal
balloons or proximal
reference measurements
for proximal balloons

M

Medial Dissection

Address Significant
Dissection⁵

Criteria:
Dissection penetrates
medial layer, and is greater
than 1 quadrant arc

A

Apposition

Address Gross
Malapposition

Criteria:
Malapposition indicator
shows longer than 3 mm⁴
of significant (≥ 0.3 mm
from wall⁵) apposition

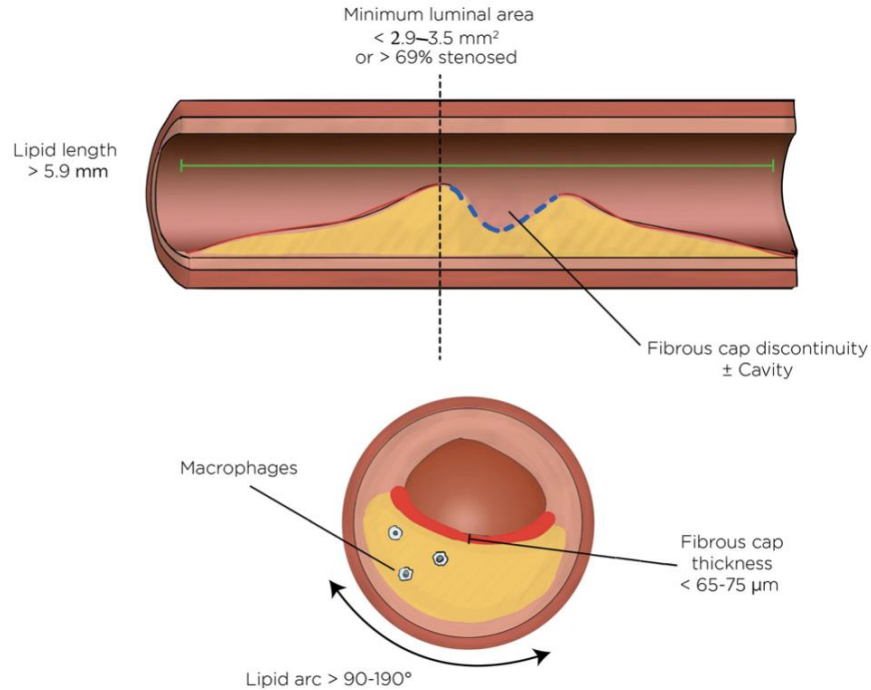
X

Xpansion

Confirm Expansion^{2,6}

Criteria:
 $\geq 80\%$ acceptable,
 $\geq 90\%$ expansion is optimal

COMPLETE-2 OCT



Study	Year	No. patients	Study design
Iannaccone et al ⁵⁸	2018	209	Retrospective, multicenter
Xing et al ⁶¹	2017	1,474	Retrospective multicenter
Araki et al ⁵⁹	2020	248	Retrospective, single center
Prati et al ⁵	2020	1,003	Prospective, multicenter
Kubo et al ⁶⁰	2021	1,378	Retrospective single center

COMPLETE 2 OCT study will be the first study to assess event prediction based on OCT plaque morphology using a **prospective multivessel imaging protocol**.

Patients with STEMI/NSTEMI and multi-vessel disease constitute a high risk population and frequently have evidence TCFA - a key target population for vulnerable plaque imaging studies.

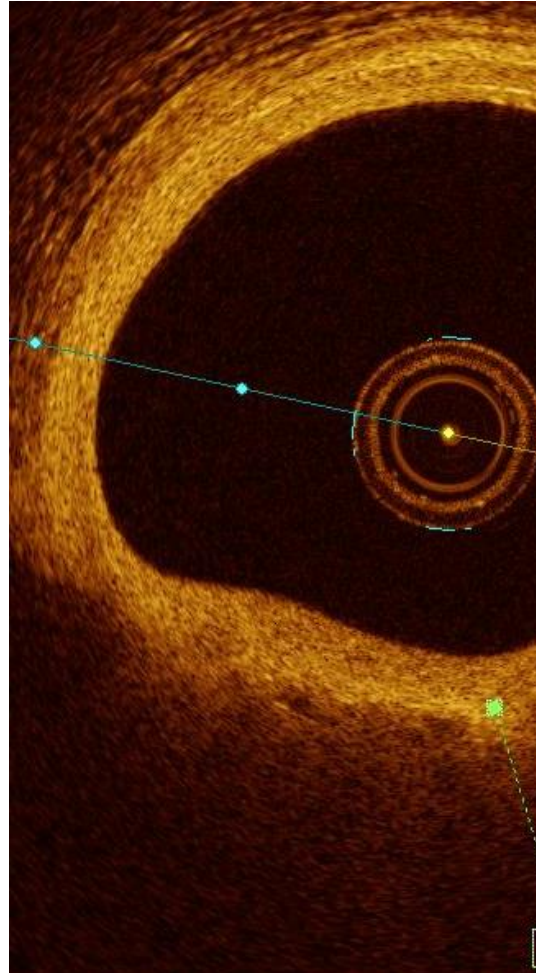


COMPLETE-2

COMPLETE-2 OCT: AI based analysis

The COMPLETE OCT study will help define OCT parameters associated with adverse clinical events that occur despite complete revascularization

Patients with high risk plaques may merit specific therapeutic options to achieve more complete plaque stabilization that is possible with current therapy



1. Lipid-Rich Plaque and Lipid Arc
2. Thin Cap Fibroatheroma (TCFA)
3. Minimum lumen area (MLA)
4. Layered/Healed Plaque

+ AI based analysis



Population Health
Research Institute
HEALTH THROUGH KNOWLEDGE

