Case 2. Anatomy vs. Physiology Approach for Complete Revascularization in ACS?

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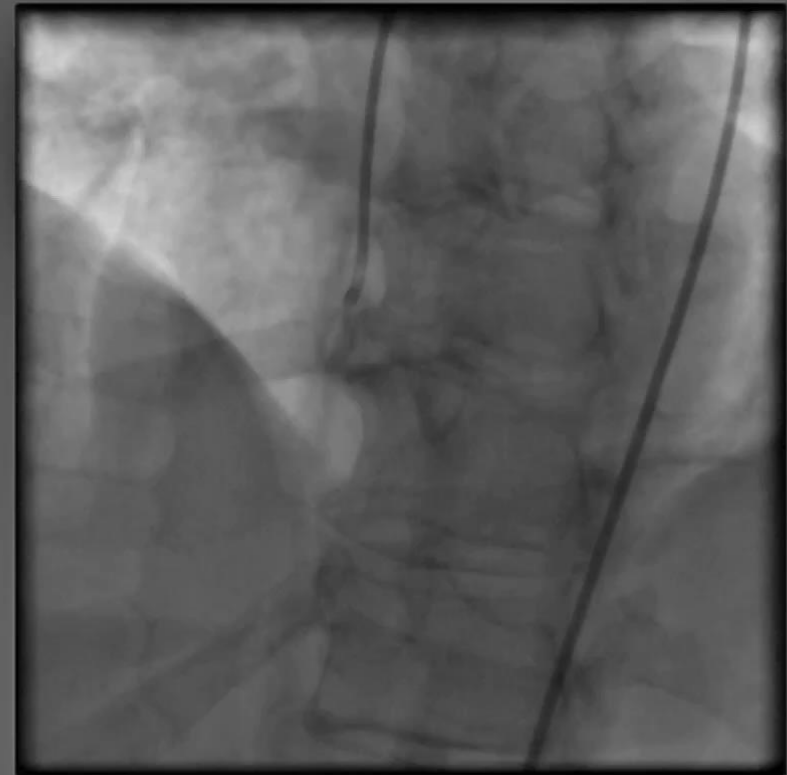Director, Interventional Cardiology

Hamilton Health Sciences

Population Health Research Institute
HEALTH THROUGH KNOWLEDGE

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McMaster University HEALTH SCIENCES

49 yo male presenting with Inferior STEMI, 2 h RSCP, transferred for primary PCI

49 yo male presenting as an Inferior STEMI, non-culprit lesion 80% LAD, 50-70% Circ

4 Years Later

New onset severe RSCP, diaphoresis, called 911. ECG on scene
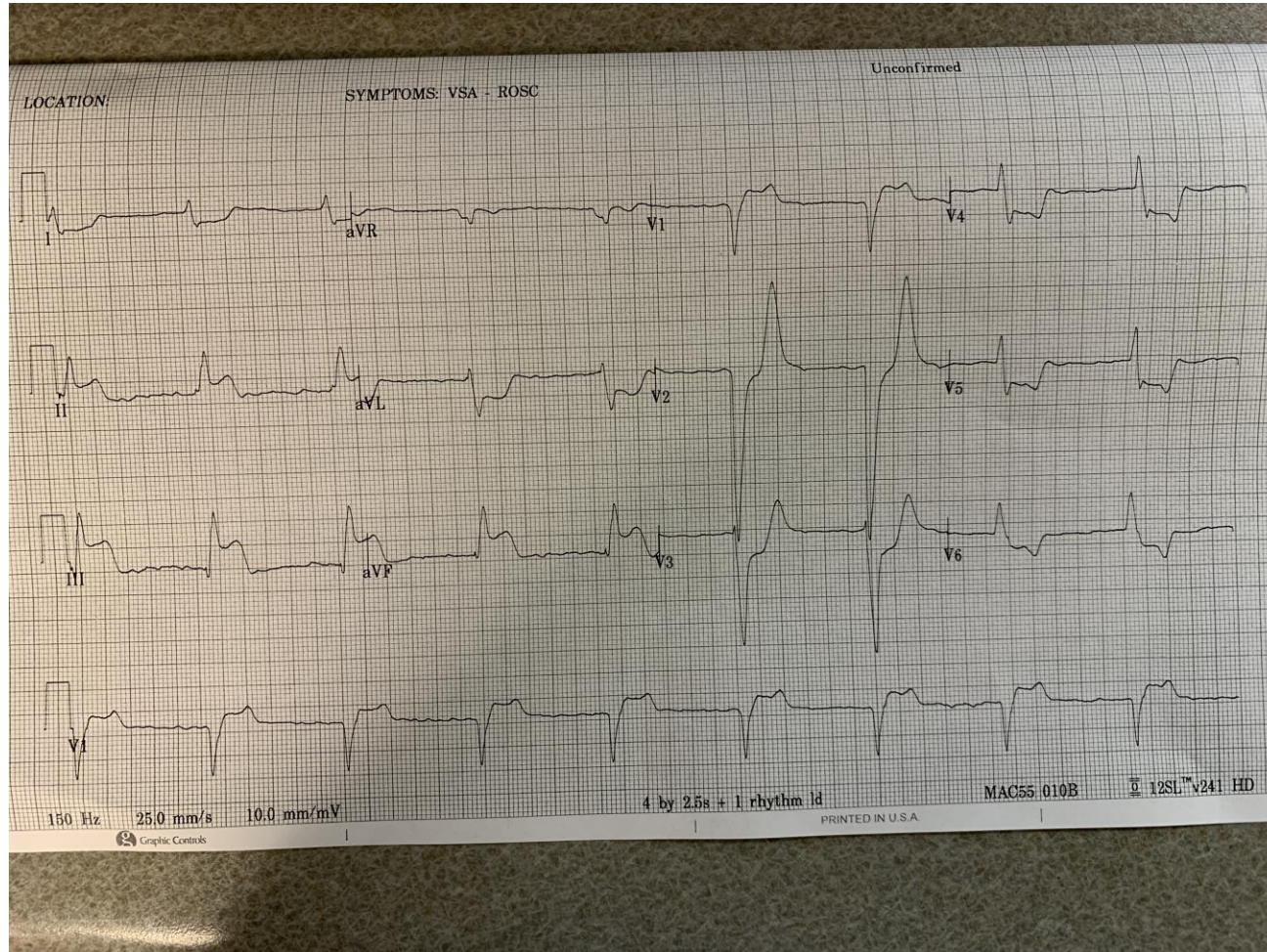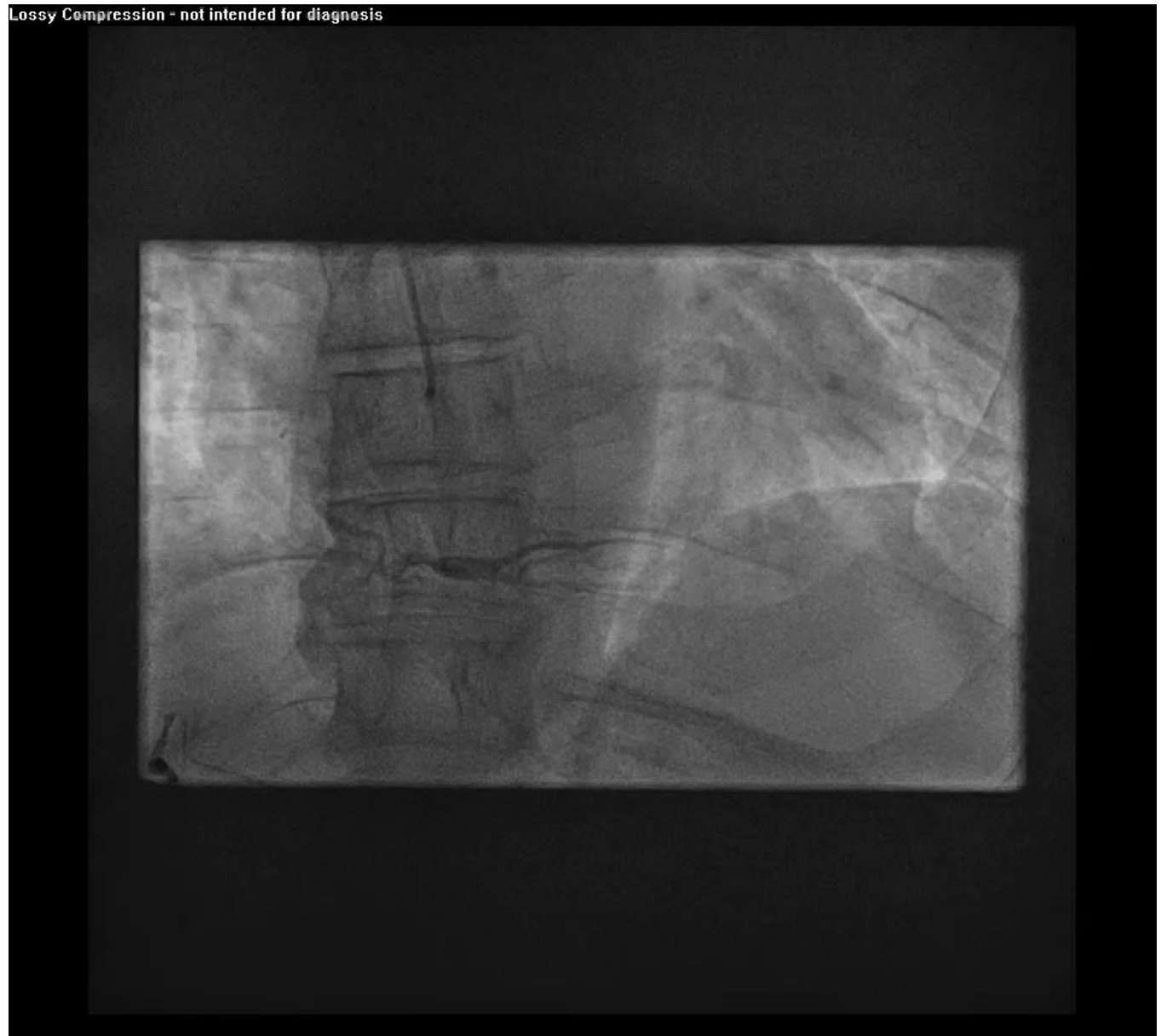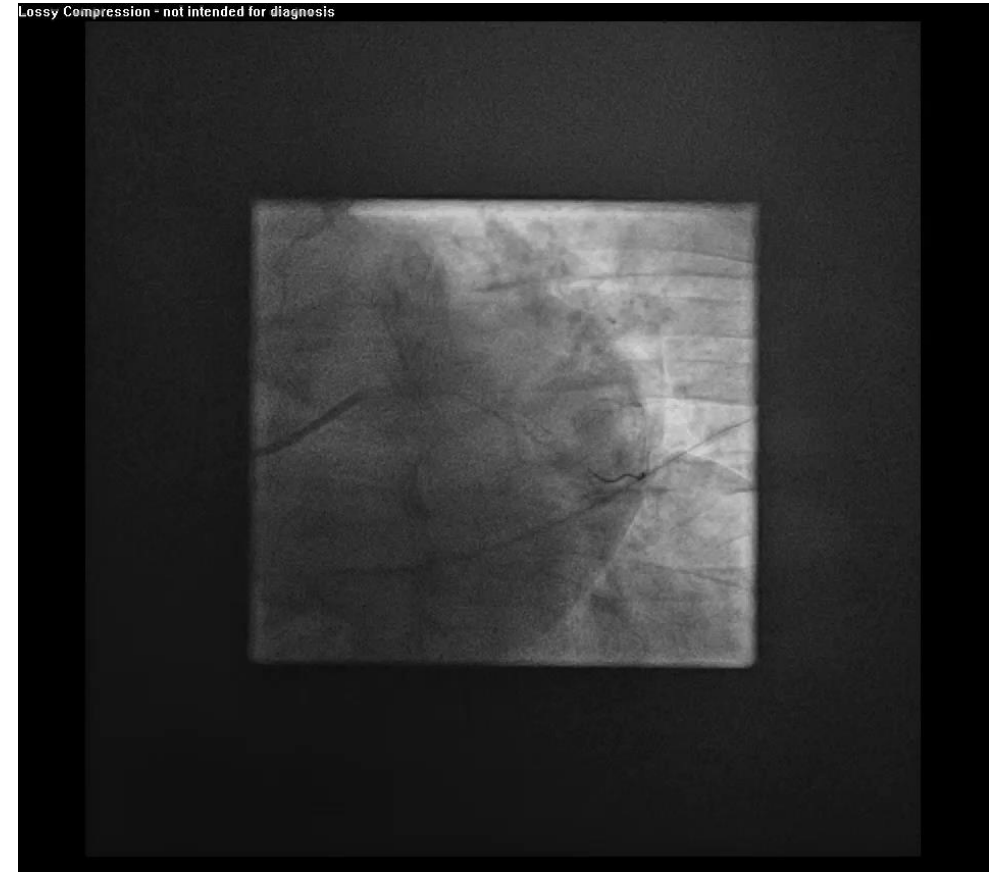
4 Years Later: 53 yo male presenting as an Inferior STEMI, patent RCA

Lossy Compression - not intended for diagnosis

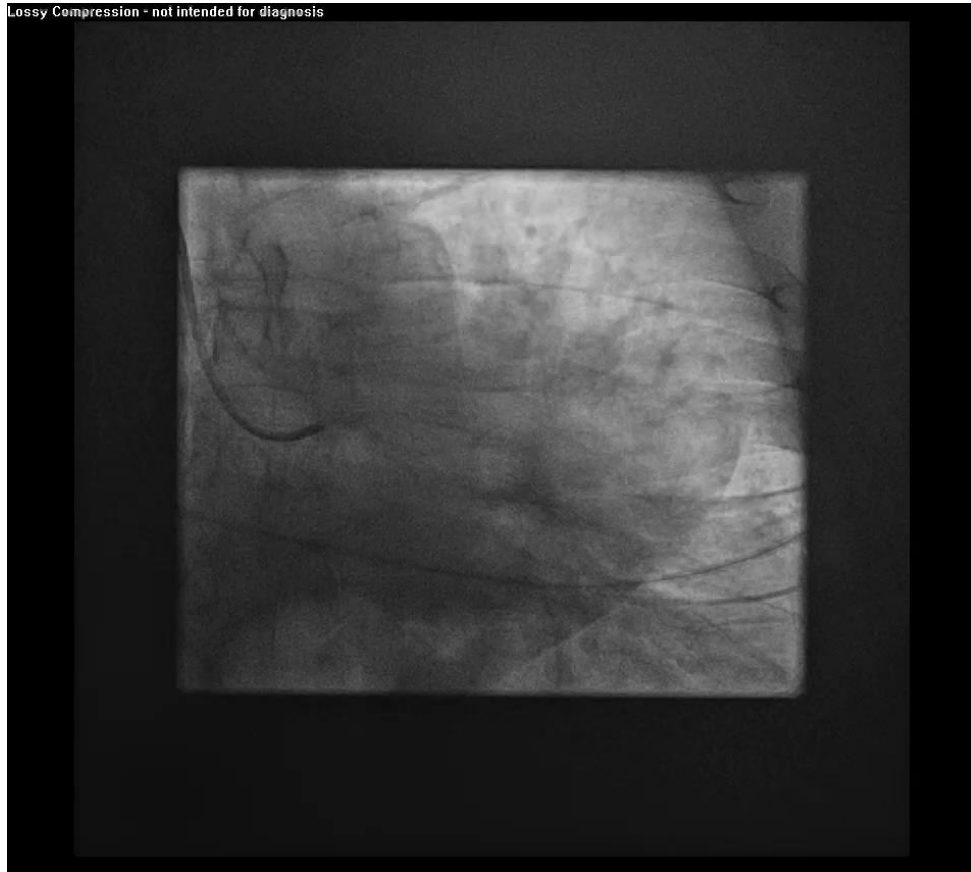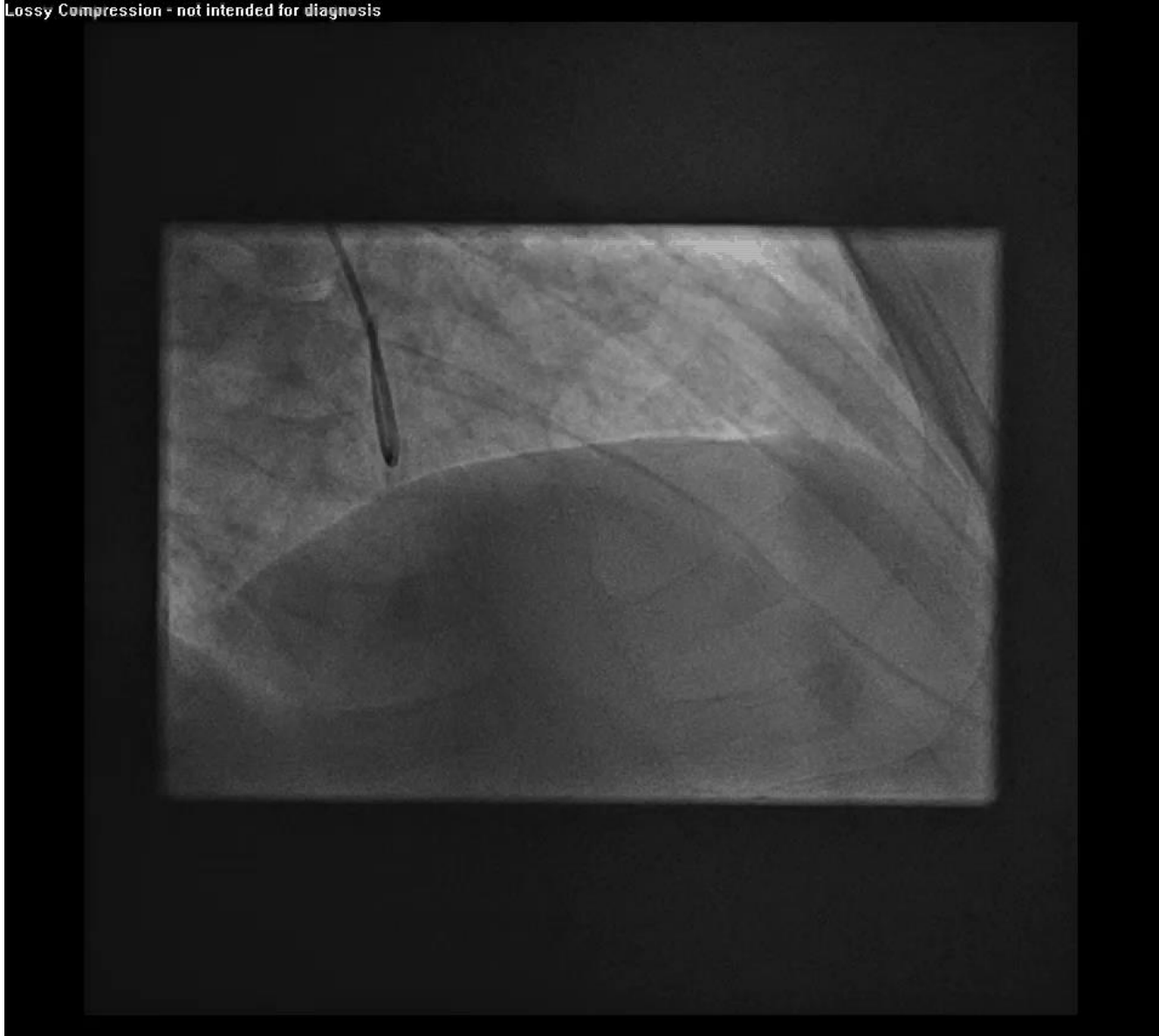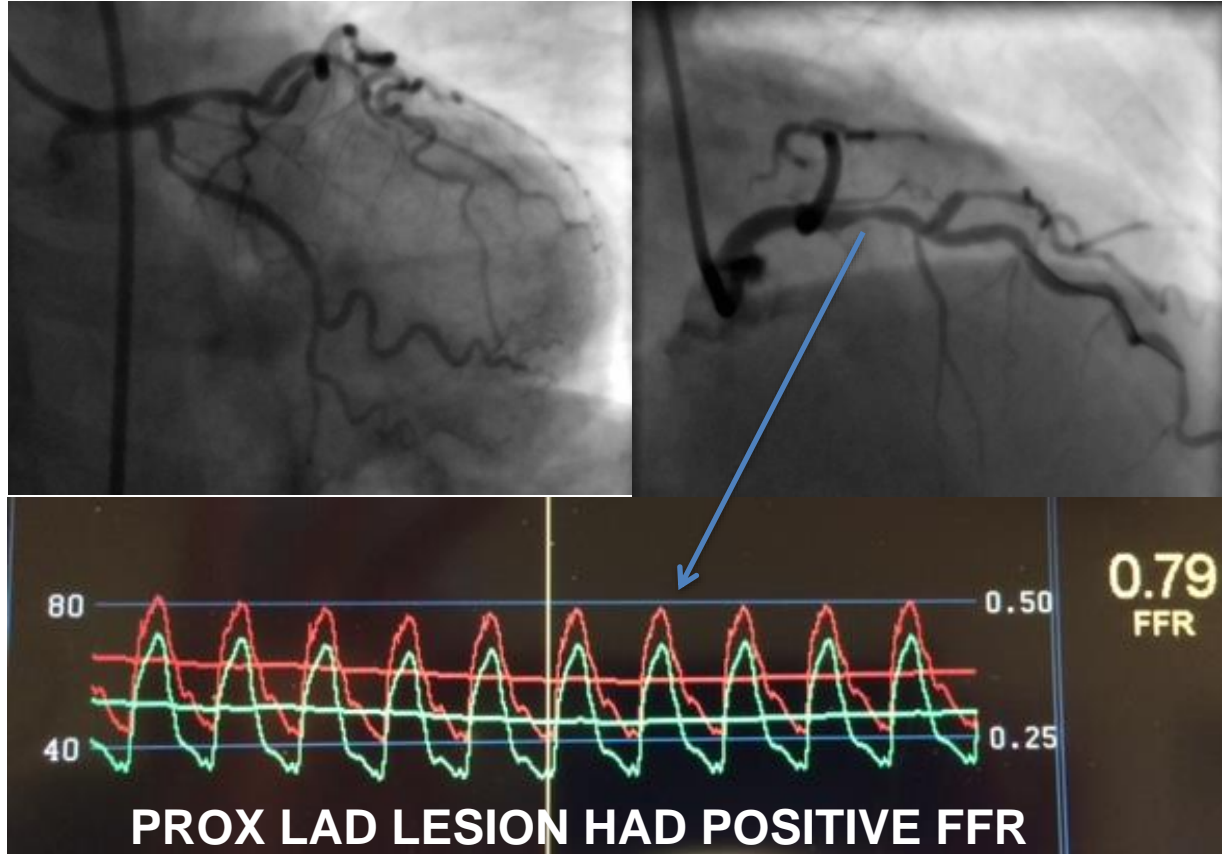# 4 Years Later: 53 yo male presenting as an Inferior STEMI, culprit lesion LCx

53 yo male presenting as an Inferior STEMI, non-culprit lesion LAD unchanged

What predicts future events from NCL's? Physiology vs Anatomy (biology)

FCT: Fibrous Cap Thickness < 65 µm

PROX LAD LESION HAD POSITIVE FFR

0.79 FFR

Overlying a lipidic plaque
Lipid arc > 90°
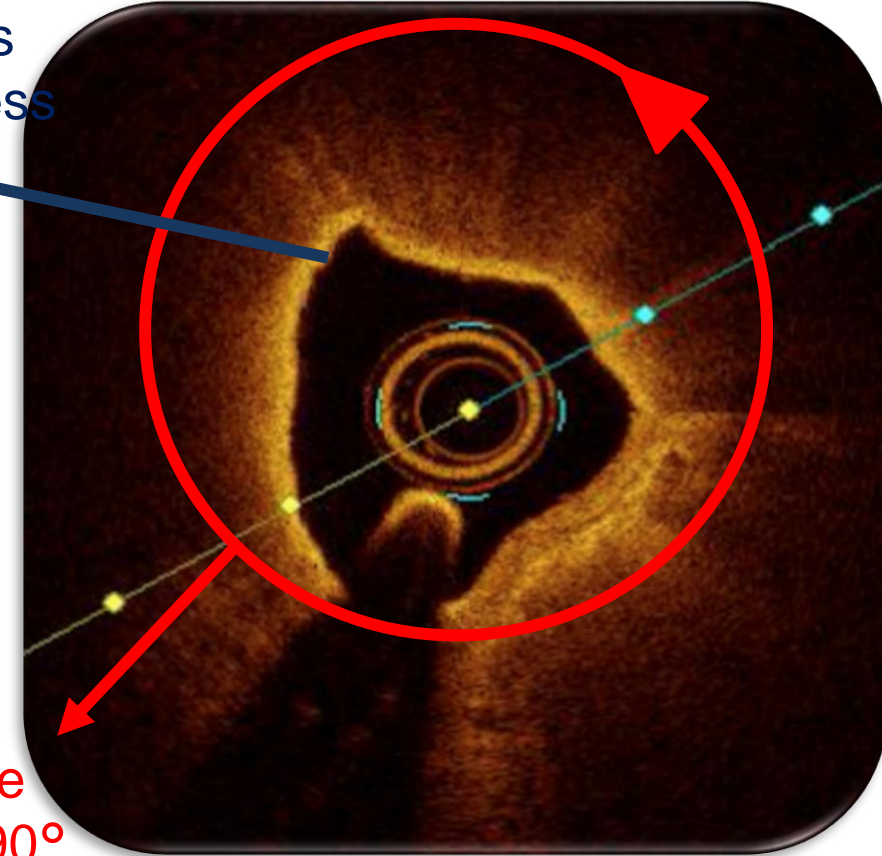
Understanding plaque morphology of non-culprit lesions in relation to physiology/angiography/image-guided revasc

Stable CAD

ACS Non-culprit

STEMI culprit

**Fibro-calcific plaques
Low Risk of Rupture**

**Plaque Rupture
Medical Emergency**

Lumen

Endothelium

• Small Lipid Core
• Few Macrophages
• No thrombus

Thick Fibrous Cap

**50% are TCFA
50% are stable plaques**

Thrombus

Platelets

• Necrotic Lipid Core
• Inflammatory Cells/Macrophages

Thin Fibrous Cap

Physiology-Guided Strategy Standard

Physiology vs Angiography Guided Strategy?
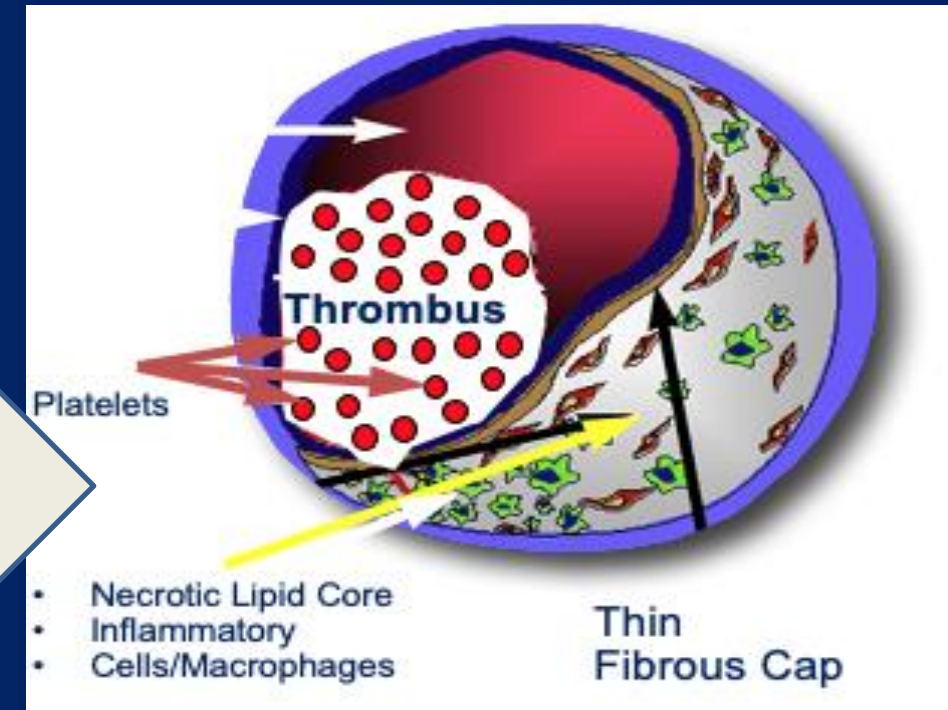
Angiography-Guided Revas Standard (PPCI)

COMPLETE Trial: Primary Outcomes

Complete revascularization was achieved in **90.1%** after NCL PCI (SYNTAX score = 0)

CV Death or New MI

Hazard Ratio 0.74
95% CI 0.60-0.91
P=0.004

NNT (median 3 years) = 37
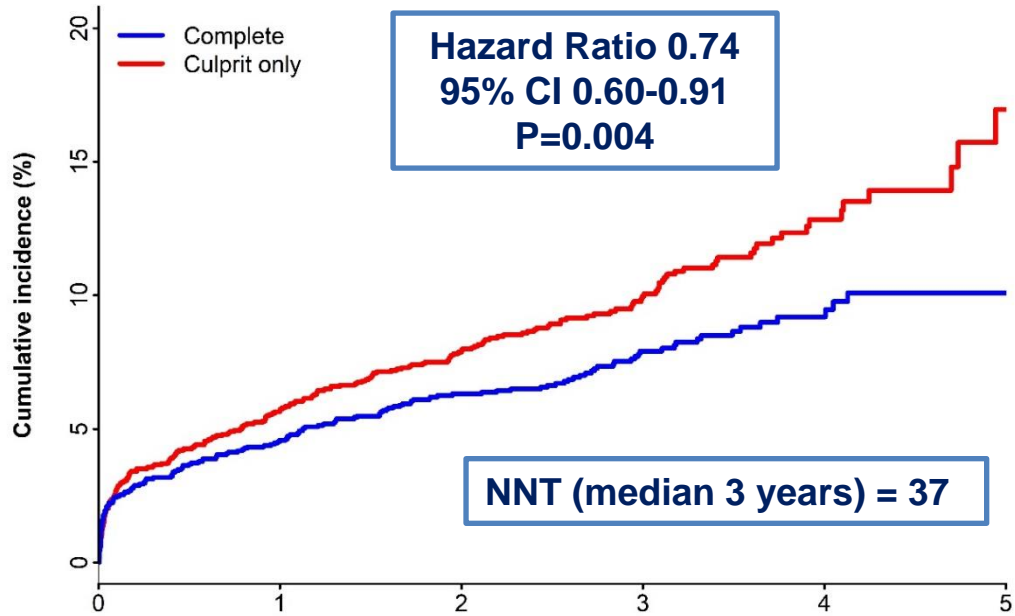
No. at Risk					
Complete	2016	1904	1677	938	337	70
Culprit only	2025	1897	1666	933	310	59

CV Death, New MI, or IDR

Hazard Ratio 0.51
95% CI 0.43-0.61
P < 0.001

NNT (median 3 years) = 13
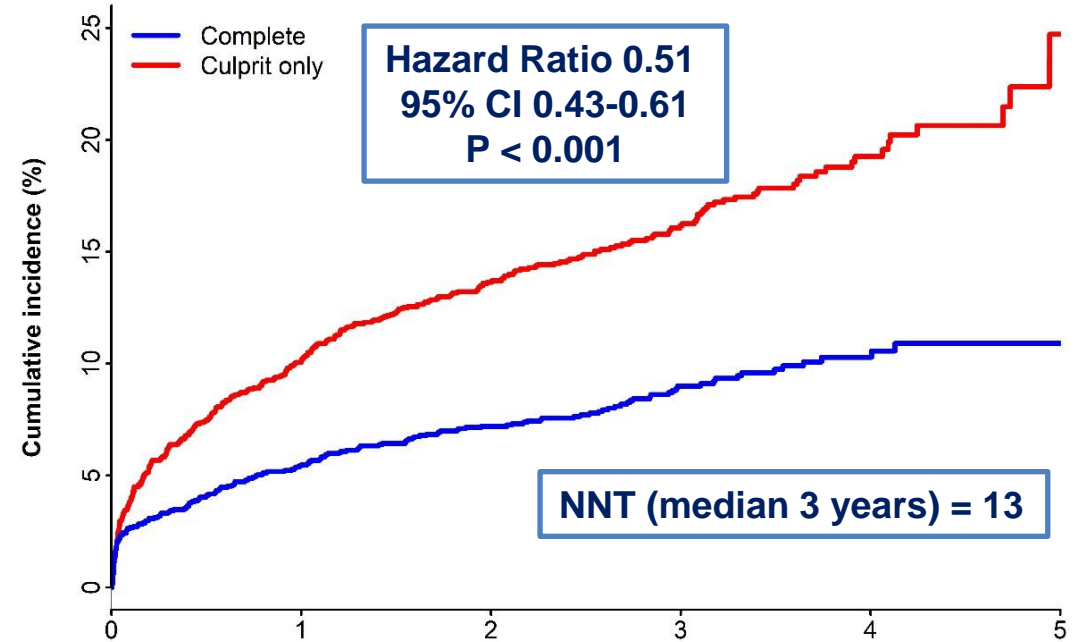
No. at Risk					
Complete	2016	1886	1659	925	329	66
Culprit only	2025	1808	1559	865	294	57

Mehta SR et al. *N Engl J Med* 2019

Outcomes by NCL Stenosis QCA Severity: Greater Benefit if Tighter NCL's

CV Death and New MI

Sheth T et al. *J Am Coll Cariol.* 2020
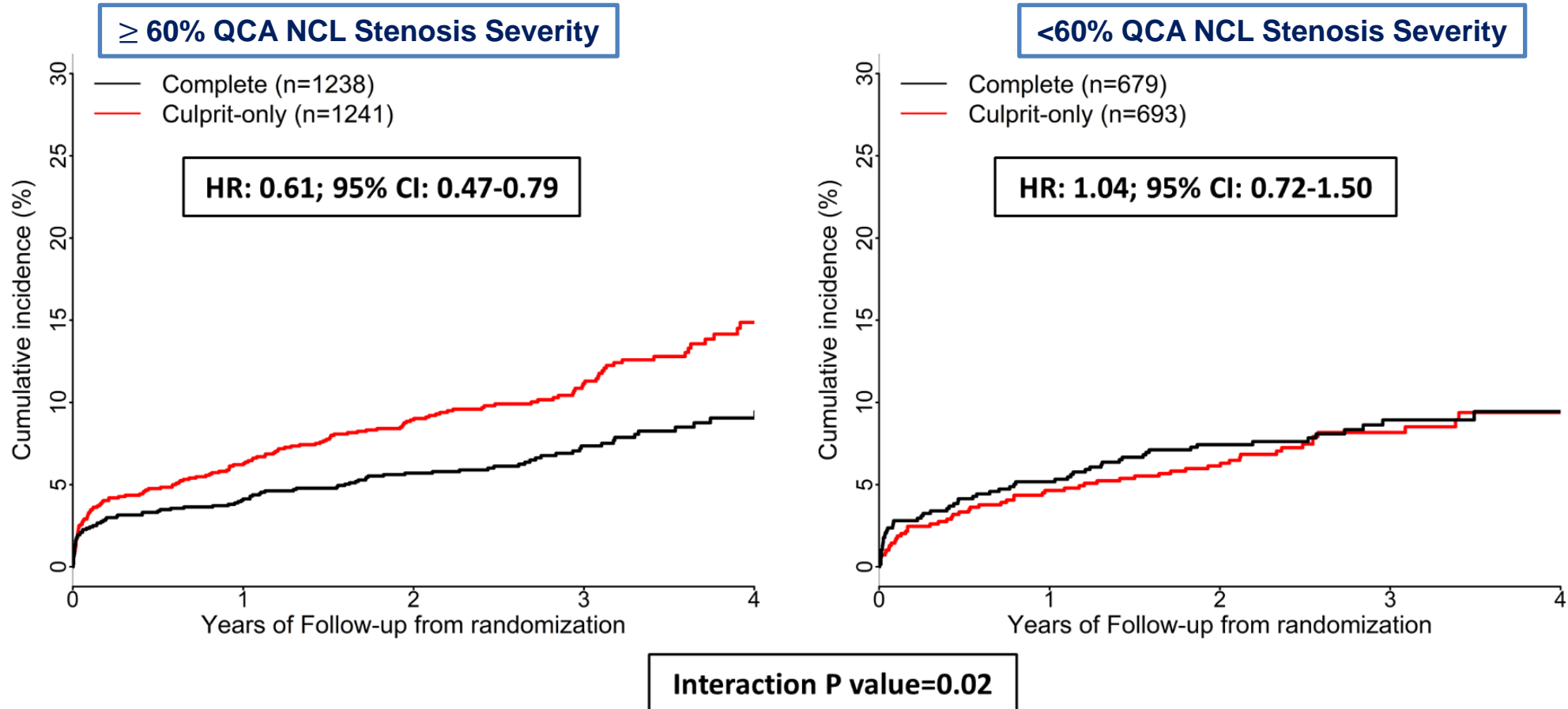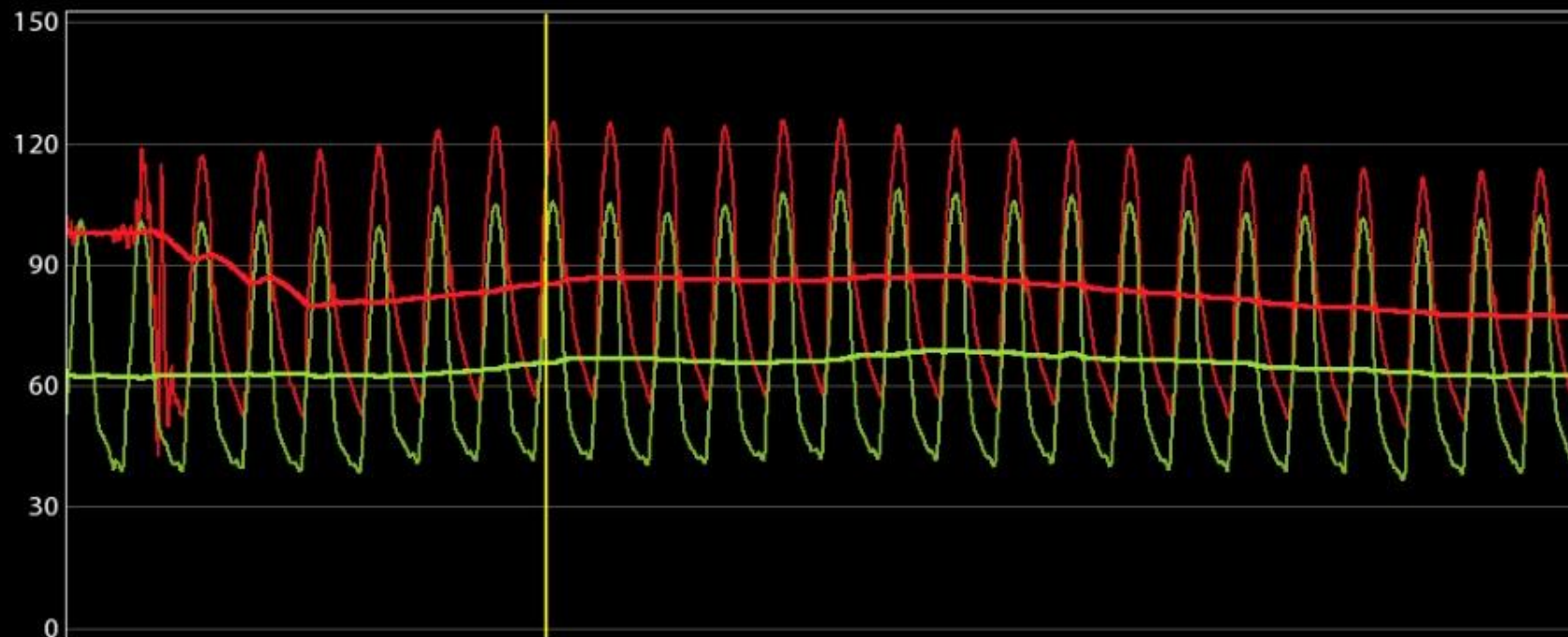
Pa **86**

Pd **66**

FFR **0.77**

Time **6.5**

10:13 FFR 0.90
10:11 FFR 0.90
10:06 FFR 0.77
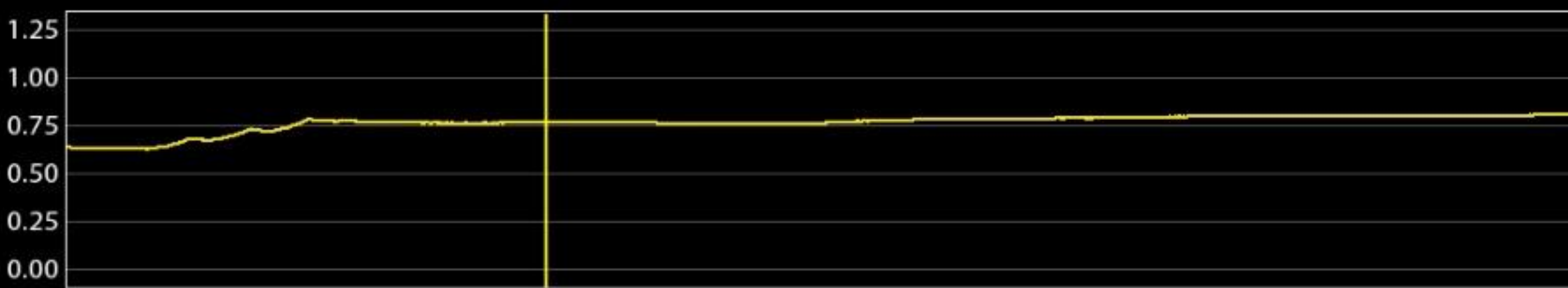
<Vessel>   <Step>   <Drug>   1/3   10:06:41

Live ▶

Patient   Live   Review   Archive

OCT COMPLETE: Imaging Protocol

— OCT imaged segment (staged non-culprit PCI procedure)
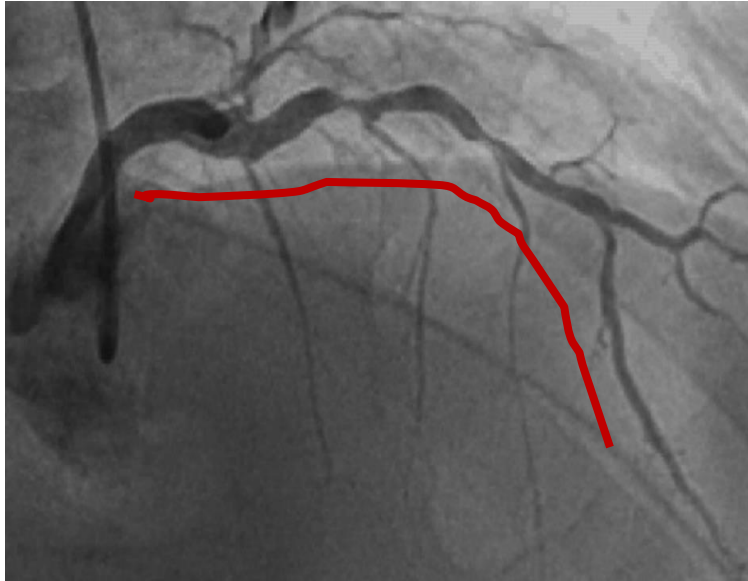
Target 1 (LAD)
Obstructive NCL
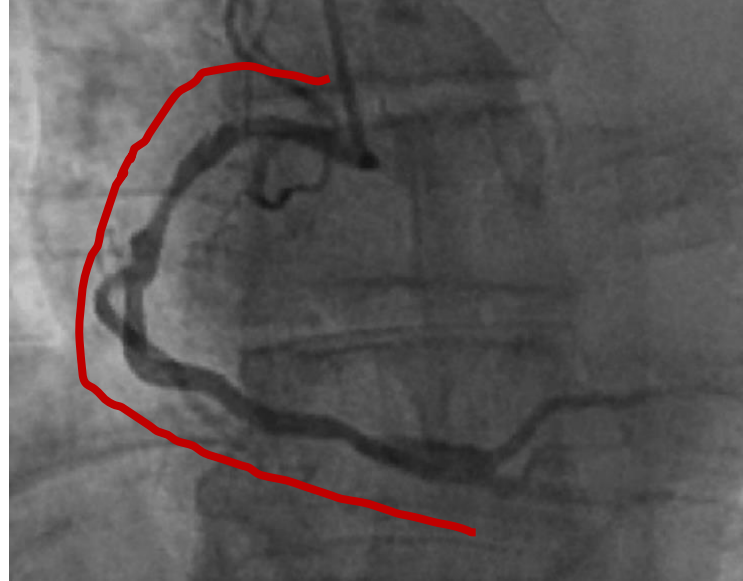
Target 2 (RCA)
Additional vessel
Obstructive or Non-obstructive lesions
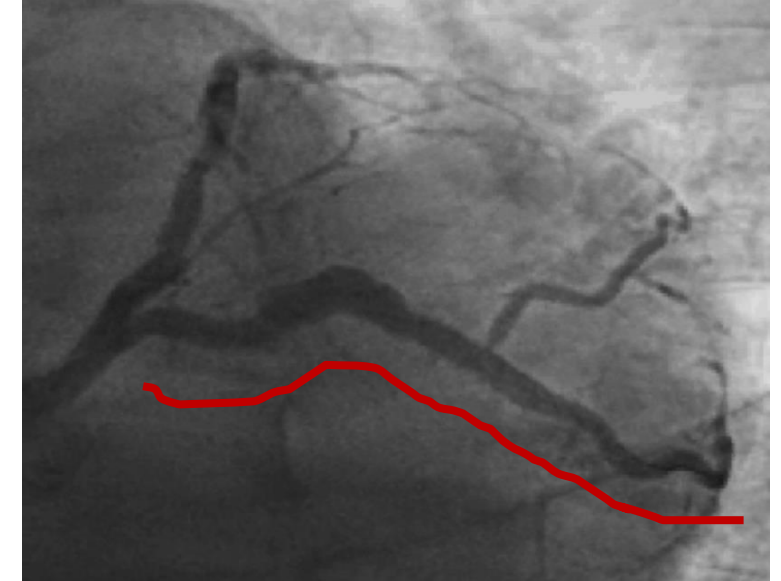
Target 3 (LCX)
STEMI vessel
If $\geq$ 50 mm unstented segment

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

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

Pinilla-Echeverri, N et al. Circ Cardiovasc Int 2020

Results: Prevalence of TCFA (per patient)
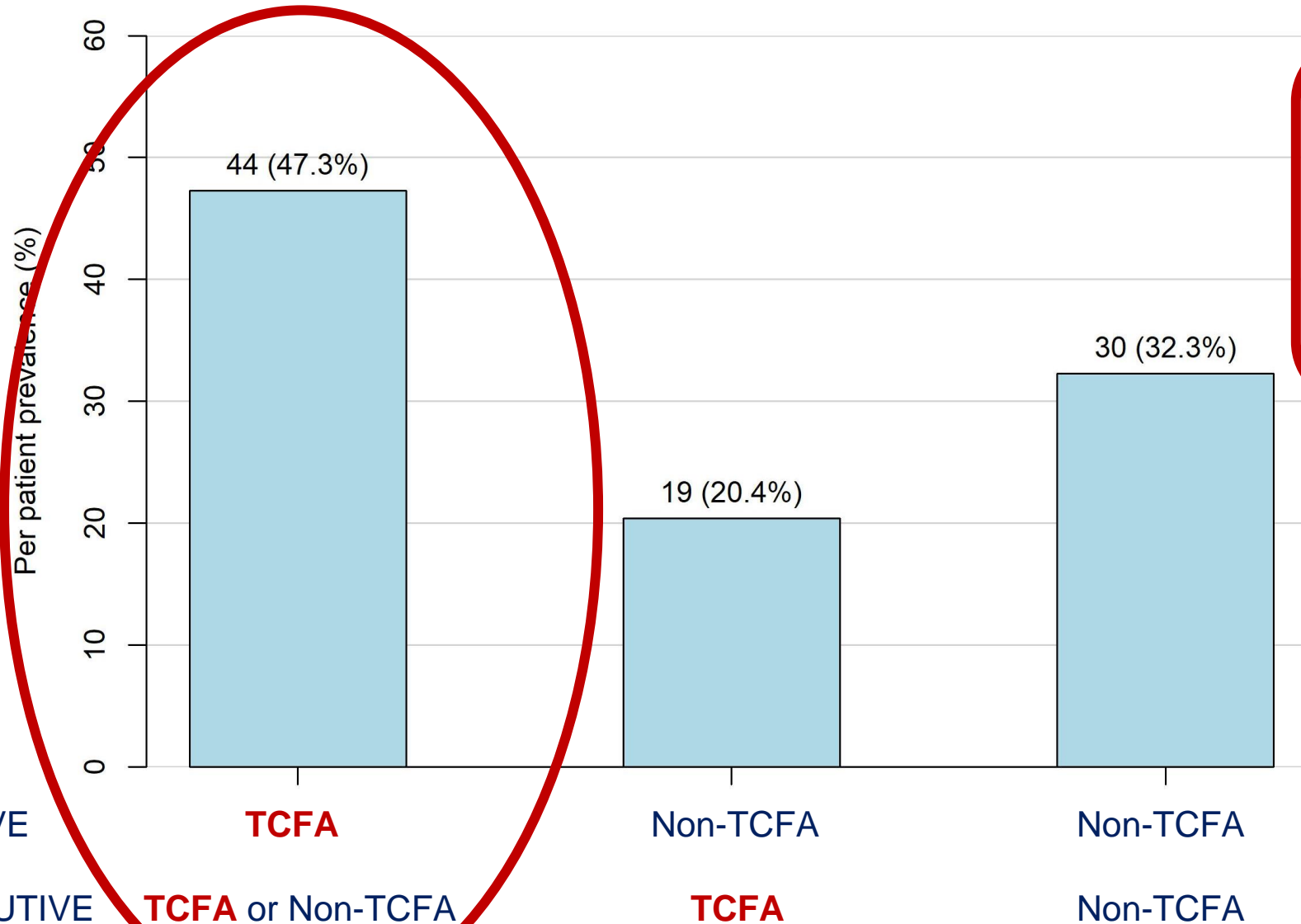
Half of patients had an obstructive non-culprit lesion containing vulnerable plaque

44 (47.3%)

19 (20.4%)

30 (32.3%)

Per patient prevalence (%)

| OBSTRUCTIVE | TCFA | Non-TCFA | Non-TCFA |
| NON-OBSTRUTIVE | TCFA or Non-TCFA | TCFA | Non-TCFA |

Pinilla-Echeverri, N. Circ Cardiovasc Int. 2020

Primary Outcome: Prevalence of TCFA (per lesion)
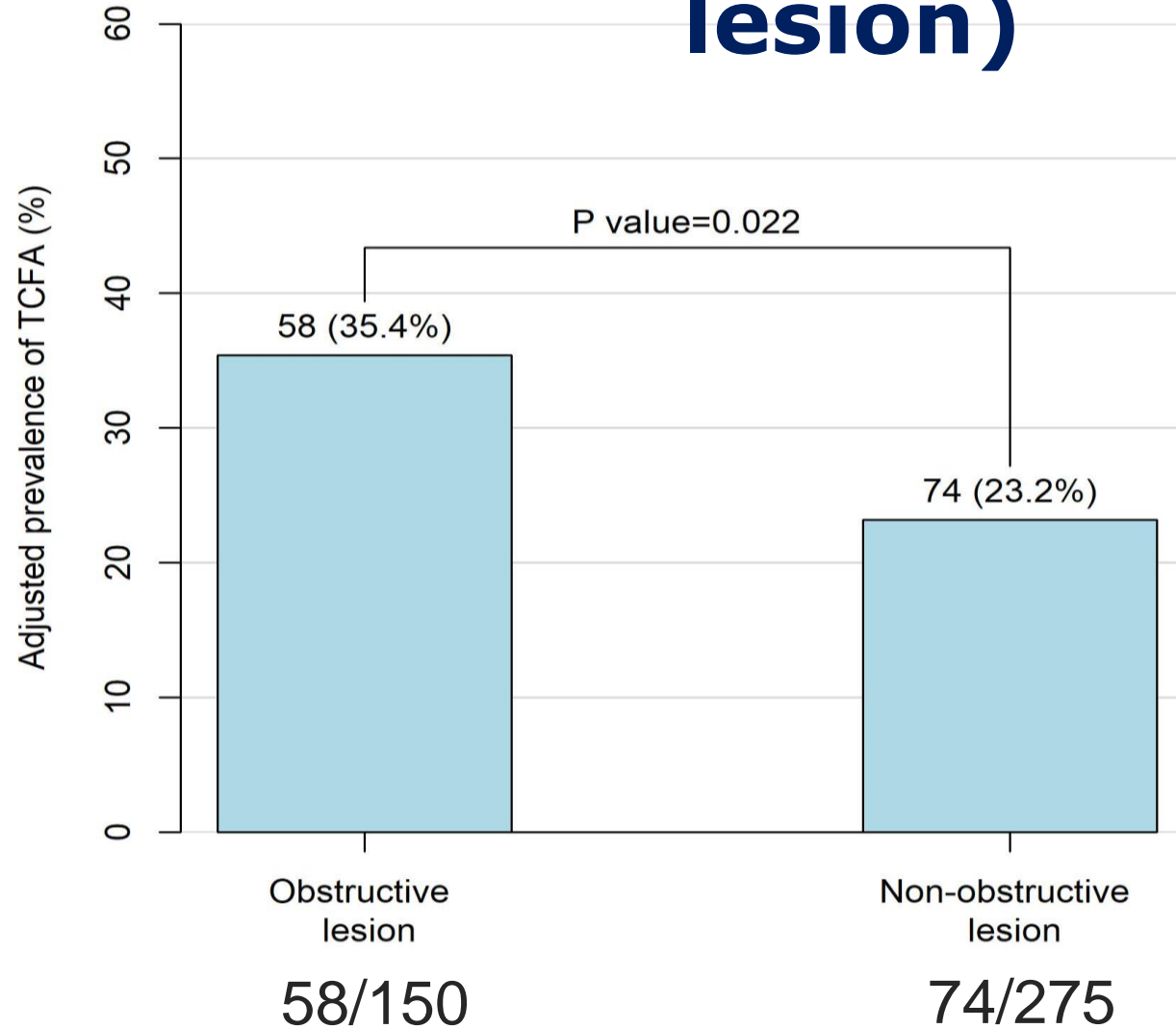
Obstructive non-culprit lesions are most likely to be vulnerable

P value=0.022

58 (35.4%)

74 (23.2%)

Obstructive lesion

Non-obstructive lesion

58/150

74/275

TCFA: Thin Cap Fibro Atheroma

Pinilla-Echeverri N. Circ Cardiovasc Int 2020

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

	TCFA (N=58)	Non-TCFA (N=92)	P value
Lesion Length (mm)	23.1	20.8	0.16
Number of l 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

COMPLETE TRIAL

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HEALTH SCIENCES

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

J. Tian et al. J Am Coll Cardiol 2014;63:2209–16
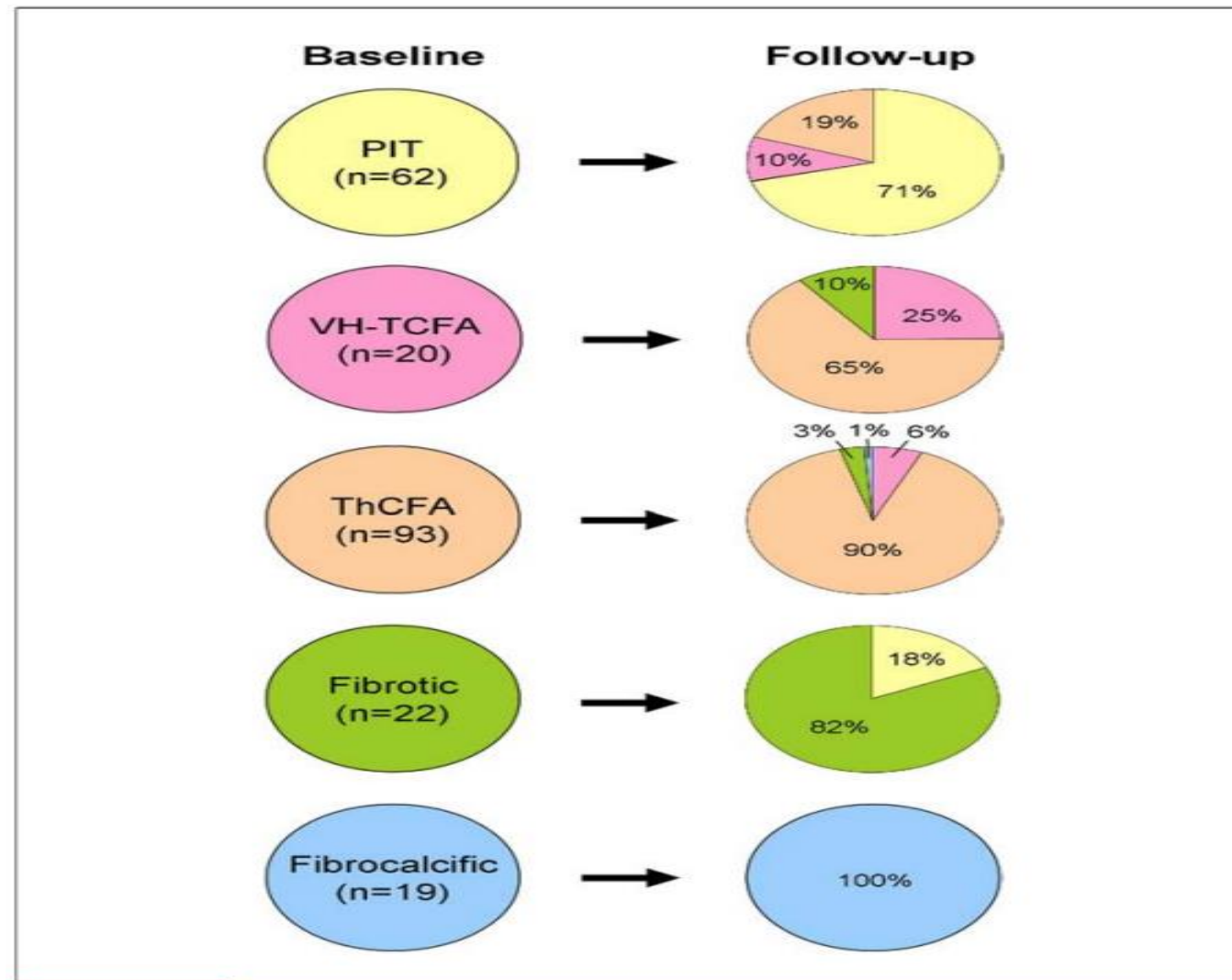
Flower-MI: Angiography vs Physiology-guided NCL PCI

56 primary outcome events

Table 3. Prespecified Clinical Outcomes at 1 Year.*

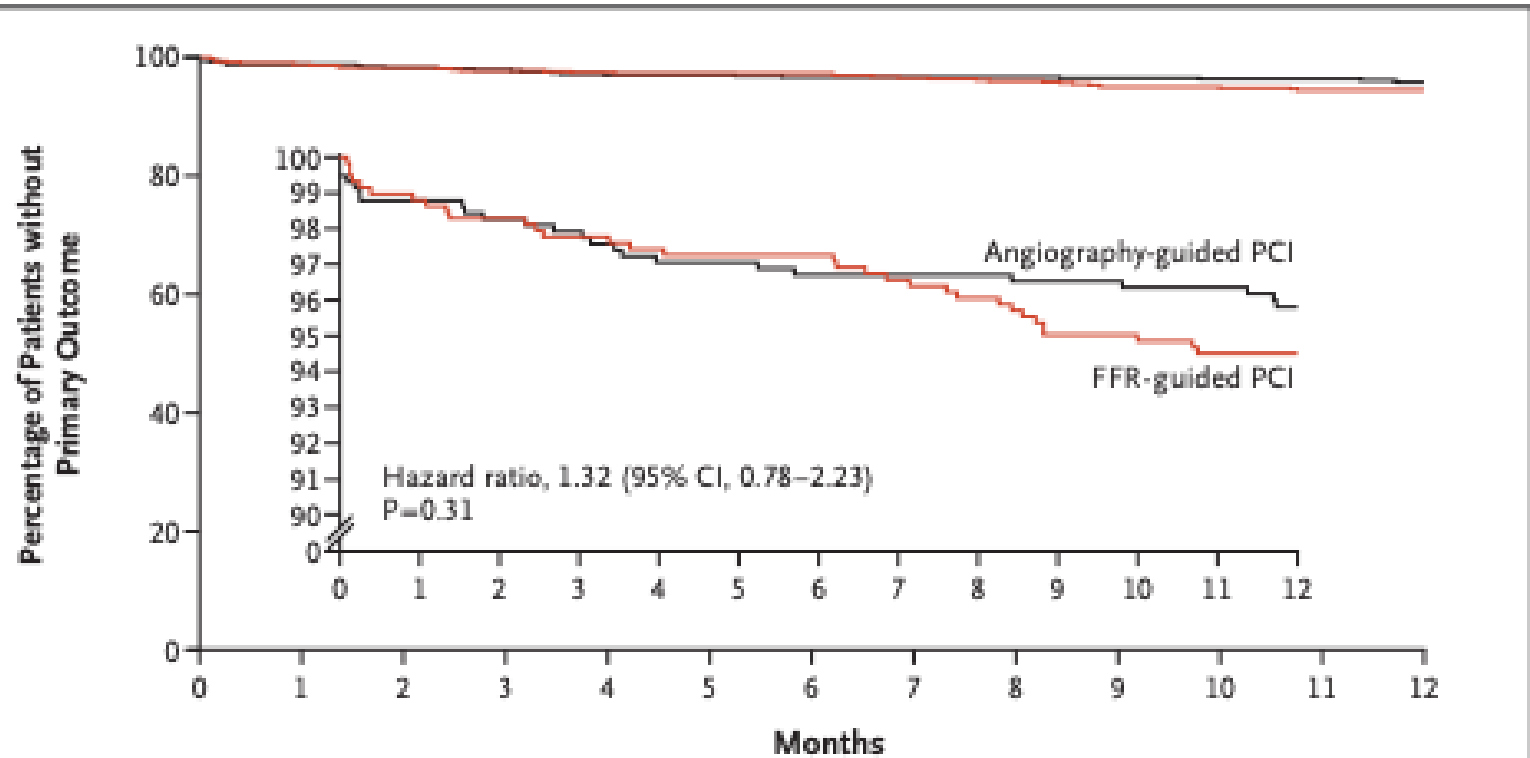| Outcomes	FFR-Guided Group (N=586)	Angiography-Guided Group (N=577)	Hazard Ratio or Difference (95% CI)†	P Value
Primary outcome				
Composite outcome — no. (%)‡	32 (5.5)	24 (4.2)	1.32 (0.78–2.23)	0.31
Death from any cause	9 (1.5)	10 (1.7)	0.89 (0.36–2.20)	
Nonfatal myocardial infarction§	18 (3.1)	10 (1.7)	1.77 (0.82–3.84)	
Unplanned hospitalization leading to urgent revascularization				
Patients with condition — no. (%)	15 (2.6)	11 (1.9)	1.34 (0.62–2.92)	
Treatment of target lesions in nonculprit artery by urgent revascularization — no./total no. (%)	8/15 (53.3)	3/11 (27.3)	—	
Secondary outcomes				
Key outcomes — no. (%)				
Stent thrombosis	4 (0.7)	6 (1.0)	0.65 (0.19–2.32)	
Any revascularization¶	38 (6.5)	26 (4.5)	1.45 (0.88–2.38)	
Hospitalization for heart failure	9 (1.5)	11 (1.9)	0.82 (0.34–1.98)	
Hospitalization for recurrent ischemia	32 (5.5)	19 (3.3)	1.68 (0.95–2.97)	
Any hospitalization in a cardiology department or service	68 (11.6)	46 (8.0)	1.49 (1.03–2.17)	
Functional status				
Mean no. of antianginal medications used per patient‖	1.0±0.5	1.0±0.5	1.01 (0.90–1.14)**	
QALY based on EQ-5D-5L score††	0.86±0.19	0.87±0.18	0.01 (0.00–0.01)**	
Recurrent ischemia				
Patients with condition — no. (%)	32 (5.5)	19 (3.3)	0.82 (0.21–3.24)‡‡	
Patients with CCS class ≥II — no./total no. (%)§§	20/32 (62.5)	13/19 (68.4)	—	

Figure 2. Kaplan–Meier Curves of the Primary Outcome.

The primary outcome was a composite of death from any cause, nonfatal myocardial infarction, or unplanned hospitalization leading to urgent revascularization. The inset shows the same data on an expanded y axis.

Puymirat E. et al. NEJM 2021;285:297-308

FRAME-MI: Angiography vs Physiology-guided NCL PCI
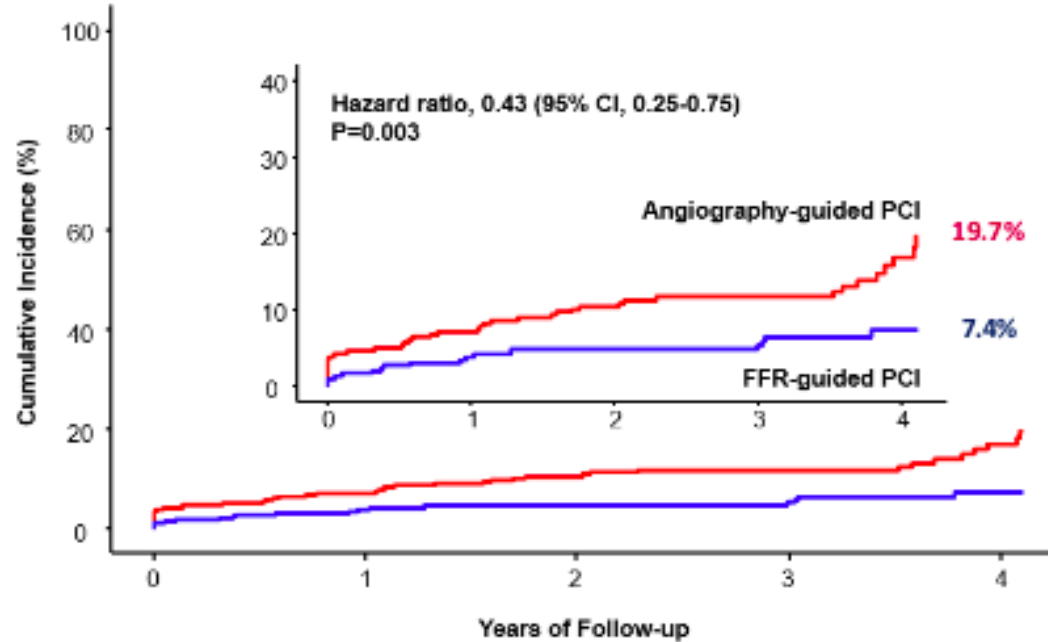

58 primary outcome events

Primary end point

A composite of death, MI, or repeat revascularization

Clinical outcomes

End Point	FFR-guided PCI (N=284)	Angiography-guided PCI (N=278)	Hazard Ratio (95% CI)	P Value
Death, myocardial infarction, and repeat revascularization	18 (7.4%)	40 (19.7%)	0.43 (0.25-0.75)	0.003
All-cause Death	5 (2.1%)	16 (8.5%)	0.30 (0.11-0.83)	0.020
Cardiac death	3 (1.4%)	15 (8.2%)	0.19 (0.06-0.67)	0.010
Myocardial infarction	7 (2.5%)	21 (8.9%)	0.32 (0.13-0.75)	0.009
Procedure-related myocardial infarction	3 (1.1%)	11 (4.0%)	0.26 (0.07-0.94)	0.041
Spontaneous myocardial infarction	4 (1.4%)	10 (5.0%)	0.39 (0.12-1.23)	0.108
Repeat revascularization	10 (4.3%)	16 (9.0%)	0.61 (0.28-1.34)	0.216
Infarct-related artery	4 (2.2%)	8 (5.0%)	0.49 (0.15-1.61)	0.237
Non-infarct related artery	7 (2.6%)	12 (5.7%)	0.56 (0.22-1.43)	0.230
Definite stent thrombosis	0 (0.0%)	1 (0.4%)	NA	NA
Cerebrovascular accident	4 (1.4%)	3 (1.1%)	1.30 (0.29-5.81)	0.730
Contrast-induced nephropathy	2 (0.7%)	1 (0.4%)	1.97 (0.18-21.67)	0.581

Hazard ratio, 0.43 (95% CI, 0.25-0.75)
P=0.003

Angiography-guided PCI — 19.7%

FFR-guided PCI — 7.4%

No. at Risk

Angiography-guided PCI	278	257	223	173	74
FFR-guided PCI	284	271	237	186	79

Joo-Yong Hahn. Presented at ESC 2022

EDITORIAL

COMPLETE-2

Anatomy vs. physiology: how should we achieve complete revascularization in acute coronary syndromes?

Shamir R. Mehta* and Brian P. McGrath

Comparison of trials assessing FFR guided vs angiographically guided PCI of non-culprit lesions

	FRAME-AMI	FLOWER-MI
Primary Outcomes Death, myocardial infarction, repeat revascularisation	7.4% vs 19.7% HR 0.43 (0.25-0.75)	5.5% vs 4.2% HR 1.32 (0.78-2.23)
	562 patients	1171 patients
	52.8% STEMI 47.25% NSTEMI	100% STEMI
Non-culprit lesion Epicardial coronary/major side branch ≥50% stenosis ≥2mm diameter	Median 3.5 years follow-up	1 year follow-up
	60% index procedure 40% staged PCI	96.2% staged PCI

Mehta SR, McGrath BP. Eur Heart J 2023

Study Design

COMPLETE-2

STEMI or NSTEMI with Multivessel Coronary Artery Disease
At least one additional non-culprit lesion ≥2.5 mm diameter and ≥50% stenosis

N=5100

Exclusion Criteria: Planned/prior CABG surgery, Absence of clearly identifiable culprit lesion based on angiographic appearance and/or ECG changes and/or regional wall motion abnormalities, NCL TIMI flow ≤2, Planned medical treatment of all qualifying NCLs, CTO presence (if CTO is the only qualifying NCL), NCL presence in same vessel as culprit (if it is the only qualifying NCL)

Randomization
Stratified by STEMI or NSTEMI

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

COMPLETE-2 OCT
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

Median Follow-Up: 3.5 Years

Primary Outcomes

Efficacy: Time to first occurrence of the composite of CV death, new MI, or ischemia-driven revascularization

Safety: Time to first occurrence of the composite of clinically significant bleeding, stroke, stent thrombosis, or contrast-associated acute kidney injury

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