

How Should I Treat non-culprit lesions in a patient with STEMI

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Disclosure

- No conflict of interest

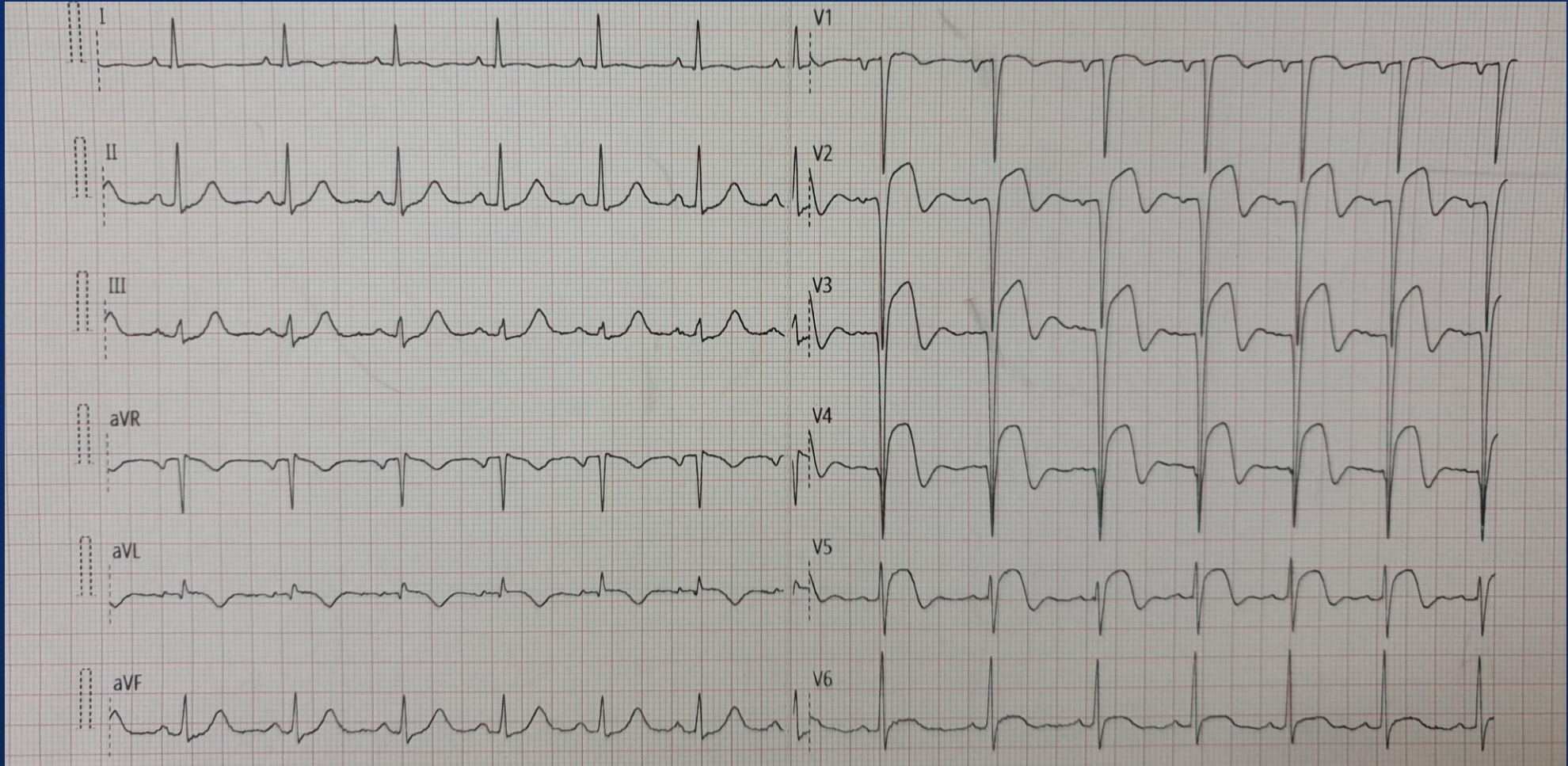
Introduction

- 30-50% of patients with STEMI undergoing primary PCI have multivessel disease
- There is uncertainty on how best to manage these non-culprit lesions:
 - *Routinely revascularize them with PCI?*
 - *Manage them conservatively with guideline-directed medical therapy alone?*
- FFR has emerged as one of the tools of decision making, but its applicability has not been widely proven

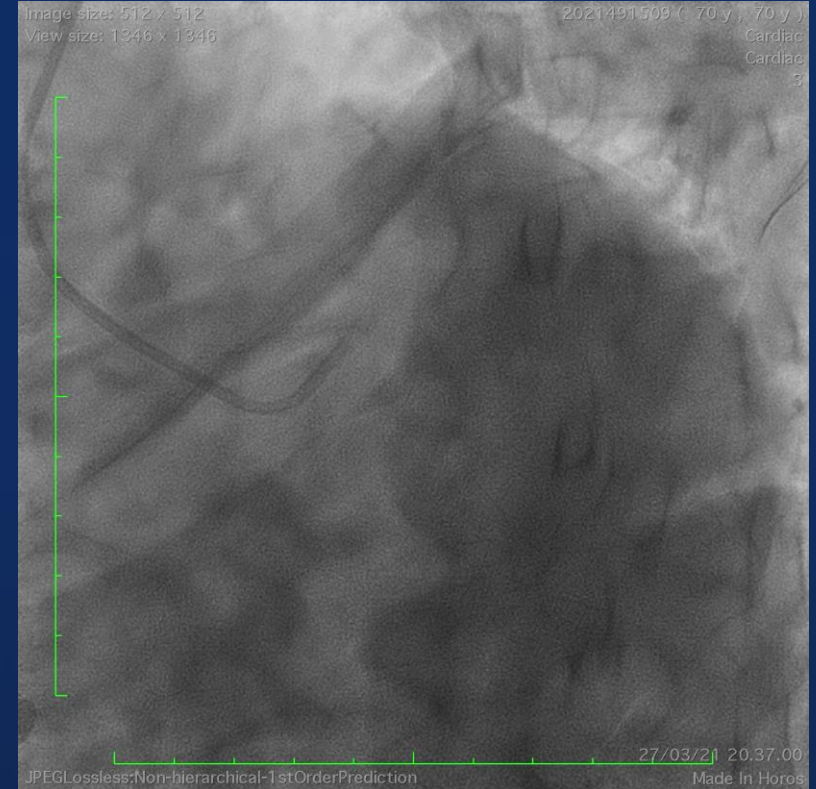
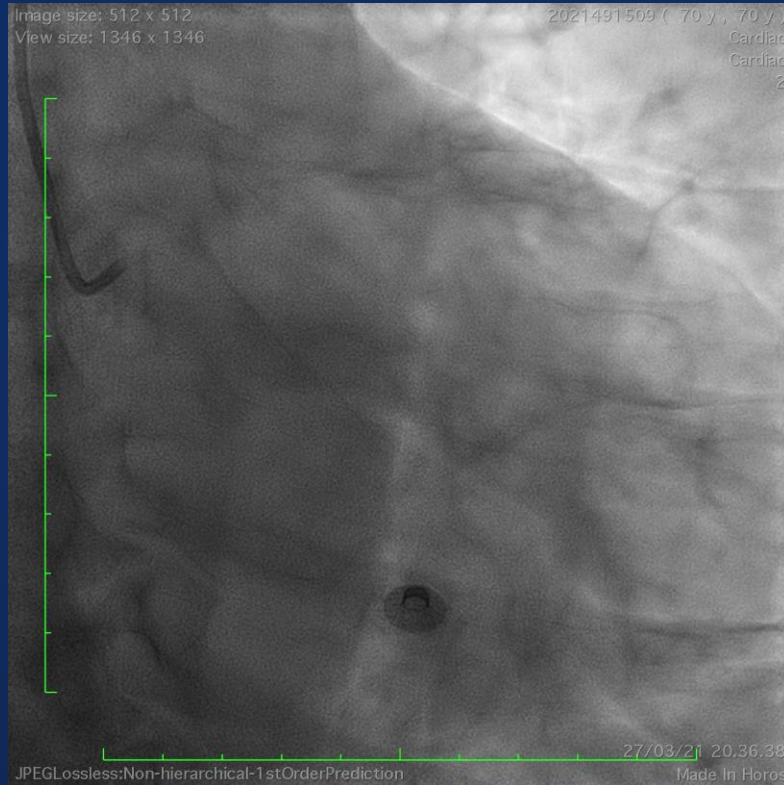
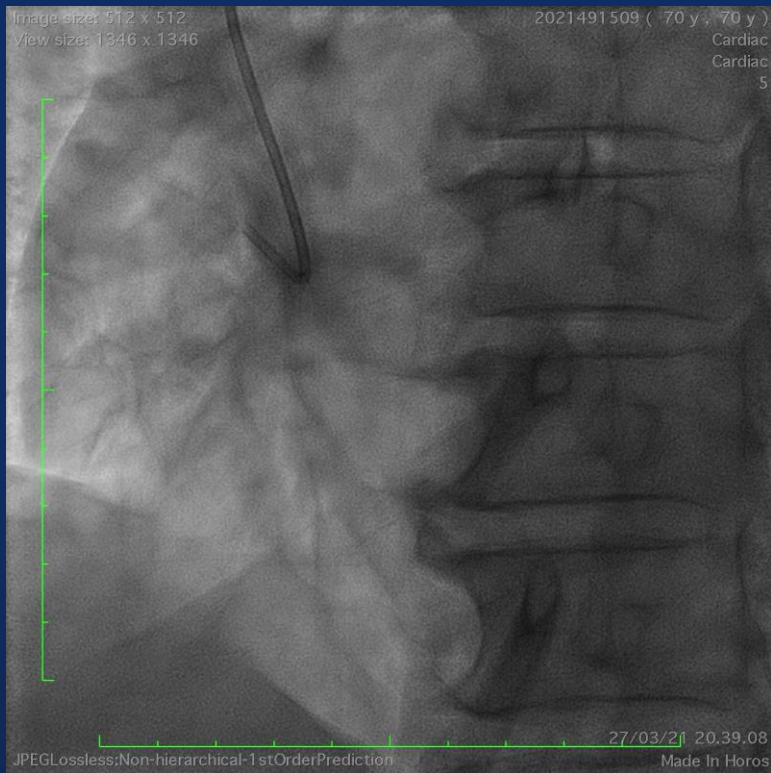
Case Illustration

- Male, 70 y.o
- Acute Anterior STEMI onset 8 hours
- Risk factor: Hypertension, Diabetes
- BP 151/95 mmHg, HR 73 bpm
- Physical examination within normal limit
- Echocardiography: EF 40%, hypokinetic anterior segment, good RV function (TAPSE 20 mm)

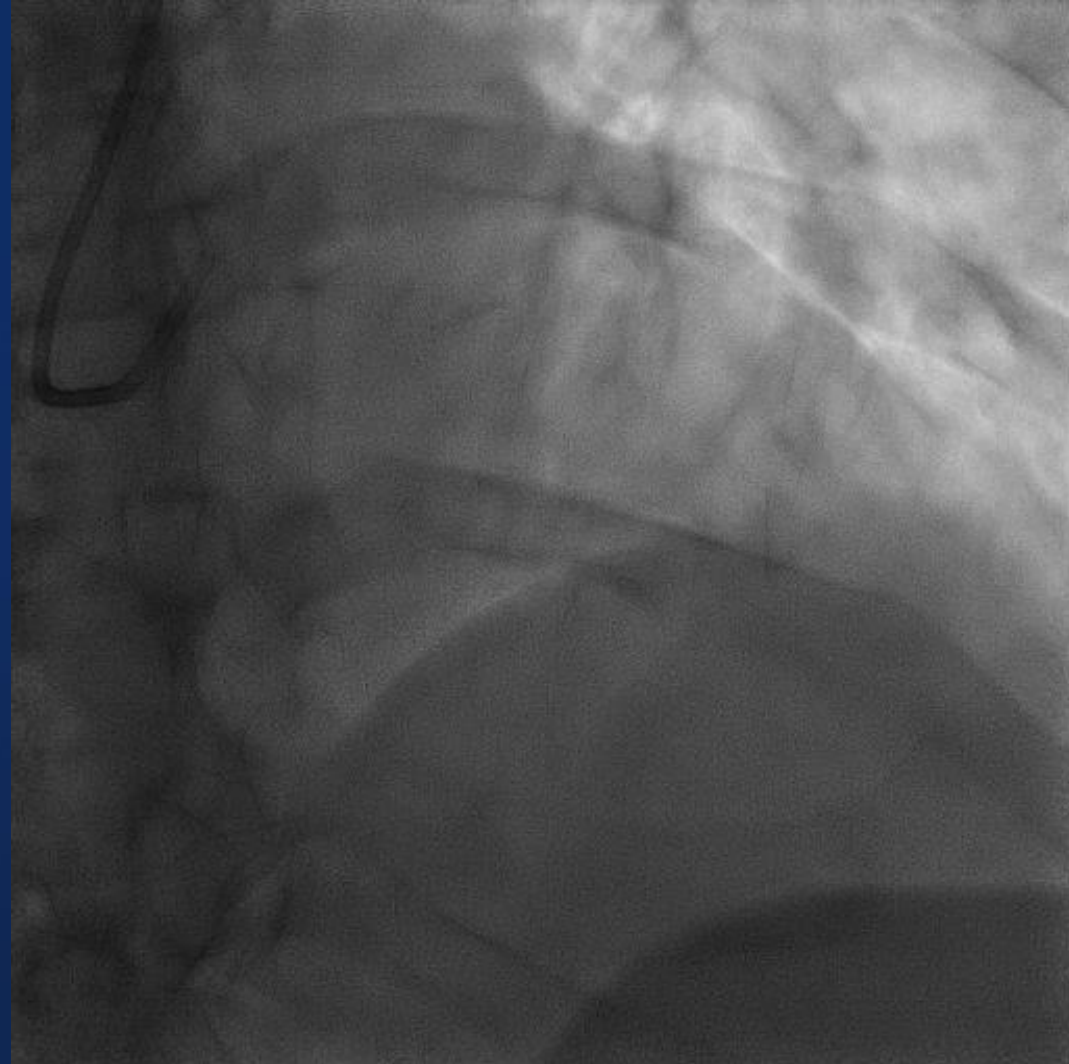
ECG



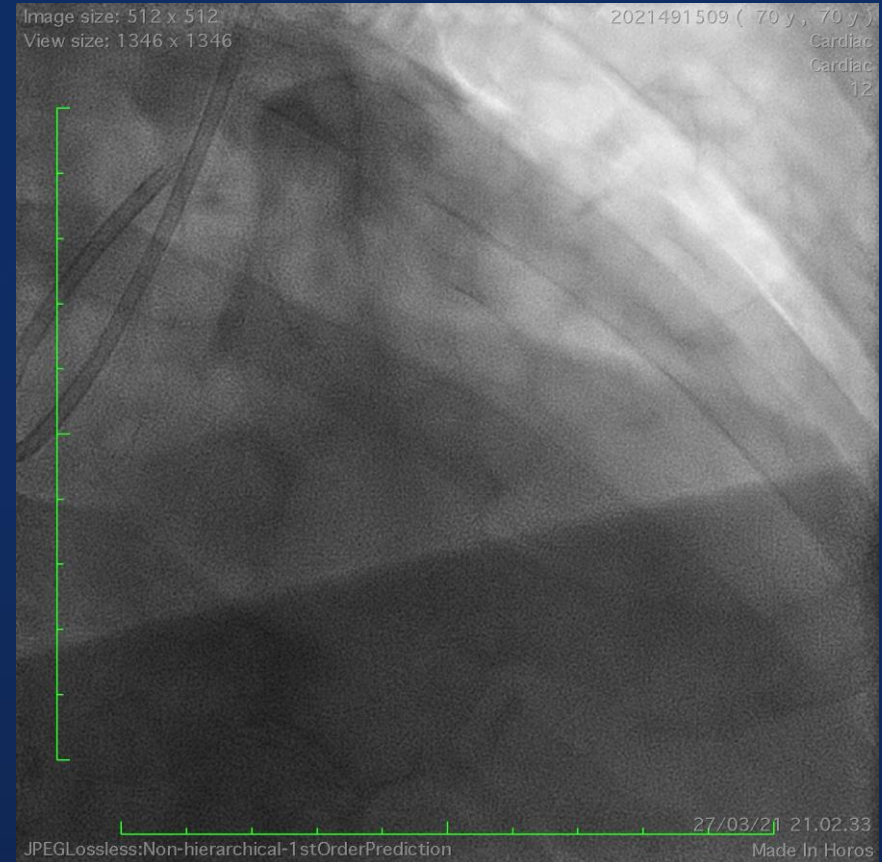
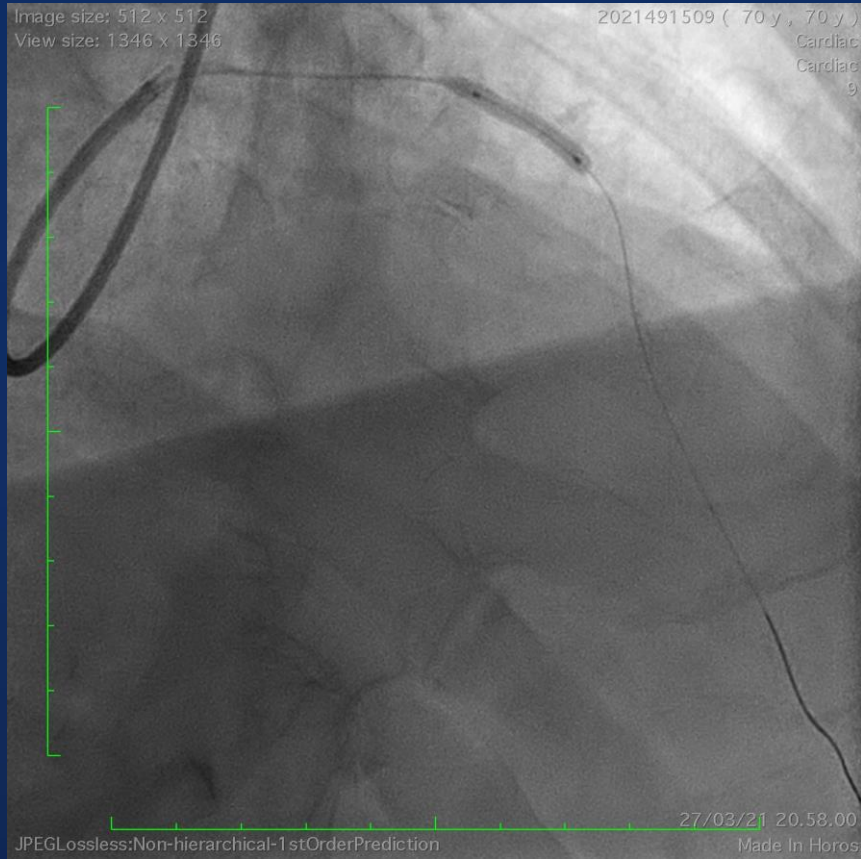
Primary PCI at 3 AM



LAD as Culprit



POBA LAD

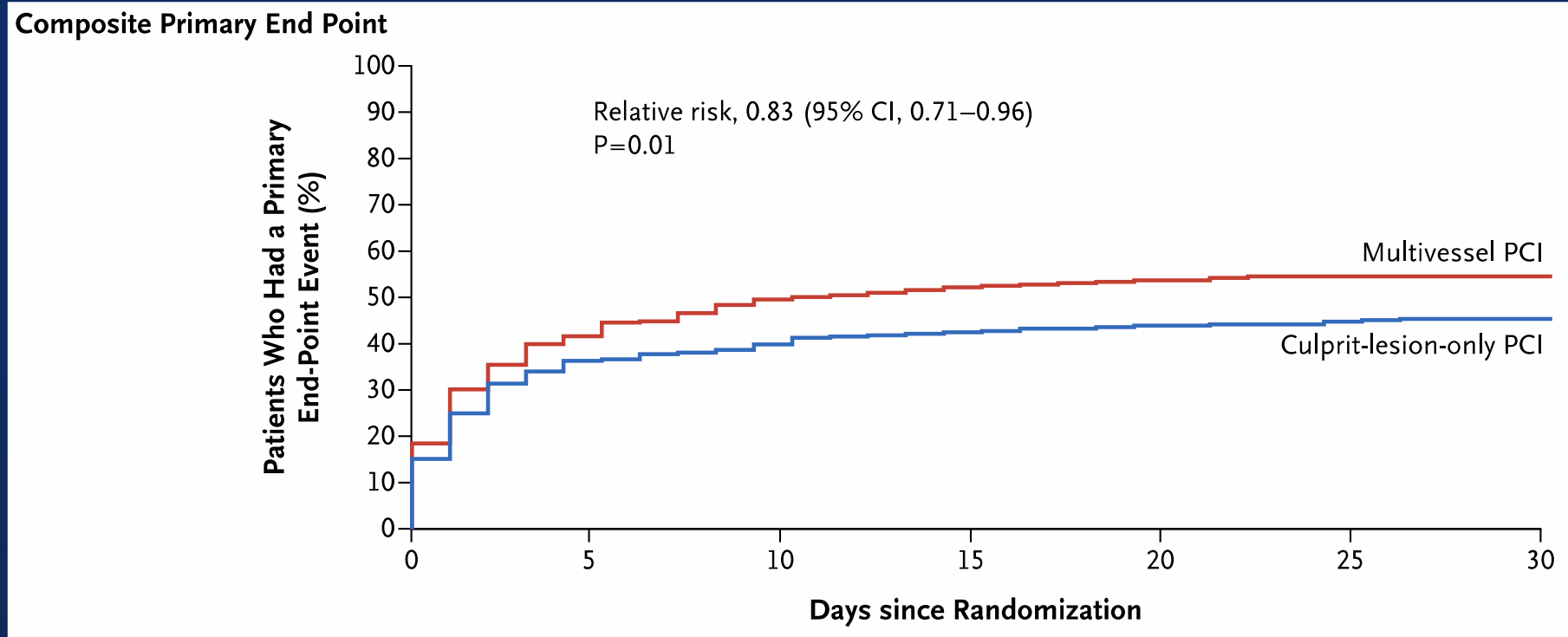


**Ok, LAD is open now
Then what?**

Discussion points

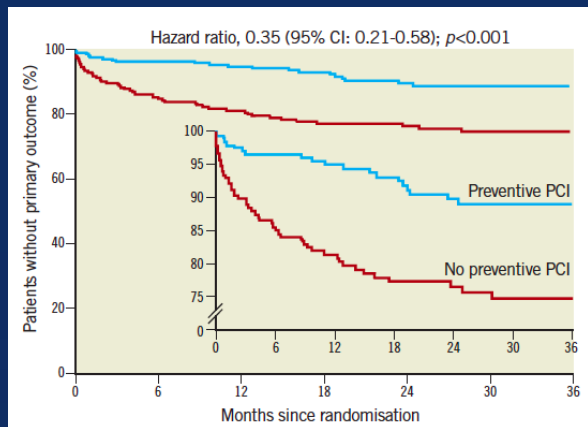
- Timepoint of non-culprit lesion treatment (acute, staged in-hospital, staged after discharge) ?
- FFR or Angio guided PCI acute or staged ?
- Value of FFR in MV-STEMI situation ?

CULPRIT SHOCK Trial

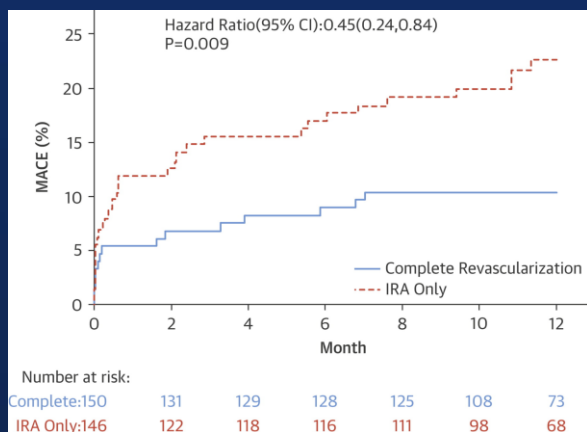


Complete versus Culprit-only

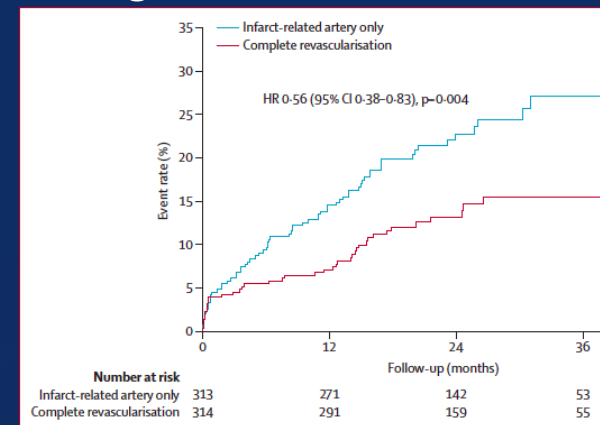
PRAMI trial (n=456)
Wald et al. NEJM 2013



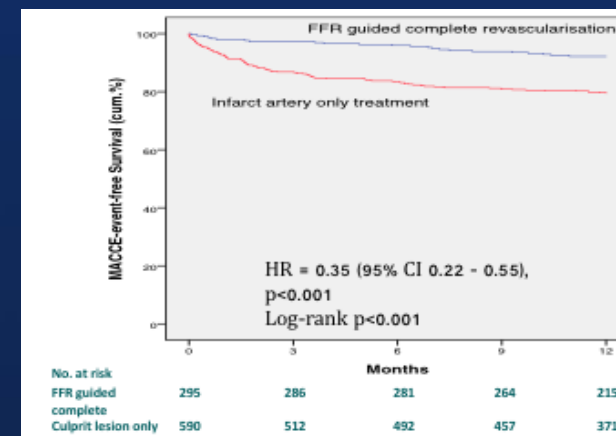
CvLPRIT trial (n=296)
Gershlick et al. JACC 2015



PRIMULTI trial (n=627)
Engstrøm et al. Lancet 2015



COMPARE-ACUTE trial (n=885)
Smits et al. NEJM 2017





STEMI WITH MULTIVESSEL CAD AND SUCCESSFUL PCI TO THE CULPRIT LESION
MVD defined as at least one additional non-culprit lesion ≥ 2.5 mm diameter and $\geq 70\%$ stenosis or 50-69% with FFR ≤ 0.80

Exclusion Criteria: Intent to revascularize NCL, planned surgical revascularization, prior CABG

RANDOMIZATION
Stratified for intended timing of NCL PCI:
During initial hospitalization or after discharge (max 45 d)

Actual Time to study NCL PCI in Complete Group (median)
During initial hospitalization: 1 day (IQR 1-3)
After hospital discharge: 23 days (IQR 12.5-33.5)

COMPLETE REVASCULARIZATION
Routine staged PCI* of all suitable non-culprit lesions with the goal of complete revascularization
N=2016

CULPRIT-LESION-ONLY REVASCULARIZATION
No further revascularization of non-culprit lesions, guideline-directed medical therapy alone
N=2025

*Everolimus-eluting stents strongly recommended

Guideline-Directed Medical Therapy
ASA, P2Y12 inhibitor (Ticagrelor strongly recommended), Statin, BB, ACE/ARB + Risk Factor Modification

MEDIAN FOLLOW-UP: 3 YEARS

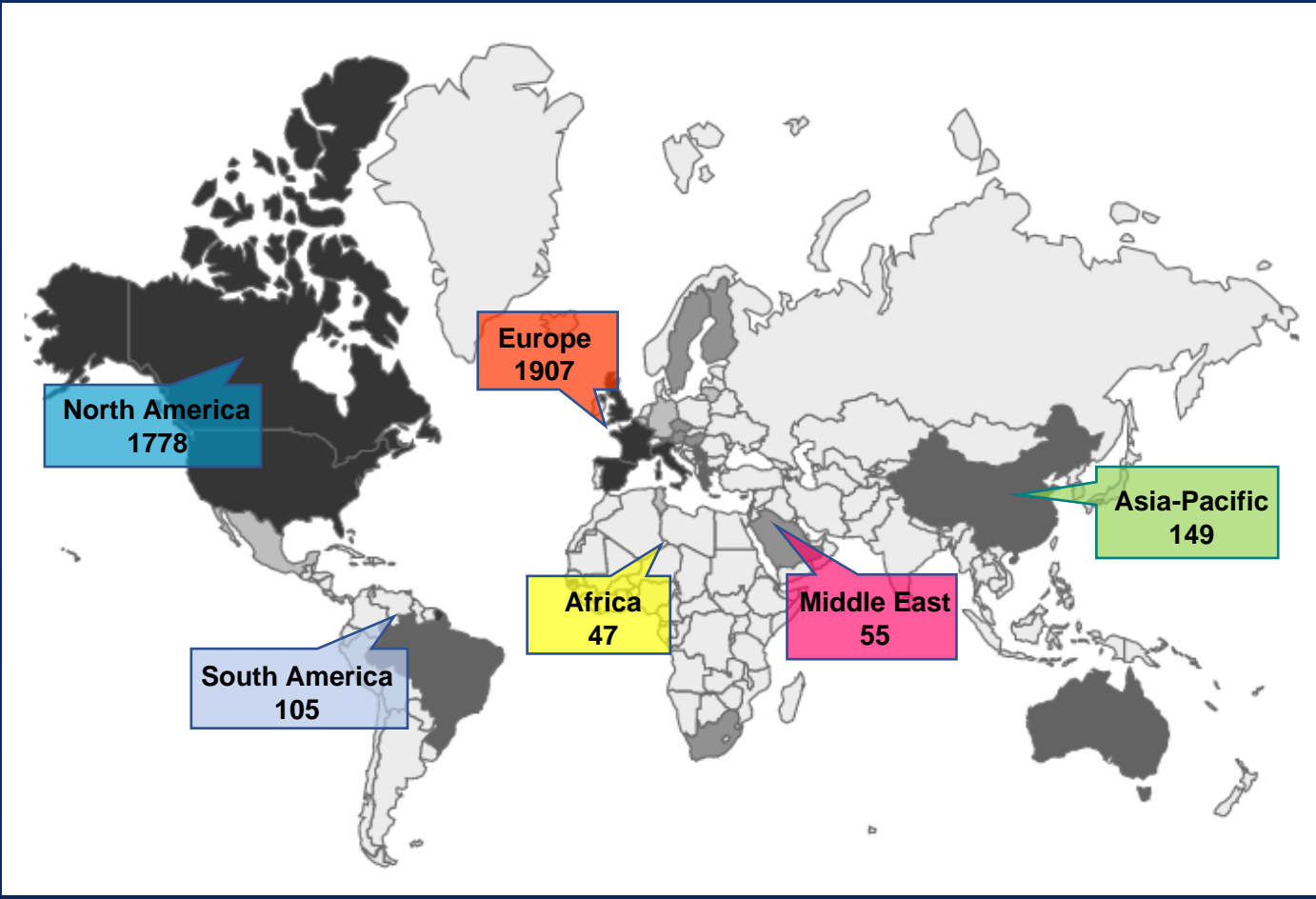
Co-PRIMARY OUTCOMES:
1. Composite of CV death or new MI
2. Composite of CV death, new MI or IDR

KEY SECONDARY OUTCOME: CV death, new MI, IDR, unstable angina, NYHA class IV heart failure



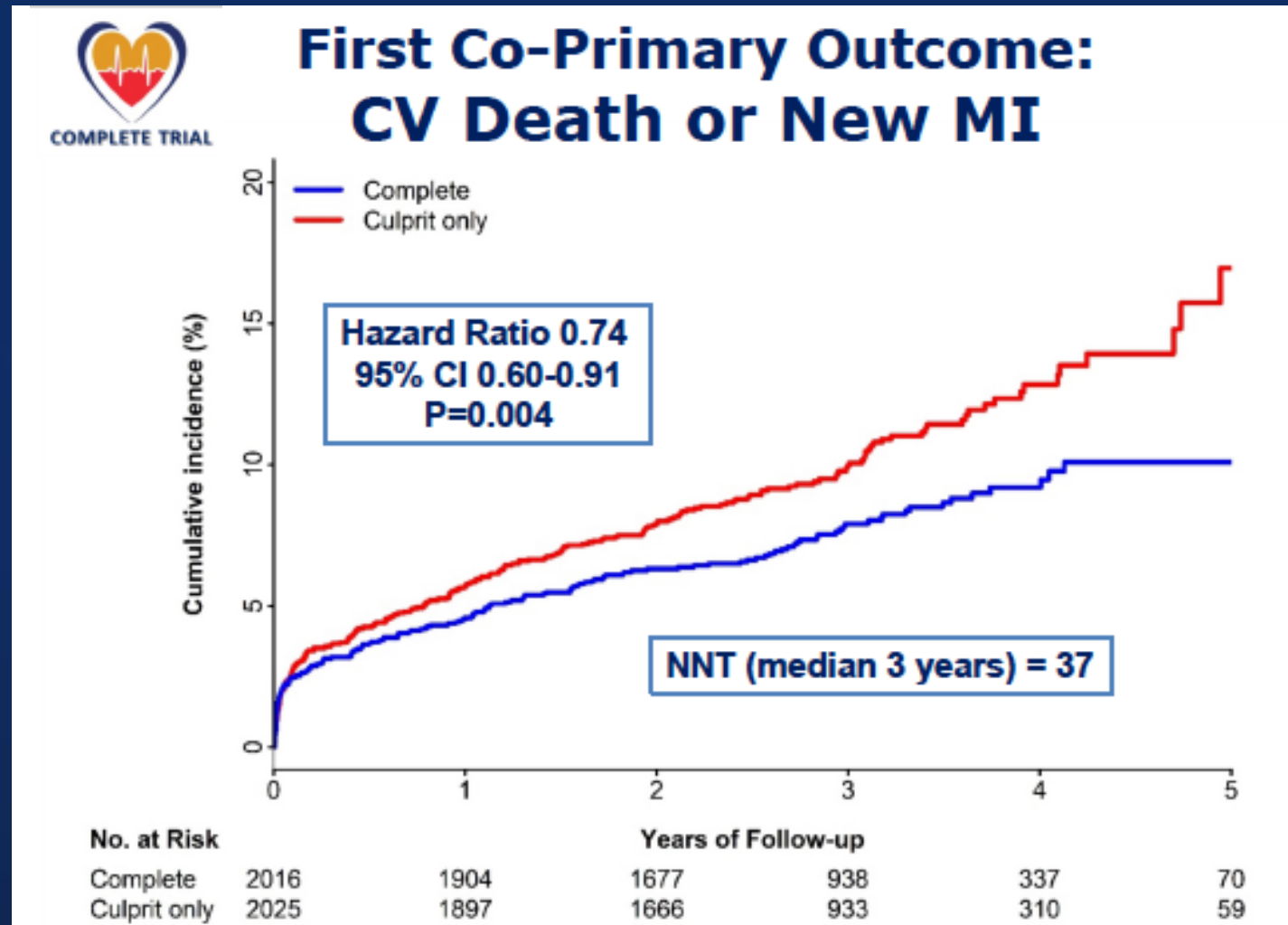
Global Recruitment

140 centers, 31 countries



- Australia
- Austria
- Belgium
- Brazil
- Canada
- China
- Colombia
- Czech Republic
- Finland
- France
- Germany
- Greece
- Hungary
- Israel
- Italy
- Kuwait
- Lithuania
- Macedonia
- Mexico
- Poland
- Portugal
- Romania
- Saudi Arabia
- Serbia
- South Africa
- Spain
- Sweden
- Switzerland
- Tunisia
- United Kingdom
- USA

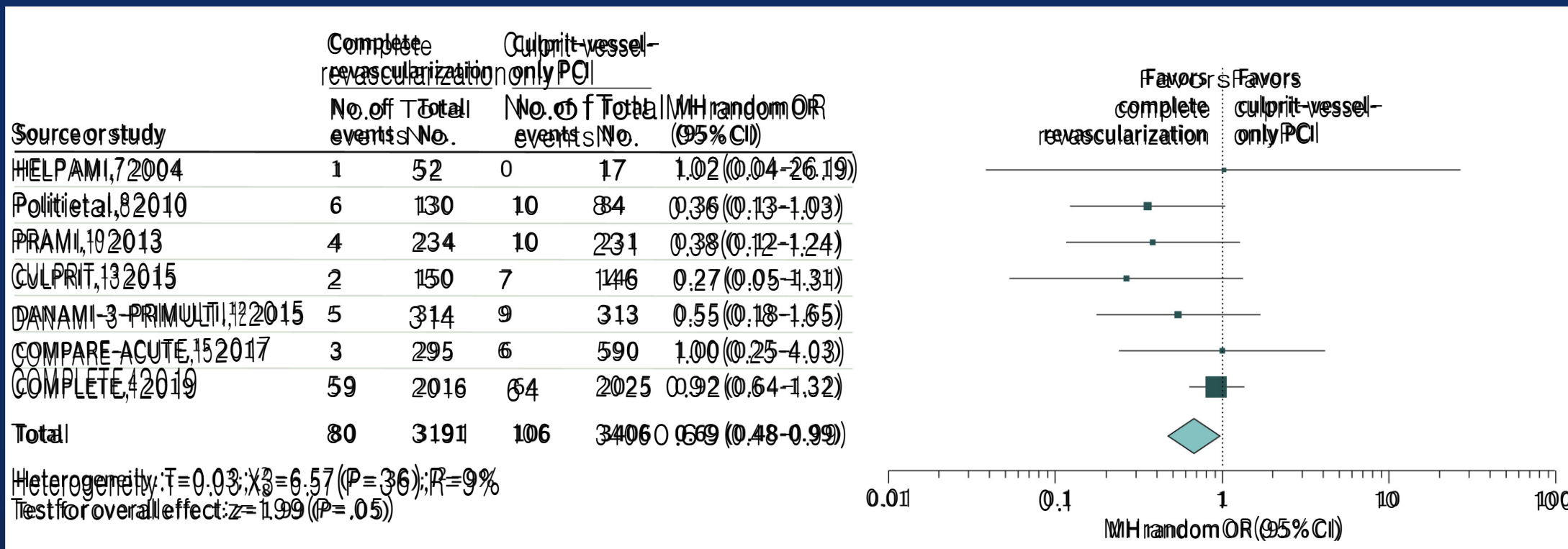
COMPLETE TRIAL (n= 4041)



Mehta et al. NEJM 2019

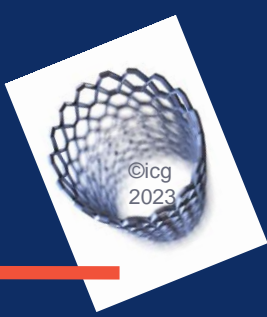
Complete vs Culprit Revascularization in STEMI

A Systematic review and Meta analysis of 7030 patients

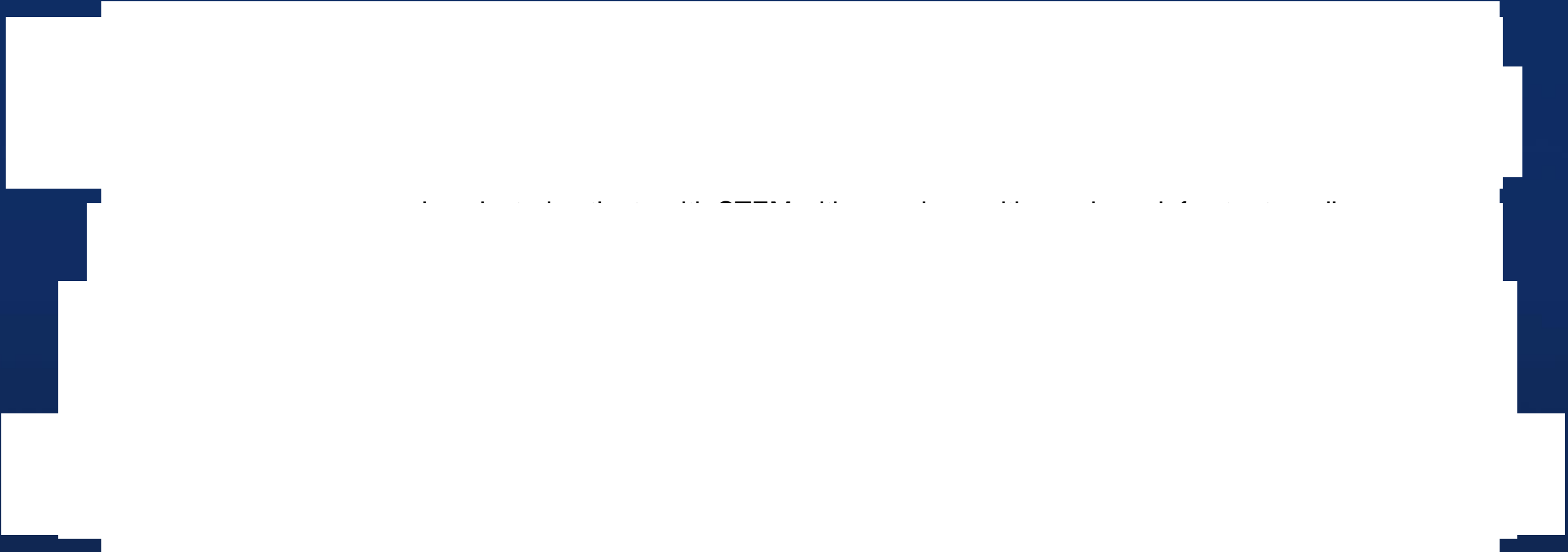


Bainey KR et al. JAMA Cardiol. 2020

Revascularization Guidelines 2021



Recommendations for Revascularization of Non-Infarct Artery in STEMI



Lawton JS, et al. 2021 ACC/AHA/SCAI guideline for coronary artery revascularization. *J Am Coll Cardiol.* 2022;79:e21-e129.

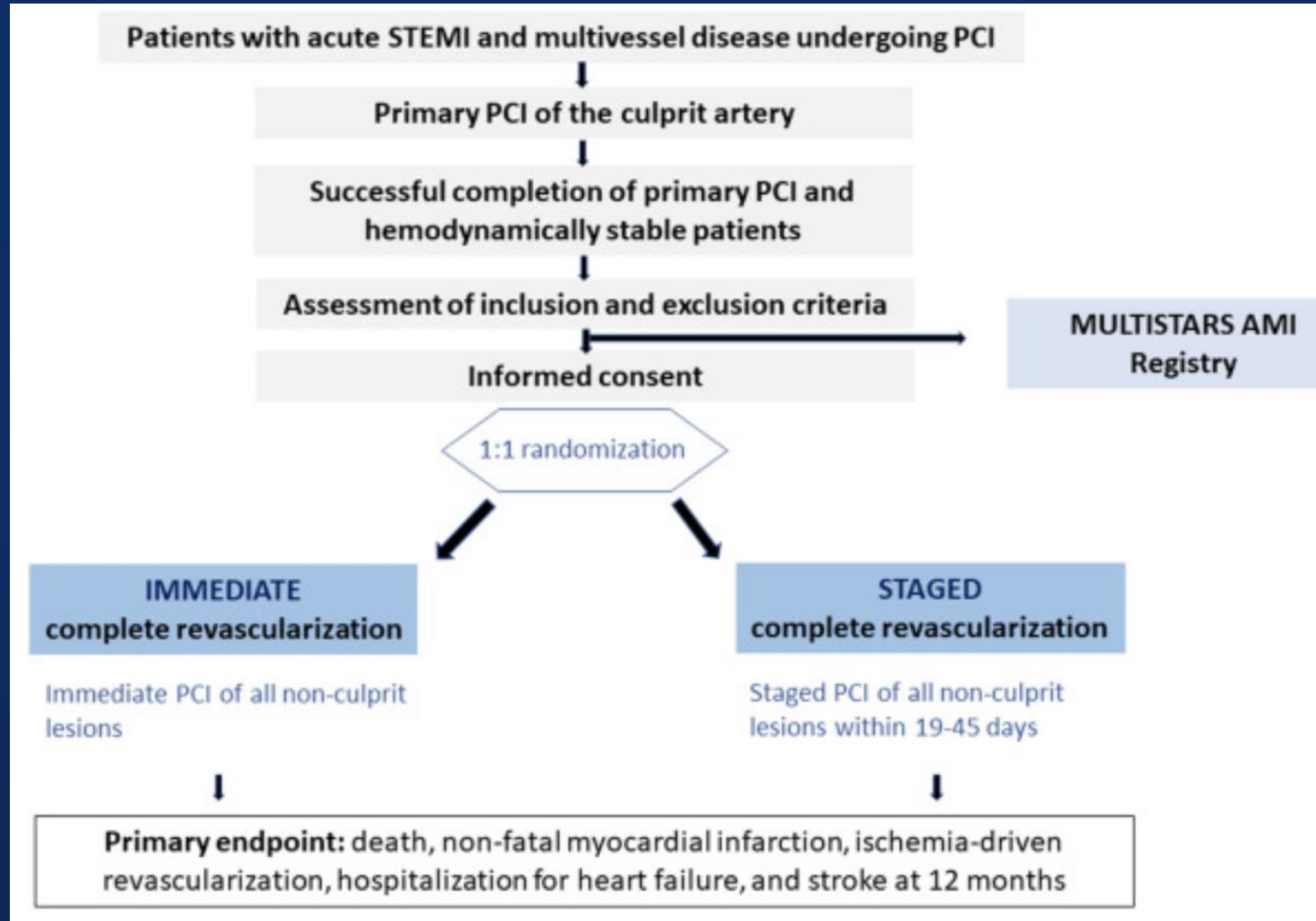
Current issue

The question has now shifted from

WHETHER to perform complete revascularization to
WHEN to perform complete revascularization

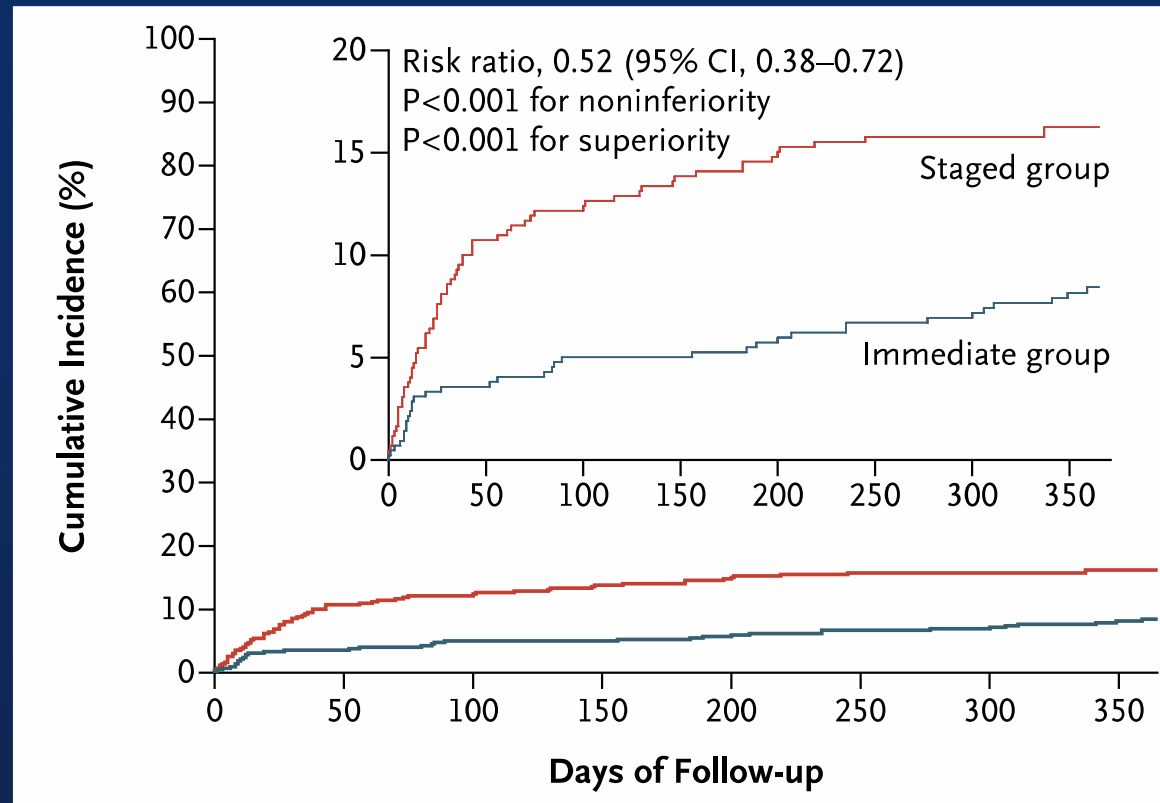
...and also HOW?

Trial Design MULTISTARS AMI



Timing of Complete Revascularization with Multivessel PCI for Myocardial infarction

MULTISTARS AMI Trial



19-45 days after onset

BIOVASC Trial study design

**ACS with multivessel disease and clear culprit lesion
N=1525**

Multivessel disease was defined as two or more coronary arteries with a diameter of ≥ 2.5 mm and $\geq 70\%$ stenosis by visual estimation or positive coronary physiology testing.

1:1 Randomization

**Immediate complete revascularization
during the index procedure
N=764**

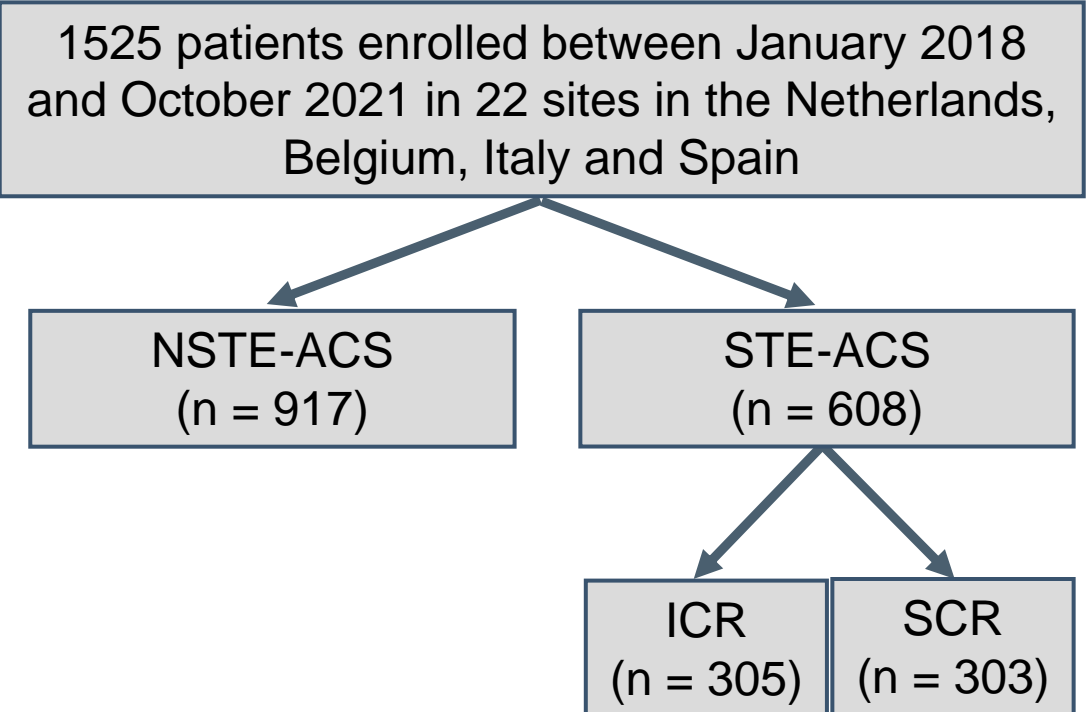
**Staged complete revascularization
within 6 weeks from the index procedure
N=761**

Composite primary outcome of all-cause mortality, myocardial infarction, any unplanned ischemia-driven revascularization and cerebrovascular events at 1-year post index procedure

Biovasc STEMI

BIOVASC Trial – STE-ACS population

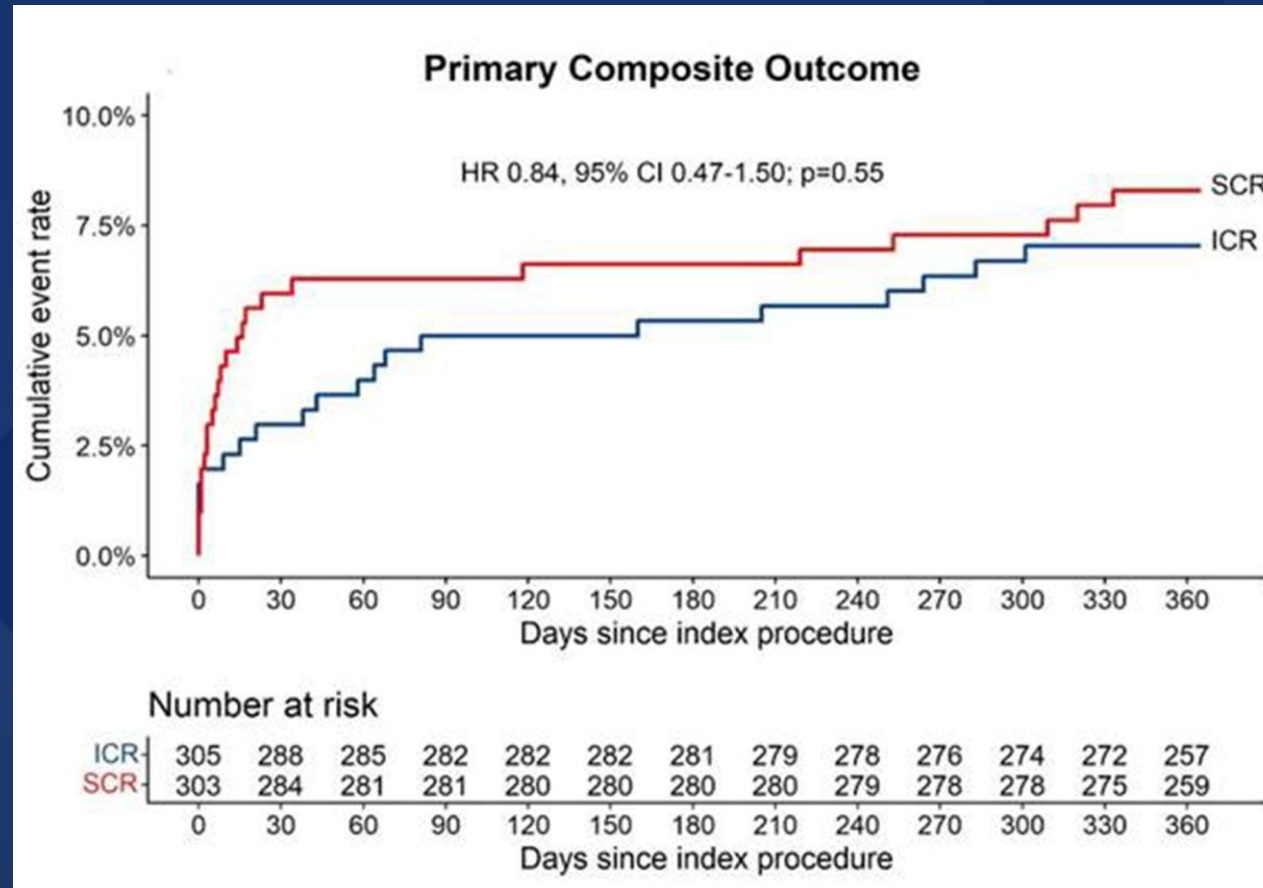
- **DESIGN:** Substudy of a prospective, open-label, non-inferiority, randomised trial
- **OBJECTIVE:** To compare immediate complete revascularization (ICR) with staged complete revascularization (SCR)
- **ENDPOINTS:** All-cause mortality, myocardial infarction unplanned ischemia driven revascularization or cerebrovascular events



BIOVASC STEMI

29th
TCTAP2024

Primary Composite Outcome at 1 year



In patients with STEMI and multivessel disease, immediate complete revascularization was associated with similar clinical outcomes at 1 year compared with staged complete revascularization

How can we best identify which non-culprit lesions to revascularize?

(Anatomy vs Physiology)

Multivessel disease in haemodynamically stable STEMI patients undergoing PPCI

Complete revascularization is recommended either during the index PCI procedure or within 45 days.^{508–511,531}

I

A

It is recommended that PCI of the non-IRA is based on angiographic severity.^{511,524}

I

B

Invasive epicardial functional assessment of non-culprit segments of the IRA is not recommended during the index procedure.

III

C

STEMI: When to Perform Physiology?

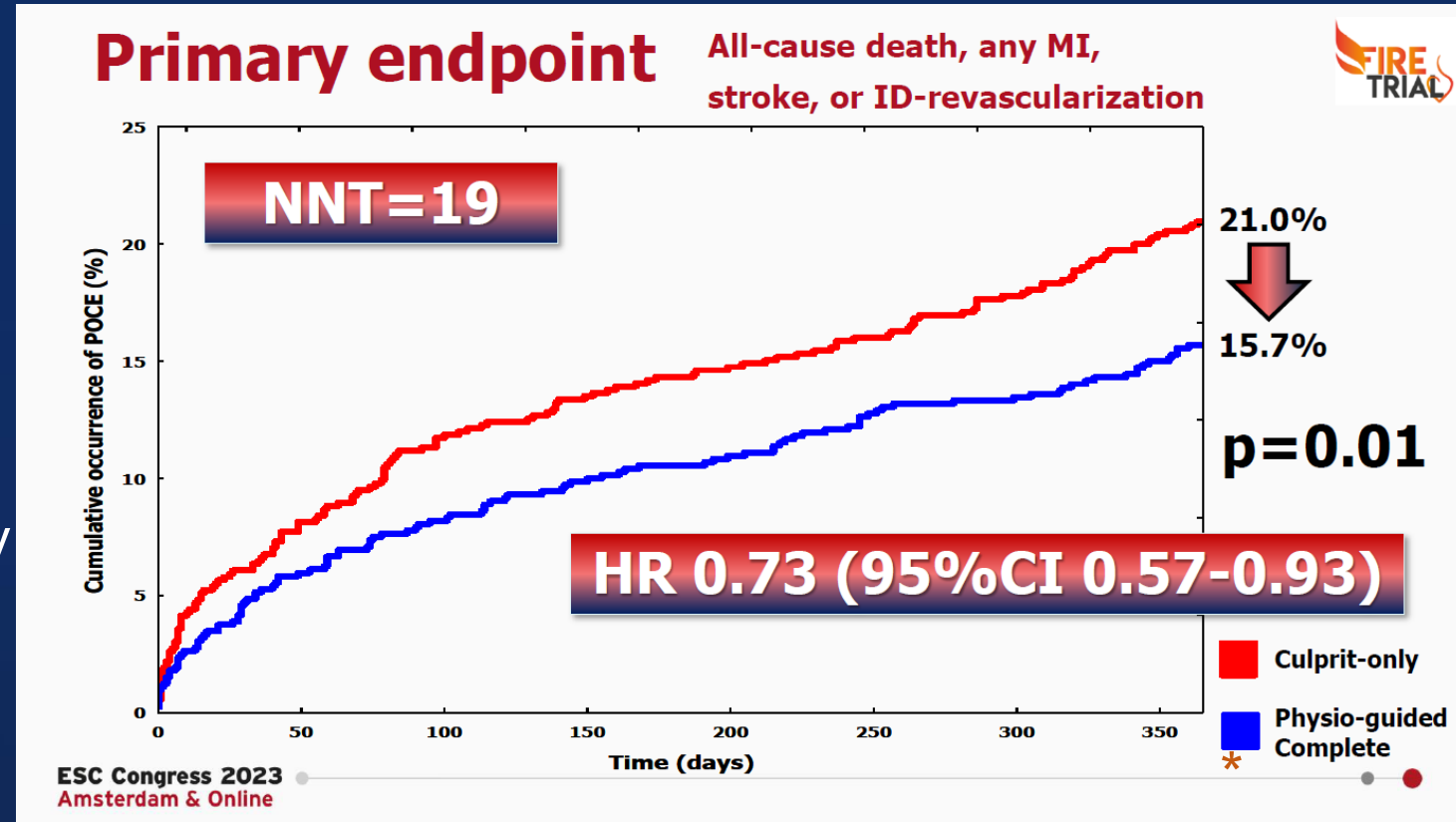
- Story is evolving
- STEMI: Physiologic evaluation of **culprit** lesion usually not performed
- Evaluation of **non-culprit** lesions (NCL) can be performed
 - flow not reduced in regions remote from the culprit vessel's area of injury
- Increasing interest for patients with concomitant MVD
 - 50% of STEMI patients have MVD

Physiology study in STEMI

- **Do all NCLs warrant revascularization?**
 - A secondary analysis of COMPLETE: the benefit of complete revascularization is in 2/3 of NCL with ~80% severity, and no benefit for less severe lesions
 - Coronary physiology in only 37 patients (<1%)
- **Do all NCLs warrant revascularization?**
 - With a more selective approach, could adverse events could be prevented?
 - stroke, heart failure, acute kidney injury, stent thrombosis, and bleeding
 - Any downside to being selective?
 - Deferral of less severe lesions could leave behind inflamed lesions with high propensity for plaque rupture while not being functionally significant
- **FIRE study, FRAME-AMI study, FLOWER study**

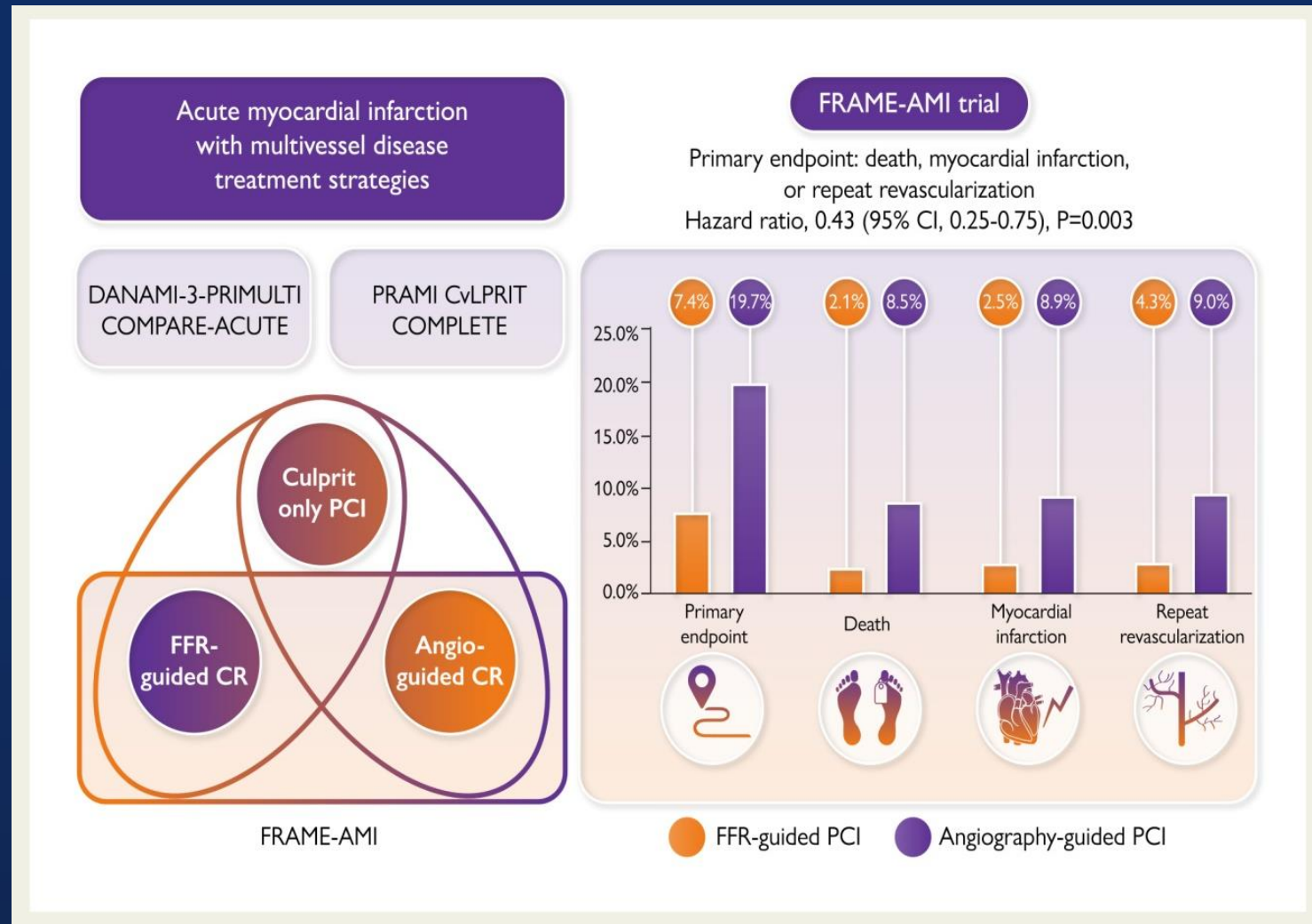
FIRE Trial

- MI (clear culprit) and MVD
 - 1445 patients
 - Median age 80 years
 - 35% STEMI, 65% NSTEMI
 - Non-culprit lesions >50% stenosis
- Strategy of *selective* revascularization of NCL using coronary physiology* (day 3) reduced MACE c/w culprit-only strategy
- 51% of lesions evaluated by physiology were deferred!



FRAME-AMI Trial

- MI and MVD
 - RCT, 14 centers, Korea
 - 2016-2020, 3.5 years
 - N=562 patients
 - 47% STEMI, 53% NSTEMI
 - Non-culprit lesions >50%
- Strategy of *selective* revascularization of NCL using FFR reduced MACE c/w angiography-guided approach
- 36% of lesions evaluated by FFR were deferred



FRAME-AMI and FLOWER Trials

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

Primary Outcomes

Death, myocardial infarction, repeat revascularisation

Non-culprit lesion

Epicardial coronary/major side branch
≥50% stenosis
≥2mm diameter

FRAME-AMI

7.4% vs 19.7%
HR 0.43 (0.25-0.75)

54 events

562 patients

52.8% STEMI
47.25% NSTEMI *

Median 3.5 years follow-up

60% index procedure
40% staged PCI

FLOWER-MI

5.5% vs 4.2%
HR 1.32 (0.78-2.23)

56 events

1171 patients

100% STEMI

1 year follow-up

96.2% staged PCI

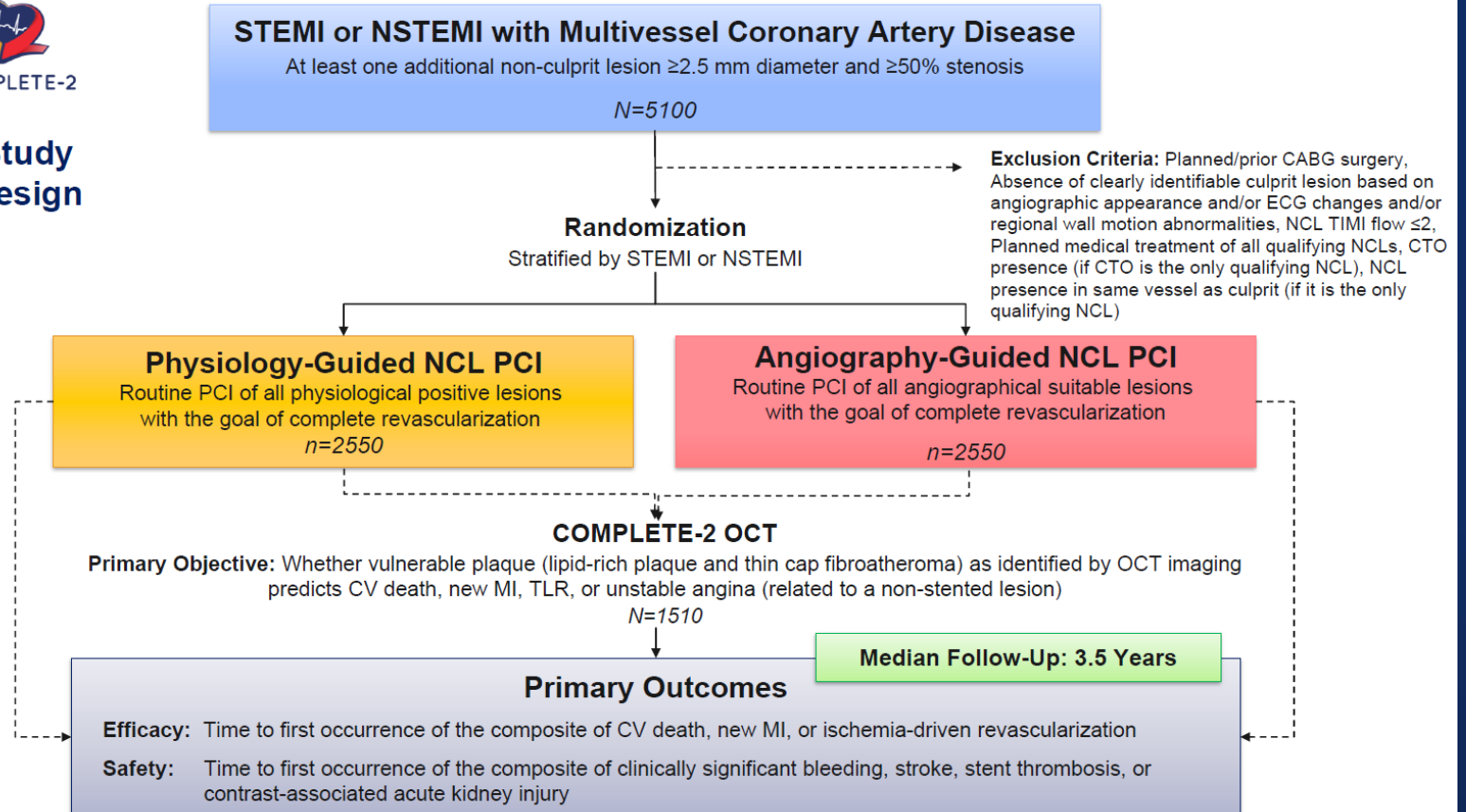
Underpowered

COMPLETE-2 Trial-currently enrolling

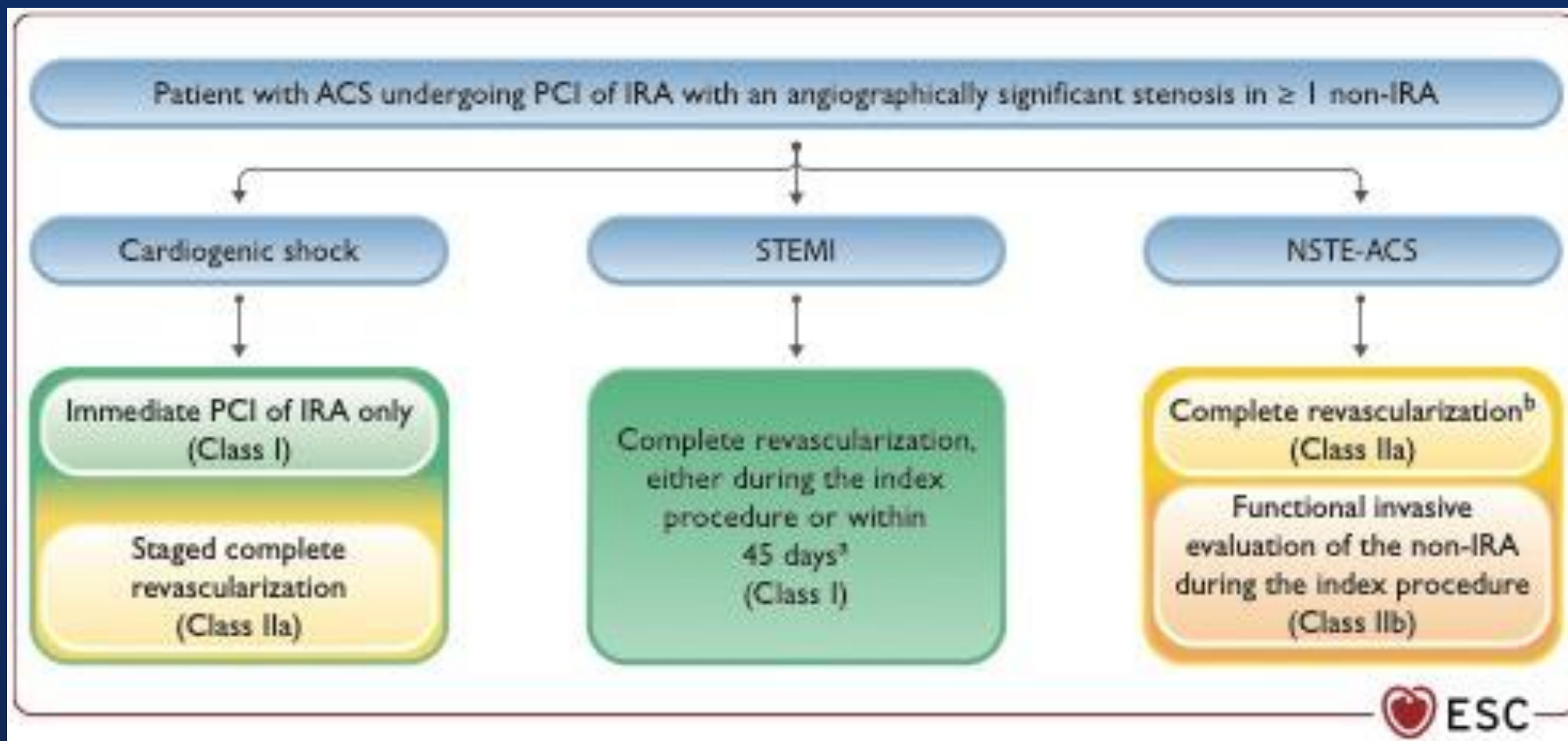
- Will a physiology-guided approach to NCL permit safe deferral of PCI in an ACS population?
- Large OCT substudy: Does plaque morphology predict future events?



Study Design



Algorithm for the management of ACS patients with multivessel CAD

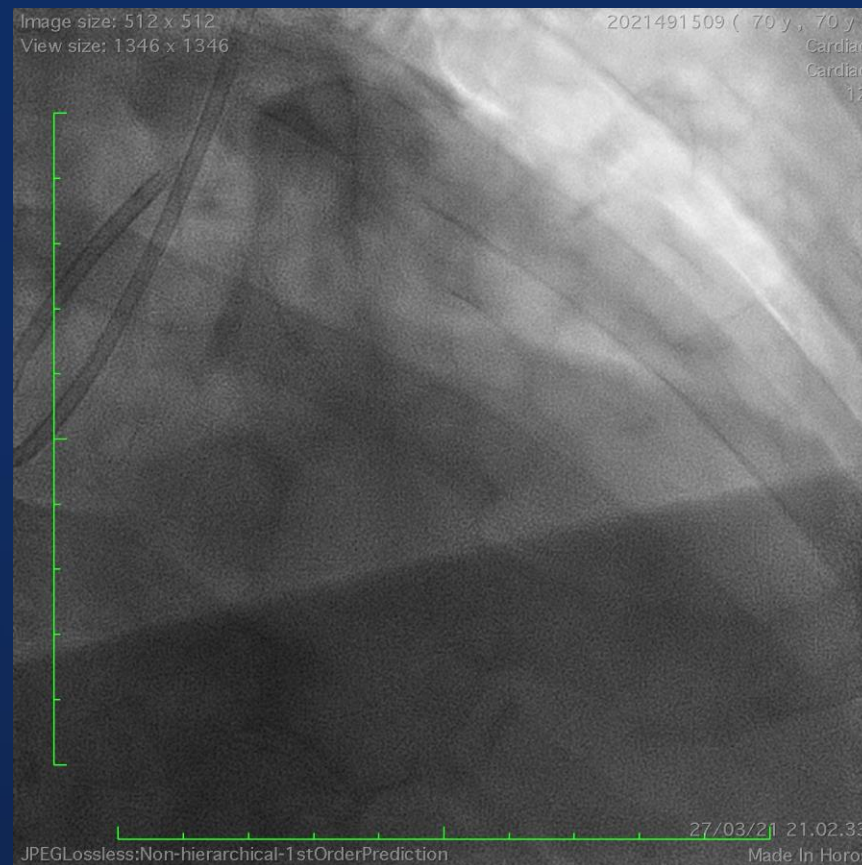
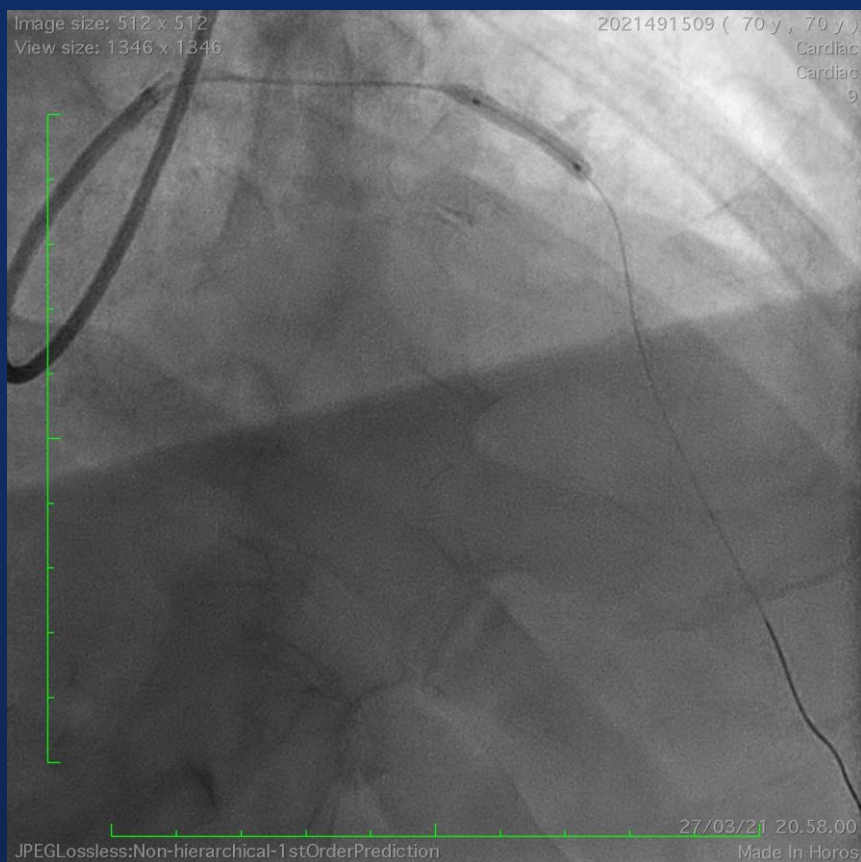


Who should NOT get non-IRA PCI?

- Lesion subsets at high risk for additional dysfunction
 - Calcified vessels requiring atherectomy
 - Stable saphenous vein graft disease
- Lesions where procedure may be prolonged
 - Vessel tortuosity
 - CTO
- Insignificant territory
- Renal dysfunction
- Shock

Back to our case....

Anterior STEMI with CAD 3VD



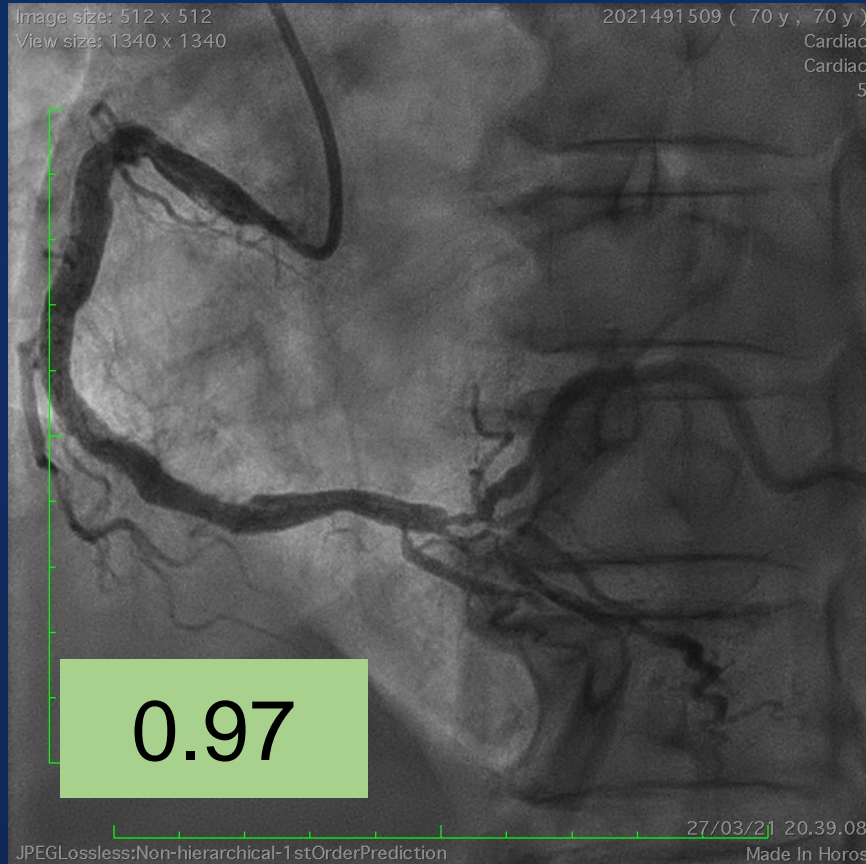
Heart Team Discussion

- Debatable RCA lesion significance : angiographic significant lesion, dominant ,but short & distal
- Small caliber LCx – not ideal for graft



iFR & IVUS-guided PCI

iFR RCA – day 3



- Non-significant
- Conservative strategy

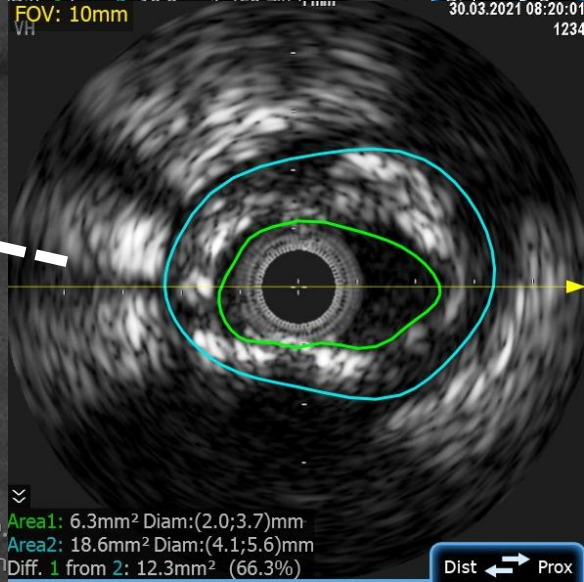
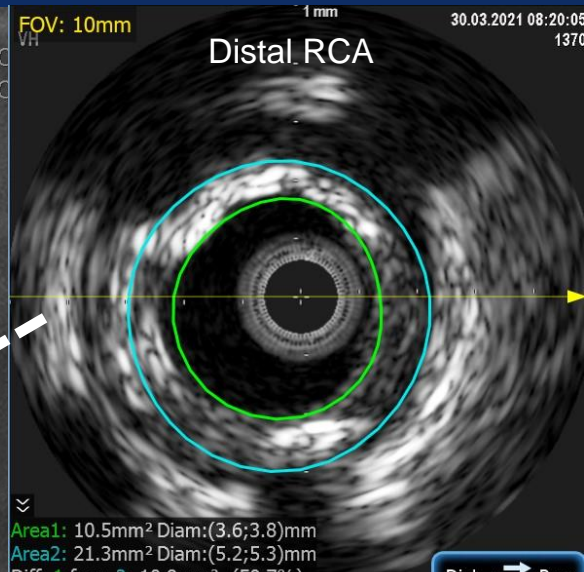
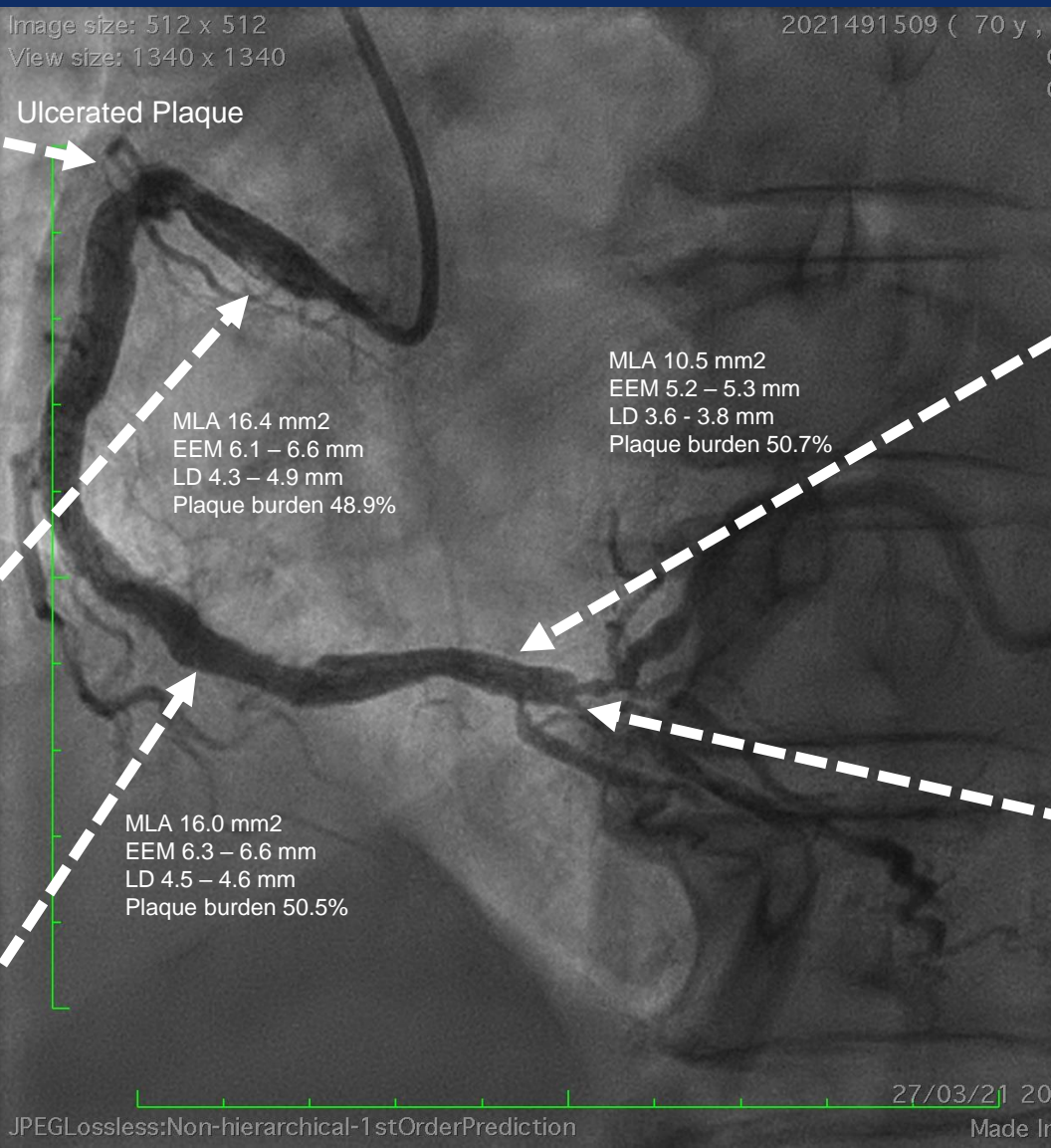
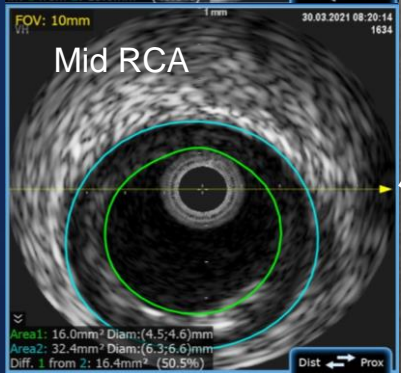
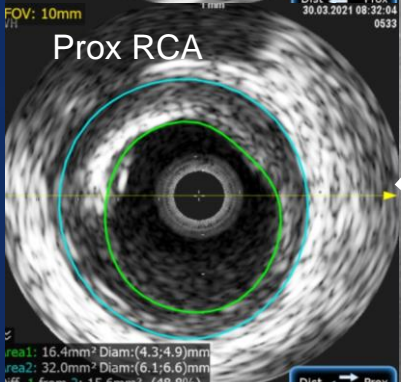
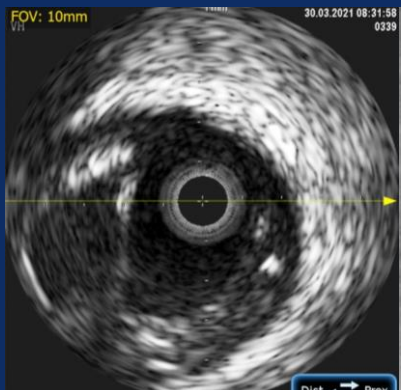


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View size: 1340 x 1340

2021491509 (70 y)

Ulcerated Plaque

MLA 16.4 mm²
EEM 6.1 – 6.6 mm
LD 4.3 – 4.9 mm
Plaque burden 48.9%

MLA 10.5 mm²
EEM 5.2 – 5.3 mm
LD 3.6 - 3.8 mm
Plaque burden 50.7%

MLA 16.0 mm²
EEM 6.3 – 6.6 mm
LD 4.5 – 4.6 mm
Plaque burden 50.5%

Distal RCA

Prox RCA

Mid RCA

FOV: 10mm

FOV: 10mm

FOV: 10mm

FOV: 10mm

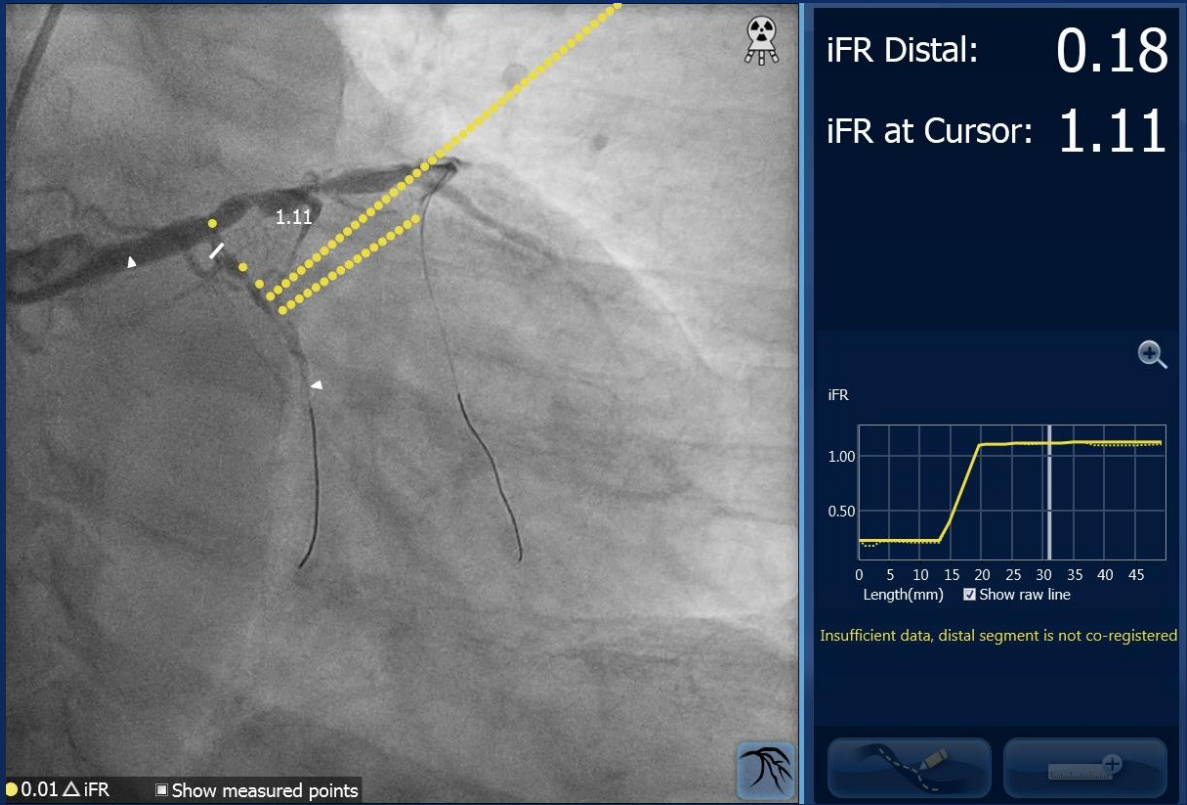
FOV: 10mm

FOV: 10mm

Dist ← Prox

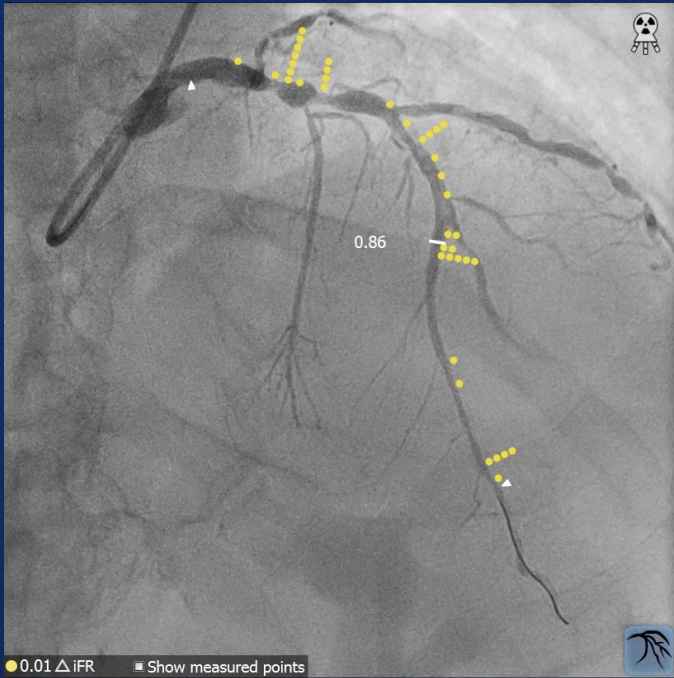
Dist ← Prox

iFR LCx + Pullback

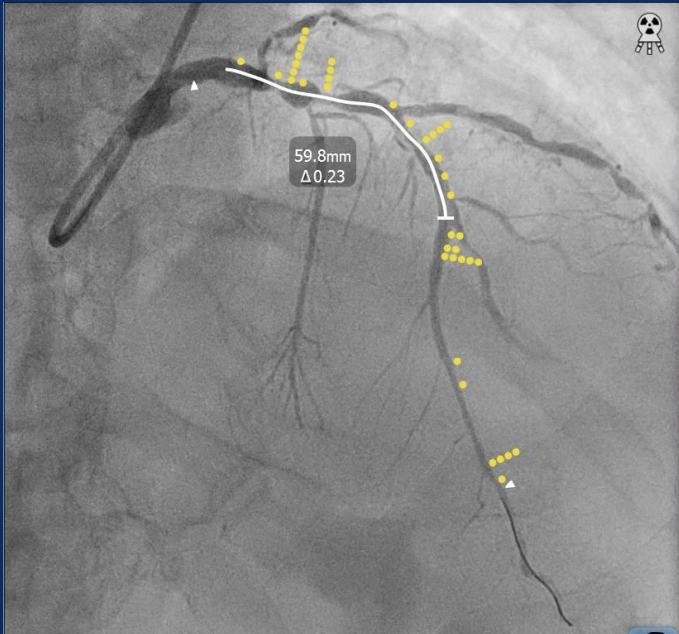
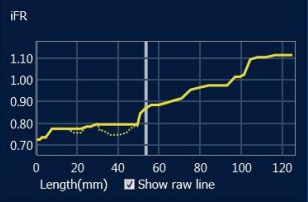


- Significant lesion
- Small vessel caliber

iFR LAD



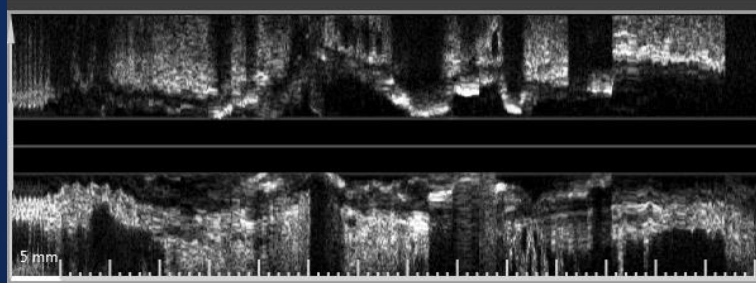
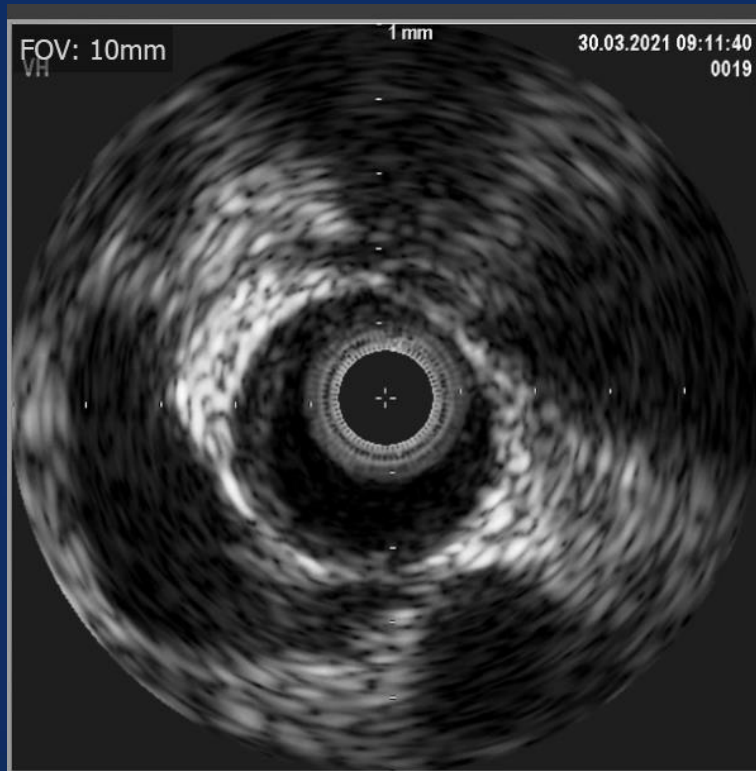
iFR Distal: 0.72
iFR at Cursor: 0.86



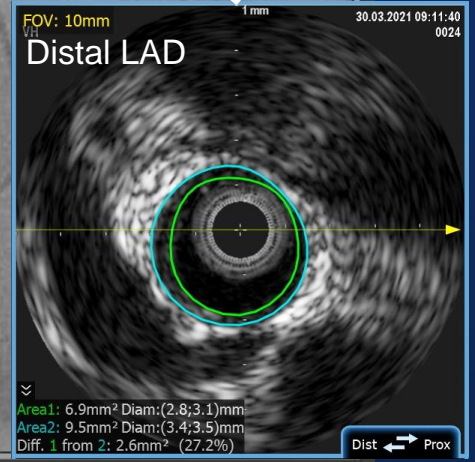
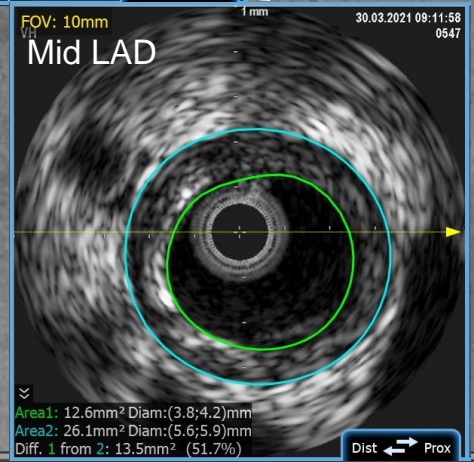
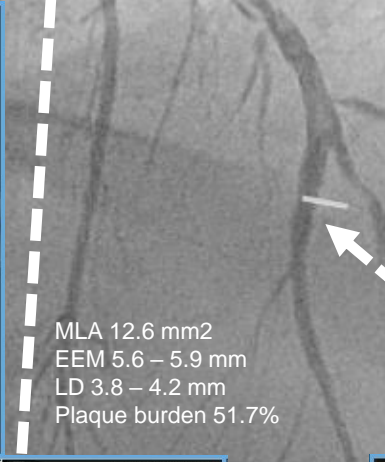
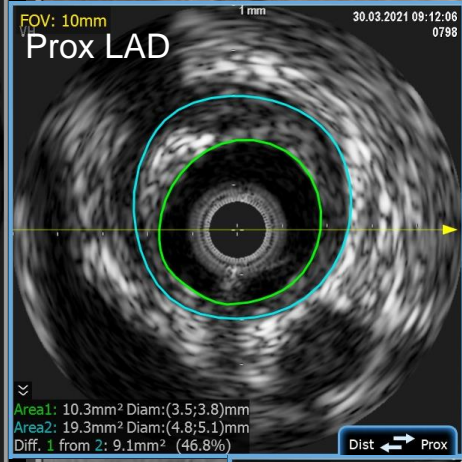
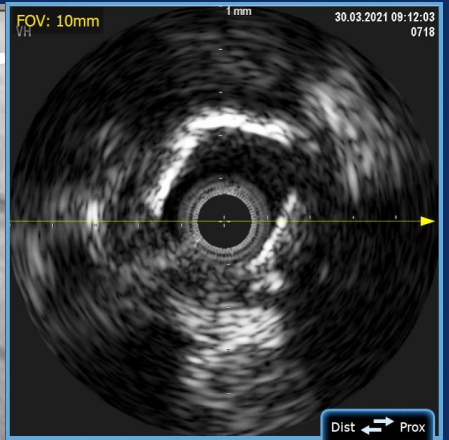
iFR Distal: 0.72
iFR Estimate: 0.95



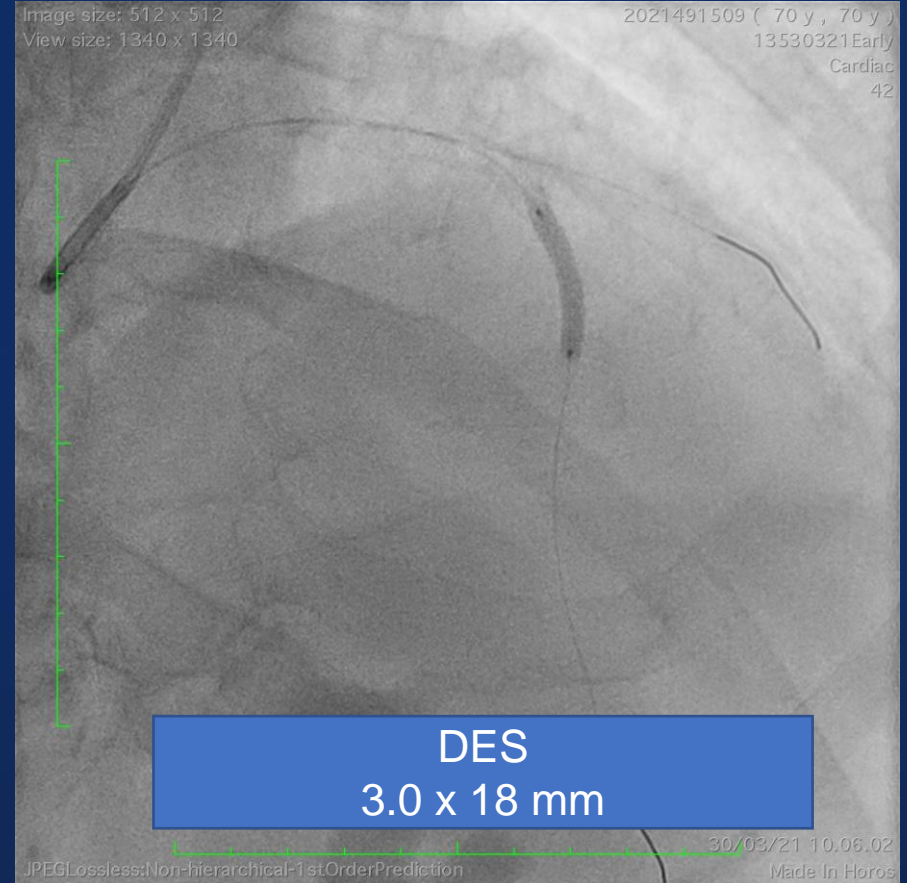
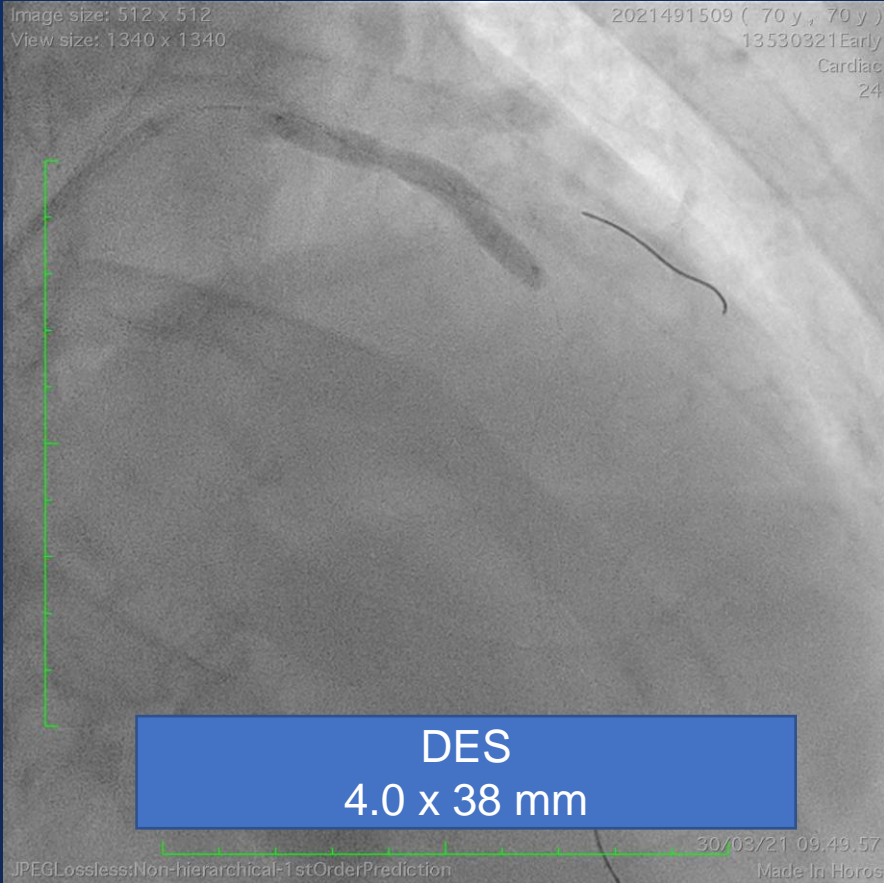
Stent length estimation by iFR : **59.8 mm**



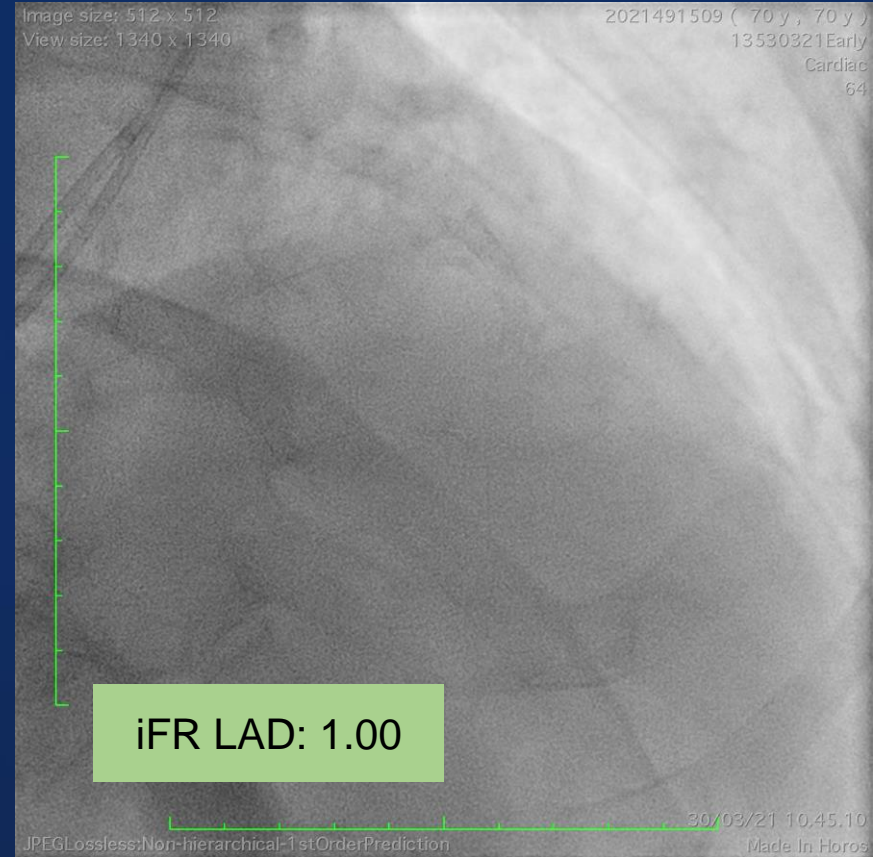
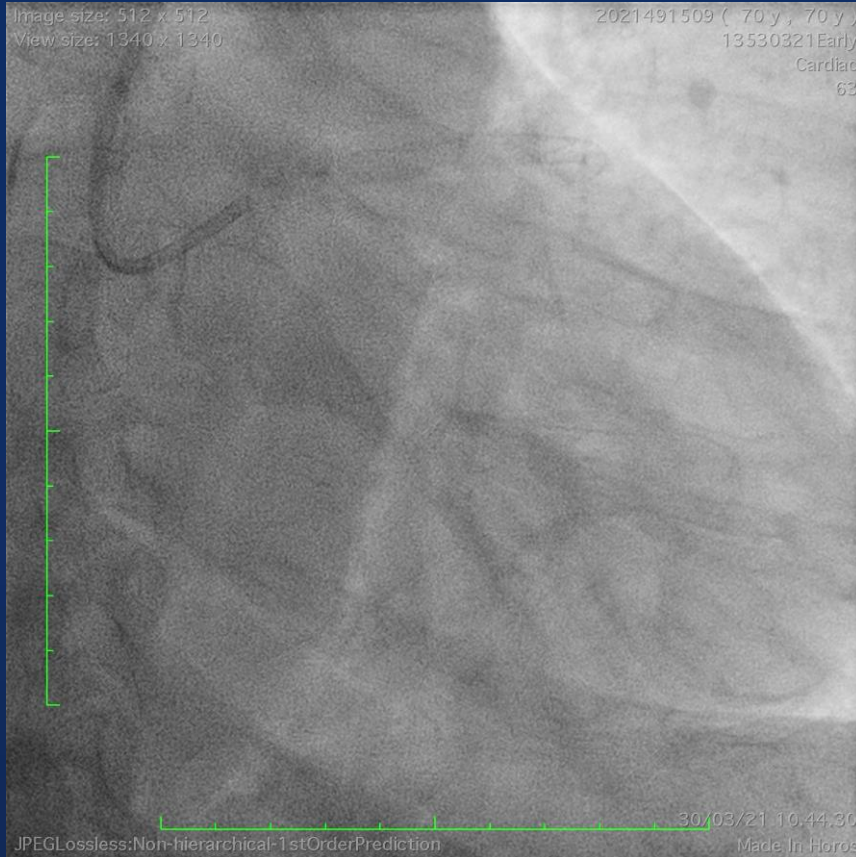
Pre – PCI IVUS LAD

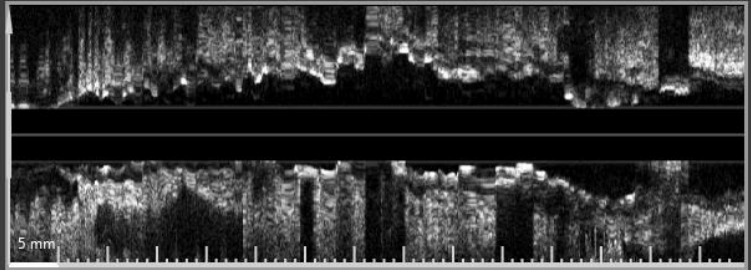


PCI LAD

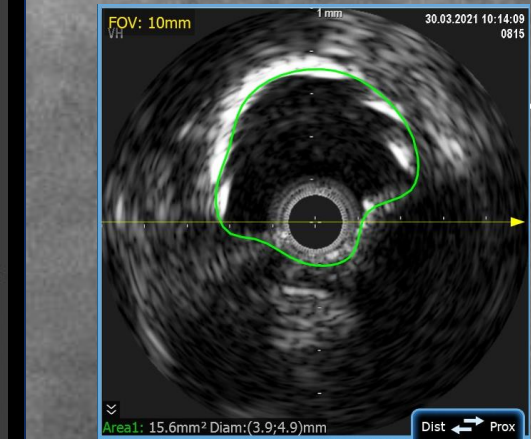
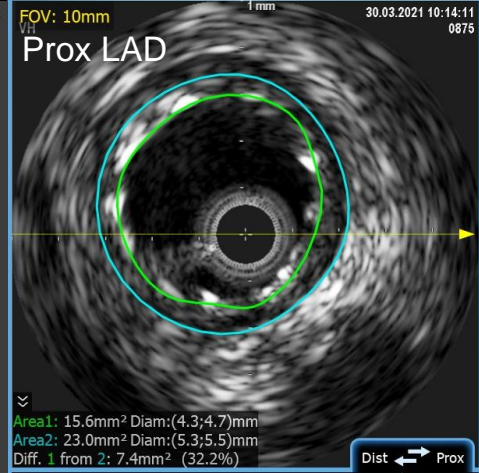


POBA LCX + Final Angiography



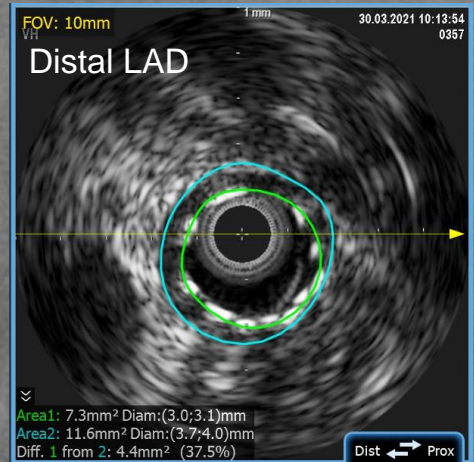


Post – PCI IVUS LAD

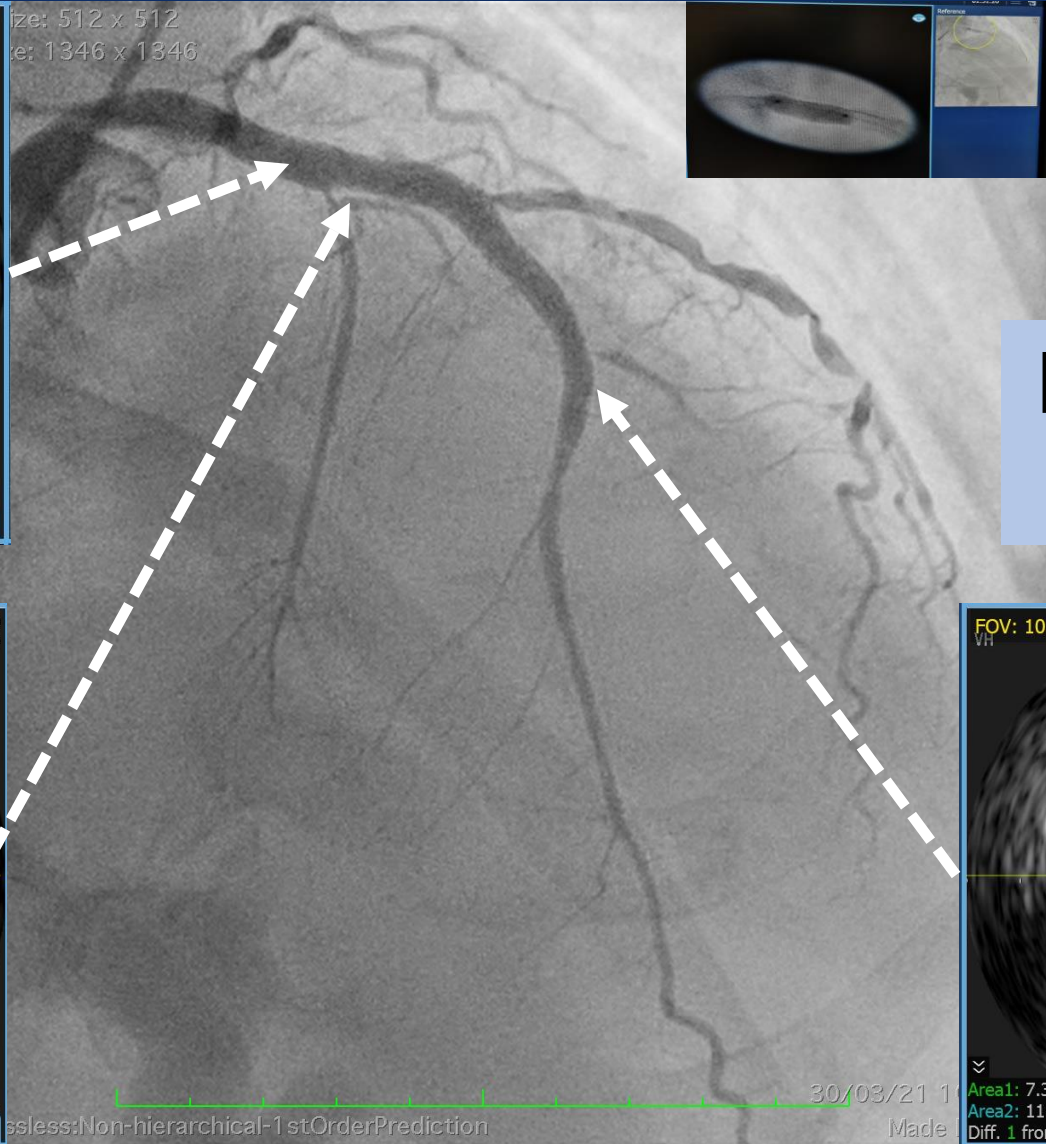
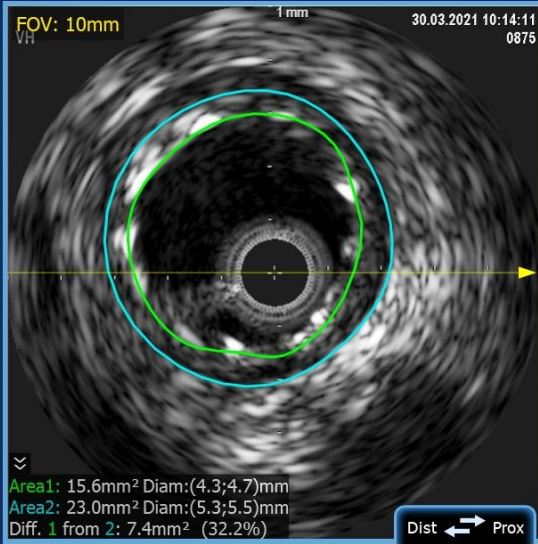


MSA 15.6 mm²
Diameter 4.3 – 4.7 mm

MSA 7.3 mm²
Diameter 3.0 – 3.1 mm

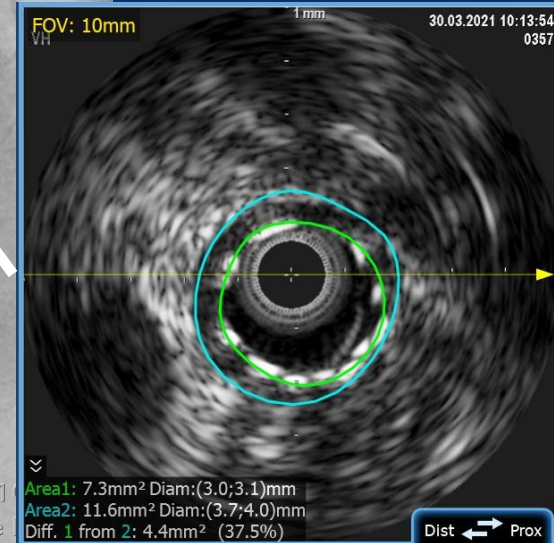
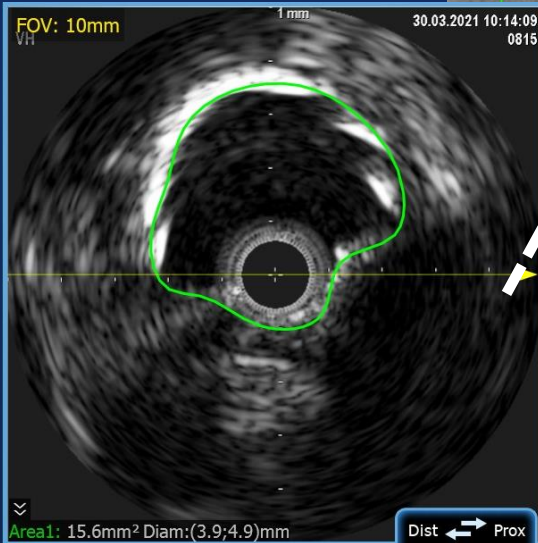


- M No Medial Dissection
- A Well Apposed
- X Well Expanded



NC 4.5 x
12

**POST-PCI
LAD IVUS**



Take home message

1. STEMI with MVD, complete revascularization is the way to go
 - Consider at the same time if tight type-A lesion
 - Will stage most other lesion (within 45 days)
 - POBA-only culprit (or DES) and consider surgery if high Syntax score
2. In staging case, consider physiology-guided for moderate non culprit lesion and angio-guided for significant non culprit lesion