CUORE
E NON SOLO
INTERVENTIONAL
CARDIOLOGY
14/15.04.23
GENOVA

CORONARY IMAGING & PHYSIOLOGY
INNOVATION IN TRANSCATHETER INTERVENTIONS

Terapia antitrombotica nel paziente con SCA: il meccanismo guida la terapia?

UNIVERSITÀ DEGLI STUDI DI GENOVA

OSPEDALE POLICLINICO SAN MARTINO
Sistema Sanitario Regione Liguria
Istituto di Ricovero e Cura a Carattere Scientifico

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UOSD Cardiologia Interventistica
IRCCS Ospedale Policlinico San Martino
Università degli Studi di Genova

Genova, 14-15 aprile 2023

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DI GENOVA

Disclosures

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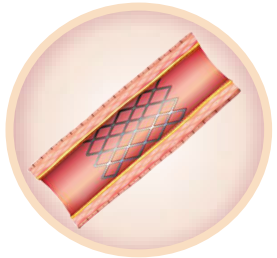
- Consulting or lecturing fees from: Abbott Vascular, Amgen, Medtronic, and Terumo.

Balancing ischemic and bleeding risk



ESC
European Society of Cardiology

Thrombotic or ischemic risk

High thrombotic risk defined as:

- **Complex coronary artery disease** based on individual clinical judgement with knowledge of patients' cardiovascular history and/or coronary anatomy
- PLUS at least 1 among 7 additional **risk enhancers** (e.g., DM, PAD, recurrent MI, etc.) or 5 **technical aspects**

Bleeding risk

High bleeding risk defined as:

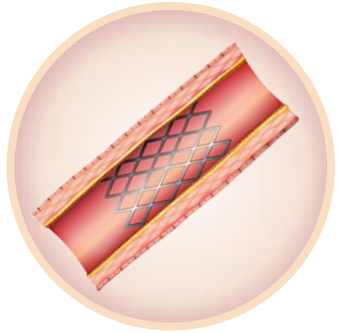
- At least 1 among 10 major **ARC-HBR** criteria
- At least 2 among 6 minor ARC-HBR criteria
- **PRECISE-DAPT** score ≥25

Collet JP, et al. Eur Heart J. 2021;42:1289-1367

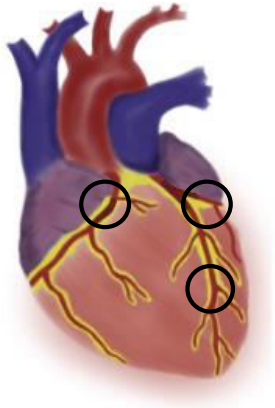
Thrombotic or ischemic risk

TECHNICAL ASPECTS

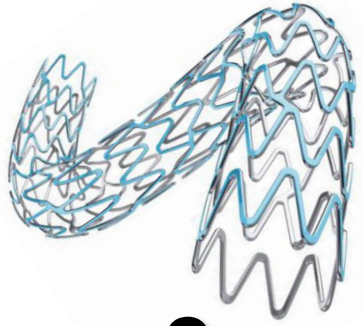
1
At least 3 stents implanted



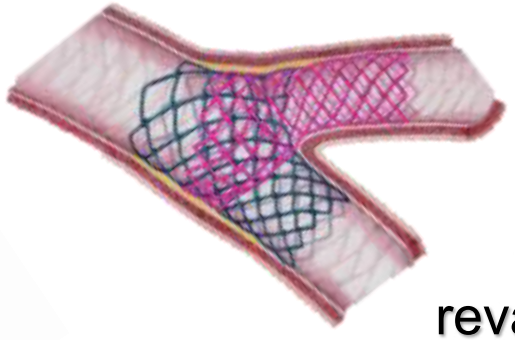
5
History of stent thrombosis



2
At least 3 lesions treated



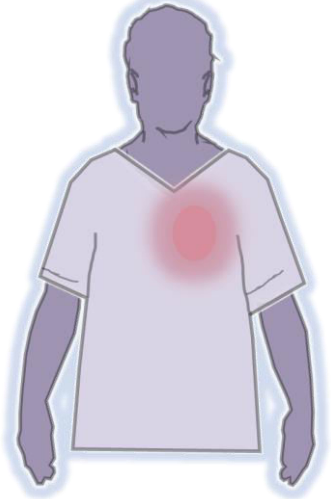
3
Total stent length >60 mm



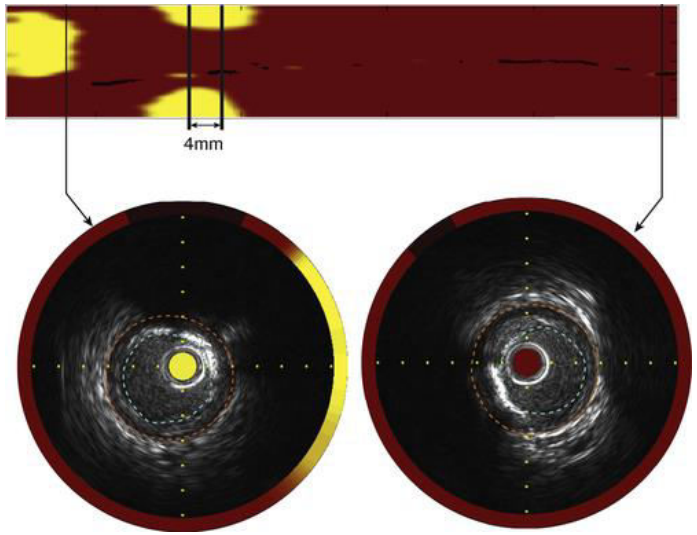
4
Complex revasularization (left main, 2-stent bifurcation, CTO, stenting of last remaining vessel

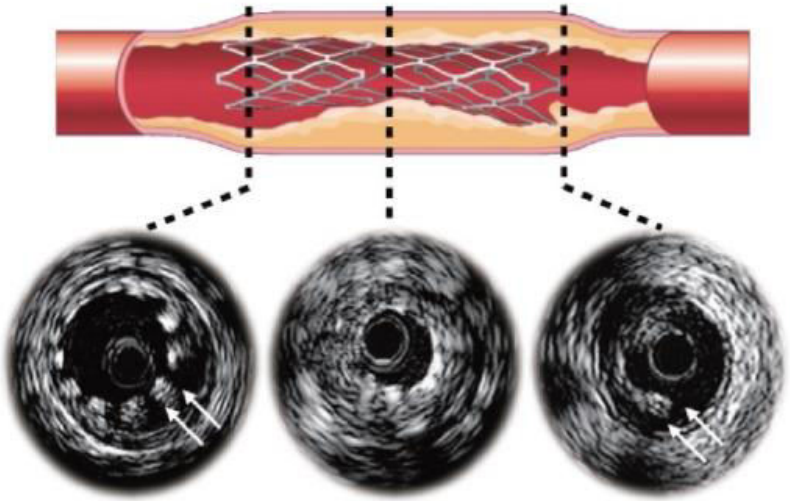
Further refining ischemic risk after ACS?

1
Mechanisms of ACS (rupture vs erosion)



2
Pancoronary vulnerability (TCFA, plaque burden, LCBI)

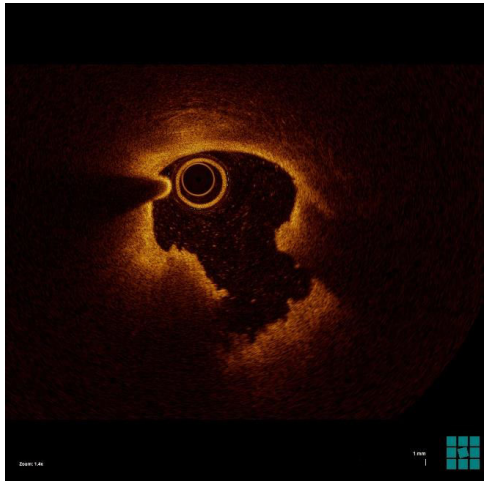




3
Suboptimal stent findings (underexpansion, malapposition, edge dissection)

Not all ACS are born equal

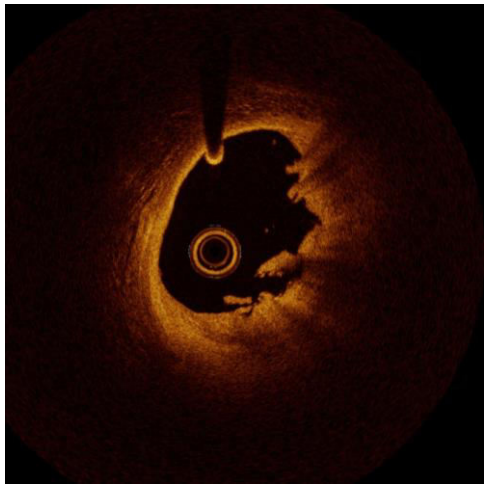
Plaque rupture (60-70%)



Disrupted vessel integrity

- Lipid-rich/TCFA
- Larger thrombus burden
- > Red thrombus

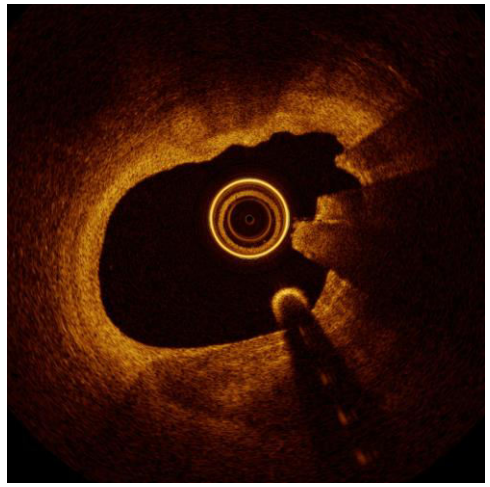
Plaque erosion (30-40%)



Preserved vessel integrity

- Fibrous plaque/ThCFA
- Smaller thrombus burden
- > White (platelet-rich) thrombus

Eruptive calcified nodule (5-8%)



Disrupted vessel integrity

- Protruding calcium
- Substantive calcium prox/dist
- Mixed thrombus

Different pathological entities

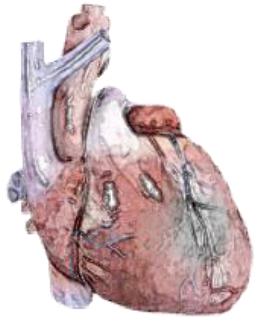
- Different clinical outcome
- Different response to medical therapy and PCI
- Different pancoronary atherosclerotic burden and “vulnerability”

Jia H, et al. J Am Coll Cardiol 2013;19:1748-1758

Higuma T, et al. JACC Cardiovasc Interv 2015;8:1166-1176

Intact fibrous cap *versus* plaque rupture

SINGLE-CENTER, PROSPECTIVE STUDY



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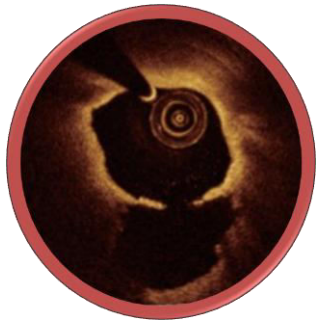
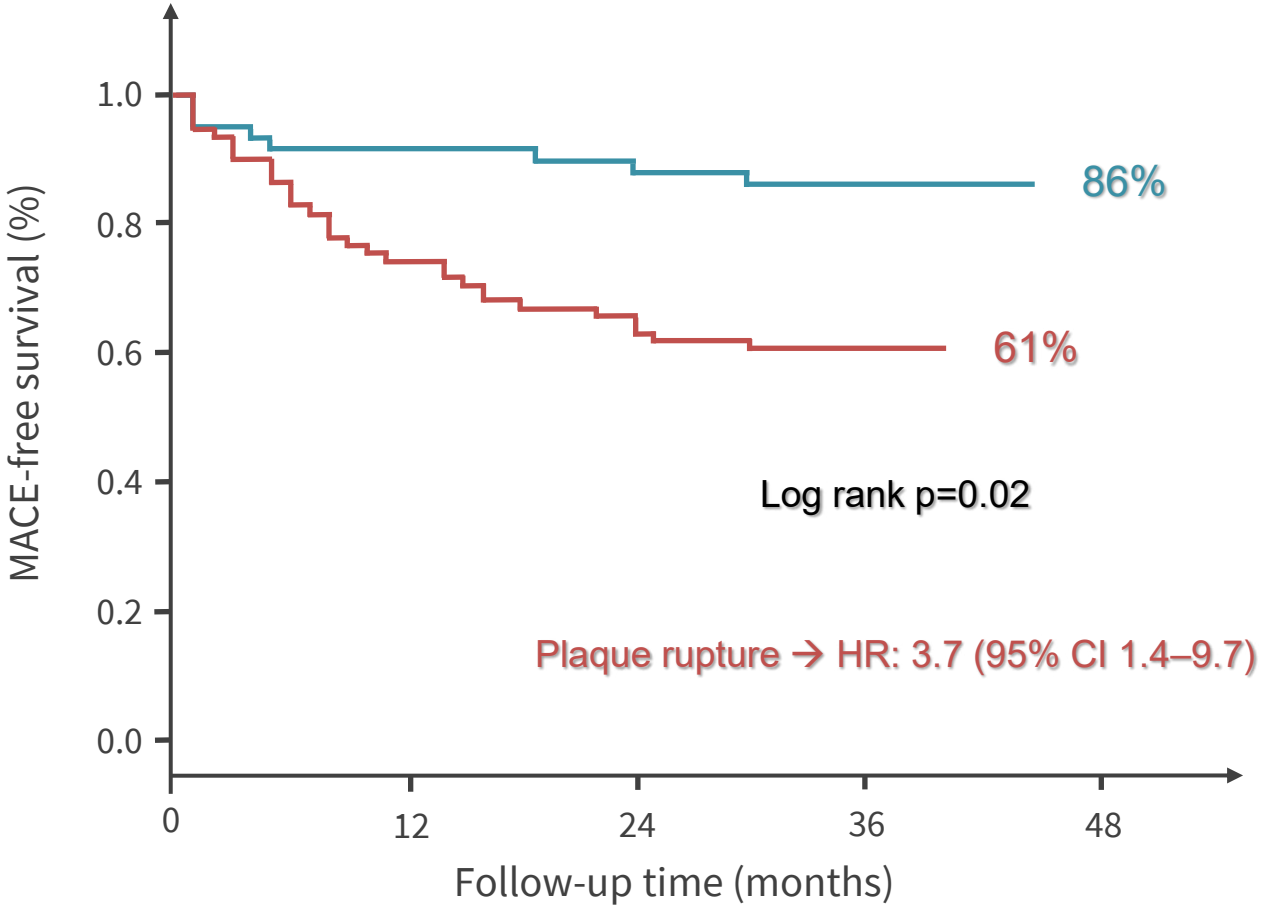
Patients with **ACS** undergoing **OCT imaging** of the culprit lesion

Plaque rupture *vs* **Intact fibrous cap**



N=82 (59%)

N=57 (41%)



MACEs were significantly lower in patients with IFC than in those with plaque PR

Niccoli G, et al. Eur Heart J 2015;36:1377-1384

Pancoronary vulnerability in patients with plaque rupture versus erosion

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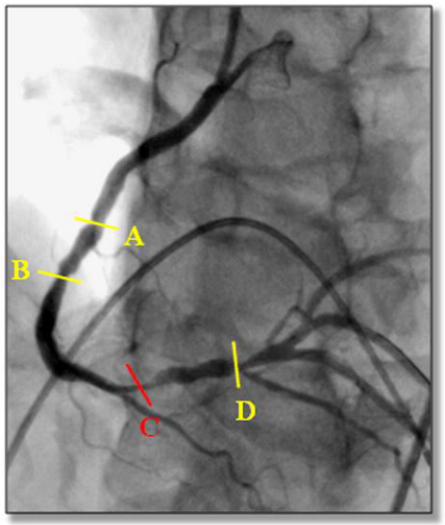
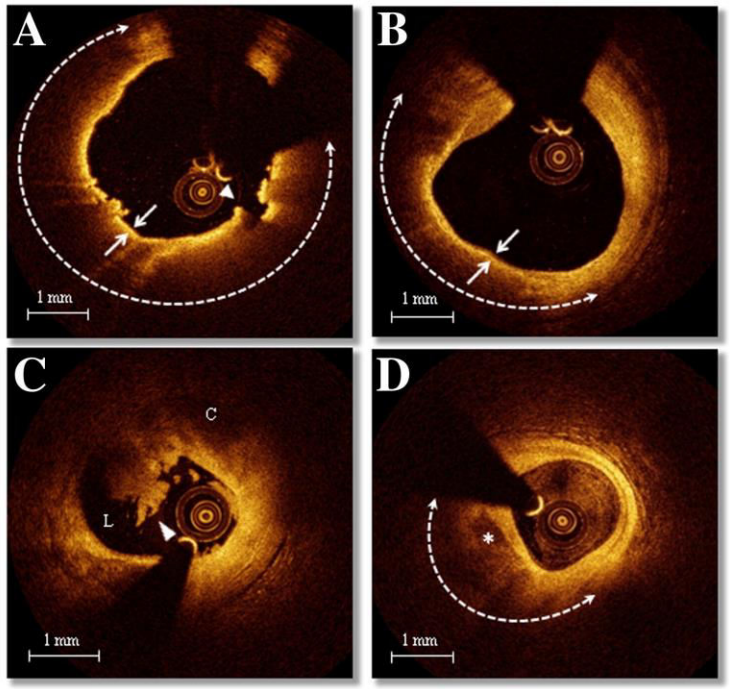
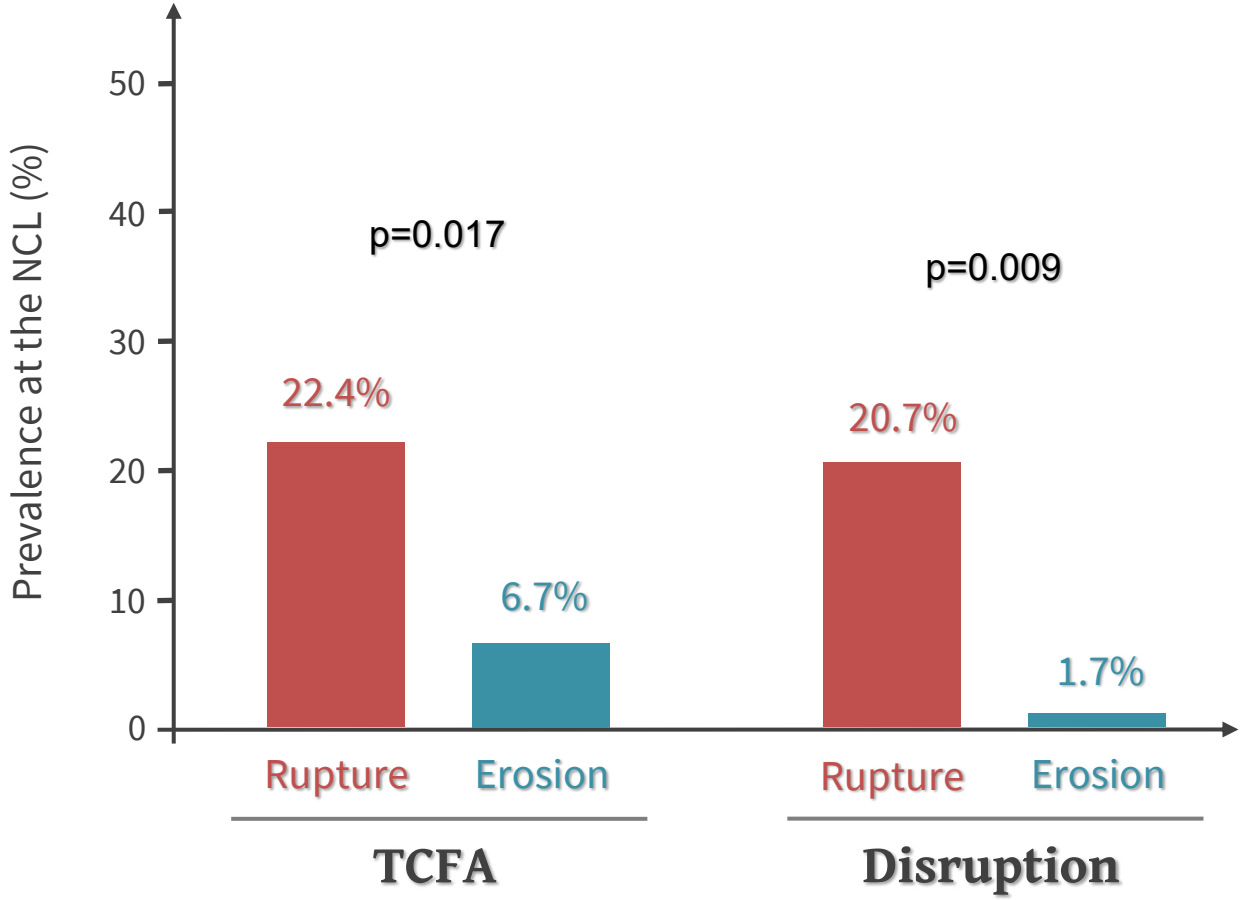
RETROSPECTIVE MULTICENTER STUDY (MGH OCT REGISTRY)

3-VESSEL OCT STUDY



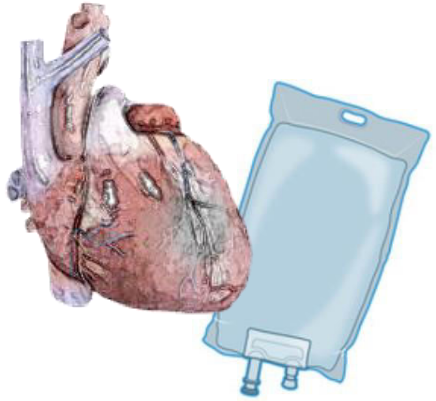




Patients with plaque rupture have greater pancoronary vulnerability

Plaque rupture *versus* erosion: response to fibrinolysis

RETROSPECTIVE SINGLE-CENTER STUDY



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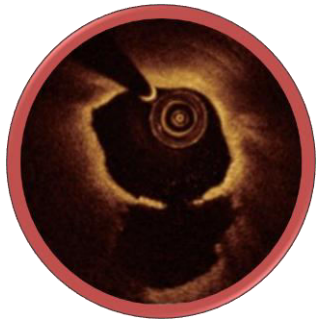
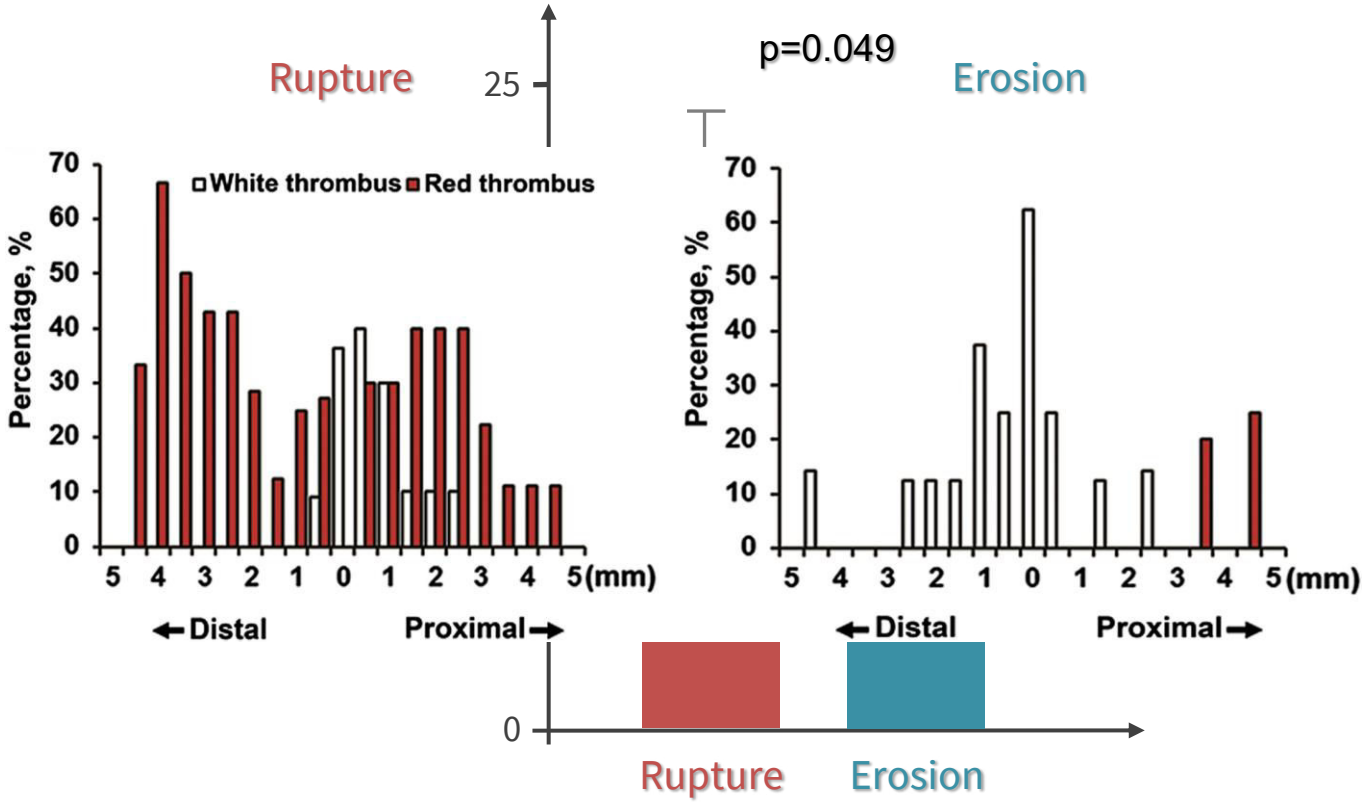
Patients with **STEMI** treated with **TENECTEPLASE** with successful fibrinolysis undergoing **OCT imaging** of the culprit lesion

Plaque rupture *vs* **Intact fibrous cap**

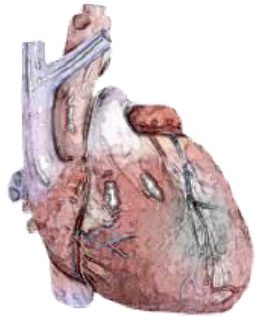




Hu S, et al. J Am Coll Cardiol 2014;13:1336-1338

OCT-based diagnosis and medical management of ACS caused by plaque erosion

CASE SERIES, MULTICENTER



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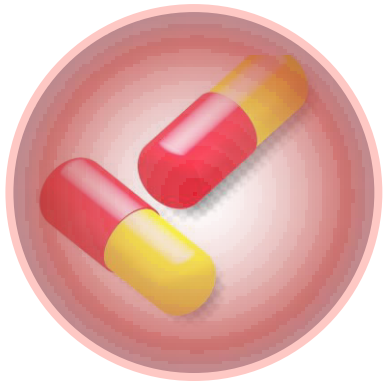
Patients with **STEMI** undergoing **OCT imaging** of the culprit lesion

With a diagnosis of

INTACT FIBROUS CAP

Medically treated



PCI with stent

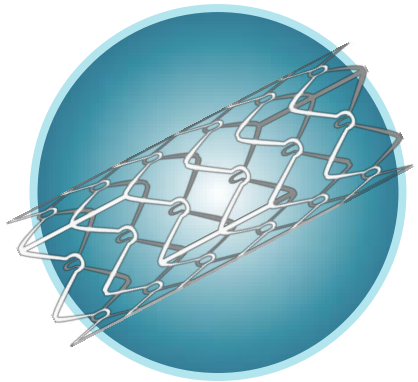


Table 2. Procedural Characteristics

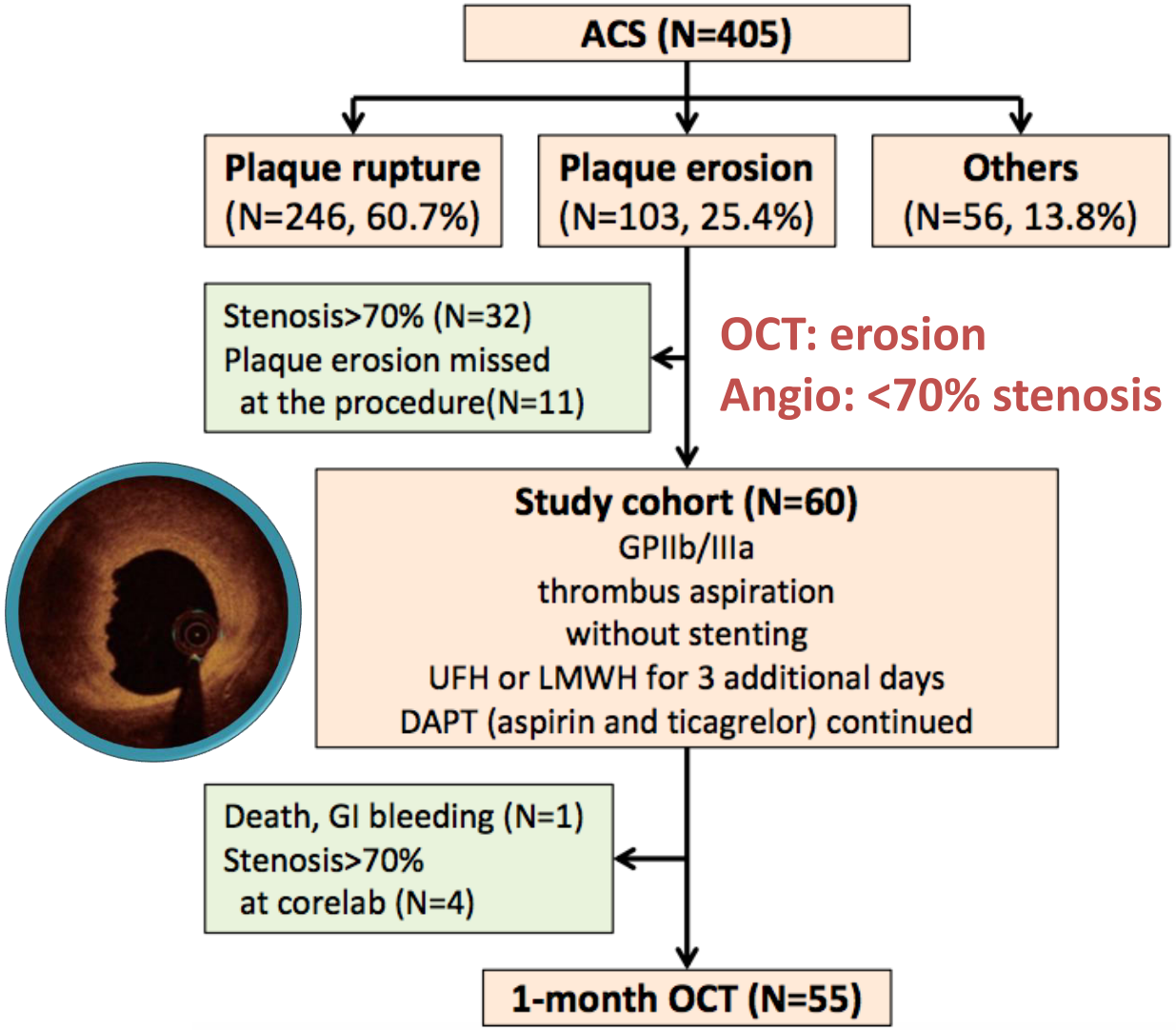
	Group 1 (n = 12)	Group 2 (n = 19)	p Value
Glycoprotein IIb/IIIa inhibitors	4 (33	4 (21)	0.73
ADP antagonists			0.042
Clopidogrel	7 (58)	18 (95)	
Prasugrel	5 (42)	1 (5)	
Angiographic analysis			
Pre-aspiration DS, %	79.4 ± 33.3	87.9 ± 17.3	0.95
Post-aspiration DS, %	27.1 ± 19.4	32.0 ± 35.2	0.48
Pre-aspiration TIMI flow grade ≤2	9 (75)	15 (79)	0.85
Post-aspiration TIMI flow grade ≤2	1 (8)	0	0.81
Total ischemic time, h	3.5 ± 3.0	3.6 ± 2.3	0.82

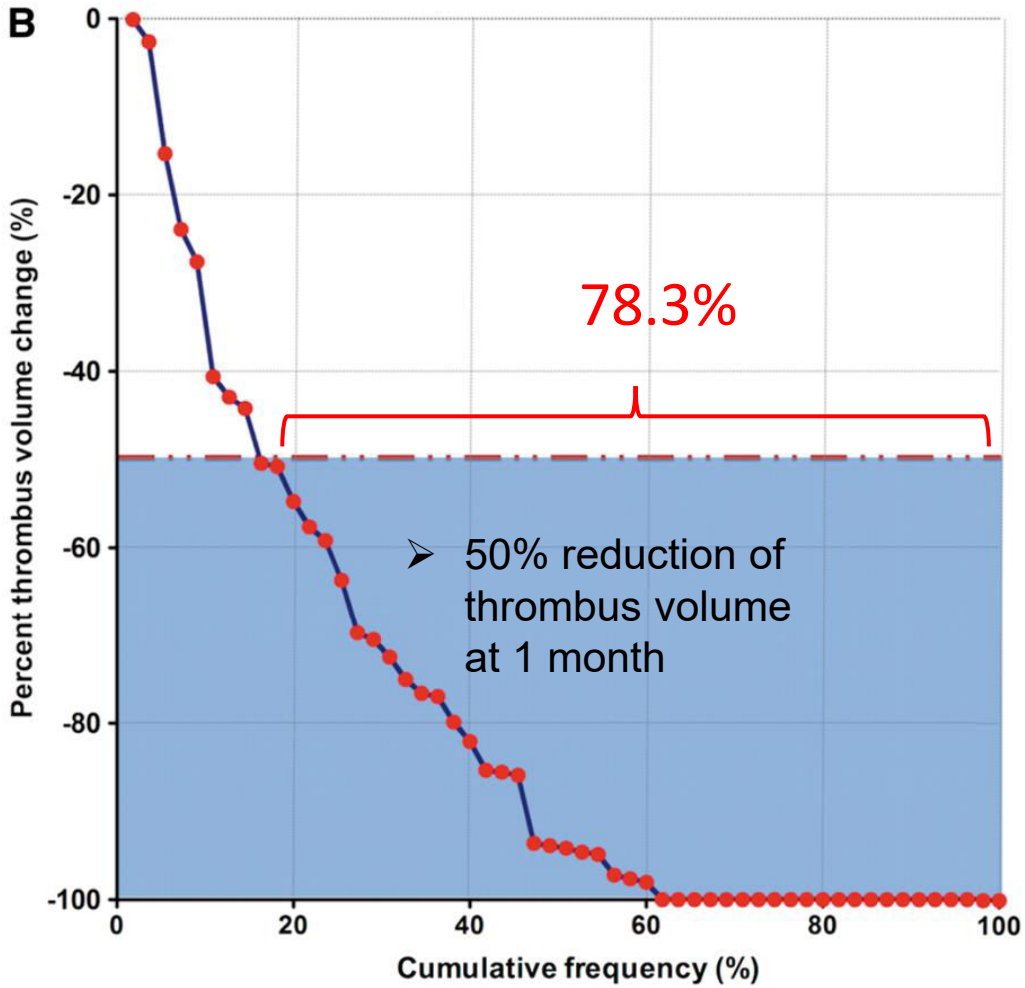
Values are n (%) or mean ± SD.
ADP = adenosine diphosphate; DS = diameter stenosis; TIMI = Thrombolysis In Myocardial Infarction.

Median follow-up 753 days: 1 TLR in group 2

Prati F, et al. JACC Cardiovasc Imaging 2013;6:283-287

The EROSION study



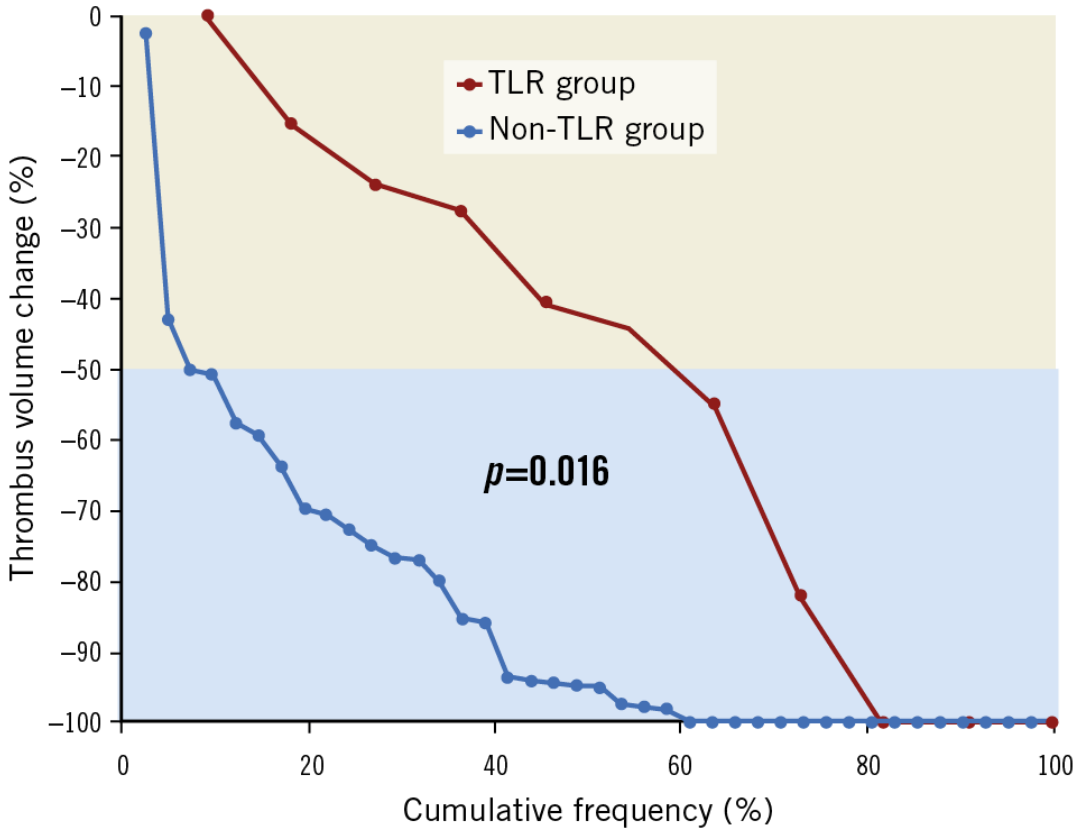


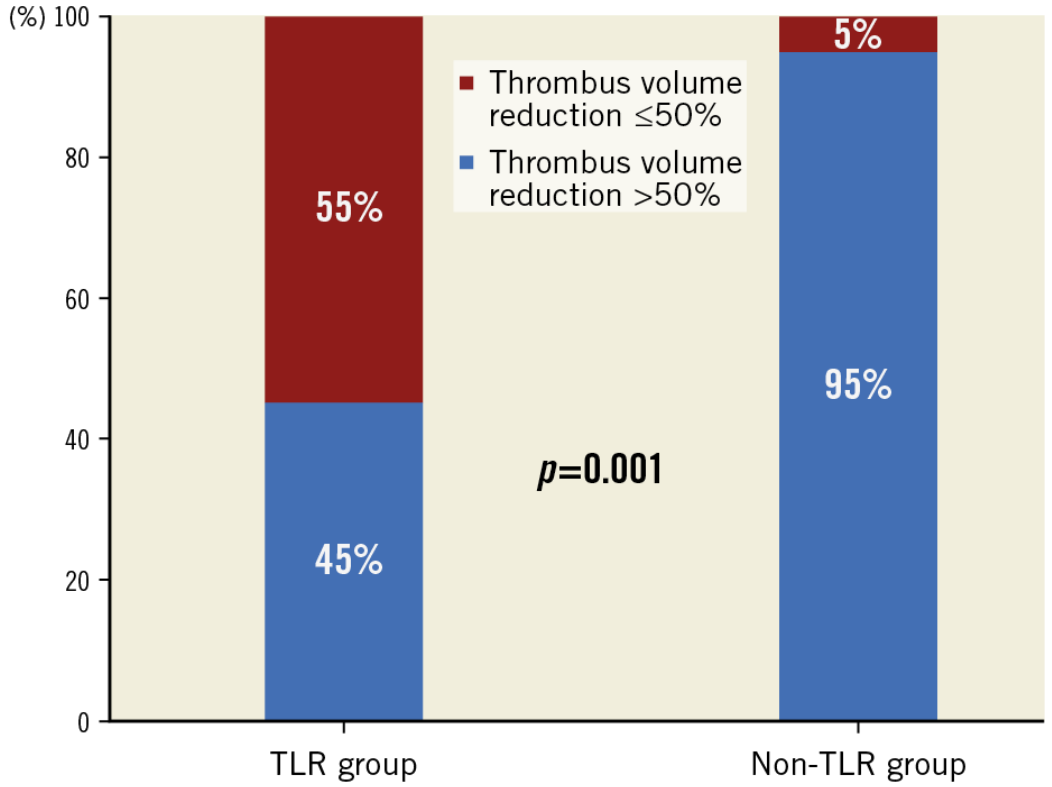
Jia H, et al. Eur Heart J 2017;38:792-800

The EROSION study: 4-year follow-up

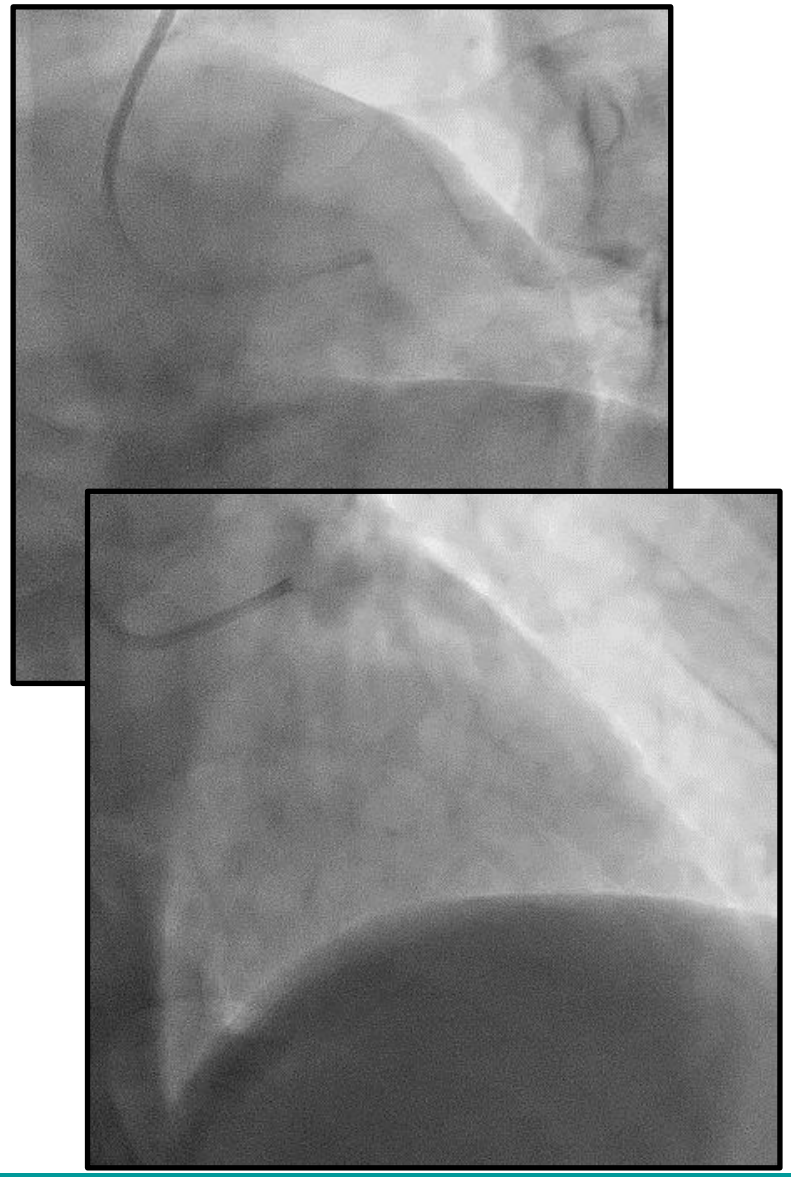
NO patient had death, MI, stroke, HF, unstable angina induced rehospitalization or CABG
Only 1 GI bleeding requiring interruption of ticagrelor after 3 months

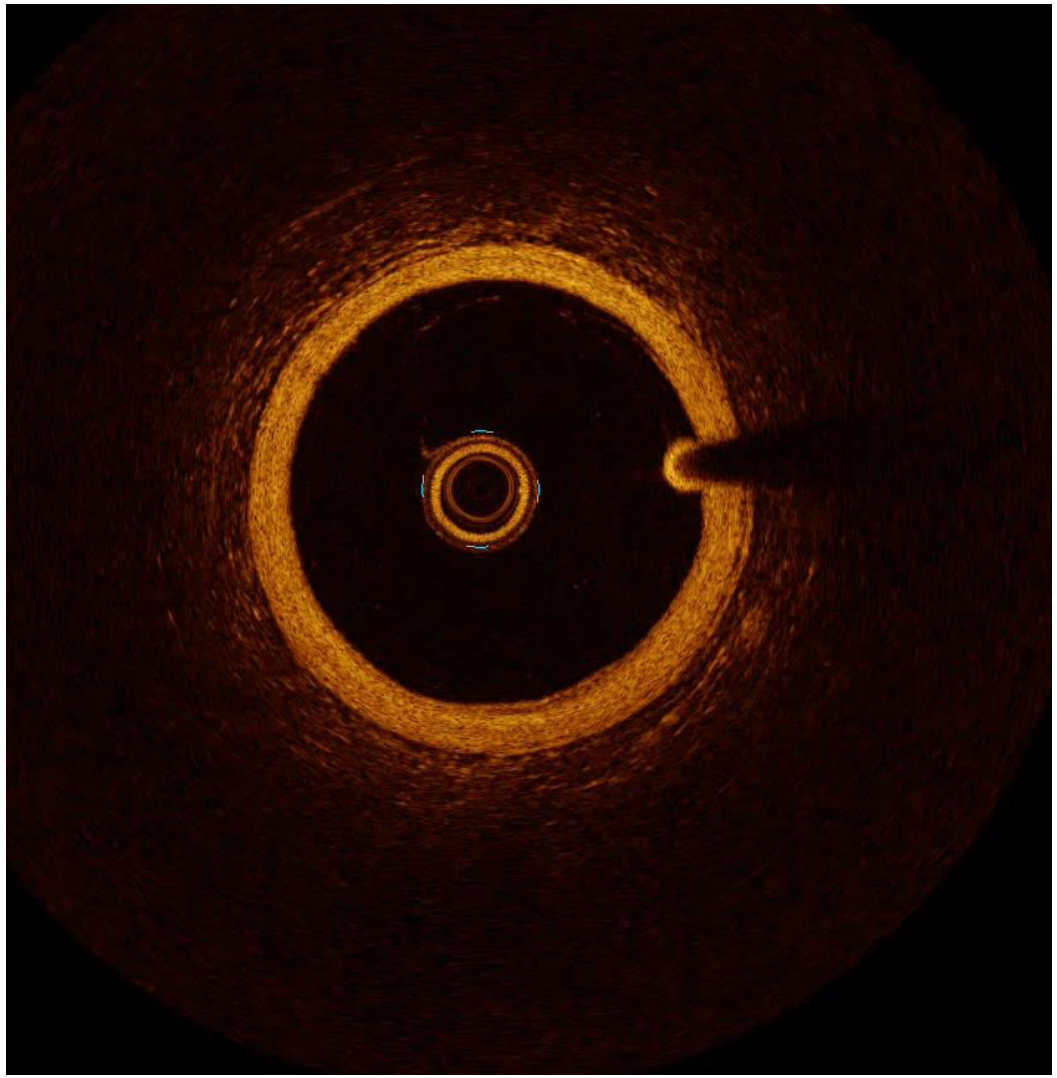
TLR in 11 patients (21%)



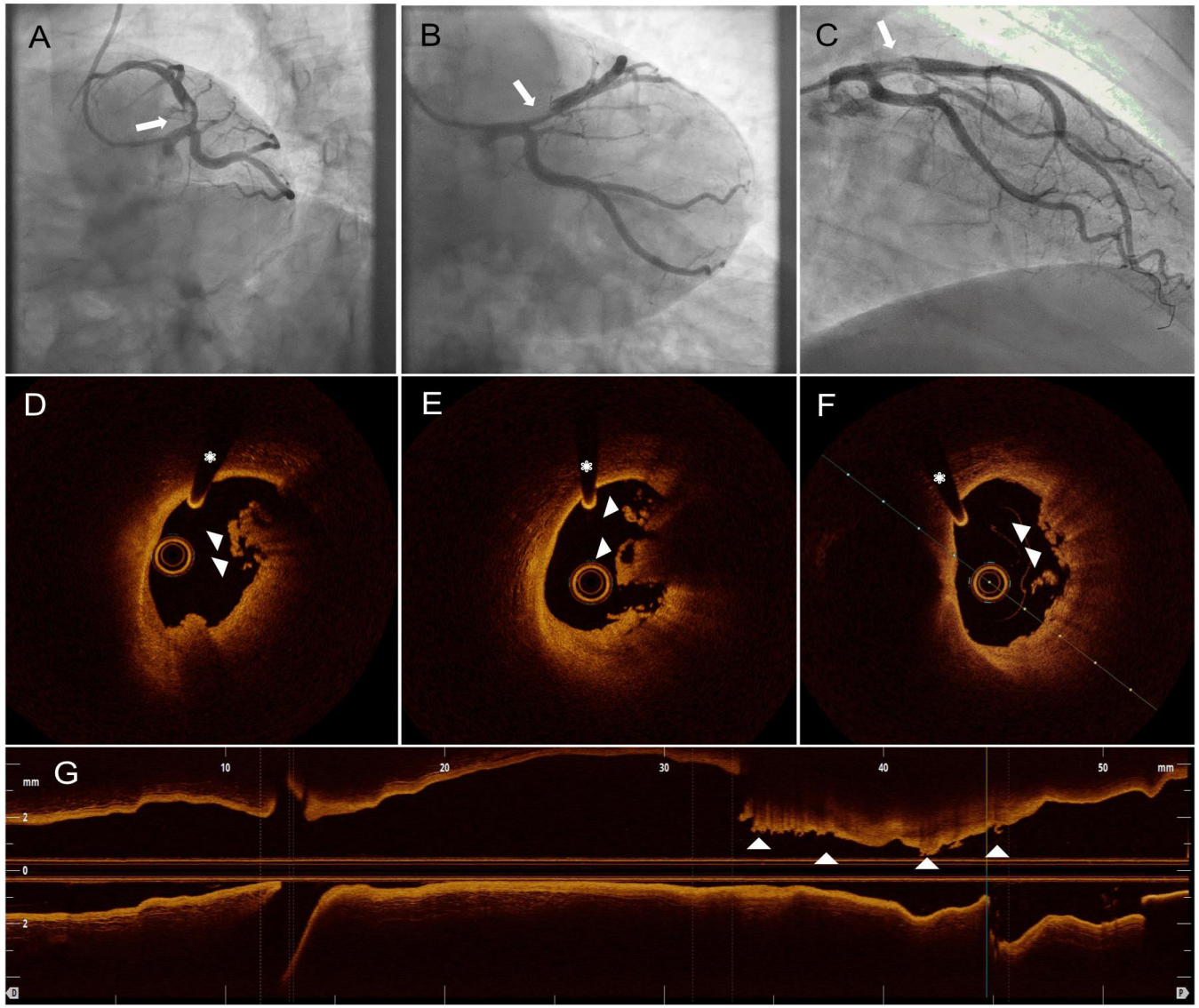


Clinical case (45 yo male, STEMI)



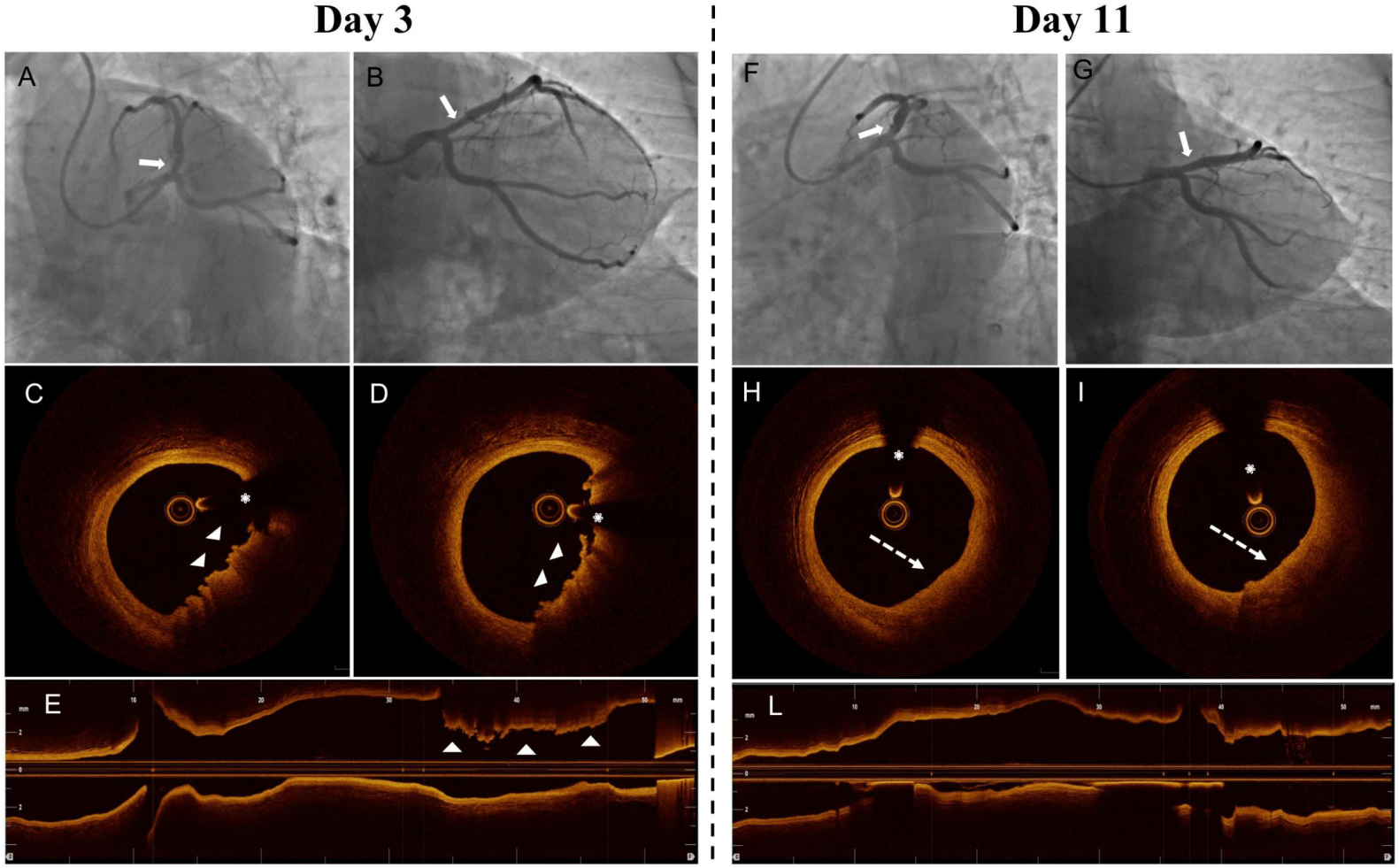


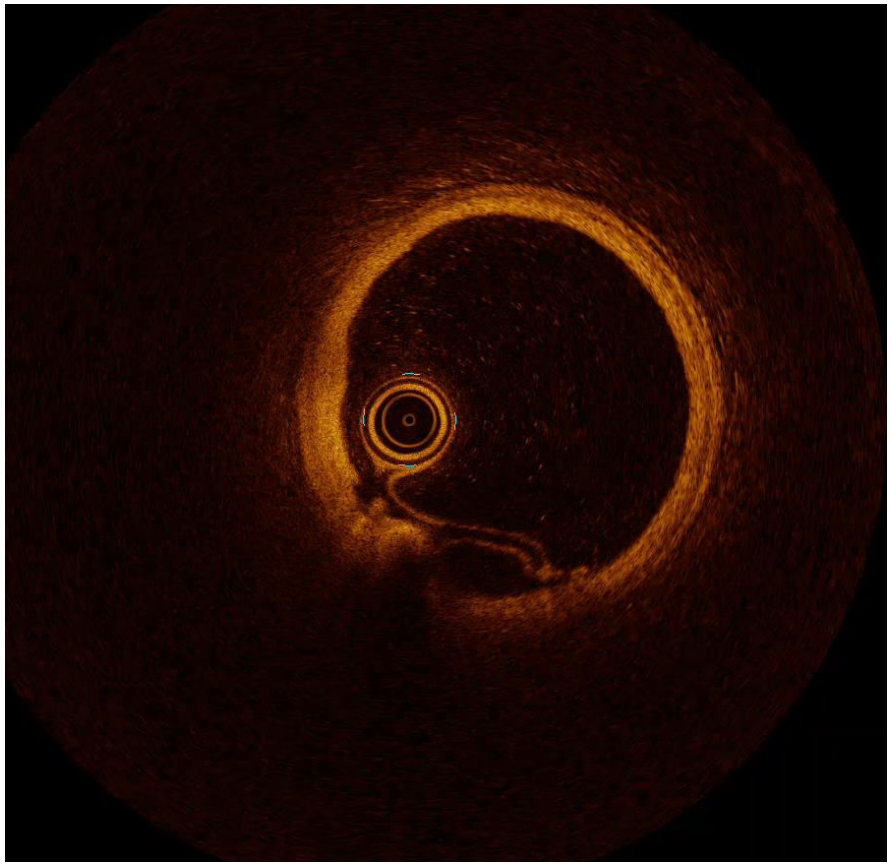
Clinical case (45 yo male, STEMI)



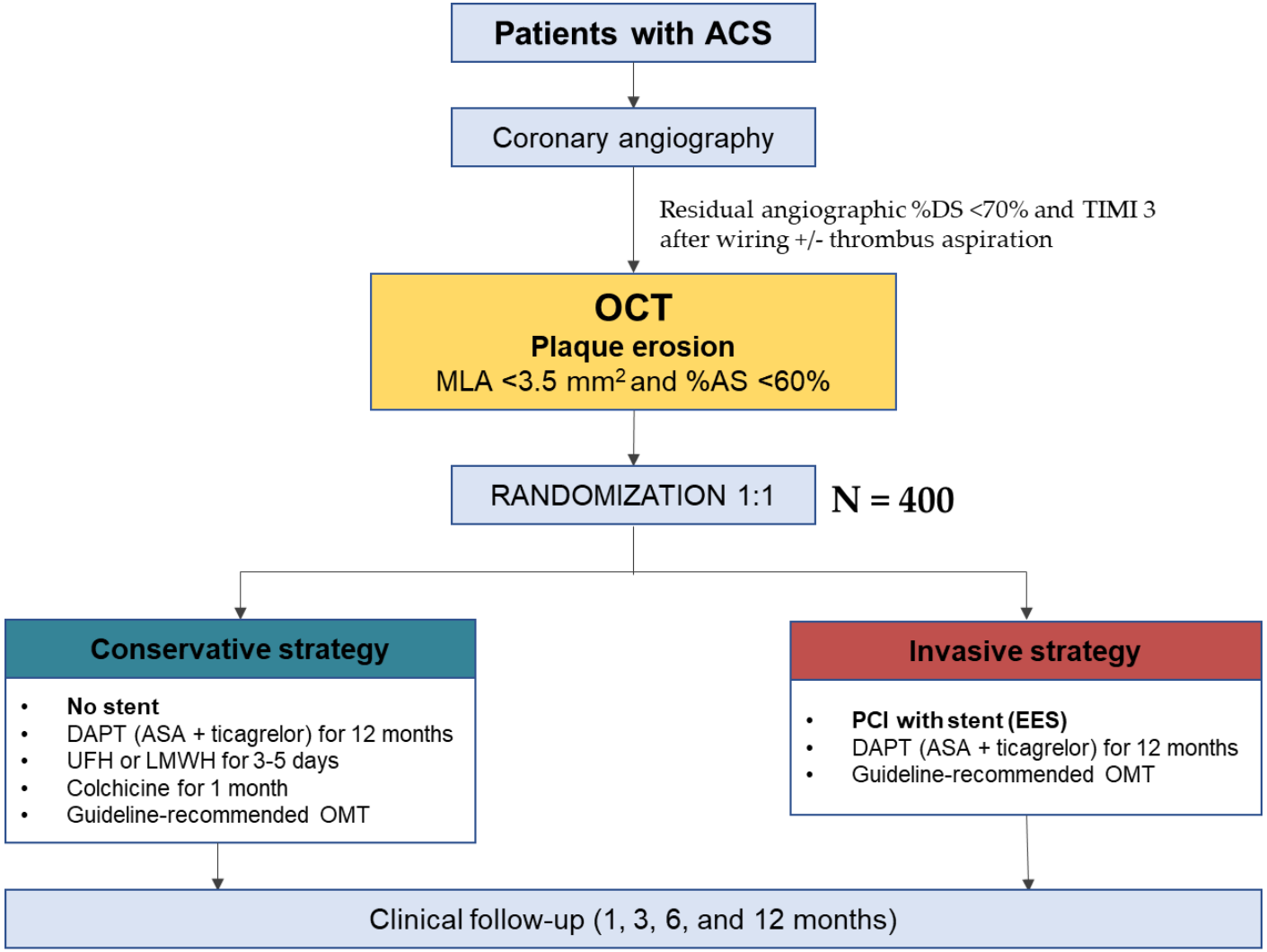
- Thrombus aspiration
- Left main to LAD stenting avoided
- **ASA, ticagrelor, UFH i.v. infusion**
- Transferred in the CCU
- Planned control CAG after 3 days

Clinical case (45 yo male, STEMI)





The CONCEPT-ACS Trial



CONCEPT-ACS trial

- MULTICENTER
- PROSPECTIVE
- OPEN-LABEL
- **NON-INFERIORITY**

Funded by Ministero della Salute (RF "Young Researcher" cod. GR-2021-12375365)

PI: Dr. R. Vergallo

Primary endpoint: MACE (composite of cardiac death, MI, UA requiring hospitalization, or TLR)

Intravascular imaging- *versus* angiography-guided PCI: The RENOVATE COMPLEX PCI trial

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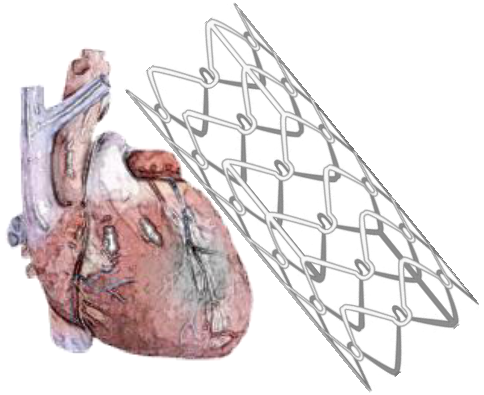
PROSPECTIVE, MULTIC



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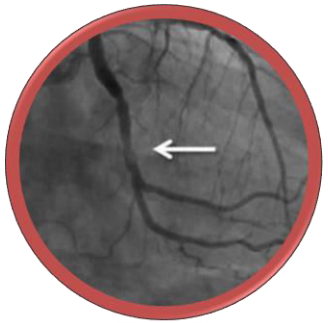
patients with IHD undergoing PCI with stenting

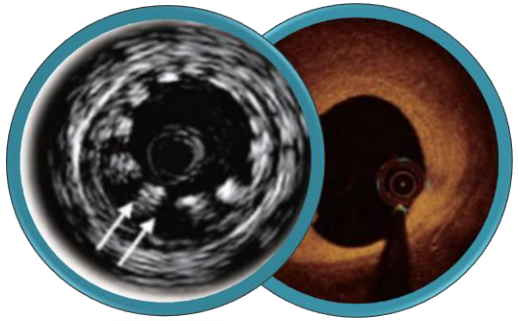
RANDOMIZED

Angiography-guided PCI

1:1

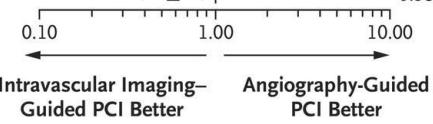
Intravascular imaging-guided PCI





IVUS 75% - OCT 25%

Subgroup	Intravascular Imaging–Guided PCI	Angiography-Guided PCI	Hazard Ratio (95% CI)
	no. of events/total no. of patients (cumulative incidence, %)		
Overall	76/1092 (7.7)	60/547 (12.3)	0.64 (0.45–0.89)
Type of imaging devices			
Intravascular ultrasonography	59/800 (8.0)	60/547 (12.3)	0.66 (0.46–0.95)
Optical coherence tomography	15/278 (5.8)	60/547 (12.3)	0.47 (0.27–0.83)
Type of complex coronary lesions			
True bifurcation	23/233 (10.3)	13/126 (11.8)	0.97 (0.49–1.93)
Chronic total occlusion	9/220 (5.0)	13/99 (14)	0.30 (0.13–0.71)
Unprotected left main coronary artery disease	9/138 (6.8)	11/54 (25)	0.31 (0.13–0.76)
Diffuse long coronary-artery lesion	36/617 (6.5)	31/281 (11.9)	0.52 (0.32–0.83)
Multivessel PCI involving ≥2 major coronary arteries	36/409 (9.5)	22/213 (11.7)	0.84 (0.50–1.44)
Lesion necessitating use of ≥3 stents	16/208 (8.1)	6/97 (6)	1.24 (0.49–3.18)
Lesion with in-stent restenosis	22/158 (15.6)	12/78 (17)	0.90 (0.45–1.82)
Severely calcified lesion	11/157 (7.3)	11/74 (17)	0.46 (0.20–1.06)
Ostial lesions of major coronary artery	8/182 (4.4)	9/69 (16)	0.33 (0.13–0.85)
Initial presentation			
Stable ischemic heart disease	25/532 (5.0)	27/275 (10.4)	0.46 (0.27–0.80)
Acute coronary syndrome	51/560 (10.4)	33/272 (14.6)	0.74 (0.48–1.15)
Age			
<65 yr	36/517 (7.8)	23/238 (10.6)	0.72 (0.42–1.21)
≥65 yr	40/575 (7.4)	37/309 (13.6)	0.57 (0.36–0.88)
Sex			
Male	66/869 (8.3)	46/431 (11.7)	0.70 (0.48–1.02)
Female	10/223 (5.2)	14/116 (14.5)	0.35 (0.16–0.80)
Diabetes mellitus			
Yes	45/394 (12.9)	26/223 (12.3)	0.97 (0.60–1.57)
No	31/698 (4.7)	34/324 (12.2)	0.41 (0.25–0.67)
Chronic kidney disease			
Yes	22/203 (13.3)	19/93 (23)	0.51 (0.27–0.93)
No	54/889 (6.4)	41/454 (9.9)	0.66 (0.44–0.99)
Left ventricular ejection fraction			
<50%	22/210 (12.0)	12/84 (15)	0.72 (0.35–1.45)
≥50%	54/882 (6.7)	48/463 (11.8)	0.58 (0.39–0.85)



Risk of MACE associated with “vulnerable” NCL in patients with ACS (per patient analysis)

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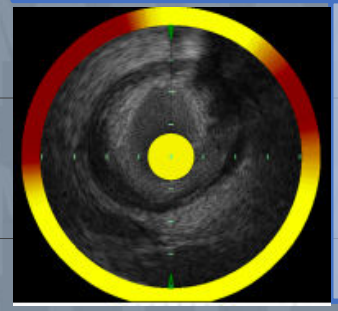
Jiang et al, JACC 2023

Pts with at least 1 NCL with:
- TCFA, and
- MLA <3.5 mm²

Jiang et al.
HR 5.23 (95% CI 2.98-9.17)

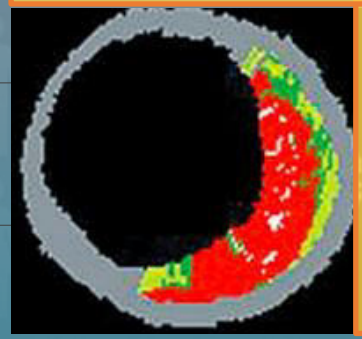
PROSPECT II



Pts with at least 1 NCL with:
- PB ≥70%, and
- maxLCBI$_{4mm}$ ≥324.7

PROSPECT II
HR 2.62 (95% CI 1.57-4.38)

PROSPECT



Pts with at least 1 NCL with ≥2 high-risk features:
- TCFA,
- PB ≥70%, and/or
- MLA ≤4 mm²

PROSPECT
HR 2.66 (95% CI 1.62-4.26)

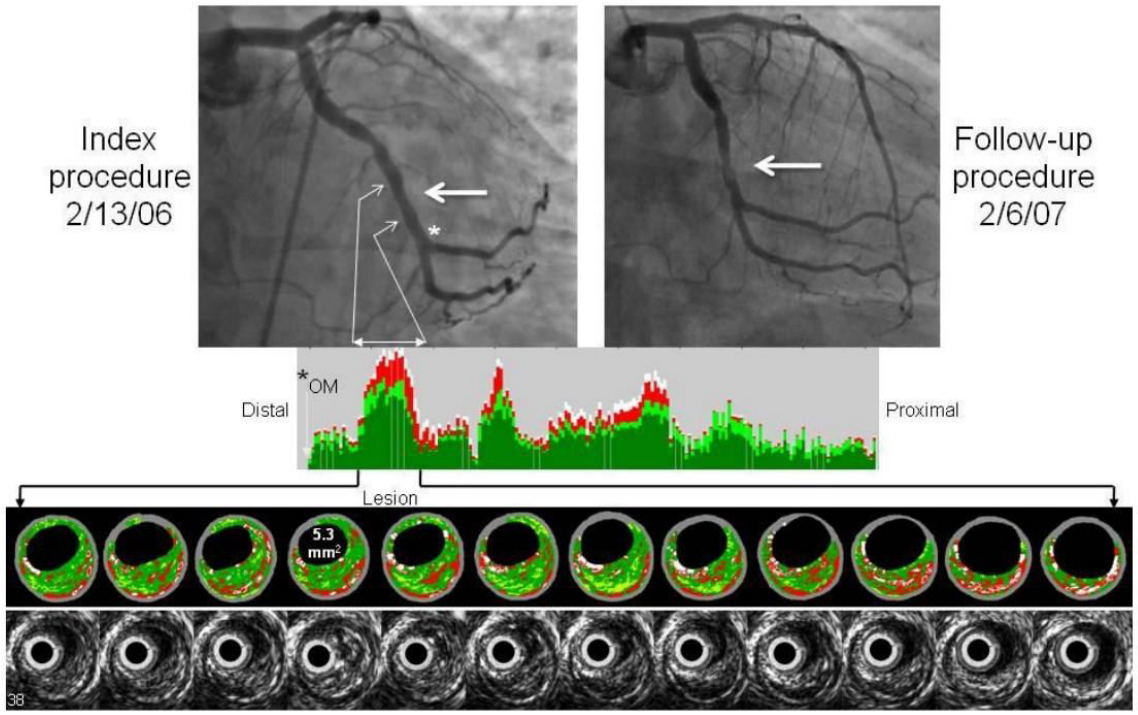
Hazard ratio

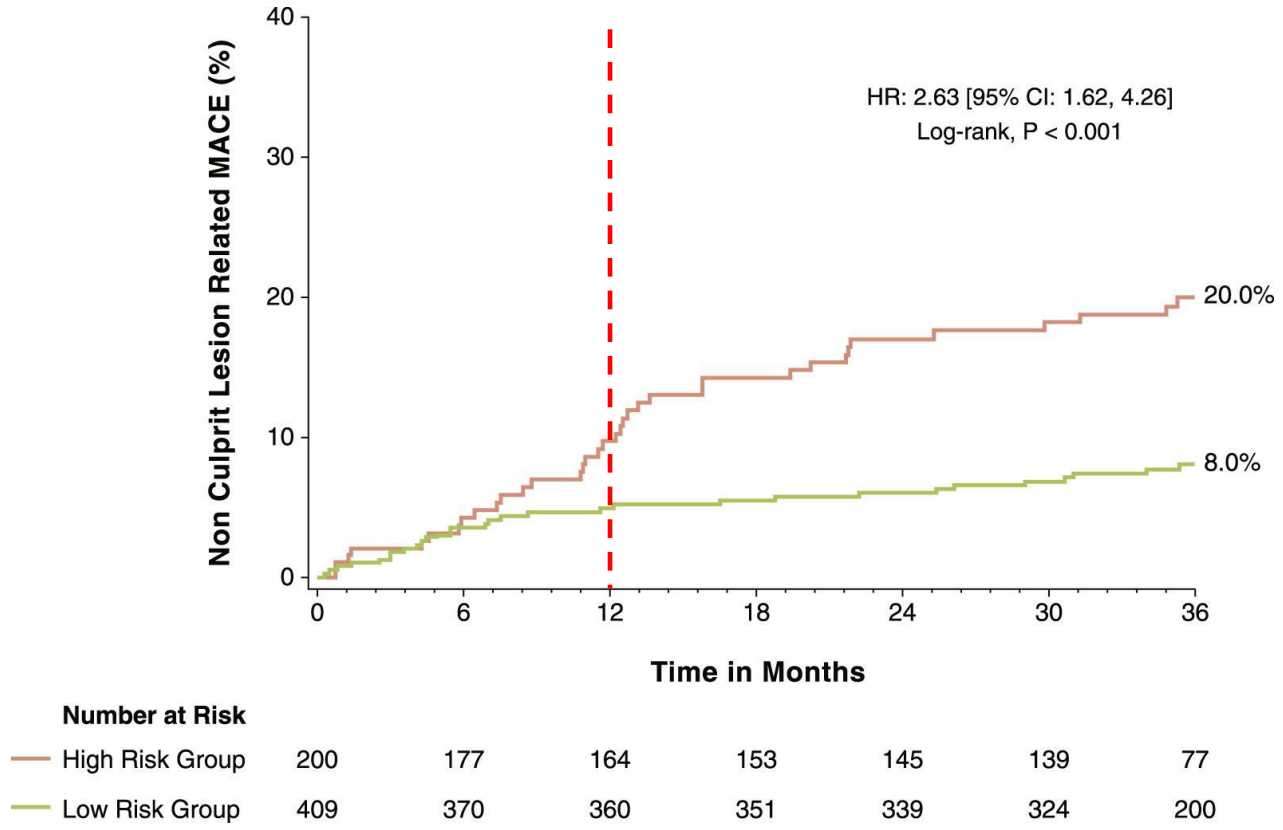
0 1 2 3 4 5 6

0 5 10 15 20 25 30 35

Prevalence (%)

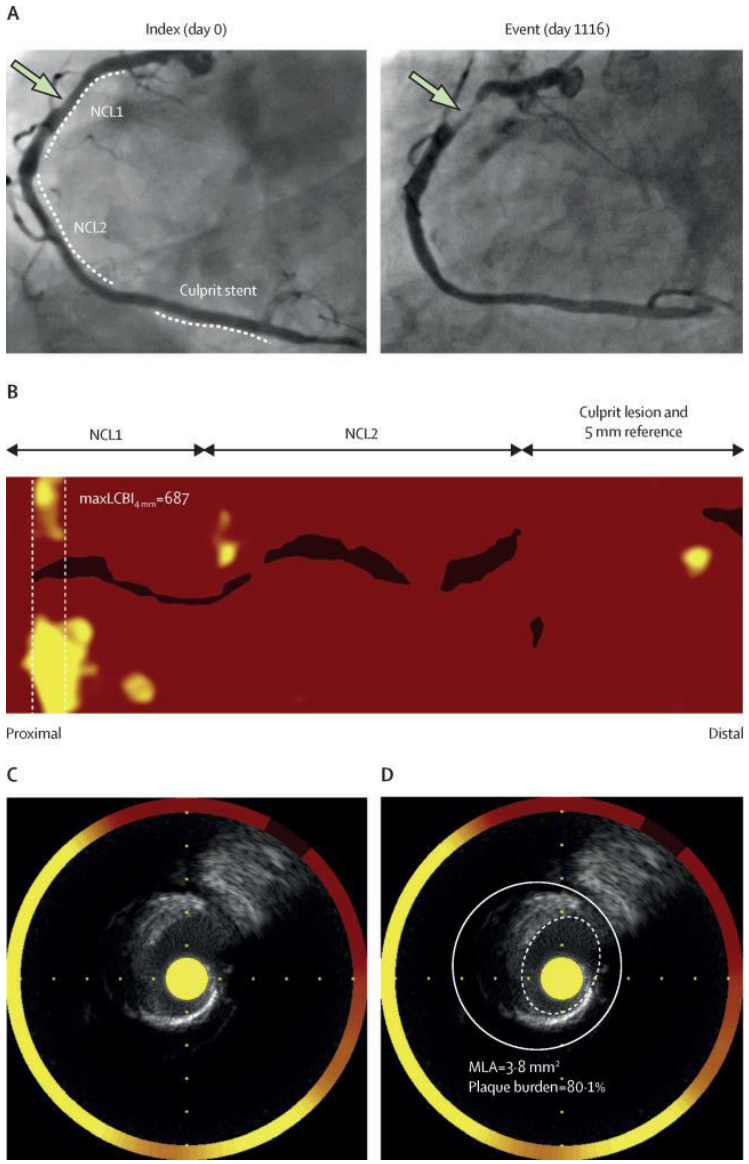
Timing of NCL-related events (PROSPECT)

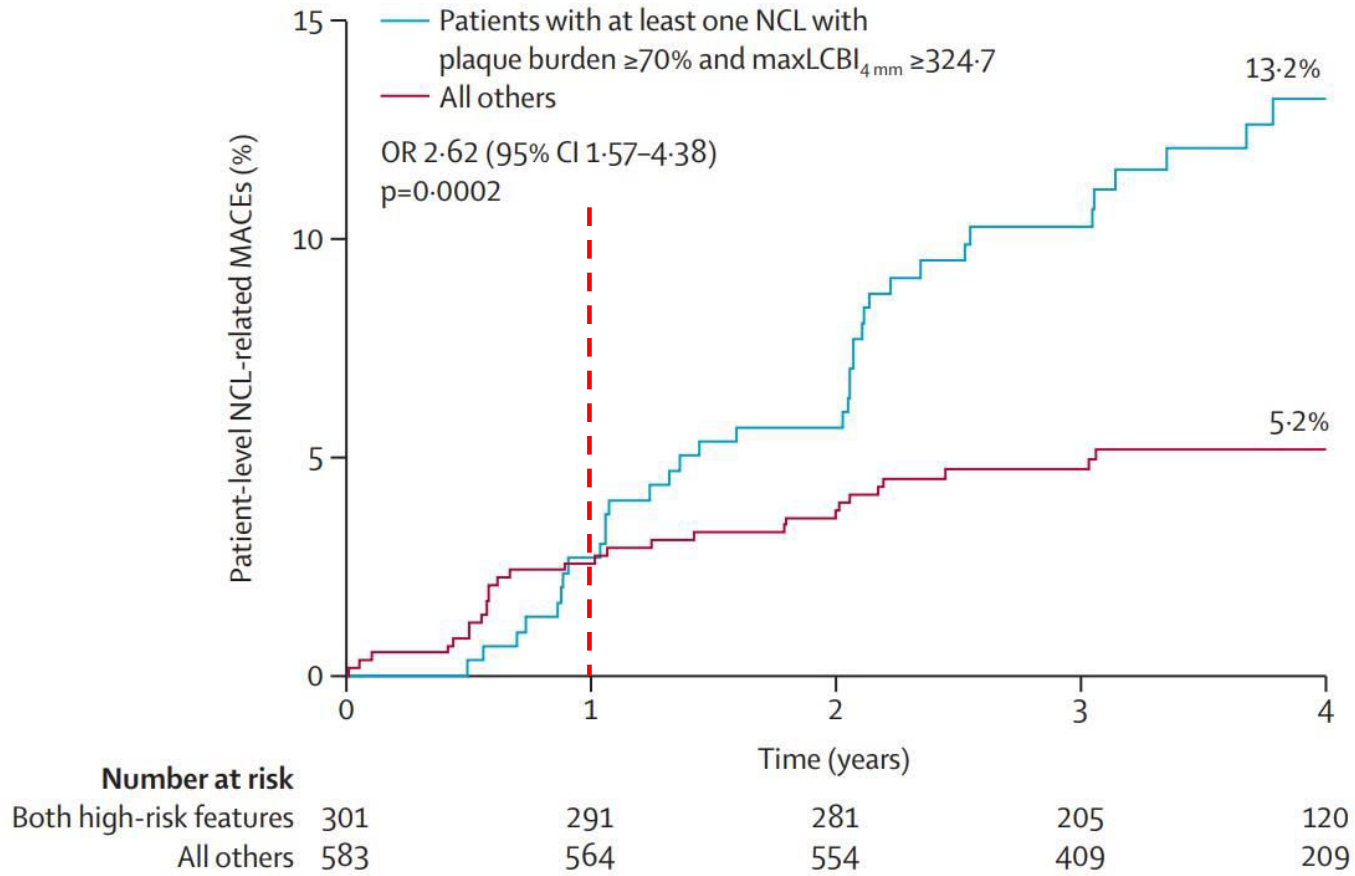




Stone GW, et al. N Engl J Med 2011;364:226-235; Bourantas CV, et al. JACC Cardiovasc Imag2013;12:1263-1272

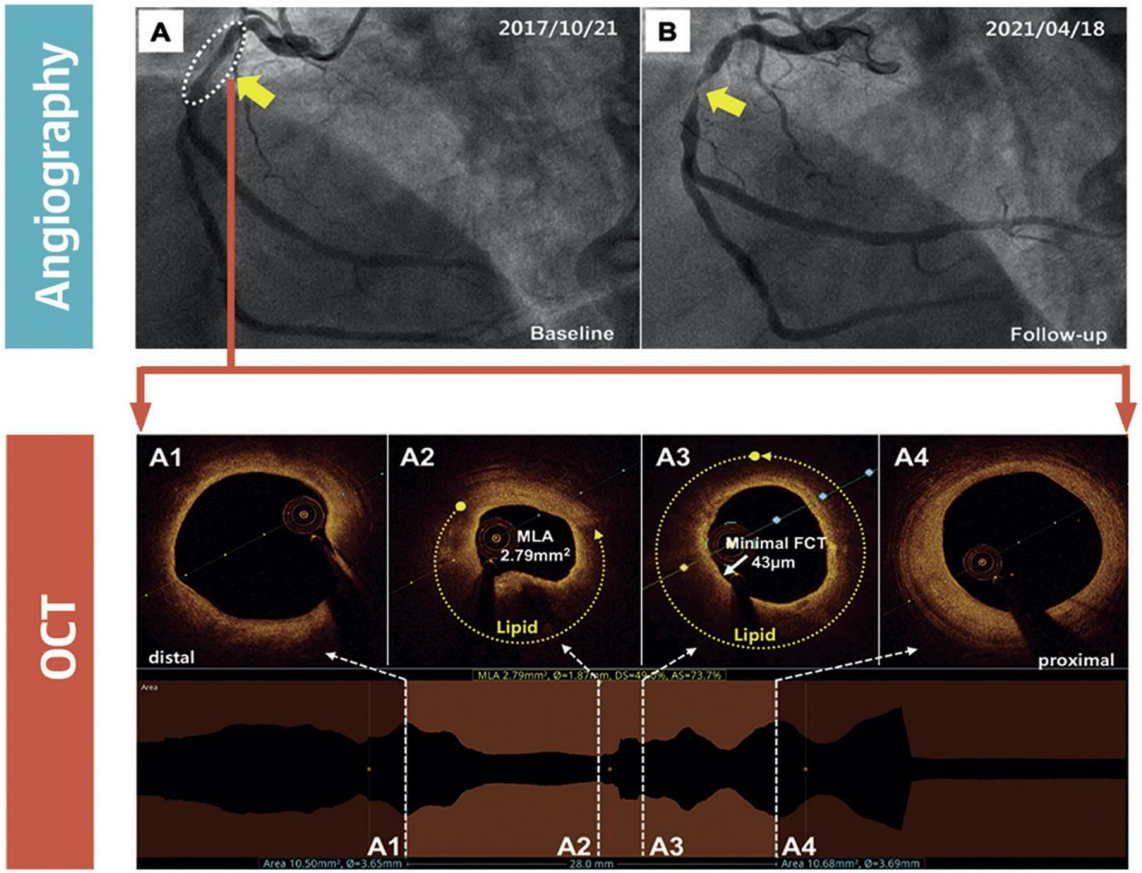
Timing of NCL-related events (PROSPECT II)



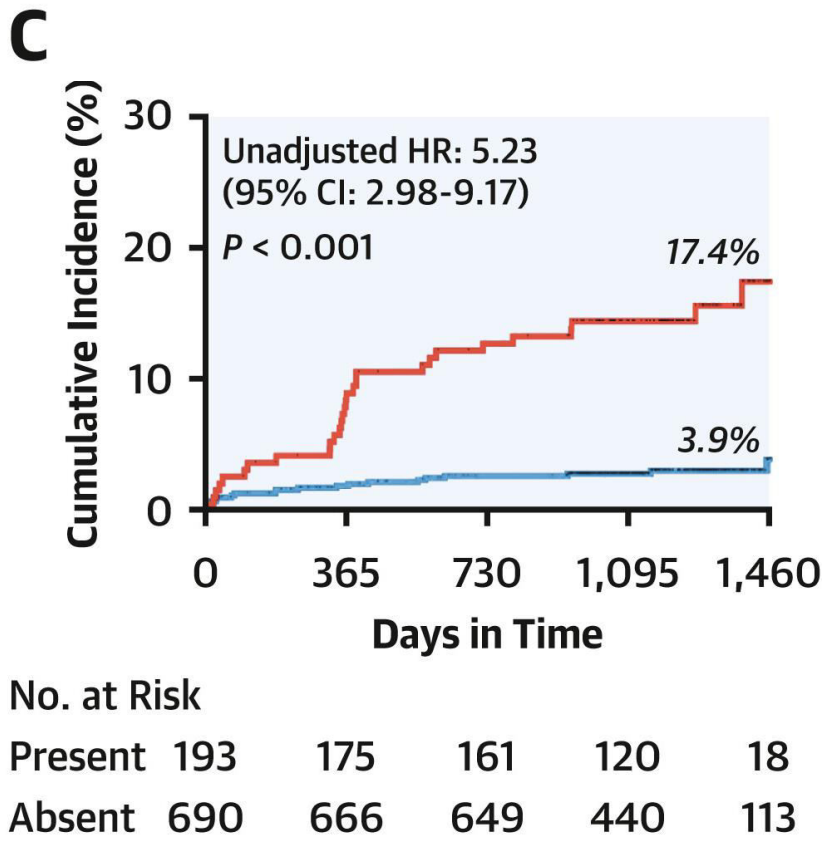


Erlinge D, et al. Lancet 2021;397:985-995

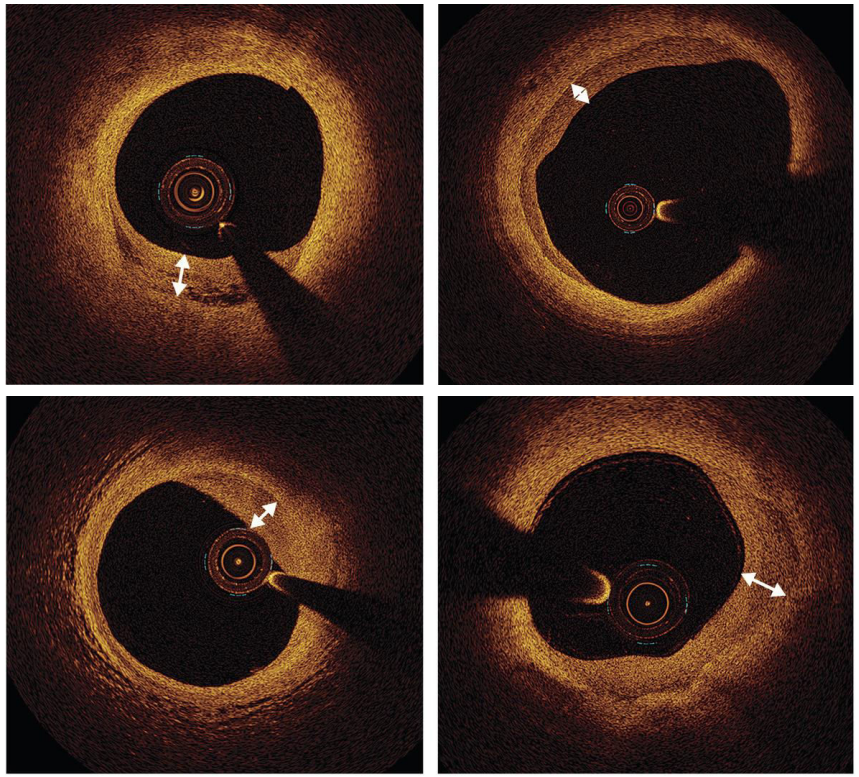
Timing of NCL-related events (3-vessel OCT study)



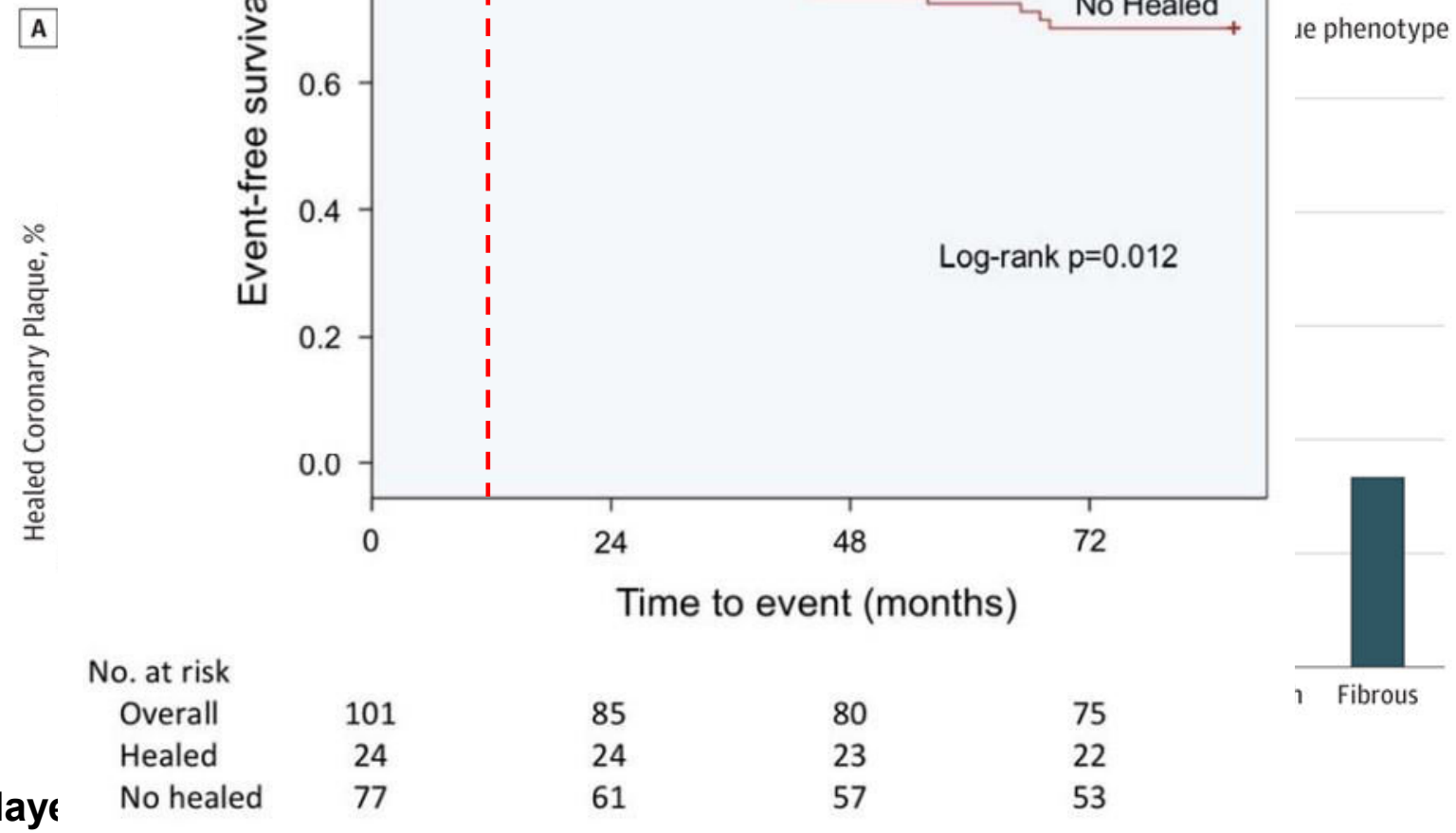
TCFA + MLA <3.5 mm²



Plaque healing and ACS



Healed (laye



Vergallo R, Porto I, et al. JAMA Cardiol 2019;4:321-329

Vergallo R, and Crea F. N Engl J Med 2020; 383:846-857

Can imaging help to personalize antithrombotic therapy? (N.B. NO DATA, but points for discussion)

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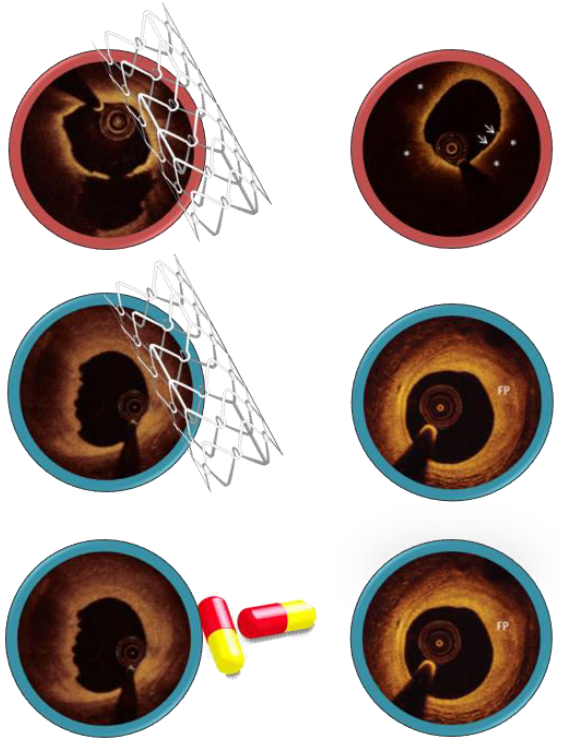
Culprit **Non-culprit**



Standard DAPT

I | A

Prolonged DAPT

IIa | A
IIb | A

High
Moderate

Short DAPT

IIa | B → ASA
IIa | A → P2Y12i

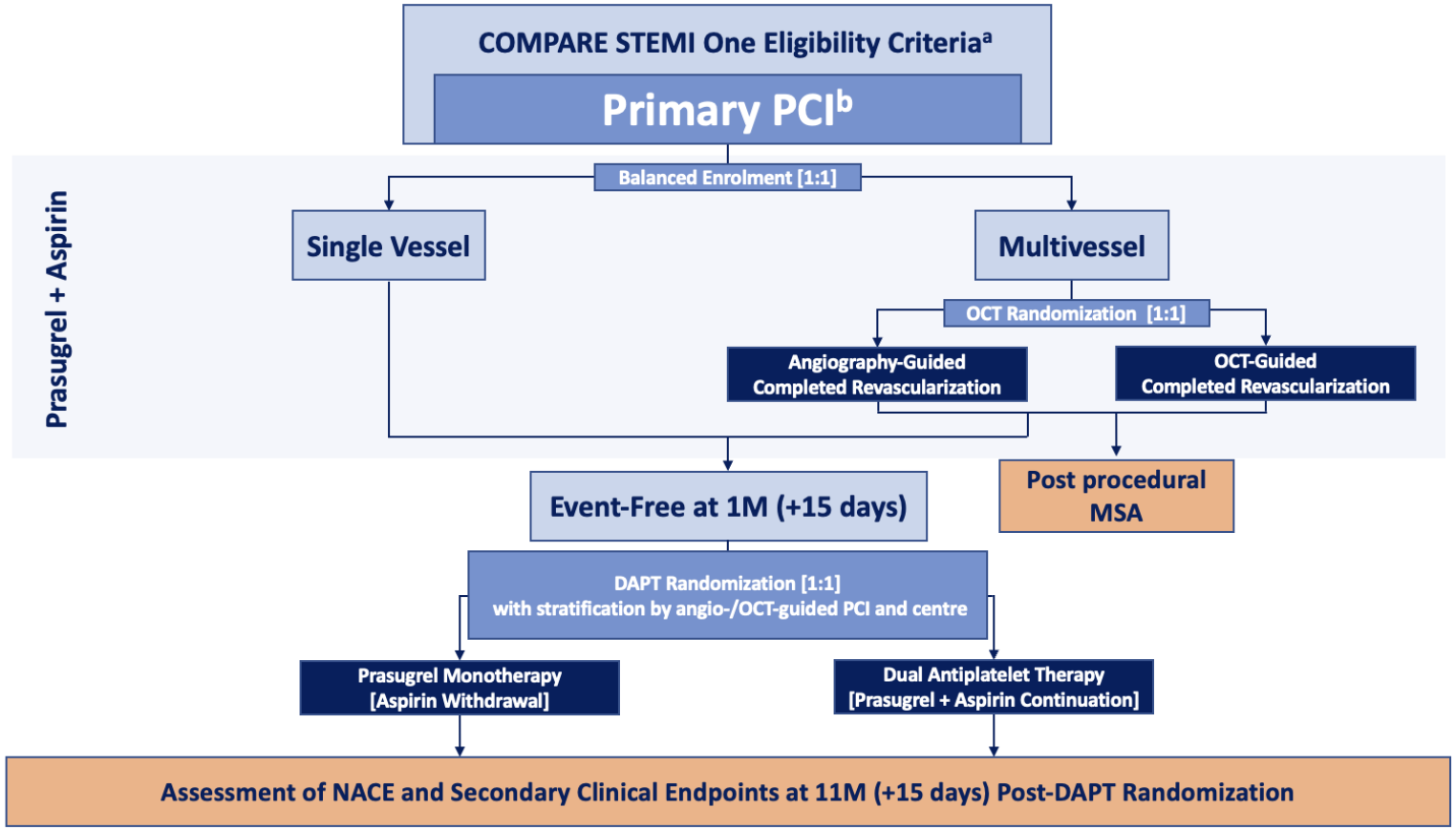
De-escalation

IIb | A → Clop
→ Halved dose

Collet JP, et al. Eur Heart J. 2021;42:1289-1367

COMPARE STEMI ONE trial

N=1656 patients



[a] Loading with prasugrel among inclusion criteria.
[b] Revascularization only of the culprit lesion is recommended.

Study Chair: Dr P.C. Smits

Principal Investigator: Dr V. Paradies

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Università di Ferrara

Germany
Segeberger Kliniek, Bad Segeberger
Herzzentrum Dresden, Dresden

Courtesy of V. Paradies

Closing remarks

- The choice of anti-thrombotic strategy in patients with ACS always needs a **careful balance** between bleeding and ischemic risk of the single patient.
- **ACS population is very heterogeneous**, and patients with plaque rupture and erosion have different thrombotic risk, both related to the unstable plaque and to the pancoronary atherosclerotic phenotype.
- The opportunity to further **refine ischemic risk** of ACS patients who received **intracoronary imaging** is fascinating, but needs to be tested against **costs** and real clinical benefit. There are **very limited data** on this regard, and future dedicated studies are needed.

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CUORE
E NON SOLO
INTERVENTIONAL
CARDIOLOGY
14/15.04.23
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CORONARY IMAGING & PHYSIOLOGY
INNOVATION IN TRANSCATHETER INTERVENTIONS

Terapia antitrombotica nel paziente con SCA: il meccanismo guida la terapia?

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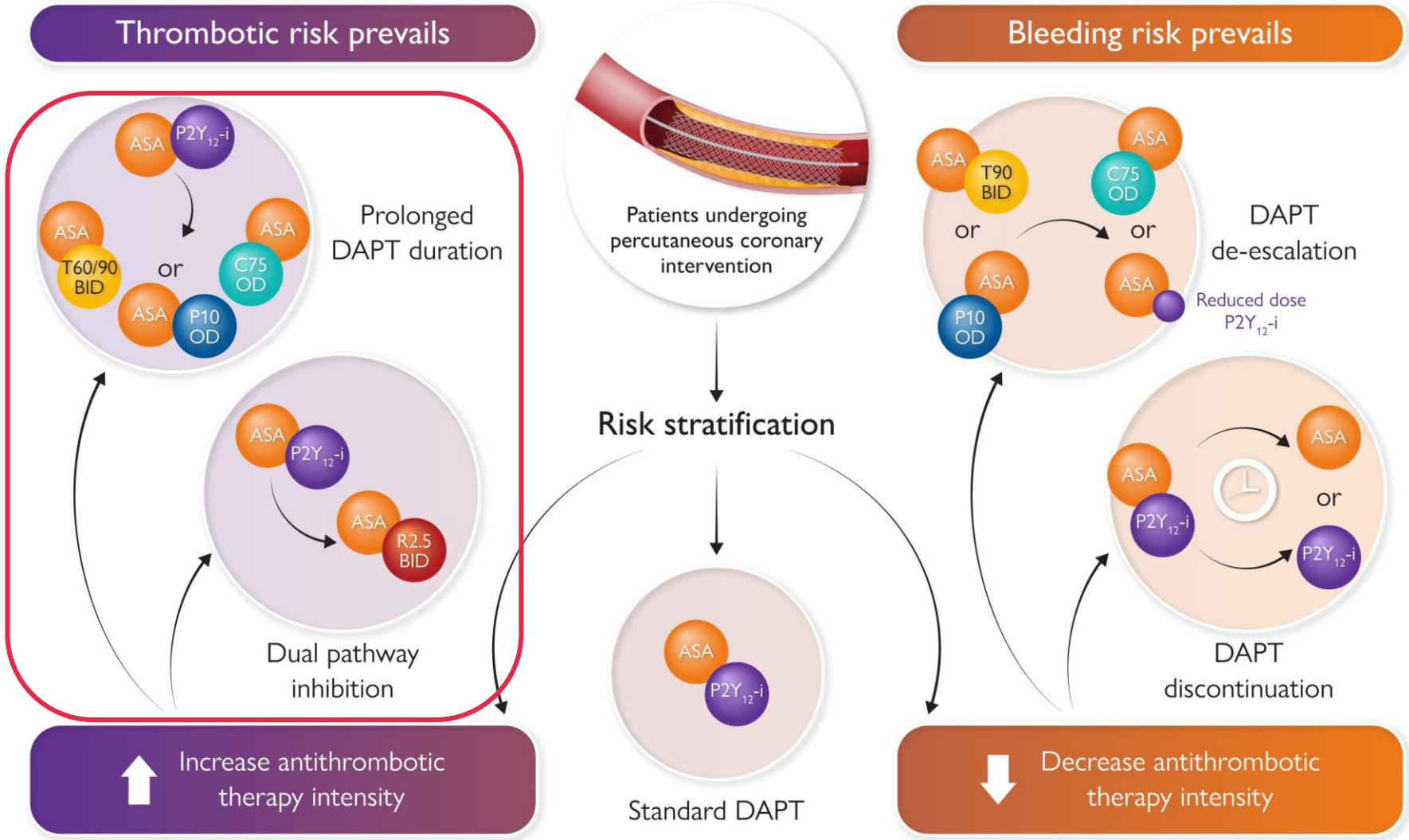
Genova, 14-15 aprile 2023

Balancing ischemic and bleeding risk



Capodanno D and Greco A. Eur Heart J 2022;11:969-971

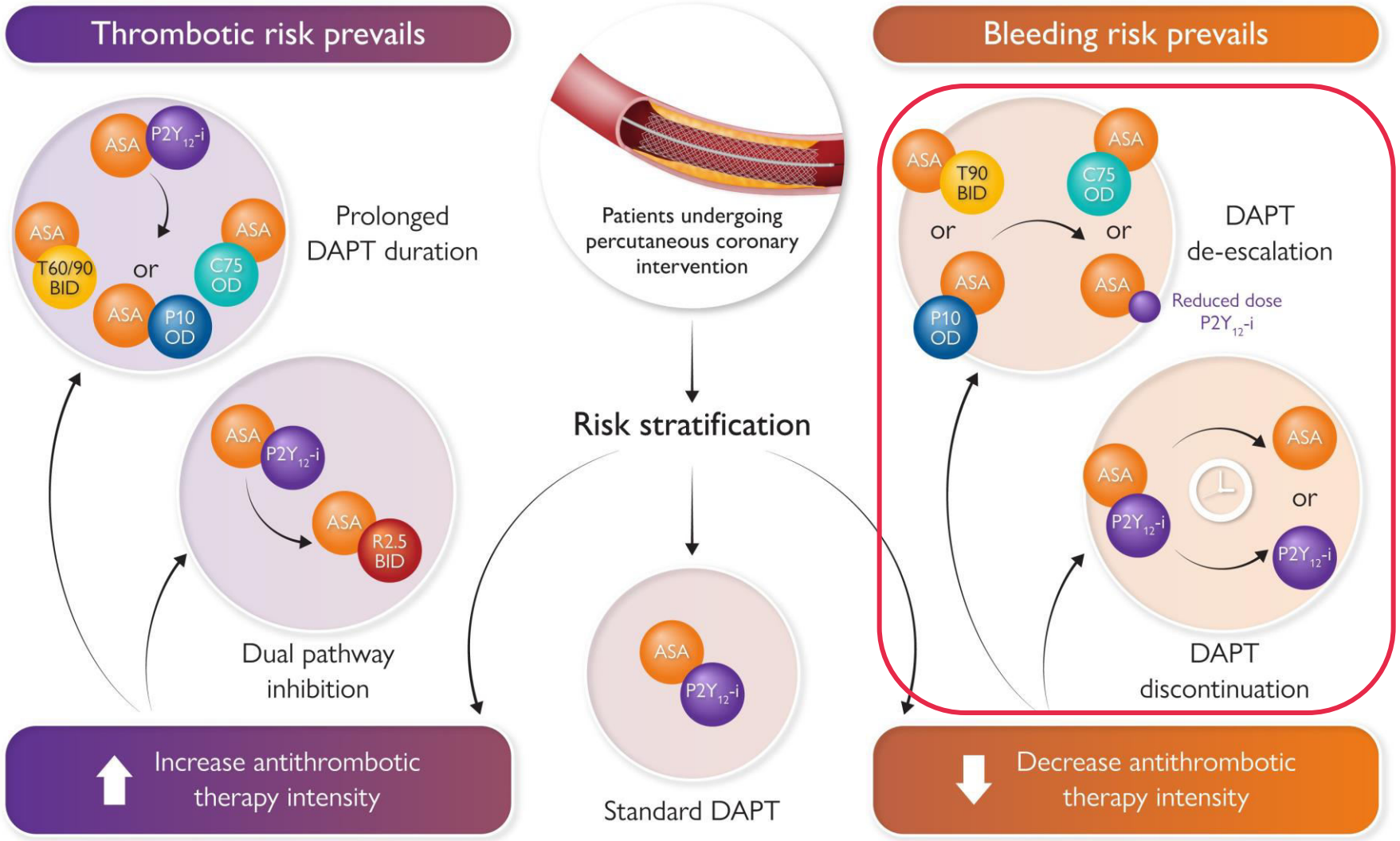
Long-term DAPT or dual pathway inhibition

2020 ESC Guidelines for the management of NSTE-ACS

The Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC)

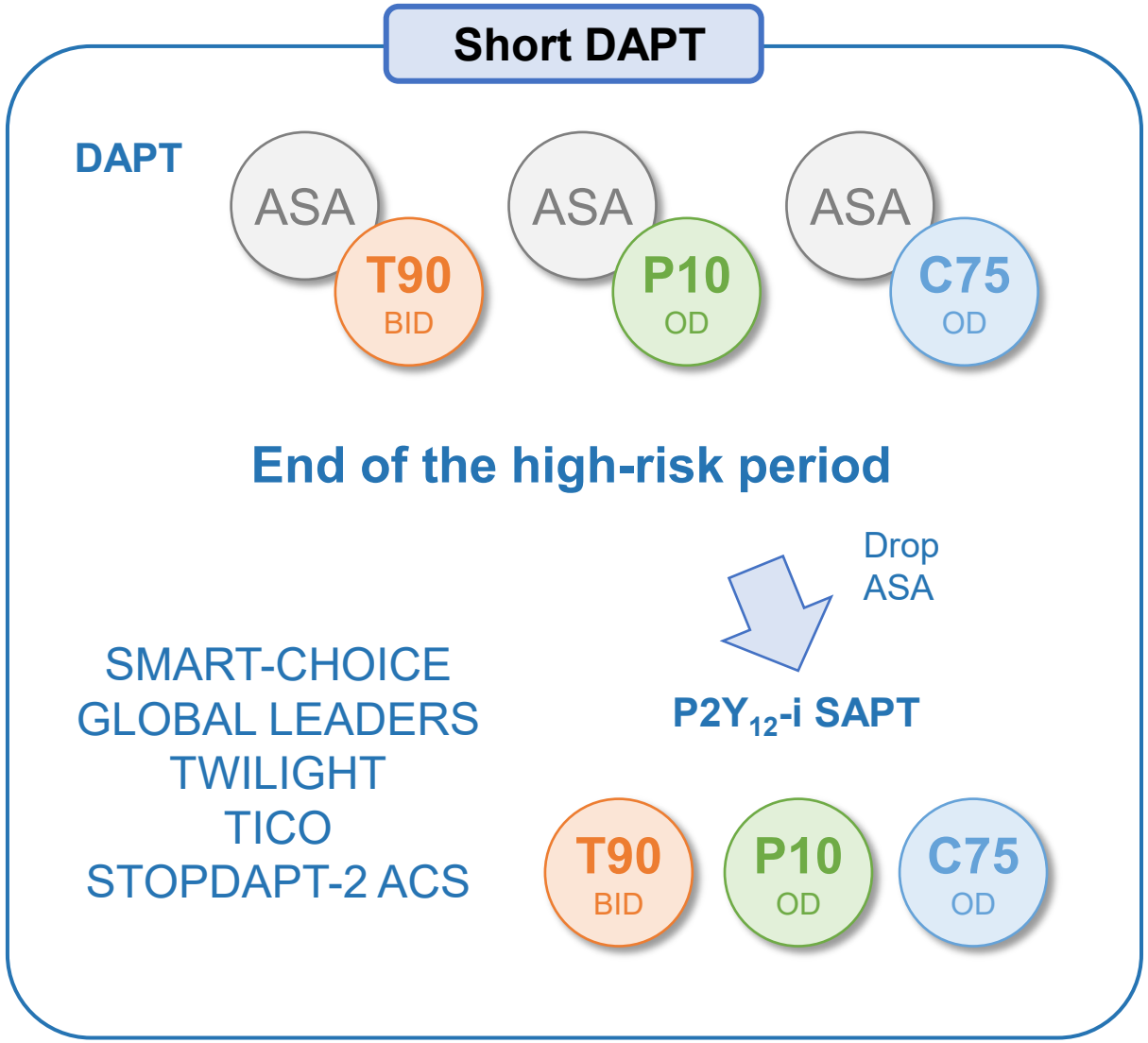
Prolonging antithrombotic treatment duration	Class	Level
Adding a second antithrombotic agent to aspirin for extended long-term secondary prevention should be considered in patients with a high risk of ischaemic events and without increased risk of major or life-threatening bleeding.	IIa	A
Adding a second antithrombotic agent to aspirin for extended long-term secondary prevention may be considered in patients with moderately increased risk of ischaemic events and without increased risk of major or life-threatening bleeding.	IIb	A

Balancing ischemic and bleeding risk



Capodanno D and Greco A. Eur Heart J 2022;11:969-971

$P2Y_{12}$ inhibitor SAPT in ACS



Short DAPT (→$P2Y_{12}$-i) vs standard DAPT

NMA (5 trials, N=35,931)	RR (95% CI)
All-cause death	0.83 (0.66 – 1.05)
NACE	0.85 (0.73 – 0.98)
MACE	0.91 (0.78 – 1.06)
Cardiovascular death	0.58 (0.23 – 1.48)
Myocardial infarction	1.09 (0.90 – 1.33)
Stroke	1.15 (0.80 – 1.66)
Stent thrombosis	1.07 (0.71 – 1.62)
Clinically relevant bleeding	0.59 (0.43 – 0.80)
Major bleeding	0.54 (0.43 – 0.67)
Minor bleeding	0.80 (0.65 – 0.99)

Laudani C, et al. JACC Cardiovasc Interv. 2022;15:268-277

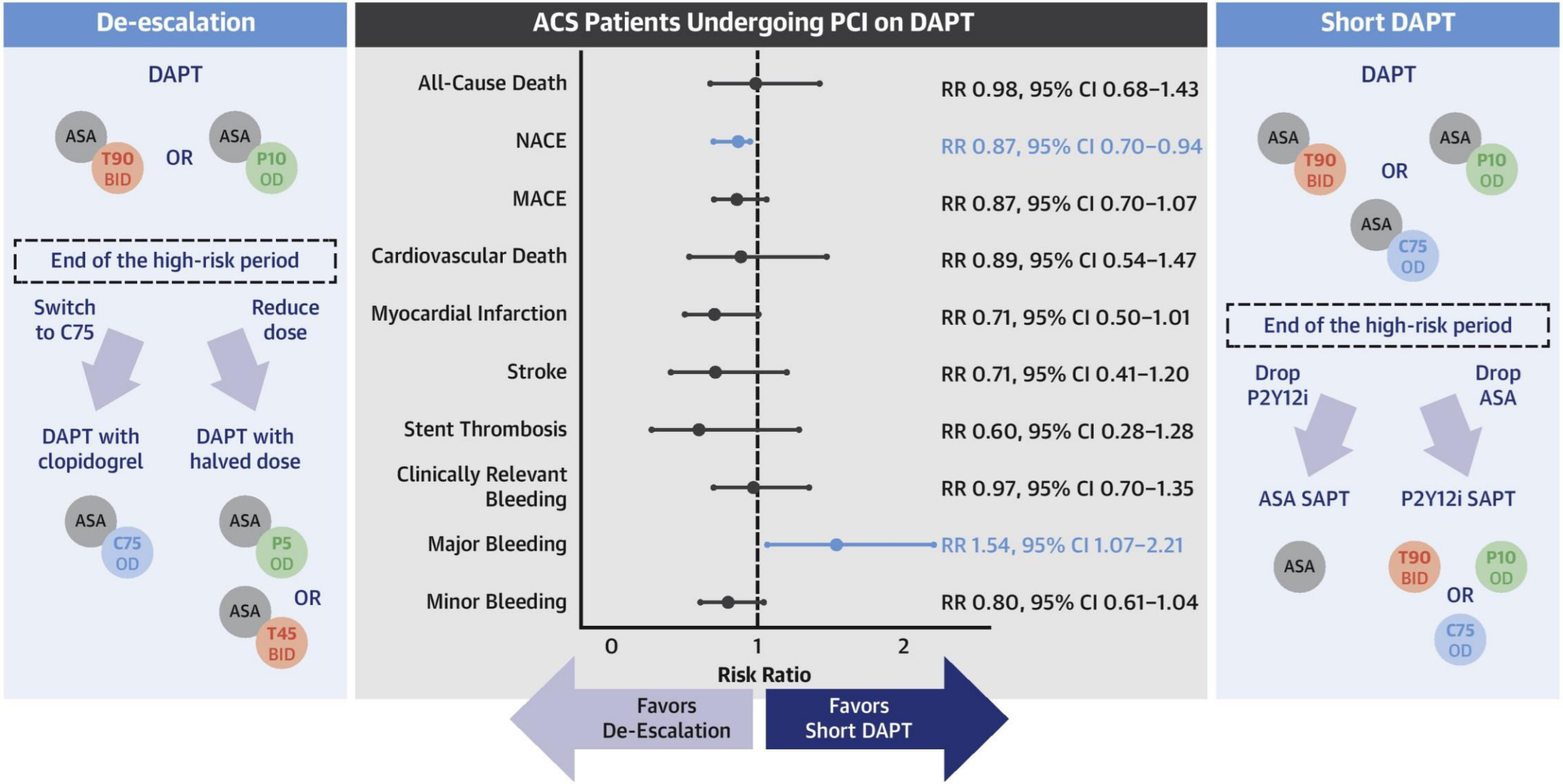
Short DAPT

2020 ESC Guidelines for the management of NSTE-ACS

The Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC)

Shortening antithrombotic treatment duration	Class	Level
After stent implantation with high risk of bleeding (e.g., PRECISE-DAPT ≥25 or ARC-HBR criteria met), discontinuation of $P2Y_{12}$ receptor inhibitor therapy after 3 months should be considered.	IIa	B
After stent implantation in patients undergoing a strategy of DAPT, stopping aspirin after 3-6 months should be considered, depending on the balance between the ischaemic and bleeding risk.	IIa	A

Short DAPT vs de-escalation



Laudani C, et al. JACC Cardiovasc Interv. 2022;15:268-277

De-escalation

2020 ESC Guidelines for the management of NSTE-ACS

The Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC)

Shortening antithrombotic treatment duration	Class	Level
De-escalation of $P2Y_{12}$ receptor inhibitor treatment (e.g., with a switch from prasugrel or ticagrelor to clopidogrel) may be considered as an alternative DAPT strategy, especially for ACS patients deemed unsuitable for potent platelet inhibition. De-escalation may be done unguided based on clinical judgment or guided by platelet function testing or CYP2C19 genotyping, depending on patient's risk profile and availability of respective assays.	IIb	A

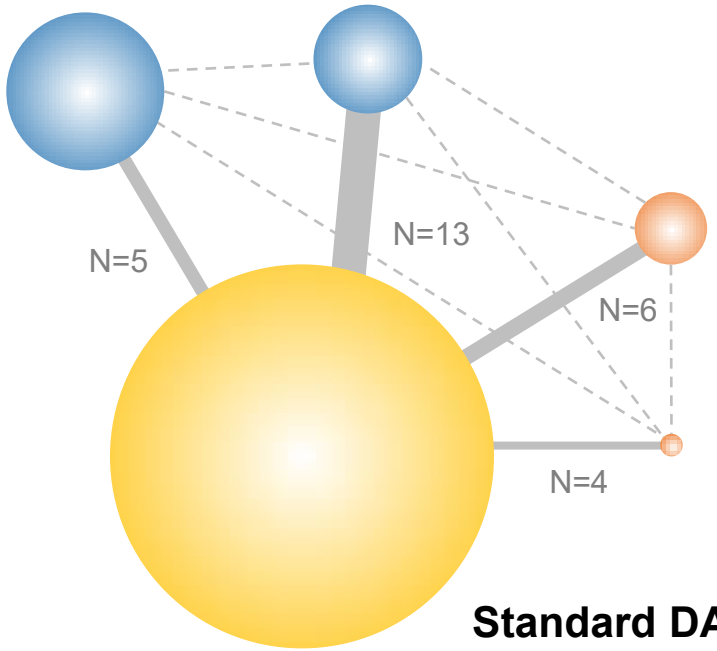
DAPT strategies in patients with ACS

Indirect network meta-analysis

50,602 patients from 29 studies

Short DAPT (→ P2Y$_{12}$i) (N=10,478)

Short DAPT (→ aspirin) (N=7,226)

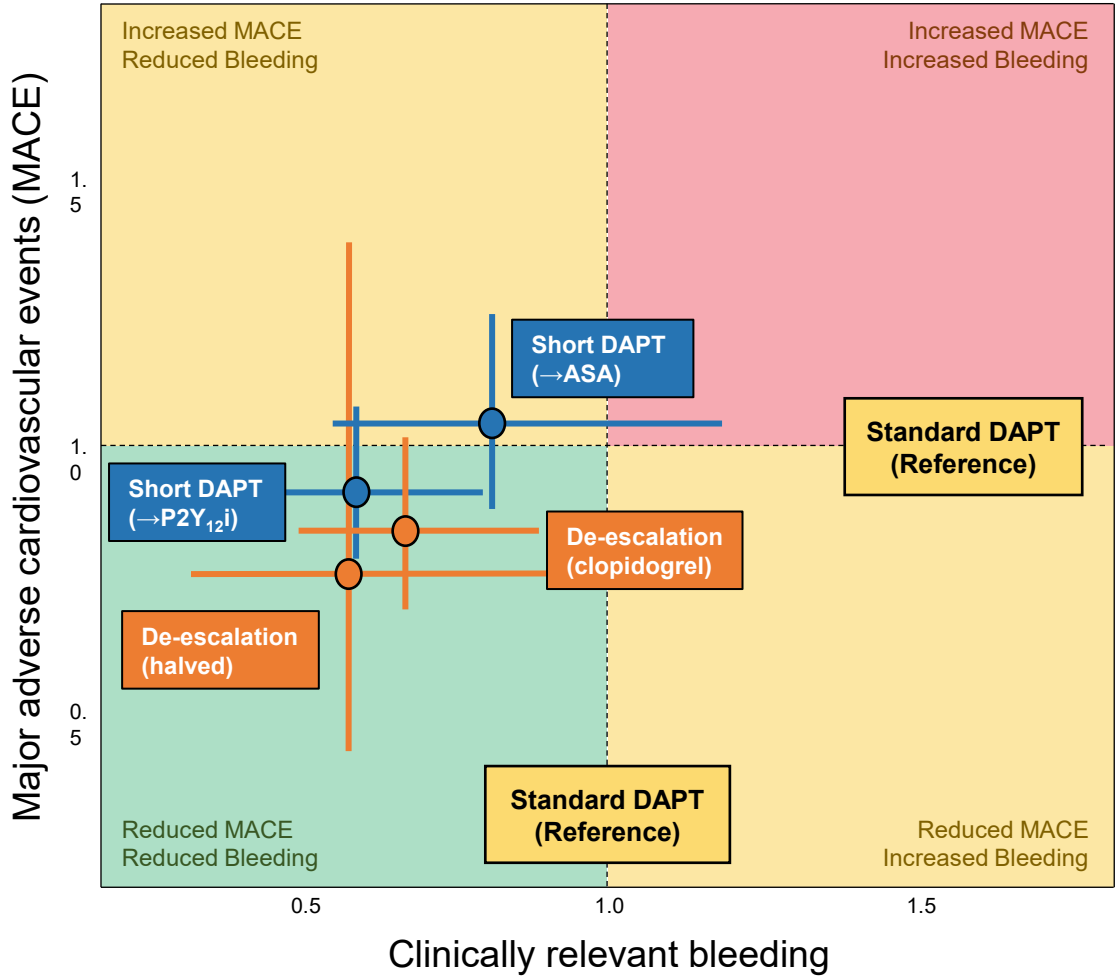


De-escalation (→ clopidogrel) (N=4,805)

De-escalation (→ halved dose) (N=1,512)

Standard DAPT (N=25,453)

Bivariate analysis (MACCE vs CRB)



Laudani C, et al. JACC Cardiovasc Interv. 2022;15:268-277

The CONCEPT-ACS Trial

- MULTICENTER
- PROSPECTIVE
- OPEN-LABEL
- **NON-INFERIORITY**

Funded by Ministero della Salute (RF "Young Researcher" cod. GR-2021-12375365)

PI: Dr. R. Vergallo

CONCEPT-ACS trial

Patients with ACS

Coronary angiography

Residual angiographic %DS <70% and TIMI 3 after wiring +/- thrombus aspiration

OCT
Plaque erosion
MLA <3.5 mm^2 and %AS <60%

RANDOMIZATION 1:1 N = 400

Conservative strategy

- **No stent**
- DAPT (ASA + ticagrelor) for 12 months
- UFH or LMWH for 3-5 days
- Colchicine for 1 month
- Guideline-recommended OMT

Invasive strategy

- **PCI with stent (EES)**
- DAPT (ASA + ticagrelor) for 12 months
- Guideline-recommended OMT

Clinical follow-up (1, 3, 6, and 12 months)