

The 26th TCTAP 2021 Virtual

**Hot Topics I: Imaging & Physiology
What Imaging Talks About the Vessel**

Imaging Detection of Vulnerable Plaques at High Risk of Developing ACS

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Disclosure statement of financial interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

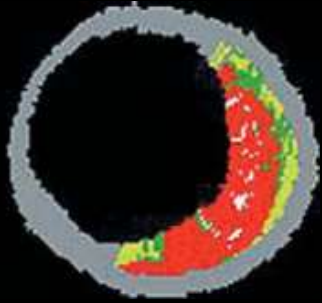

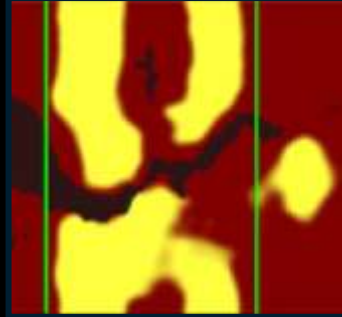

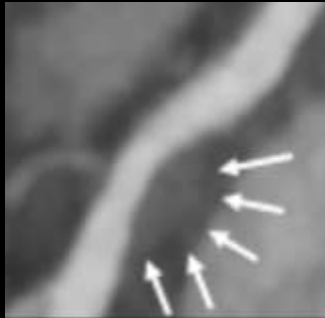
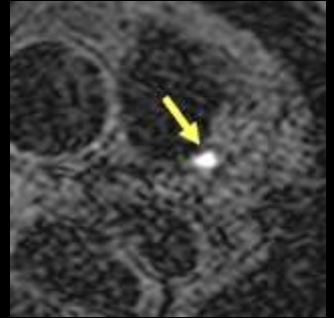
Affiliation/Financial Relationship

Company

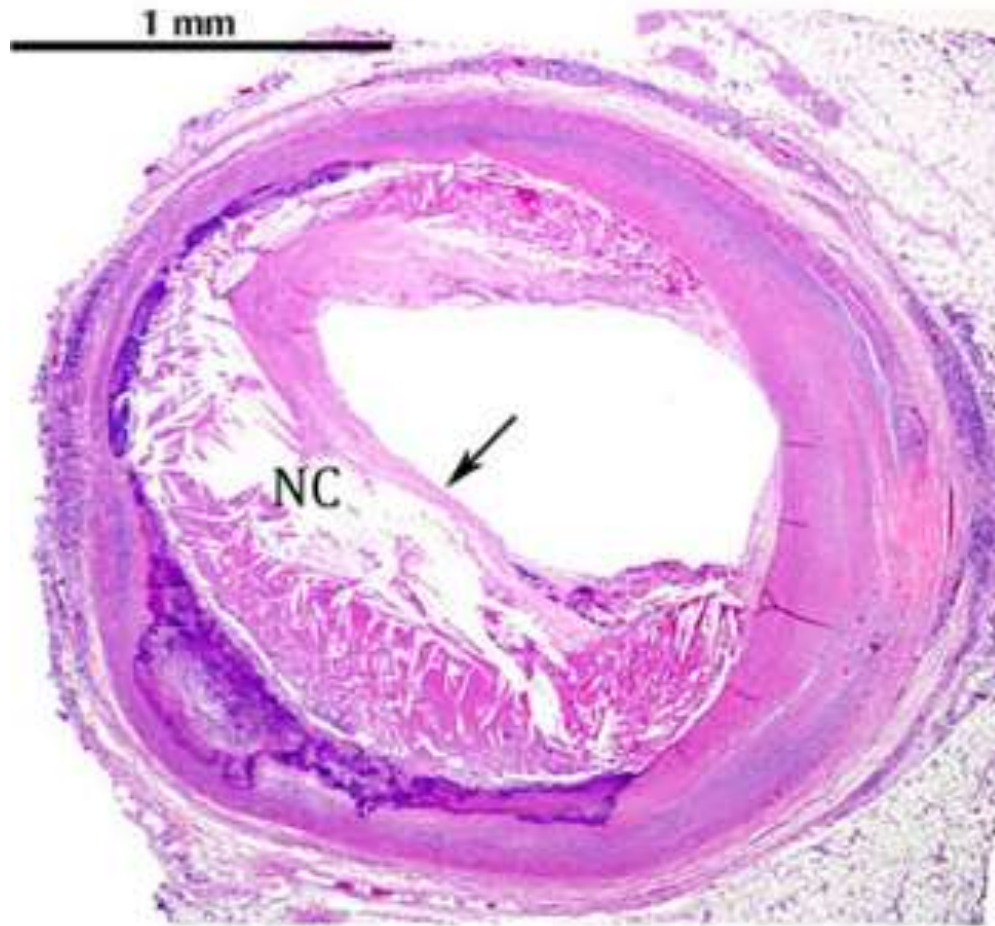
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| • Grant/Research Support | • No |
| • Consulting Fees/Honoraria | • No |
| • Major Stock Shareholder/Equity | • No |
| • Royalty Income | • No |
| • Ownership/Founder | • No |
| • Intellectual Property Rights | • No |
| • Other Financial Benefit | • No |



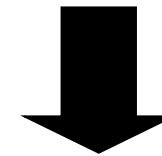
Detection of vulnerable plaque

Modality	IVUS/VH	Angio- scopy	NIRS	OCT	CT	MRI
Procedure	Invasive				Non-invasive	
Image						
Predictors	PB>70% MLA<4mm ² VH-TCFA	Yellow plaque	maxLCBI(4) >400	FCT<75μm Lipid >180° MLA<3.5mm ² Macrophage	Low density plaque	High intensity plaque

Rupture-prone plaque

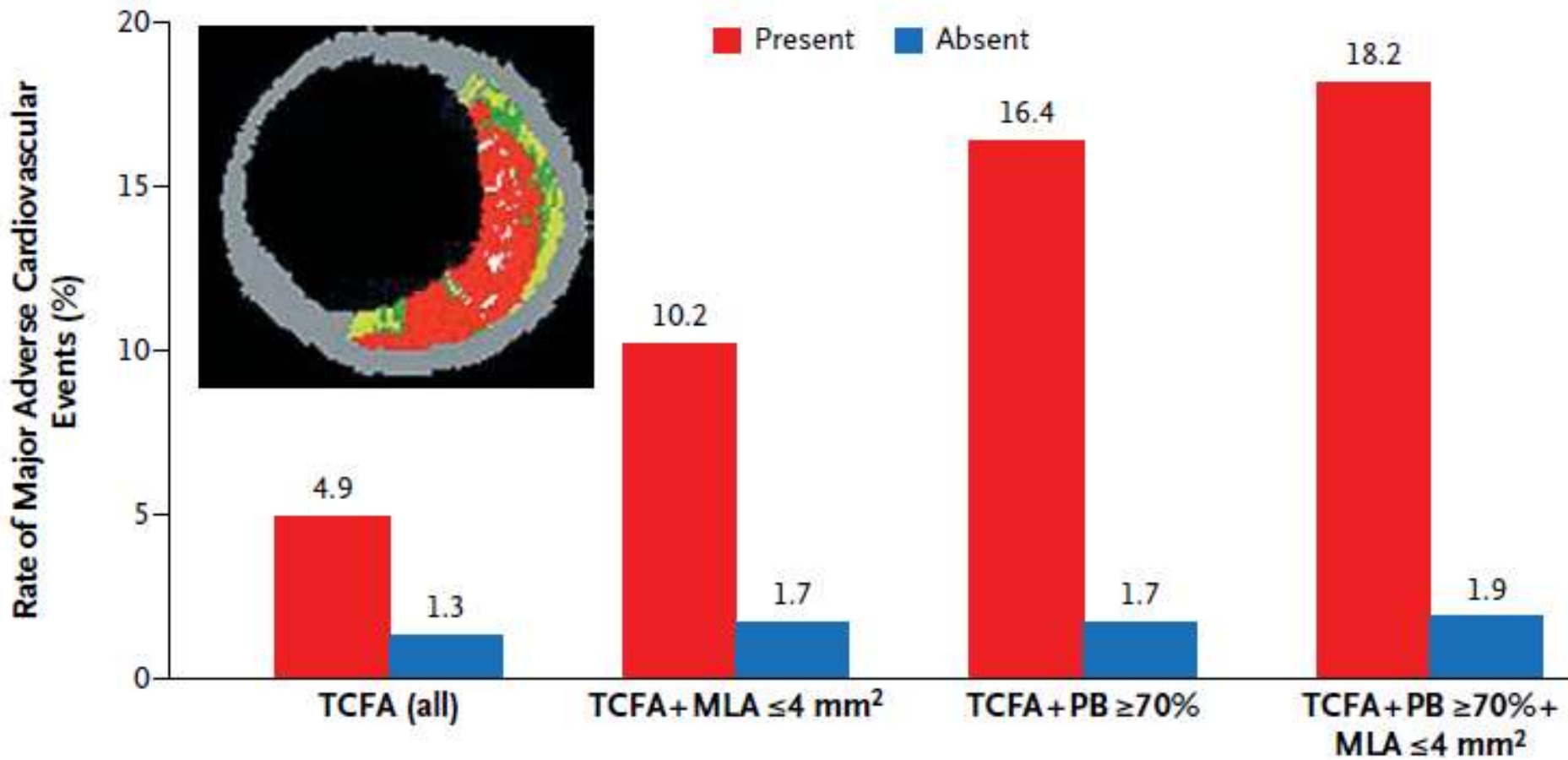


- Large lipid necrotic-core
- Thin fibrous cap $<65\mu\text{m}$
- Positive remodeling
- Large plaque burden
- Macrophages



**Thin-cap fibroatheroma
(TCFA)**

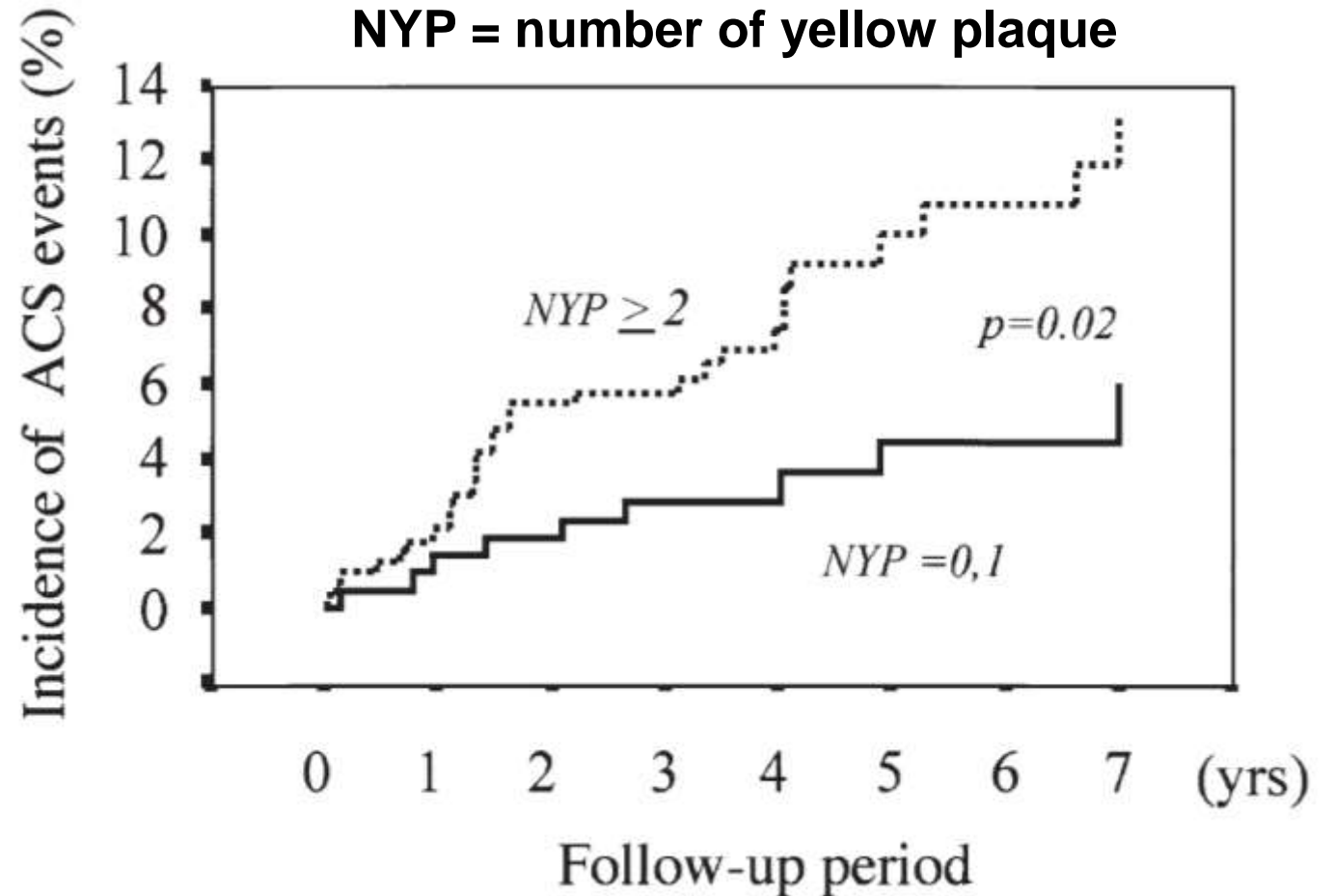
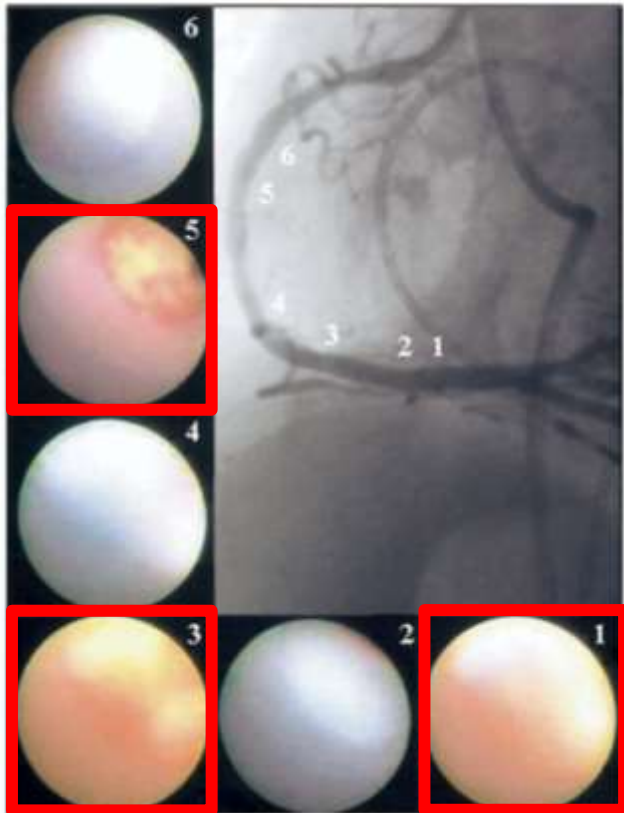
VH-IVUS: PROSPECT study



Lesion hazard ratio (95% CI)	3.90 (2.25–6.76)	6.55 (3.43–12.51)	10.83 (5.55–21.10)	11.05 (4.39–27.82)
P value	<0.001	<0.001	<0.001	<0.001
Prevalence (%)	46.7	15.9	10.1	4.2

Angioscopy: intensive yellow plaque

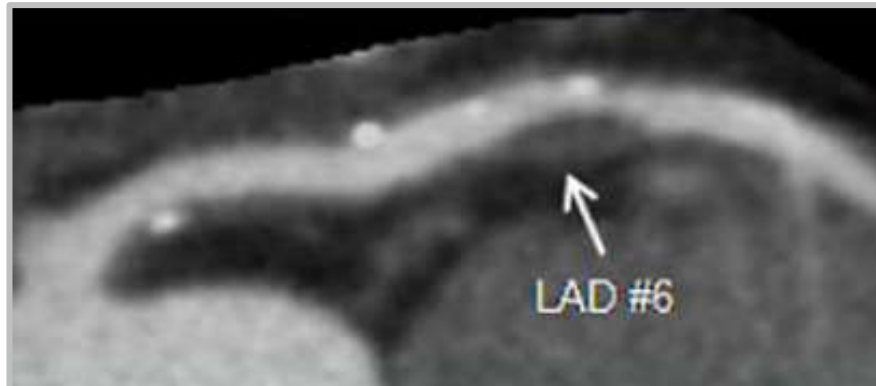
Multiple-yellow plaque



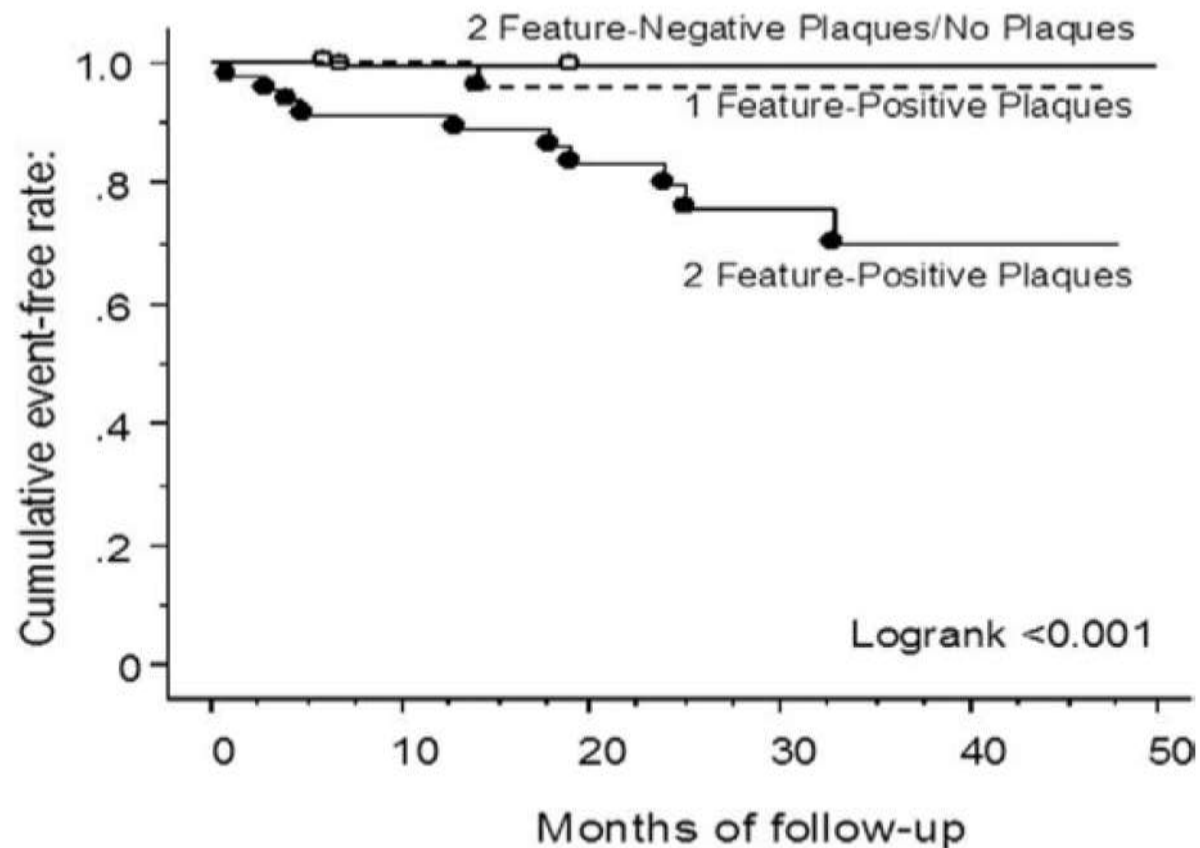
Patients with multiple yellow plaques had a higher risk of follow-up ACS events than those without multiple yellow plaques. Angioscopy would be useful to detect **vulnerable patients**.

CT: low attenuation plaque

Two vulnerable features of CT

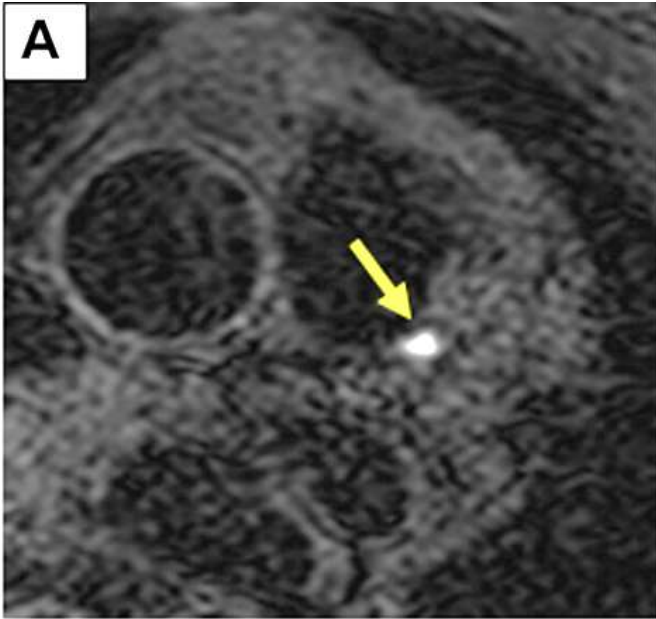


- (1) Low attenuation plaque (< 30HU)
- (2) Positive remodeling (Remodeling index > 1.1)

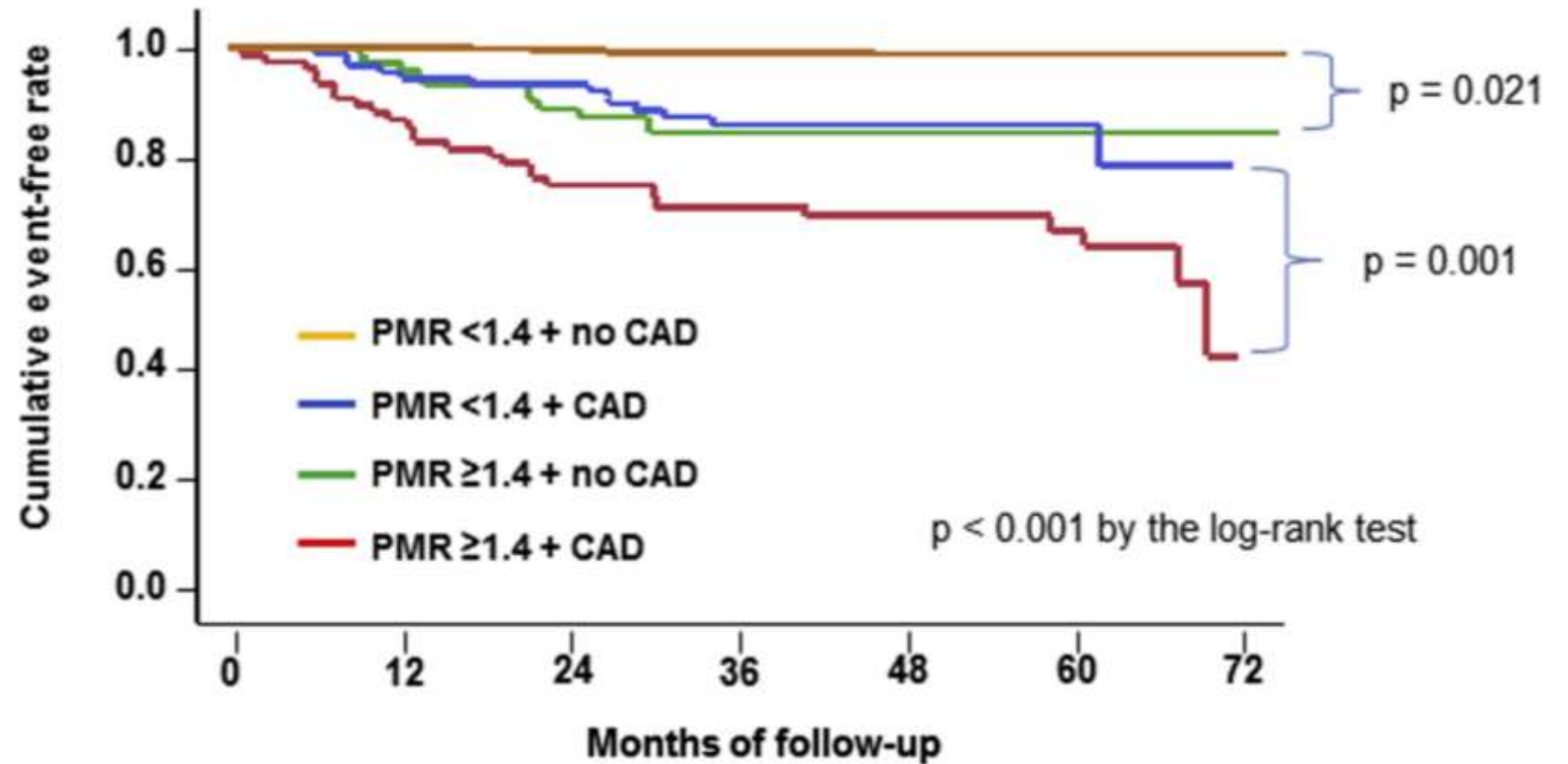


The patients demonstrating positive vessel remodeling with low-attenuation plaques on CT angiography were at a higher risk of follow-up ACS events when compared with patients having lesions without these characteristics.

MRI: high-intensity plaque (HIP)

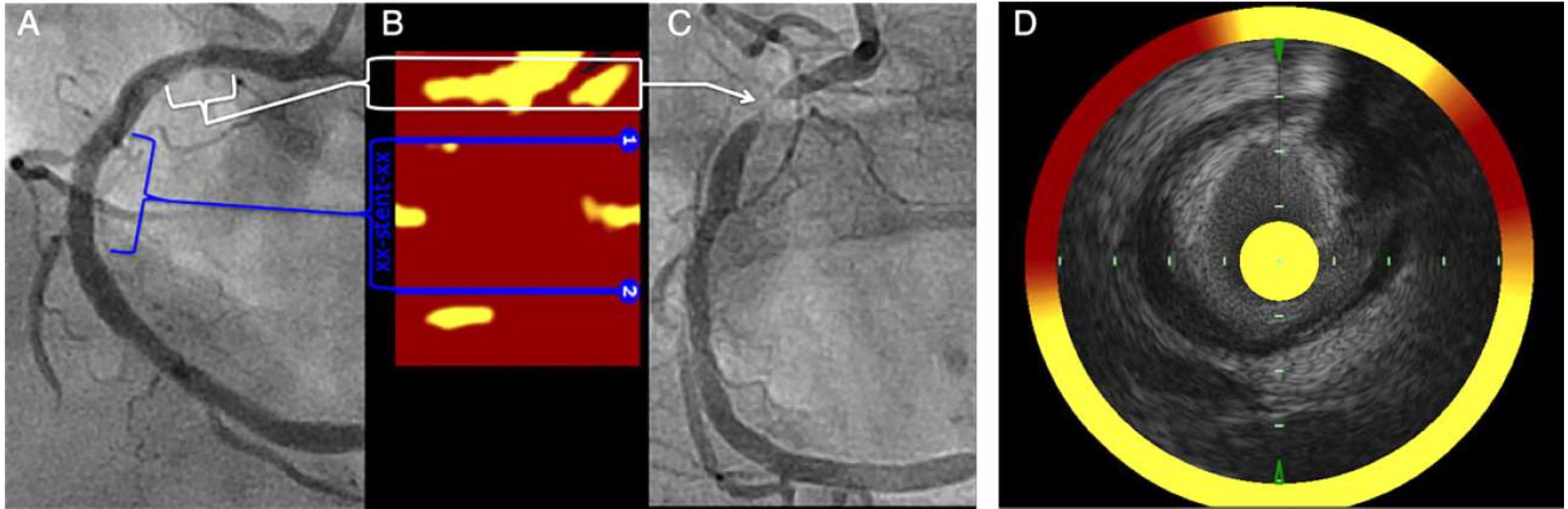


Non-contrast T1WI



Coronary event-free survival was worst in the group with plaque-to-myocardium signal intensity ratios (PMRs) \geq 1.4 and coronary artery disease (CAD) (red line) and best in the group with PMRs <1.4 but no CAD group (orange line). The rate in the group with PMRs \geq 1.4 and no CAD (green line) was intermediate but comparable with that in the group with PMRs <1.4 and CAD (blue line).

NIRS: lipid-core plaque (LCP)

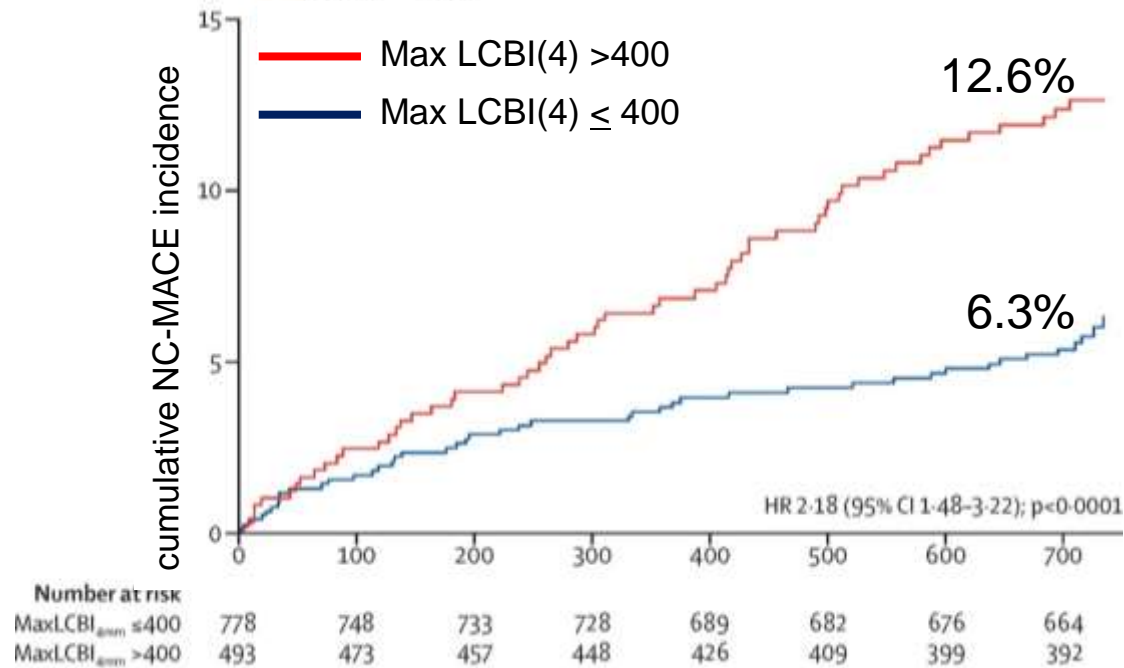


Case. 64-year-old male . (A) Angiography at index catheterization after stenting the mid-RCA is shown . (B) Baseline NIRS chemogram obtained after stent placement demonstrates **a large LCP (maxLCBI4mm 694)** at the site of mild stenosis (white box). (C) Seven months later the patient presented with non-fatal ACS secondary to a de novo culprit lesion in the proximal RCA at the site of the previously demonstrated large LRP (white arrow). (D) A combined cross-sectional NIRS-IVUS image of the proximal RCA lesion at baseline demonstrates a large non-stenotic LRP. LRP = lipid-rich plaque.

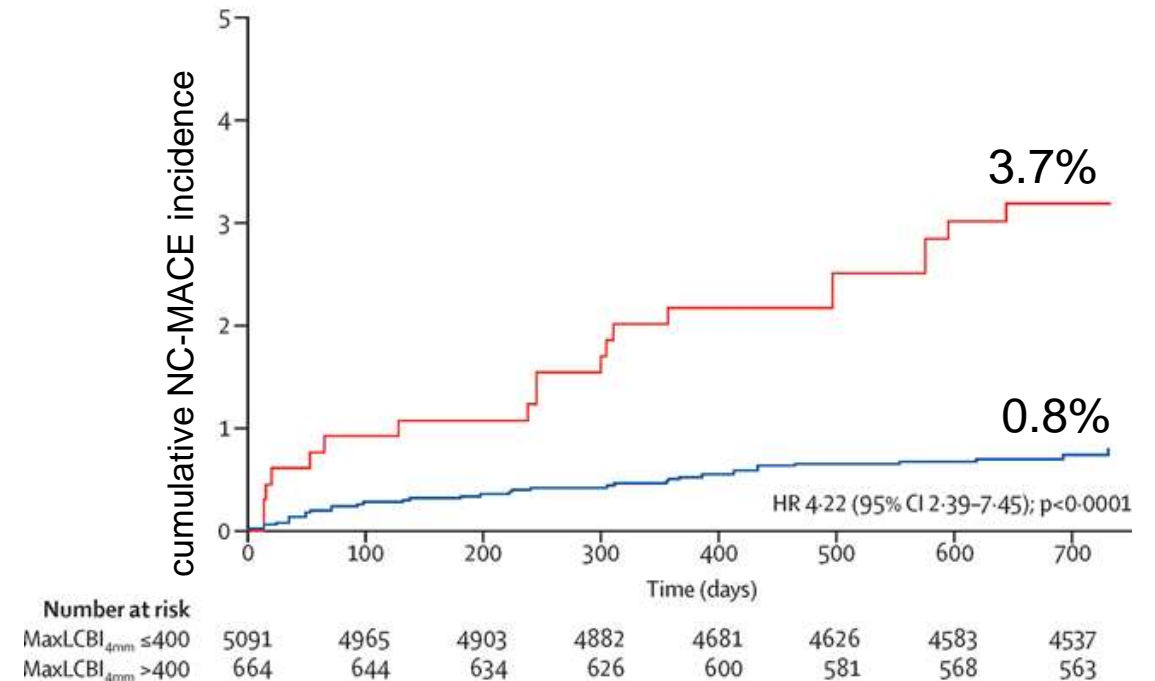
NIRS: LRP study

The LRP study aimed to establish the relationship between LRPs detected by NIRS-intravascular ultrasound imaging at unstented sites and subsequent coronary events from new culprit lesions.

Patient level



Plaque level

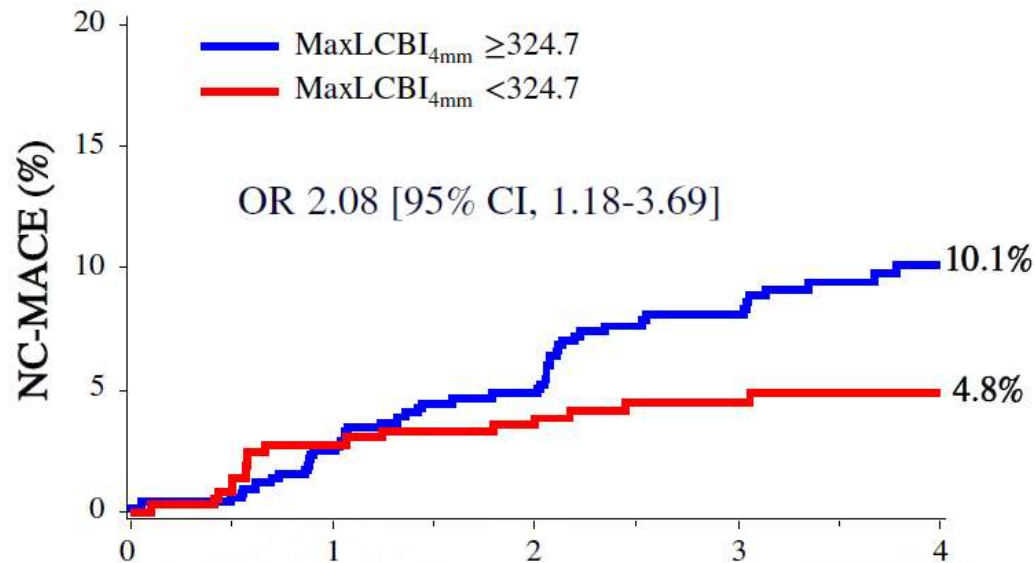


Using binary cutoff of maxLCBI(4) >400, NIRS-IVUS can identify both patients and non-culprit coronary plaques at high risk for future events.

NIRS: PROSPECT II study

NIRS-IVUS was performed in 3 coronary arteries after successful treatment for recent MI. Untreated “non-culprit” lesions were identified by IVUS and their lipid content was assessed by blinded NIRS.

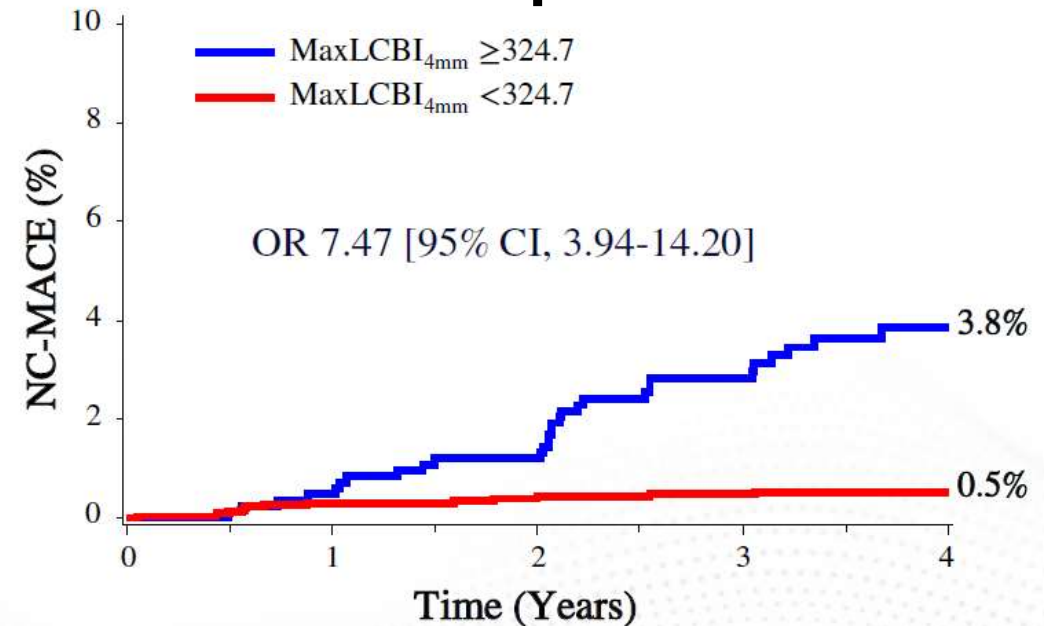
Patient level



Number at risk :

	0	1	2	3	4
≥324.7	520	503	490	359	202
<324.7	364	352	345	255	127

Plaque level

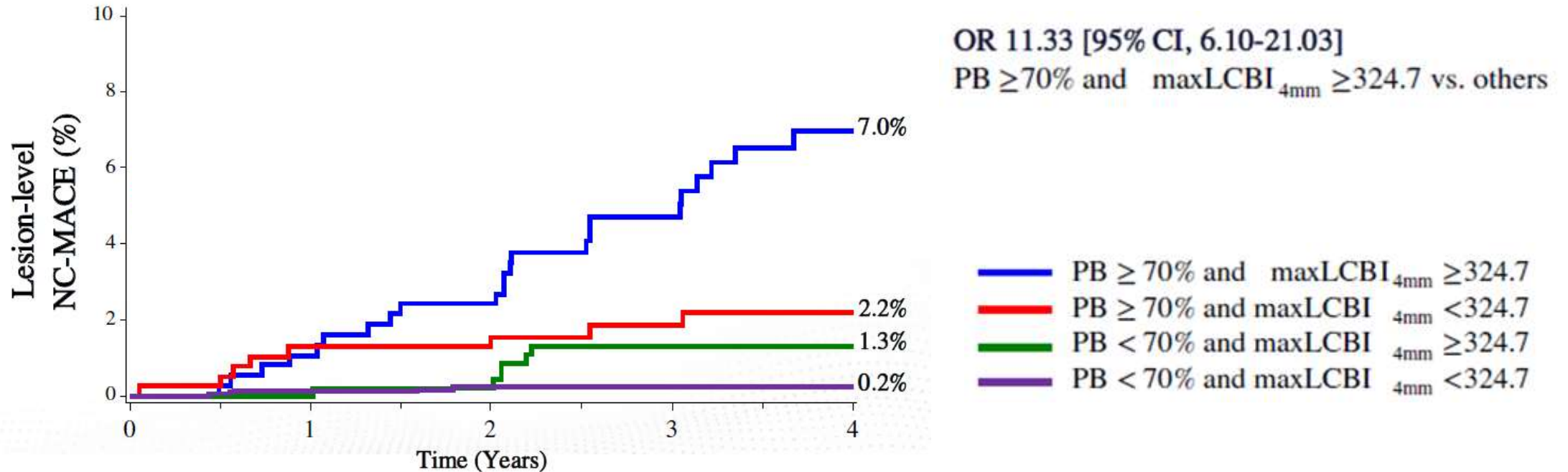


	0	1	2	3	4
≥324.7	851	837	830	621	359
<324.7	2,649	2,623	2,610	1,976	1,092

NIRS identified lipid-rich angiographically non-flow-limiting plaques that were responsible for future coronary events.

NIRS: PROSPECT II study

MaxLCBI 4mm ≥ 324.7 and PB $\geq 70\%$ were independently associated with lesion-level NCL-MACE in multivariable analysis.

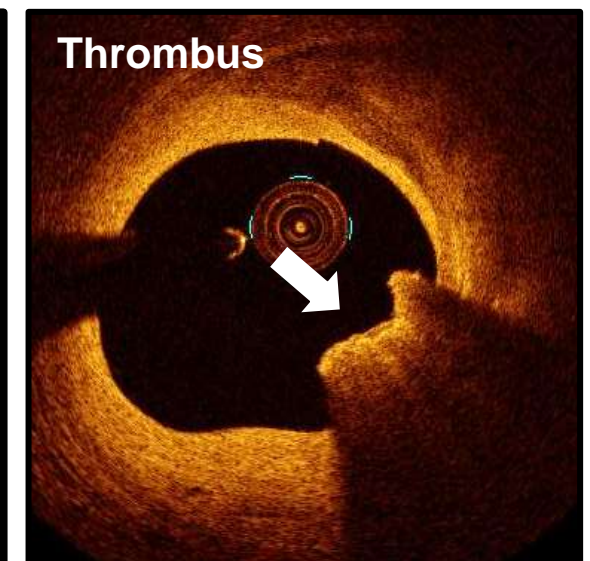
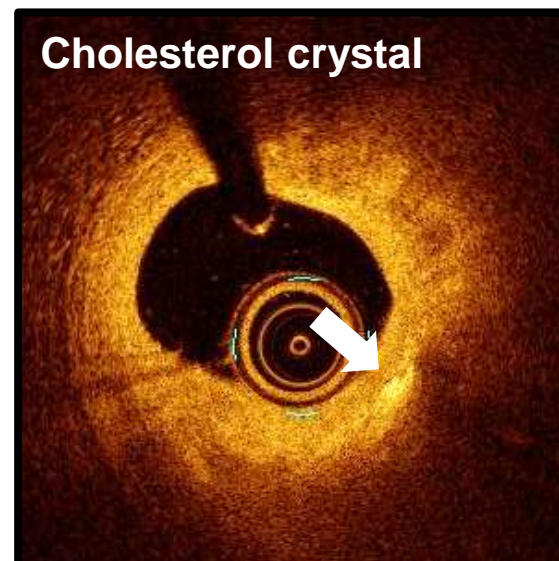
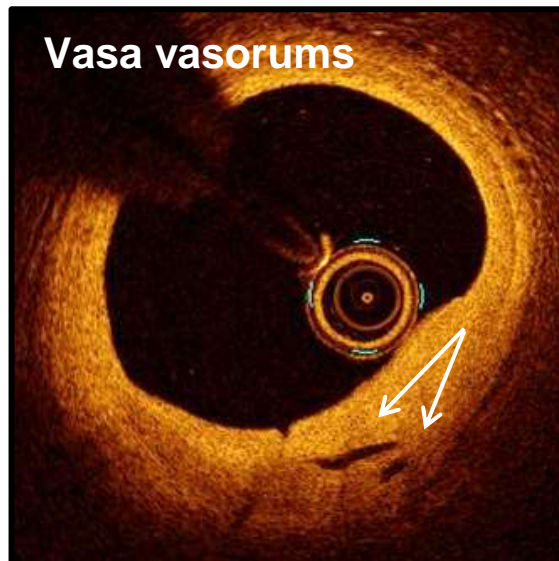
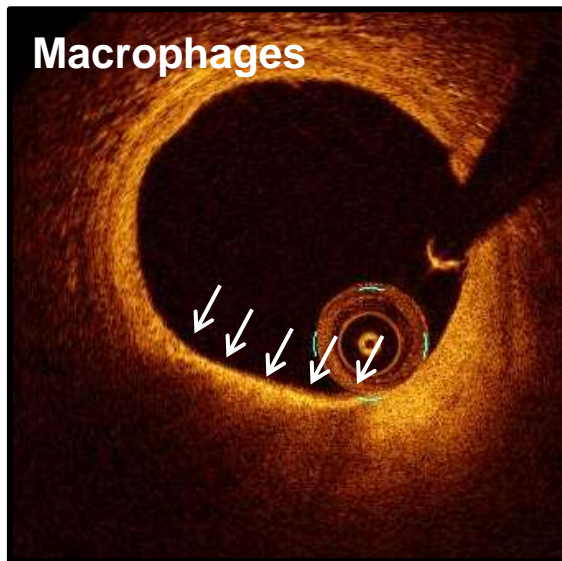
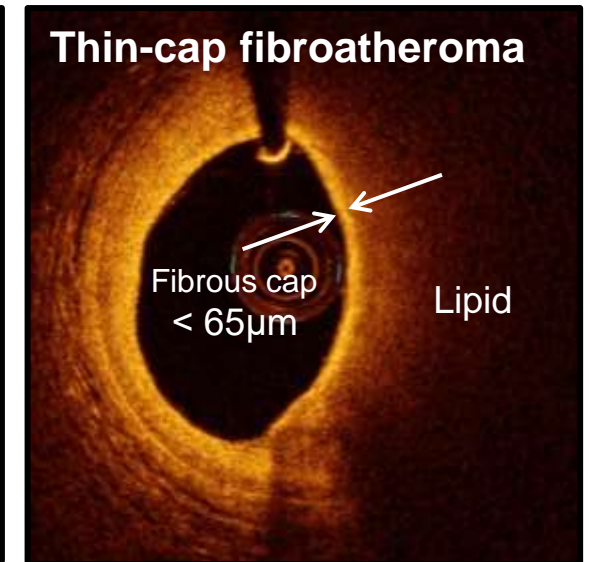
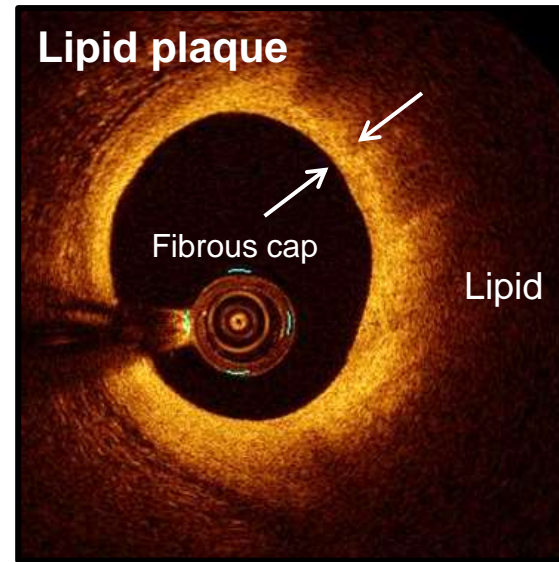
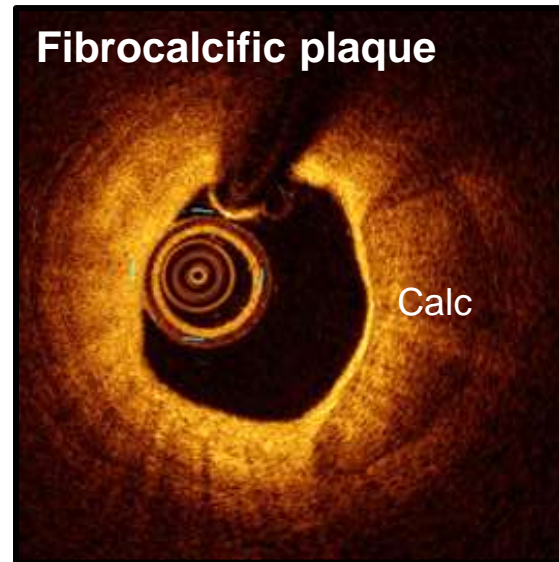
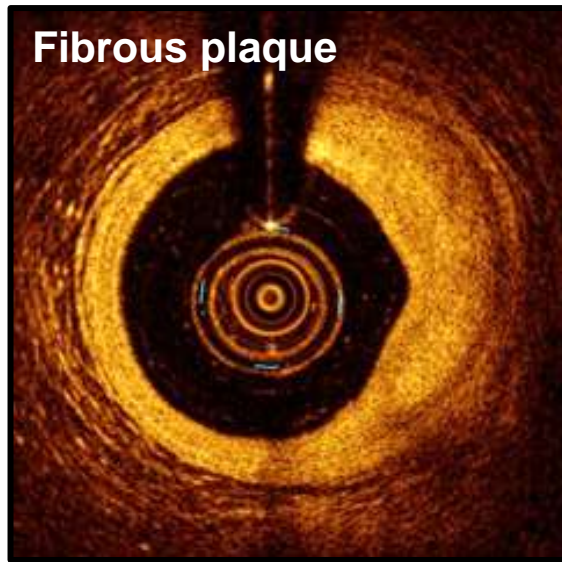


Number at risk:

PB $\geq 70\%$ and maxLCBI _{4mm} ≥ 324.7	374	368	362	271	162
PB $\geq 70\%$ and maxLCBI _{4mm} < 324.7	391	383	381	293	168
PB $< 70\%$ and maxLCBI _{4mm} ≥ 324.7	477	469	468	350	197
PB $< 70\%$ and maxLCBI _{4mm} < 324.7	2,258	2,240	2,229	1,683	924

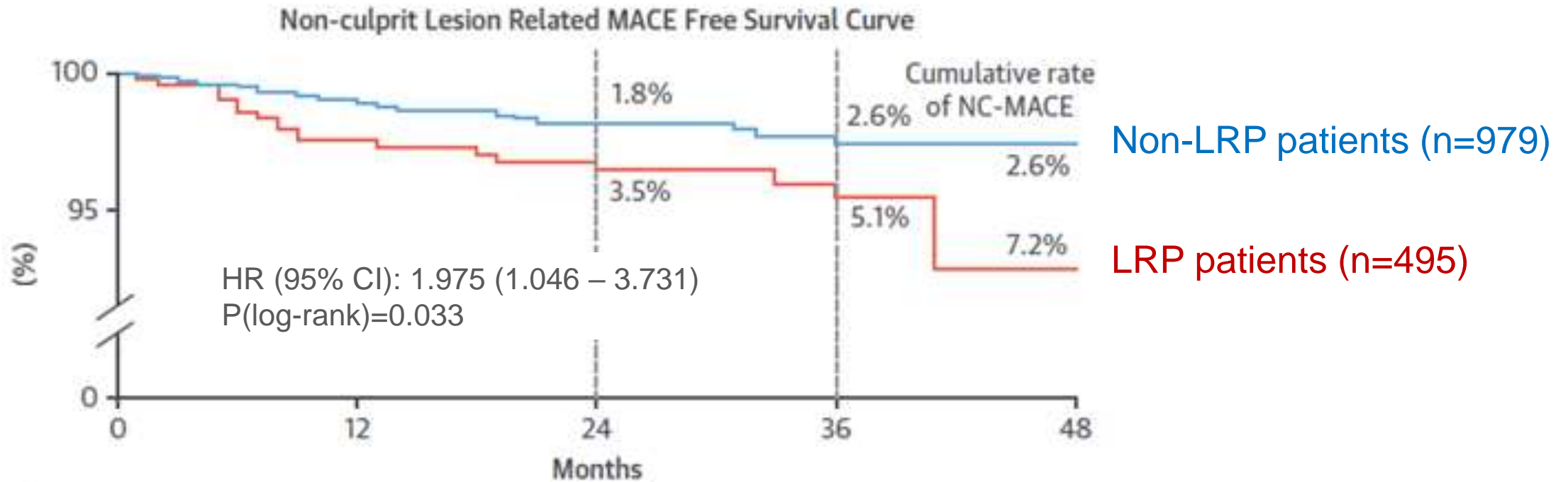
The combination of lipid-rich plaque and large plaque burden identified vulnerable plaques that placed patients at especially high risk for future MACE.

OCT images of coronary plaques



OCT: MGH registry (patient level analysis)

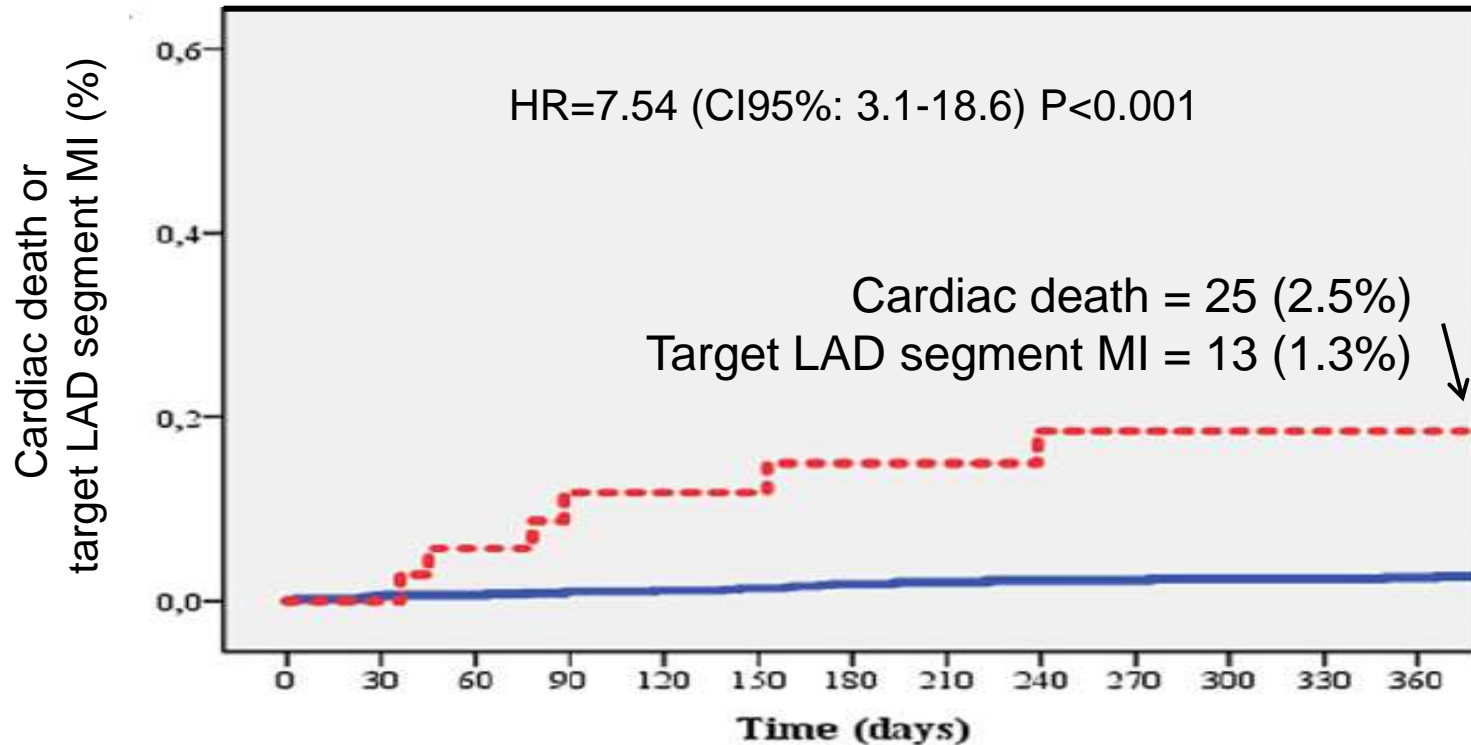
This study investigated the clinical significance of OCT-derived lipid-rich plaque (LRP) in the nonculprit region of the target vessel in 1,474 patients undergoing PCI.



Patients with LRP in the non-culprit region of the PCI-targeted vessel showed significantly higher risk of future MACE compared to those without LRP.

OCT: CLIMA study (patient level analysis)

The CLIMA study investigated the relationship between OCT-determined plaque morphology of the proximal LAD and 12 months clinical outcome in 1,003 patients.



Simultaneously presence of

- (1) MLA < 3.5 mm²,
- (2) fibrous cap thickness < 75 μm,
- (3) lipid arc > 180, and
- (4) macrophages

YES

No

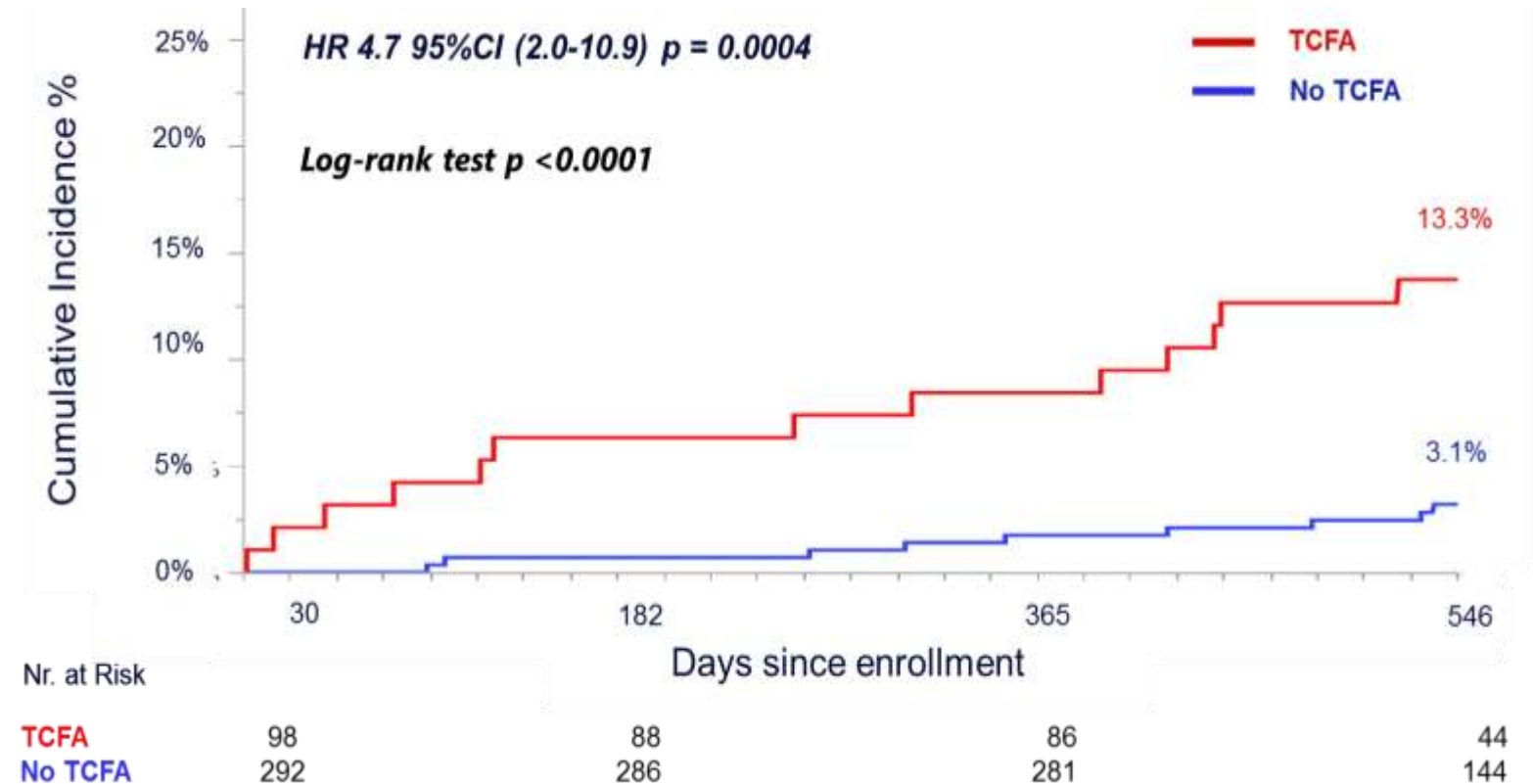
Patients with these four plaque features in proximal LAD showed significantly higher incidence of subsequent acute coronary event compared to patients without these four plaque features.

OCT: COMBINE OCT-FFR study (plaque level analysis)

COMBINE enrolled DM patients with at least 1 coronary lesions with angiographic diameter stenosis 40-80% and FFR >0.80 (defined as target lesions).

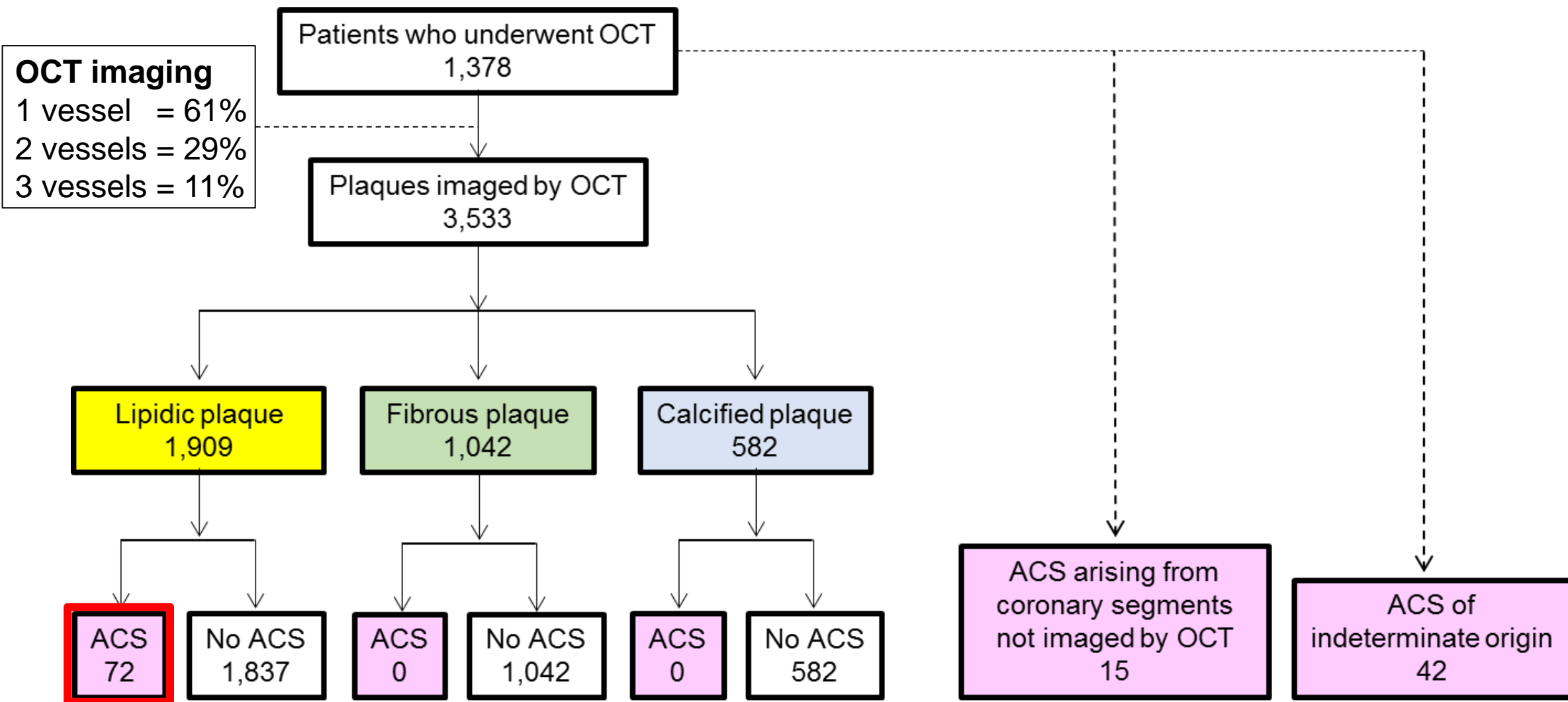
Primary endpoint
Target lesion related MACE
Composite of

- Cardiac death
- Target vessel MI,
- Clinically-driven TLR
- Hospitalisation due to unstable or progressive angina



Patients with TCFAs had a significant increase in target-lesion related MACE as compared to patients without TCFA. OCT-derived TCFA is a high risk plaque for future MACE.

OCT: Wakayama registry (plaque level analysis)

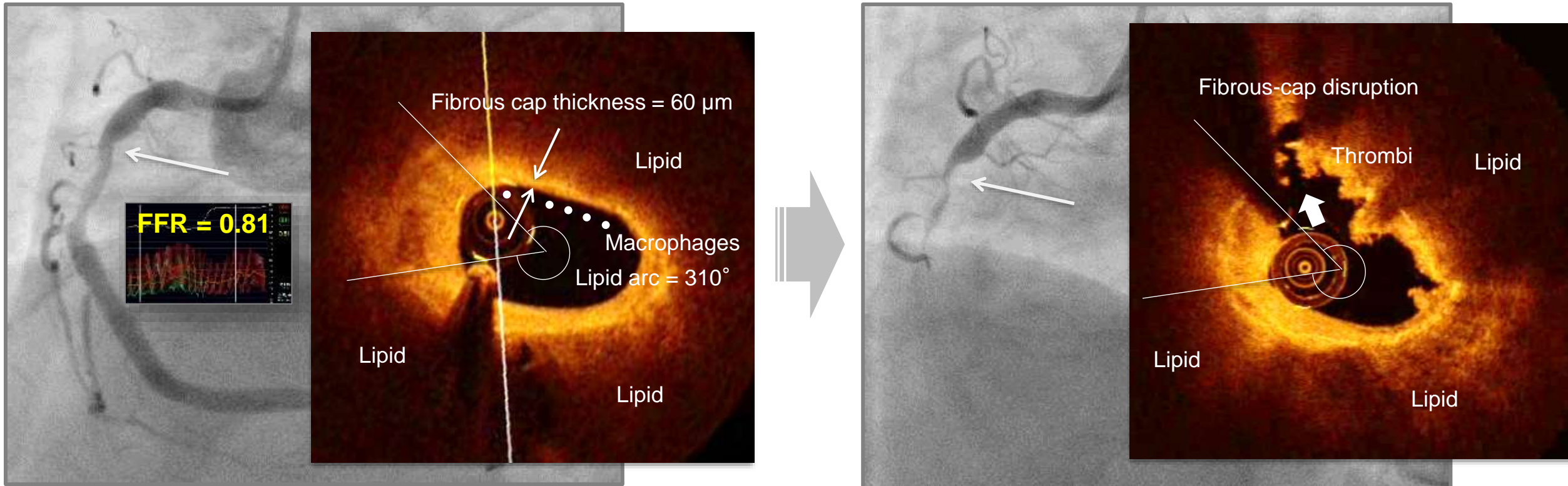


Follow-up period = median 6 years (IQR: 5-9 years)

ACS event arising from LRP+TCFA

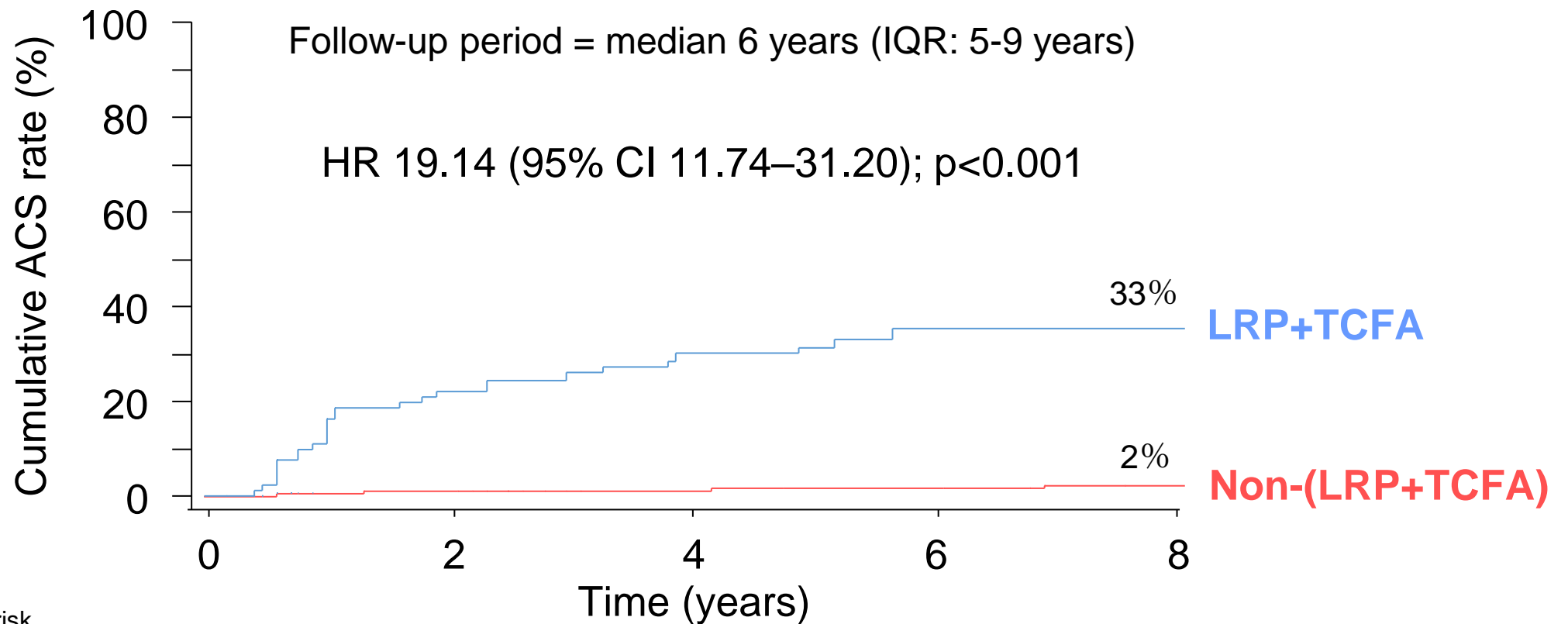
Baseline

10 months



Baseline angiogram showed moderate stenosis in the proximal right RCA. Baseline OCT characterized the plaque as both LRP and TCFA (maximum lipid arc 310° [asterisks], minimum fibrous cap thickness 60μm [arrow heads], minimum lumen area 2.27mm², and presence of OCT-derived macrophage infiltration [dots]). This plaque was associated with AMI 10 months after baseline imaging. Follow-up angiography showed that the stenosis developed into an occlusion. Follow-up OCT showed rupture (arrow) of the plaque that was imaged during baseline OCT.

Kaplan-Meier curves



Number at risk

LRP+TCFA

Non-(LRP+TCFA)

83

63

50

27

9

1,826

1,756

1,535

928

532

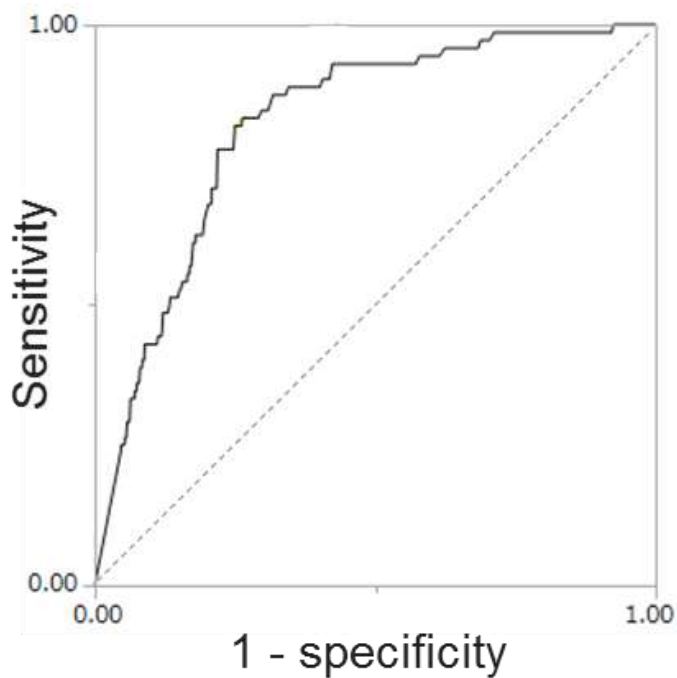
Lipidic plaques that were characterized as both LRP and TCFA had a significantly higher risk of follow-up ACS than lipidic plaques that did not have those characteristics.

OCT predictors

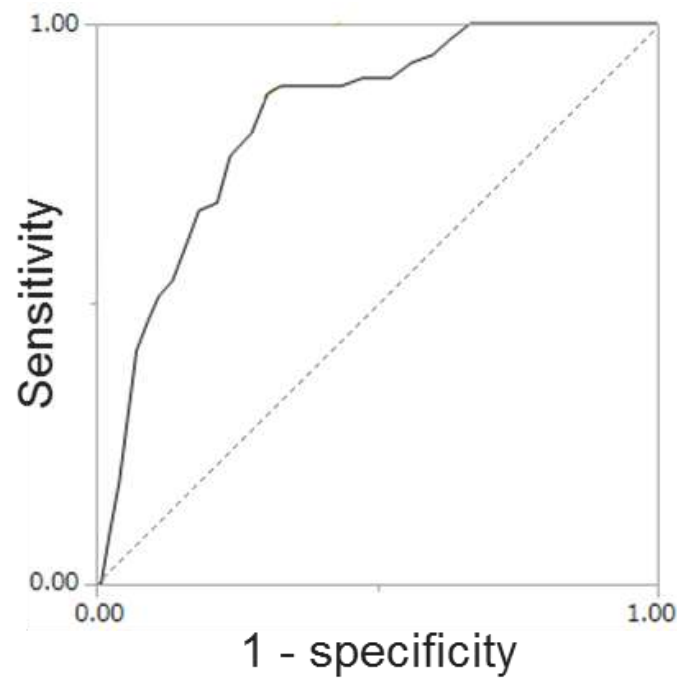
	Univariate analysis HR (95% CI)	P	Multivariate analysis HR (95% CI)	P
Max lipid arc	1.01 (1.00-1.01)	<0.001	1.01 (1.01-1.01)	<0.001
Lipid length	1.03 (0.98-1.08)	0.193	-	-
Min fibrous-cap thickness	0.98 (0.98-0.99)	<0.001	0.99 (0.98-0.99)	<0.001
Macrophages	4.83 (2.80-8.34)	<0.001	1.06 (0.58-1.95)	0.850
Microvasculature	0.72 (0.38-1.38)	0.324	-	-
Cholesterol crystal	0.97 (0.50-1.89)	0.925	-	-
Min lumen area	0.73 (0.63-0.84)	<0.001	0.78 (0.67-0.90)	<0.001

Optimal cutoffs to predict ACS

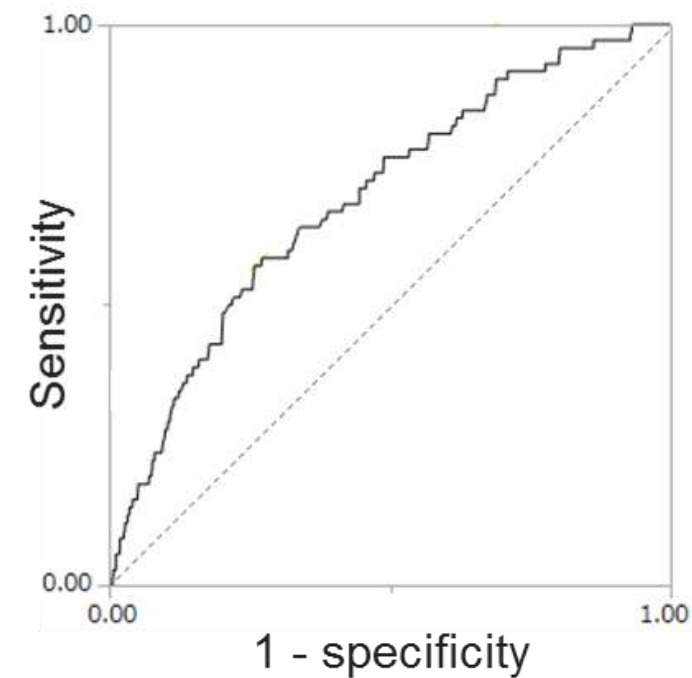
Maximum lipid arc
Cut-off $\geq 185^\circ$
AUC = 0.82



Minimum fibrous cap thickness
Cut-off $\leq 150\mu\text{m}$
AUC = 0.83

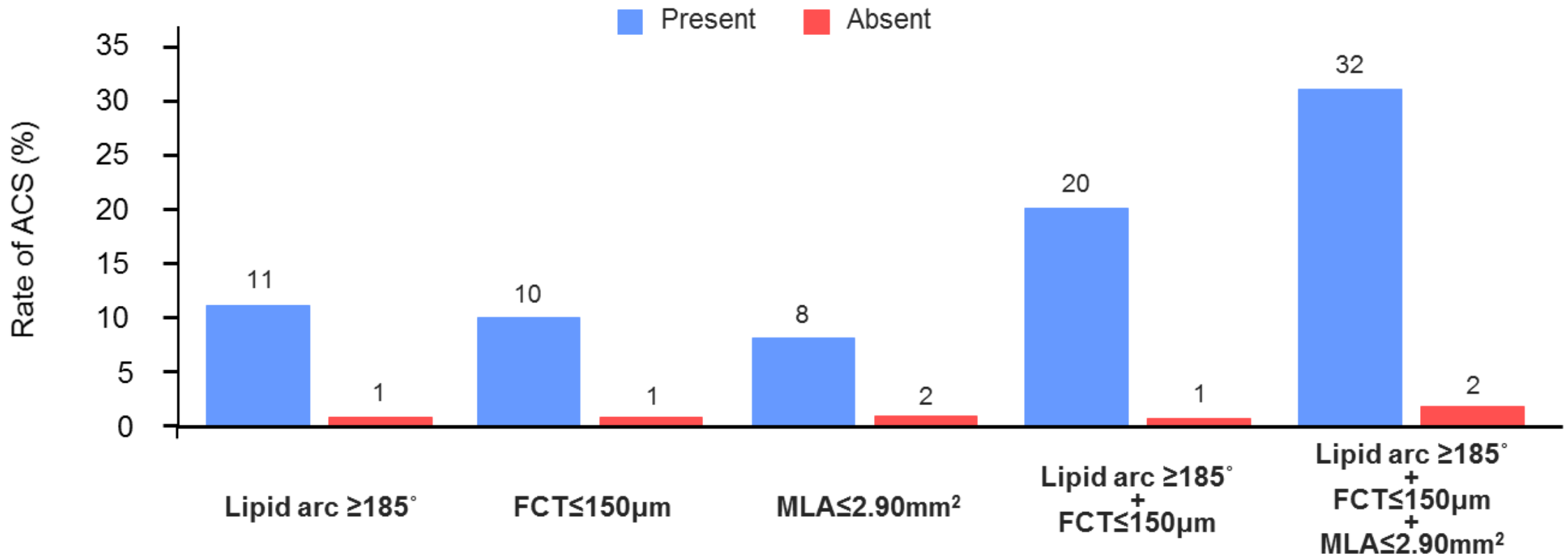


Minimum lumen area
Cut-off $\leq 2.90\text{mm}^2$
AUC = 0.69



Based on ROC curve analysis, the optimal cutoffs to predict ACS were maximum lipid arc of $\geq 185^\circ$, minimum fibrous cap thickness of $\leq 150\mu\text{m}$, and minimum lumen area of $\leq 2.90\text{mm}^2$.

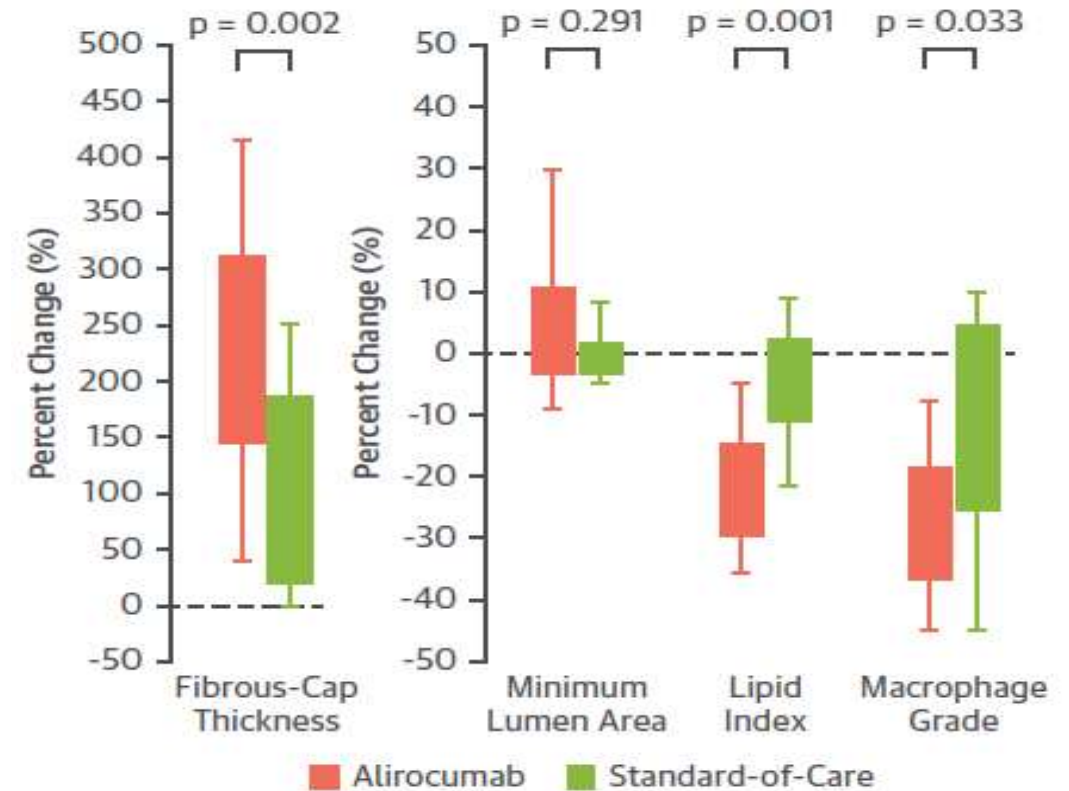
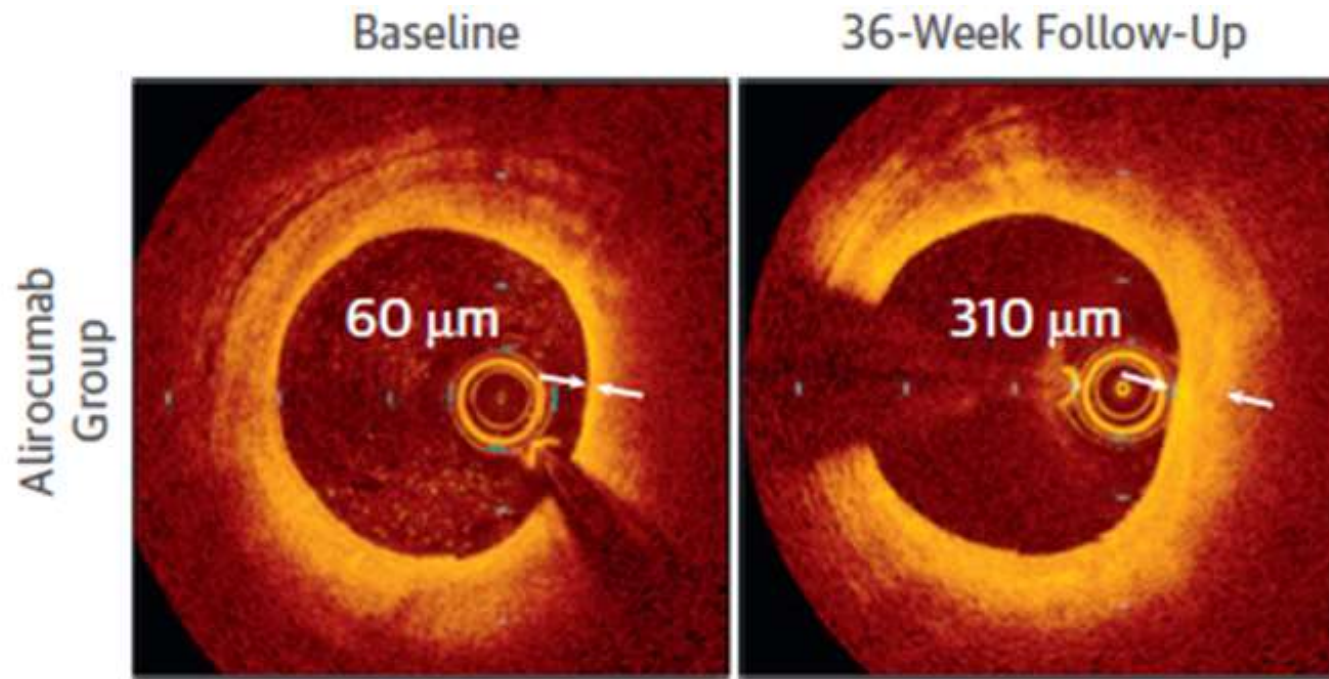
Rate of ACS



No. of plaques	543	1366	623	1286	531	1378	278	1631	105	1804
No. of ACS	60	12	63	9	42	30	55	17	34	38
HR (95%CI)	13.24 (7.01-24.68)		11.08 (6.06-20.27)		4.56 (2.63-7.90)		2.63 (1.64-4.23)		2.63 (1.64-4.23)	
P value	<0.001		<0.001		<0.001		<0.001		<0.001	
Prevalence	28%		33%		28%		15%		6%	

Plaque stabilization with PCSK9i: ALTAIR study

The ALTAIR study assessed the effect of adding the PCSK9 inhibitor Alirocumab to Rosuvastatin in patients with TCFA during 36-week follow-up period.



Addition of Alirocumab was associated with a significantly greater increase in fibrous cap thickness and significantly greater percentage decreases in lipid index and macrophage grade.

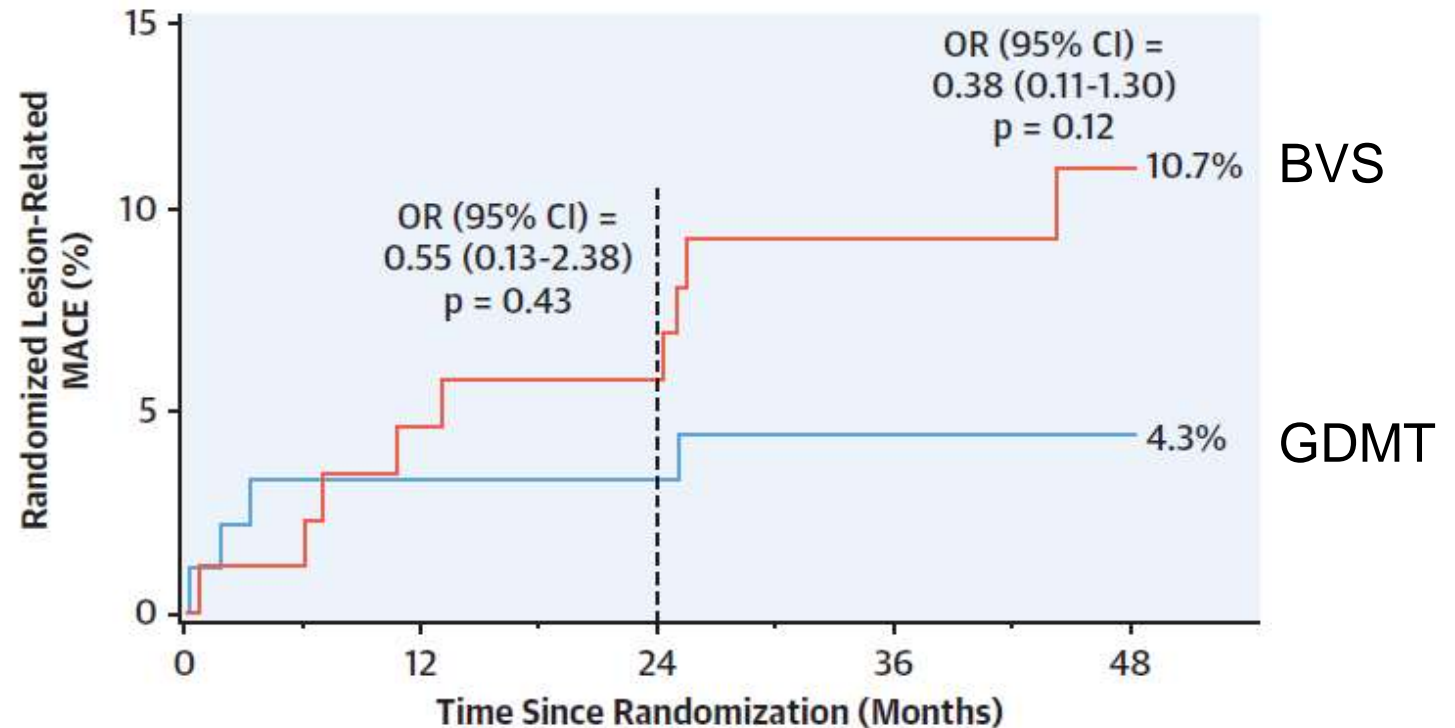
Prophylactic PCI for VP: PROSPECT ABSORB study

Non-flow-limiting stenoses (Angiographic DS <70% and IVUS plaque burden \geq 65%) were randomized to treatment with an **BVS plus GDMT vs. GDMT alone**.

The secondary (non-powered) clinical effectiveness endpoint

Randomized lesion-related MACE at latest follow-up

- Cardiac death
- MI
- Unstable angina
- Progressive angina



PCI of angiographically mild lesions with large plaque burden was associated with favorable long-term clinical outcomes.

Conclusion

- Imaging can be used to identify both patients and non-culprit plaques at high risk for future events and should be considered for use in patients undergoing cardiac catheterisation with possible PCI.
- Studies for the use of imaging-guided therapy should be done to address and mitigate the high risk for MACE of these patients and plaques.





Thank you!