

Approach to FFR-Negative and TCFA-Positive Coronary Lesions How Can We Manage It?

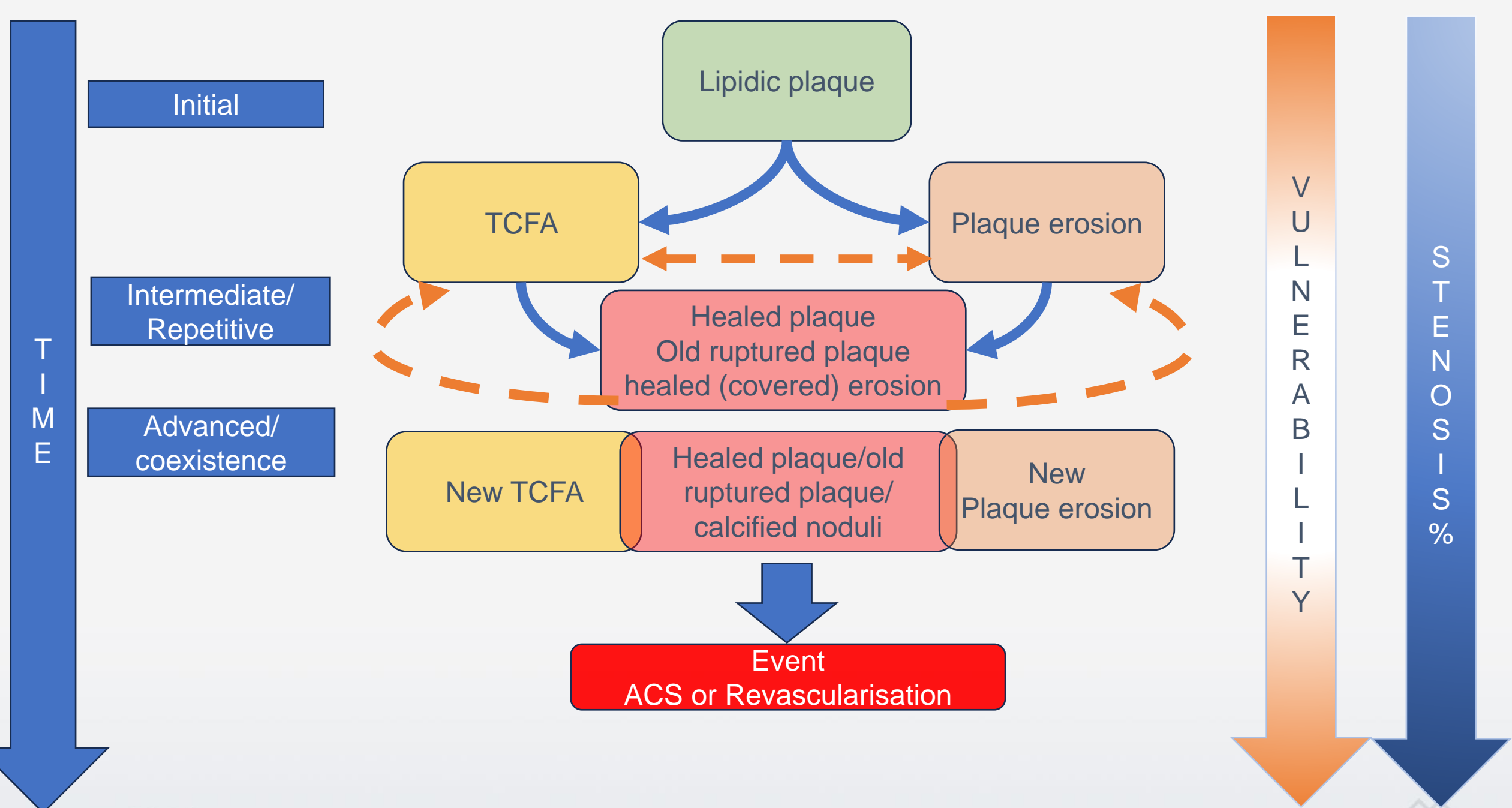
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- Wojciech Wojakowski: Abbott Vascular lecture fees



Initial

Lipidic plaque

TCFA

Plaque erosion

Intermediate/
Repetitive

Healed plaque
Old ruptured plaque
healed (covered) erosion

Advanced/
coexistence

New TCFA

Healed plaque/old
ruptured plaque/
calcified noduli

New
Plaque erosion

Event

ACS or Revascularisation

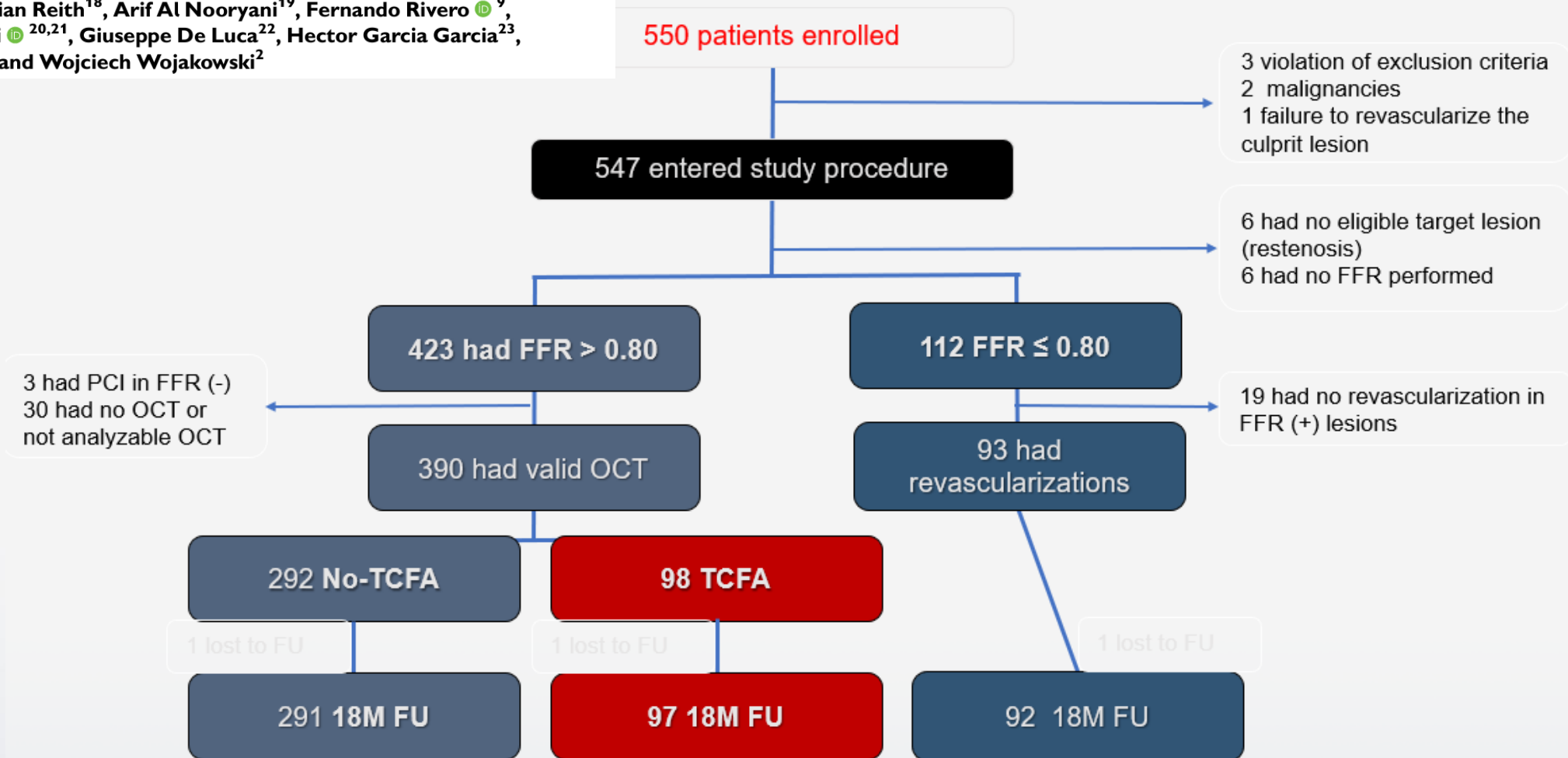
VULNERABILITY

STENOSIS %

Thin-cap fibroatheroma predicts clinical events in diabetic patients with normal fractional flow reserve: the COMBINE OCT-FFR trial

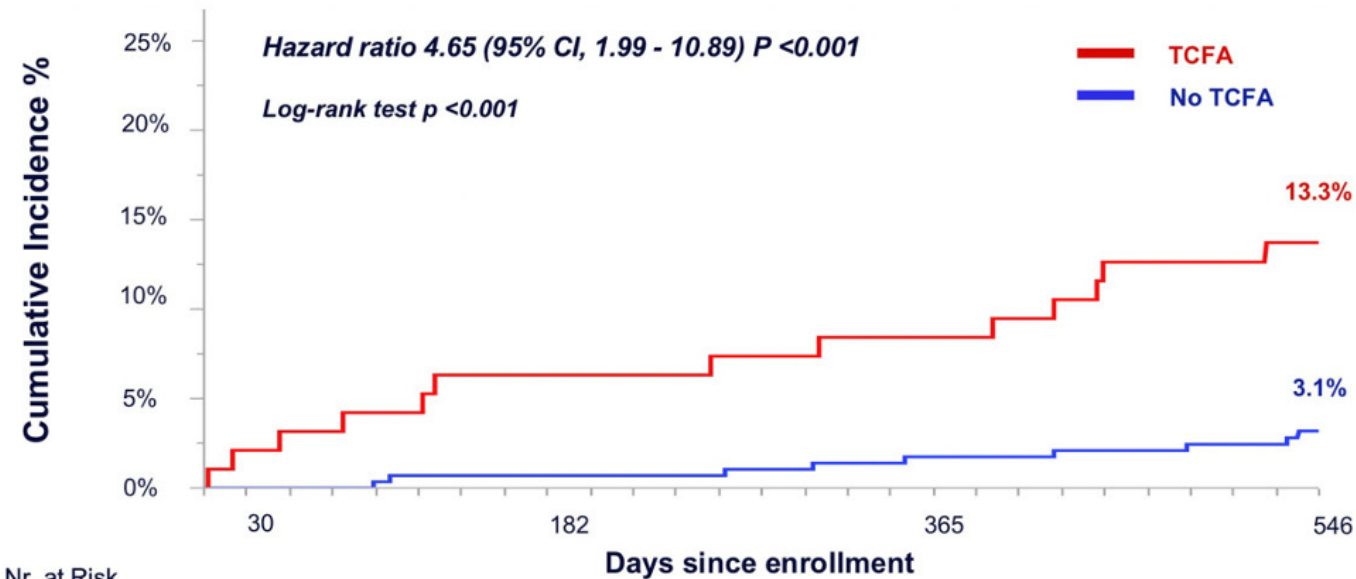
Elvin Kedhi^{1,2*}, Balazs Berta^{3,4}, Tomasz Roleder⁵, Rencus S. Hermanides⁴, Enrico Fabris⁶, Alexander J.J. Ijsselmuiden⁷, Floris Kauer⁸, Fernando Alfonso⁹, Clemens von Birgelen^{10,11}, Javier Escaned¹², Cyril Camaro¹³, Mark W. Kennedy¹⁴, Bruno Pereira¹⁵, Michael Magro¹⁶, Holger Nef¹⁷, Sebastian Reith¹⁸, Arif Al Nooryani¹⁹, Fernando Rivero⁹, Krzysztof Malinowski^{20,21}, Giuseppe De Luca²², Hector Garcia Garcia²³, Juan F. Granada^{24,25}, and Wojciech Wojakowski²

Impact of OCT-TCFA on clinical outcomes in patients with DM and FFR-negative lesions.



Variables	FFR(-)/TCFA(+), n = 98	FFR(-)/TCFA(-), n = 292	P-value
Age, years, median (IQR)	70 (59–76)	68 (62–74)	0.87
BMI, kg/m ² , mean (IQR)	29 (27–33)	29 (26–32)	0.99
Male sex, n (%)	65 (66.3)	180 (61.6)	0.41
Insulin-dependent DM, n (%)	35 (35.7)	100 (34.2)	0.79
Oral antidiabetics, n (%)	82 (83.7)	240 (82.2)	0.74
Smoking status, n (%)			
Current smoking	22 (22.4)	53 (18.7)	0.42
Previous smoking	23 (34.8)	64 (31.1)	0.57
Hypercholesterolemia, n (%)	61 (62.2)	171 (58.8)	0.54
Hypertension, n (%)	75 (76.5)	214 (73.8)	0.59
Previous ACS, n (%)	42 (42.9)	97 (33.2)	0.08
Previous PCI, n (%)	41 (41.8)	103 (35.3)	0.24
Previous CABG, n (%)	4 (4.1)	8 (2.7)	0.51
Previous CVA, n (%)	12 (12.2)	20 (6.8)	0.09
SCD at presentation, n (%)	77 (78.6)	215 (73.6)	0.78
ACS at presentation, n (%)	21 (21.4)	77 (26.4)	0.78
MI at presentation, n (%)	12 (12.2)	50 (17.1)	0.25
Total no. of lesions, n (per patient)	204 (2.08)	493 (1.69)	0.02
1 vessel disease	38 (38.8%)	157 (53.8%)	0.01
2 vessel disease	49 (50.0%)	114 (39.0%)	0.07
3 vessel disease	11 (11.2%)	21 (7.2%)	0.29
Lesions revascularized, n (per patient)	81 (0.83)	152 (0.52)	0.003
FFR-negative target lesions, n (per patient)	123 (1.26)	341 (1.17)	0.50
Distribution FFR-negative lesions			0.14
Left main	1 (0.8%)	5 (1.5%)	
LAD	45 (36.6%)	156 (45.7%)	
CX	33 (26.8%)	93 (27.3%)	
RCA	44 (35.8%)	87 (25.5%)	
Total cholesterol, mg/dL, median (IQR)	161 (142–189)	154 (135–193)	0.18
LDL-cholesterol, mg/dL, median (IQR)	88 (82–93)	91 (81–99)	0.52
Triglycerides, mg/mL, median (IQR)	168 (120–242)	150 (106–231)	0.25
Hemoglobin A1c, %, median (IQR)	7.3 (6.7–7.9)	7.3 (6.6–8.1)	0.78

	FFR(-)/TCFA(+), <i>n</i> = 104a	FFR(-)/TCFA(-), <i>n</i> = 341	P-value
Quantitative OCT analysis, median (IQR)			
MLA, mm ²	2.35 (1.70–3.18)	2.60 (1.90–3.50)	0.09
% area stenosis, %	65 (57–73)	62 (53–70)	0.07
Lesion length, mm	27.65 (18.10–36.10)	20.10 (14.10–29.60)	<0.001
Proximal RLD, mm	3.10 (2.70–3.50)	3.00 (2.60–3.50)	0.63
Distal RLD, mm	2.50 (2.30–3.00)	2.60 (2.20–3.00)	0.68
Qualitative OCT analysis			
Fibrous cap thickness, μm, median (IQR)	60 (56–63)	151 (109–218)	–
Calcification present, <i>n</i> (%)	91 (87.5)	292 (85.6)	0.99
Calcium arc, °, median (IQR)	112 (80–192)	159 (88–244)	0.02
Protruding calcification, <i>n</i> (%)	36 (34.6)	157 (46.0)	0.04
Cholesterol clefts, <i>n</i> (%)	75 (72.8)	149 (44.1)	<0.001
Lipidic plaque, <i>n</i> (%)	104 (100)	201 (58.9)	<0.001
Lipidic arc, °, median (IQR)	241 (193–287)	169 (126–214)	<0.001
Neovascularization, <i>n</i> (%)	88 (84.6)	232 (68.0)	0.002
Macrophage infiltration, <i>n</i> (%)	72 (69.9)	157 (46.0)	<0.001



Nr. at Risk

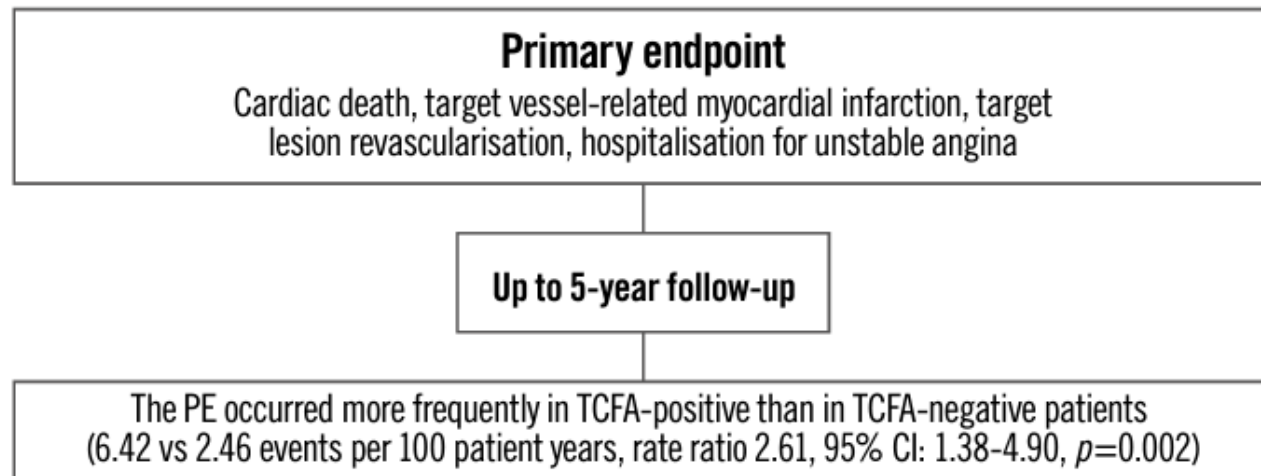
	30	182	365	546
TCFA	98	88	86	44
No TCFA	292	286	281	144

Variable	FFR(-)/TCFA(+) (n = 98)	FFR(-)/TCFA(-) (n = 292)	Hazard ratio (95% confidence interval)	P-value
Primary endpoint, ^a n (%)	13 (13.3)	9 (3.1)	4.65 (1.99–10.89)	<0.001
Cardiac death, n (%)	0 (0)	1 (0.34)	–	–
Death (any), n (%)	0 (0)	3 (1.03)	–	–
TV MI, n (%)	4 (4.1)	0 (0)	–	–
Spontaneous MI (any), n (%)	8 (8.2)	3 (1.0)	8.26 (2.19–31.14)	0.002
CD-TLR, n (%)	11 (11.2)	4 (1.4)	8.72 (2.78–27.39)	<0.001
Revascularization (any), n (%)	17 (17.3)	17 (5.8)	3.26 (1.66–6.38)	<0.001
Unstable angina requiring hospitalization, n (%)	6 (6.1)	5 (1.7)	3.76 (1.15–12.32)	0.03
Cardiac death and TV MI, n (%)	4 (4.1)	1 (0.3)	12.84 (1.44–114.92)	0.02
Death and any MI, n (%)	9 (9.2)	6 (2.0)	4.70 (1.68–13.22)	0.003
Cardiac Death, TV MI and CD-TLR, n (%)	11 (11.2)	5 (1.7)	7.0 (2.43–20.14)	<0.001
Death, MI and revascularization, n (%)	17 (17.3)	20 (6.8)	2.77 (1.45–5.28)	0.002

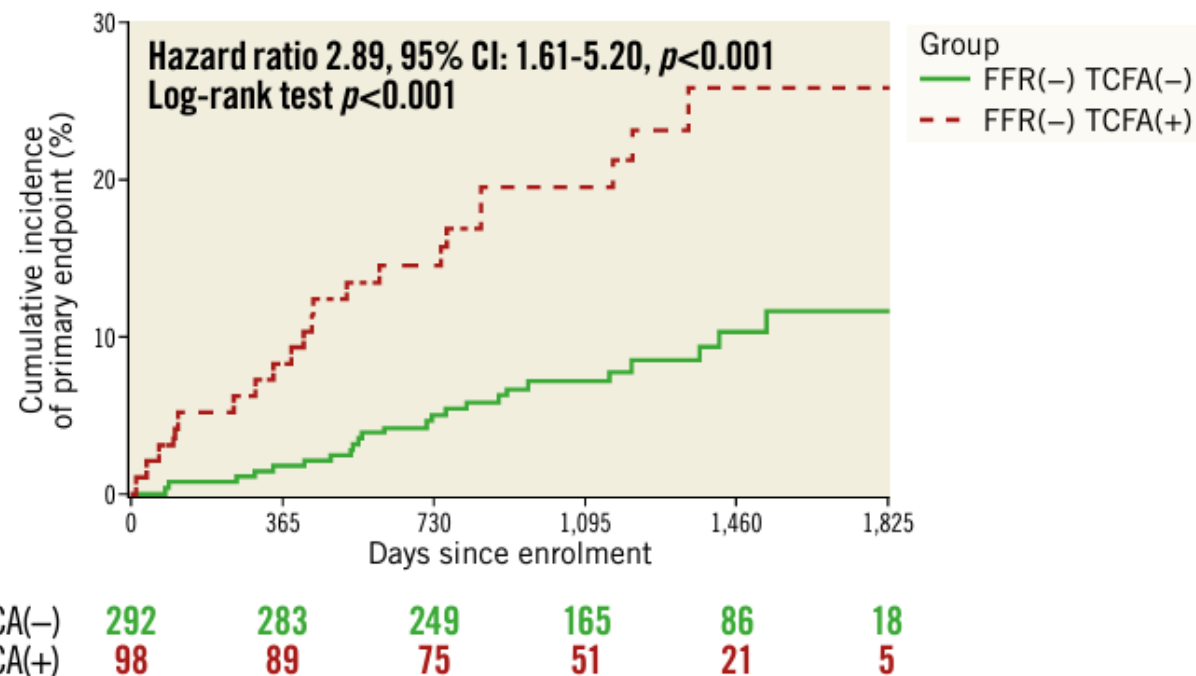
Long-term outcomes of patients with normal fractional flow reserve and thin-cap fibroatheroma

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Variables	Total	FFR(-)/TCFA(+) 98	FFR(-)/TCFA(-) 292	Hazard ratio 95% confidence interval	p-value
Primary endpoint, n (%)	45 (11.54)	21 (21.43)	24 (8.22)	2.891 (1.609;5.195)	<0.001
Cardiac death or TVR-MI or TLR	39 (10.00)	20 (20.41)	19 (6.51)	3.432 (1.831;6.433)	<0.001
Cardiac death or TVR-MI	19 (4.87)	8 (8.16)	11 (3.77)	2.398 (0.964;5.962)	0.06
Cardiac death, n (%)	12 (3.08)	2 (2.04)	10 (3.42)	0.580 (0.127;2.648)	0.48
TVR-MI, n (%)	7 (1.80)	6 (6.12)	1 (0.34)	18.233 (2.195;151.458)	0.007
TLR	26 (6.67)	17 (17.35)	9 (3.08)	6.086 (2.712;13.656)	<0.001
Unstable angina ^a	17 (4.36)	10 (10.20)	7 (2.40)	4.504 (1.713;11.846)	0.002
MI spontaneous, n (%)	20 (5.14)	10 (10.20)	10 (3.44)	3.107 (1.293;7.466)	0.011
All revascularisation	55 (14.10)	27 (27.55)	28 (9.59)	3.199 (1.885;5.429)	<0.001
Death or MI or revascularisation	75 (19.23)	31 (31.63)	44 (15.07)	2.390 (1.509;3.786)	<0.001
Death or MI	42 (10.77)	16 (16.33)	26 (8.90)	1.968 (1.056;3.669)	0.033
Death, n (%)	21 (5.38)	5 (5.10)	16 (5.48)	0.931 (0.341;2.541)	0.89



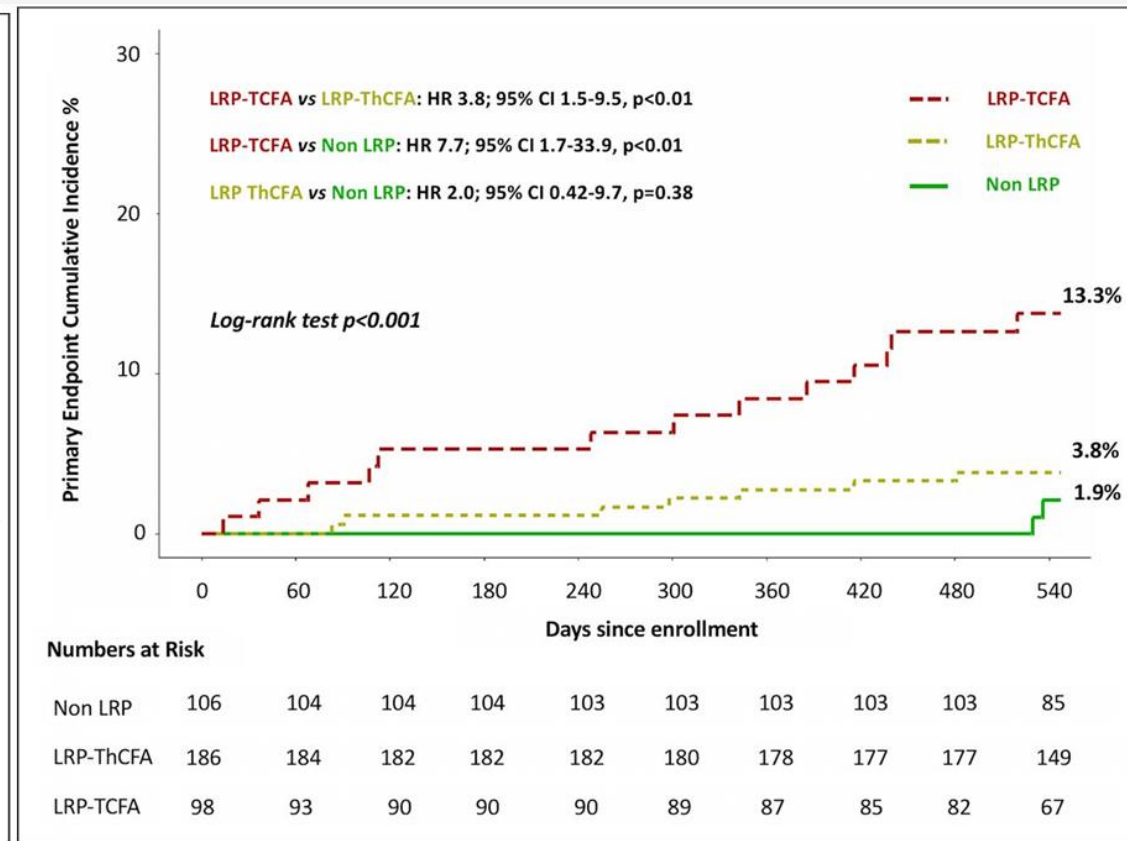
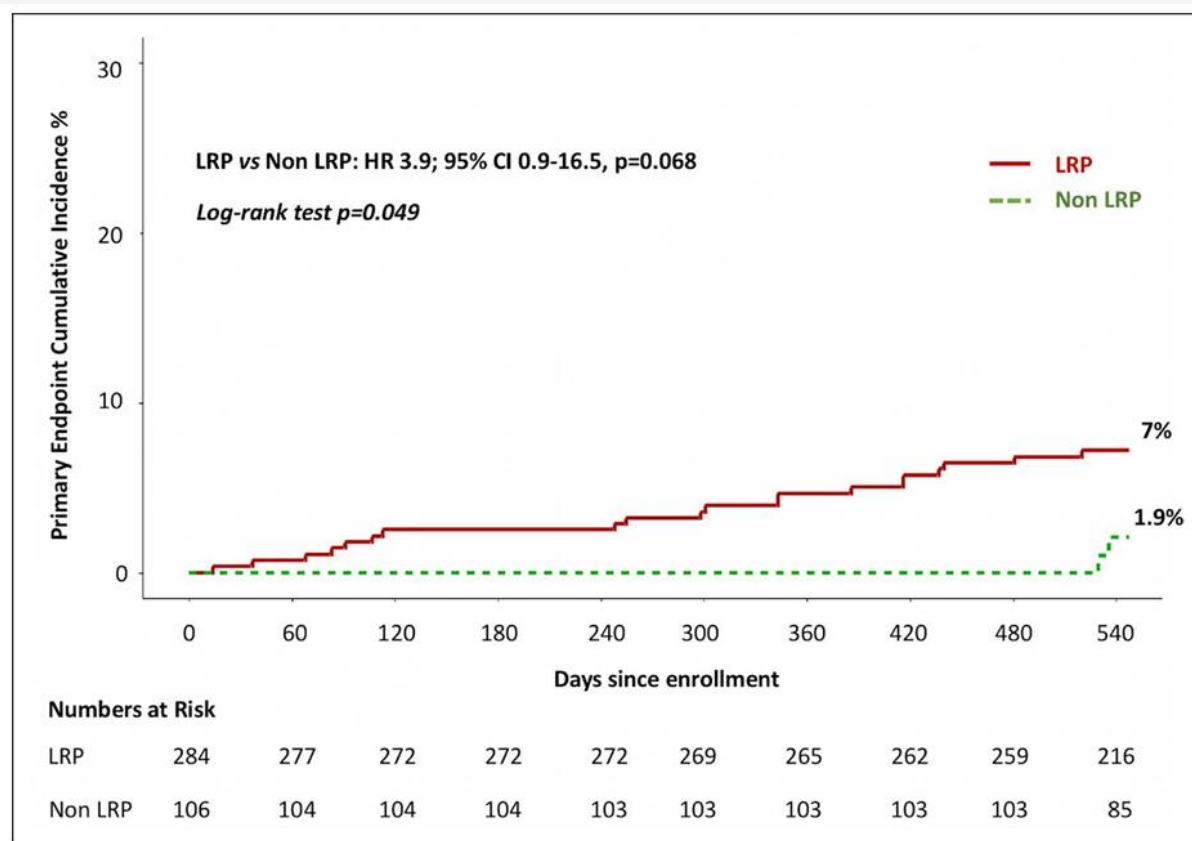
Kaplan-Meier curves for primary endpoint



Thin-Cap Fibroatheroma Rather Than Any Lipid Plaques Increases the Risk of Cardiovascular Events in Diabetic Patients: Insights From the COMBINE OCT-FFR Trial

Enrico Fabris MD, PhD; Balasz Berta MD, PhD; Tomasz Roleder, MD, PhD; Rencus S. Hermanides, MD, PhD; Alexander J.J. IJsselmuiden, MD, PhD; Floris Kauer MD; Fernando Alfonso MD, PhD; Clemens von Birgelen, MD, PhD; Javier Escaned MD, PhD; Cyril Camaro MD, PhD; Mark W. Kennedy, MD, PhD; Bruno Pereira MD; Michael Magro MD, PhD; Holger Nef, MD, PhD; Sebastian Reith, MD, PhD; Magda Roleder-Dylewska MD; Pawel Gasior MD, PhD; Krzysztof Malinowski Msc; Giuseppe De Luca MD, PhD; Hector M. Garcia-Garcia MD, PhD; Juan F. Granada MD; Wojciech Wojakowski MD, PhD; Elvin Kedhi MD, PhD

Natural history of OCT-detected TCFA, ThCFA, and non-LRP



Outcomes	Total	Non-LRP	ThCFA	TCFA	P value	TCFA vs ThCFA		TCFA vs non-LRP		ThCFA vs non-LRP	
						HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Primary end point CD, TVR-MI, TLR, UA, n (%)	22 (5.64%)	2 (1.89%)	7 (3.78%)	13 (13.27%)	<0.01	3.8 (1.5–9.5)	<0.01	7.7 (1.7–33.9)	<0.01	2.0 (0.42–9.7)	0.38
CD, TVR-MI, TLR, n (%)	16 (4.10%)	0	5 (2.69%)	11 (11.22%)	<0.01	4.4 (1.5–12.8)	<0.01
CD, TVR-MI, UA, n (%)	16 (4.10%)	2 (1.89%)	4 (2.15%)	10 (10.20%)	<0.01	5.1 (1.8–16.1)	<0.01	5.8 (1.3–26.4)	0.02	1.1 (0.2–6.2)	0.88
CD, n (%)	1 (0.26%)	0	1 (0.54%)	0
TVR-MI, n (%)	4 (1.03%)	0	0	4 (4.08%)
TLR, n (%)	15 (3.85%)	0	4 (2.15%)	11 (11.22%)	<0.01	5.5 (1.77–17.4)	<0.01
UA, n (%)	11 (2.82%)	2 (1.89%)	3 (1.61%)	6 (6.12%)	0.11	4.0 (0.997–15.9)	0.051	3.4 (0.7–17.0)	0.13	0.9 (0.1–5.1)	0.87

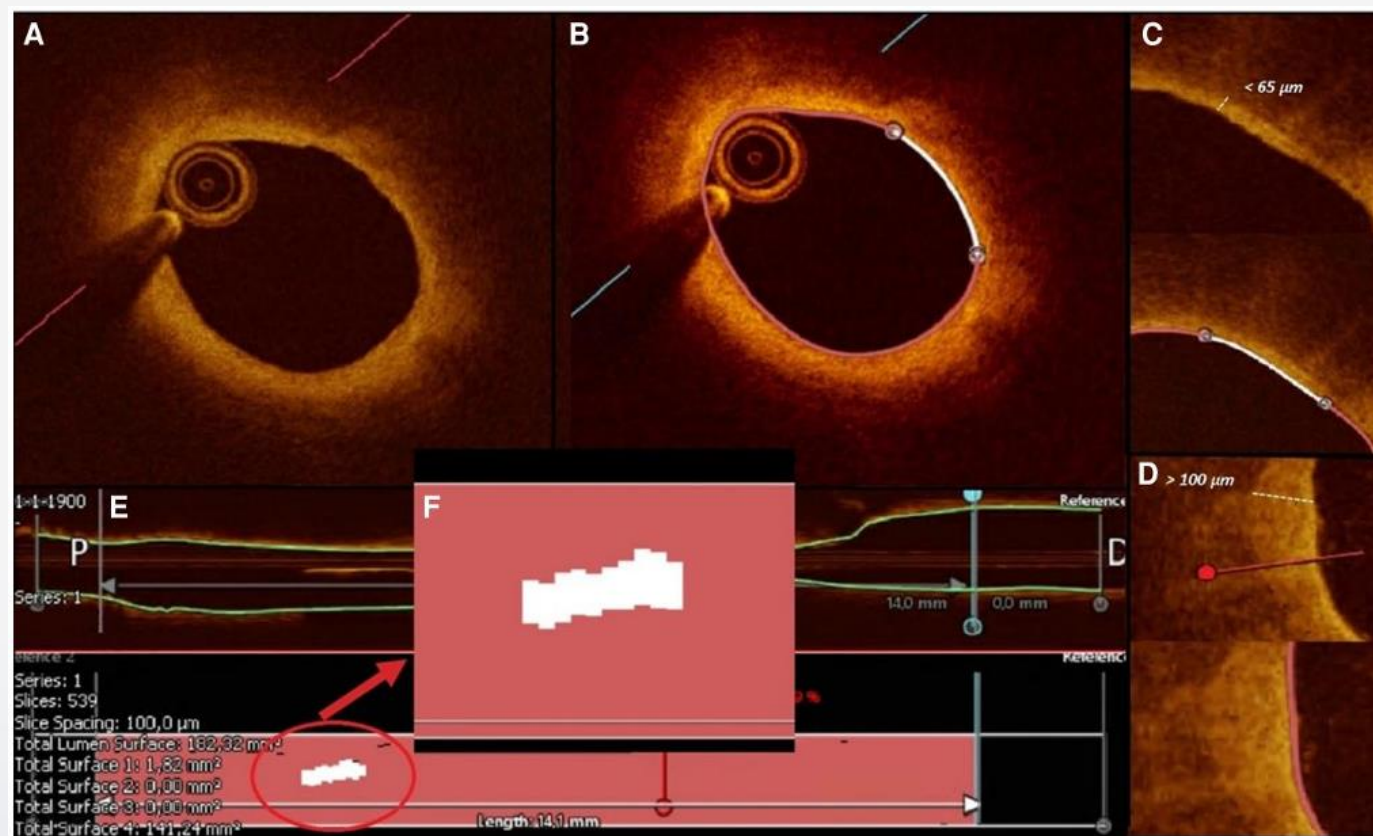
CD indicates cardiac death; HR, hazard ratio; LRP, lipid rich plaque; TCFA, thin-cap fibroatheroma; ThCFA, thick-cap fibroatheroma; TLR, target-lesion revascularization; TVR-MI, target vessel related myocardial infarction; and UA, hospitalization due to unstable angina.

Variables	HR	95% CI	P value
ThCFA	1.78	0.37–8.62	0.47
TCFA	6.79	1.50–30.72	0.013
ACS presentation	3.00	1.29–6.97	0.011
Statin at discharge	0.69	0.27–1.80	0.452
% area stenosis at minimal lumen area	1.55	1.01–2.38	0.047

Morphological characteristics of lesions with thin cap fibroatheroma—a substudy from the COMBINE (OCT-FFR) trial

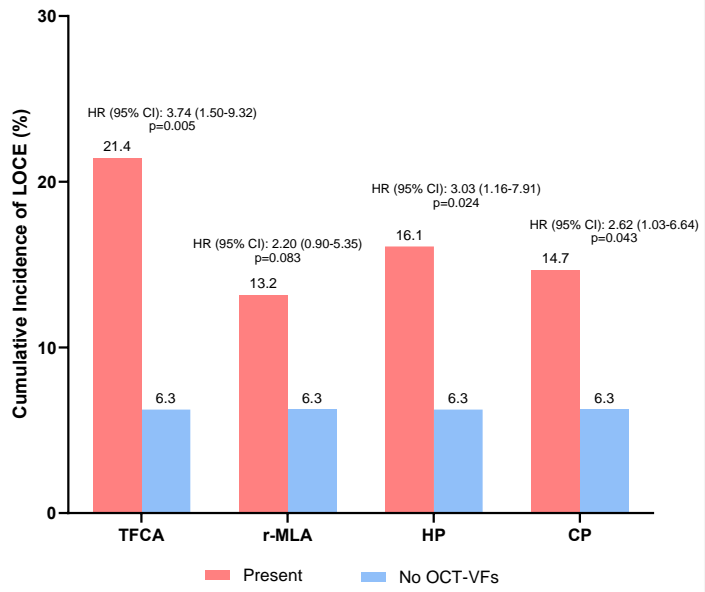
Magda Roleder-Dylewska¹, Pawel Gasior¹, Tobias M. Hommels⁵, Tomasz Roleder^{1,3}, Balasz Berta^{4,5}, Hui Ying Ang^{6,7}, Jaryl Chen Koon Ng^{6,7}, Rencus S. Hermanides⁵, Enrico Fabris⁸, Alexander J.J. Ijsselmuiden⁹, Floris Kauer¹⁰, Fernando Alfonso¹¹, Clemens von Birgelen^{12,13}, Javier Escaned¹⁴, Cyril Camaro¹⁵, Mark W. Kennedy^{16,17}, Bruno Pereira¹⁸, Michael Magro¹⁹, Holger Nef²⁰, Sebastian Reith²¹, Krzysztof Malinowski²², Giuseppe De Luca²³, Hector M. Garcia Garcia²⁴, Juan F. Granada^{25,26}, Wojciech Wojakowski¹, and Elvin Kedhi^{1,2*}

Do any qualitative or quantitative OCT variables in combination with TCFA improve the identification of lesions at risk for MACE

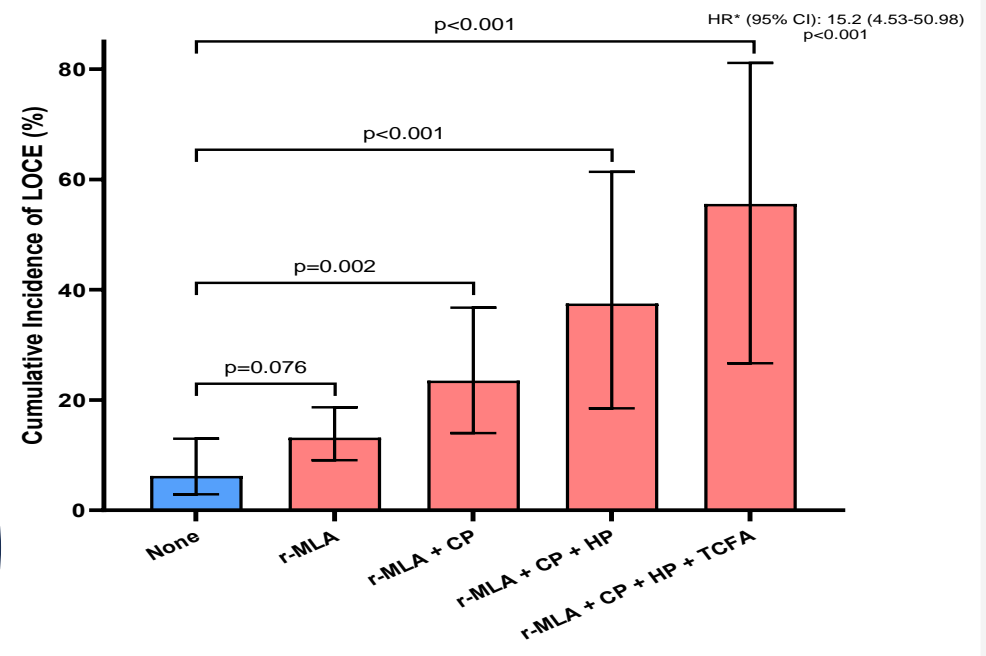


Parameter	MACE (n = 13)	Non-MACE(n = 85)	P value
TCFA area surface (IQR)—mm ²	0.19 (0.07–0.33)	0.37 (0.18–0.76)	0.03
Total lesion surface (IQR)—mm ²	190(86–249.5)	221.5(145–271.5)	0.09
TCFA length (IQR)—mm	0.20 (0.15–0.35)	0.30 (0.20–0.58)	0.06
TCFA to MLA distal localization—no. (%)	2 (15.4)	22 (25.9)	0.58
TCFA to MLA proximal localization—no. (%)	11 (84.6)	52 (61.2)	0.13
TCFA arc (IQR)—°	33.00 (24.0–43.5)	49.00 (36.0–63.0)	0.02
Localization of the TCFA—no. (%)			
LAD	7 (53.9)	27 (31.8)	0.15
CX	4 (30.8)	22 (25.9)	0.15
RCA	2 (15.4)	35 (42.4)	0.15
FFR value	0.85 ± 0.04	0.89 ± 0.05	0.02
Lesion length (IQR)—mm	22.10 (11.1–35.1)	27.20 (18.6–36.1)	0.31
Proximal lumen diameter (IQR)—mm	3.45 (3.0–3.8)	3.40 (3.1–3.8)	0.94
Distal lumen diameter (IQR)—mm	2.50 (2.5–2.9)	2.70 (2.5–3.2)	0.13
Min. lumen diameter (IQR)—mm	1.20 (1.1–1.6)	1.50 (1.2–1.7)	0.04
MLA (IQR)—mm ²	1.80 (1.3–2.3)	2.40 (1.8–3.2)	0.02
Stenosis reference (IQR)—%	67.00 (55.5–76.5)	64.00 (57.5–72.0)	0.24
Lumen volume (IQR)—mm	118.40 (50.1–141.6)	138.10 (85.6–185.9)	0.14
Calcific plaque—no. (%)	10 (76.9)	75 (88.2)	0.26
Calcium arc (IQR)—°	150.00 (94.0–210.0)	116.00 (76.0–200.0)	0.59
Protruding calcification—no. (%)	5 (38.5)	30 (35.3)	0.82
Cholesterol Cleft—no. (%)	10 (76.9)	60 (70.6)	0.64
Lipid plaque—no. (%)	13 (100)	85 (100)	
Lipid arc (IQR)—°	206.00 (193.0–299.0)	240.00 (191.5–285.5)	0.88
Plaque rupture—no. (%)	3 (23.1)	28 (32.9)	0.47
Plaque erosion—no. (%)	2 (15.4)	9 (10.6)	0.61
Healed plaque—no. (%)	7 (53.9)	18 (21.2)	0.01
New micro vessels—no. (%)	10 (76.9)	72 (84.7)	0.48

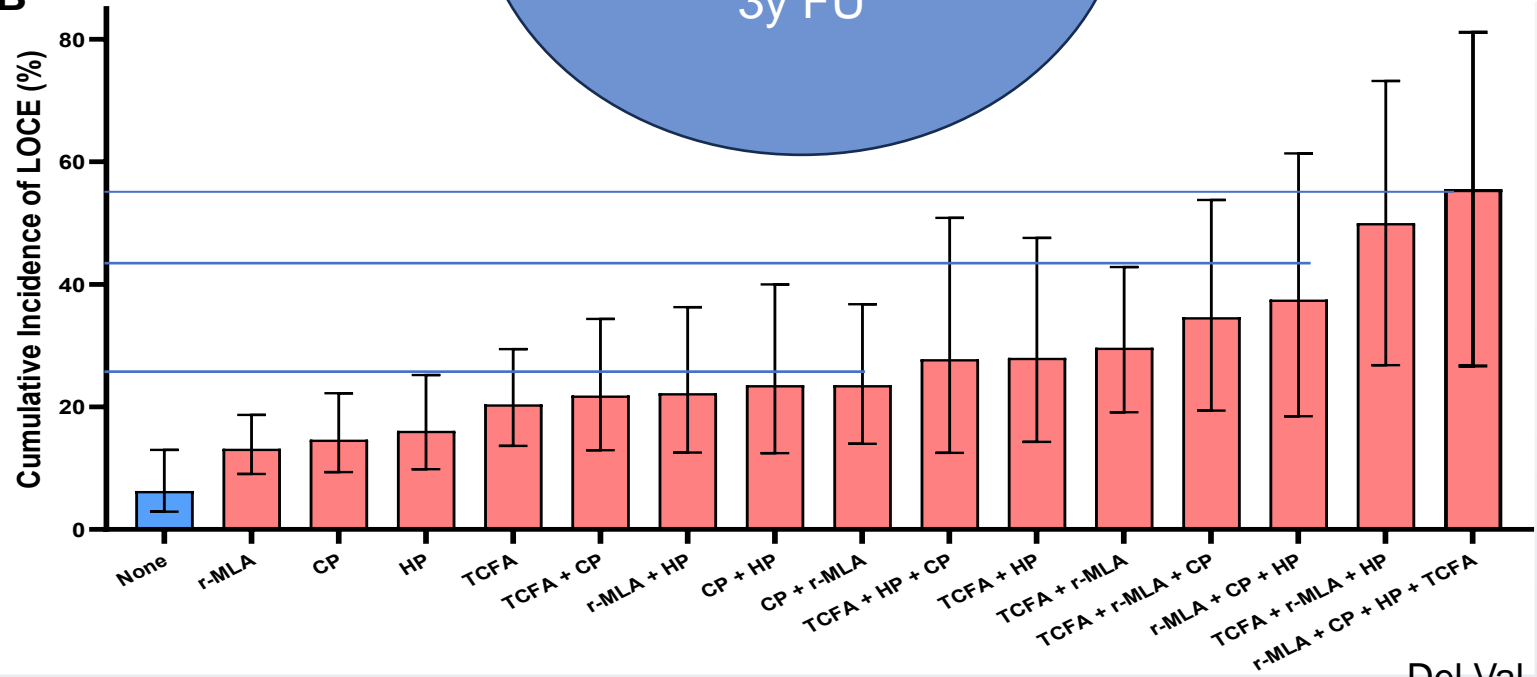
A



TCFA & ≥1 other predictor very high LOCE event rates 25-57% at average 3y FU



B



Best cut-off MLA
2.5mm²

Is stenting the right treatment for VP?

OCT guided
stenting has a low
event rate of
LOCE

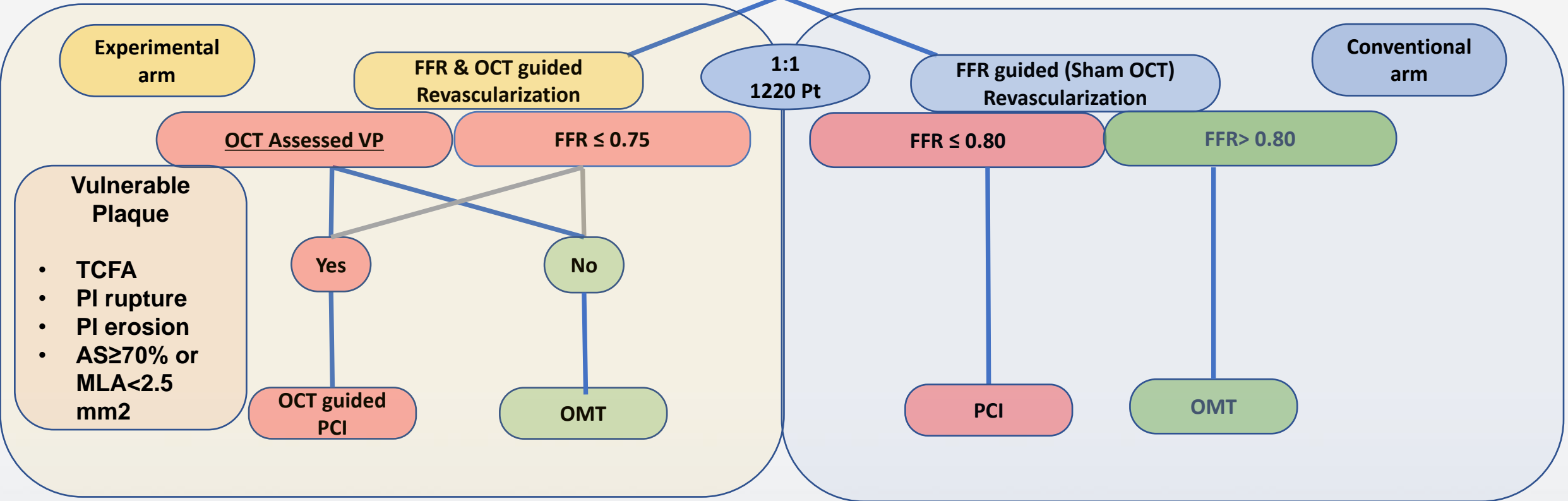
Stenting
Complications

VP risk

Tailored VP risk
evaluation

Stenting) might be considered for VP with a high degree of vulnerability (on top of aggressive medical treatment, while **early phase VP can benefit from aggressive medical treatment alone**

Patients with MVD (> 2 Lesions \geq 50% stenosis)
Any clinical presentation (aiming 50% ACS & 30-35% DM)

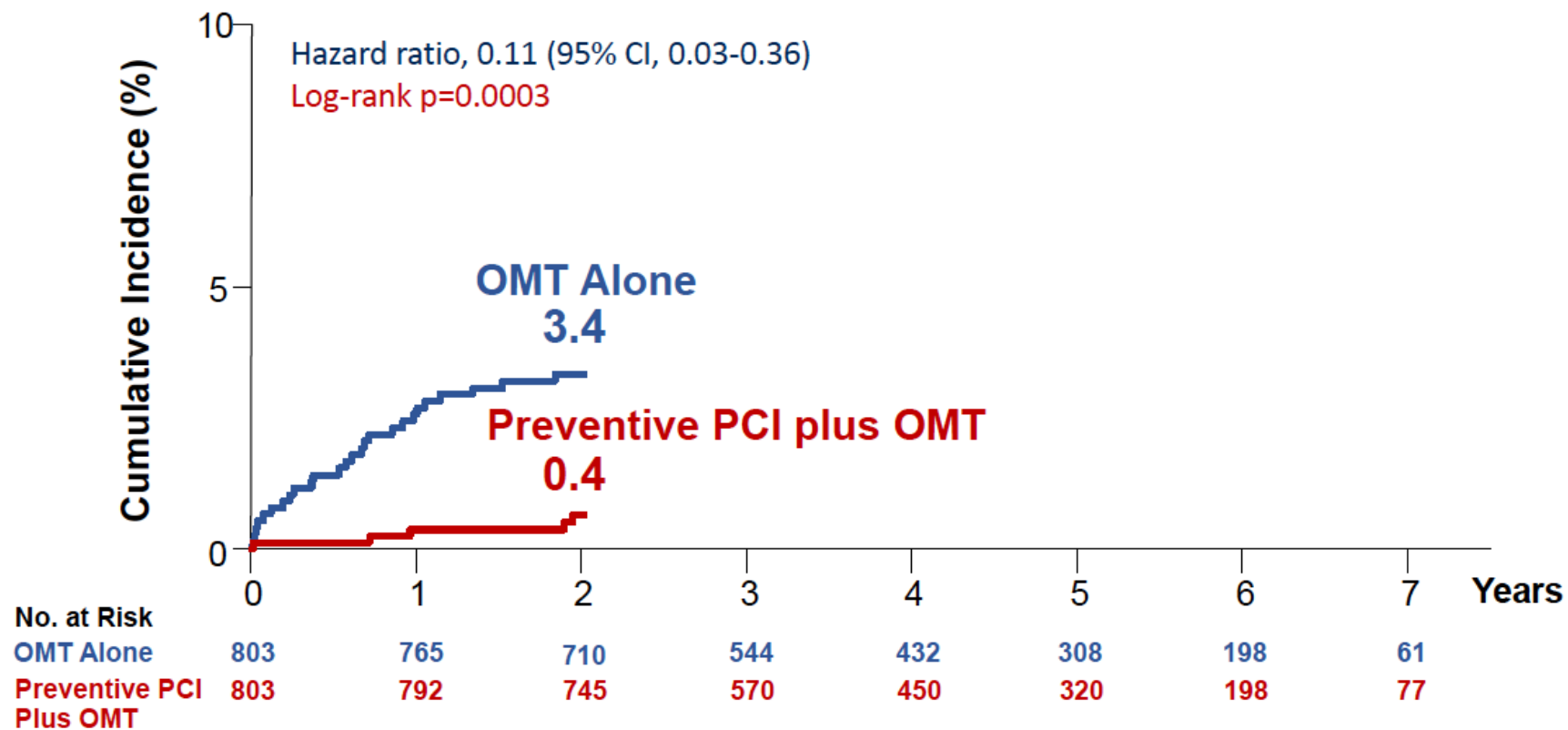


International (Global 50 centers worldwide), Randomized, Single-blinded, Sham-controlled, Superiority Trial
PE: **Cardiac death** or **any myocardial infarction** or **any clinically-driven revascularization** at 2y

Expected PE recuction of 50%

Primary Composite Outcome: Target Vessel Failure at 2 Year F/U

PREVENT



Anatomic Characteristics

PREVENT

	Preventive PCI plus OMT (N=831)	OMT alone (N=841)
Qualifying criteria for target lesions[†]	N=831	N=841
MLA <4.0 mm ² by gray-scale IVUS or OCT	809 / 831 (97%)	817 / 841 (97%)
Plaque burden >70% by gray-scale IVUS	792 / 815 (97%)	805 / 831 (97%)
Large lipid-rich plaque by NIRS (maxLCBI _{4mm} >315)	99 / 348 (28%)	94 / 369 (26%)
TCFA defined by OCT or radiofrequency IVUS	39 / 571 (7%)	40 / 679 (6%)
Target lesion location		
Left anterior descending artery	416 (50%)	400 (48%)
Left circumflex artery	170 (20%)	147 (17%)
Right coronary artery	245 (29%)	294 (35%)
Median FFR values of target lesions	0.87 (0.83 – 0.90)	0.86 (0.83 – 0.90)
QCA of target lesions		
Diameter stenosis — %	56.6 (9.2)	52.6 (9.8)
Minimal lumen diameter — mm	1.3 (0.3)	1.5 (0.4)
Reference vessel diameter — mm	3.1 (0.4)	3.1 (0.5)
Lesion length — mm	23.6 (8.5)	19.3 (8.3)

Data are median (inter-quartile range), or n (%). †Preventive percutaneous coronary intervention group n=485; optimal medical therapy group n=358.

Summary

- In non-ischemic lesions OCT-TCFA is a strong predictor of MACE
- Role of PCI in treatment of non-ischemic TCFAs are under evaluation in RCTs