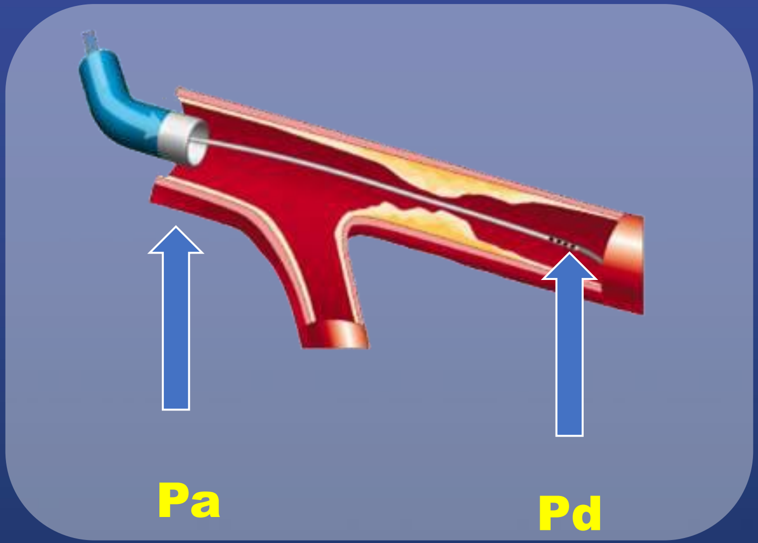
Physiology

Fractional Flow Reserve

Under the maximal hyperemia

$$FFR = \frac{Qs_{max}}{Qn_{max}} = \frac{(P_d - \cancel{P_v})/\cancel{R}}{(P_a - \cancel{P_v})/\cancel{R}}$$

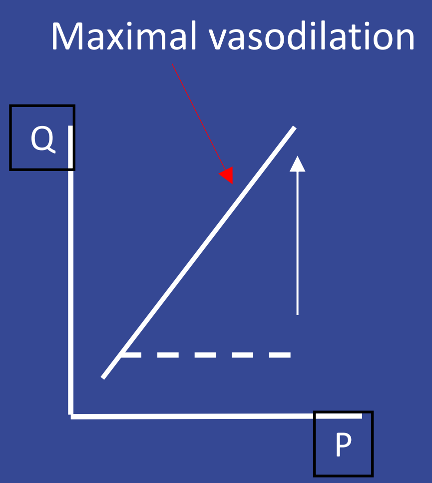
$$= \frac{Pd}{Pa}$$



Importance of Maximum Hyperemia

$$FFR = \frac{Q_S^{max}}{Q_N^{max}}$$

$$= \frac{Pd}{Pa}$$



During maximal vasodilation, the ratio of *stenotic flow* to n*ormal flow* is proportional to their respective driving pressures.

This is exactly the definition of the FFR: the ratio of *distal coronary pressure* to *aortic pressure*.

Importance of Maximum Hyperemia

Insufficient hyperemia

↓

Underestimation of pressure gradient

↓

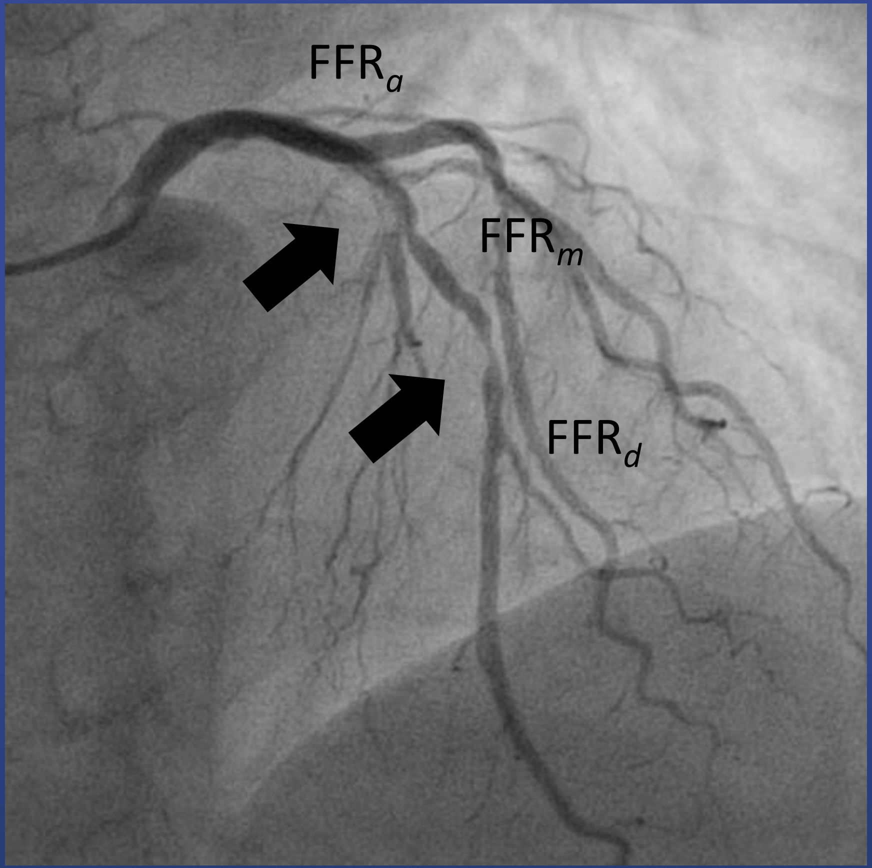
Overestimation of FFR

↓

Underestimation of Stenosis Severity

Coronary Tandem Lesions

Multiple stenoses in series along one coronary artery



Rule of Big Delta

If FFRa-FFRm > FFRm-FFRd

→ Proximal Lesion Tx First

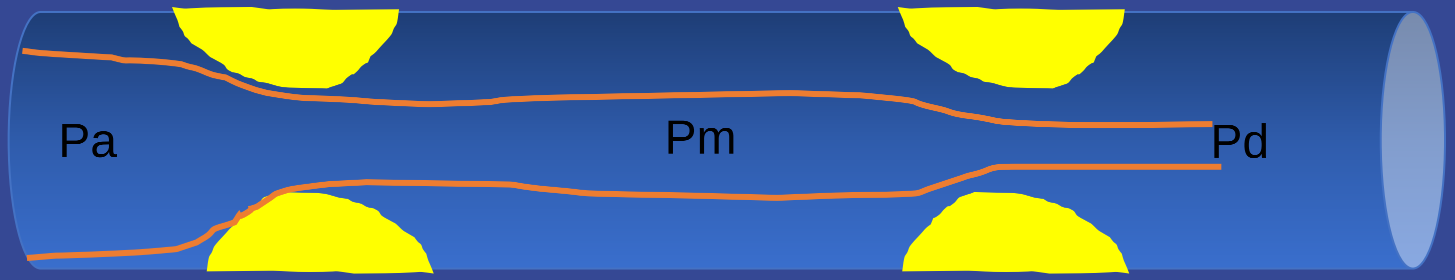
If FFRa-FFRm < FFRm-FFRd

→ Distal Lesion Tx First

Courtesy of SJ PARK

Coronary Tandem Lesions

Multiple stenoses in series along one coronary artery



"a" lesion

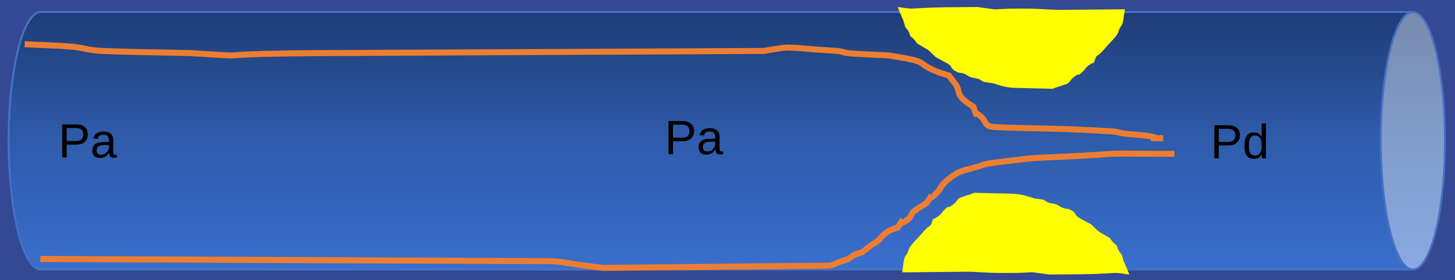
"b" lesion

FFRa = Pa-Pm/Pa

FFRb = Pd-Pm/Pm (at maximal hyperemia)

Coronary Tandem Lesions

Multiple stenoses in series along one coronary artery



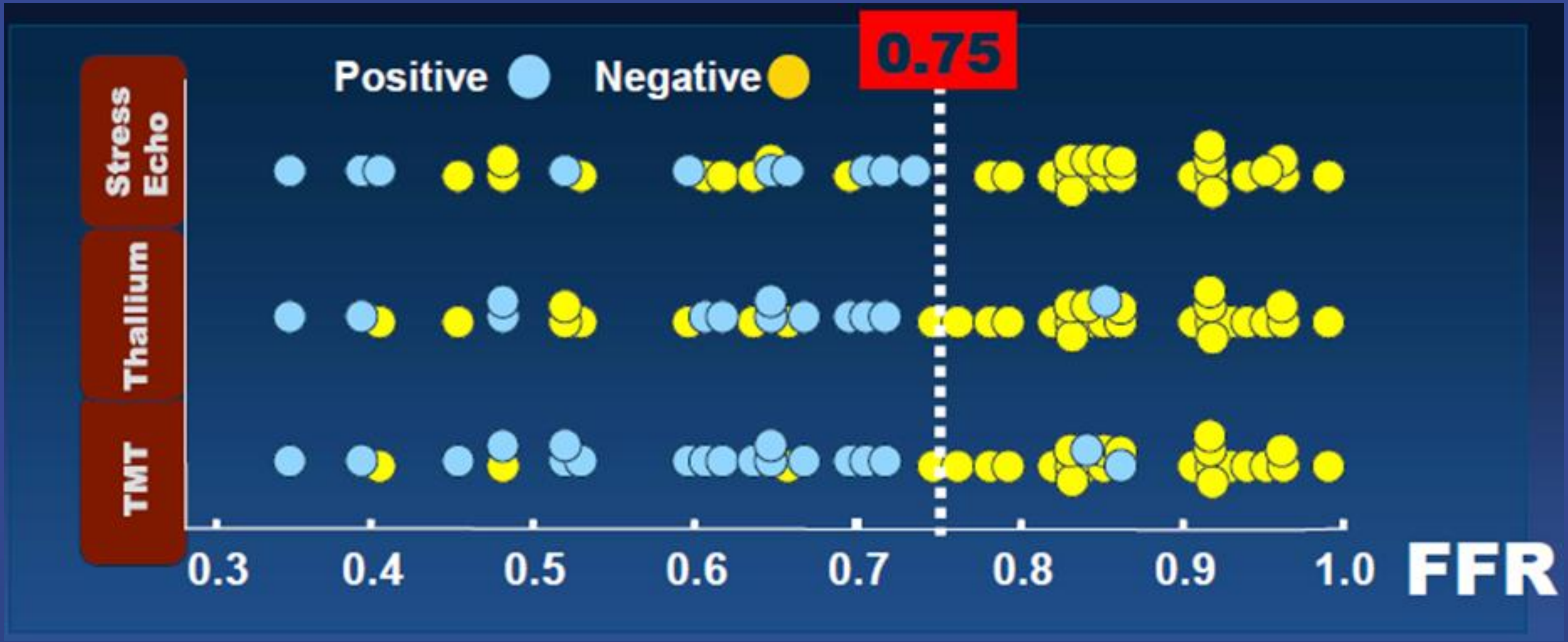
If “a” lesion is removed

FFR of “b” lesion will change

FFRb = Pd-Pa/Pa (At maximal hyperemia)

First Validation of FFR

Comparison with 3 non-invasive functional studies



N = 45 patients

Sensitivity 88%, Specificity 100%, PPV 10%, NPV 88%

N Engl J Med 1996;334:1703-8

FFR Cut-Off Value

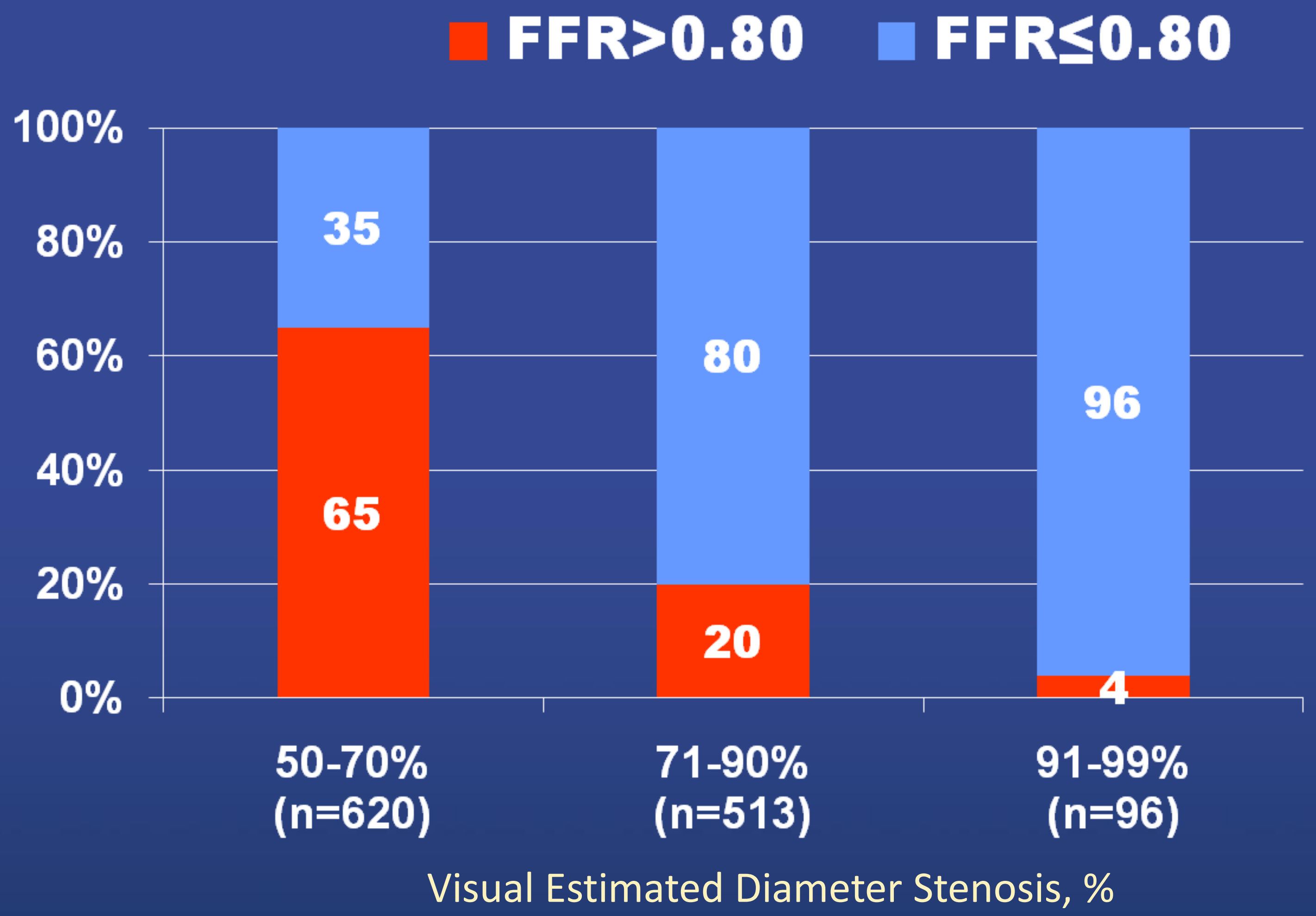
0 ⟷ 0.75 ⟷ 0.80 ⟷ 1.0

Significant	grey zone	Non-significant

Author	Number	Stress Test	BCV	Accuracy
Pijls et al.	60	X-ECG	0.74	97
DeBruyne et al.	60	X-ECG/SPECT	0.72	85
Pijls et al.	45	X-ECG/SPECT/pacing/DSE	0.75	93
Bartunek et al.	37	DSE	0.68	90
Abe et al.	46	SPECT	0.75	91
Chamuleau et al.	127	SPECT	0.74	77
Caymaz et al.	40	SPECT	0.76	95
Jimenez-Navarro et al.	21	DSE	0.75	90
Usui et al.	167	SPECT	0.75	79
Yanagisawa et al.	167	SPECT	0.75	76
Meuwissen et al.	151	SPECT	0.74	85
DeBruyne et al.	57	MIBI-SPECT post-MI	0.78	85
Samady et al.	48	MIBI-SPECT post-MI	0.78	85

Visual-Functional Mismatch (I)

From FAME Study



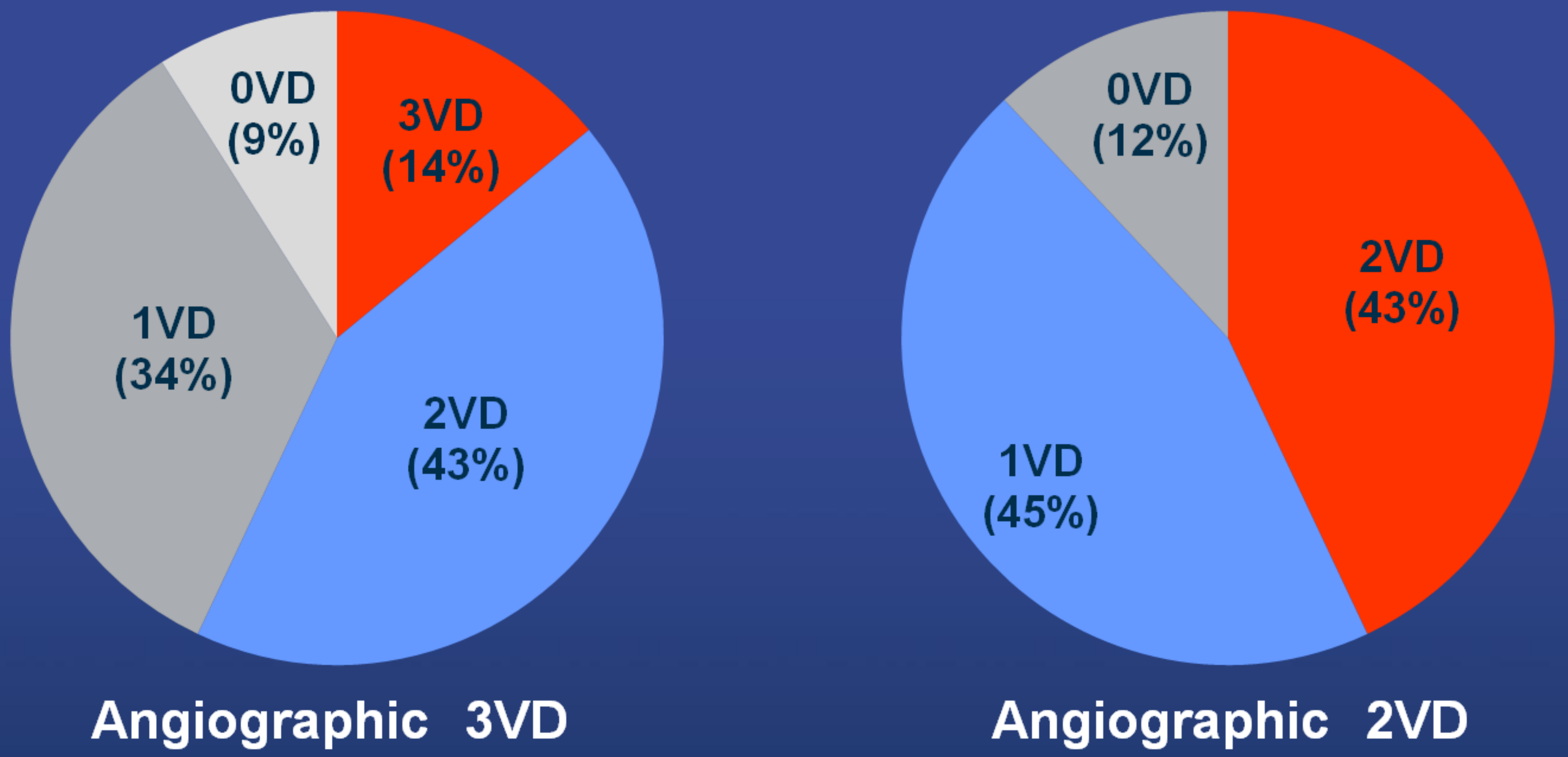
Mismatch 36.3%

J Am Coll Cardiol 2010;55:2816–21

Visual-Functional Mismatch (II)

From FAME Study

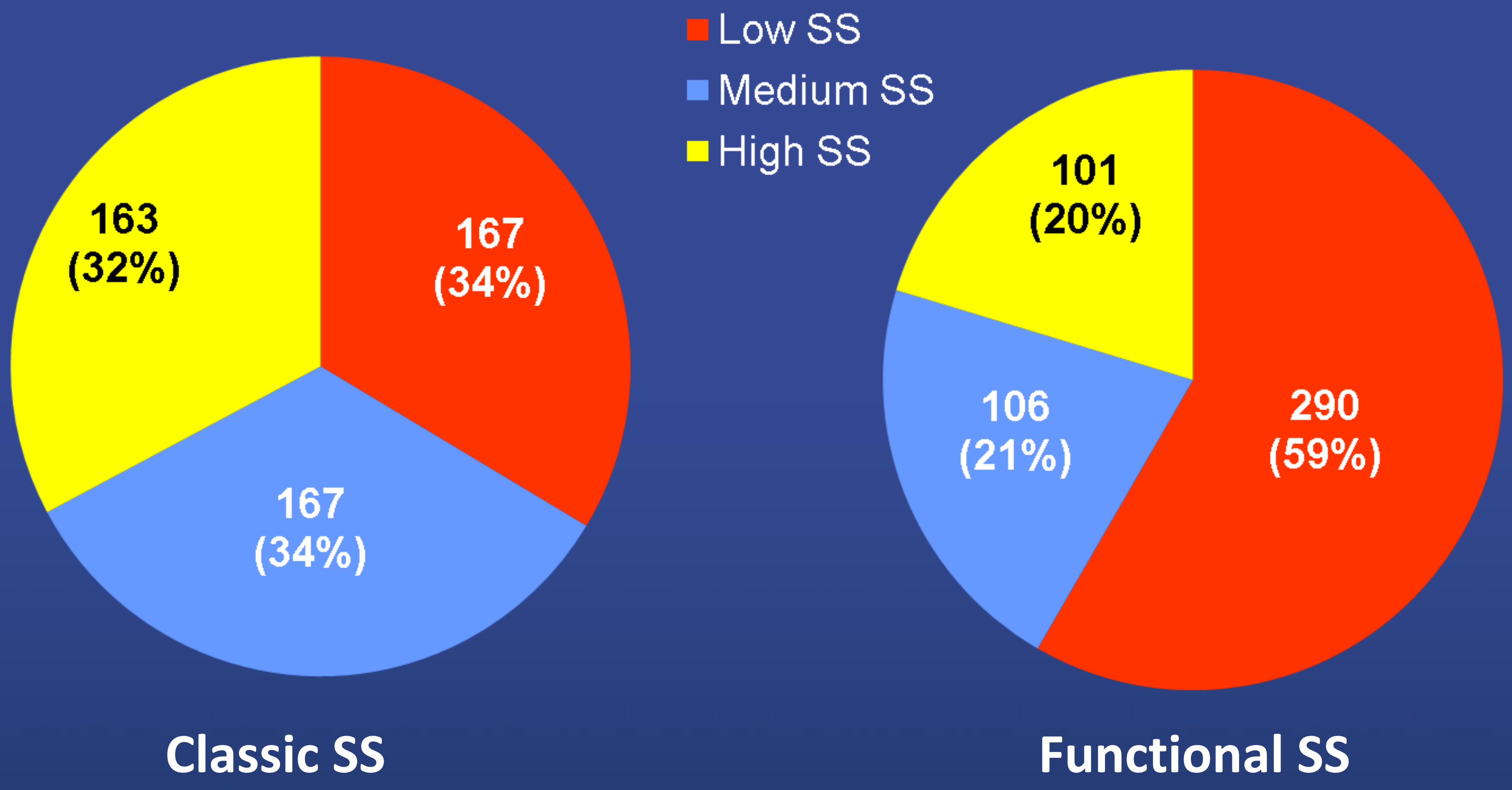
Functionally Diseased Coronary Arteries



J Am Coll Cardiol 2010;55:2816–21

Visual-Functional Mismatch (III)

Functional SYNTAX Score in FAME



Nam et al. J Am Coll Cardiol 2011;58:1211–18

FAME @ 2yr FU

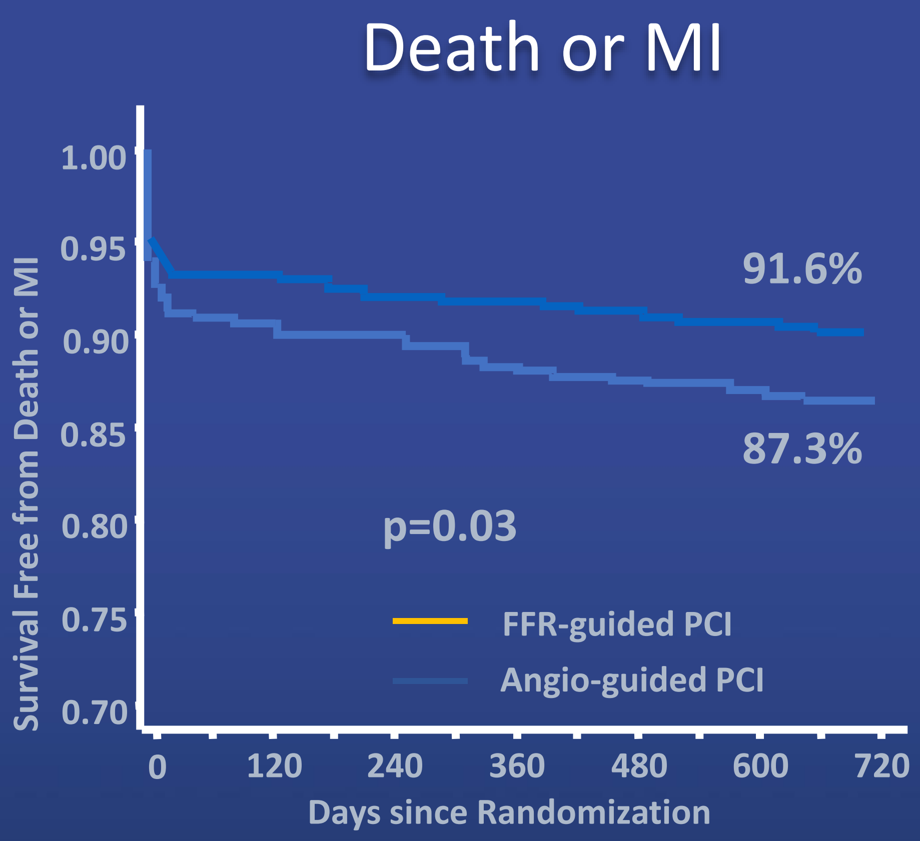
A total of 1,005 patients with multivessel CAD were randomly assigned

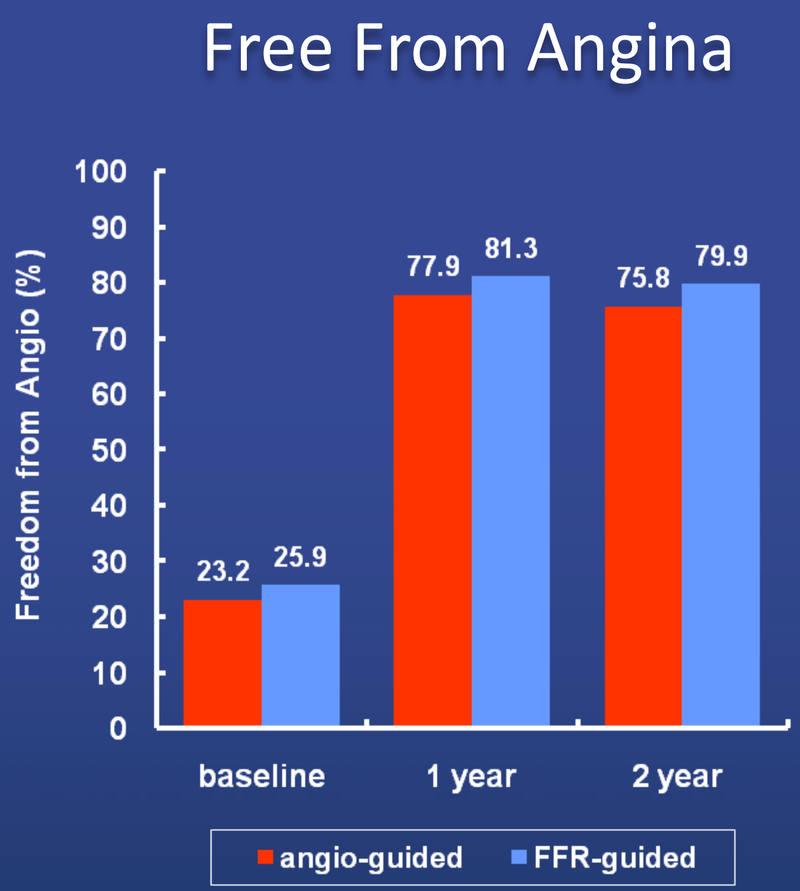
	Angio-Guided N=496	FFR-Guided N=509	p value
Total no. of MACE	139	105	
Individual Endpoints			
Death	19 (3.8)	13 (2.6)	0.25
MI	48 (9.7)	31 (6.1)	**0.03**
CABG or repeat PCI	61 (12.3)	53 (10.4)	0.35
Composite Endpoints			
Death or MI	63 (12.7)	43 (8.4)	**0.03**
Death, MI, CABG, or re-PCI	110 (22.2)	90 (17.7)	0.07
Total no. of MACE	139	105	

J Am Coll Cardiol 2010;56:177-84

FAME @ 2yr FU

A total of 1,005 patients with multivessel CAD were randomly assigned

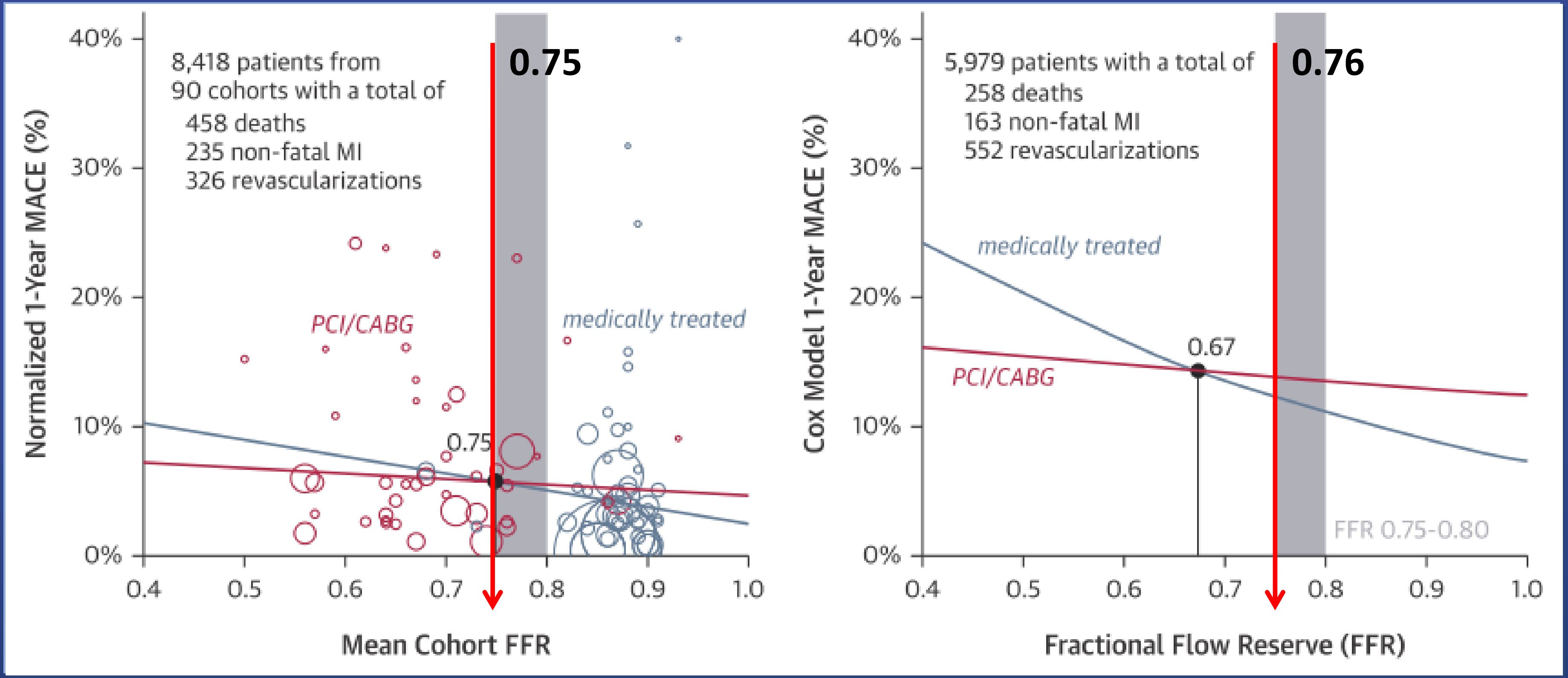




J Am Coll Cardiol 2010;56:177–84

Prognostic Value of FFR on Clinical Outcomes

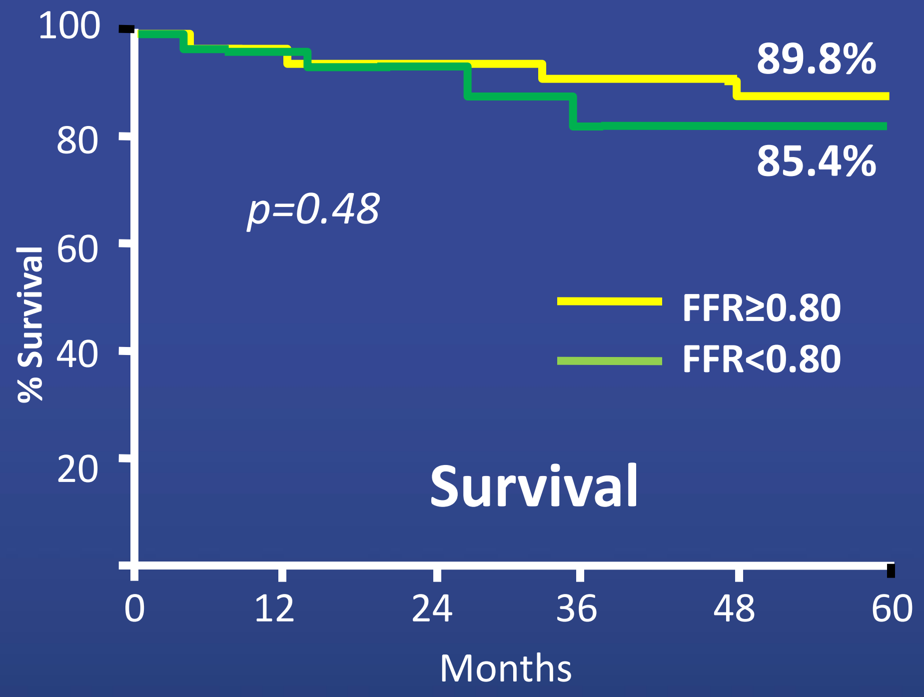
6,961 pts, 9,173 lesions

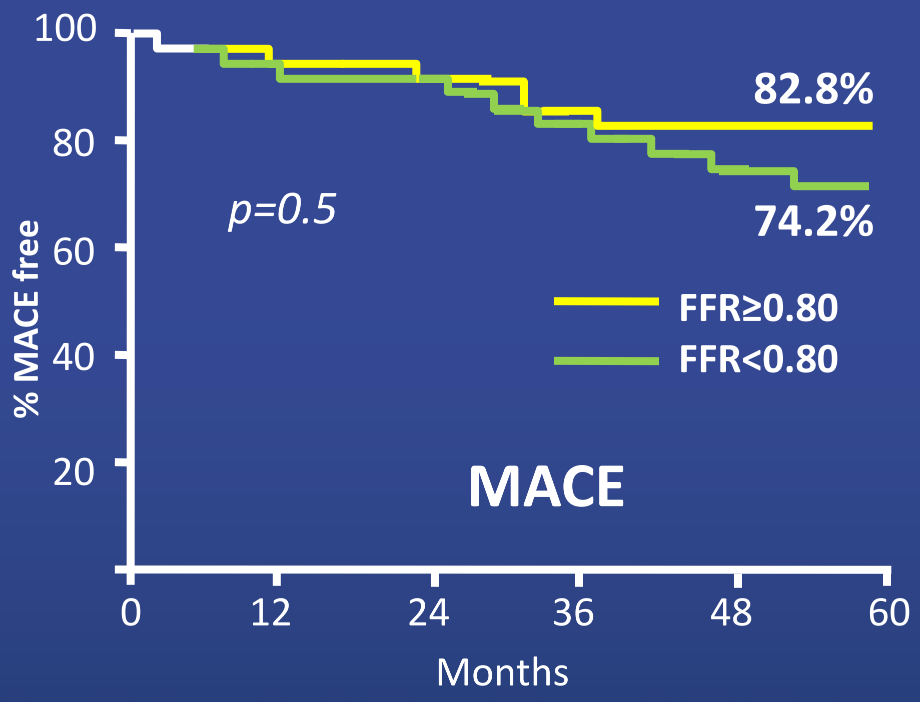


Johnson et al, JACC 2014;64:1641-54

FFR guided PCI in Equivocal LMCA

- In 213 patients with an equivocal LMCA stenosis
- FFR ≥0.80: Medication (n=138) vs. FFR<0.80: CABG (n=75)

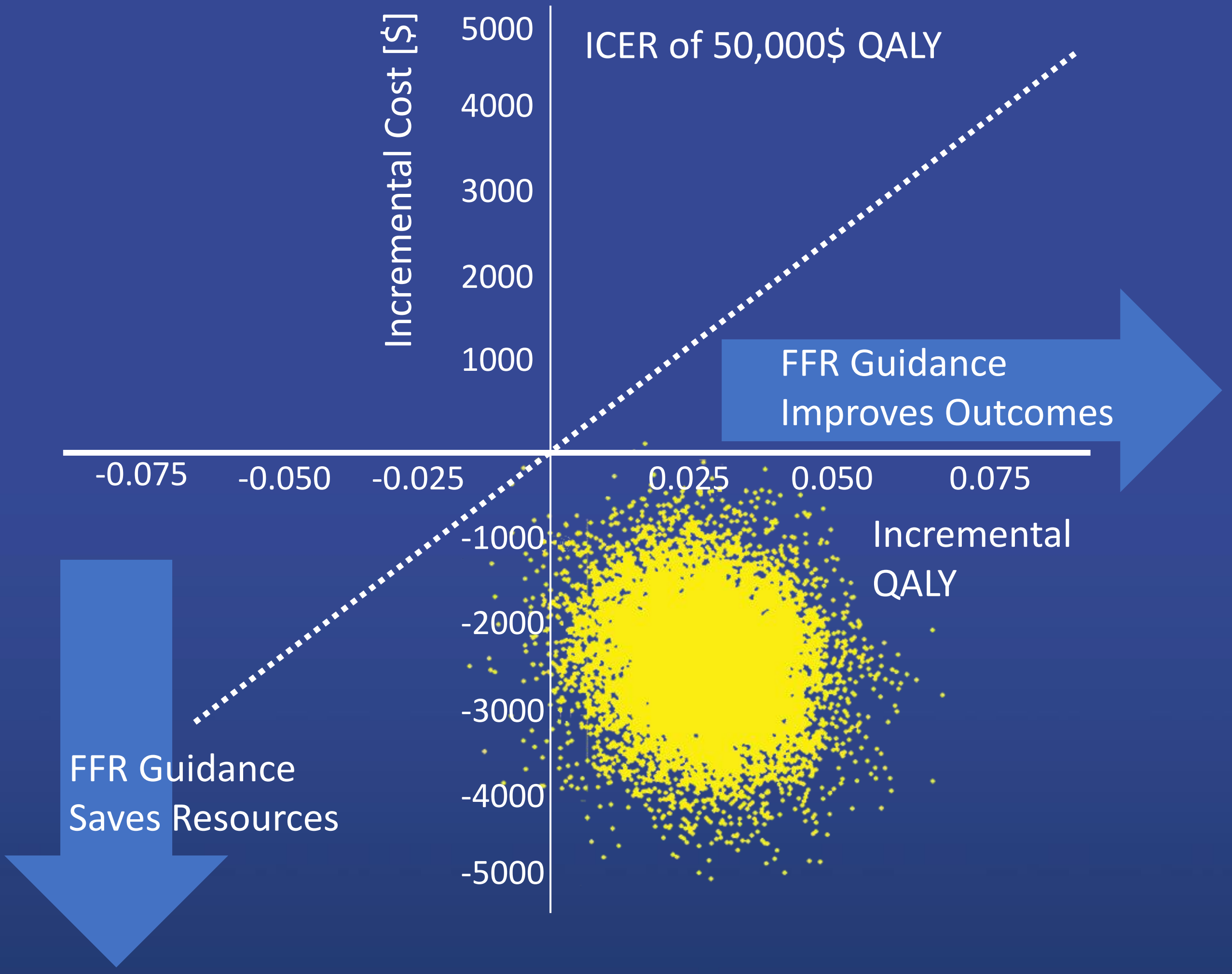




An FFR-guided strategy showed the favorable outcome.

Circulation. 2009;120:1505-1512

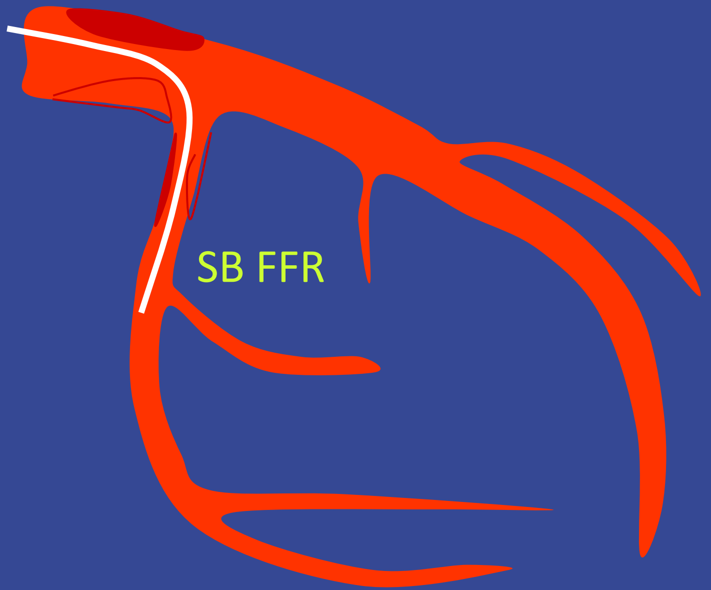
Saving Costs and Improving Outcomes By FFR guidance



Circulation2010;122:2545-2550

Use of IVUS vs. FFR in SB Assessment

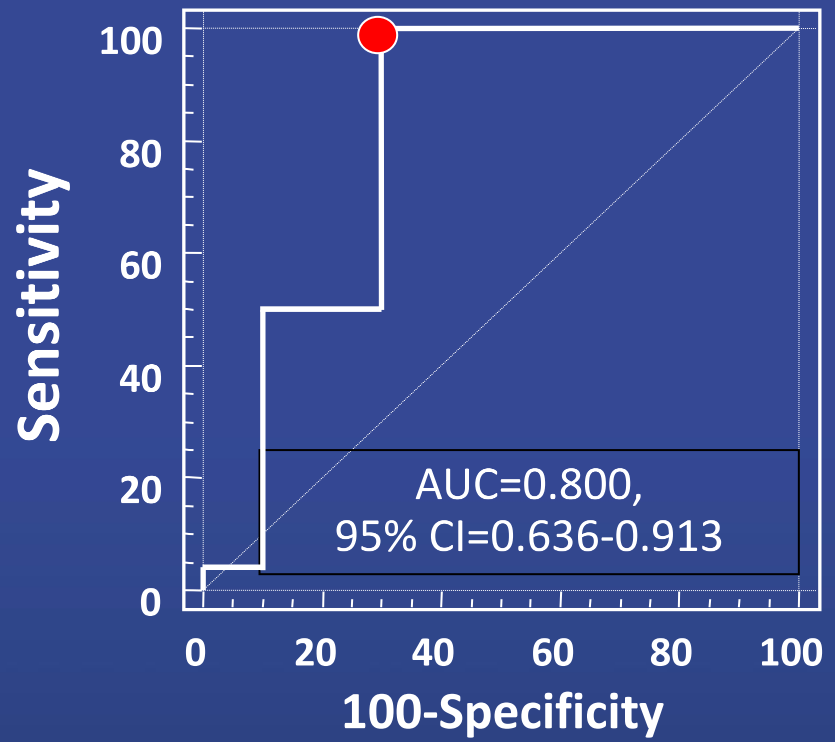
After LM Cross-over



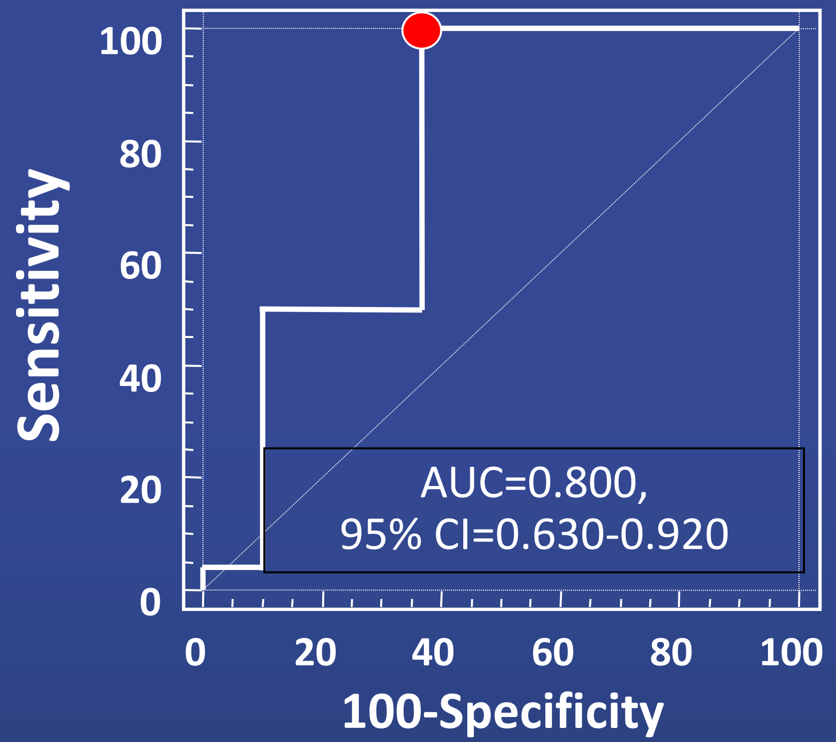
	SB-pullback IVUS	SB FFR
Advantage	▪ Confirm the anatomical compromise and MLA loss ▪ Mechanism of SB jailing	▪ Confirm the functional SB compromise
Pitfalls	▪ MLA-FFR mismatch ▪ No MLA criteria ▪ Low feasibility	▪ Minority - not feasible

Functional Compromise of LCX after LM Cross-Over Stenting

Preporcedural MLA and plaque burden of poststenting LCX FFR < 0.80



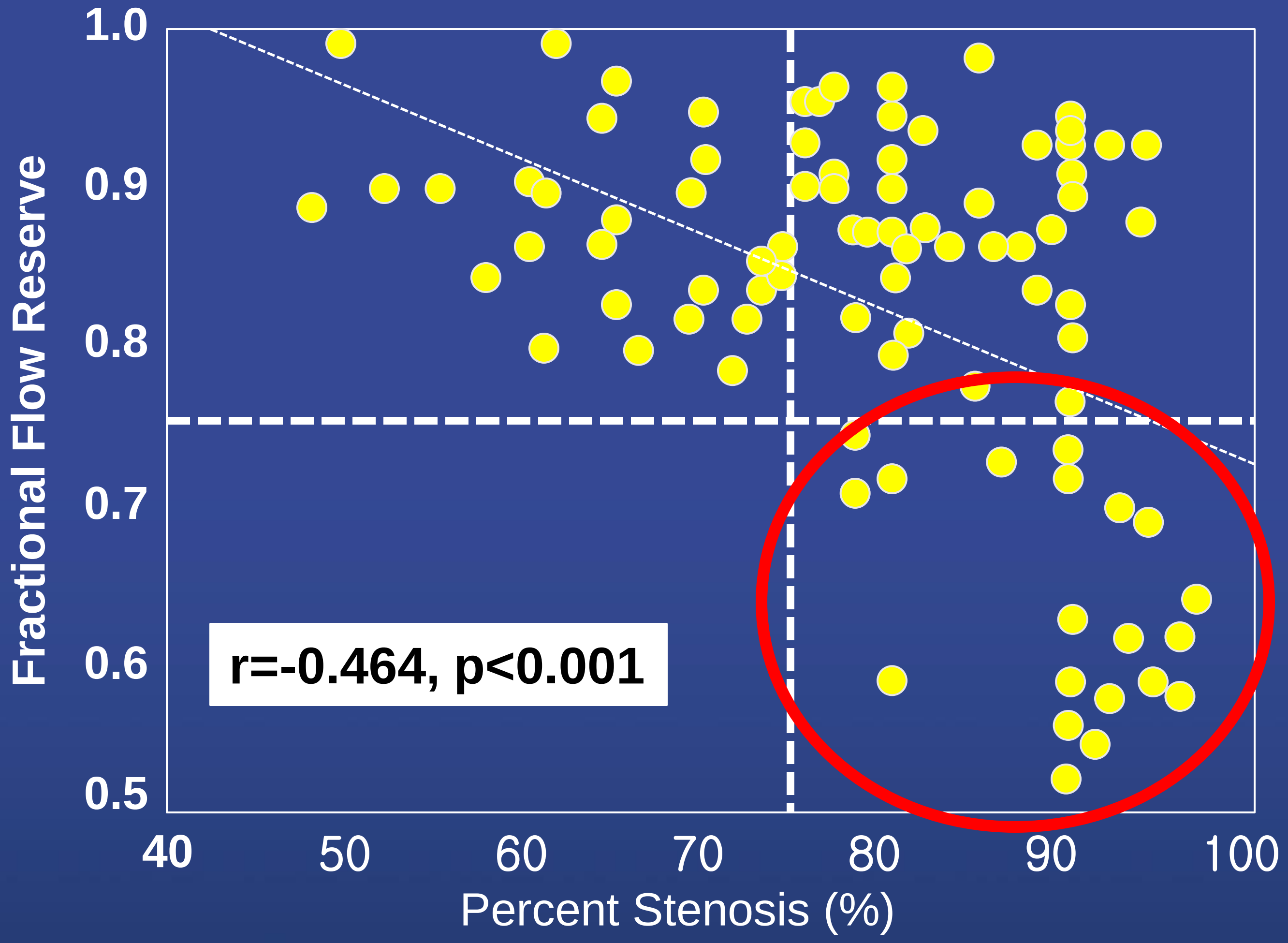
MLA 3.7 mm²



Plaque burden 56%

Kang SJ et al. Catheter Cardiovasc Interv.

FFR of the Jailed Side Branch

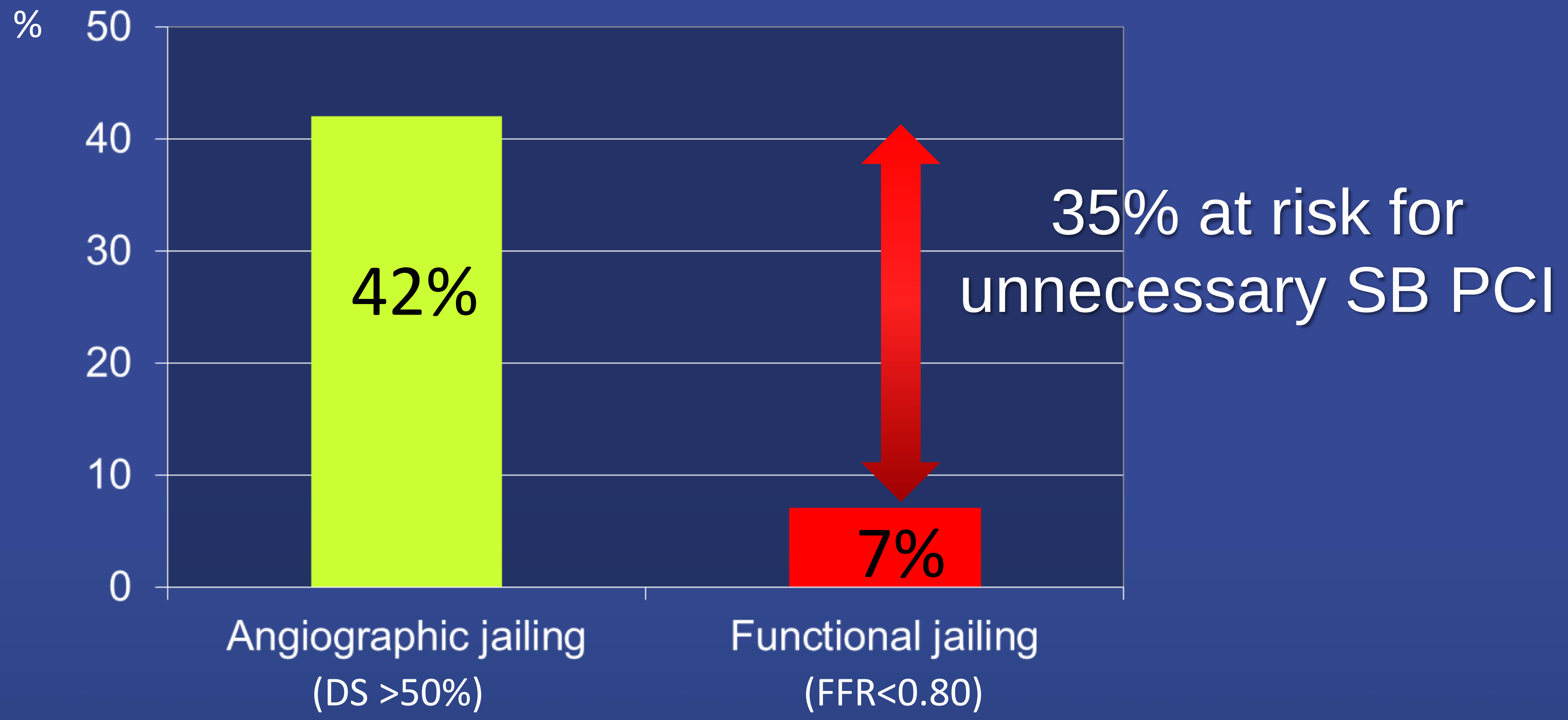


Only 27% among SB with > 75% has FFR < 0.75

Koo BK et al JACC 2005; 46: 633

Functional LCX Compromise

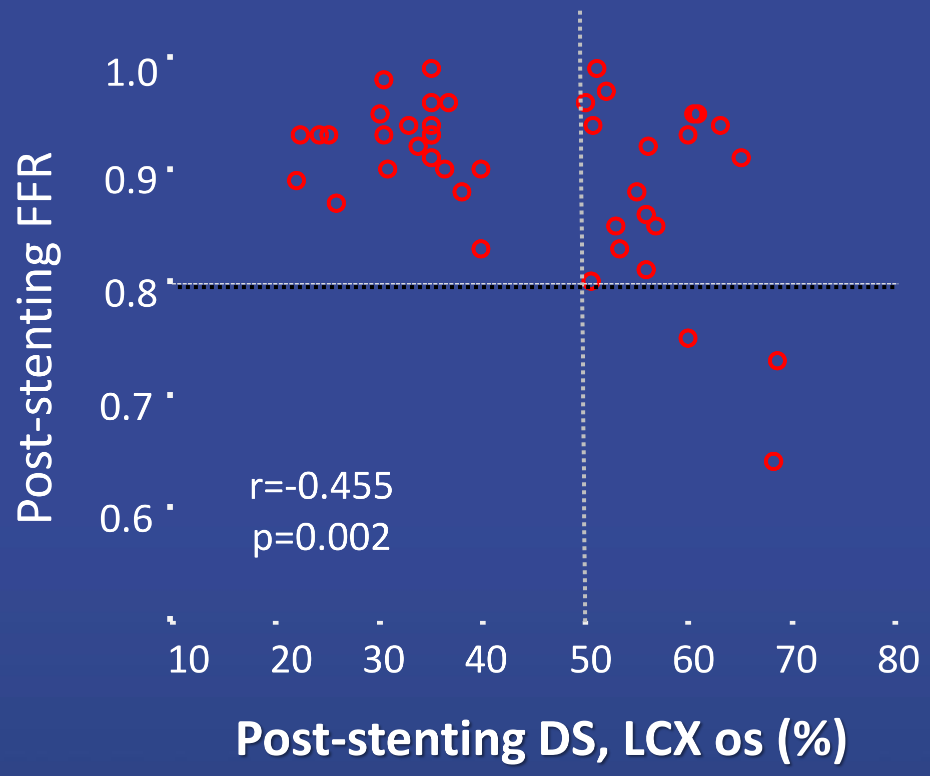
In LMCA Bifurcations (LCX ostial DS<50%)

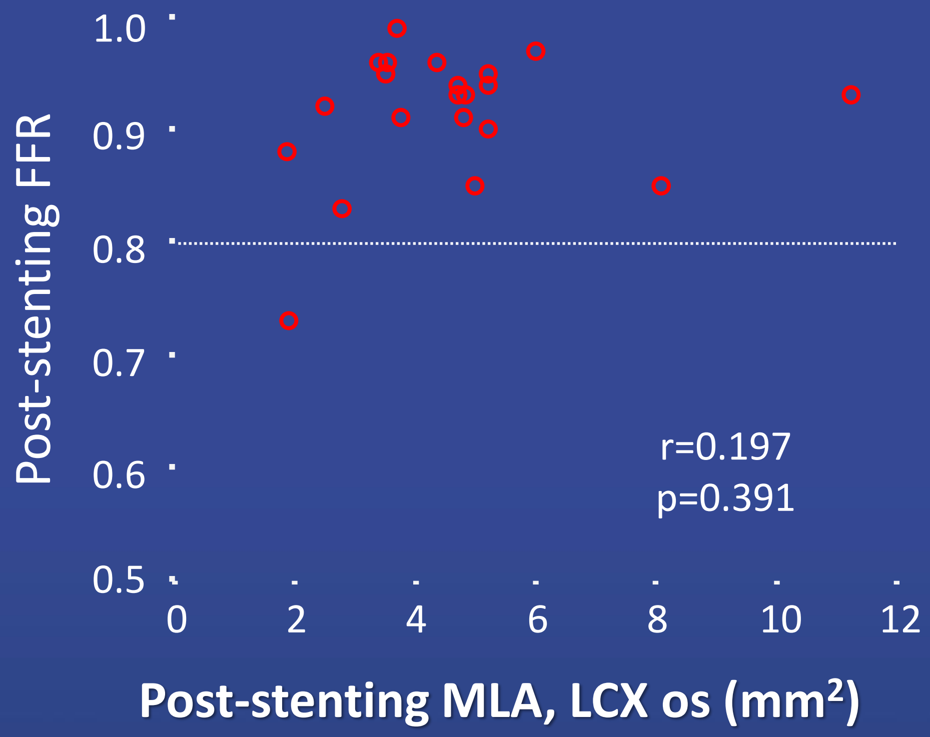


Kang et al. Catheter Cardiovasc Interv 2014;83(4):545-52

When Pre-PCI LCX Ostial DS<50%, Just Do Single Stent!

LMCA Bifurcation
Post-stenting LCX Stenosis

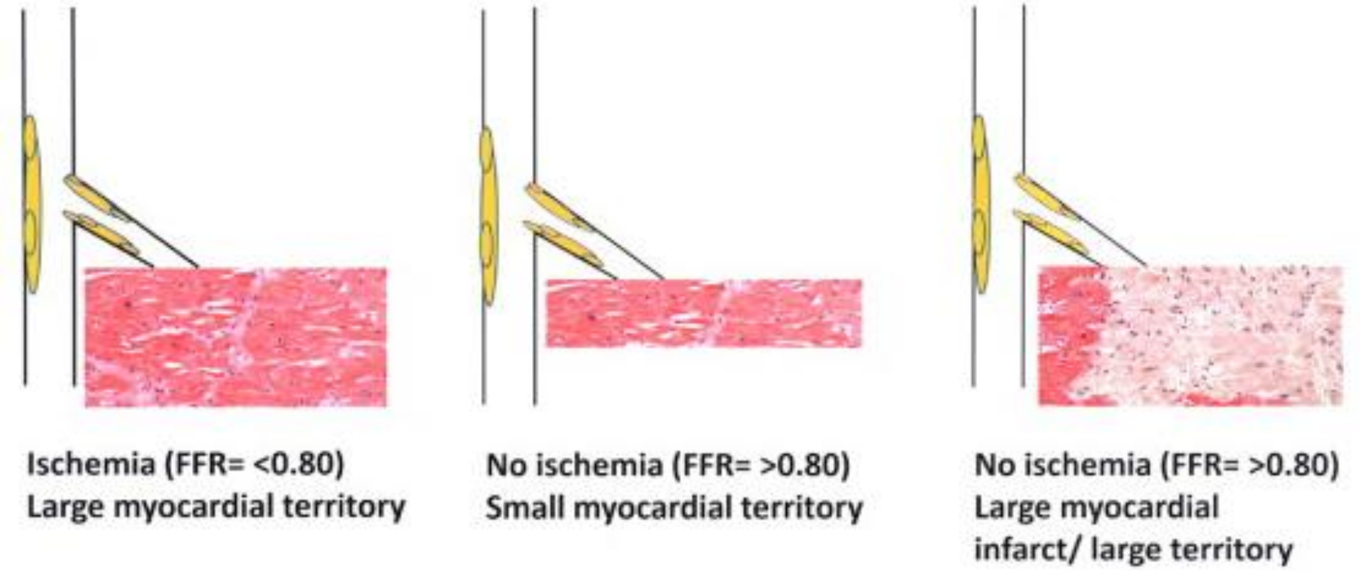




Kang et al. Catheter Cardiovasc Interv 2014;83:542-52

Why Mismatch?

- Lesion eccentricity of SB
- Negative remodeling of ostium
- Various size of myocardium
- Strut artifacts
- Focal carina shift



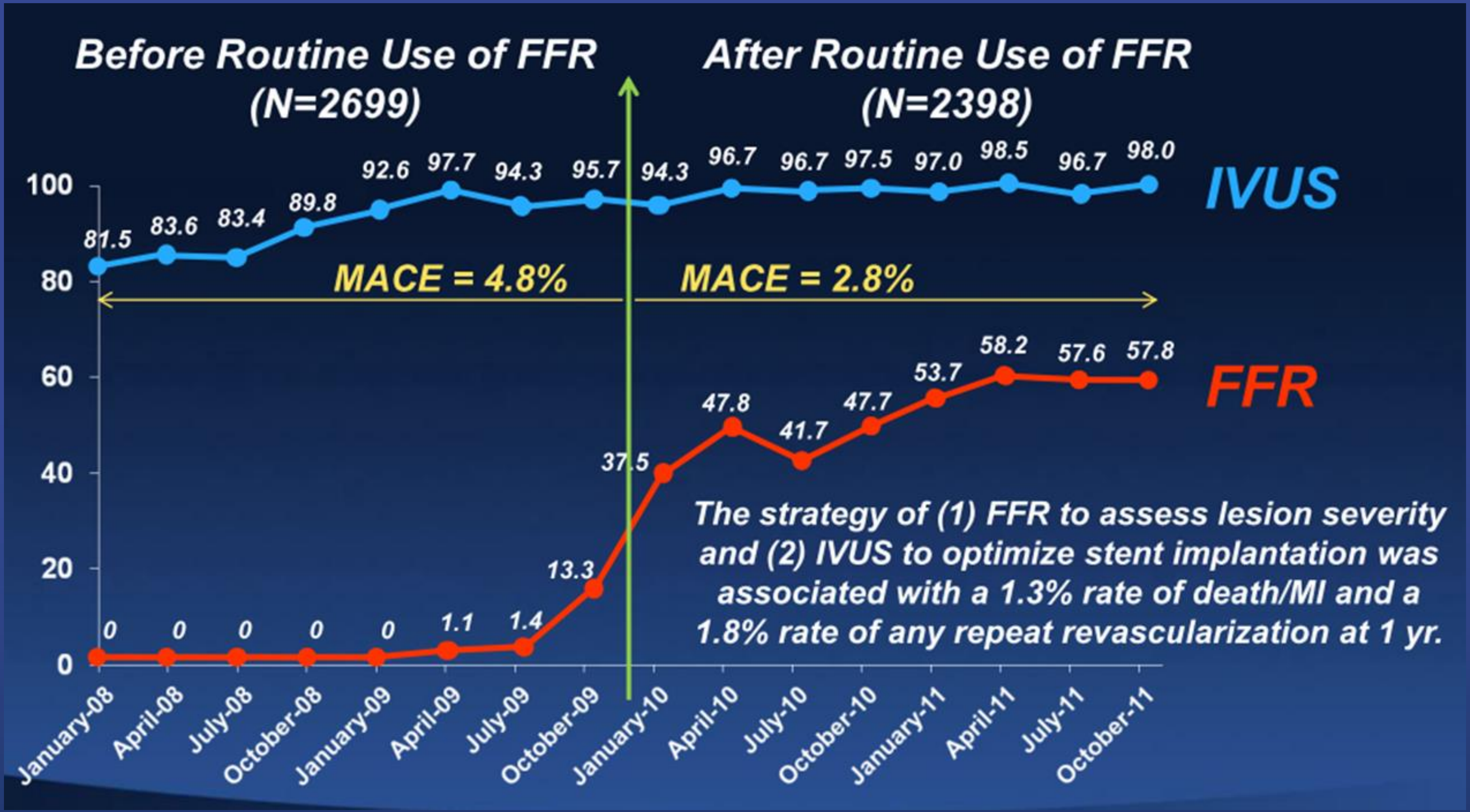
Sachdeva et al. Am J Cardiol 2011;107:1794-5

The Use of FFR

- Single Vessel Stenting
- Multivessel Stenting
- Complex Bifurcation Stenting
- Full Metal Jaket

- Deferral of PCI under OMT
- Single Vessel Stenting
- Simple Bifurcation Stenting
- Selected Stent Implantation

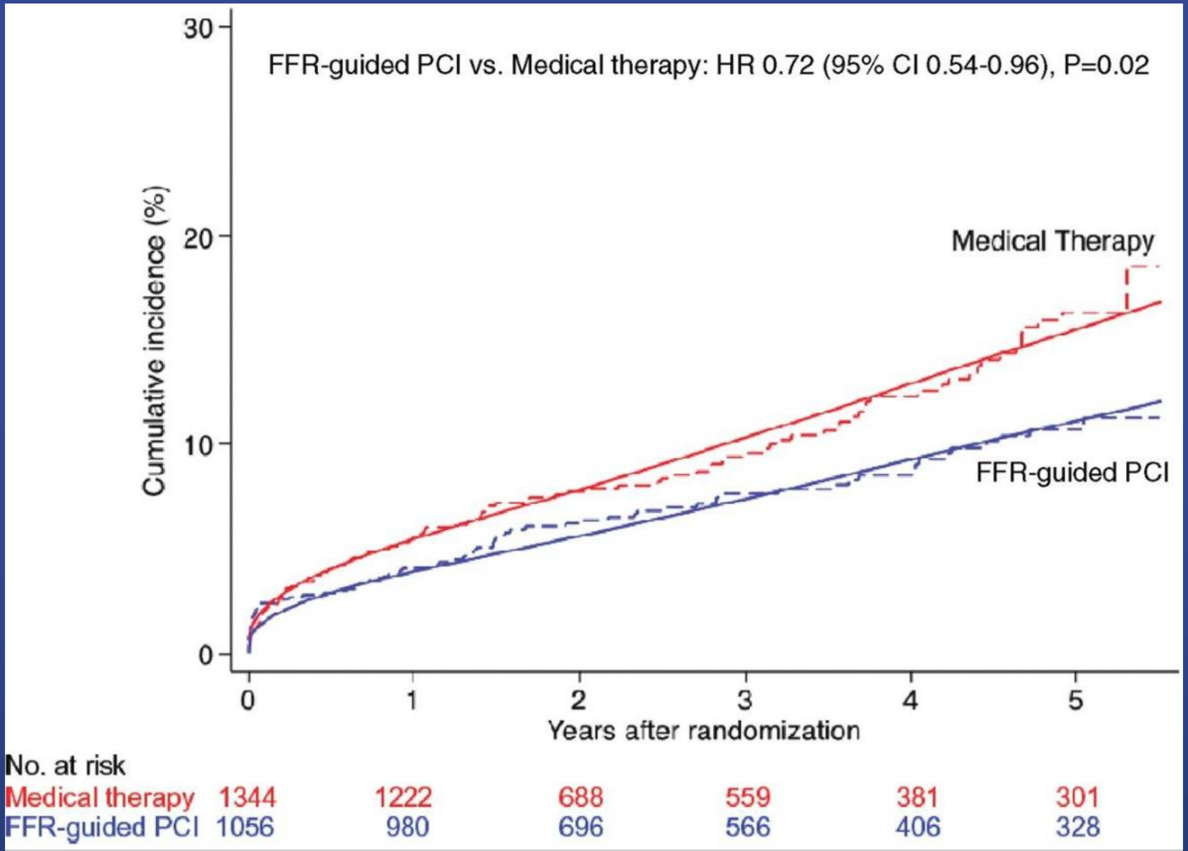
Between Jan 2008 and Dec 2011, 5097 pts underwent PCI at Asan Medical Center, Seoul, Korea and were followed for 1 year



SJ Park et al. Eur Heart J 2013;34:3353-61

FFR–Guided Multivessel Angioplasty in SCAD

- Stable coronary artery disease
- Meta-analysis of 3 randomized control trials
  - FAME 2 study
  - DANAMI-3-PRIMULTI
  - Compare-Acute
- Primary composite end-point : cardiac death or MI
  HR 0.72 (95% CI 0.54-0.96)



FFR–Guided Multivessel Angioplasty in Myocardial Infarction

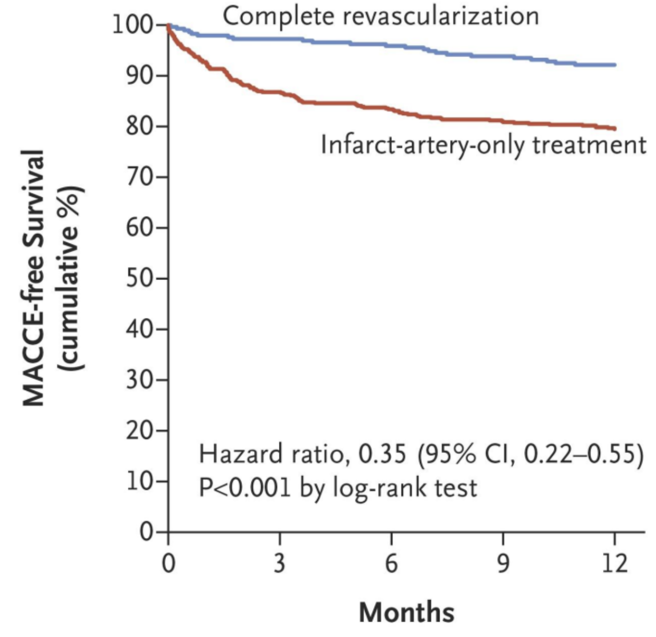
COMPARE-ACUTE trial

- 885 patients with STEMI and multivessel
- underwent primary PCI
- Randomization(1:2)

Complete revascularization of non–infarct-related coronary arteries guided by FFR (295 patients)

VS

No revascularization of non–infarct-related coronary arteries (590 patients)



No. at Risk					
Complete revascularization	295	286	281	264	215
Infarct artery	590	512	492	457	371

Smits PC et al. N Engl J Med 2017;376:1234-1244

FFR–Guided Multivessel Angioplasty in STEMI

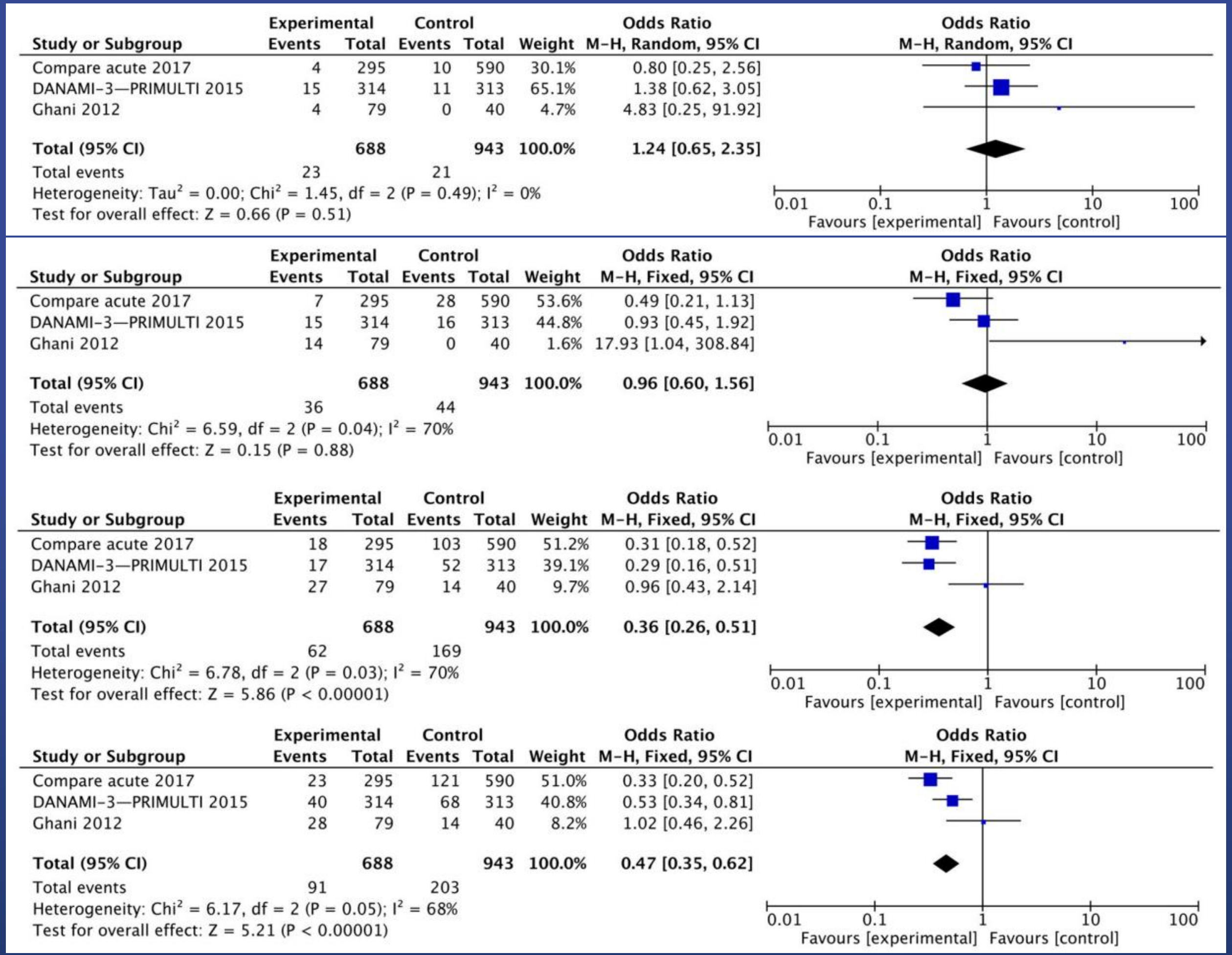
Complete revascularization by FFR vs culprit only revascularization

All cause mortality
HR 1.24 [0.65-2.35]

Non-fatal MI
HR 0.96 [0.60-1.56]

Repeat revascularization
HR 0.36 [0.26-0.51]

MACE
HR 0.47 [0.35-0.62]



Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
Compare acute 2017	4	295	10	590	30.1%	0.80 [0.25, 2.56]
DANAMI-3—PRIMULTI 2015	15	314	11	313	65.1%	1.38 [0.62, 3.05]
Ghani 2012	4	79	0	40	4.7%	4.83 [0.25, 91.92]
Total (95% CI)		**688**		**943**	**100.0%**	**1.24 [0.65, 2.35]**
Total events	23		21			

Heterogeneity: Tau² = 0.00; Chi² = 1.45, df = 2 (P = 0.49); I² = 0%
Test for overall effect: Z = 0.66 (P = 0.51)

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Compare acute 2017	7	295	28	590	53.6%	0.49 [0.21, 1.13]
DANAMI-3—PRIMULTI 2015	15	314	16	313	44.8%	0.93 [0.45, 1.92]
Ghani 2012	14	79	0	40	1.6%	17.93 [1.04, 308.84]
Total (95% CI)		**688**		**943**	**100.0%**	**0.96 [0.60, 1.56]**
Total events	36		44			

Heterogeneity: Chi² = 6.59, df = 2 (P = 0.04); I² = 70%
Test for overall effect: Z = 0.15 (P = 0.88)

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Compare acute 2017	18	295	103	590	51.2%	0.31 [0.18, 0.52]
DANAMI-3—PRIMULTI 2015	17	314	52	313	39.1%	0.29 [0.16, 0.51]
Ghani 2012	27	79	14	40	9.7%	0.96 [0.43, 2.14]
Total (95% CI)		**688**		**943**	**100.0%**	**0.36 [0.26, 0.51]**
Total events	62		169			

Heterogeneity: Chi² = 6.78, df = 2 (P = 0.03); I² = 70%
Test for overall effect: Z = 5.86 (P < 0.00001)

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Compare acute 2017	23	295	121	590	51.0%	0.33 [0.20, 0.52]
DANAMI-3—PRIMULTI 2015	40	314	68	313	40.8%	0.53 [0.34, 0.81]
Ghani 2012	28	79	14	40	8.2%	1.02 [0.46, 2.26]
Total (95% CI)		**688**		**943**	**100.0%**	**0.47 [0.35, 0.62]**
Total events	91		203			

Heterogeneity: Chi² = 6.17, df = 2 (P = 0.05); I² = 68%
Test for overall effect: Z = 5.21 (P < 0.00001)

Wang et al. BMC Cardiovascular Disorders (2019) 19:49

Pitfalls with Pressure Measurement

- Introducer needle
- Height of the fluid-filled transducer
- Equalization
- Hyperemia
- Drift
- Guiding catheter wedging
- Side holes
- Whipping
- Accordion effect

Instantaneous wave-Free Ratio (iFR)

$$\Delta P = \Delta Q \times R \longrightarrow \Delta P \approx \Delta Q \times R$$

Changes in pressure across a stenosis
under constant and minimized coronary resistance can be **a surrogate for blood flow to myocardium**.

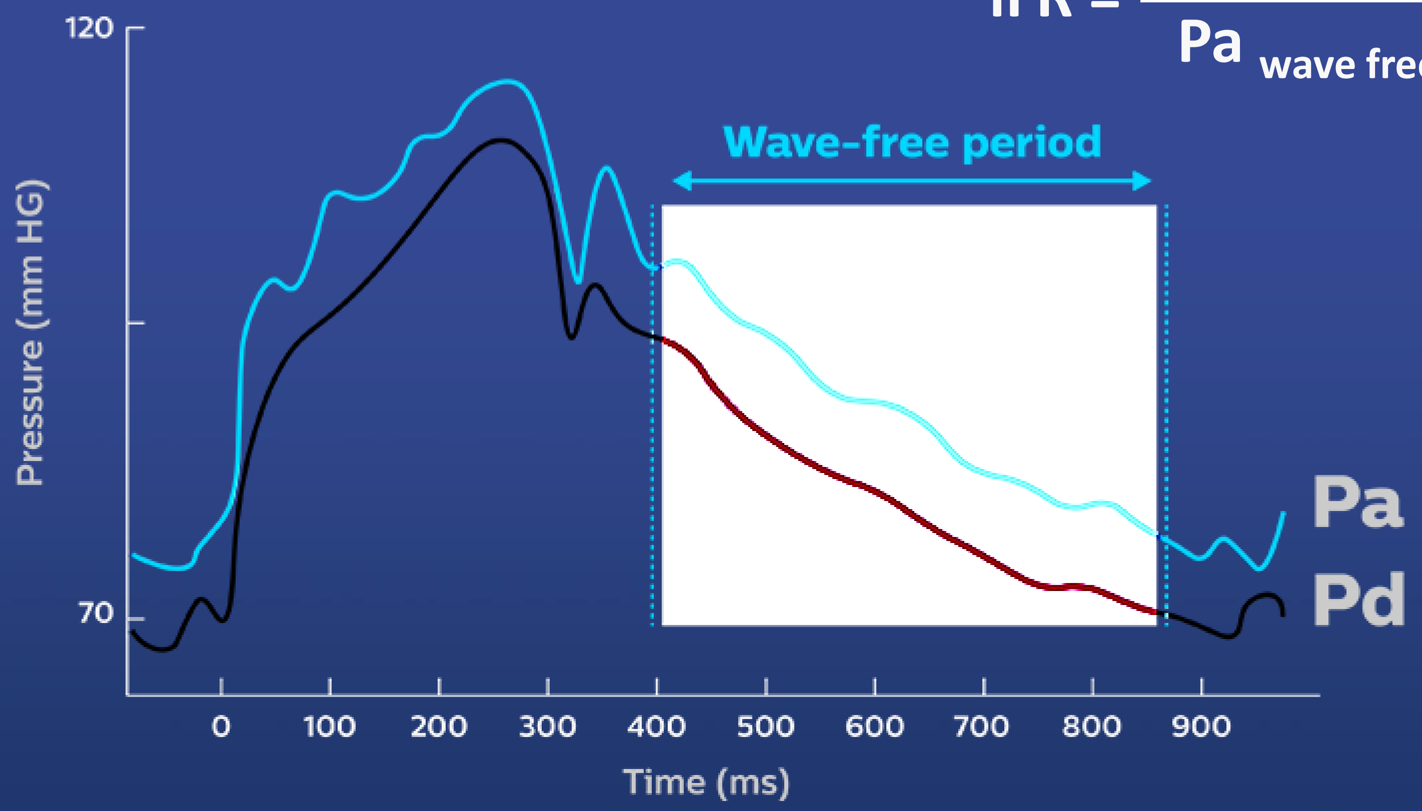
For minimizing intracoronary resistance during measurment

- FFR : adenosine infusion, average over several cycles
- iFR : **wave free period**, instantaneous pressure

Instantaneous wave-Free Ratio (iFR)

- Wave free period ; resistance naturally constant and minimized in the cardiac cycle

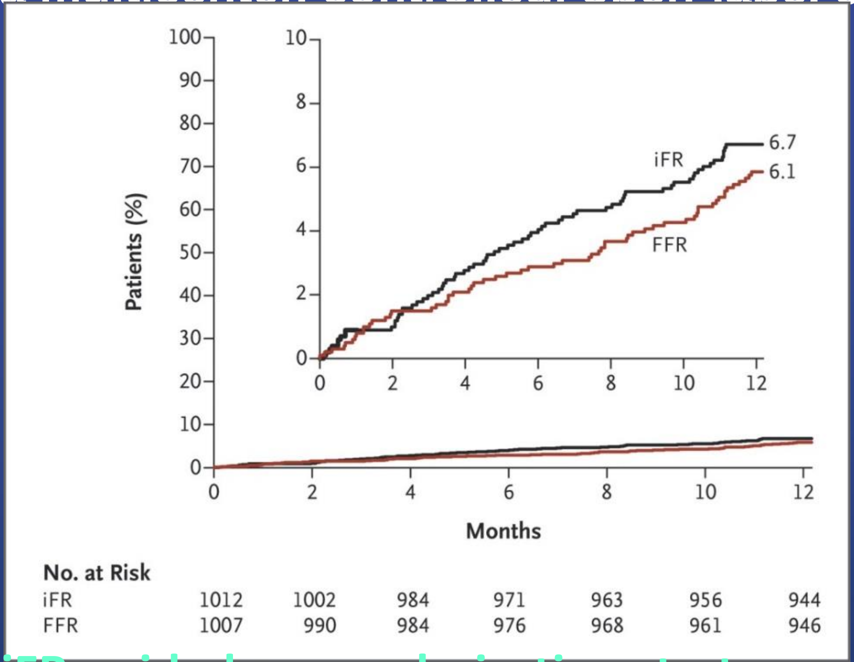
$$iFR = \frac{Pd_{\text{wave free period}}}{Pa_{\text{wave free period}}}$$



iFR vs FFR to Guide PCI

iFR-SWEDEHEART trial

- 2037 participants with stable angina or an acute coronary syndrome
- Underwent coronary revascularization
- Randomization (1:1)
- a multicenter, controlled, open-label clinical trial



iFR-guided

VS

FFR-guided

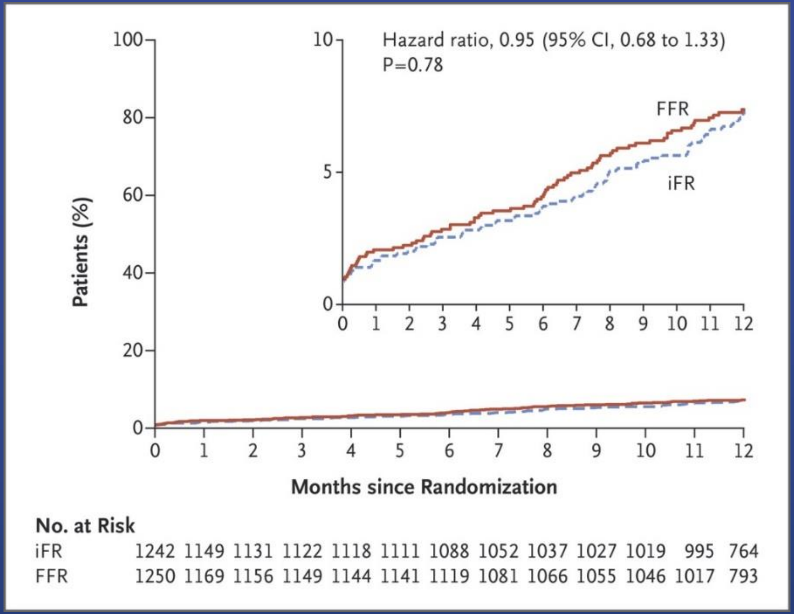
An iFR-guided revascularization strategy was noninferior to an FFR-guided revascularization strategy with respect to the rate of MACE(1yr)

Götberg M et al. N Engl J Med 2017. DOI: 10.1056/NEJMoa1616540

Use of the Instantaneous Wave-free Ratio

DEFINE-FLAIR trial

- 2492 patients with coronary artery disease
- Underwent coronary revascularization
- Randomization (1:1)
- a multicenter, international, blinded trial



iFR-guided

VS

FFR-guided

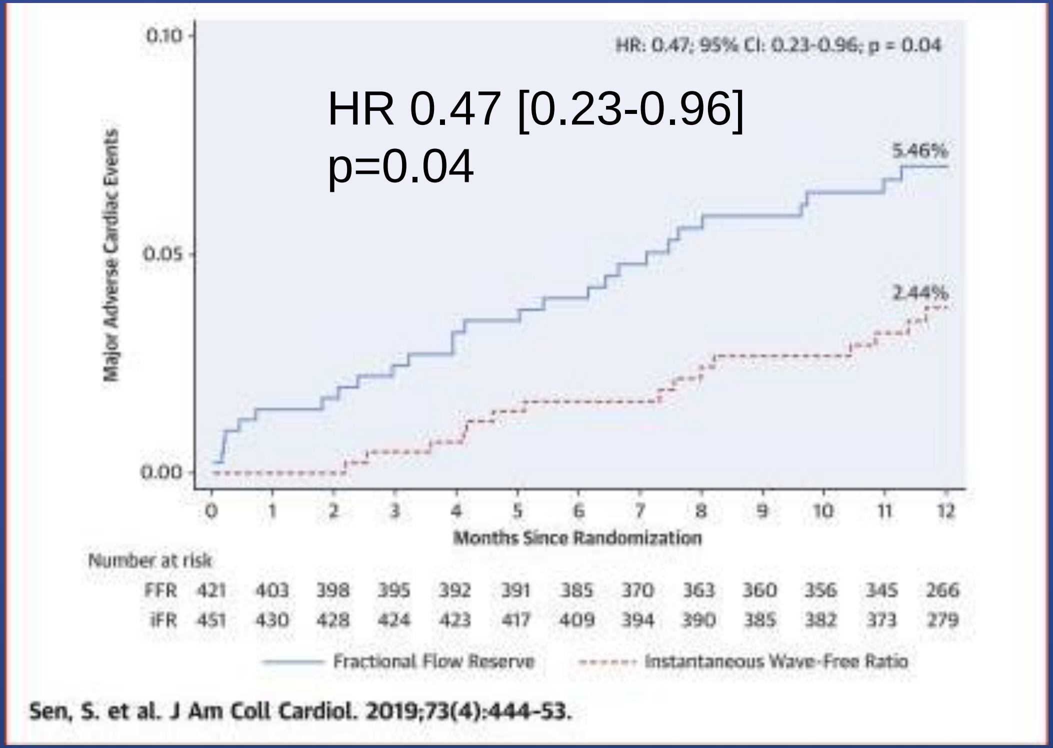
Coronary revascularization guided by iFR was noninferior to revascularization guided by FFR with respect to the risk of MACE(1yr)

Davies JE et al. N Engl J Med 2017. DOI: 10.1056/NEJMoa1700445

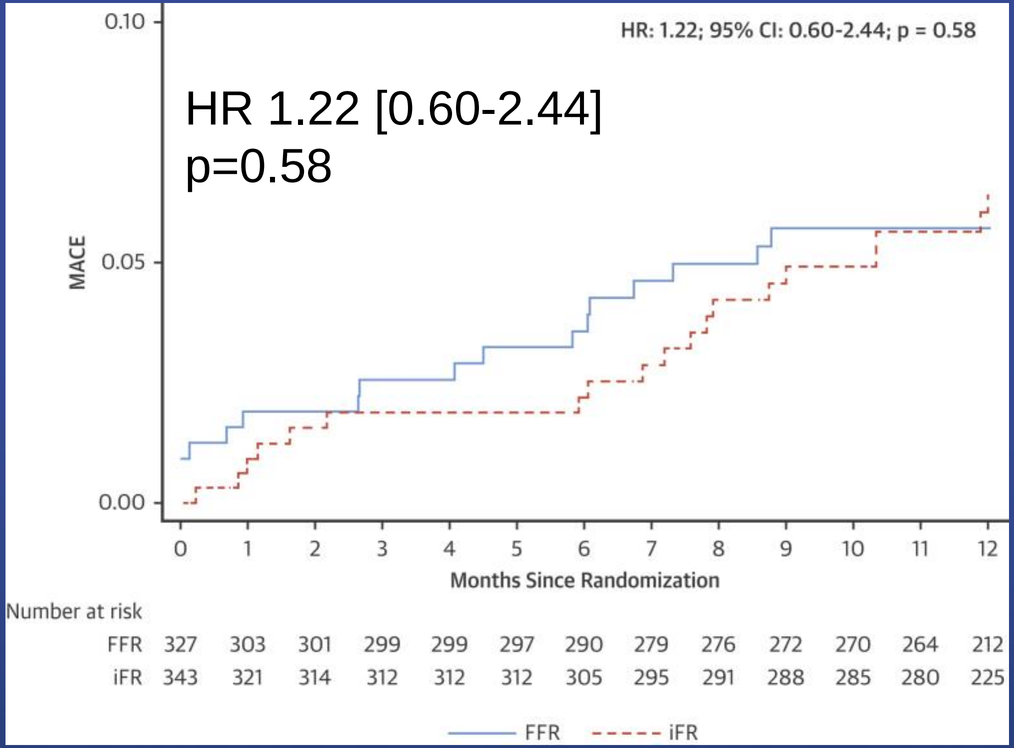
iFR vs FFR in LAD lesions

DEFINE-FLAIR trial sub-study

LAD lesion



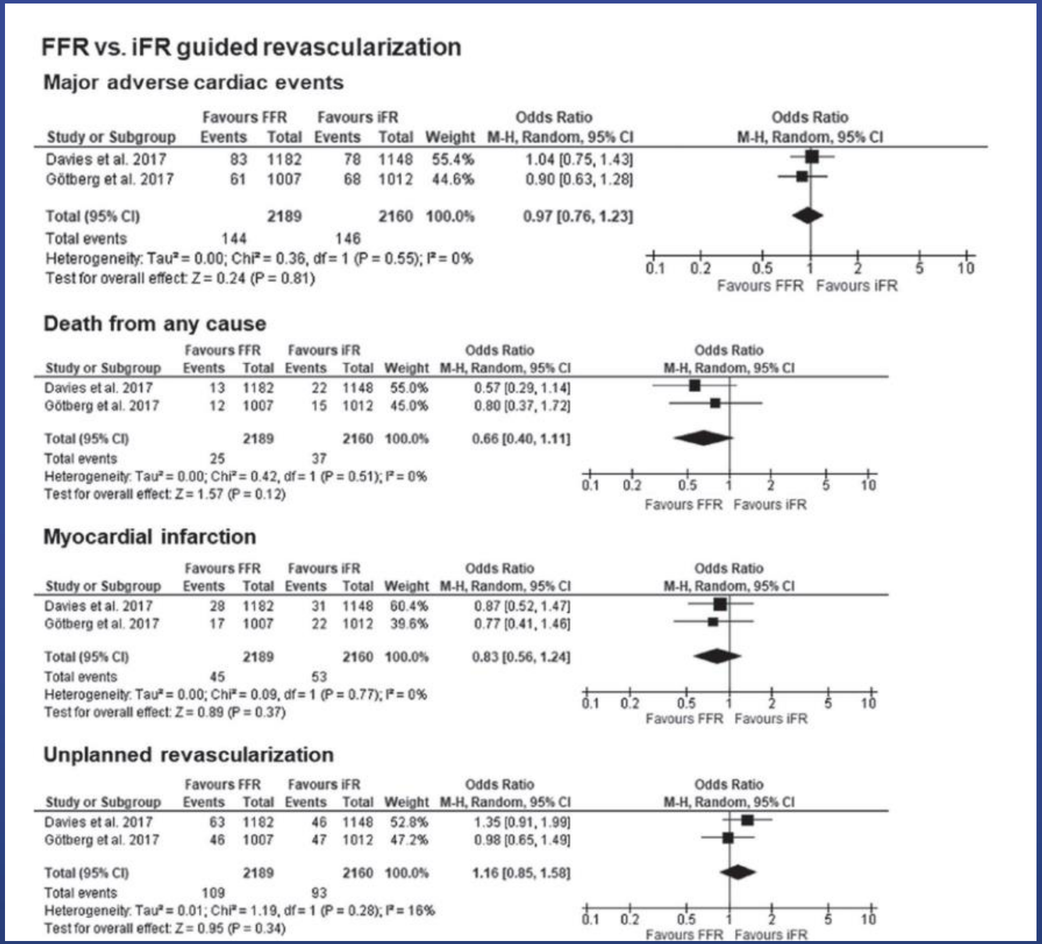
Non-LAD lesion



Sayan Sen et al. J Am Coll Cardiol. 2019 Feb 5; 73(4): 444–453.

iFR vs FFR to Guide PCI

META-ANALYSIS OF ANGIOGRAPHY, IFR AND FFR GUIDED PCI



iFR-SWEDHEART study
DEFINE-FLAIR study

significant lower numbers in chest discomfort (P<0.001) when using iFR

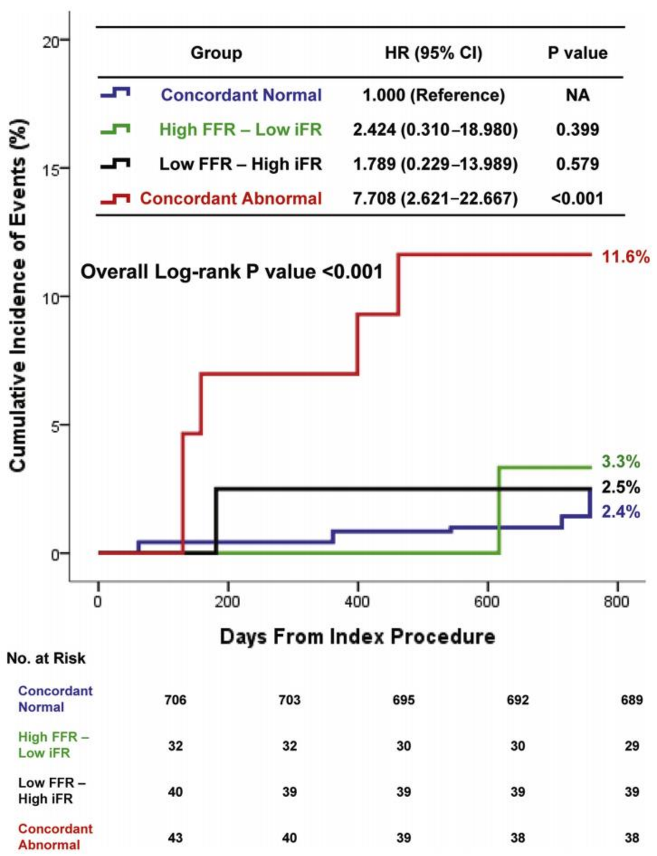
There is no significant superiority of FFR over iFR

Baumann et al. Exp Ther Med. 2019 Mar;17(3):1939-1951. doi: 10.3892/etm.2019.7156. Epub 2019 Jan 7.

iFR vs FFR concordance

3V FFR-FRIENDS substudy

- Comparison of 2-Year Clinical Outcomes of Lesions Classified by FFR and iFR in Deferred Lesions



- 821 deferred lesion (n=374)
- Primary outcome : MACE at 2 years

- Group 1 : FFR > 0.80 and iFR > 0.89
- Group 2 : FFR > 0.80 and iFR ≤ 0.89
- Group 3 : FFR ≤ 0.80 and iFR > 0.89
- Group 4 : FFR ≤ 0.80 and iFR ≤ 0.89

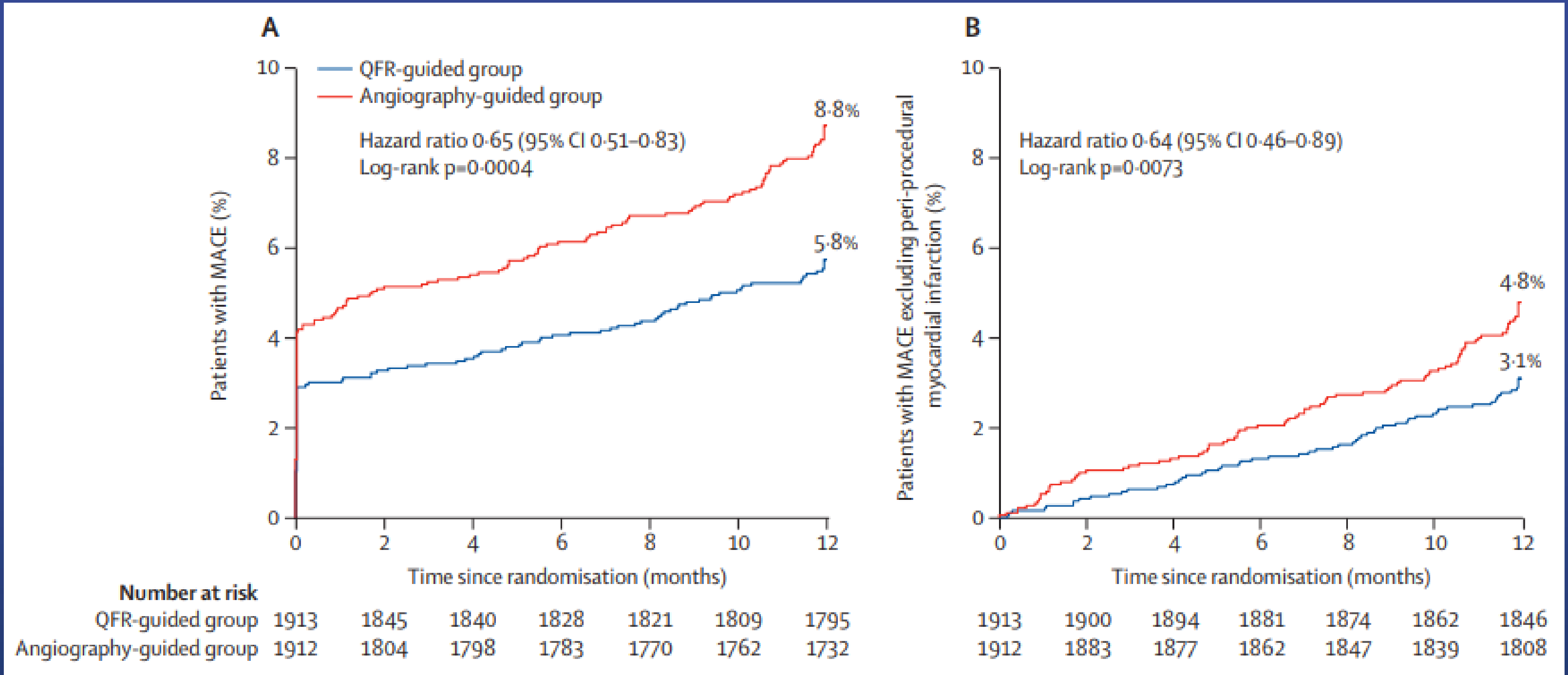
The discordant results between FFR and iFR were not associated with the increased risk of MACE. The risk of MACE was significantly increased only in lesions with abnormal results of both FFR and iFR.

Lee J, Shin E, Nam C et al. JACC Cardiovasc Interv 2017;10(24):2506

FAVOR III China

QFR-guided PCI versus Angiography-guided PCI

Death/MI or Ischemic Driven Revascularization



Xu bo et al. Lancet 2021; 398: 2149–59

FLOWER MI

In Patients with STEMI
Undergoing Complete Revascularization
(n=1171)

R

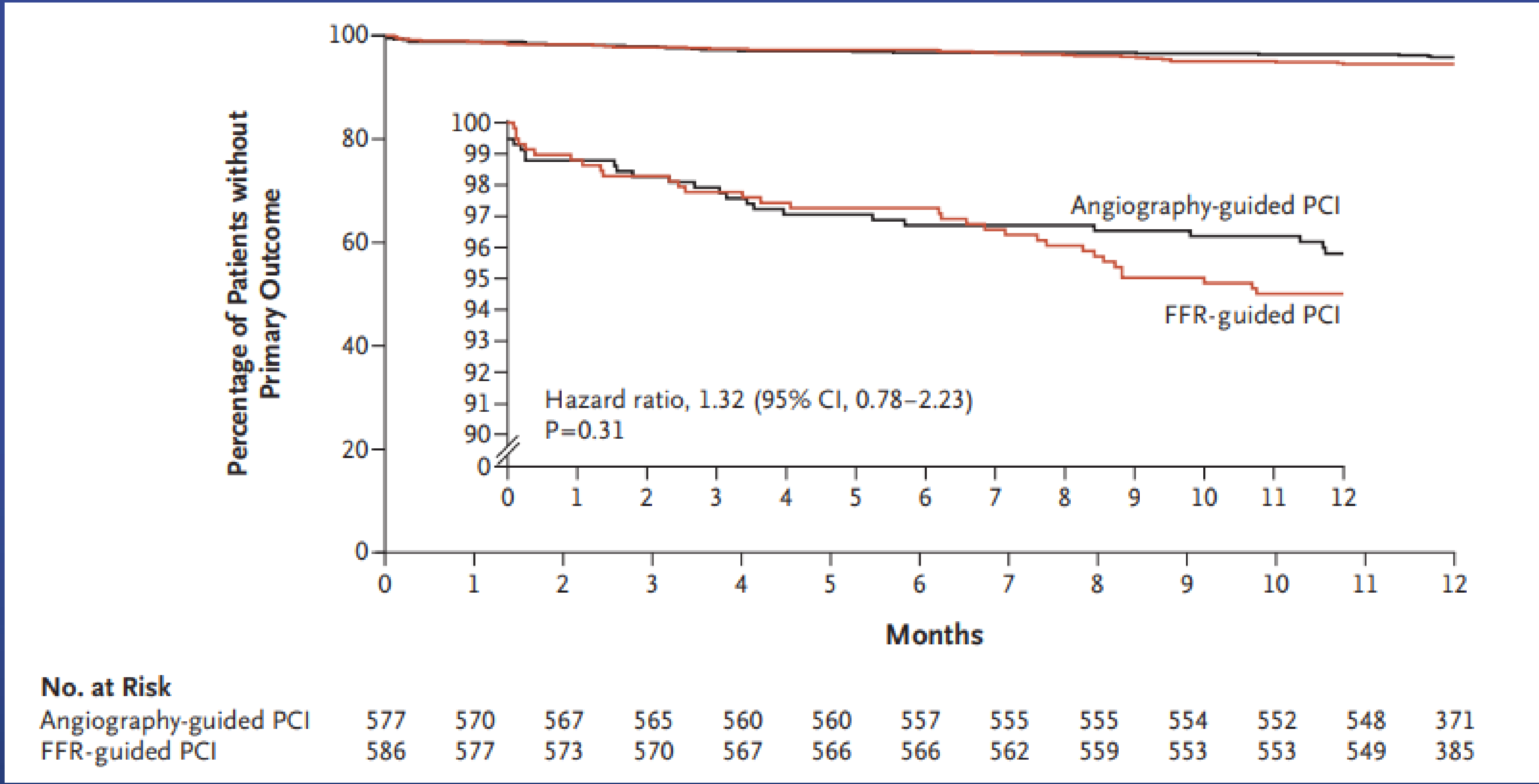
FFR Guided PCI
(n=590)

Angio Guided PCI
(n=581)

Primary Endpoint at 1 year:
Death from any cause, nonfatal myocardial infarction or unplanned hospitalization leading to urgent revascularization

Etienne Puymirat et al. N Engl J Med 2021;385:297-308

FLOWER MI



Etienne Puymirat et al. N Engl J Med 2021;385:297-308

FUTURE

Multivessel CAD Patients at Angiography
3 stenosis > 50% per patient
(n=927)

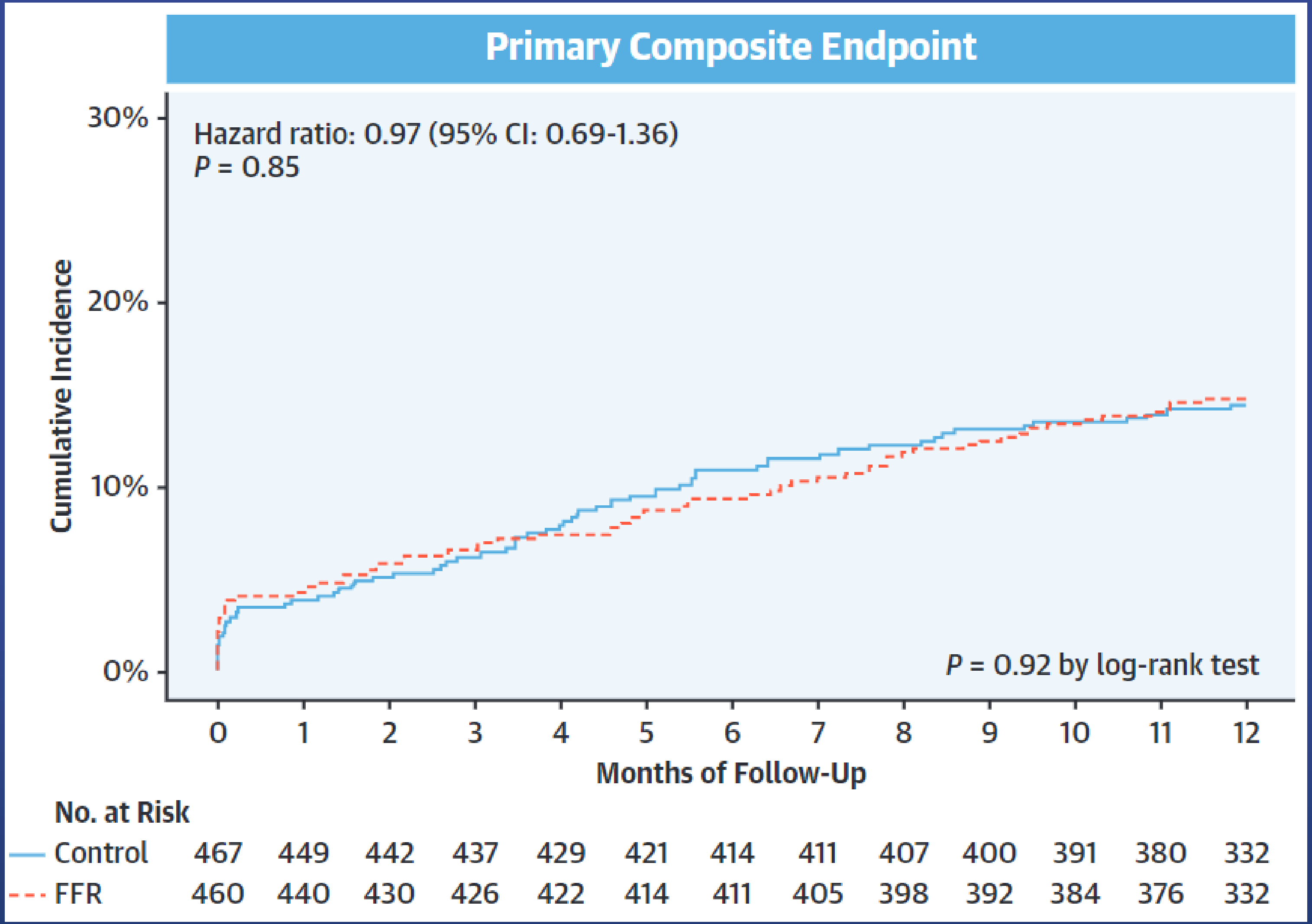
R

Angiography Evaluation only (>50% Stenosis) (n=467)	FFR in all target lesions 43% (FFR > 0.80) (n=460)

Primary Endpoint at 1 year:
Death from any cause, nonfatal myocardial infarction, Stroke, or unplanned revascularization

Gilles Rioufol et al. JACC 2021;78:9;1875-1885

FUTURE



Gilles Rioufol et al. JACC 2021;78:9;1875-1885

FLAVOUR trial

Patients with de novo intermediate stenosis (40–70%) eligible for PCI (n=1682)

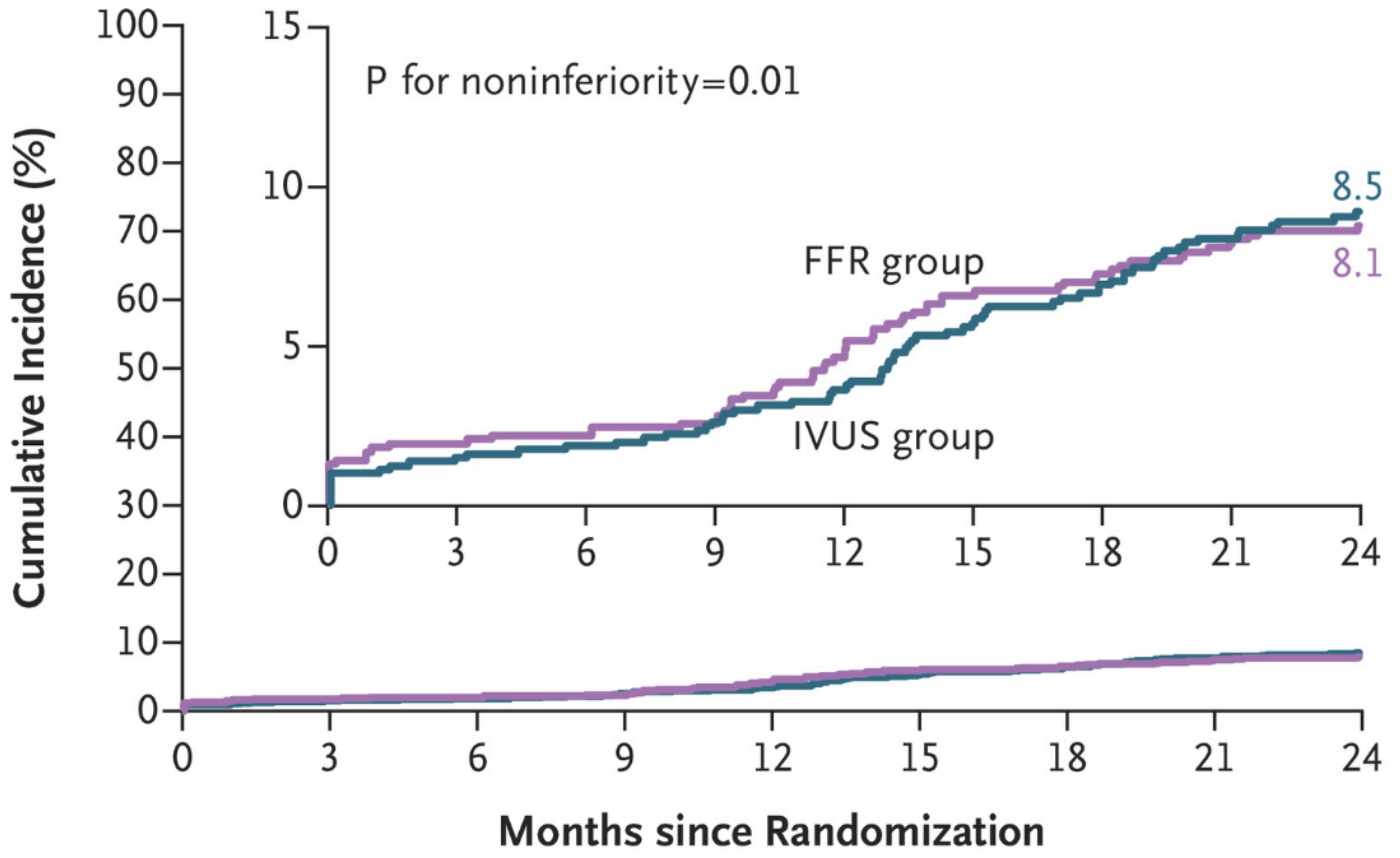
R

FFR guided PCI (n=838)	IVUS-guided PCI (n=844)

Primary Endpoint at 2 year:
Death from any cause, myocardial infarction, and any revascularization

KOO et al. JACC 2021;78:9;1875-1885

FLAVOUR trial



No. at Risk

	0	3	6	9	12	15	18	21	24
IVUS group	844	828	825	820	809	792	784	771	690
FFR group	838	818	816	812	796	781	778	770	699

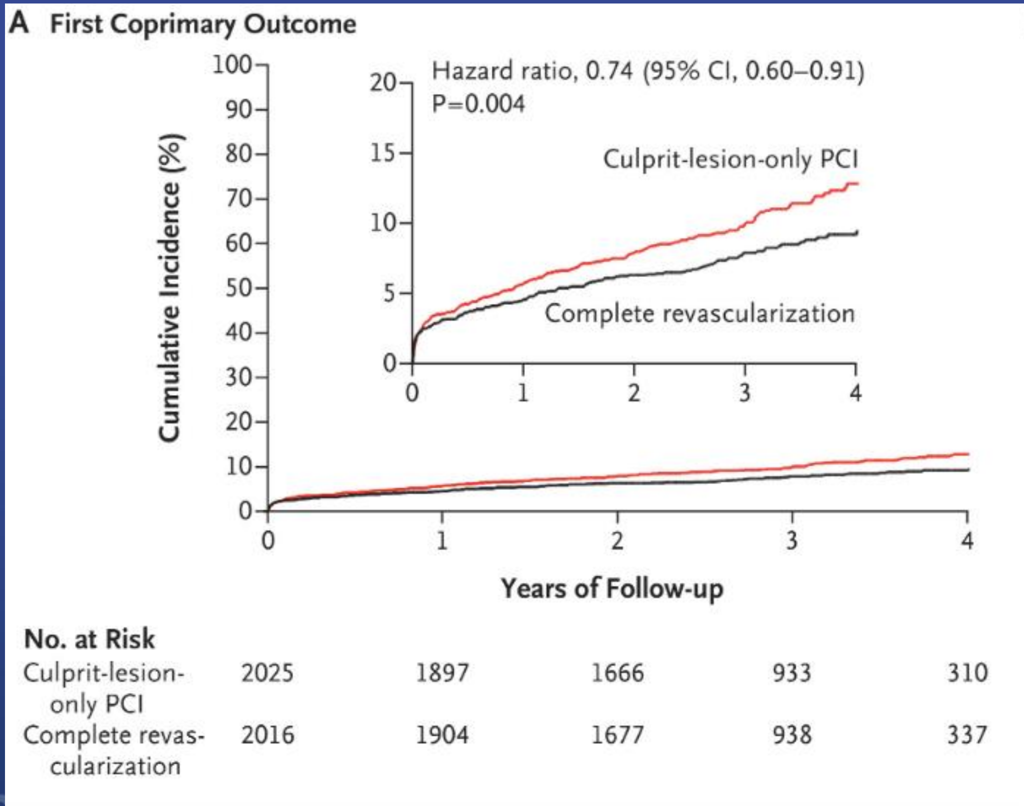
KOO et al. JACC 2021;78:9;1875-1885

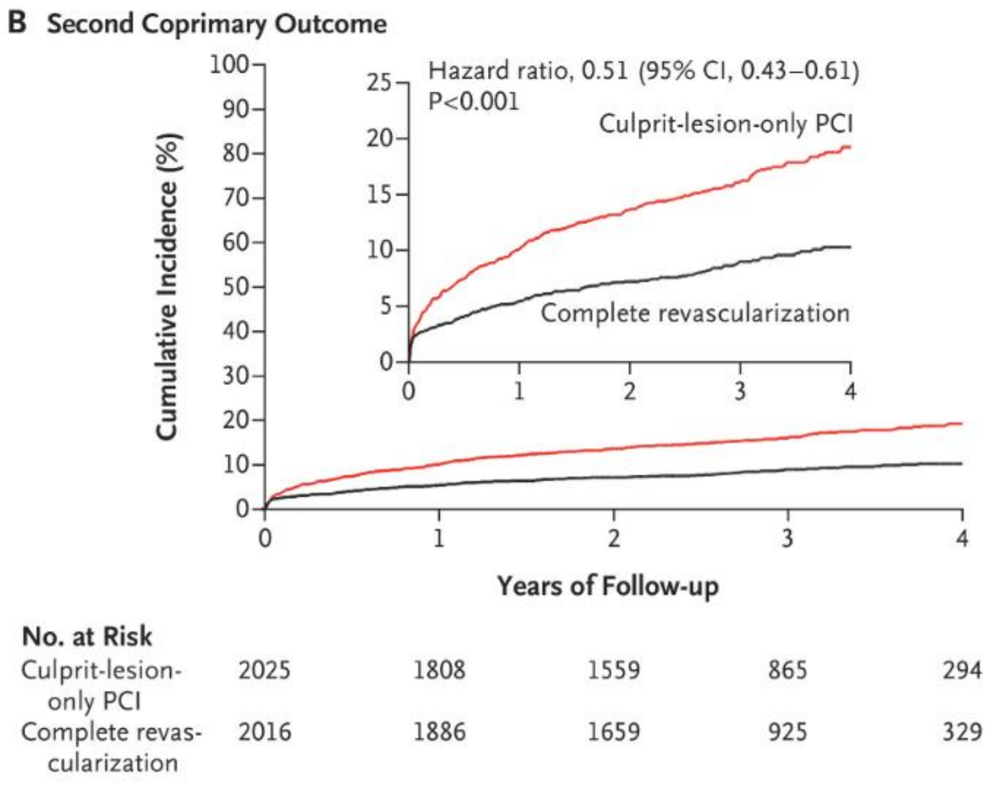
COMPLETE trial

4041 STEMI patients with non-culprit stenosis (visual > 70% or FFR < 0.80) were randomized into complete revascularization (N=2016) versus culprit-only PCI (N=2025) groups

Primary endpoint: cardiac death or new MI

Co-Primary endpoint:
cardiac death or new MI, ischemia-driven revascularization

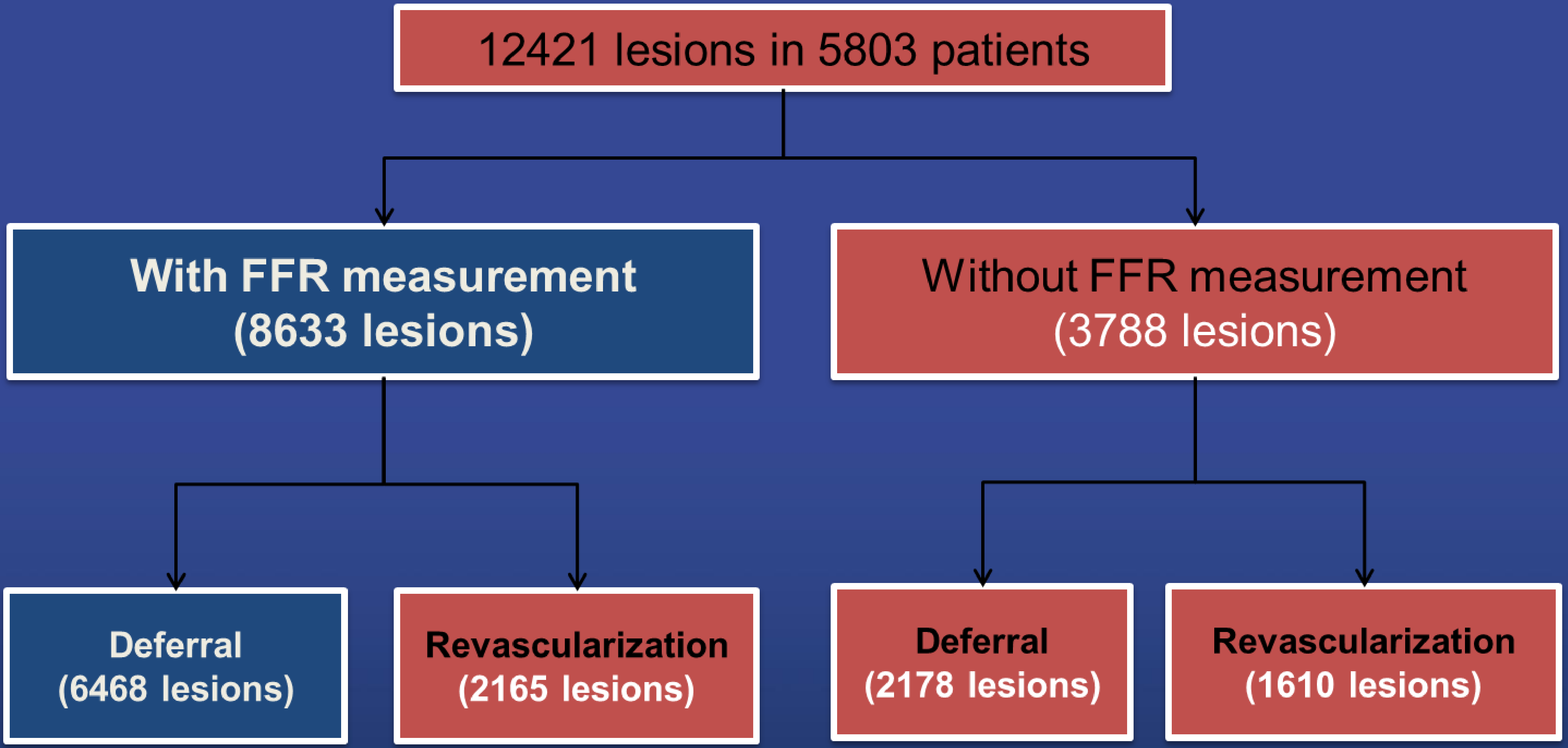




Mehta et al. NEJM 2019;381:1411-1421

Gray-zone FFR

Data from IRIS-FFR Registry



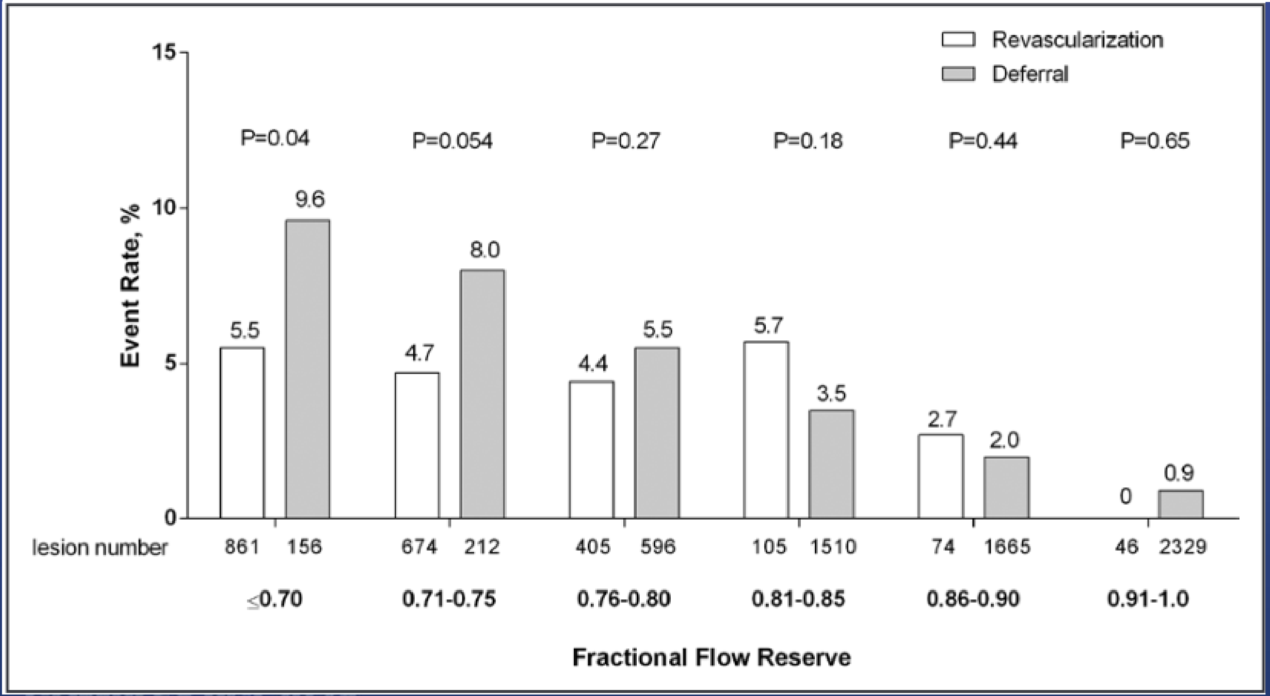
Ahn JM et al. Circulation. 2017;135(23):2241-2251.

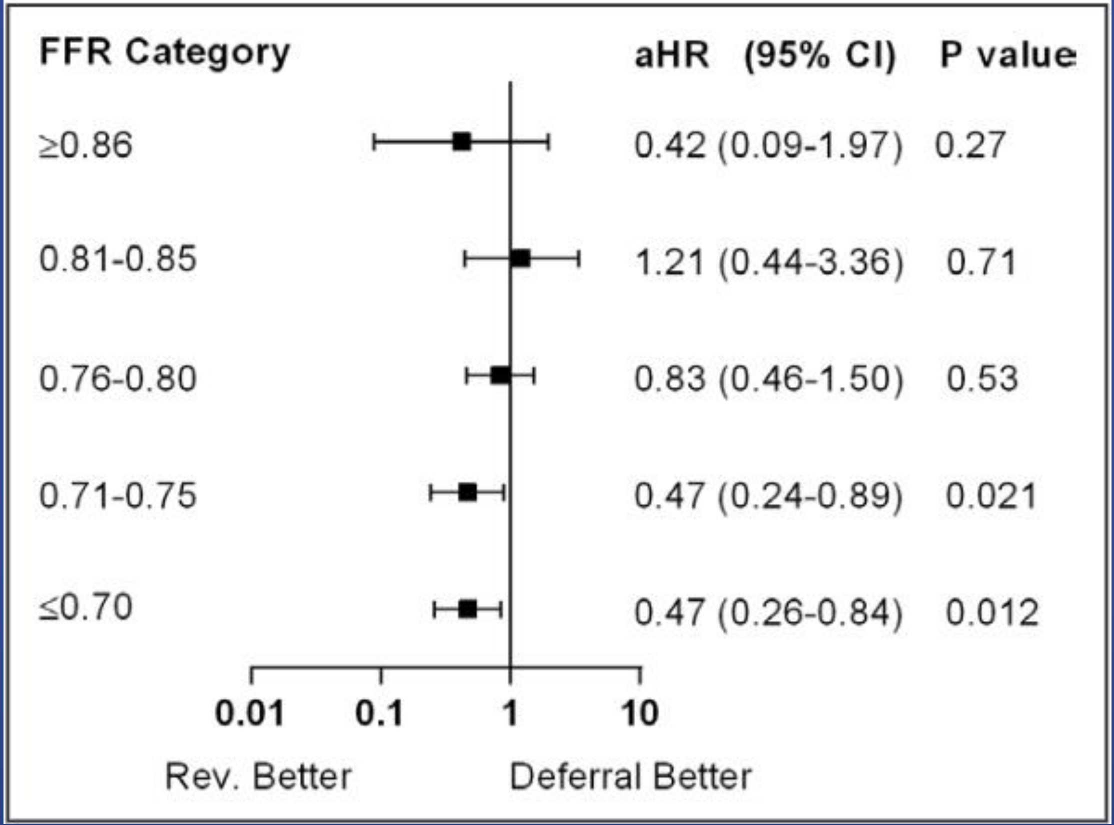
Data from IRIS-FFR Registry

ORIGINAL RESEARCH ARTICLE

Fractional Flow Reserve and Cardiac Events in Coronary Artery Disease

Data From a Prospective IRIS-FFR Registry (Interventional Cardiology Research Incooperation Society Fractional Flow Reserve)





Ahn JM et al. Circulation. 2017;135(23):2241-2251.

Defer vs. PCI in Gray-zone FFR

ESC European Society of Cardiology
European Heart Journal (2018) **0**, 1–10
doi:10.1093/eurheartj/ehy079

CLINICAL RESEARCH
Interventional cardiology

Deferred vs. performed revascularization for coronary stenosis with grey-zone fractional flow reserve values: data from the IRIS-FFR registry

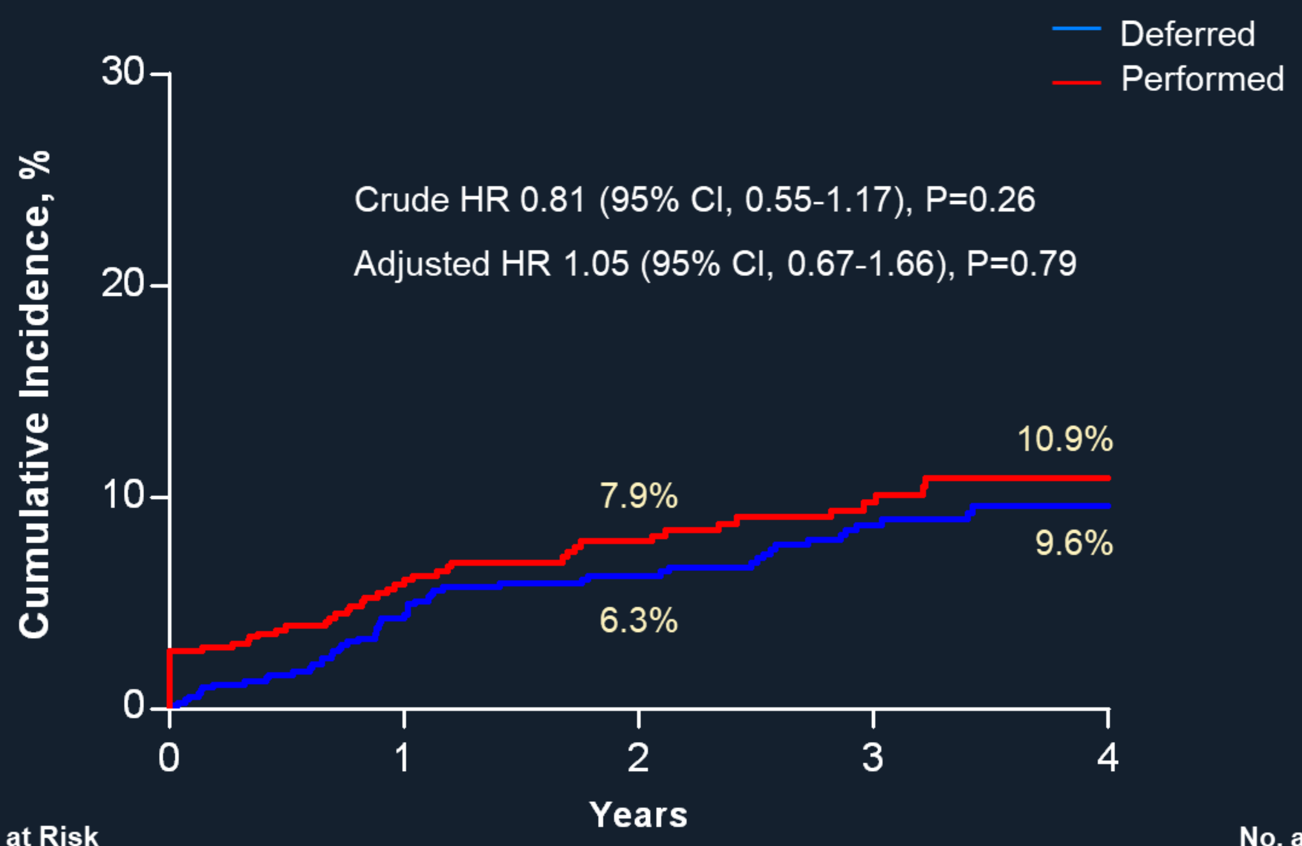
Do-Yoon Kang†, Jung-Min Ahn†, Cheol Hyun Lee, Pil Hyung Lee, Duk-Woo Park, Soo-Jin Kang, Seung-Whan Lee, Young-Hak Kim, Cheol Whan Lee, Seong-Wook Park, and Seung-Jung Park*

Heart Institute, University of Ulsan College of Medicine, Asan Medical Center, 388-1 Pungnap-dong, Songpa-gu, Seoul 138-736, South Korea

Kang DY et al. Eur Heart J. 2018;39(18):1610-1619.

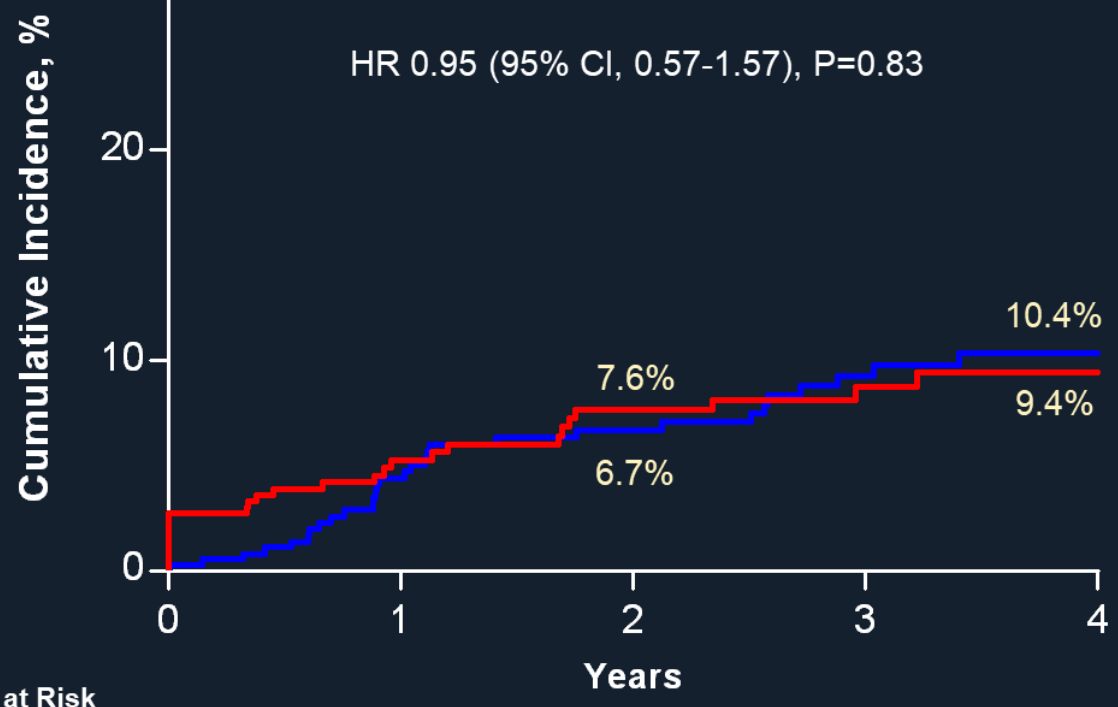
Primary End Point in Gray-zone FFR
(Death, TV-MI, Target Vessel Revascularization)

Overall Population



No. at Risk					
Deferred	683	591	493	361	171
Performed	651	449	343	247	144

Matched Population

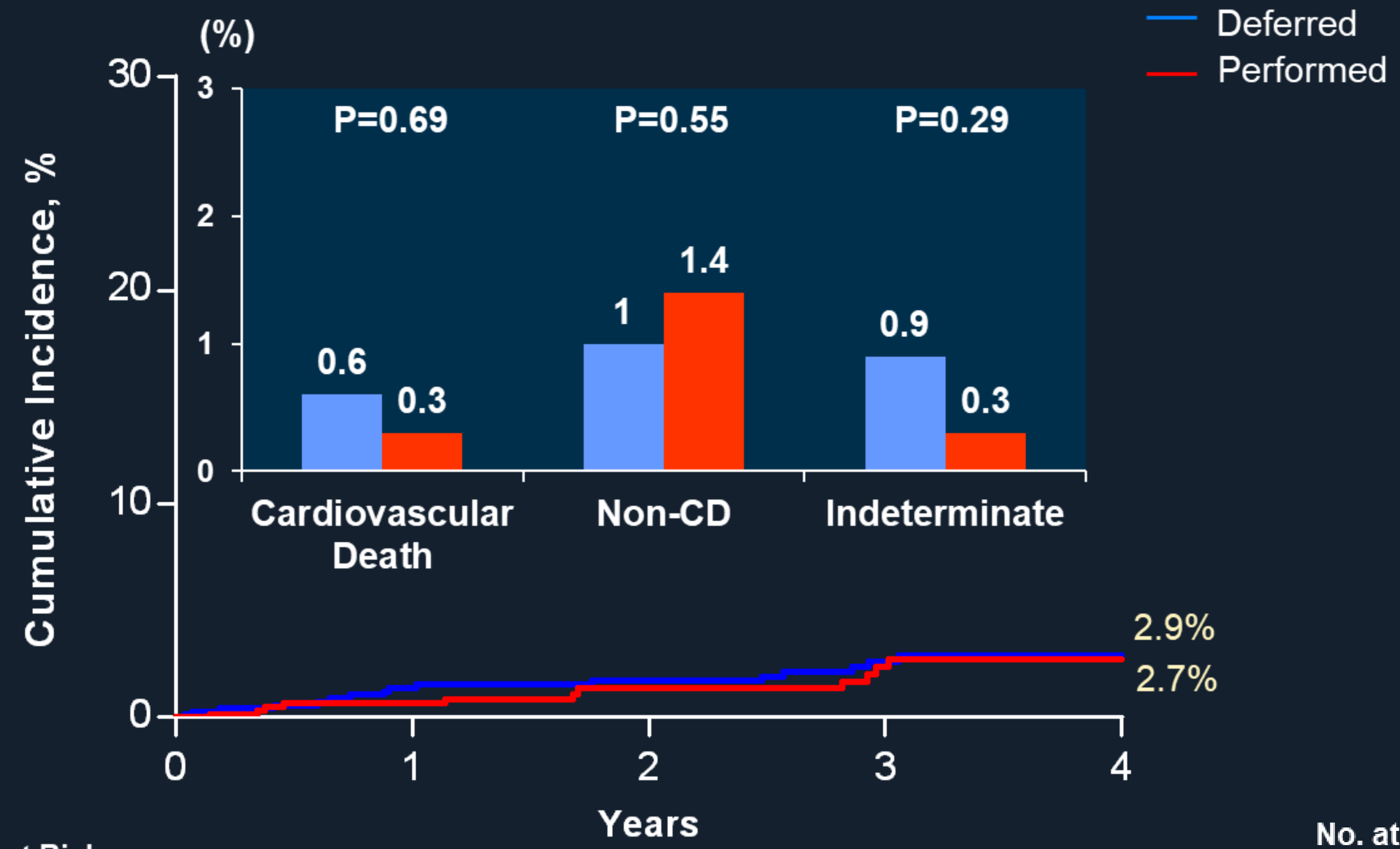


No. at Risk					
Deferred	368	308	249	186	99
Performed	368	263	204	144	84

Kang DY et al. Eur Heart J. 2018;39(18):1610-1619.

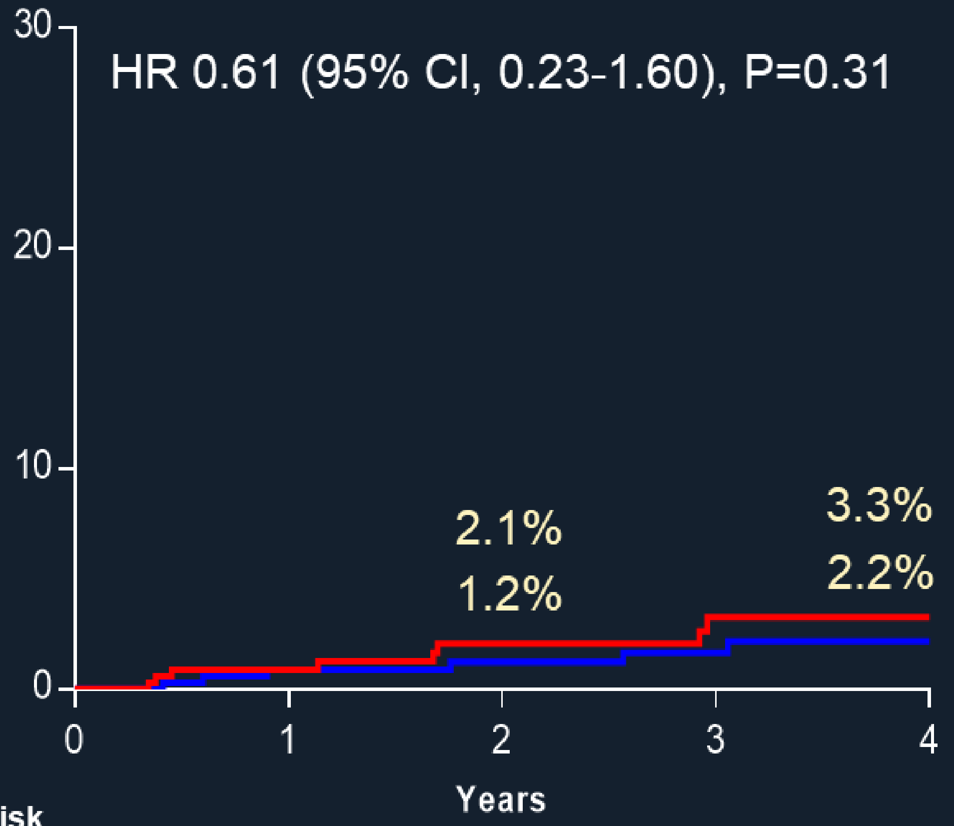
Death from any cause

Overall Population



No. at Risk					
Deferred	683	609	517	387	189
Performed	651	476	373	271	162

Matched Population

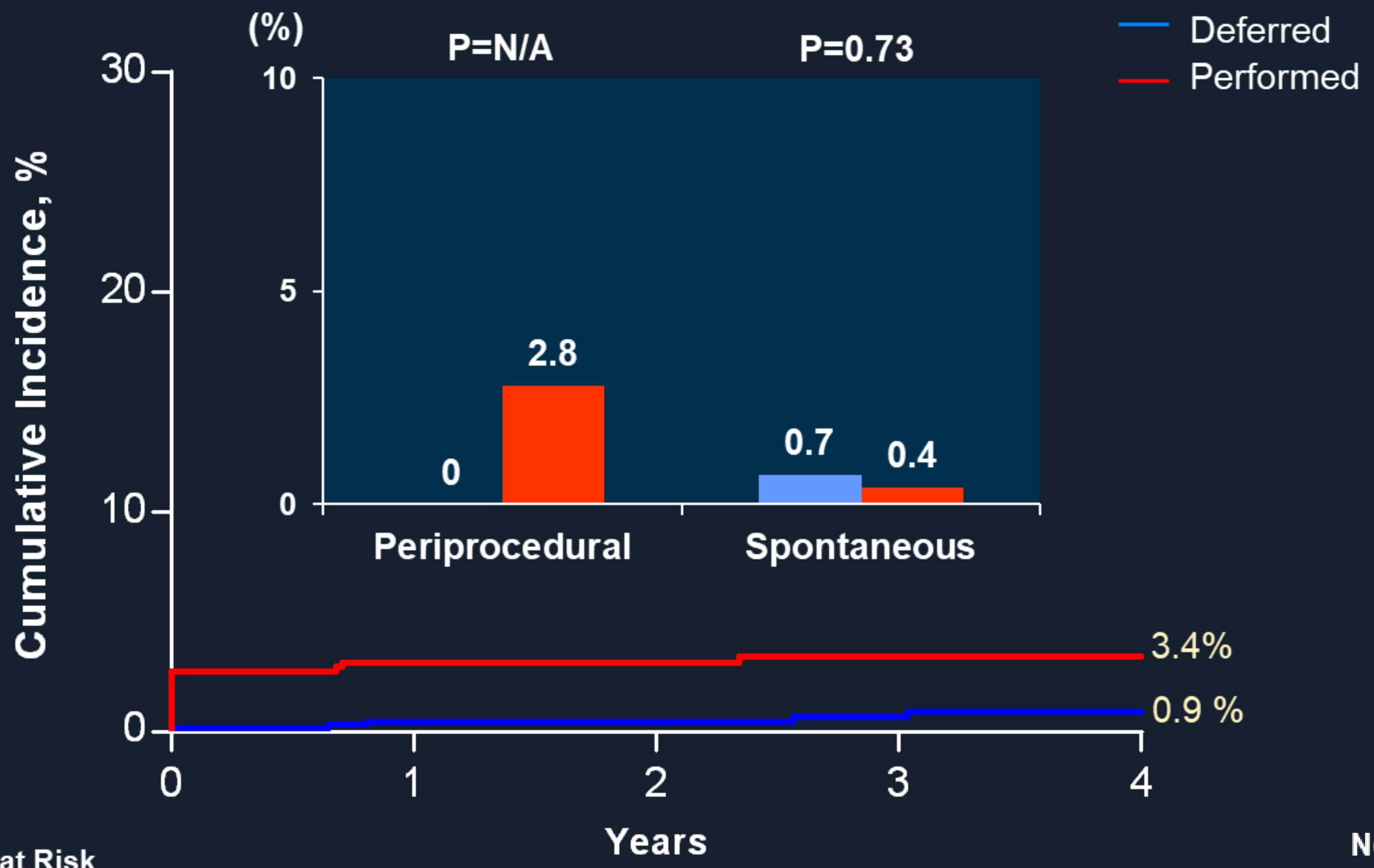


No. at Risk					
Deferred	368	319	262	201	109
Performed	368	276	222	154	89

Kang DY et al. Eur Heart J. 2018;39(18):1610-1619.

Myocardial Infarction

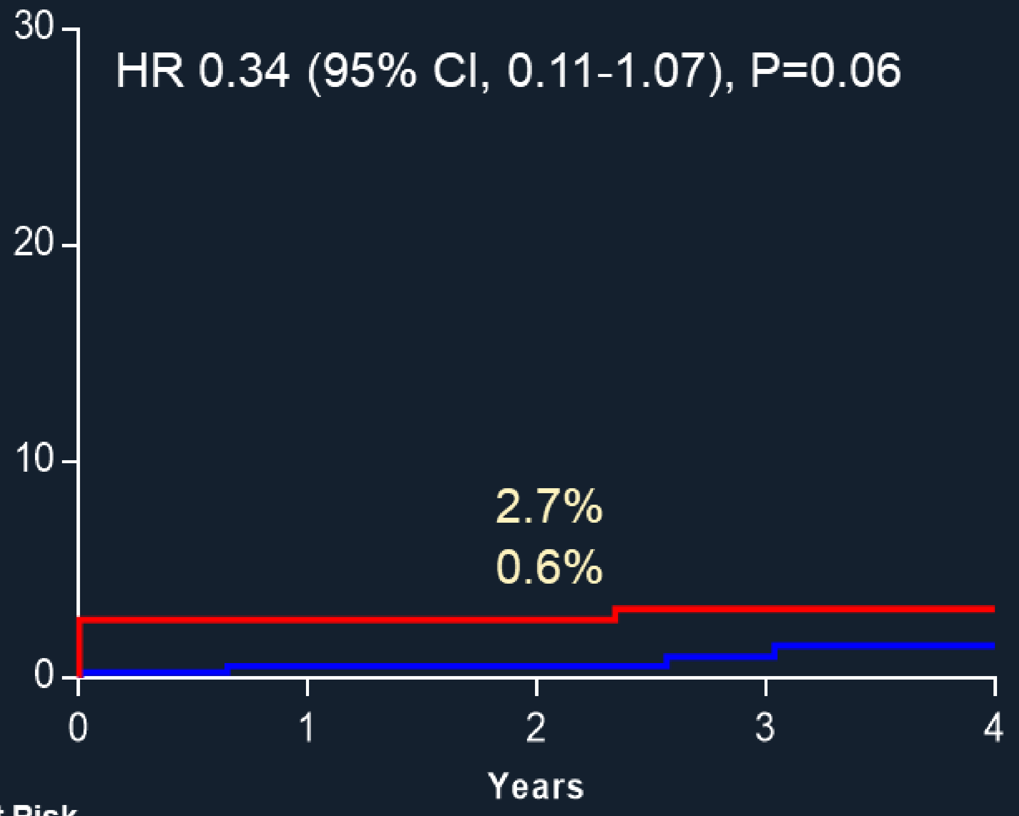
Overall Population



No. at Risk

	0	1	2	3	4
Deferred	683	606	514	387	188
Performed	651	452	353	261	156

Matched Population



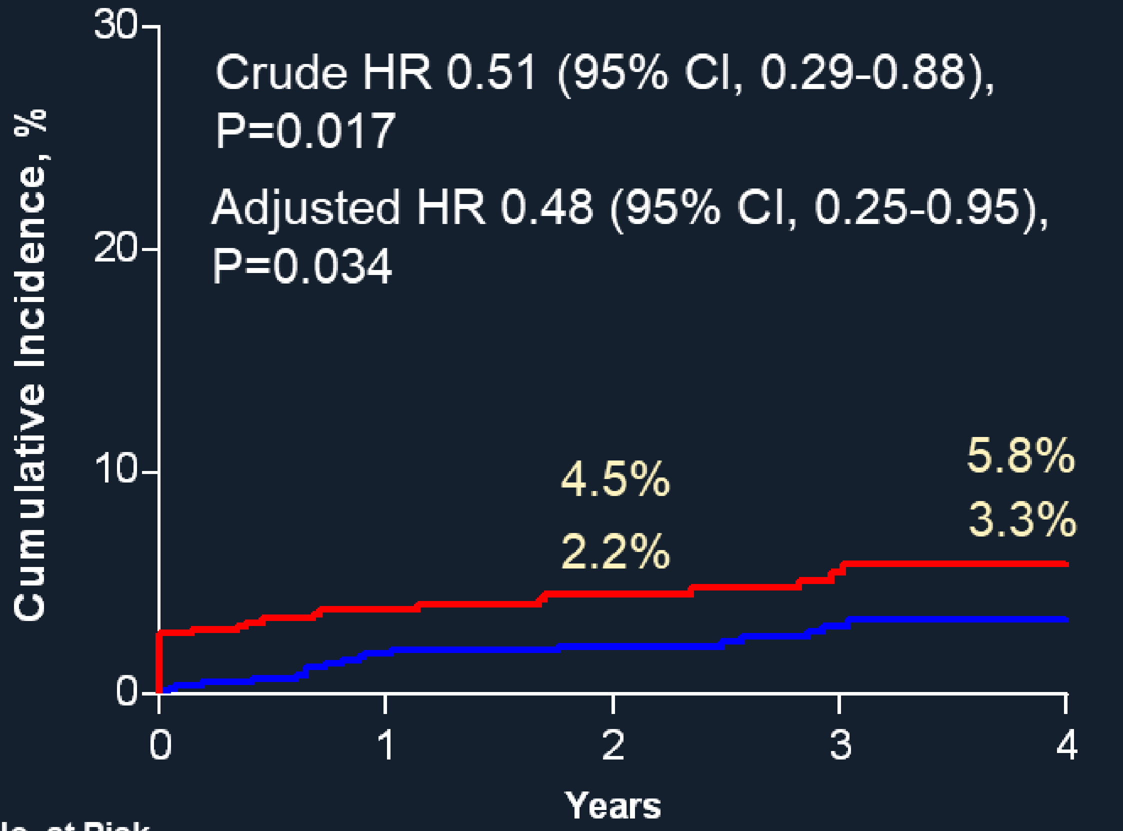
No. at Risk

	0	1	2	3	4
Deferred	368	318	260	200	109
Performed	368	264	210	151	89

Kang DY et al. Eur Heart J. 2018;39(18):1610-1619.

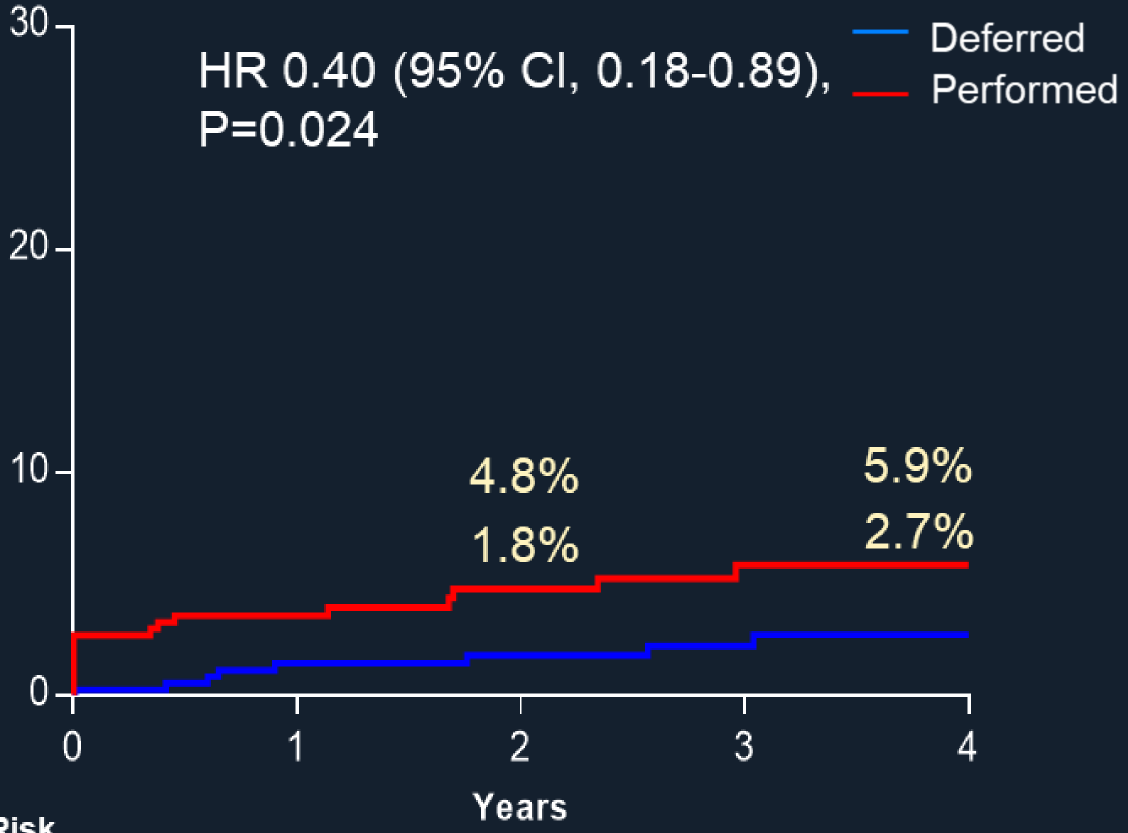
Death and Myocardial Infarction

Overall Population



No. at Risk					
Deferred	683	606	514	388	189
Performed	651	460	358	260	154

Matched Population

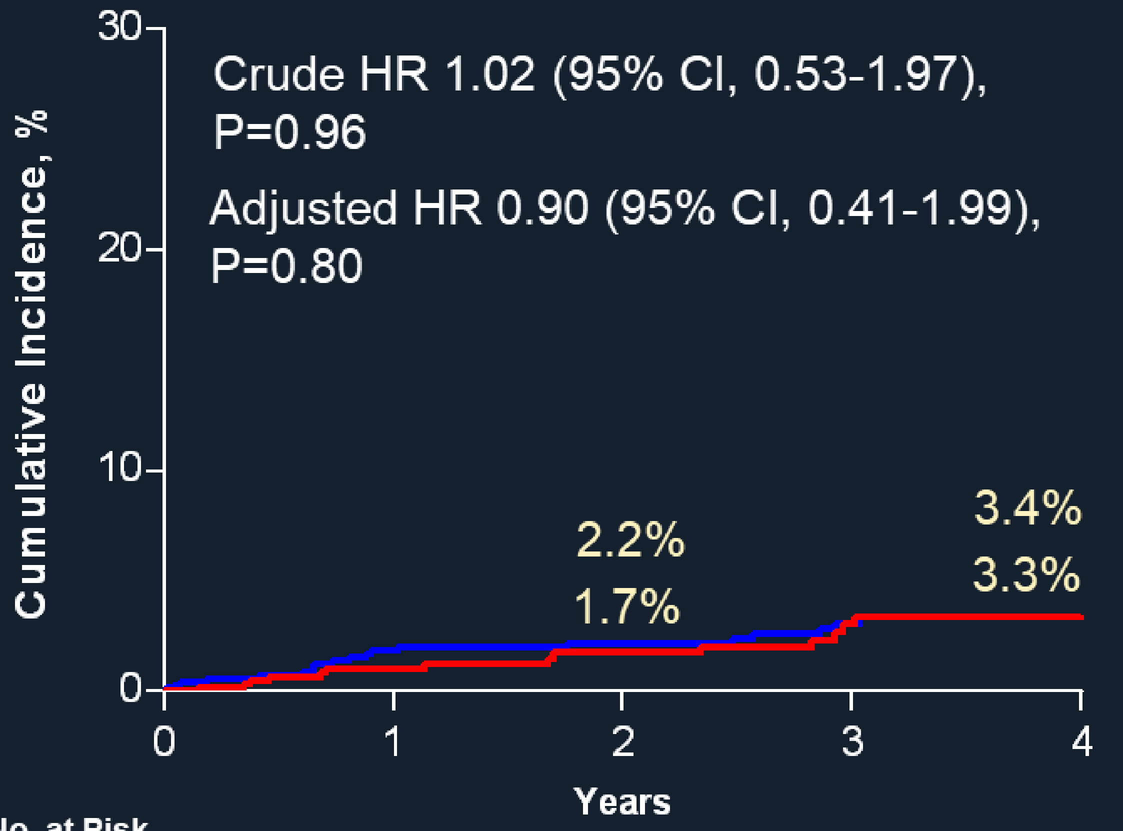


No. at Risk					
Deferred	368	317	260	200	109
Performed	368	268	212	150	87

Kang DY et al. Eur Heart J. 2018;39(18):1610-1619.

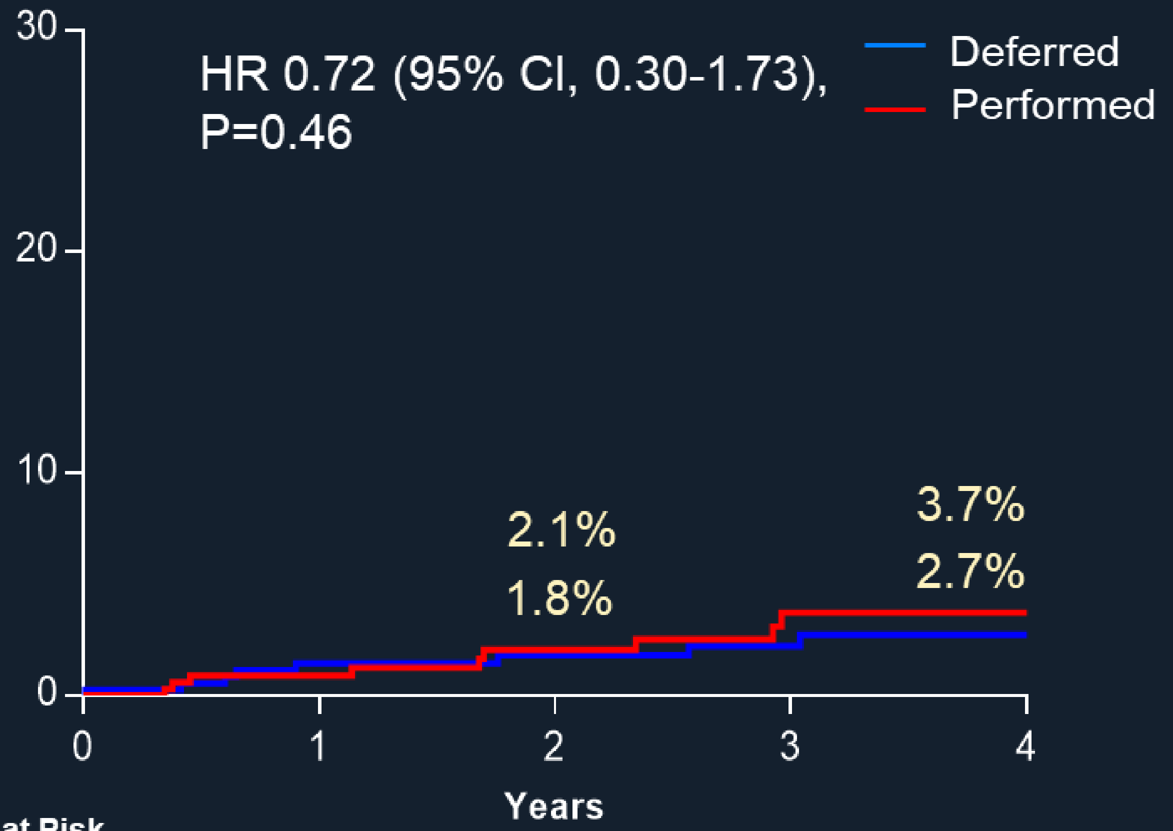
Death and Spontaneous MI

Overall Population



No. at Risk					
Deferred	683	607	515	387	189
Performed	651	475	372	272	162

Matched Population

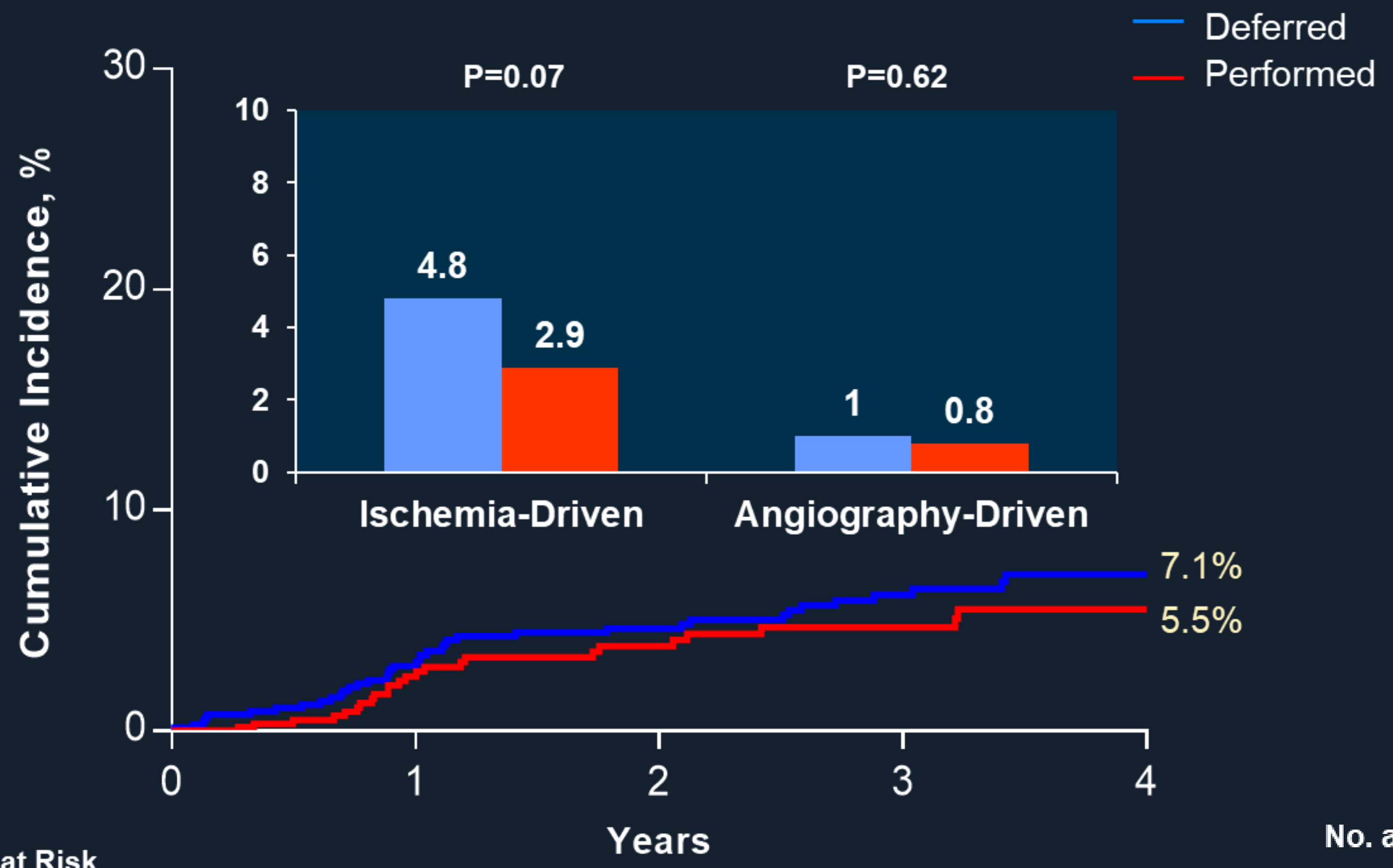


No. at Risk					
Deferred	368	318	260	200	109
Performed	368	276	219	154	90

Kang DY et al. Eur Heart J. 2018;39(18):1610-1619.

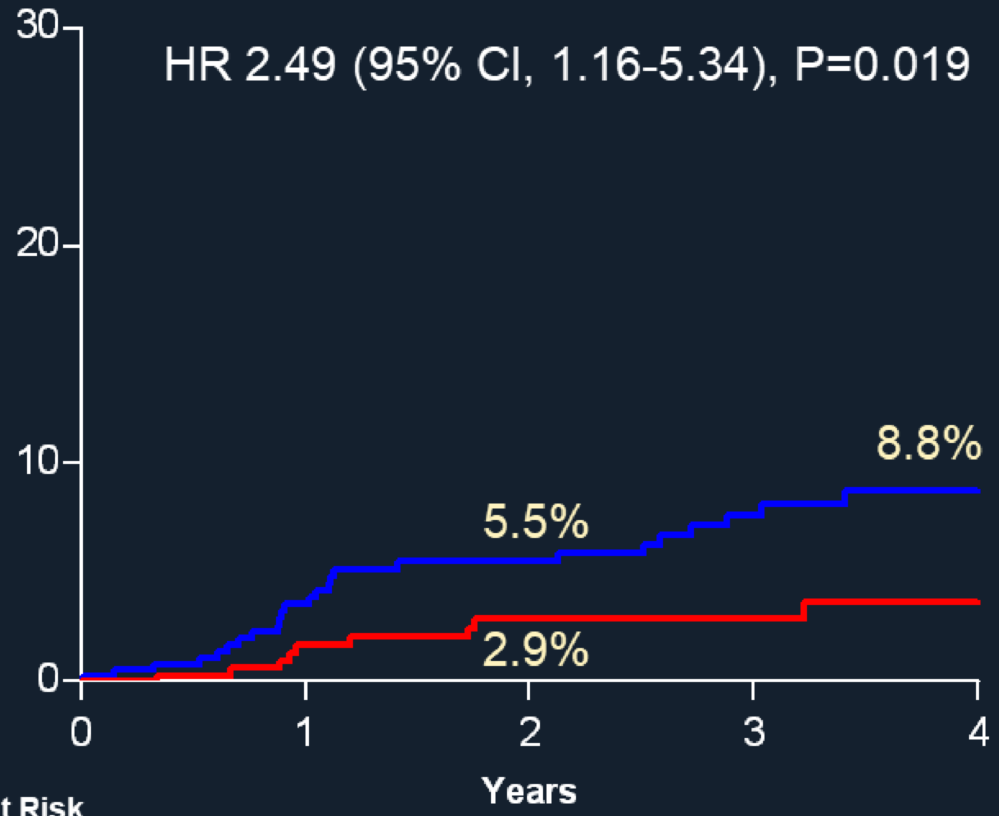
Target Vessel Revascularization

Overall Population



No. at Risk					
Deferred	683	598	500	371	176
Performed	683	467	361	261	154

Matched Population



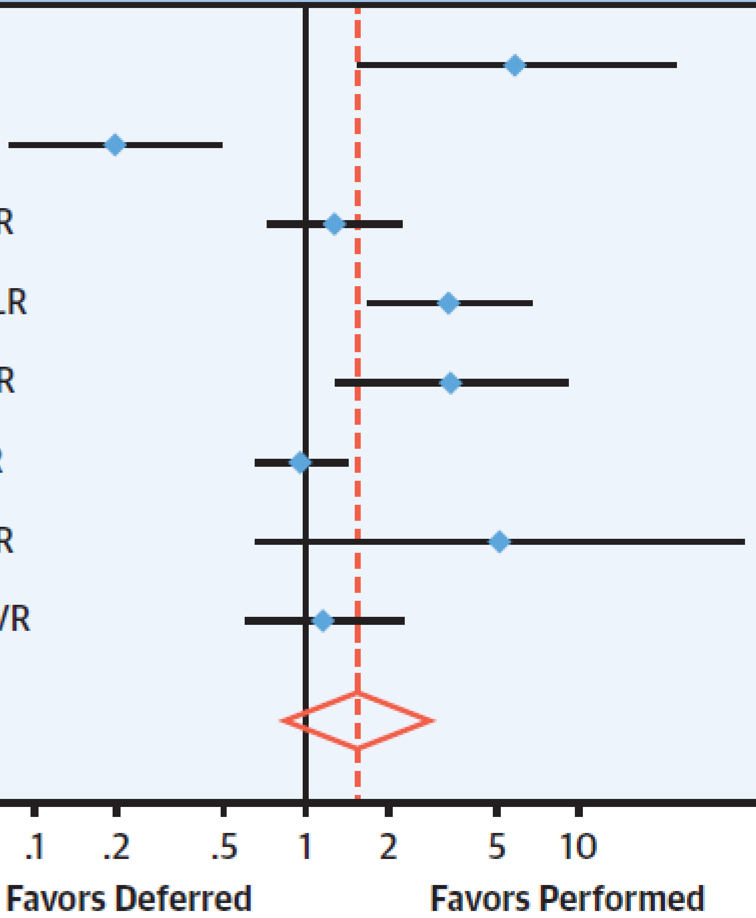
No. at Risk					
Deferred	368	309	249	186	99
Performed	368	271	211	148	87

Kang DY et al. Eur Heart J. 2018;39(18):1610-1619.

Meta-analysis

Study-Level Pooled Analysis Comparing Deferred and Performed PCI in Patients With FFR 0.75-0.80

Study	Definition Composite Outcome	OR (95% CI)	Events, Deferred	Events, Performed	% Weight
Courtis et al. 2008	Death, MI, TVR	5.88 (1.51-22.9)	10/44	3/63	9.49
Lindstaedt et al. 2010	Death, MI, TVR	0.20 (0.08-0.48)	10/48	28/49	12.70
Adjedi et al. 2016	C-death, MI, any R	1.28 (0.72-2.26)	37/266	21/187	15.05
Agarwal et al. 2017	C-death, TL-MI, TLR	3.36 (1.68-6.73)	19/48	31/190	14.19
Kubo et al. 2018	Death, TV-MI, TVR	3.41 (1.28-9.06)	35/185	5/78	12.10
Kang et al. 2018	C-death, MI, TVR	0.95 (0.64-1.40)	55/683	55/651	16.14
Du et al. 2019	C-death, MI, any R	5.13 (0.64-40.9)	10/129	1/62	5.91
ILIAS registry 2021	C-death, TV-MI, TVR	1.16 (0.59-2.25)	22/219	17/193	14.41
Overall Random Effects Model $Z = 1.35$ ($P = 0.178$), $I^2 = 81.0\%$		1.53 (0.82-2.86)	198/1,622	161/1,473	100.00



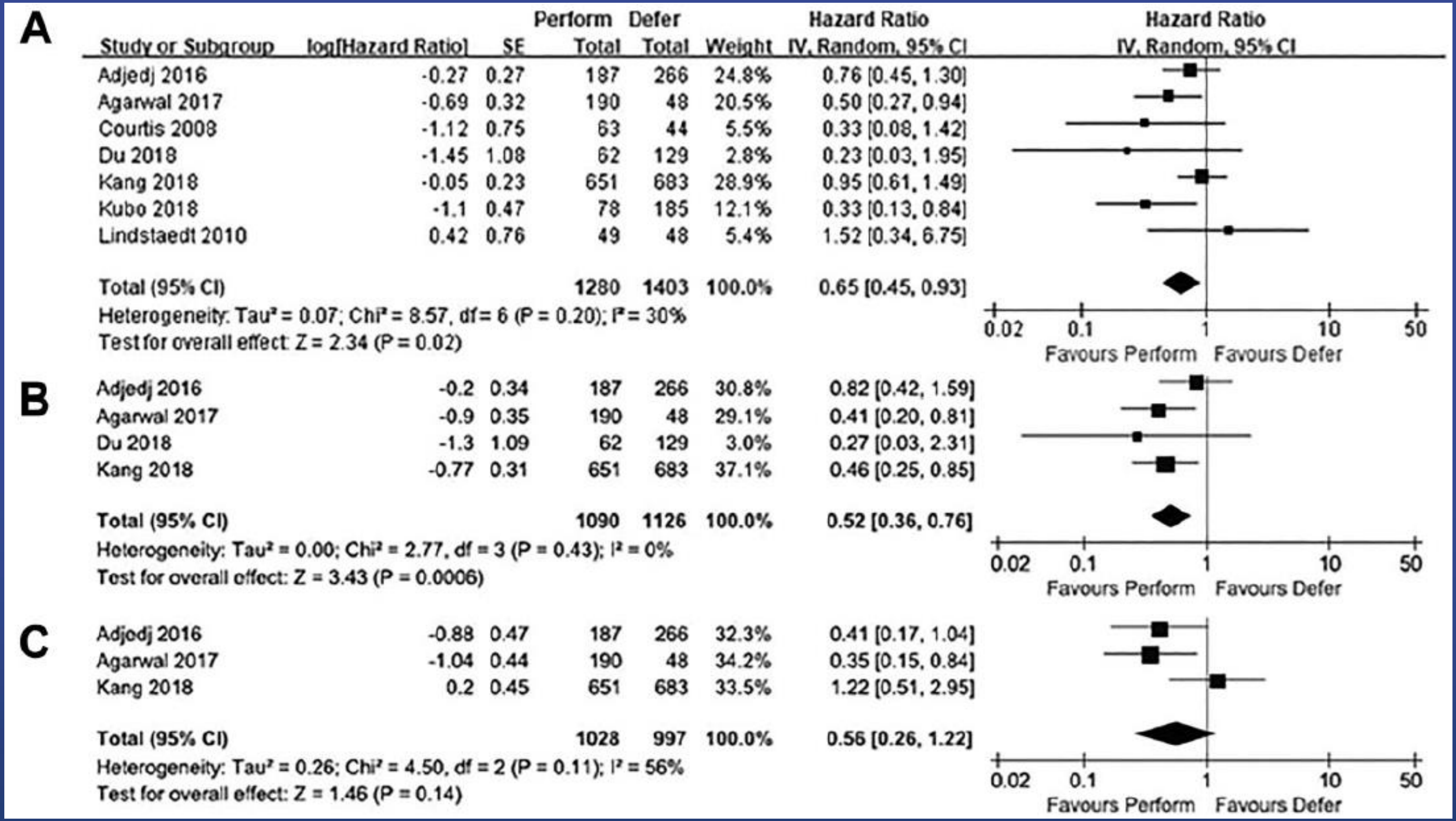
Kim J et al. JACC CV Interv. 2022;15(10):1033-1043.

Meta-analysis

MACE

TVR

Death



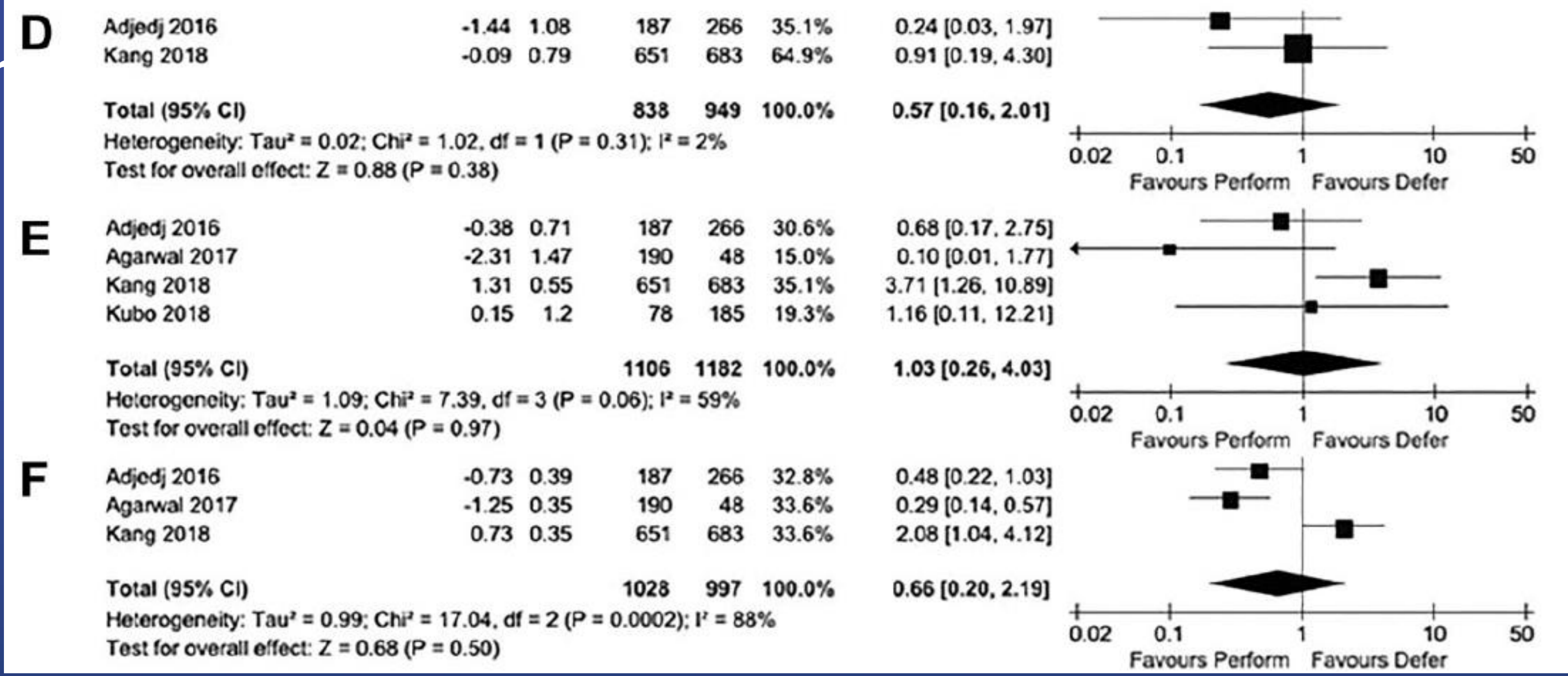
Du Y et al. Angiology. 2020;71(1):48-55.

Meta-analysis

Cardiac Death

MI

Death or MI



D

Adjedj 2016	-1.44	1.08	187	266	35.1%	0.24 [0.03, 1.97]
Kang 2018	-0.09	0.79	651	683	64.9%	0.91 [0.19, 4.30]
Total (95% CI)			**838**	**949**	**100.0%**	**0.57 [0.16, 2.01]**

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 1.02$, df = 1 (P = 0.31); $I^2 = 2\%$
Test for overall effect: Z = 0.88 (P = 0.38)

E

Adjedj 2016	-0.38	0.71	187	266	30.6%	0.68 [0.17, 2.75]
Agarwal 2017	-2.31	1.47	190	48	15.0%	0.10 [0.01, 1.77]
Kang 2018	1.31	0.55	651	683	35.1%	3.71 [1.26, 10.89]
Kubo 2018	0.15	1.2	78	185	19.3%	1.16 [0.11, 12.21]
Total (95% CI)			**1106**	**1182**	**100.0%**	**1.03 [0.26, 4.03]**

Heterogeneity: $Tau^2 = 1.09$; $Chi^2 = 7.39$, df = 3 (P = 0.06); $I^2 = 59\%$
Test for overall effect: Z = 0.04 (P = 0.97)

F

Adjedj 2016	-0.73	0.39	187	266	32.8%	0.48 [0.22, 1.03]
Agarwal 2017	-1.25	0.35	190	48	33.6%	0.29 [0.14, 0.57]
Kang 2018	0.73	0.35	651	683	33.6%	2.08 [1.04, 4.12]
Total (95% CI)			**1028**	**997**	**100.0%**	**0.66 [0.20, 2.19]**

Heterogeneity: $Tau^2 = 0.99$; $Chi^2 = 17.04$, df = 2 (P = 0.0002); $I^2 = 88\%$
Test for overall effect: Z = 0.68 (P = 0.50)

Du Y et al. Angiology. 2020;71(1):48-55.

GzFFR RCT : Defer vs. PCI in Gray-zone FFR

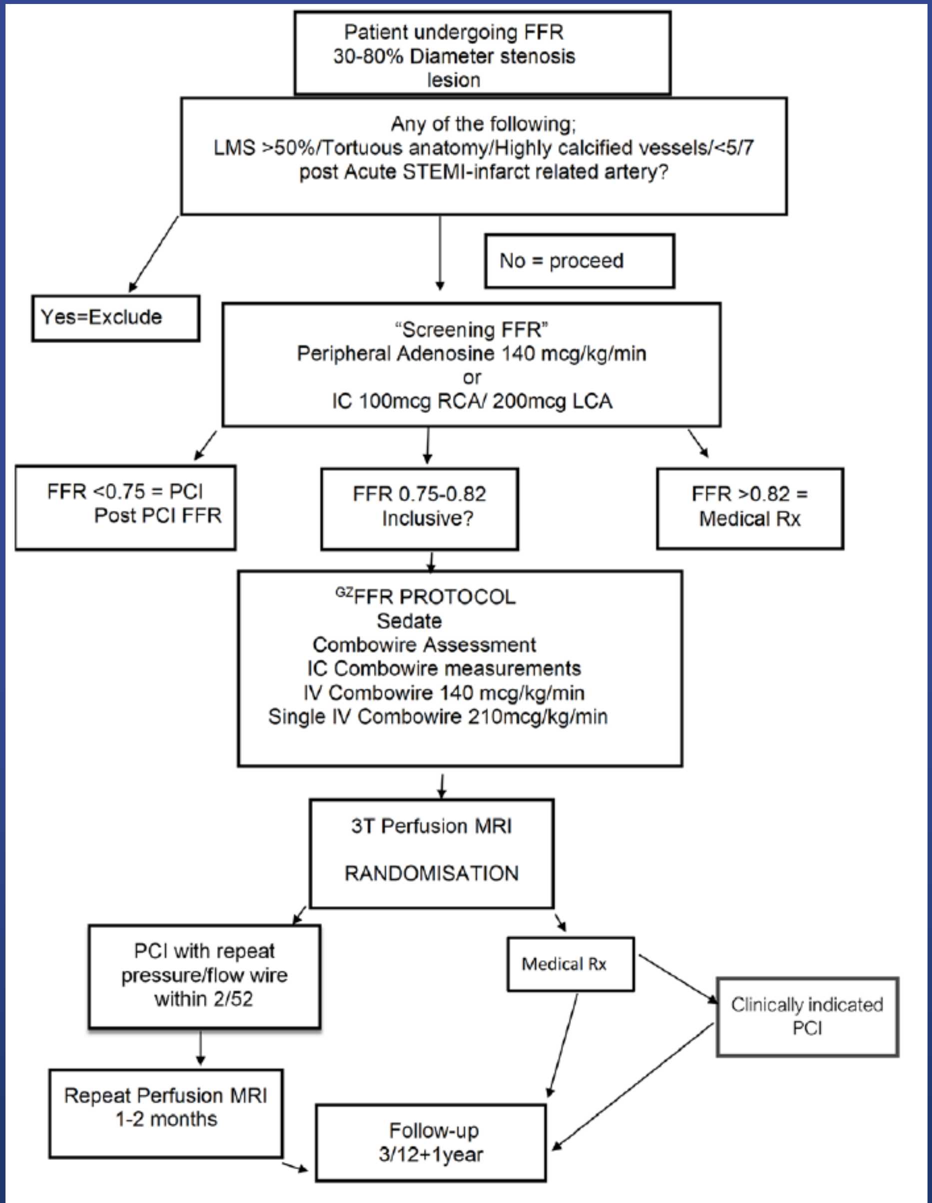


Table 1 Risk factors according to treatment strategy and symptom status, previous cardiac history and mode of presentation at time of recruitment

Variable	OMT n=52	PCI n=52
Age	61 (SD 9.0)	60 (SD 8.0)
Male	39 (75%)	40 (76.9%)
Female	13 (25%)	12 (23.1%)
Current smoker	13 (25%)	21 (40.3%)
Previous smoking	13 (25%)	11 (21.1%)
HTN	**44 (84.6%)**	**31 (59.6%)**
Hyperlipidaemia	31 (59.6%)	38 (73.1%)
T2DM	10 (19.2%)	10 (19.2%)
IDDM	2 (3.8%)	2 (3.8%)
FHX CAD	38 (73.1%)	33 (63.5%)
PVD	4 (7.7%)	6 (11.5%)
Cerebrovascular disease	4 (7.7%)	4 (7.7%)

Hennigan B et al. Heart. 2020.

GzFFR RCT : Defer vs. PCI in Gray-zone FFR

Table 3 Quantitative coronary angiographic data according to treatment strategy

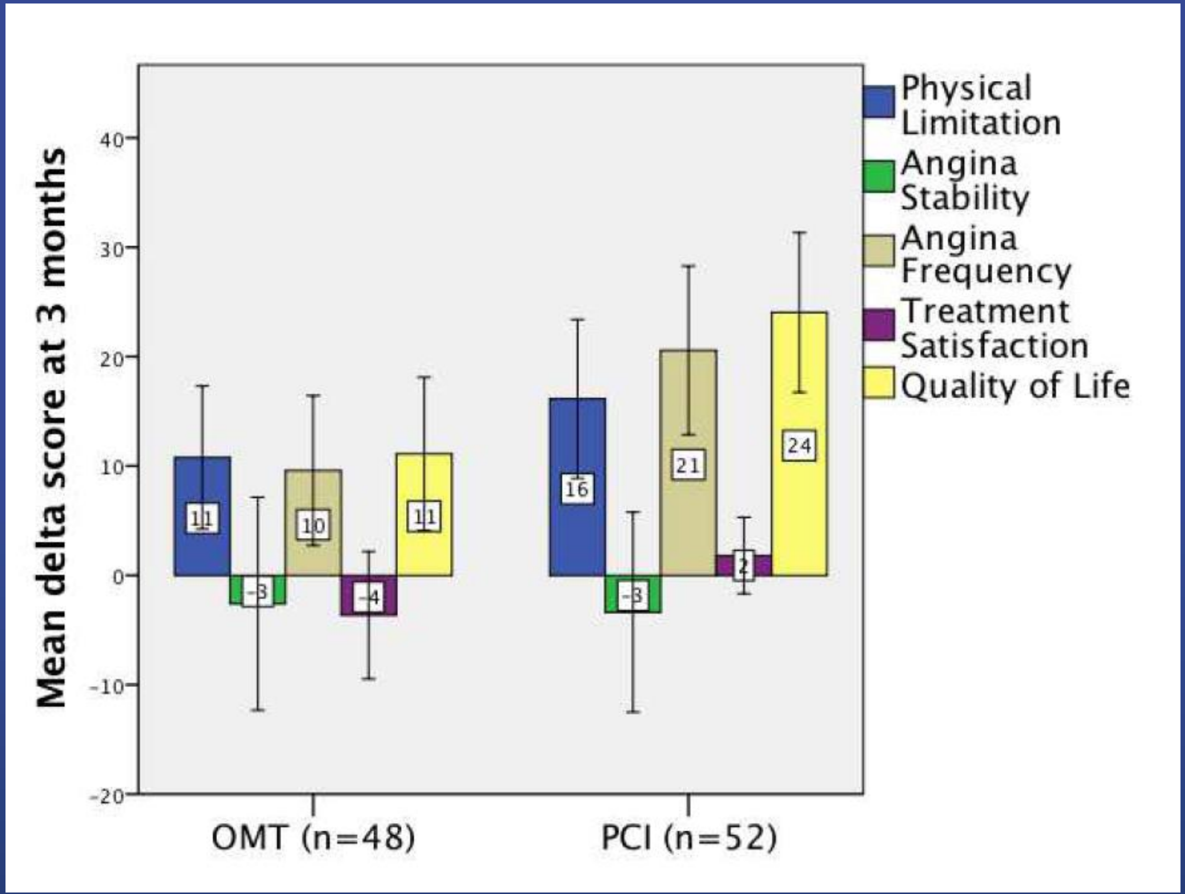
Variable	OMT (n=52)	PCI (n=52)
Diameter stenosis (%)	44 (8)	45 (10)
Area stenosis (%)	69 (8)	69 (10)
Lesion length (mm)	10 (4)	10 (4)
APPROACH Score (%)	32 (9)	32 (8)

eTable 5: This table includes all patients with MRI data at enrollment and demonstrates the numbers of patients according to the numbers of segments with detectable ischemia in the ^{GZ}FFR territory.

Total number Grey Zone FFR segments per patient with any detectable ischemia	0	1	2	3	4
Total Patient number (n=98)(%)	74(75.5%)	8(8.2%)	10(10.2%)	5(5.1%)	1(1%)

Hennigan B et al. Heart. 2020.

GzFFR RCT : Defer vs. PCI in Gray-zone FFR



Secondary outcomes at 3 months

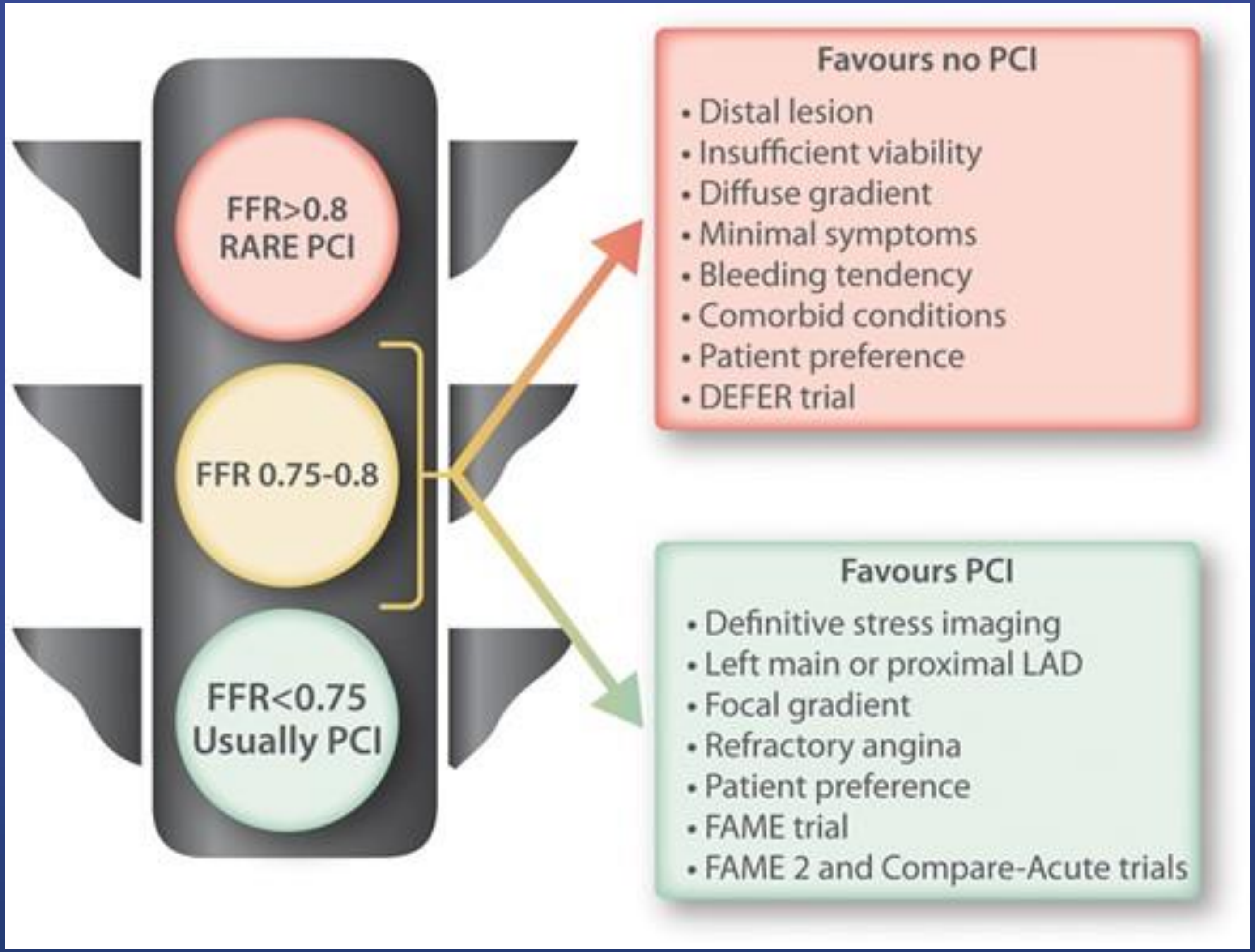
This study was not powered to detect a difference in hard clinical endpoints. All-cause mortality at 3 months was 3/52 (5.7%) in OMT group (all confirmed non-cardiac deaths) vs 0/52 (0%) in PCI group.

eTable 7: 12-month Seattle Angina Score Delta values according to treatment strategy

Questionnaire Parameter	Group	N	Mean delta	Standard. Deviation	P value
SAQ Summary Delta Score	OMT	45	9.8	18	0.208
	PCI	44	15.1	21	
Physical limitation Delta Score	OMT	45	2.9	20	0.07
	PCI	44	11.6	24	
Anginal stability Delta Score	OMT	45	.5	32	0.62
	PCI	44	-2.8	32	
Anginal frequency Delta Score	OMT	45	13.5	25	0.77
	PCI	44	15.2	29	
Treatment satisfaction Delta Score	OMT	45	-2.3	16	0.35
	PCI	44	.9	17	
Quality of Life Delta Score	OMT	45	12.9	24	0.27
	PCI	44	18.5	24	

Hennigan B et al. Heart. 2020.

Decision-Making in Gray-zone FFR



Johnson N, Zimmerman F. Eur Heart J. 2018;39(18):1620-1622.

FAME 3

1500 Multivessel CAD Patients 48 centers

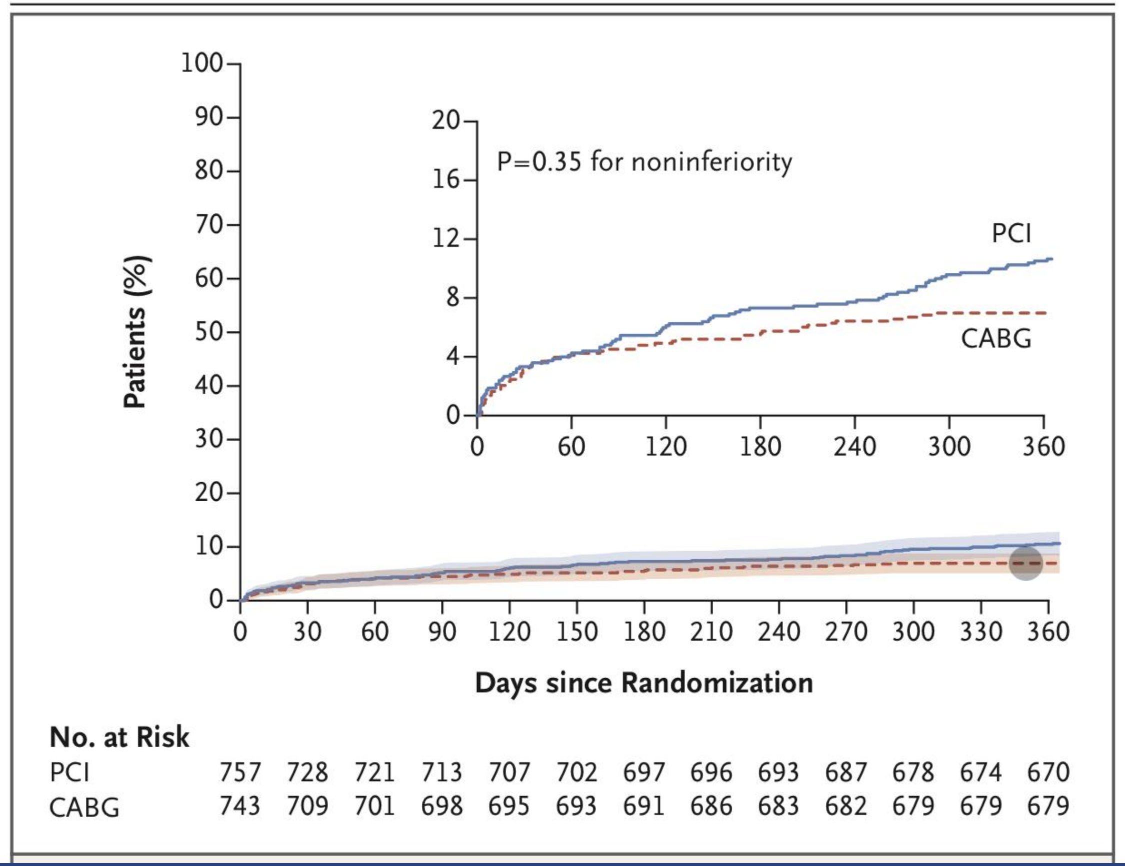
R

CABG | FFR Guided PCI

Primary Endpoint at 1 year:
Death from any cause, myocardial infarction,
Stroke, or repeat revascularization

N Engl J Med 2022;386:128-37. DOI: 10.1056/NEJMoa2112299

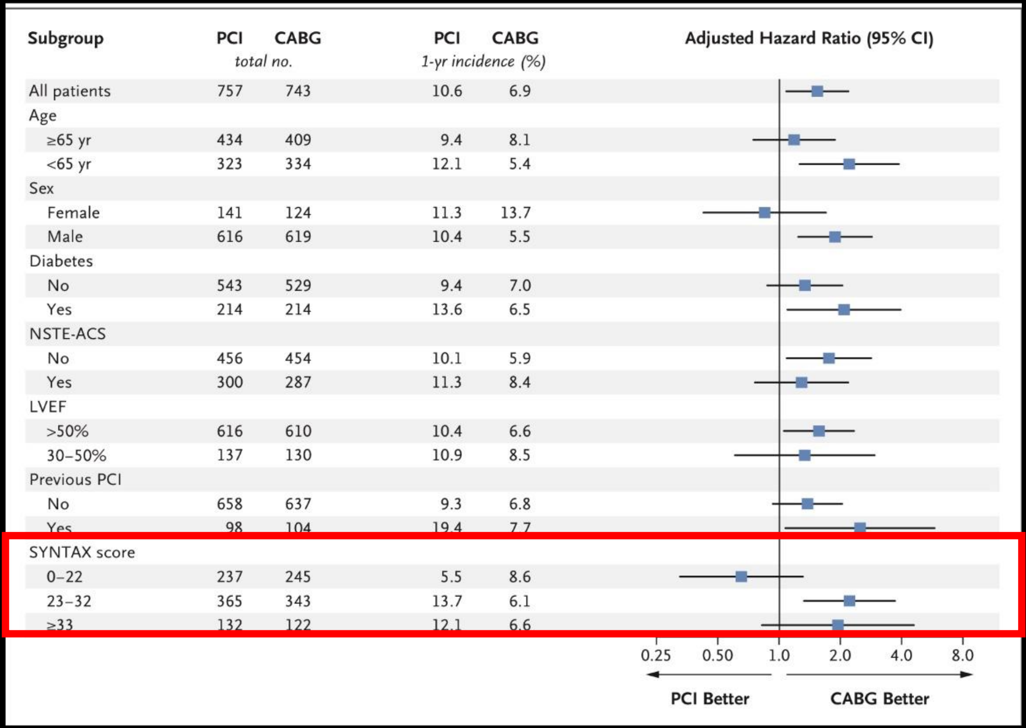
FAME 3



FFR-guided PCI did not meet criteria for non-inferiority compared with CABG in patients with angiographic three-vessel disease.

N Engl J Med 2022;386:128-37. DOI: 10.1056/NEJMoa2112299

FAME 3



Subgroup	PCI	CABG	PCI	CABG	Adjusted Hazard Ratio (95% CI)
	total no.		*1-yr incidence (%)*		
All patients	757	743	10.6	6.9	
Age					
≥65 yr	434	409	9.4	8.1	
<65 yr	323	334	12.1	5.4	
Sex					
Female	141	124	11.3	13.7	
Male	616	619	10.4	5.5	
Diabetes					
No	543	529	9.4	7.0	
Yes	214	214	13.6	6.5	
NSTE-ACS					
No	456	454	10.1	5.9	
Yes	300	287	11.3	8.4	
LVEF					
>50%	616	610	10.4	6.6	
30–50%	137	130	10.9	8.5	
Previous PCI					
No	658	637	9.3	6.8	
Yes	98	104	19.4	7.7	
SYNTAX score					
0–22	237	245	5.5	8.6	
23–32	365	343	13.7	6.1	
≥33	132	122	12.1	6.6	

* benefit with PCI among patients with low SYNTAX scores

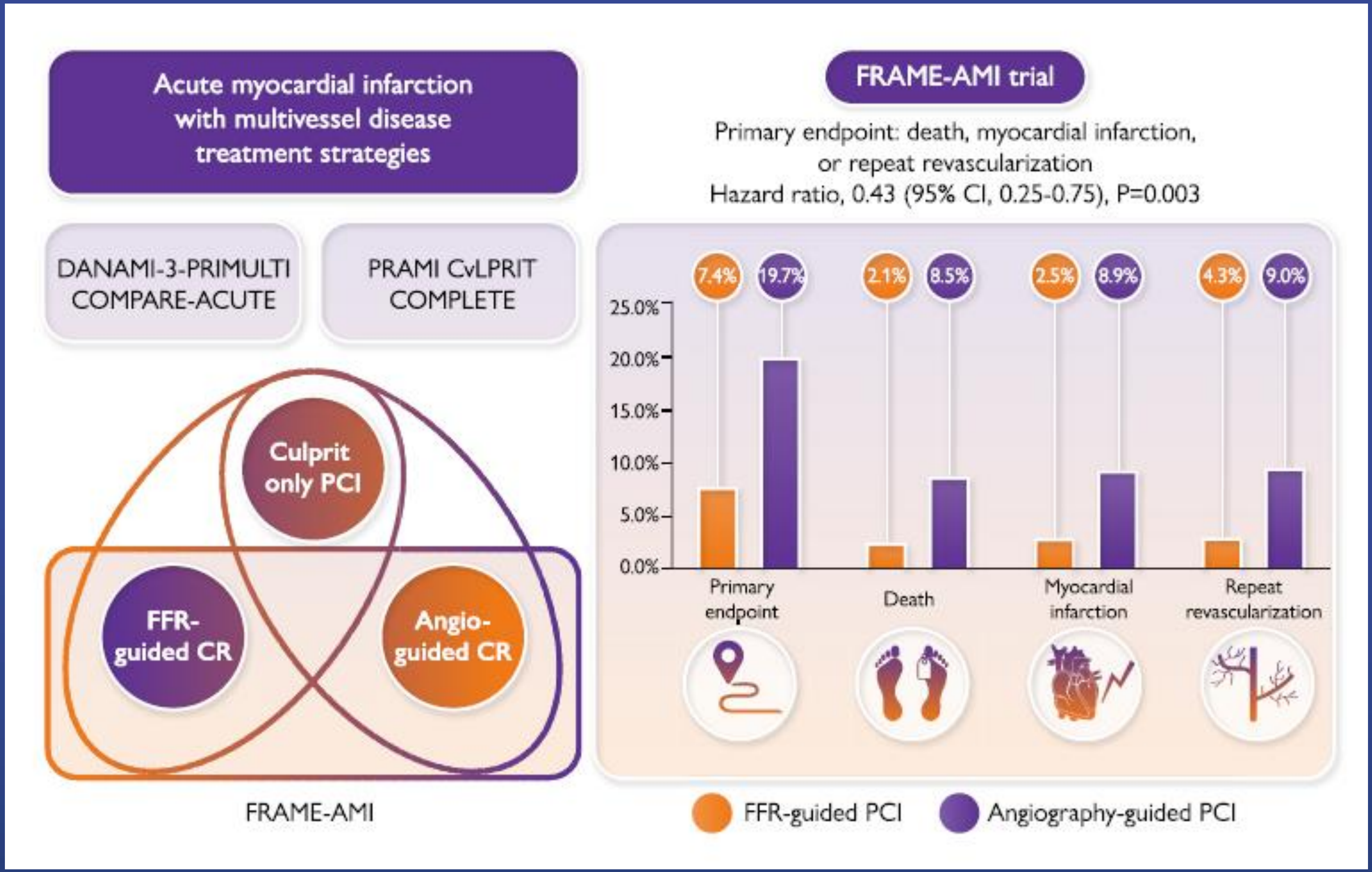
Table 2. Angiographic and Procedural Characteristics.*

Characteristic	PCI (N=757)	CABG (N=743)
Median time to procedure (IQR) — days	4 (1–13)	13 (6–26)
Median procedure duration (IQR) — min	87 (67–113)	197 (155–239)
Median length of hospital stay (IQR) — days	3 (1–7)	11 (7–16)
No. of lesions	4.3±1.3	4.2±1.2
At least one chronic total occlusion — no./total no. (%)	157/755 (20.8)	171/739 (23.1)
At least one bifurcation lesion — no./total no. (%)	522/755 (69.1)	491/739 (66.4)
SYNTAX score†	26.0±7.1	25.8±7.1
SYNTAX score category — no./total no. (%)†		
Low, 0 to 22	237/734 (32.3)	245/710 (34.5)
Intermediate, 23 to 32	365/734 (49.7)	343/710 (48.3)
High, >32	132/734 (18.0)	122/710 (17.2)
PCI characteristics		
Staged procedure — no./total no. (%)	166/750 (22.1)	NA
No. of stents	3.7±1.9	NA
Median total length of stents placed (IQR) — mm	80 (52–116)	NA
Intravascular imaging used — no./total no. (%)	87/744 (11.7)	NA
CABG characteristics		
Multiple arterial grafts — no./total no. (%)	NA	173/705 (24.5)
No. of distal anastomoses	NA	3.4±1.0
LITA used as graft — no./total no. (%)	NA	684/705 (97.0)
Off-pump surgery — no./total no. (%)	NA	168/698 (24.1)
FFR used before CABG — no./total no. (%)	NA	72/718 (10.0)

*IVUS/OCT was used in only 12% of patients

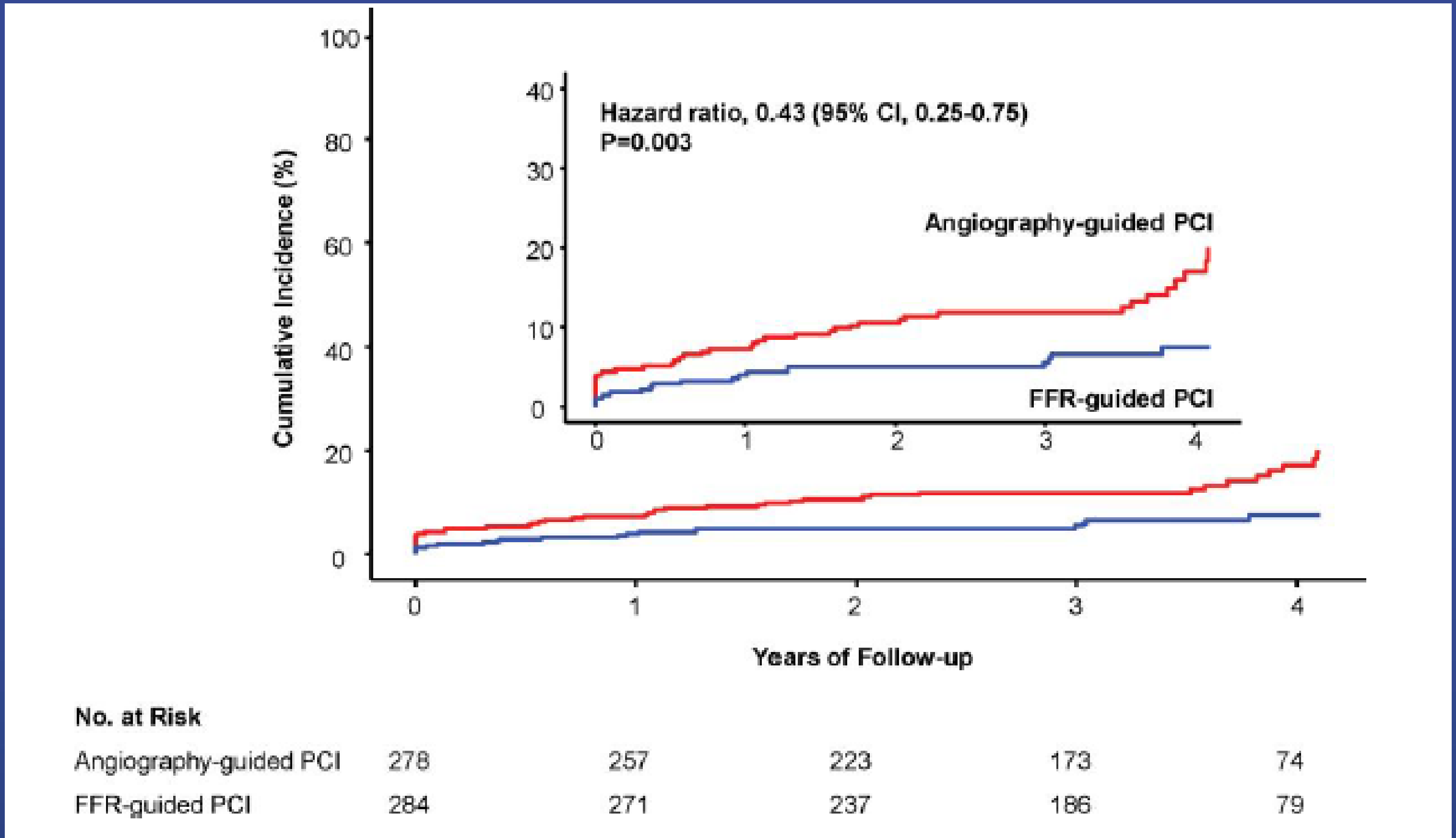
2023 Feb 7;44(6):473-484.

FRAME-AMI



JM Lee et el. Eur Heart J 2023 Feb 7;44(6):473-484

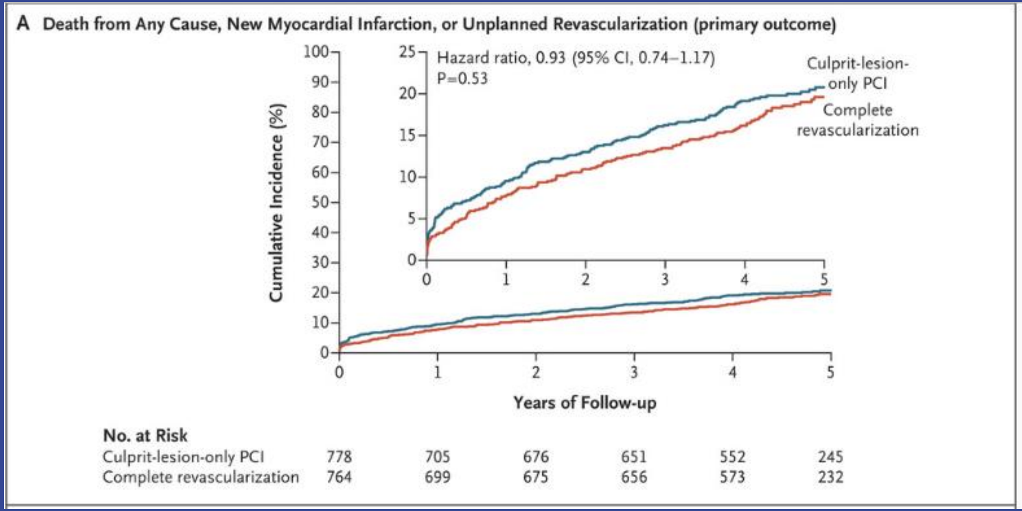
FRAME-AMI

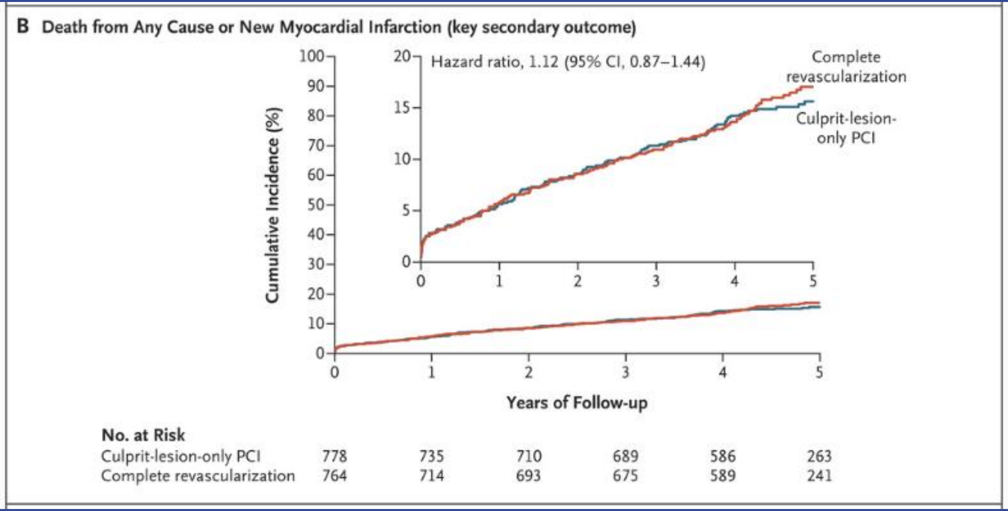


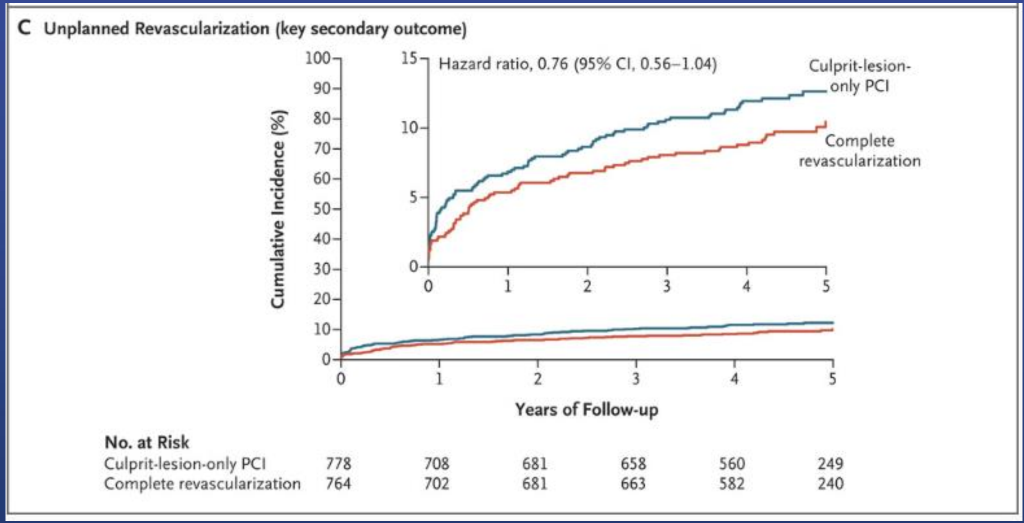
In acute MI and multivessel coronary artery disease, selective PCI using FFR was superior to routine PCI based on angiography for non-infarct-related artery lesions regarding the risk of death, MI, or repeat revascularization.

JM Lee et el. Eur Heart J 2023 Feb 7;44(6):473-484

FULL REVASC Trial

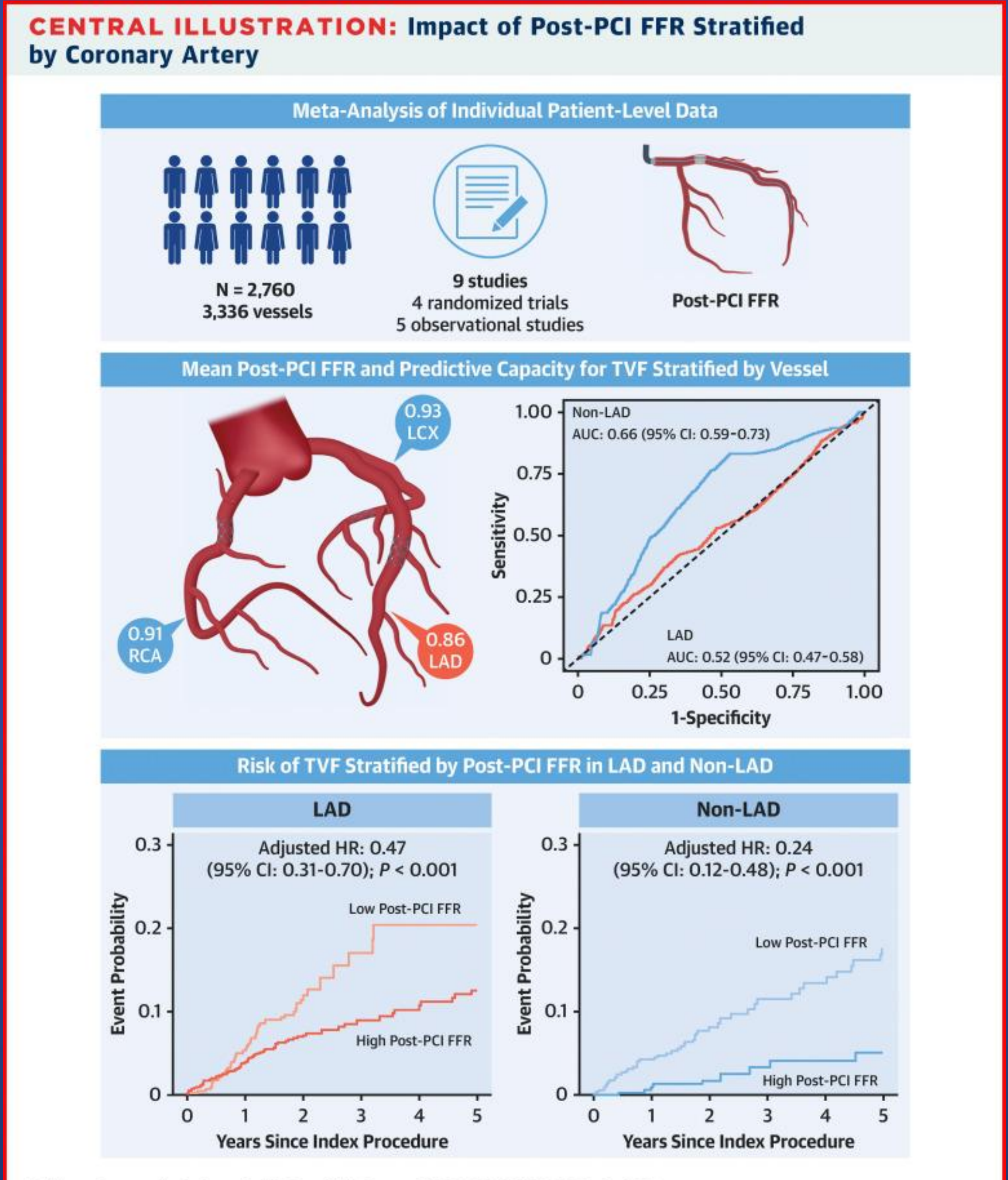






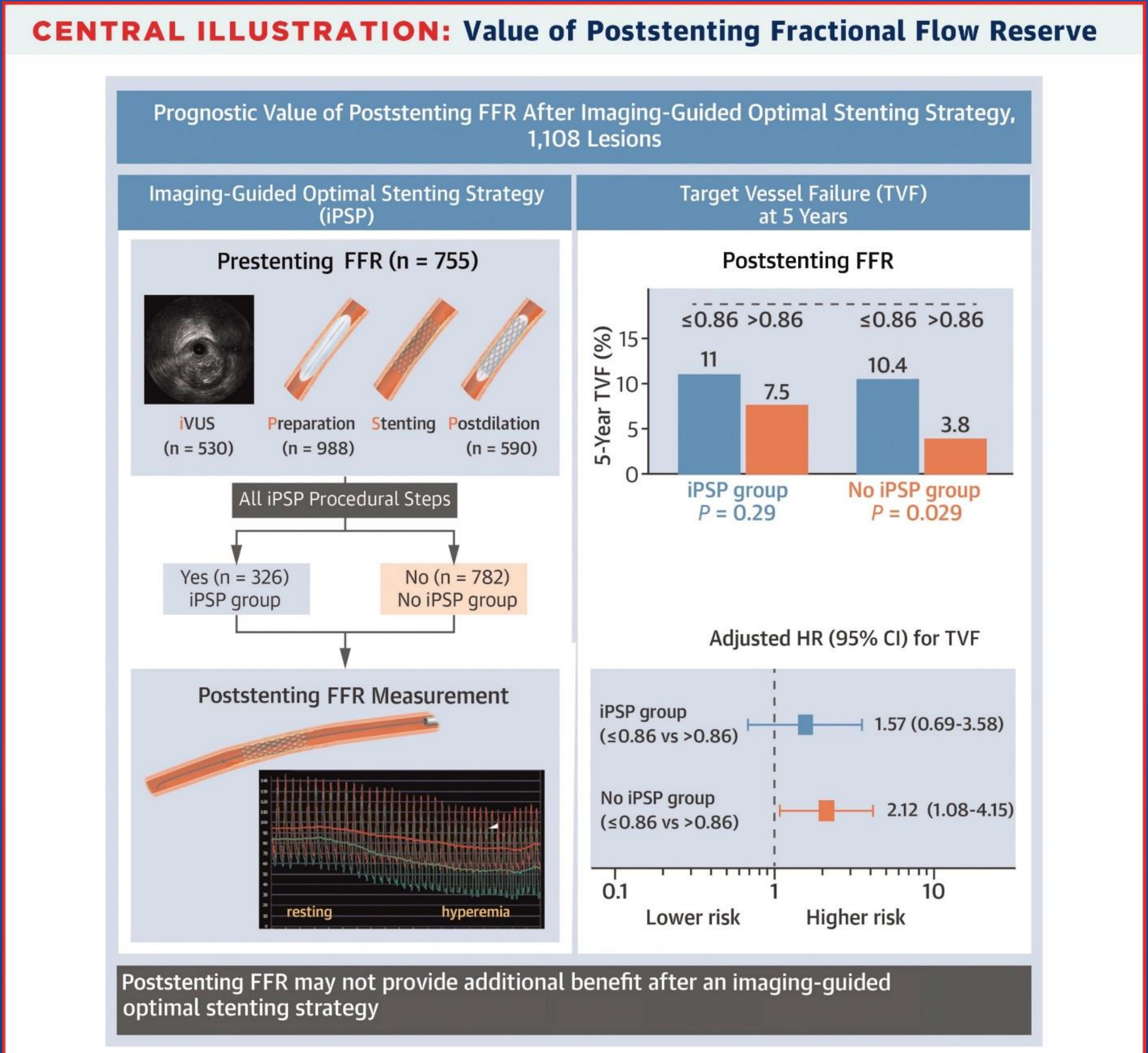
The FULL REVASC trial showed that, among patients with STEMI or very-high-risk NSTEMI and multivessel coronary artery disease, a strategy of routine FFR-guided complete revascularization was not superior to a strategy of culprit-lesion-only PCI in reducing the risk of death from any cause, myocardial infarction, or unplanned revascularization at a median follow-up of 4.8 years.

Poststenting FFR



Collet C, et al. J Am Coll Cardiol Intv. 2023;16(19):2396-2408.

Poststenting FFR

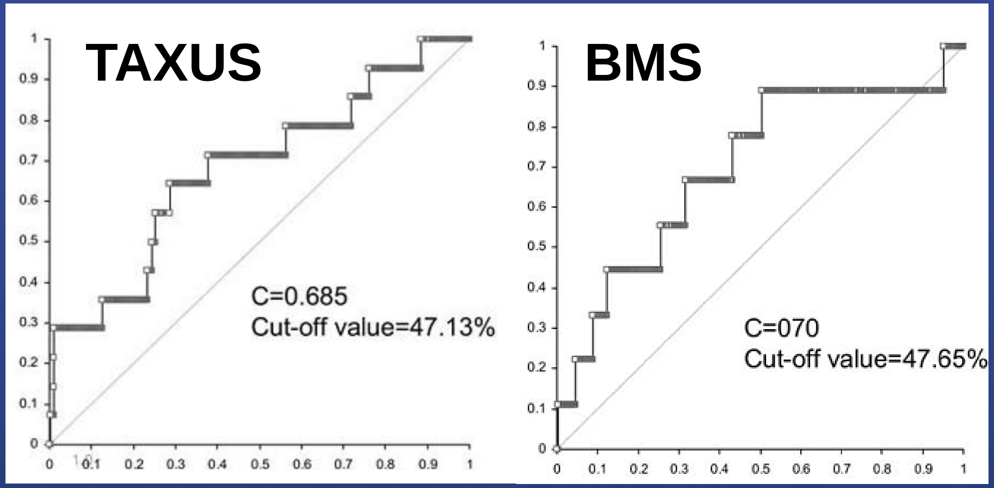


Ahn J-M, et al. J Am Coll Cardiol Intv. 2024;17(7):907-916.

IVUS

Residual Plaque Predicts Edge Restenosis

	Population	DES	F/U time	Predictor
SIRIUS[1]	6 edge restenosis vs. 162 controls	SES	8 mo	**Ref segment PB** 60% vs. 41% (p<0.01)
TAXUS[2]	276 edge stenosis	PES	9 mo	**Ref segment PB 47%**

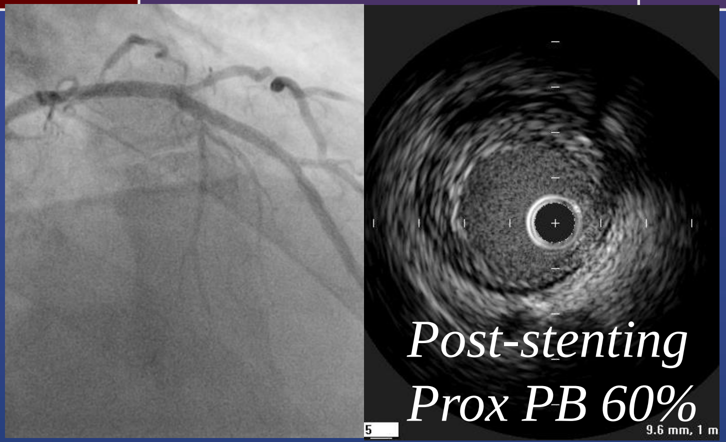


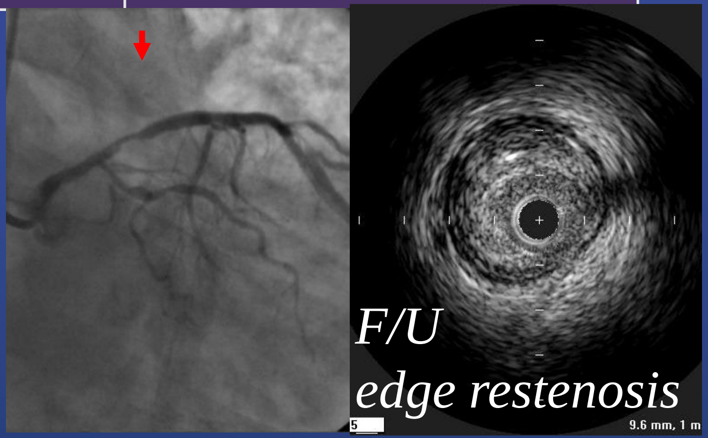
predict 9-mo edge restenosis

[1] *Am J Cardiol 2005;96:1251-3*
[2]*Liu et al. Am J Cardiol 2009;103:501-6*

Residual Plaque Predicts DES Thrombosis

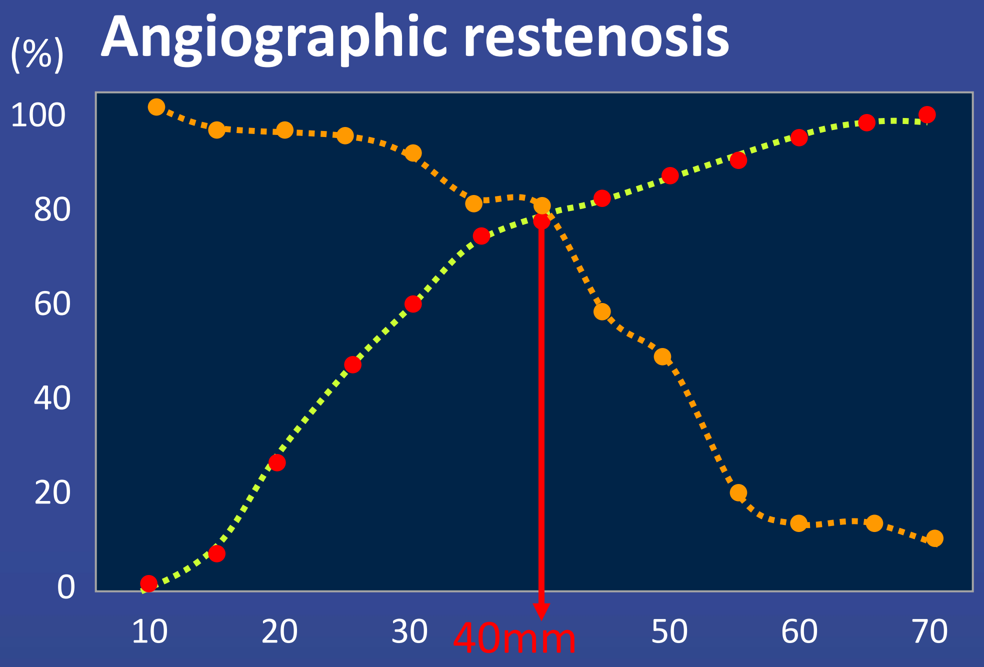
	Population	DES	Endpoint	Predictor
Fujii[1]	15 ST vs. 45 controls	SES	ST <1 mo	**Ref. PB** 62% vs. 46%
Okabe[2]	13 ST vs. 27 controls	DES	ST <1 yr	**Ref. PB** 66% vs. 56%
Liu[3]	20 ST vs. 50 controls	DES	ST <1 yr	**Ref. PB** 57% vs. 38%



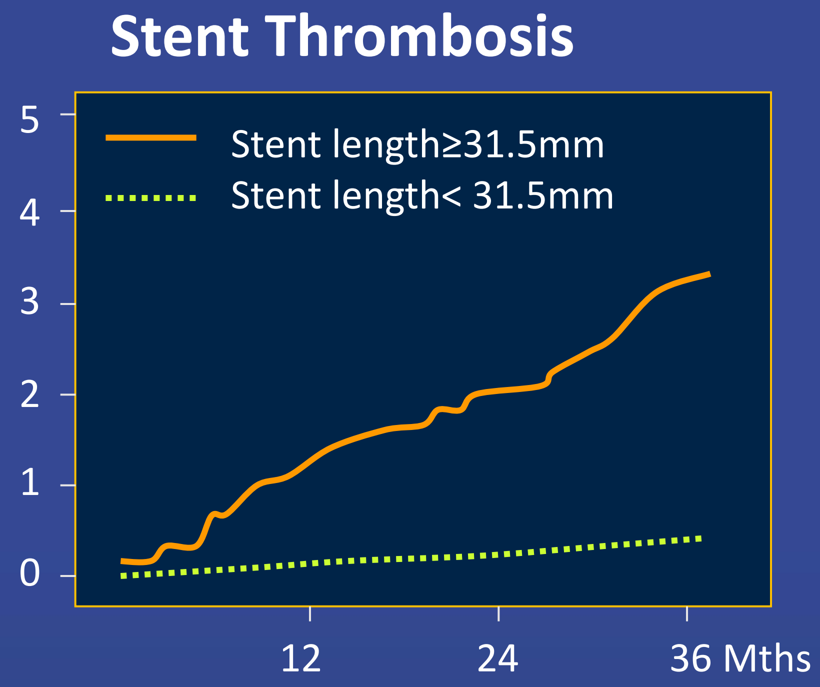


[1] *Fujii et al. J Am Coll Cardiol 2005;45:995-8*
[2] *Okabe et al. Am J Cardiol 2007;100:615-20*
[3] *Liu et al. JACC Cardiovasc Interv. 2009;2:428-34*

Stent Length Predicts DES Failure



Sensitivity 81%, Specificity 78%



HR 7.8 (95% CI 2.5–24.1)

IVUS-guided PCI is necessary to achieve full lesion coverage and to avoid the waste of stent

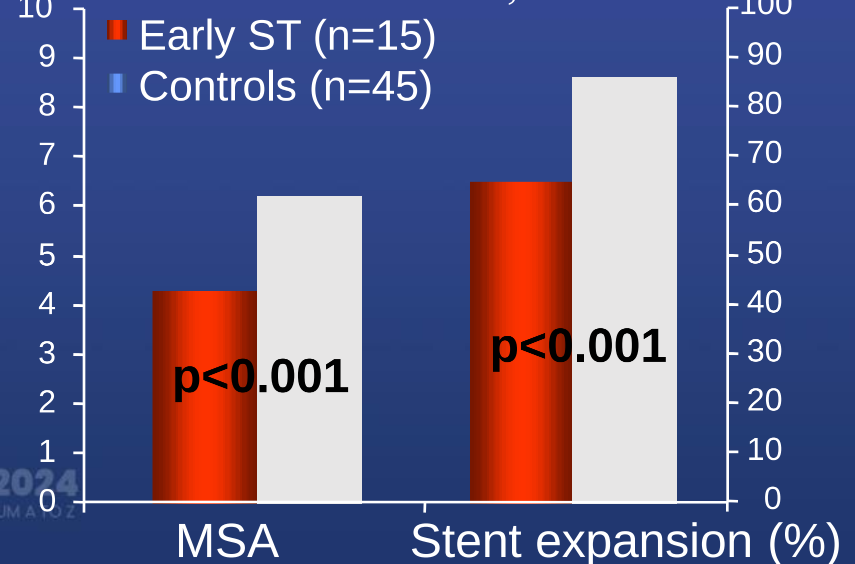
Hong et al. Eur Heart J 2006;27:1305-10

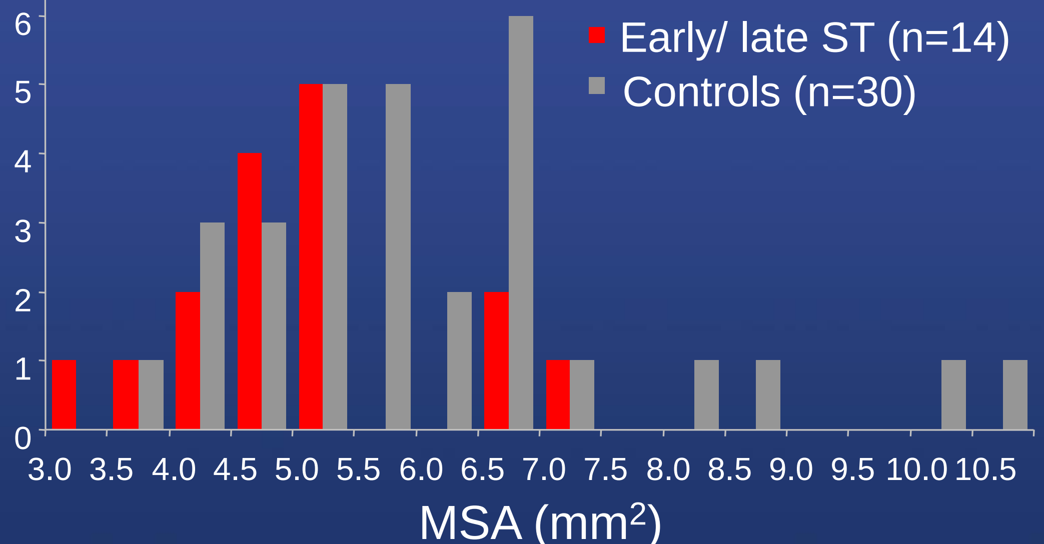
Suh et al. JACC interv 2010;3:383-9

Underexpansion Predicts DES Restenosis

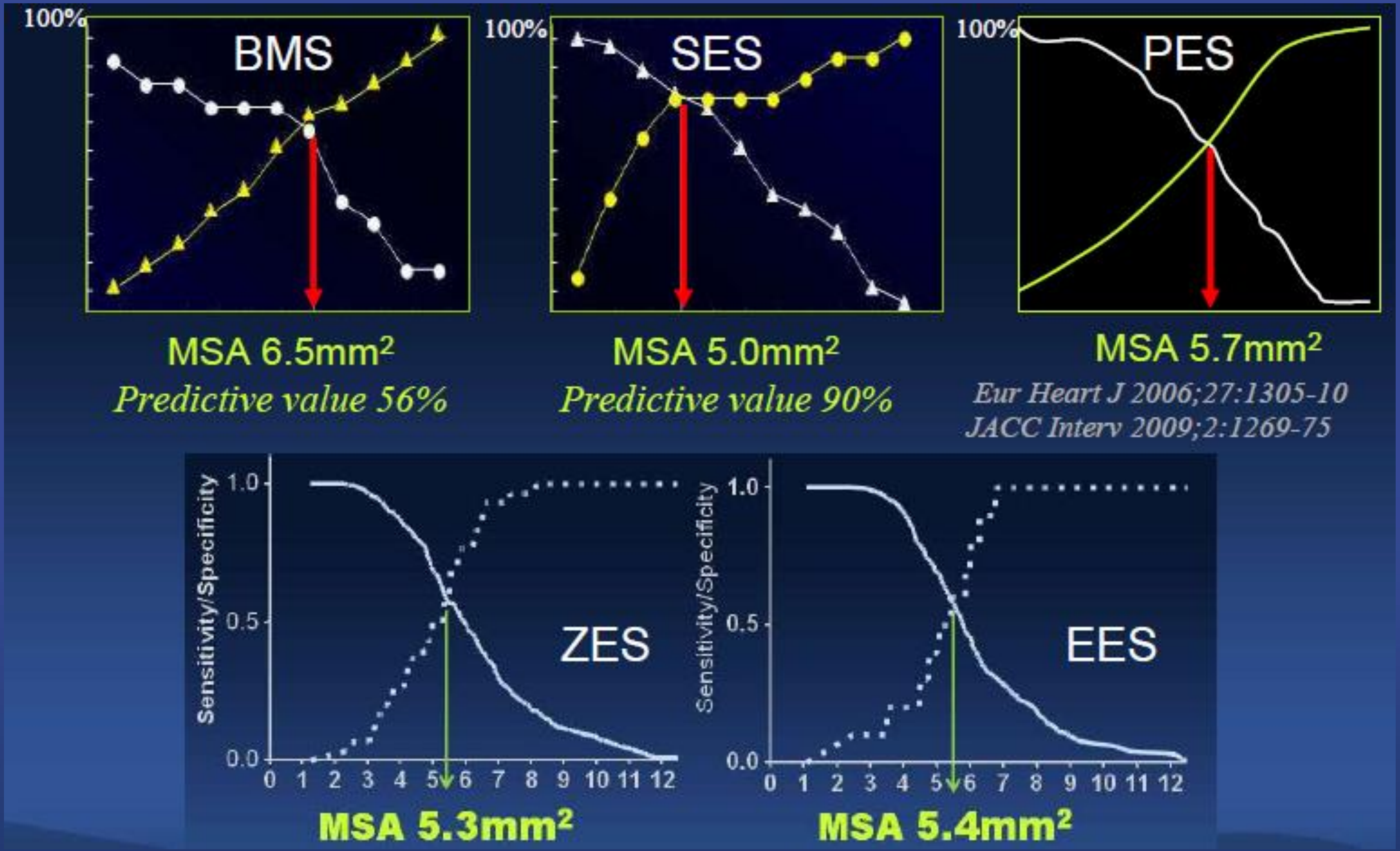
	Population	DES	Endpoint	Rate of Underexpansion
Fujii [1]	15 ST vs. 45 controls	SES	ST <1 month	<5.0mm^2 in 80% vs. 29%
Okabe [2]	13 ST vs. 27 controls	DES	ST <1 year	<5.0mm^2 in 79% vs. 40%
Liu [3]	20 ST vs. 50 controls	DES	ST <1 year	<5.0mm^2 in 85% vs. 26%

[1] *J Am Coll Cardiol 2005;45:995-8* [2] *Am J Cardiol 2007;100:615-20* [3] *JACC interv 2009;2:428-34*





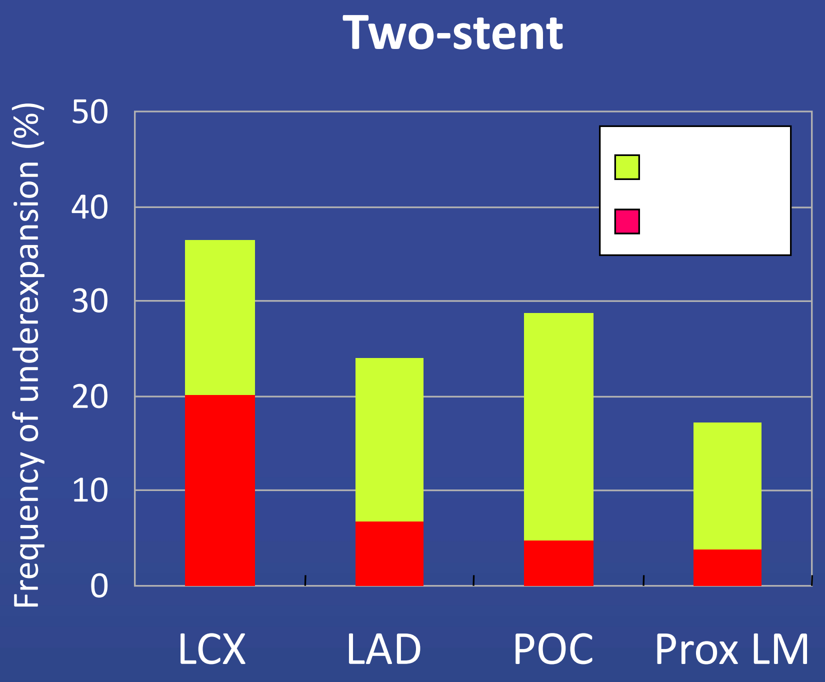
Underexpansion Predicts DES Restenosis

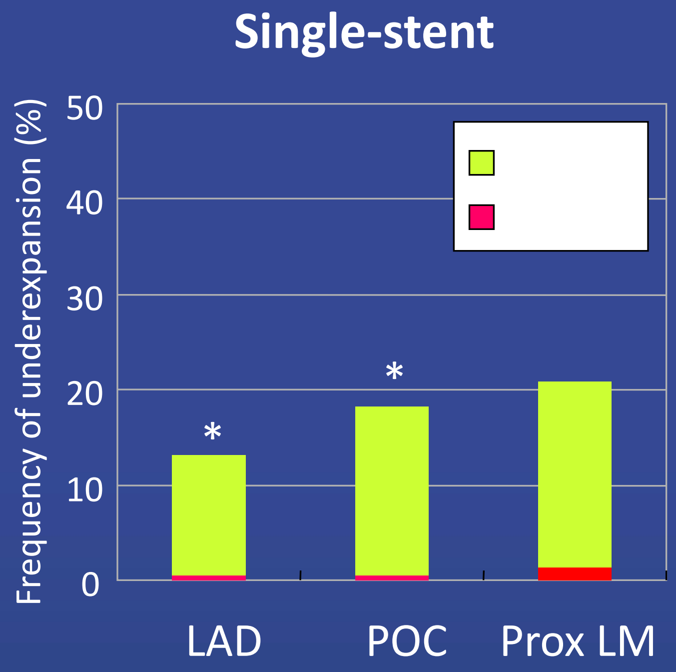


Song et al. Catheter Cardiovasc Interv 2012;

Frequency of Underexpansion and ISR

33.8% *had underexpansion of at least one stented segment*





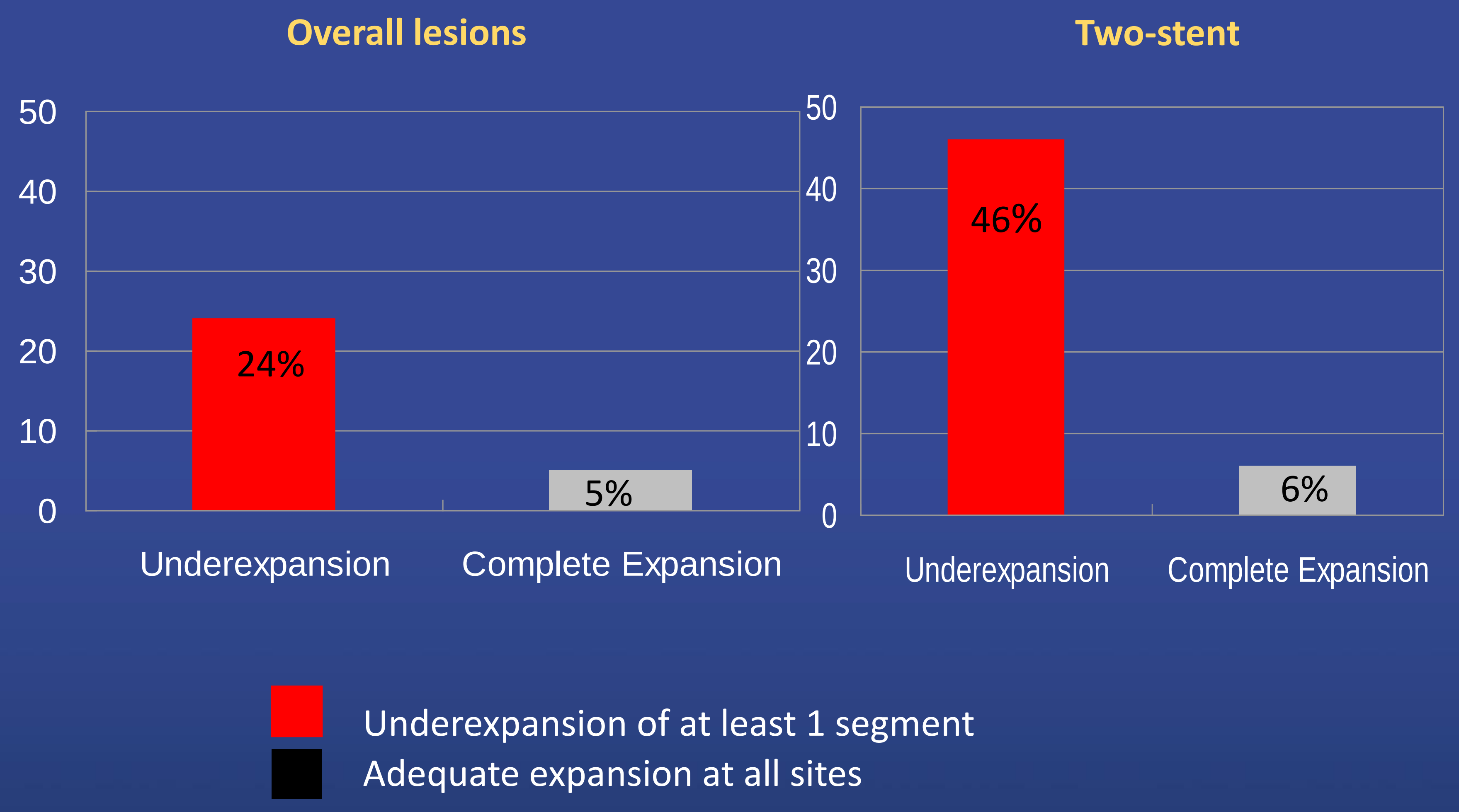
* *single-stent vs. two-stent, p<0.05*

54% had underexpansion in at least one of the 4 stented segments

27% had underexpansion in at least one of the 3 stented segments

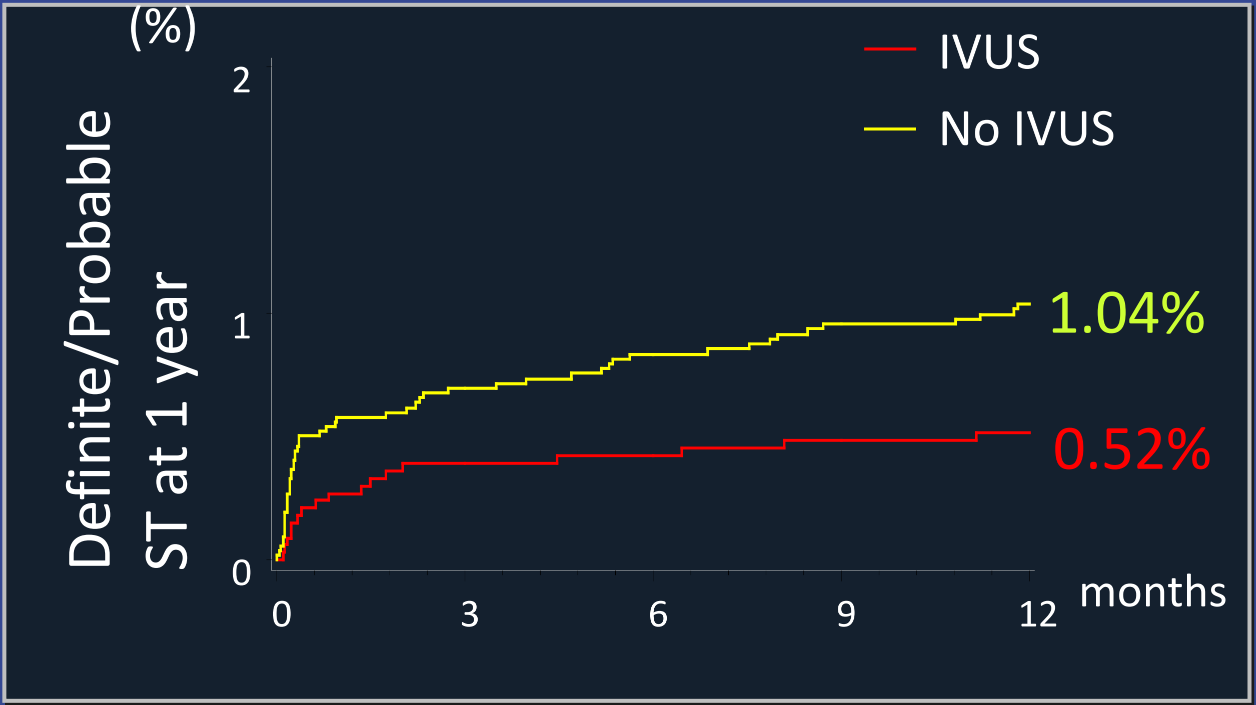
Frequency of ISR in LM Lesions

with vs without Underexpansion



Kang et al. Circ Cardiovasc Interv 2011 2011;4:1168-74

ADAPT-DES 1-year Outcomes



p=0.01
HR 0.50
95%CI 0.29-0.86

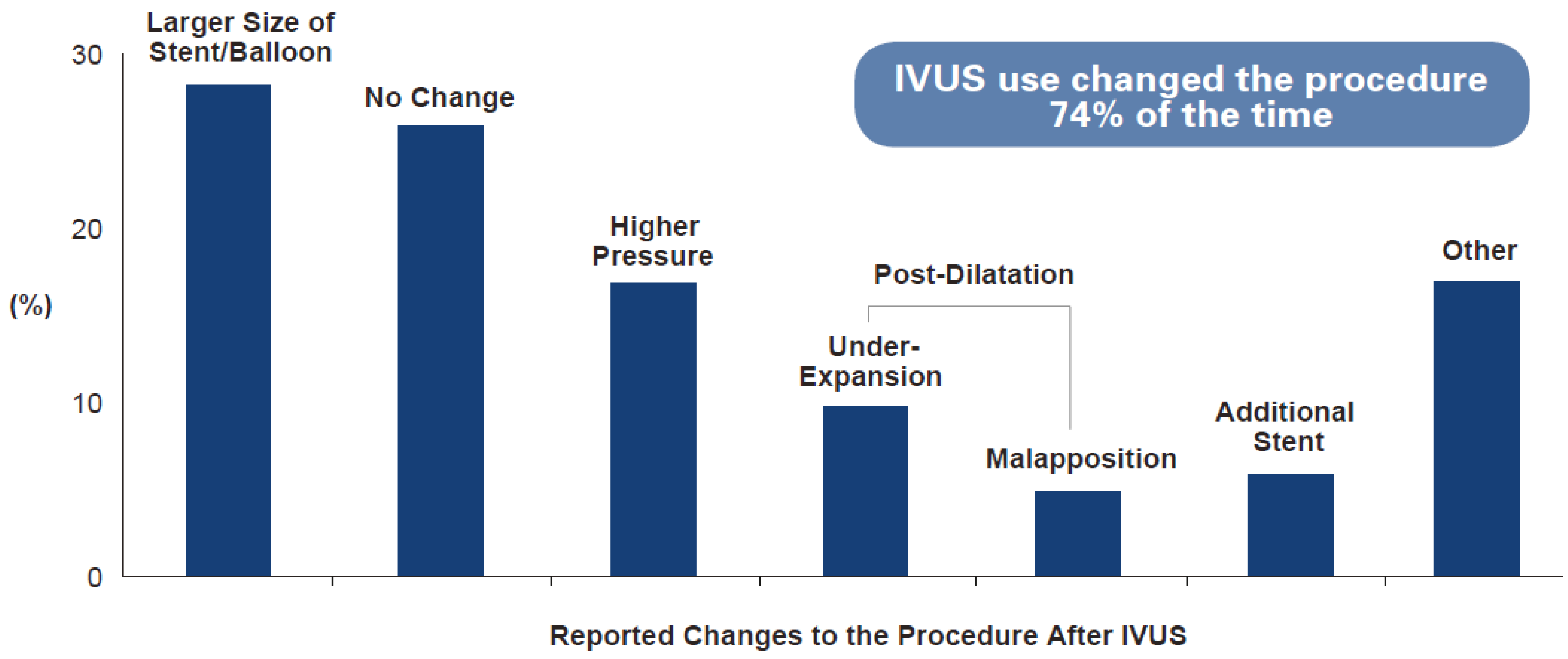
	IVUS n = 3349	No IVUS n = 5234	p Value
Definite/probable ST	0.52% (17)	1.04% (53)	0.011
All myocardial infarction	2.46% (81)	3.68% (188)	0.0022
Ischemic driven TVR*	2.42% (81)	3.95% (207)	0.0001

Maehara et al. 2013 TCT

ADAPT-DES 2-YEAR RESULTS

The largest prospective study of IVUS use to date

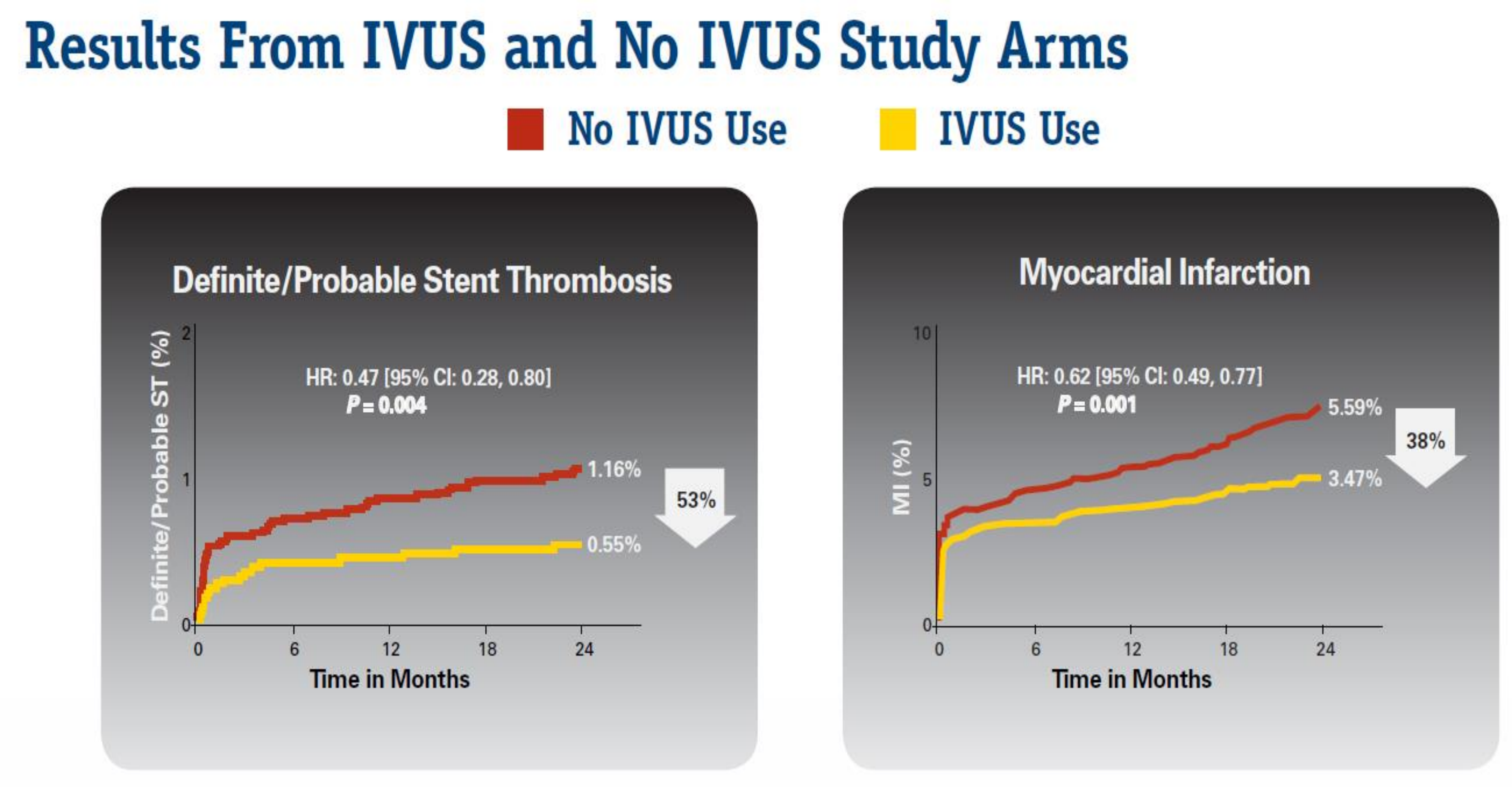
IVUS Arm Reported Improved Clinical Outcomes



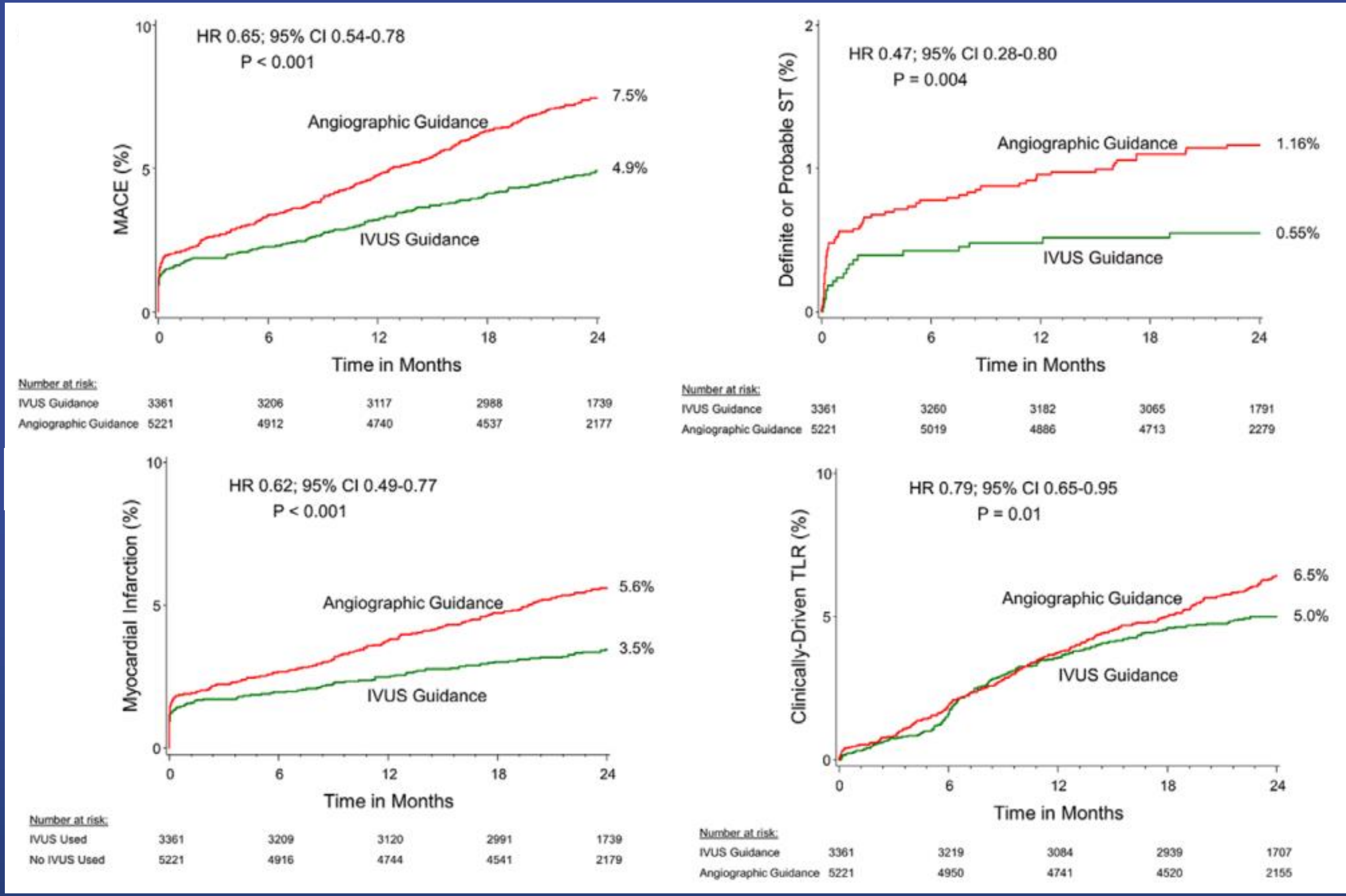
- IVUS use was associated with longer stent length and larger stent size without increasing peri-procedural MI or the number of stents
- IVUS use was associated with reduction of MACE in complex lesions

ADAPT-DES 2-YEAR RESULTS

The largest prospective study of IVUS use to date



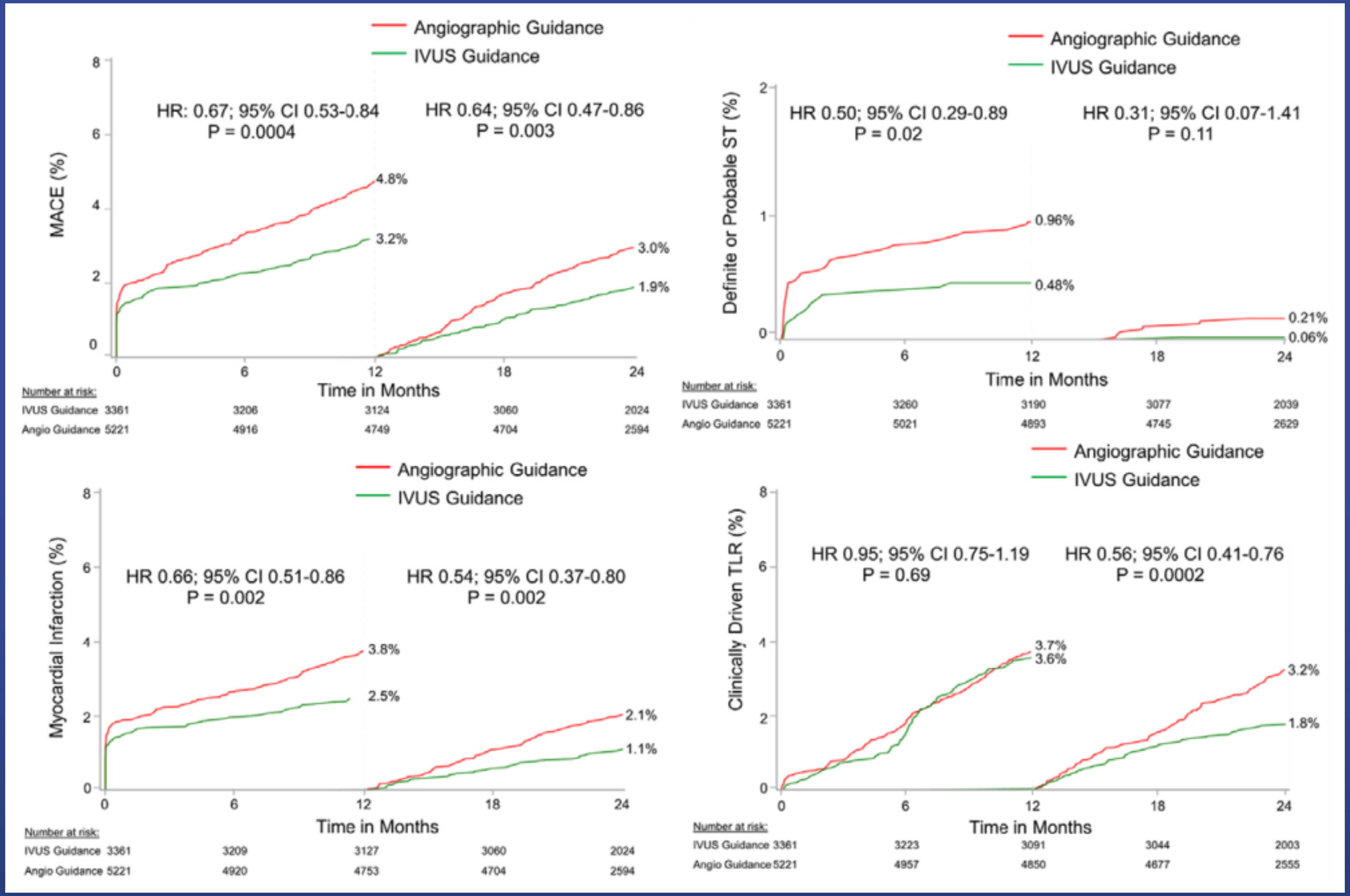
ADAPT-DES 2-years Outcomes



Maehara et al. Circ Cardiovasc Interv. 2018;11:e006243.

ADAPT-DES 2-years Outcomes

Landmark analysis between 1 and 2 year

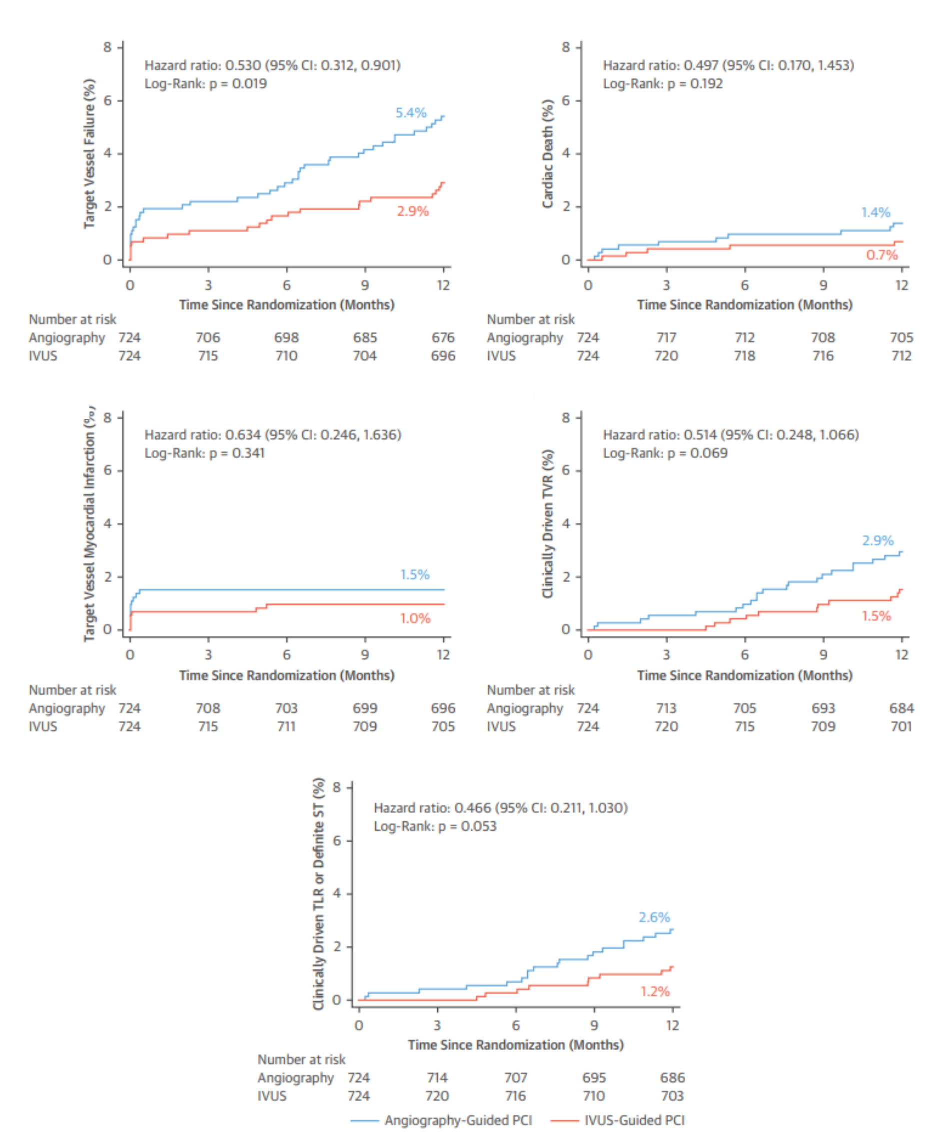


Maehara et al. Circ Cardiovasc Interv. 2018;11:e006243.

IVUS vs angio-guided DES

The ULTIMATE trial

	IVUS guidance	Angiography guidance	p value
Stent number	1.81 ± 0.80	1.76 ± 0.77	0.16
Mean stent diameter	3.14 ± 0.51	2.97 ± 0.48	<0.001
Mean stent length, mm	49.99 ± 25.10	47.38 ± 22.42	0.02
Maximum balloon diameter, mm	3.73 ± 0.56	3.51 ± 0.53	<0.001
Maximum post-dilation pressure, atm	19.7 ± 3.7	19.0 ± 3.7	<0.001



Zhang et al. JACC VOL. 72, NO. 24, 2018

IVUS vs angio-guided DES

Meta-analysis

Study/First Author (Ref. #)	Year of Publication	Number of Patients	Study Design	Type of Stent	Follow-Up Duration (Months)
Angiography vs. IVUS					
RESIST (8)	1998	76/79	Randomized	BMS	6
CRUISE (9)	2000	229/270	Randomized	BMS	9
OPTICUS (10)	2001	275/273	Randomized	BMS	12
Gaster et al. (11)	2003	54/54	Randomized	BMS	30
TULIP (12)	2003	76/74	Randomized	BMS	6–12
DIPOL (13)	2007	80/83	Randomized	BMS	6
AVID (14)	2009	406/394	Randomized	BMS	12
HOME DES IVUS (15)	2010	105/105	Randomized	DES	18
Kim et al. (16)	2013	274/269	Randomized	DES	12
AVIO (17)	2013	142/142	Randomized	DES	24
CTO-IVUS (18)	2015	201/201	Randomized	DES	12
AIR-CTO (19)	2015	115/115	Randomized	DES	24
IVUS-XPL (20)	2015	700/700	Randomized	DES	12
Tan et al. (21)	2015	62/61	Randomized	DES	24
Roy et al. (22)	2008	884/884	Observational, PSM	DES	12
MAIN-COMPARE (23)	2009	201/201	Observational, PSM	BMS/DES	36
MATRIX (24)	2011	548/548	Observational, PSM	DES	24
Kim et al. (25)	2011	487/487	Observational, PSM	DES	36
Chen et al. (26)	2012	123/123	Observational, PSM	DES	12
Wakabayashi et al. (27)	2012	637/637	Observational, PSM	BMS/DES	12
EXCELLENT (28)	2013	463/463	Observational, PSM	DES	12
De la Torre Hernandez et al. (29)	2014	505/505	Observational, PSM	DES	36
Gao et al. (30)	2014	291/291	Observational, PSM	DES	12
Hong et al. (31)	2014	201/201	Observational, PSM	DES	24

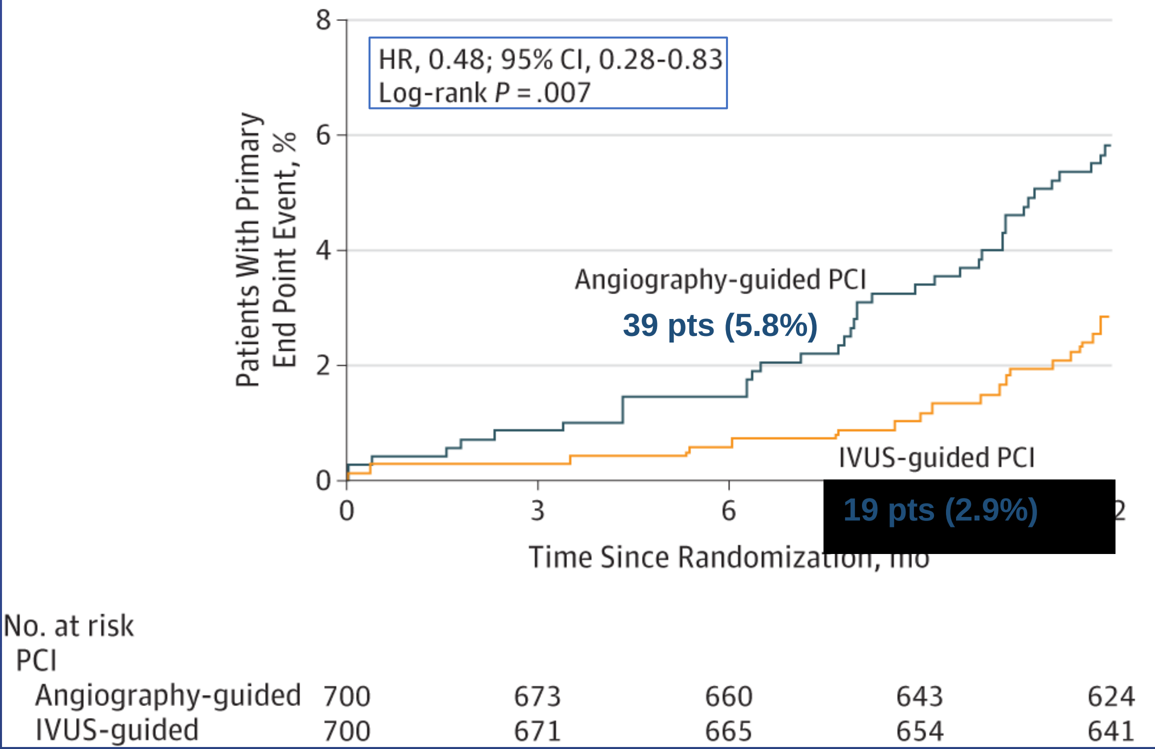
	IVUS vs angiography
Primary endpoints	
All cause mortality	0.75 [0.58-0.98]
Secondary endpoints	
MACE	0.79 [0.67-0.91]
Cardiovascular death	0.47 [0.32-0.66]
MI	0.72 [0.52-0.93]
TLR	0.74 [0.58-0.90]
ST	0.42 [0.20-0.72]

Buccheri et al. ACC Cardiovasc Interv. 2017 Dec 26;10(24):2488-2498

IVUS-XPL Randomized Clinical Trial

Effect of IVUS–Guided vs Angiography-Guided Everolimus-Eluting Stent Implantation

- Multicenter trial
- 1400 patients with long coronary lesions
  (implanted stent ≥28 mm in length)
- 1yr follow-up
- Primary end point : MACE

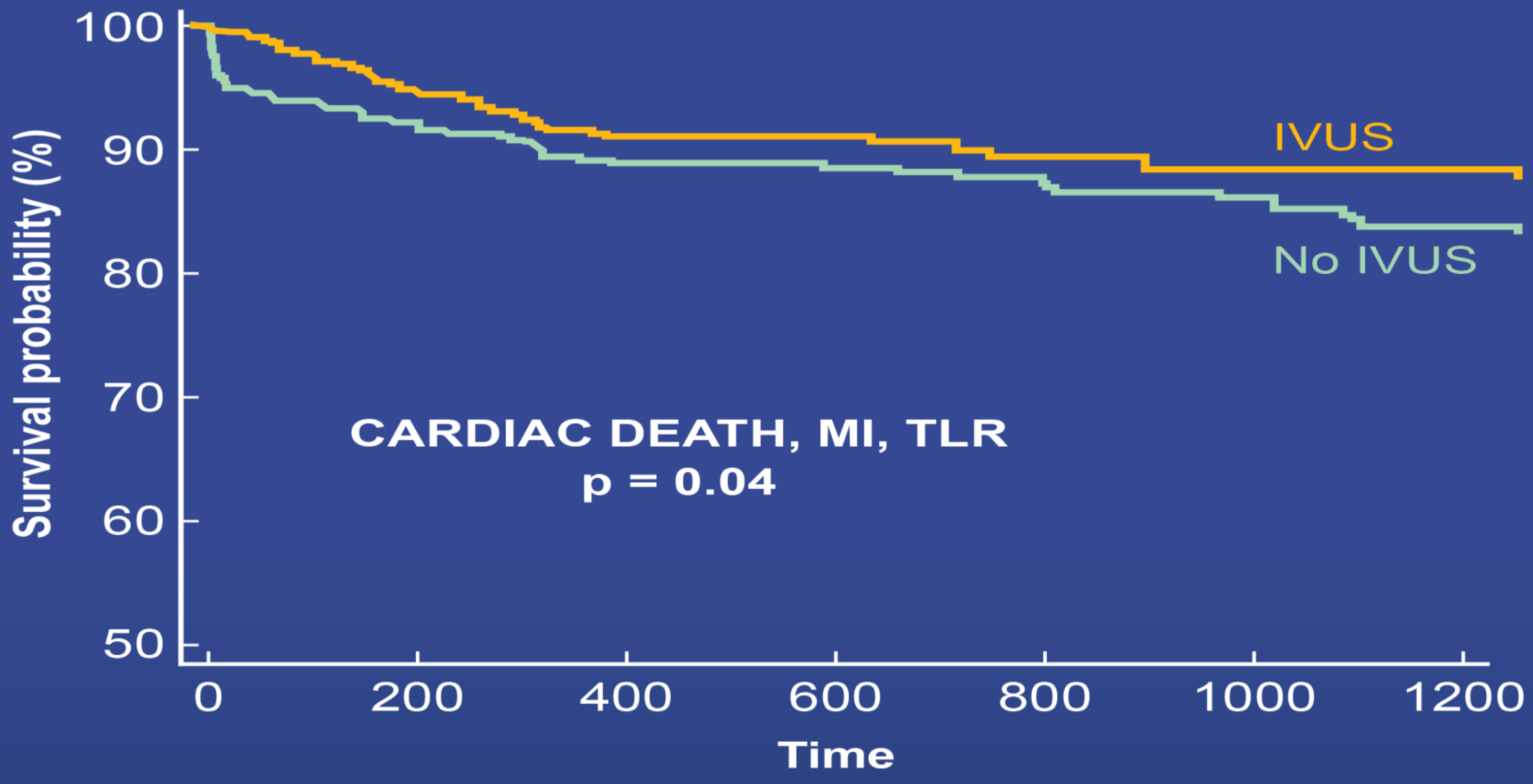


Hong et al. JAMA. 2015;314(20):2155-2163

Pooled analysis

:ESTROFA-LM, RENACIMIENTO, Bellvitge, Valdecilla

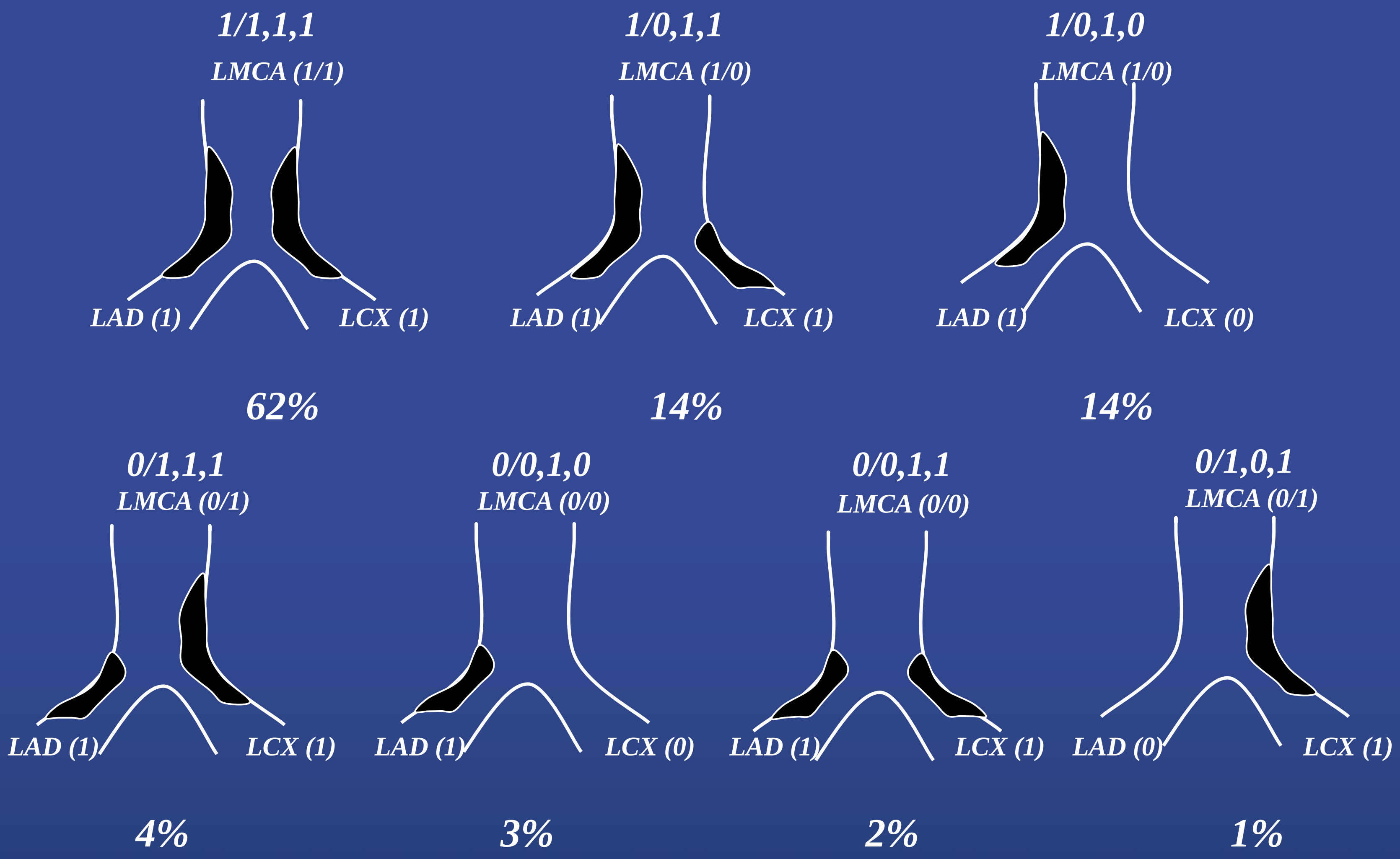
Effectiveness of IVUS on LM PCI



Pts. at risk	365 days	730 days	1095 days
IVUS	485	286	203
No IVUS	470	275	201

JoseM. de la Torre Hernandez et al. *JACC: cardiovasc interv* 2014;7:244-54

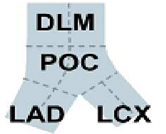
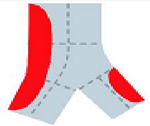
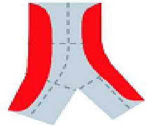
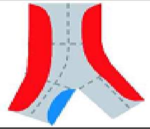
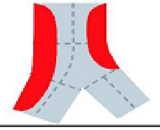
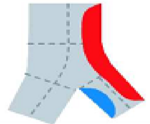
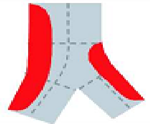
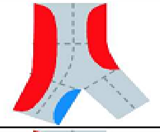
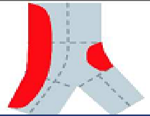
Plaque Distribution by IVUS (n=140)



In 90% plaque extends from LMCA-LAD

Oviedo C et al. Circ Cardiovasc Interv 2010;3:105-12.

Plaque Distribution by IVUS (n=82)

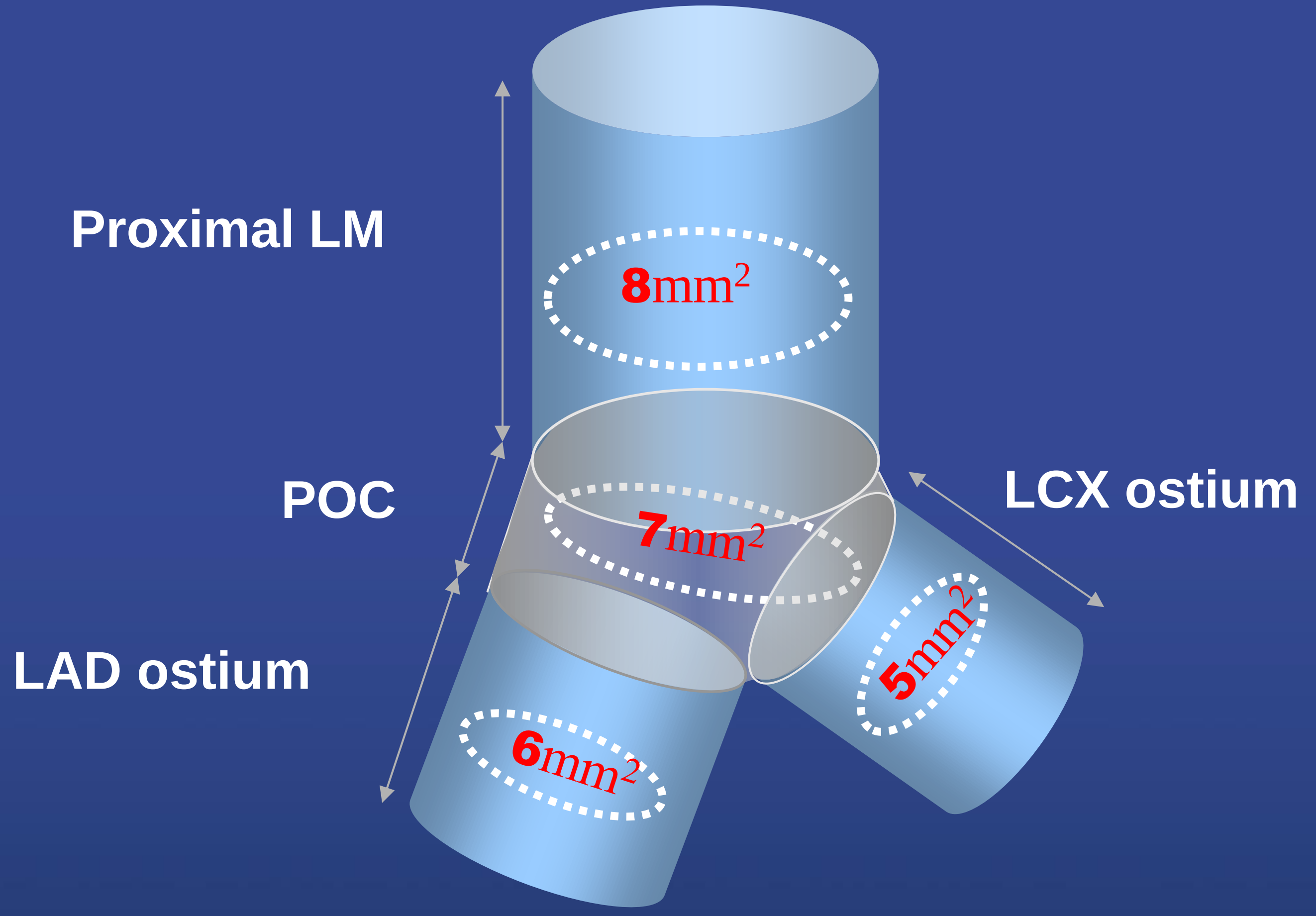
	N. (%)	LAD ostium, MLA (mm^2)	POC, MLA (mm^2)	DLM, MLA (mm^2)	LCX ostium, MLA (mm^2)
	5 (6%)	4.4±2.0	9.6±4.4	8.1±4.7	3.4±1.6
	26 (32%)	4.2±2.8	5.3±2.6	4.6±1.5	3.9±2.1
	12 (15%)	2.6±1.3	4.5±1.6	4.5±2.1	3.3±2.0
	9 (11%)	4.3±2.5	5.6±3.3	5.7±3.8	7.6±3.6
	9 (11%)	3.2±1.4	6.1±2.0	4.8±2.5	3.9±1.4
	4 (5%)	3.4±1.9	5.2±1.9	5.8±4.7	3.9±2.0
	4 (5%)	2.8±0.7	5.1±2.1	5.1±2.2	6.6±1.7
	5 (6%)	3.4±1.9	5.2±2.6	5.1±3.8	4.6±2.1

In all cases, the LM disease extended into LAD and LCX continuously.

Kang et al, Catheterization and Cardiovascular Interventions. 2011 Jul 29.

Optimal MSA

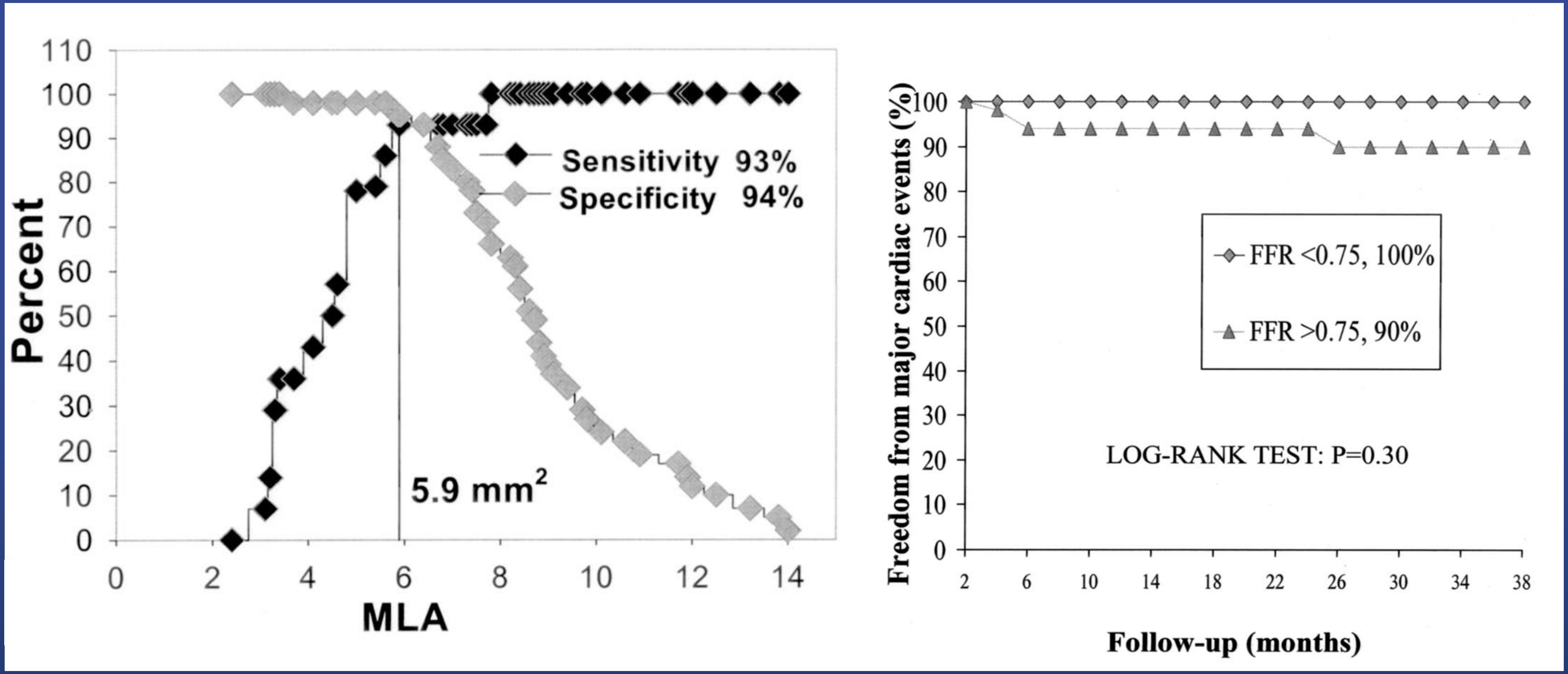
on a segmental basis



Kang et al. Circ Cardiovasc Interv 2011 2011;4:1168-74

Cut-off for Predicting LM FFR<0.75
LM MLA 6.0mm²

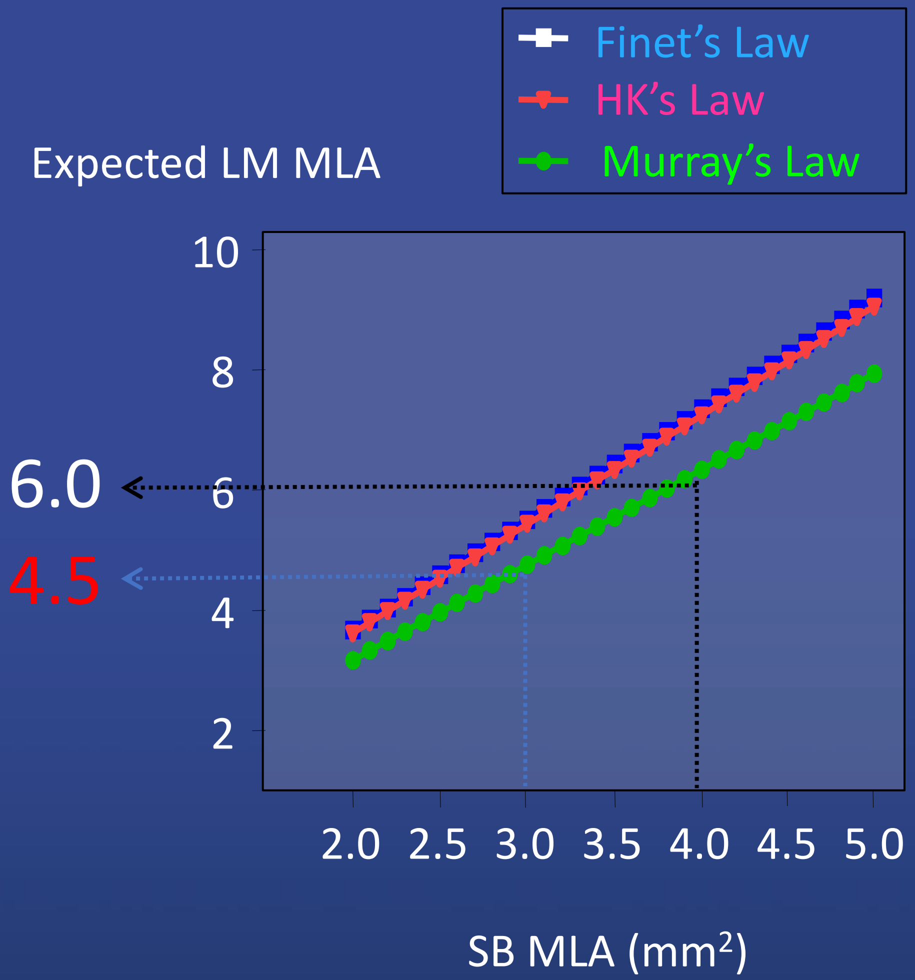
- Sum of lumen areas of two daughter vessels (Each of LAD and LCx should be 4.0mm²) = 150% of the parent LM
- **Murray's Law (*LM* r³ = *LAD* r³ + *LCx* r³)**



Jasti et al. Circulation 2004;110:2831–6

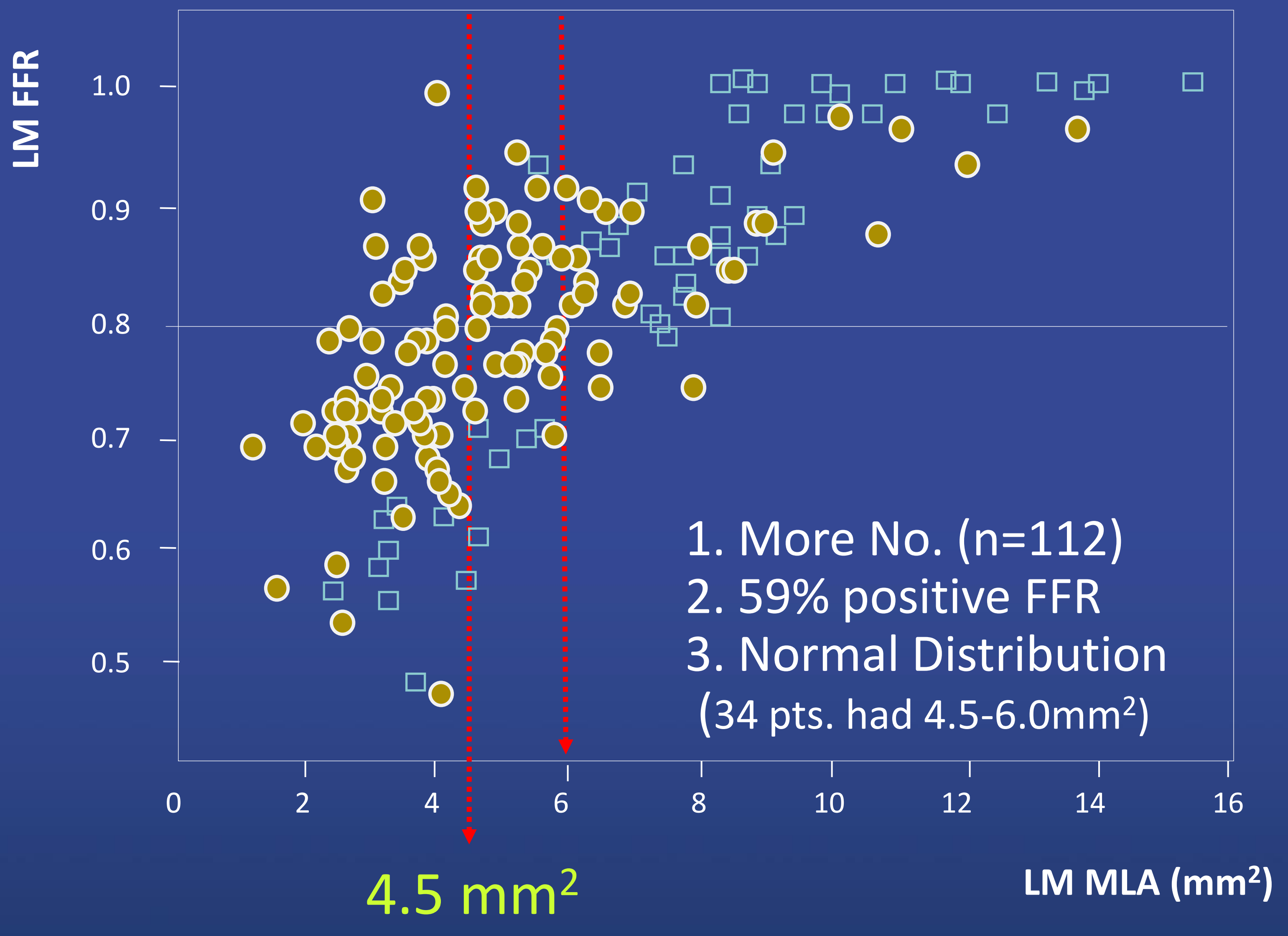
False Assumption…
The used cut-off 4.0mm² is too Big!

LAD	LCX	LM (Murray's)
3.0	3.0	4.76
3.0	2.9	4.68
3.0	2.8	4.60
3.0	**2.7**	**4.53**
3.0	2.6	4.45
3.0	2.5	4.37



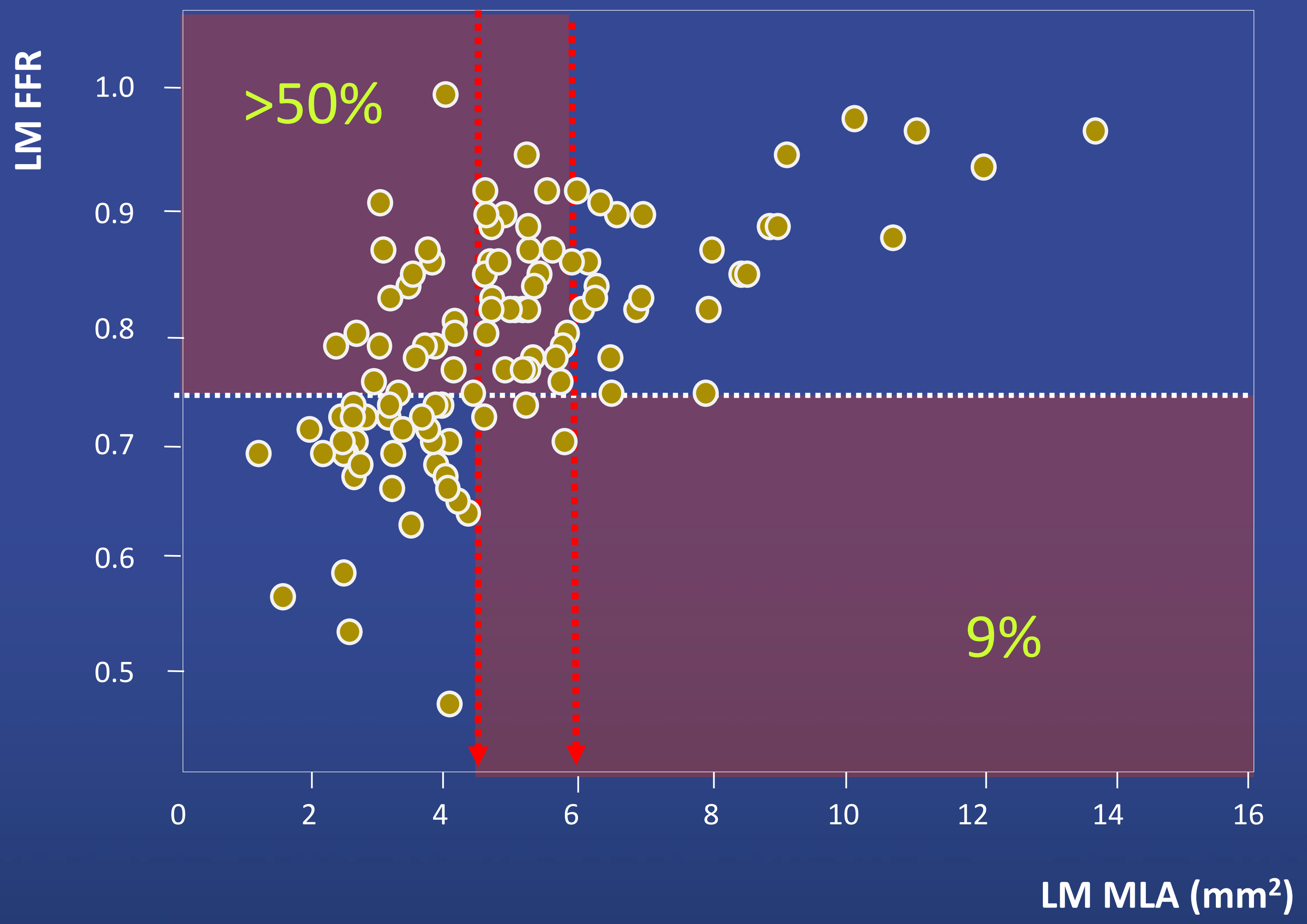
Huo et al. Eurointervention 2012;7:1310-6

AMC New Data (n=112)



Park SJ et al. JACC Interv 2014;7:868–74

AMC New Data (n=112)



Park SJ et al. JACC Interv 2014;7:868–74

- Old data (MLA 6.0mm^2) included downstream SB disease, and 32 of 55 (58%) were distal LM lesions that usually extend to the SB ostia
- Recent data (MLA 4.5mm^2) evaluated only pure LM lesions, which more reliably assessed the impact of LM-MLA on functional significance

TABLE 1. Baseline Clinical, Angiographic, and IVUS Characteristics of Patients (n=55)

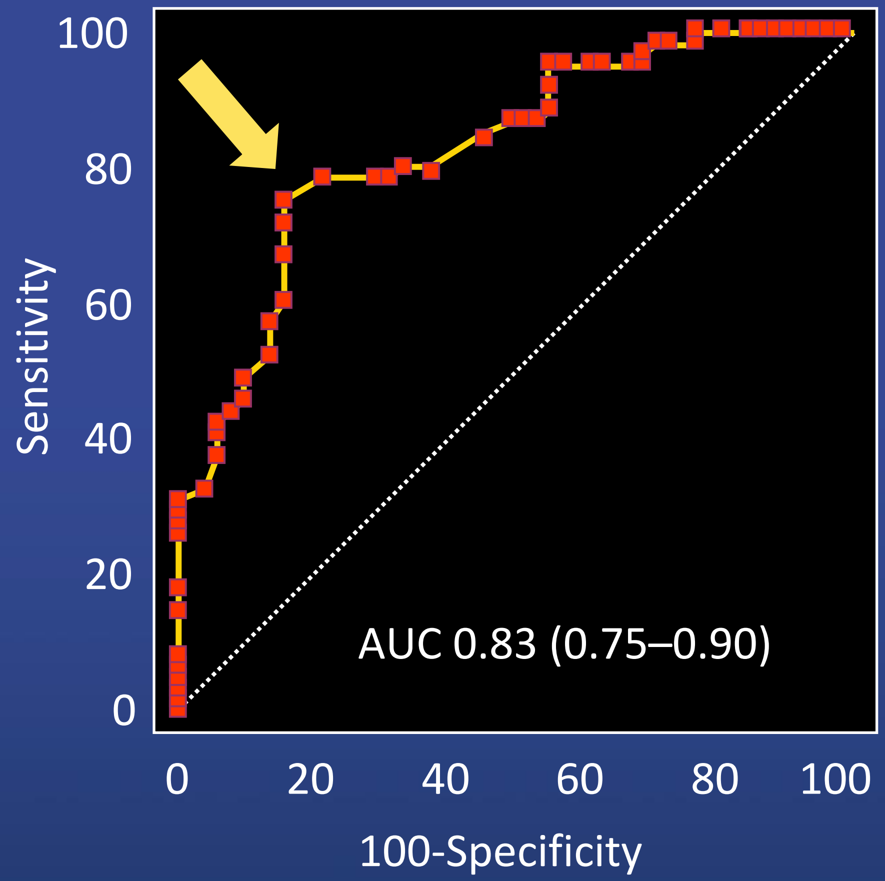
Age, y	62±11
Diabetes mellitus, n	20
Hypertension, n	50
Smoking, n	39
Prior bypass surgery, n	13
Ostial LM stenosis, n	20
Mid-LM stenosis, n	3
Distal LM stenosis, n	32

Jasti et al. Circulation 2004;110:2831-6

New LM MLA 4.5mm²

Matched with FFR <0.80

Ostial and Shaft LM Disease (N=112)



Sensitivity	79%
Specificity	80%
PPV	83%
NPV	76%

Park SJ et al. JACC Interv 2014;7:868–74

Angio-guided PCI vs. IVUS-guided PCI

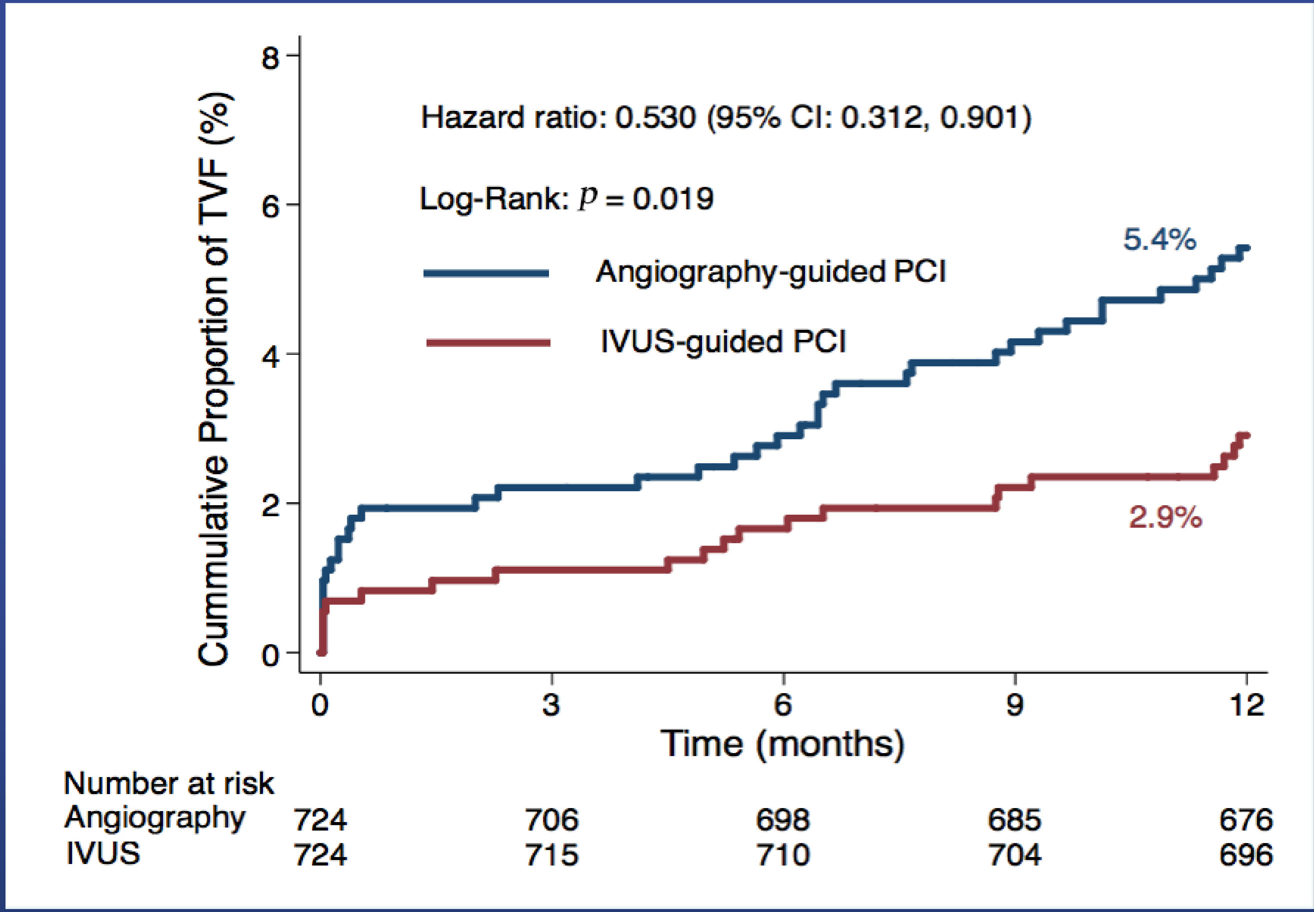
Procedural Data
ULTIMATE trial

	IVUS guidance (n=962)	Angiography guidance (n=1016)	*P*
Per lesion, n (%)			
Stent number	1.81±0.80	1.76±0.77	0.16
Mean stent length, mm	49.99±25.10	47.38±22.42	0.02
Mean stent diameter, mm	3.14±0.51	2.97±0.48	<0.001
Max balloon diameter, mm	3.73±0.56	3.51±0.53	<0.001
Max post-dilation pressure, atm	19.7±3.7	19.0±3.7	<0.001

Jun-Jie Zhang et al. TCT 2018

Angio-guided PCI vs. IVUS-guided PCI

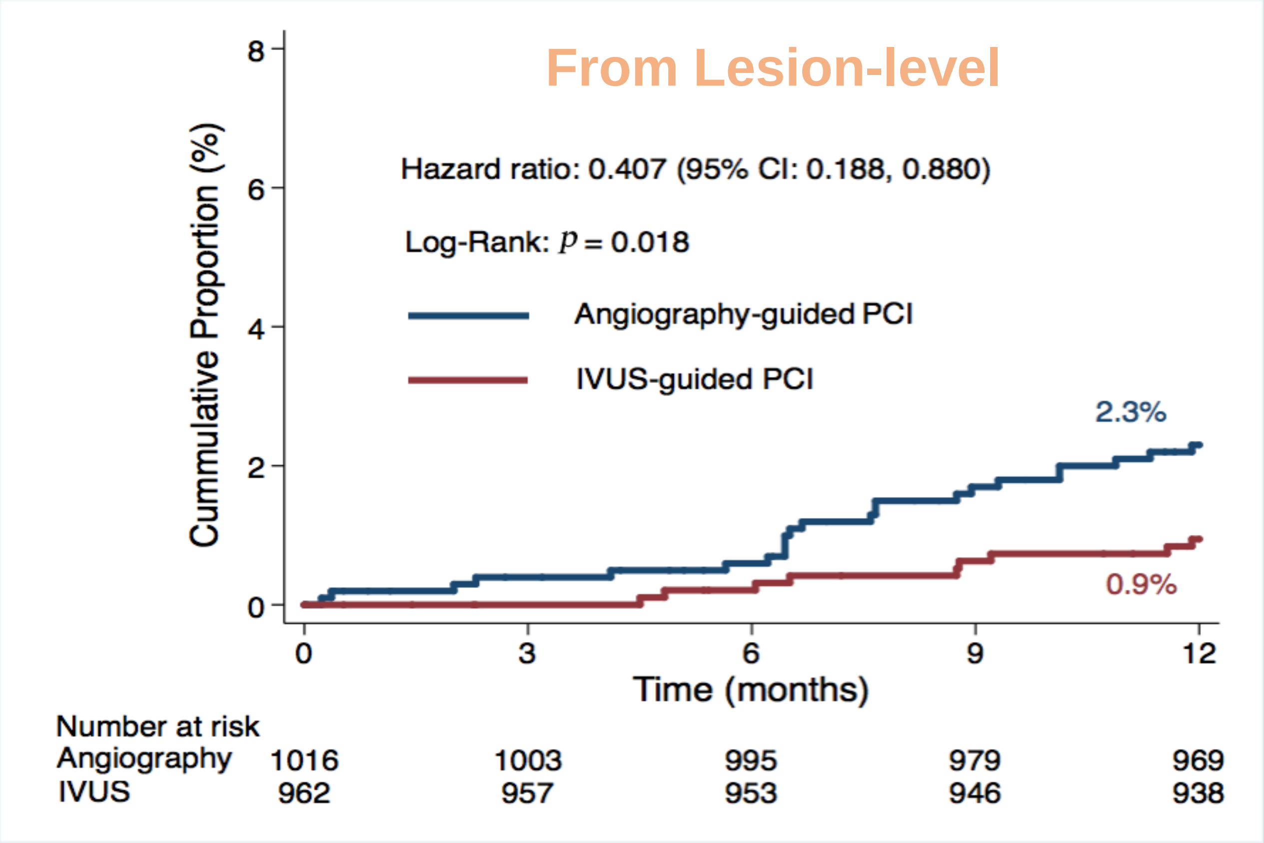
TVF at 12-months
ULTIMATE trial



Jun-Jie Zhang et al. TCT 2018

Angio-guided PCI vs. IVUS-guided PCI

CD-TLR or Definite ST at 12-month
ULTIMATE trial



Jun-Jie Zhang et al. TCT 2018

On-site Post-procedure IVUS Assessment

ULTIMATE trial

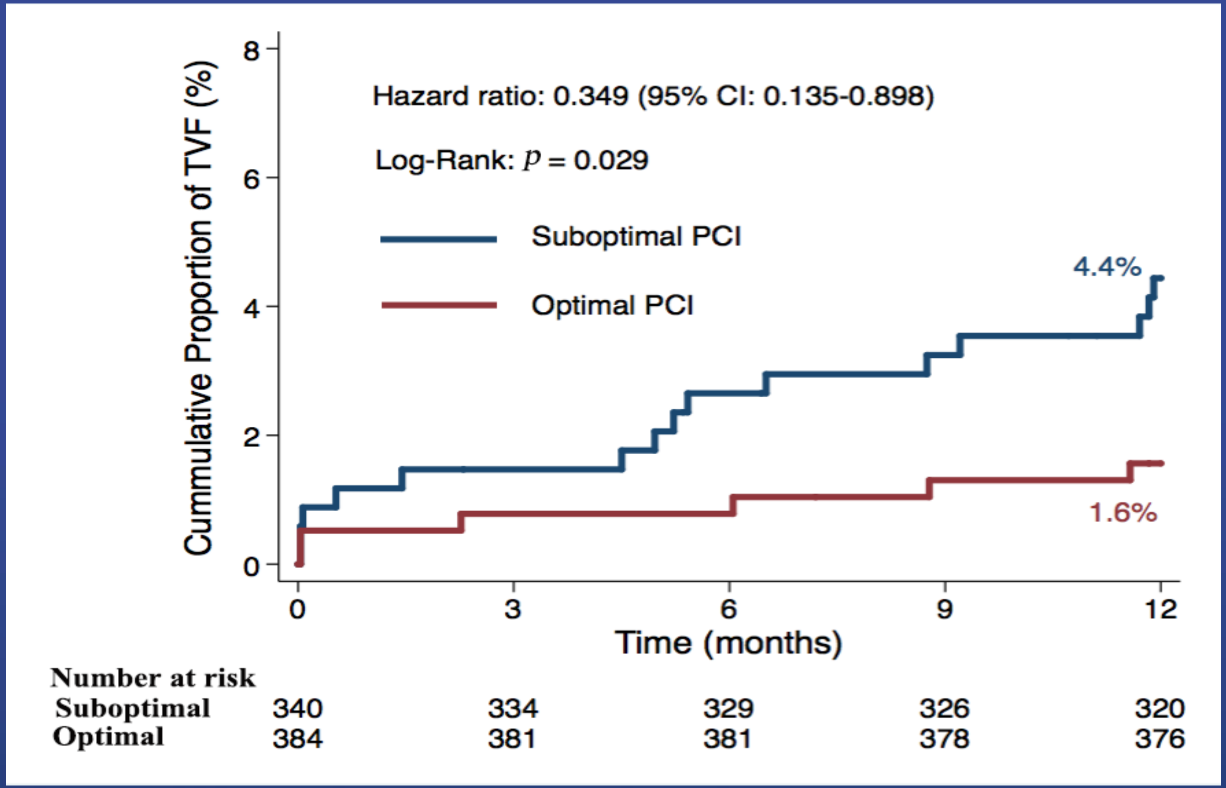
	Optimal group	Suboptimal group	*P*
Number of patients, n (%)	384 (53.0)	340 (47.0)	
Number of lesions, n (%)	578 (60.1)	384 (39.9)	
MSA, mm^2	6.09	5.45	<0.001
Prox. edge plaque burden	37.2%	51.2%	<0.001
Dist. edge plaque burden	24.2%	35.1%	<0.001

Jun-Jie Zhang et al. TCT 2018

Optimal vs. Suboptimal IVUS-guided PCI

TVF at 12-months

ULTIMATE trial

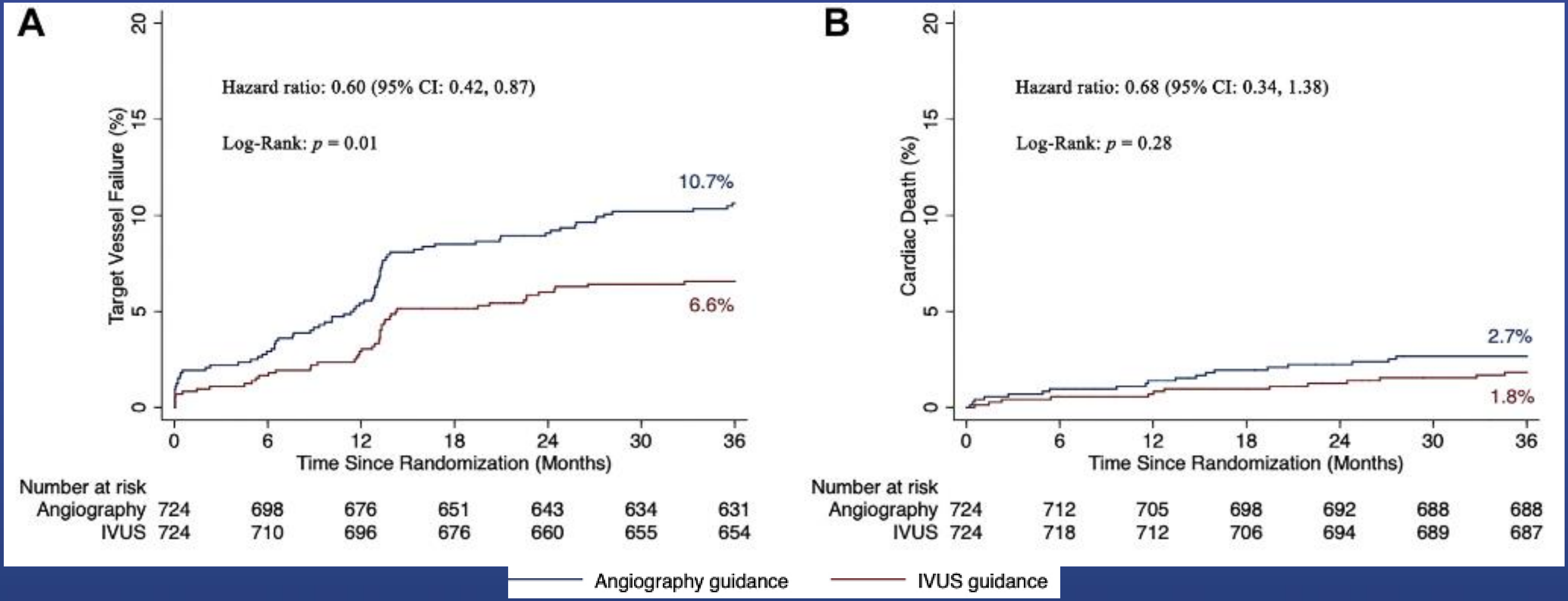


Jun-Jie Zhang et al. TCT 2018

ULTIMATE 3-Year Outcomes

Target vessel failure

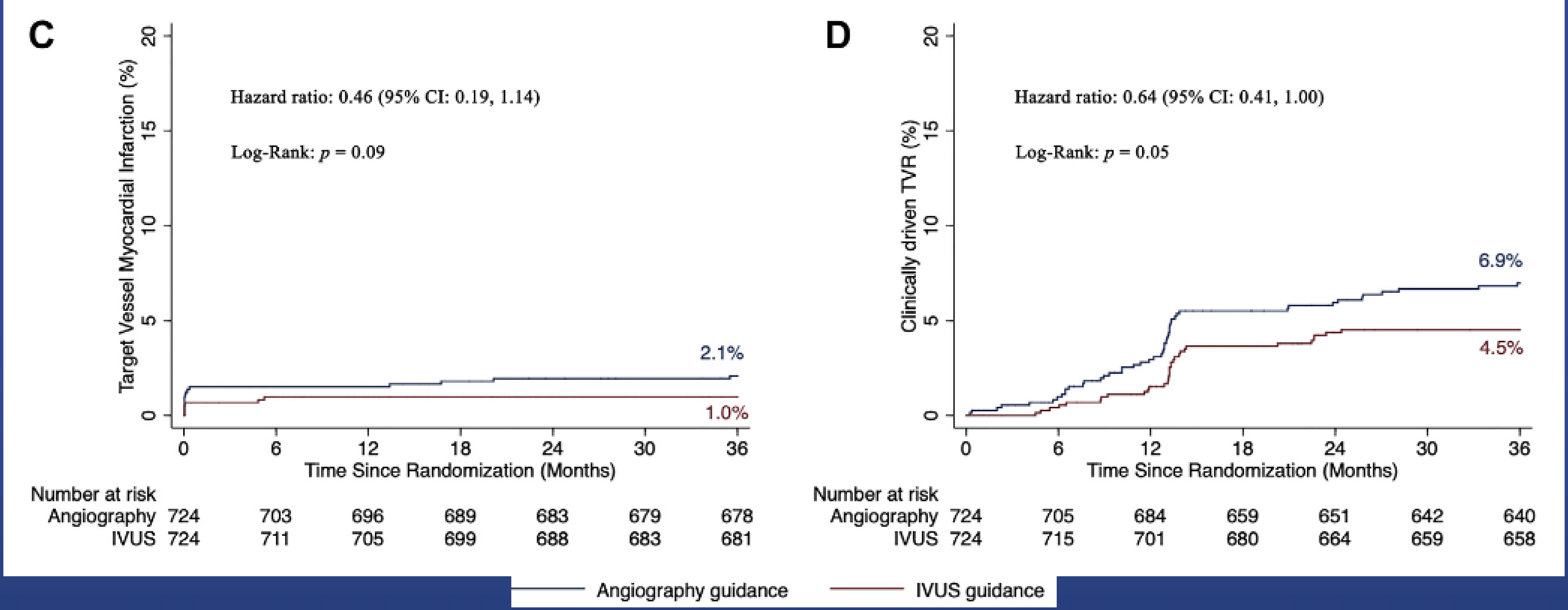
Cardiac death



Xiao-Fei Gao et al. Am Coll Cardiol Intv 2021;14:247–57

ULTIMATE 3-Year Outcomes

Target vessel MI | Clinically driven TVR



Xiao-Fei Gao et al. Am Coll Cardiol Intv 2021;14:247–57

RENOVATE-COMPLEX PCI

Prospective, multicenter, open label trial

1639 Complex CAD Patients

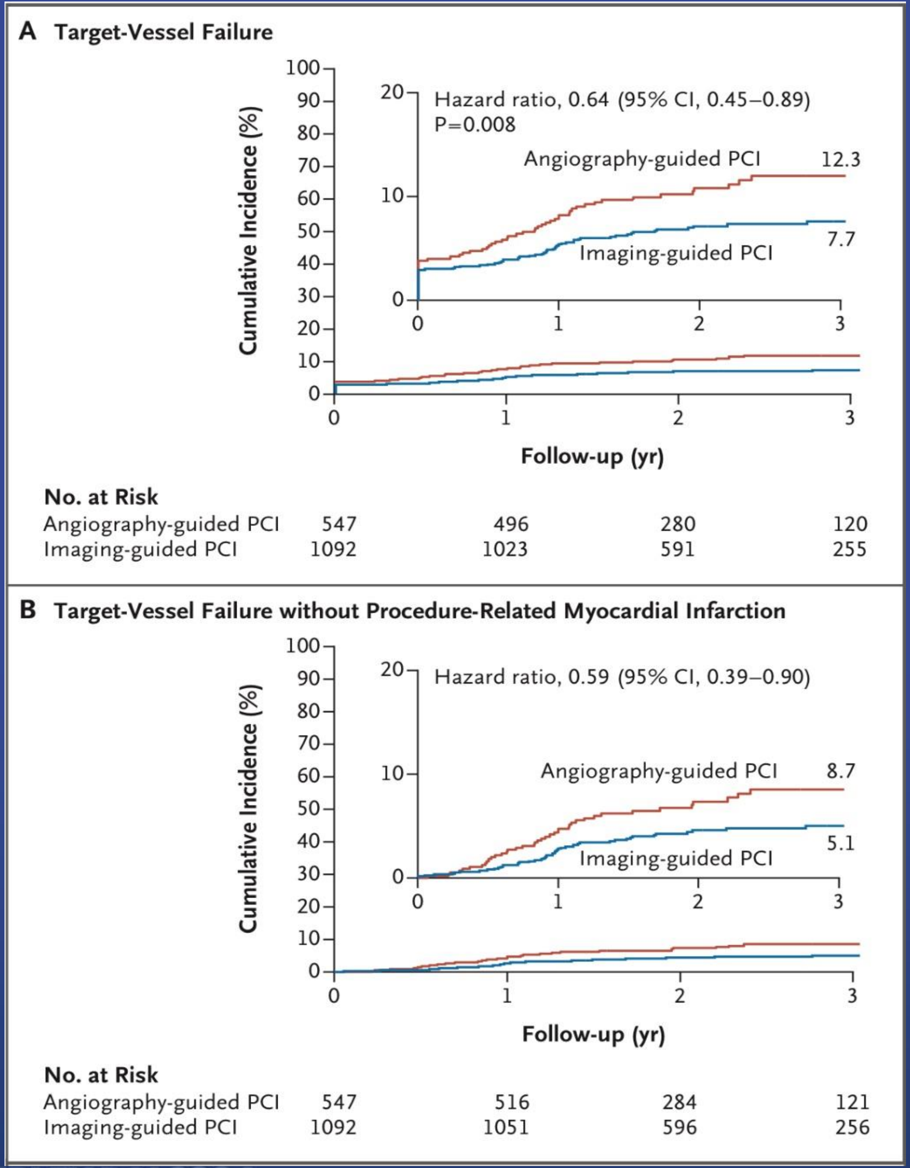
R
2:1

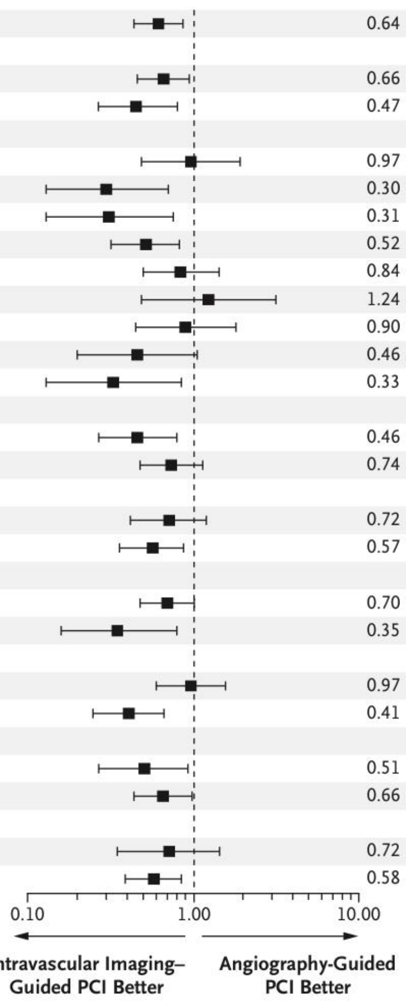
Image Guided PCI (IVUS/OCT) (n=1092)	Angio Guided PCI (n=547)

Primary Endpoint at 3 year:
Target vessel Failure = Composite Death from Cardiac cause, TVR myocardial infarction or revascularization

J.M. Lee, K.H. Choi, Y.B. Song and J.-Y. Hahn et al. DOI: 10.1056/NEJMoa2216607

RENOVATE-COMPLEX PCI





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)

J.M. Lee, K.H. Choi, Y.B. Song and J.-Y. Hahn et al. DOI: 10.1056/NEJMoa2216607

Angio-guided PCI vs. IVUS-guided PCI

Meta-analysis

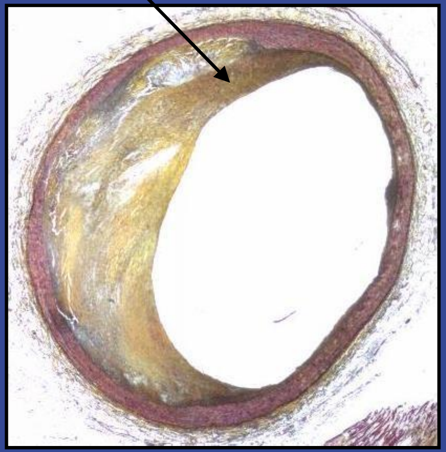
Study/First Author (Ref. #)	Year of Publication	Number of Patients	Study Design	Type of Stent	Follow-Up Duration (Months)
Angiography vs. IVUS					
RESIST (8)	1998	76/79	Randomized	BMS	6
CRUISE (9)	2000	229/270	Randomized	BMS	9
OPTICUS (10)	2001	275/273	Randomized	BMS	12
Gaster et al. (11)	2003	54/54	Randomized	BMS	30
TULIP (12)	2003	76/74	Randomized	BMS	6–12
DIPOL (13)	2007	80/83	Randomized	BMS	6
AVID (14)	2009	406/394	Randomized	BMS	12
HOME DES IVUS (15)	2010	105/105	Randomized	DES	18
Kim et al. (16)	2013	274/269	Randomized	DES	12
AVIO (17)	2013	142/142	Randomized	DES	24
CTO-IVUS (18)	2015	201/201	Randomized	DES	12
AIR-CTO (19)	2015	115/115	Randomized	DES	24
IVUS-XPL (20)	2015	700/700	Randomized	DES	12
Tan et al. (21)	2015	62/61	Randomized	DES	24
Roy et al. (22)	2008	884/884	Observational, PSM	DES	12
MAIN-COMPARE (23)	2009	201/201	Observational, PSM	BMS/DES	36
MATRIX (24)	2011	548/548	Observational, PSM	DES	24
Kim et al. (25)	2011	487/487	Observational, PSM	DES	36
Chen et al. (26)	2012	123/123	Observational, PSM	DES	12
Wakabayashi et al. (27)	2012	637/637	Observational, PSM	BMS/DES	12
EXCELLENT (28)	2013	463/463	Observational, PSM	DES	12
De la Torre Hernandez et al. (29)	2014	505/505	Observational, PSM	DES	36
Gao et al. (30)	2014	291/291	Observational, PSM	DES	12
Hong et al. (31)	2014	201/201	Observational,	DES	24

	IVUS compared with angiography Odds ratio [95% CI]
Primary outcome	
All cause mortality	0.75 [0.58-0.98]
Secondary outcome	
MACE	0.79 [0.67-0.91]
Cardiovascular death	0.47 [0.32-0.66]
MI	0.72 [0.52-0.93]
TLR	0.74 [0.58-0.90]
ST	0.42 [0.20-0.72]

Buccheri et al. JACC Cardiovasc Interv. 2017 Dec 26;10(24):2488-2498

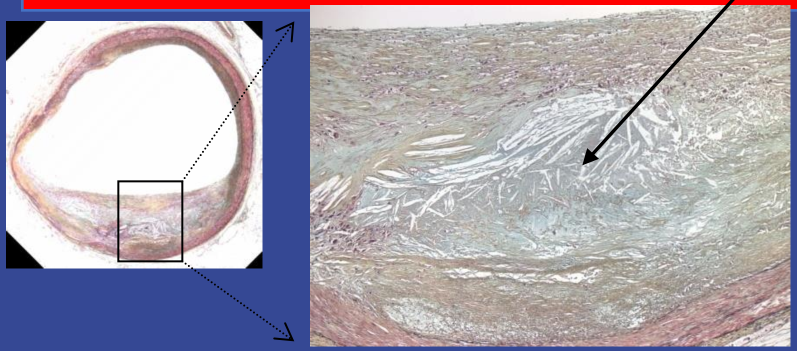
VH-IVUS

Fibrous Tissue



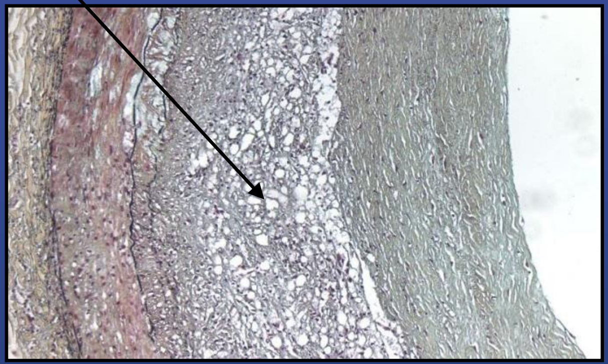
Densely packed collagen fibers with no evidence of lipid accumulation. No evidence of macrophage infiltration.

Necrotic Core



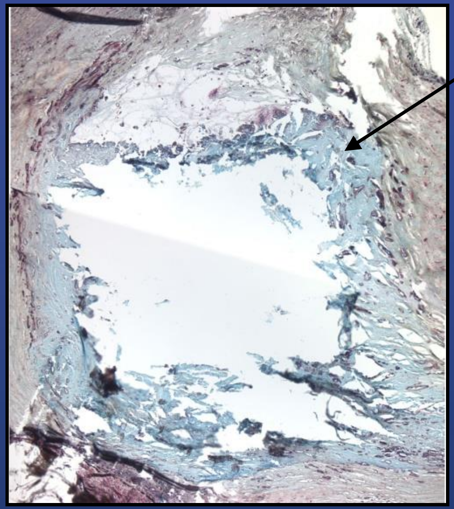
Highly lipidic necrotic region with remnants of foam cells and dead lymphocytes. No collagen fiber, Cholesterol clefts and micro calcifications

Fibro-Fatty



Loosely packed bundles of collagen fibers with regions of lipid deposition present. No cholesterol clefts or necrosis. Increase in extra-cellular matrix

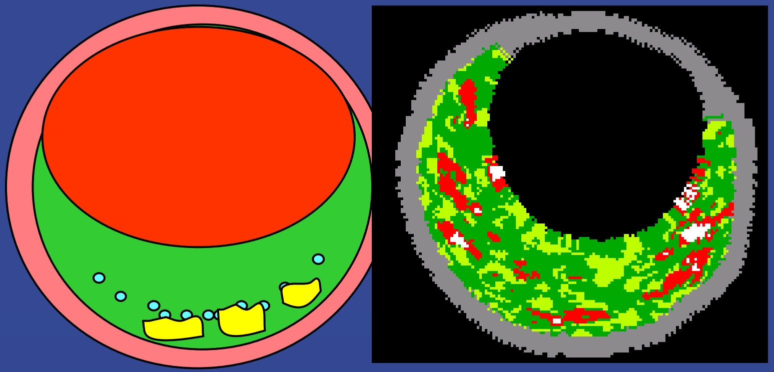
Dense Calcium



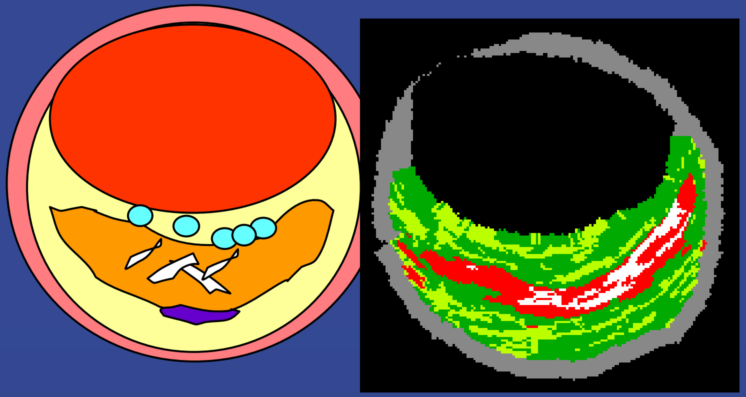
Focal dense calcium

PIT

Fibroatheroma



Plaque thickness > 600um
Fibrofatty >15%

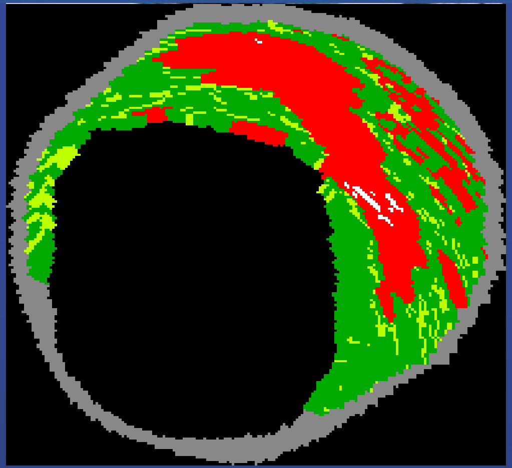


Confluent NC >10%

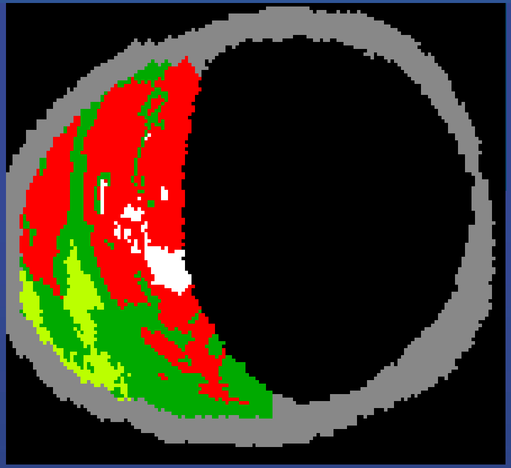
Criteria of TCFA

In at least 3 consecutive frames:

1) Necrotic core $\geq$ 10%
2) without evident overlying fibrous tissue
3) Percent atheroma area $\geq$ 40%



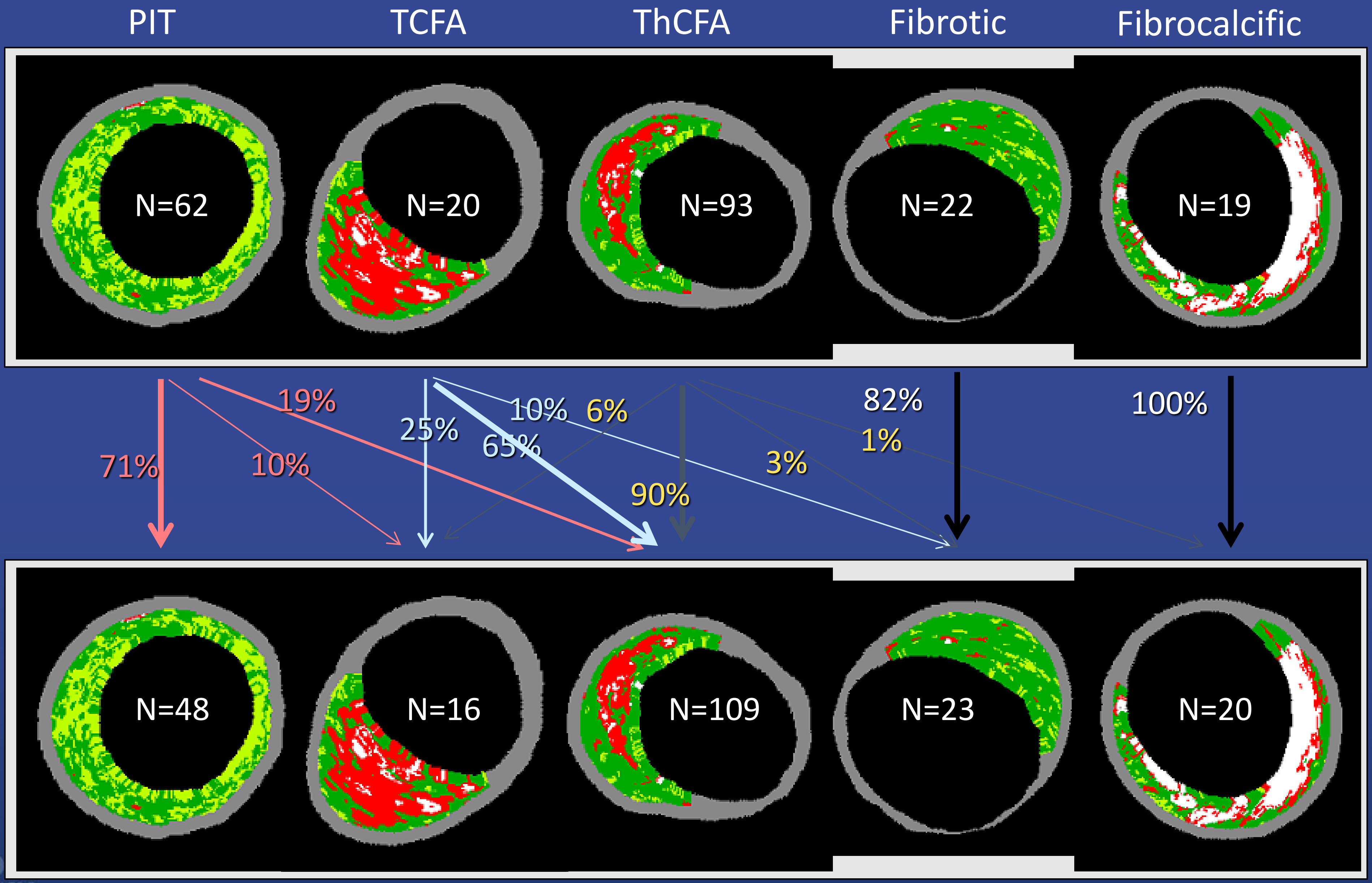
Thick fibrous cap
Low lipid conc
Low macrophage density



Thin fibrous cap
High lipid conc
High macrophage density

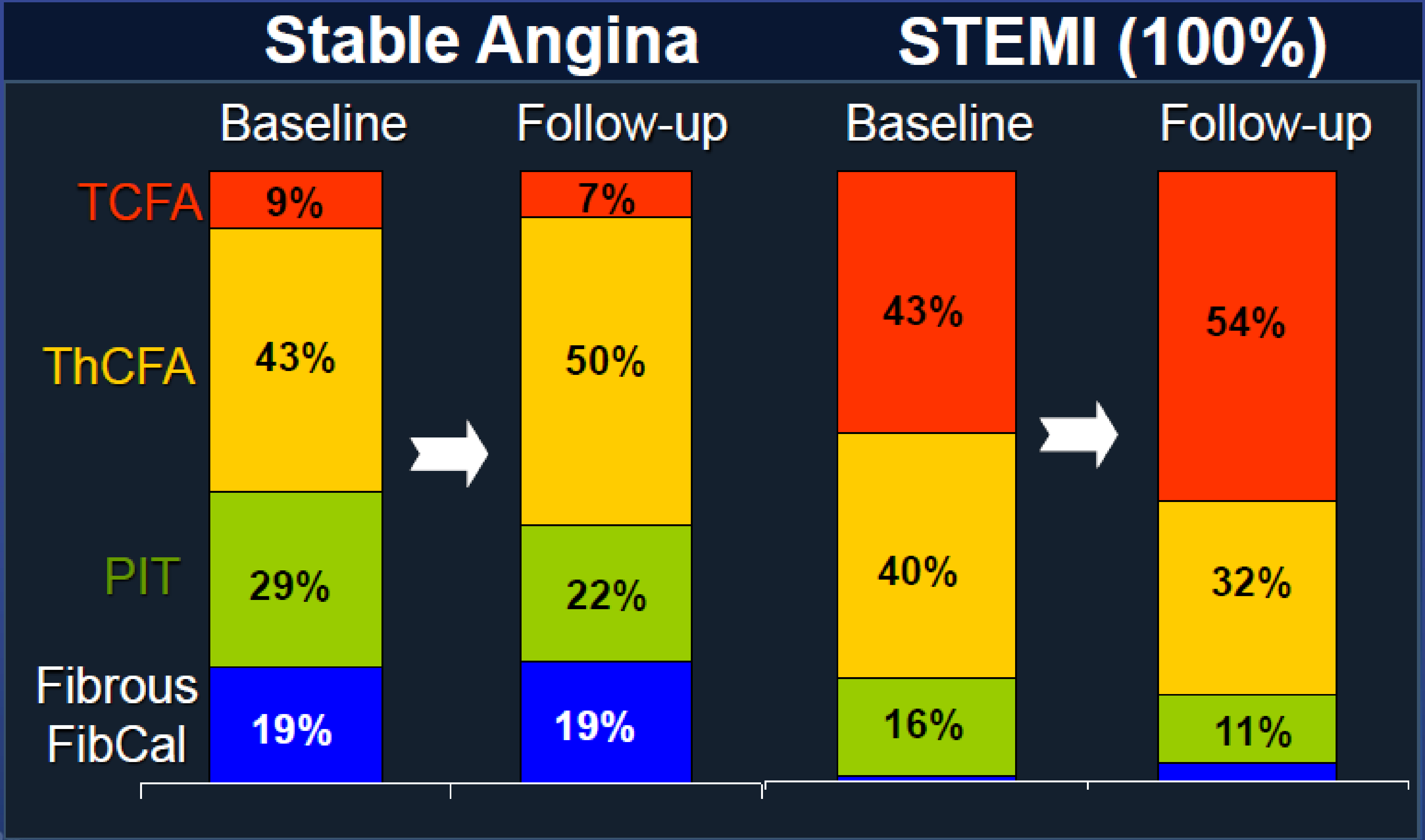
Rodriguez-Granillo et al. J Am Coll Cardiol 2005;46:2038–42

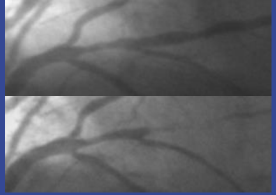
Change of Plaque Type



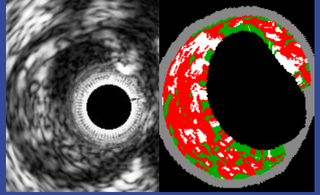
Kubo T, JACC 2010;55:1590

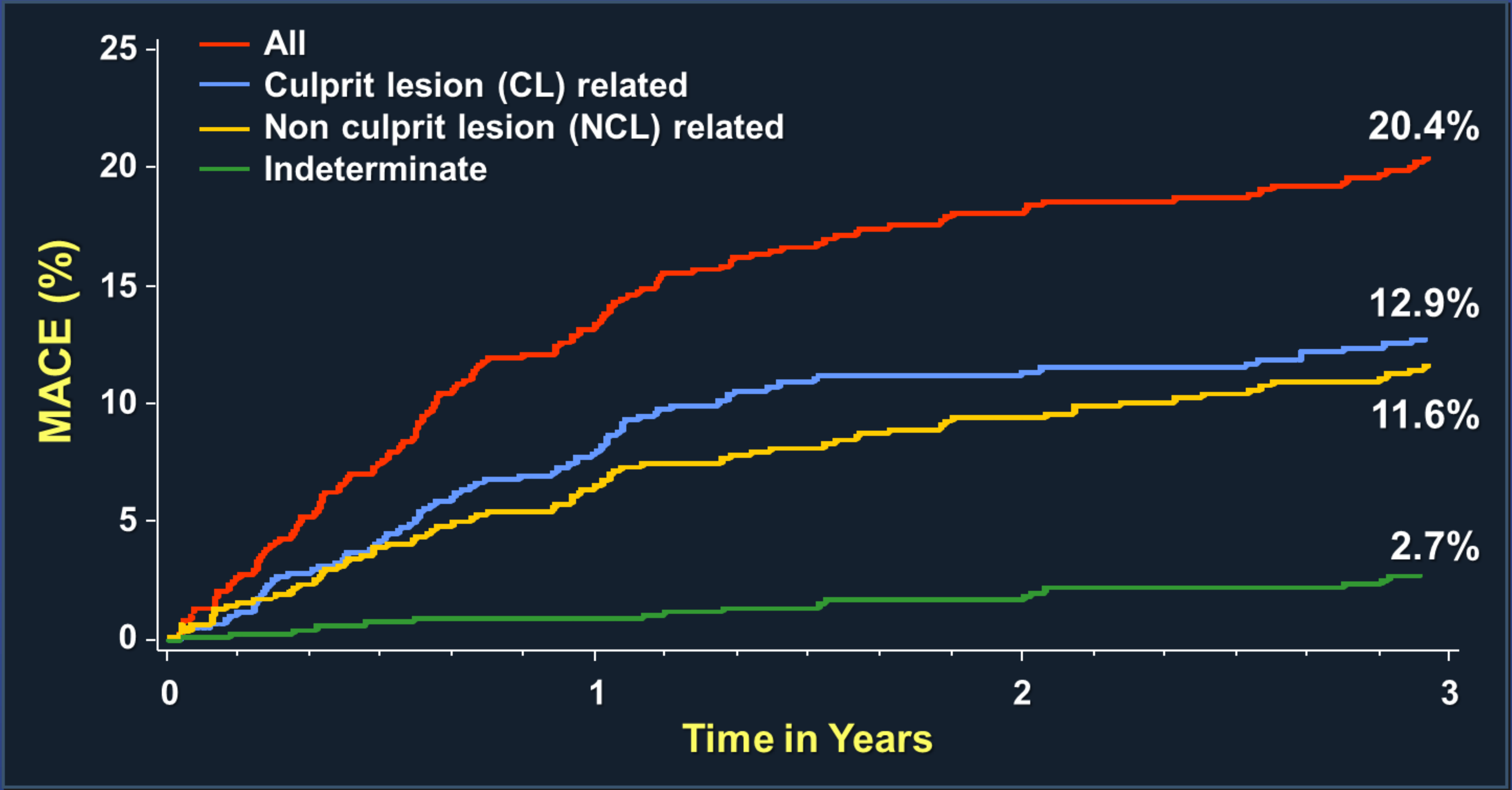
Differences in Temporal Changes of Non-Culprit Lesions





PROSPECT MACE (N=697)





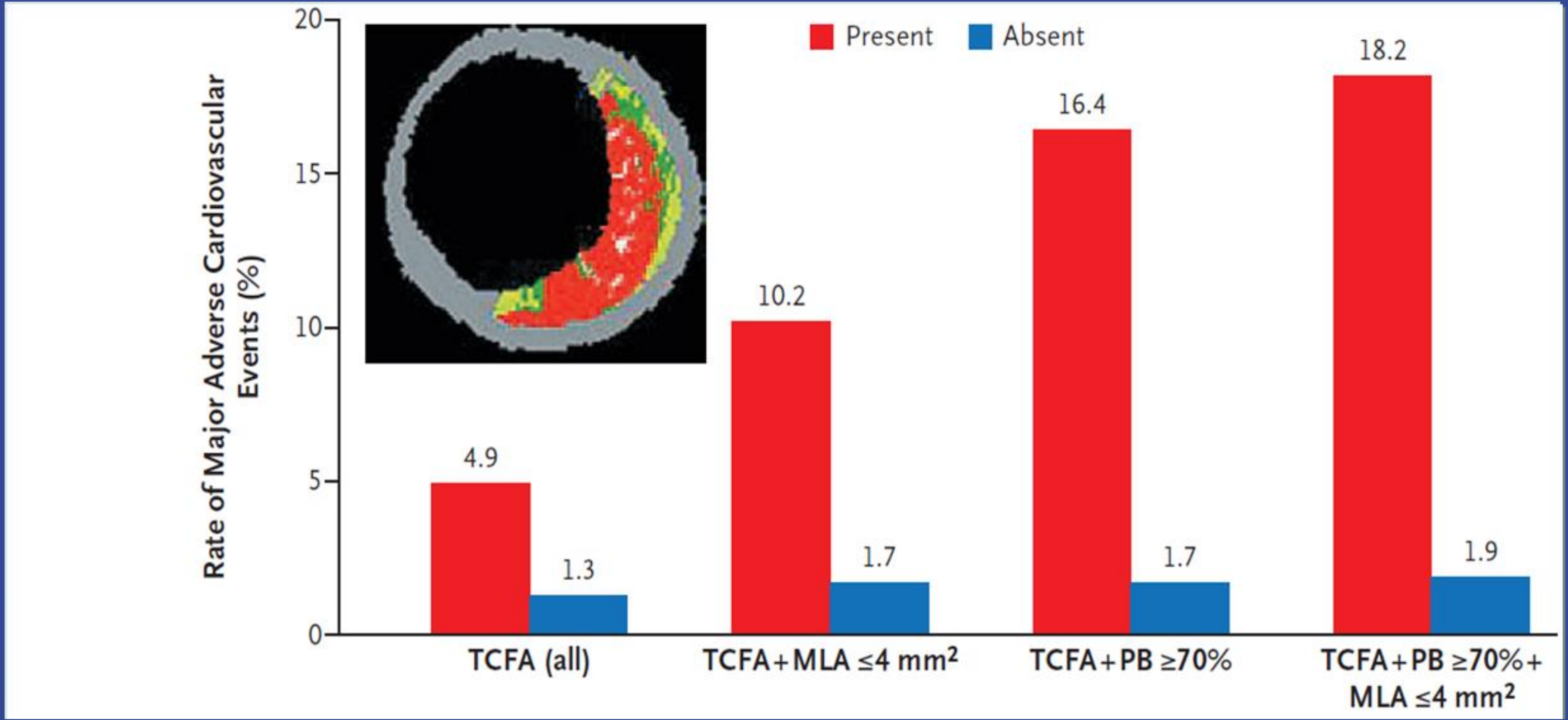
Number at risk

	0	1	2	3
ALL	697	557	506	480
CL related	697	590	543	518
NCL related	697	595	553	521
Indeterminate	697	634	604	583

Stone GW et al. NEJM 2011;364:226-35

PROSPECT 3-year MACE

*MACE = cardiac death, arrest, MI, rehospitalization for unstable/ progressive angina



Predictors	Hazard ratio (95% CI)	p
Plaque burden ≥70%	5.03 (2.51 – 10.11)	<0.001
Thin-cap fibroatheroma	3.35 (1.77 – 6.36)	<0.001
MLA ≤4.0 mm^2	3.21 (1.61 – 6.42)	0.001

Stone G et al. N Engl J med 2011;364:226-35

PROSPECT II
PROSPECT ABSORB

PROSPECT II Study

900 pts with ACS at up to 20 hospitals

in Sweden, Denmark and Norway (SCAAR)

NSTEMI or STEMI >12º

IVUS + NIRS (blinded) performed in culprit vessel(s)

Successful PCI of all intended lesions (by angio ±FFR/iFR)

↓

Formally enrolled

↓

3-vessel imaging post PCI

Culprit artery, followed by non-culprit arteries

Angiography (QCA of entire coronary tree)

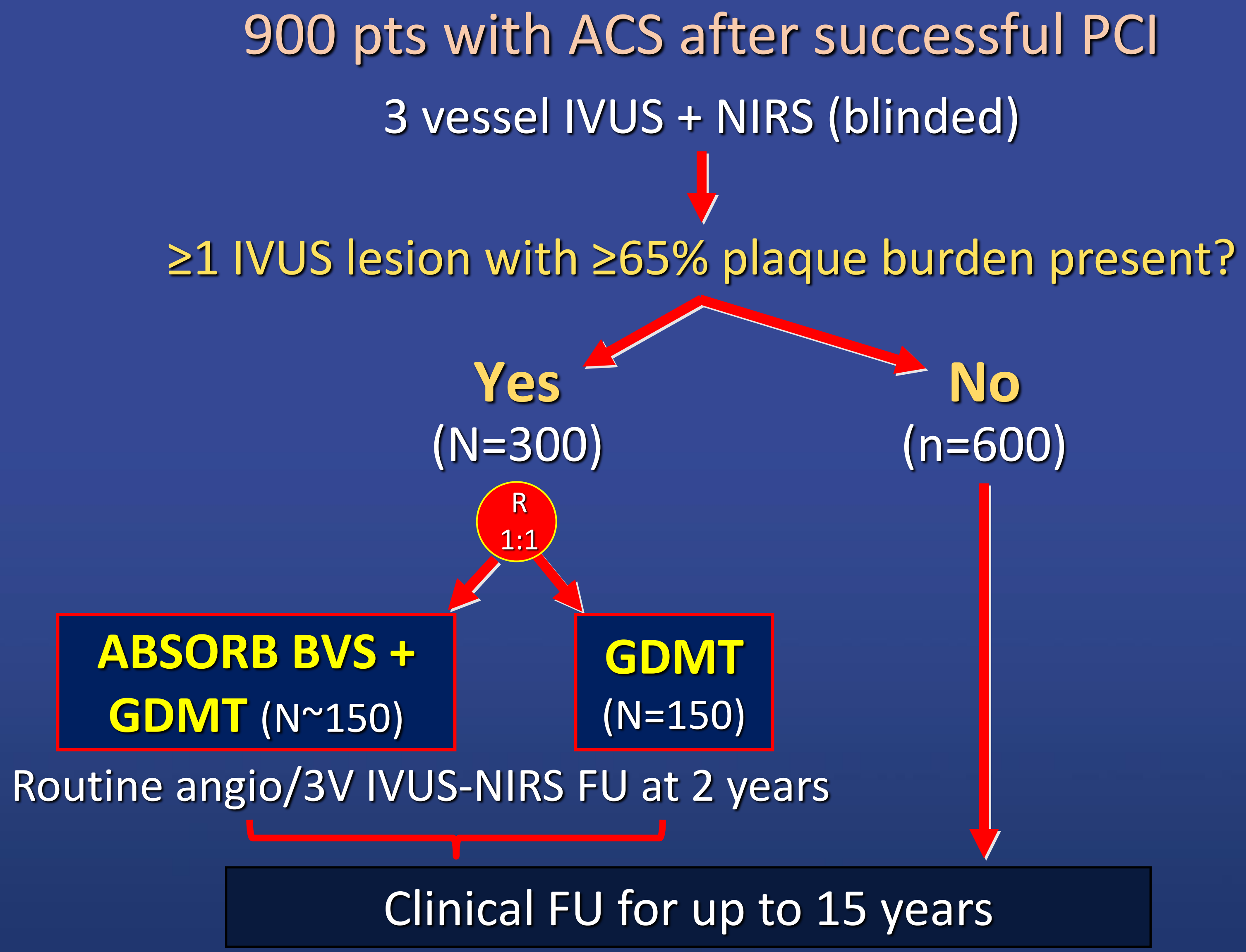
IVUS + NIRS (blinded) (prox 6-8 cm of each coronary artery)

↓

PROSPECT II
PROSPECT ABSORB

PROSPECT II Study

PROSPECT ABSORB RCT



The Preventive Coronary Intervention on Stenosis With Functionally Insignificant Stenosis With Vulnerable Plaque Characteristics

PREVENT Trial

Symptomatic or Asymptomatic CAD patients

Any epicardial coronary stenosis
with ***FFR ≥0.80*** and with ***Two*** of the following

- **IVUS MLA ≤4.0mm²**
- **IVUS Plaque Burden >70%**
- **TCFA by OCT or VH-IVUS**
- **Lipid-Rich Plaque on NIRS ($_{max}LCBI_{4mm}$>400)**

R

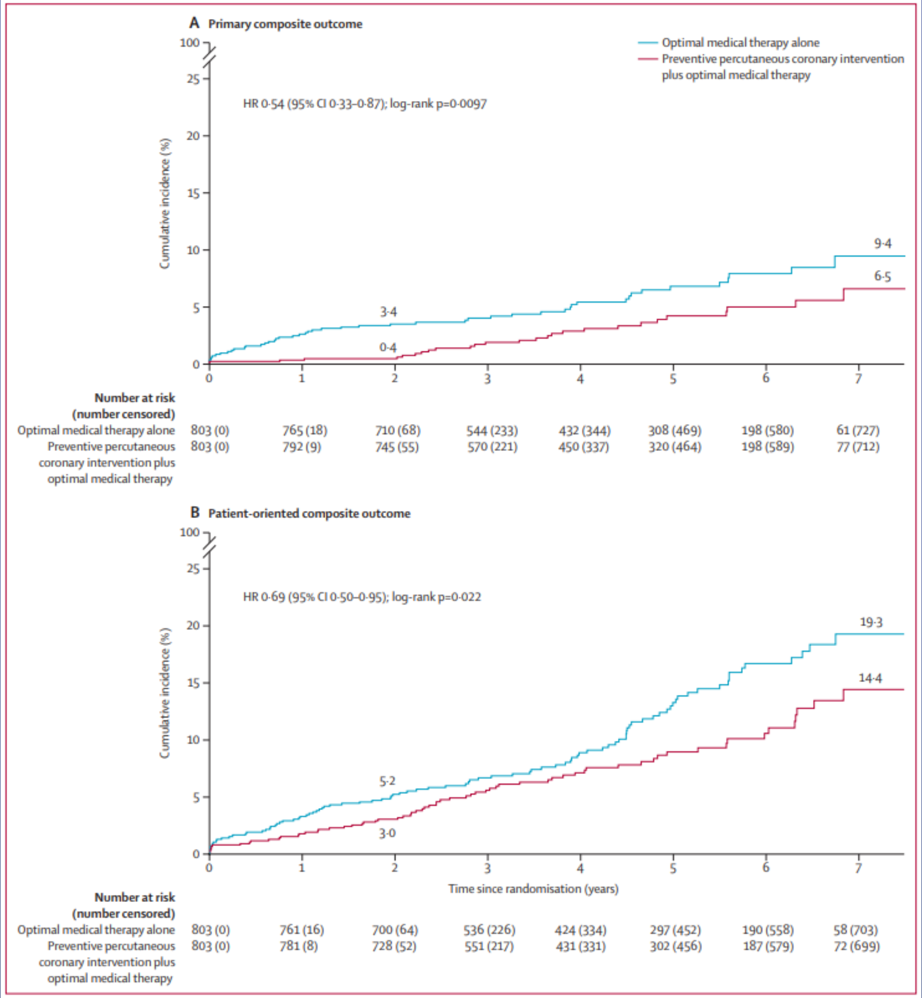
XIENCE+OMT	OMT
N=800	N=800

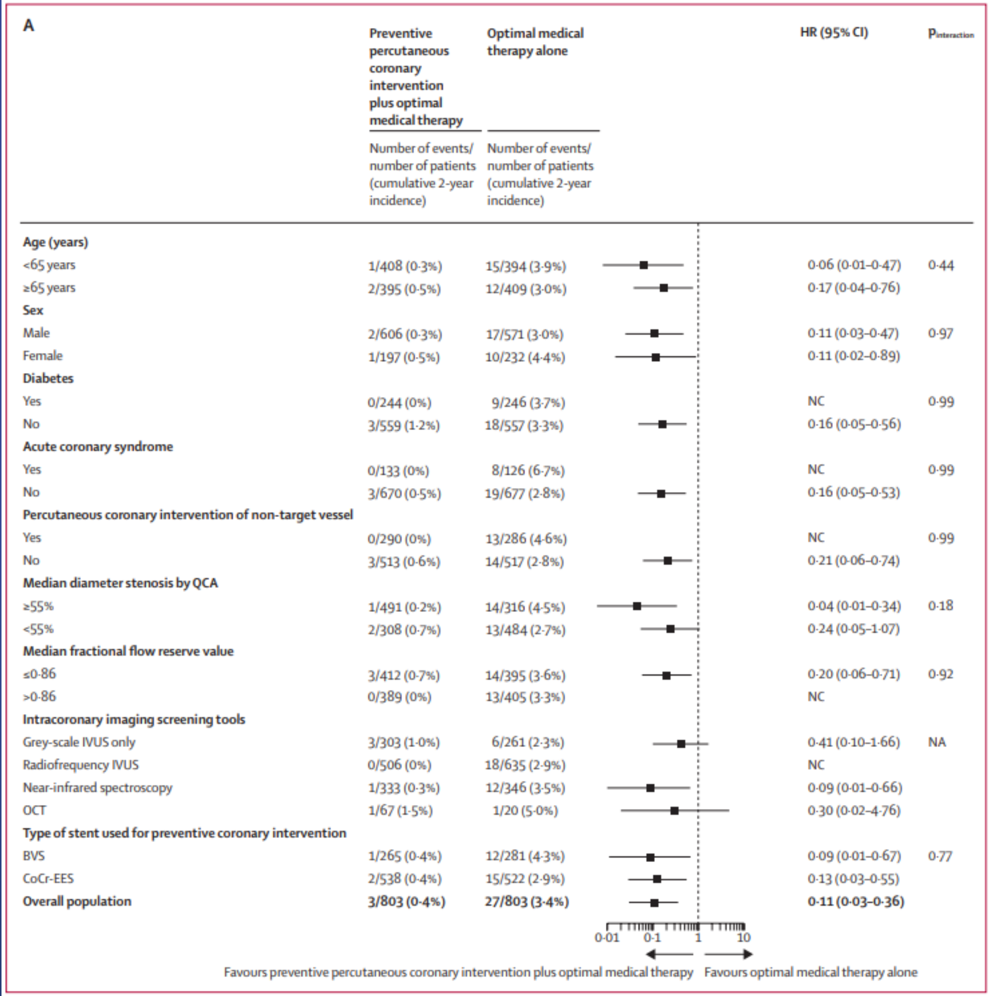
Primary endpoint at 2 years: CV death, MI, Hospitalization d/t unstable angina

OCT sub-study/ NIRS sub-study (300 patients in each arm at 2 years)

The Preventive Coronary Intervention on Stenosis With Functionally Insignificant Stenosis With Vulnerable Plaque Characteristics

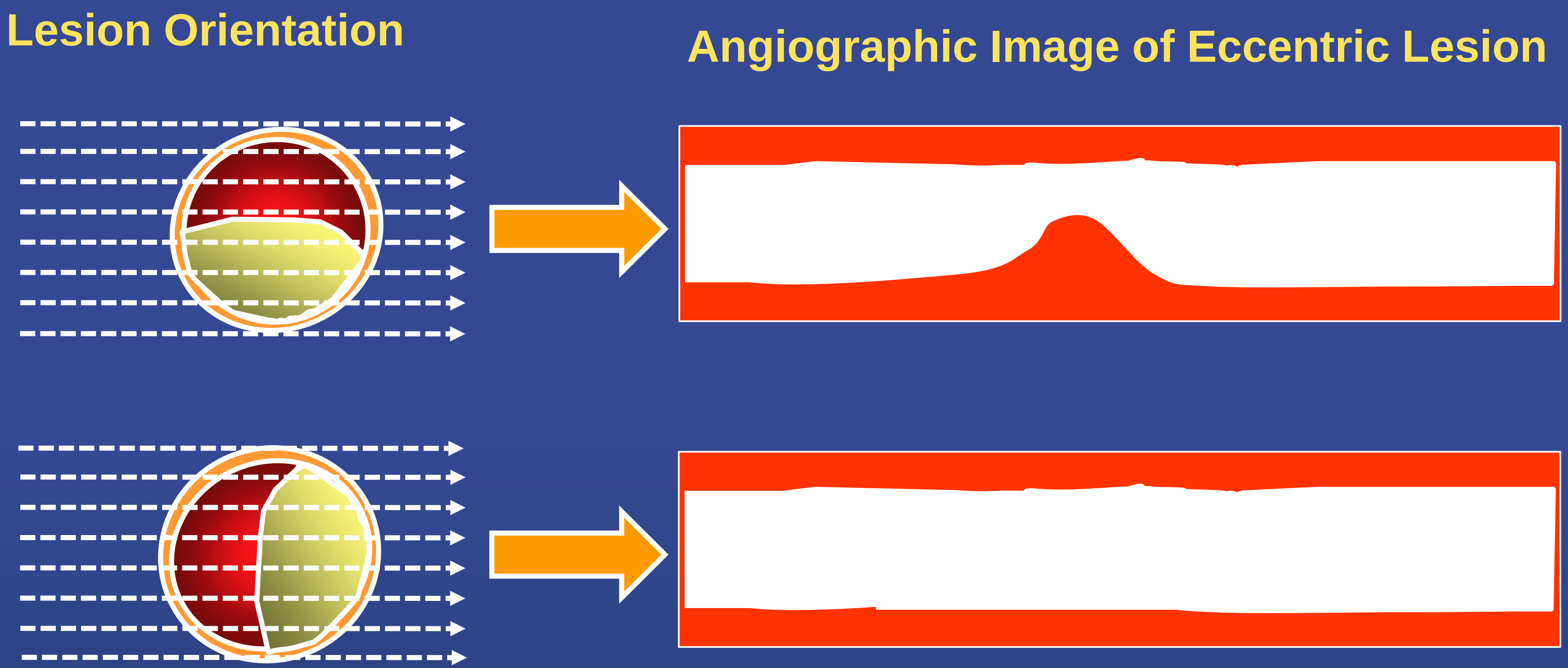
PREVENT Trial





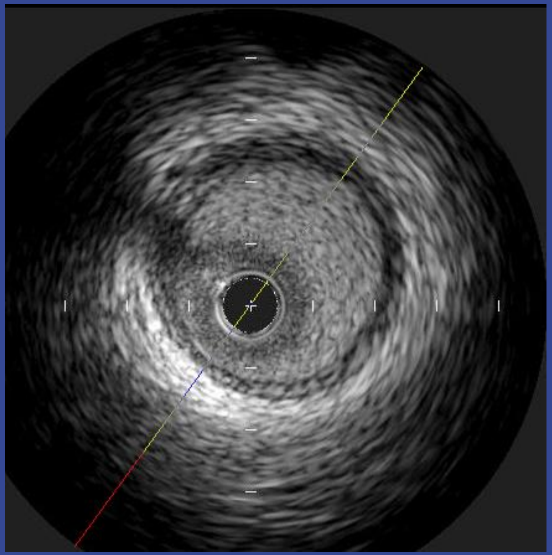
Imaging guided PCI

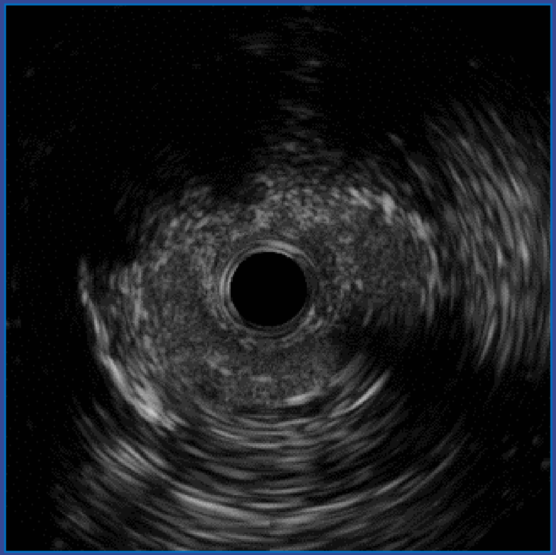
Angiography is a 'Luminography'

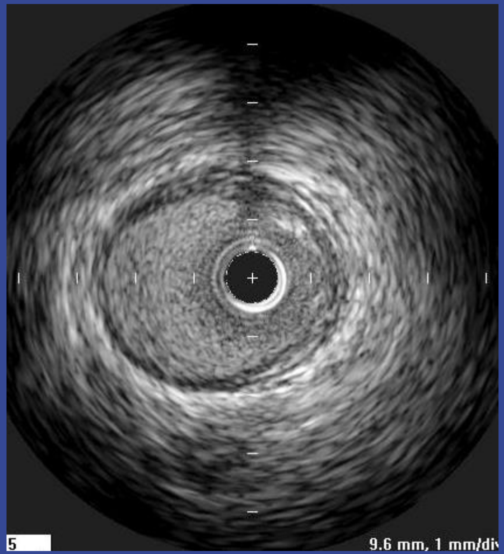


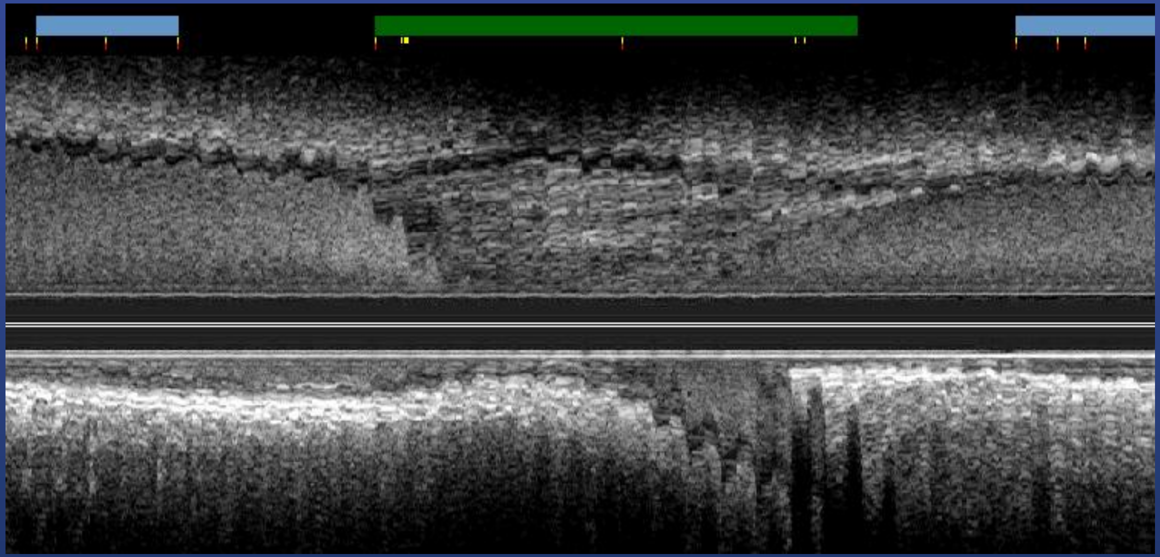
C. von Birgelen, TCT 2009

Intracoronary Imaging Visualizes the "Real" Vessel

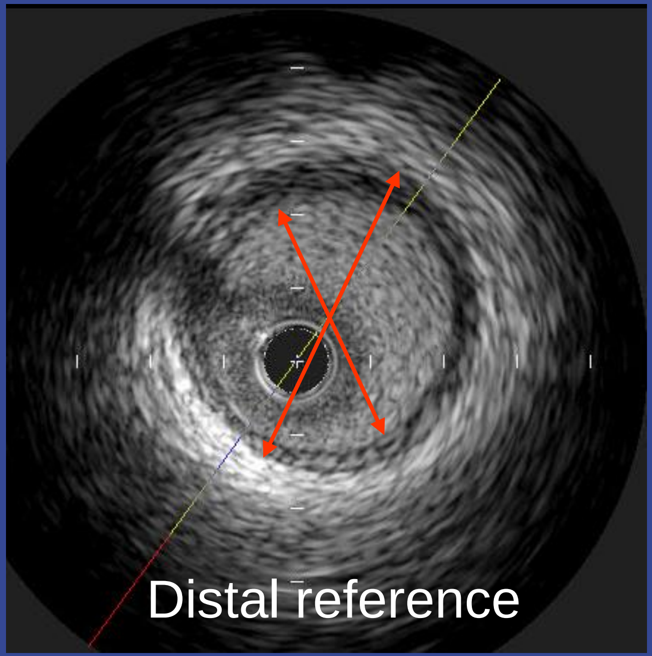


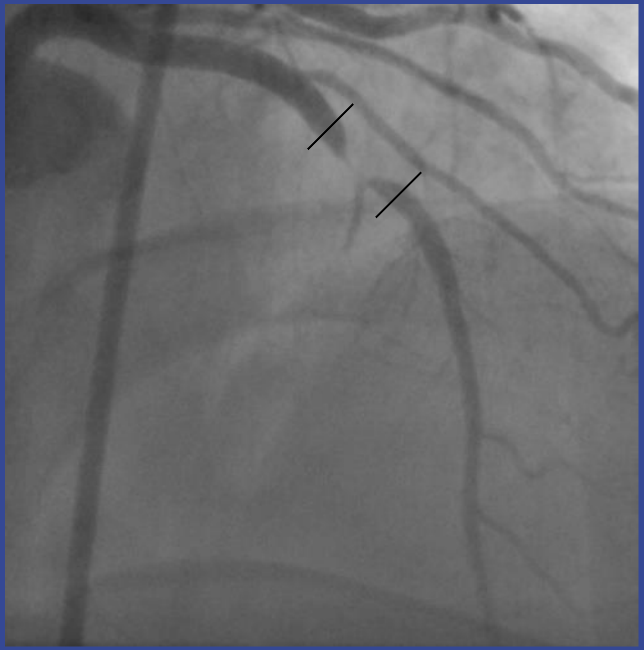


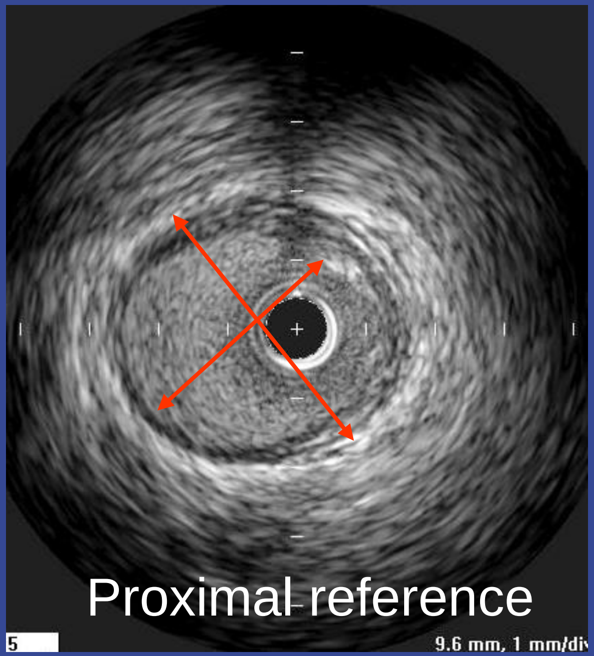


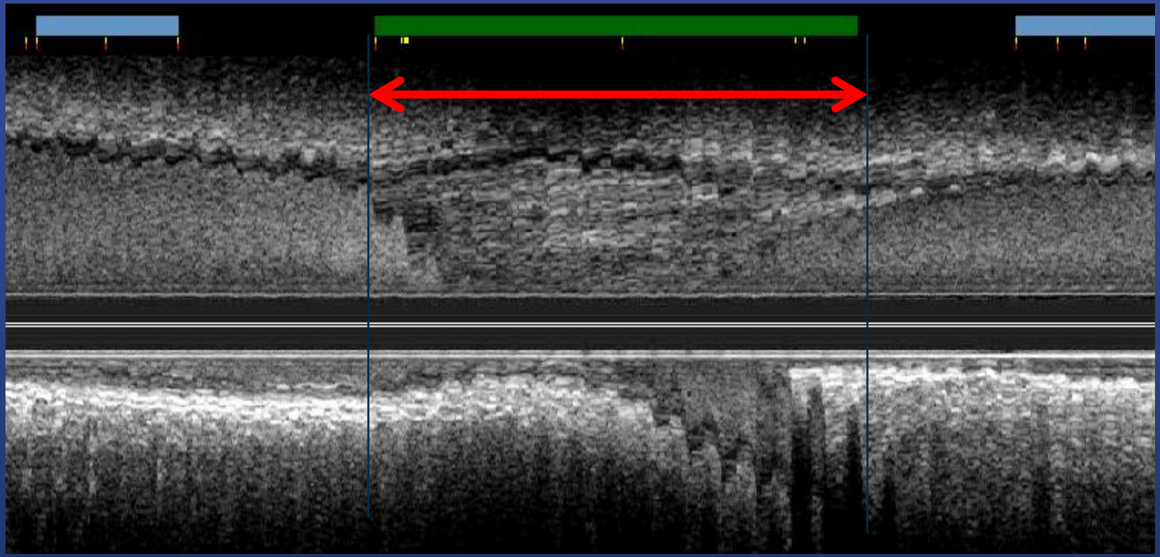


Assess Optimal Balloon / Stent Size & Landing Zone (Length)

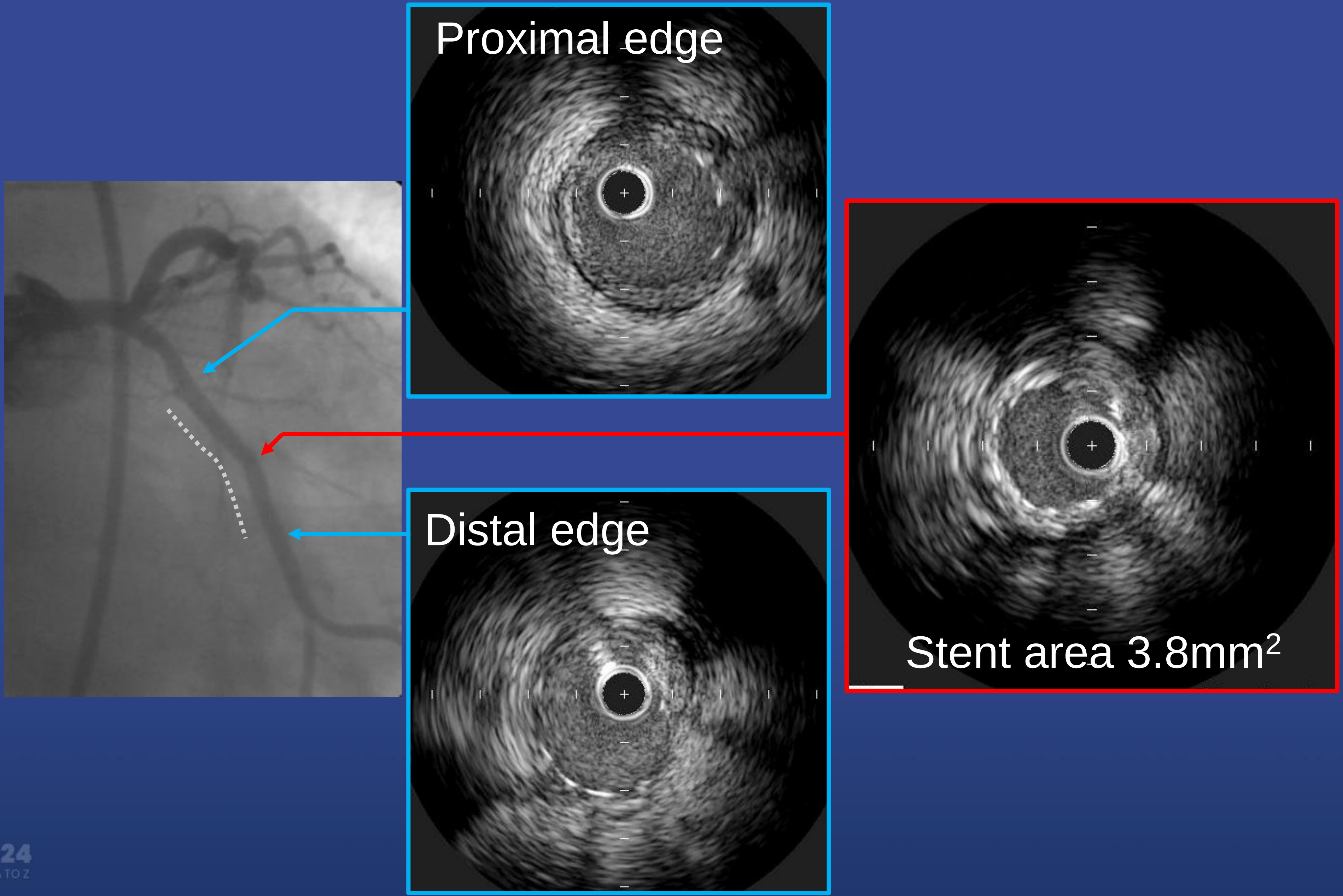




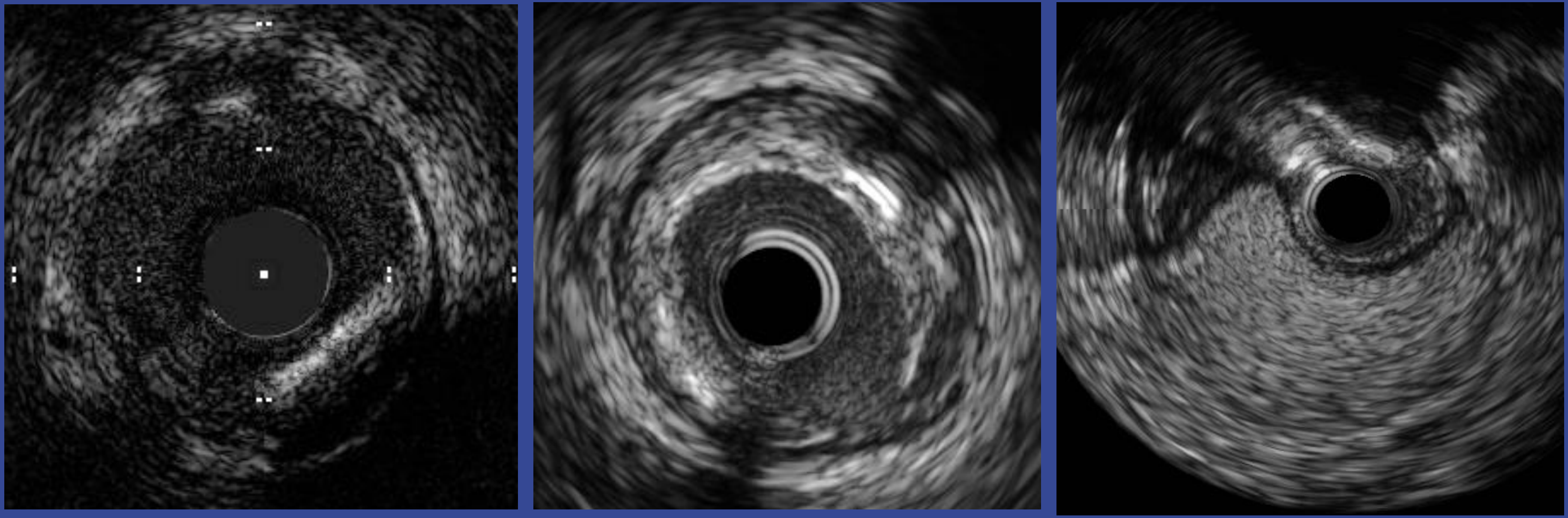




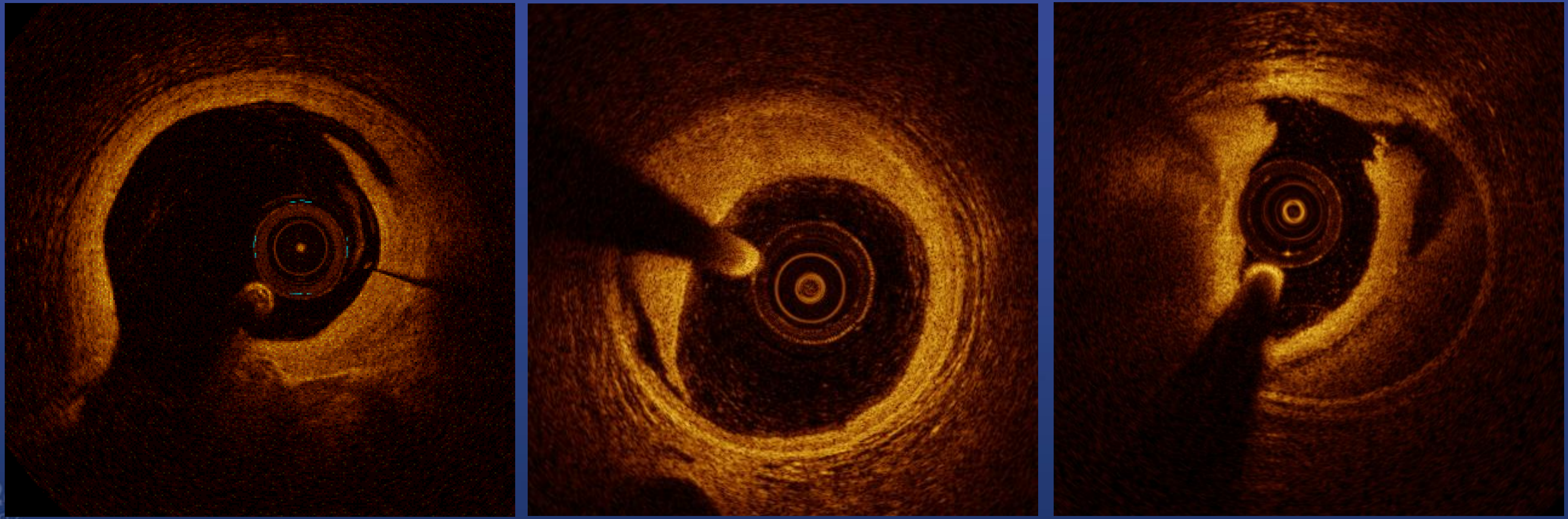
Review of Post-stenting Results (Apposition / Expansion)



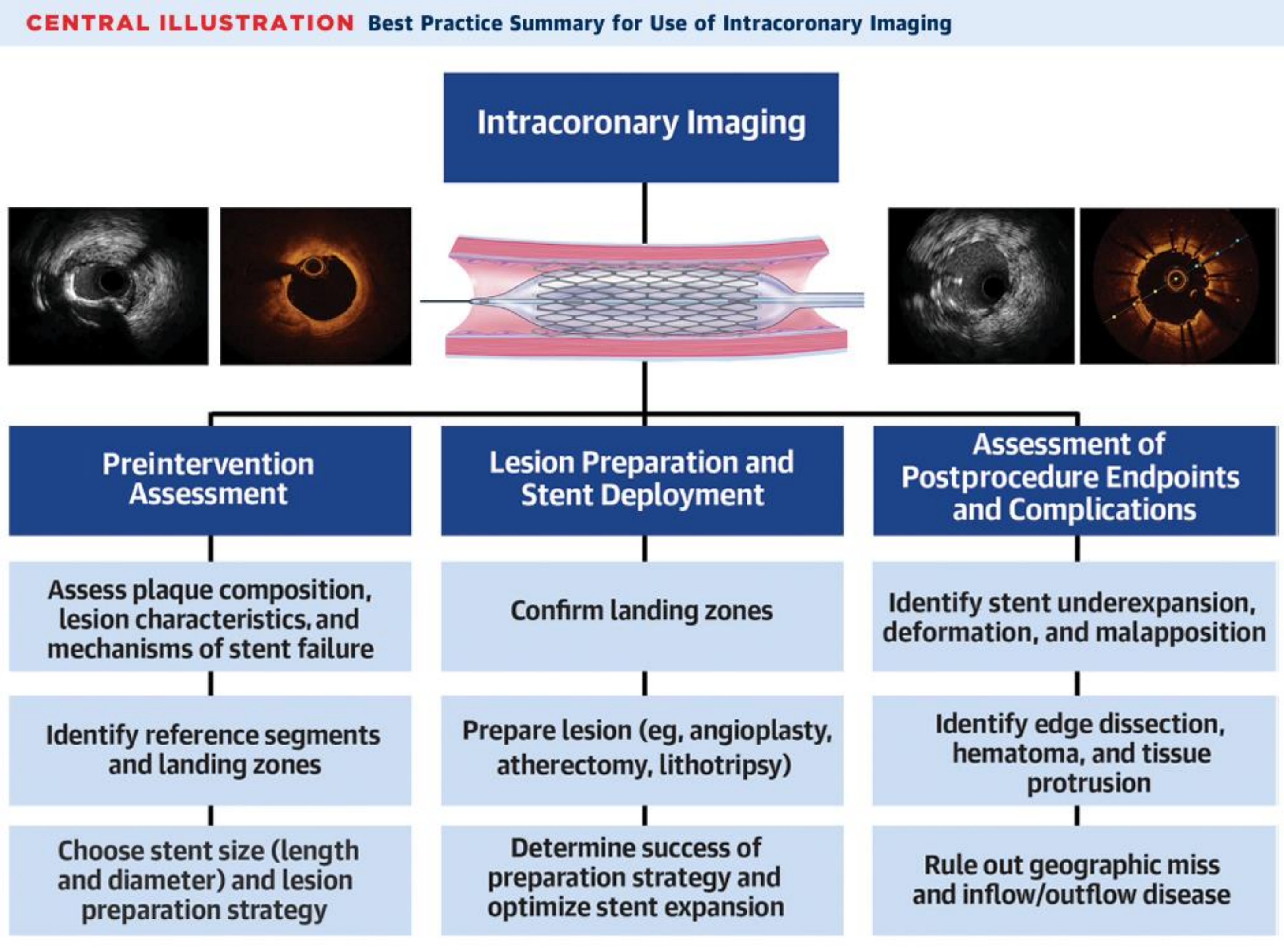
Identify Edge Problems – Dissections, Hematoma



Intimal | Medial | Intramural Hematoma



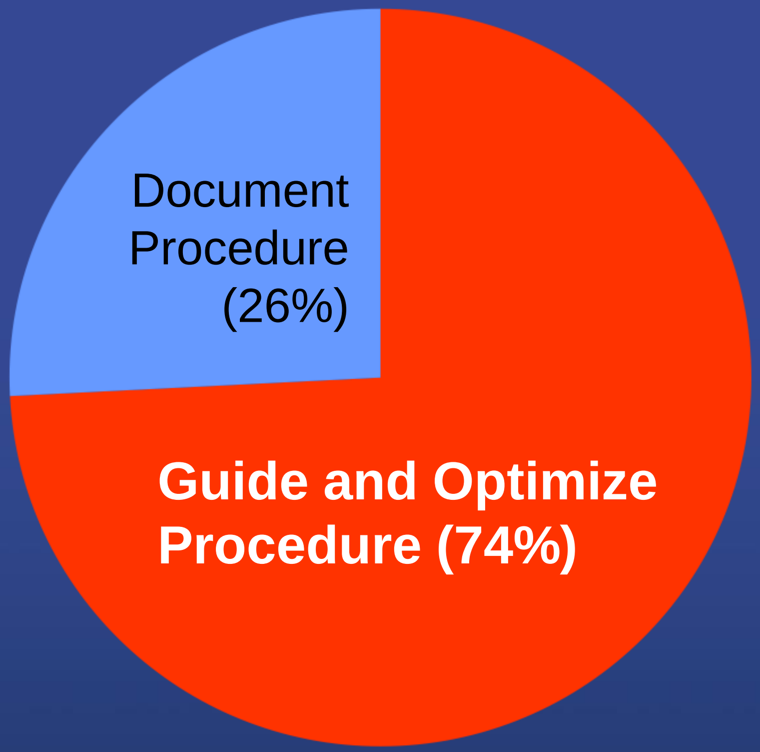
Use of intracoronary imaging

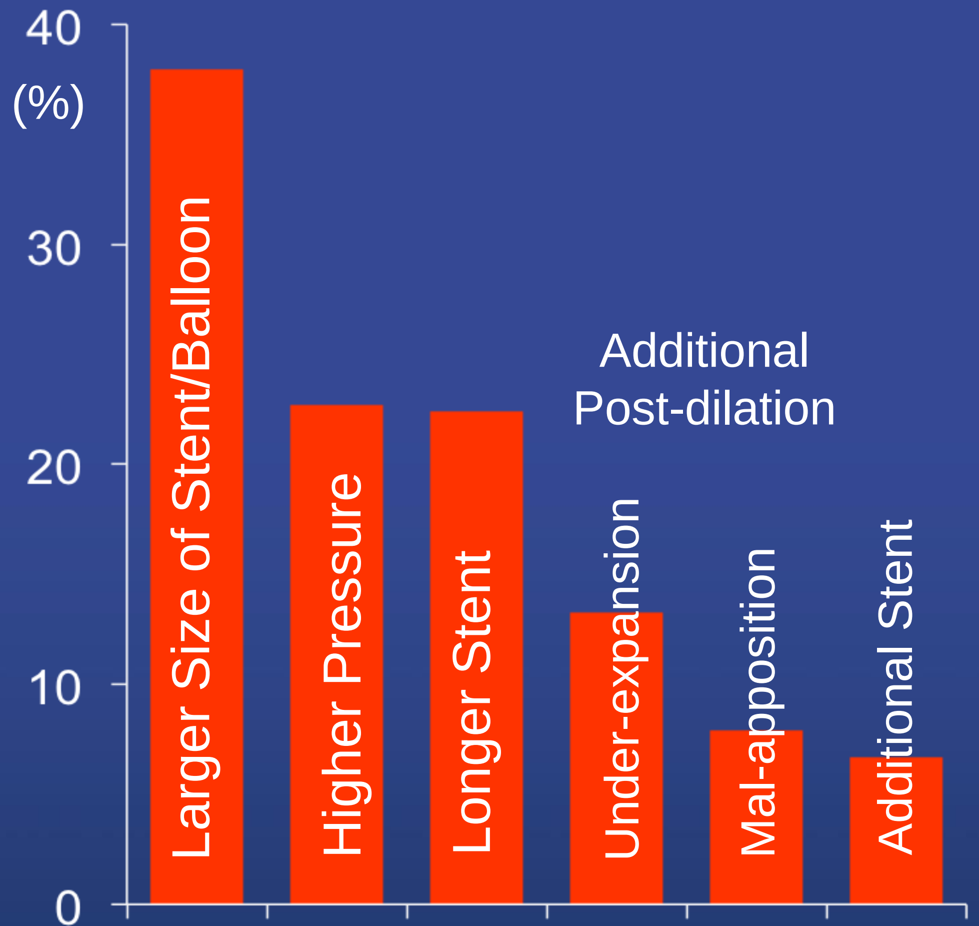


Truesdell et al. J Am Coll Cardiol. 2023;81(6):590-605.

How Intravascular Imaging Changed Procedure?

ADAPT-DES: Procedural Changes After IVUS in 74%



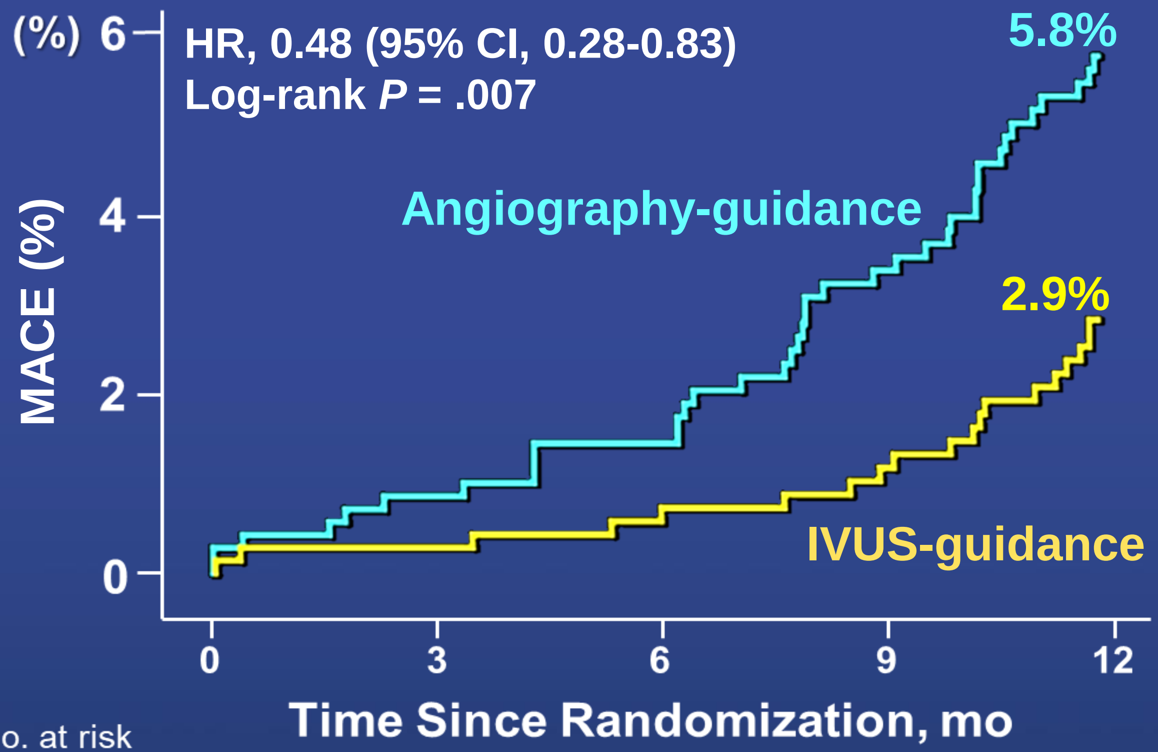


Witzenbichler et al. Circulation 2014;129:463-70

IVUS Improved Clinical Outcomes in Large RCTs

IVUS-XPL (Long lesions)

MACE (CD+TL-MI+ID-TLR)

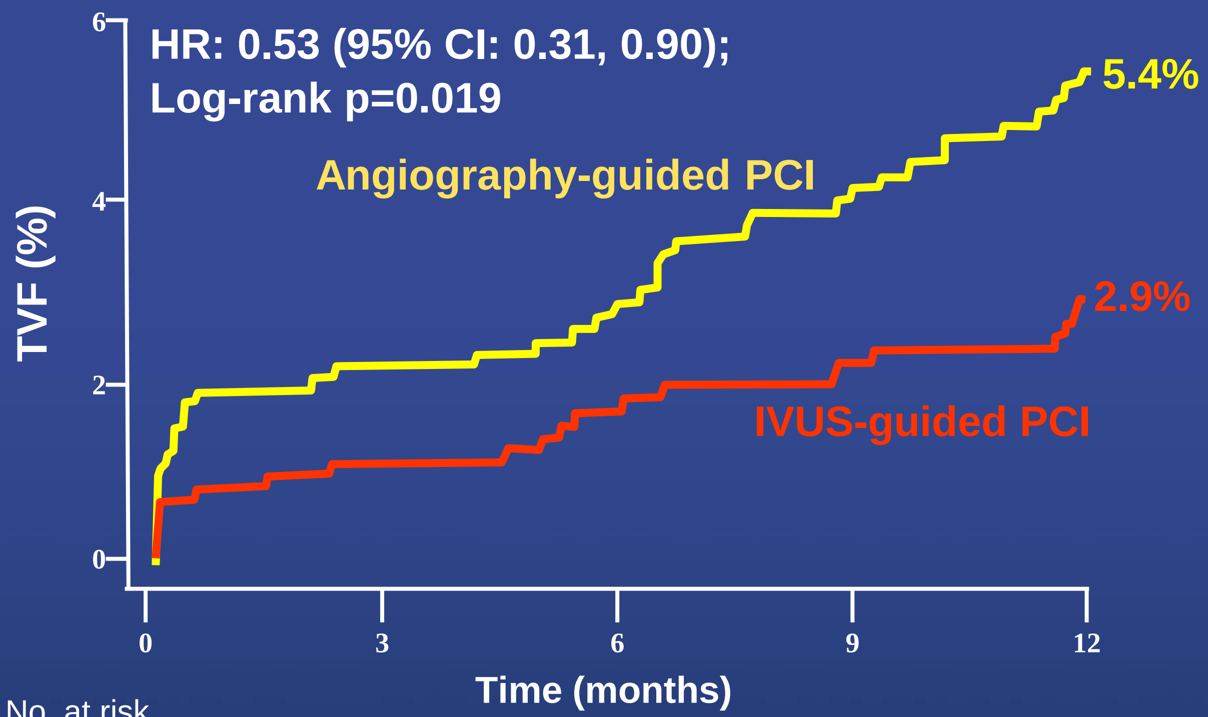


No. at risk					
Angiography arm	700	673	660	643	624
IVUS arm	700	671	665	654	641

Hong SJ, Hong MK et al. JAMA 2015;314:2155-63.

ULTIMATE (All-comer)

TVF (CD+TV-MI+CD-TVR)



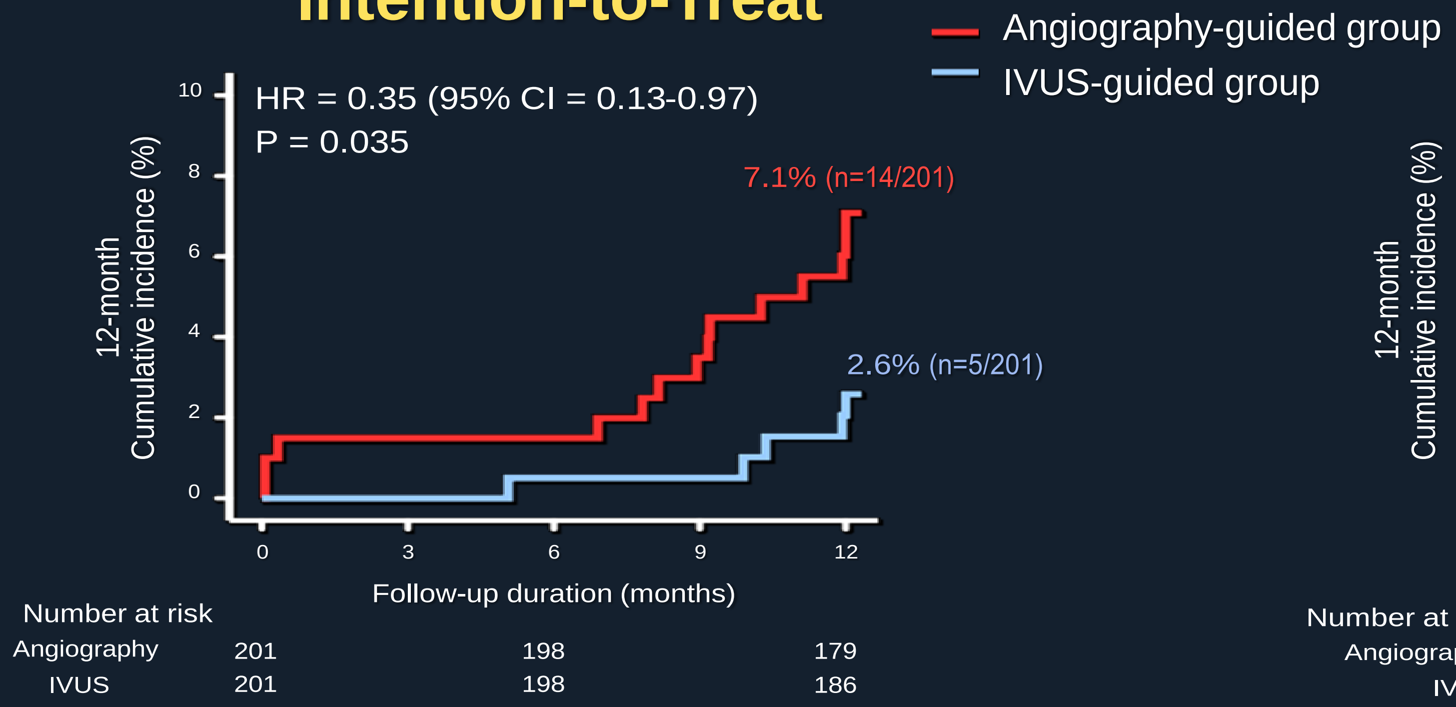
No. at risk					
Angiography	724	706	698	685	676
IVUS	724	715	710	704	696

Zhang J et al. J Am Coll Cardiol 2018;72:3126-27.

IVUS Improved Clinical Outcomes in CTO PCI

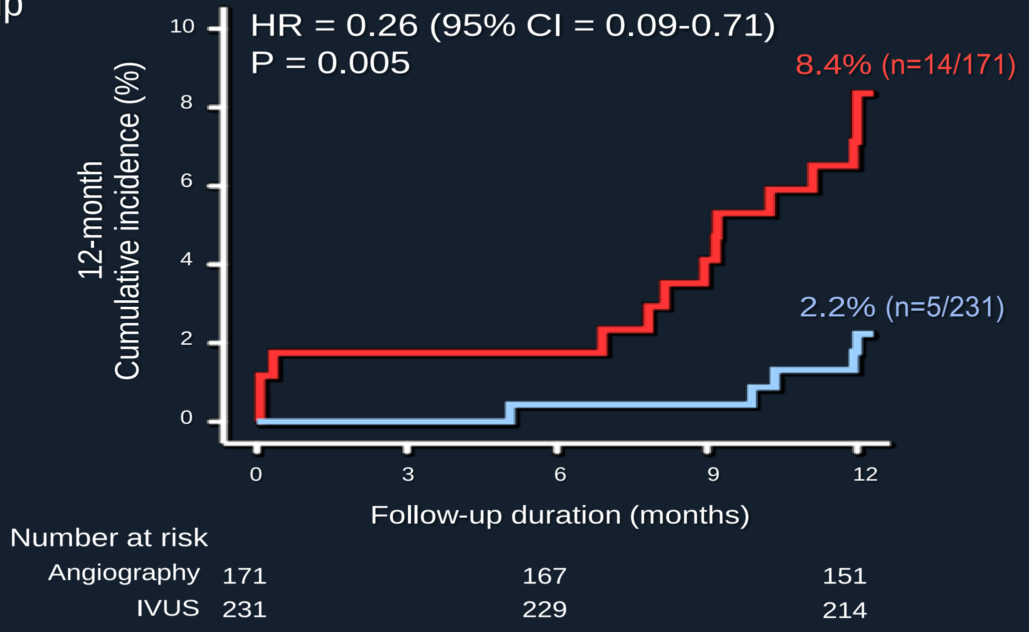
RCT (n=402), Primary endpoint : Cardiac death, MI, and TVR

Intention-to-Treat



	IVUS	Angio	P-value
Cardiac death/MI	0%	2%	0.045
TVR	2.6%	5.2%	0.186

Per Protocol



	IVUS	Angio	P-value
Cardiac death/MI	0%	2.3%	0.019
TVR	2.2%	6.1%	0.049

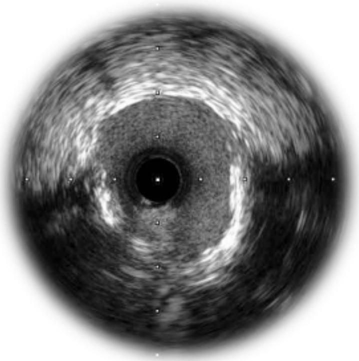
Kim BK et al. Circ Cardiovasc Interv. 2015 Jul;8(7):e002592.

IVUS Use was Associated with Better 10-yr Outcomes after LM PCI

MAIN-COMPARE Registry

Left Main Disease

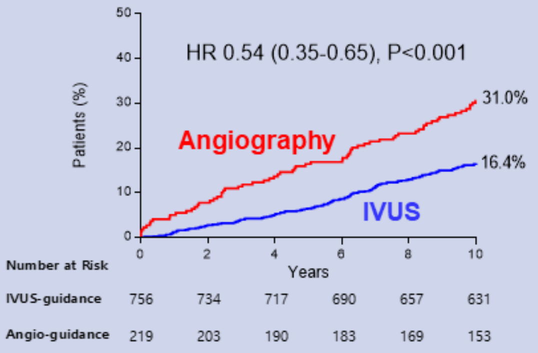
IVUS-guided PCI



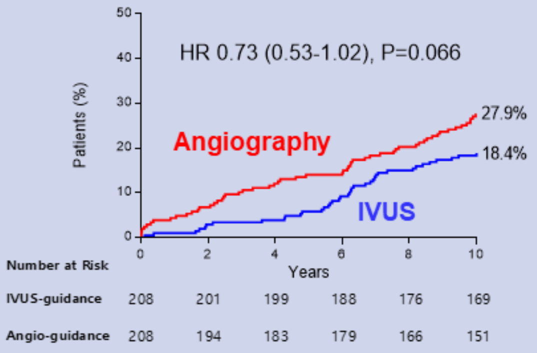
10-Year Follow-up

	Overall Population	After Propensity-score Matching
All-cause death	see chart 3 below	see chart 4 below
Composite of all-cause death, Q-wave MI, or stroke	see chart 5 below	see chart 6 below

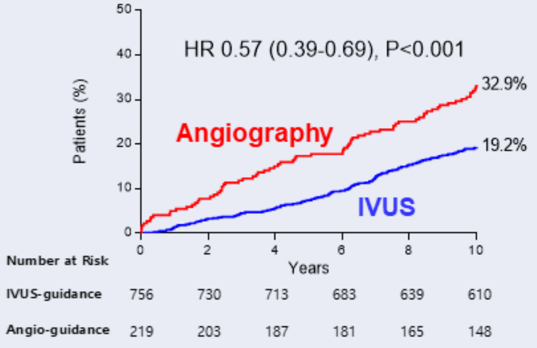
All-cause death — Overall Population



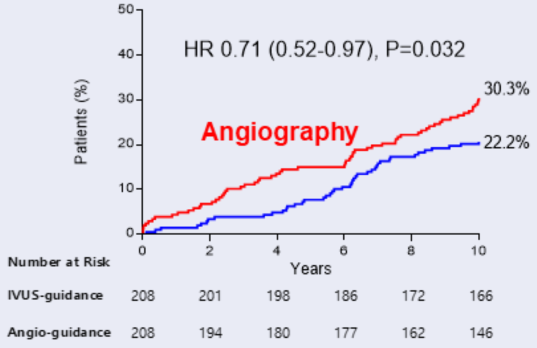
All-cause death — After Propensity-score Matching



Composite of all-cause death, Q-wave MI, or stroke — Overall Population



Composite of all-cause death, Q-wave MI, or stroke — After Propensity-score Matching



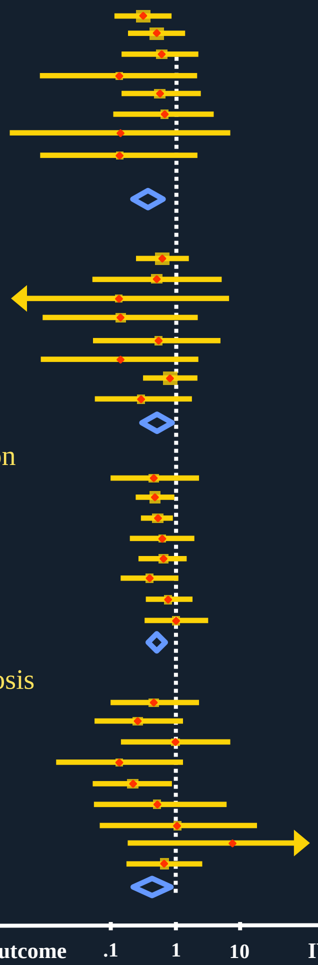
Kang DY et al, Circ Cardiovasc Interv. 2021.

Updated Meta-analysis of 10 RCTs

IVUS use was associated with Better Clinical Outcomes (N=5160)

← IVUS Better

Study	Year	OR [95% CI]	IVUS	Angio
Cardiovascular mortality				
Liu et al	2019	0.33 (0.11, 1.00)	3/167	10/169
ULTIMATE	2018	0.51 (0.18, 1.41)	5/724	10/724
IVUS-XPL	2015	0.61 (0.15, 2.43)	3/700	5/700
CTO-IVUS	2015	0.13 (0.01, 2.16)	0/201	2/201
AIR-CTO	2015	0.60 (0.15, 2.44)	3/115	5/115
Tan et al	2015	0.67 (0.11, 4.00)	2/61	3/62
Kim et al	2013	0.14 (0.00, 6.95)	0/269	1/274
AVIO	2013	0.13 (0.01, 2.16)	0/142	2/142
Zhang et al	2016	Excluded	0/42	0/42
		0.44 (0.26, 0.75)	16/2421	38/2429
MI				
ULTIMATE	2018	0.64 (0.25, 1.62)	7/724	11/724
Zhang et al	2016	0.51 (0.05, 4.99)	1/42	2/42
IVUS-XPL	2015	0.14 (0.00, 6.82)	0/700	1/700
CTO-IVUS	2015	0.13 (0.01, 2.16)	0/201	2/201
Tan et al	2015	0.52 (0.05, 5.06)	1/61	2/62
Kim et al	2013	0.14 (0.01, 2.20)	0/269	2/274
AVIO	2013	0.82 (0.34, 1.96)	10/142	12/142
HOME DES IVUS	2010	0.29 (0.05, 1.73)	1/105	4/105
		0.55 (0.32, 0.94)	20/2244	36/2250
Target lesion revascularization				
Liu et al	2019	0.42 (0.09, 1.89)	2/167	5/169
ULTIMATE	2018	0.48 (0.23, 1.02)	9/724	19/724
IVUS-XPL	2015	0.52 (0.29, 0.91)	17/700	33/700
CTO-IVUS	2015	0.62 (0.21, 1.87)	5/201	8/201
AIR-CTO	2015	0.65 (0.26, 1.61)	8/115	12/115
Tan et al	2015	0.39 (0.14, 1.10)	5/61	12/62
AVIO	2013	0.74 (0.35, 1.58)	13/142	17/274
HOME DES IVUS	2010	1.00 (0.31, 3.20)	6/105	6/105
		0.57 (0.42, 0.77)	66/2215	112/2218
Definite/probable stent thrombosis				
Liu et al	2019	0.42 (0.09, 1.89)	2/167	5/169
ULTIMATE	2018	0.26 (0.05, 1.30)	1/724	5/724
IVUS-XPL	2015	1.00 (0.14, 7.11)	2/700	2/700
CTO-IVUS	2015	0.13 (0.01, 1.30)	0/201	3/201
AIR-CTO	2015	0.21 (0.05, 0.87)	1/115	7/115
Tan et al	2015	0.52 (0.05, 5.06)	1/61	2/62
Kim et al	2013	1.02 (0.06, 16.33)	1/269	1/274
AVIO	2013	7.39 (0.15, 372.38)	1/142	0/142
HOME DES IVUS	2010	0.66 (0.19, 2.34)	4/105	6/105
		0.44 (0.24, 0.79)	13/2484	31/2492



Angiography Better →

Elgendy et al, Circ J 2019;83:1410-13

2021 ACC/AHA PCI Guideline for Intracoronary Imaging

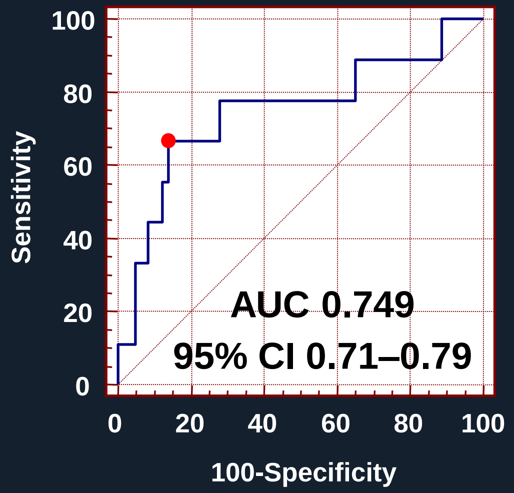
	COR	LOE
➢ In patients undergoing coronary stent implantation, IVUS can be useful for procedural guidance, particularly in cases of left main or complex coronary artery stenting, to reduce ischemic events	IIa	B
➢ In patients undergoing coronary stent implantation, OCT is a reasonable alternative to IVUS for procedural guidance, except in ostial left main disease	IIa	B
➢ In patients with stent failure, IVUS or OCT is reasonable to determine the mechanism of stent failure	IIa	C

Lawton JS et al. JACC 2021.

The Best Cut-off of Edge Restenosis

Plaque Burden <55%

433 E-ZES

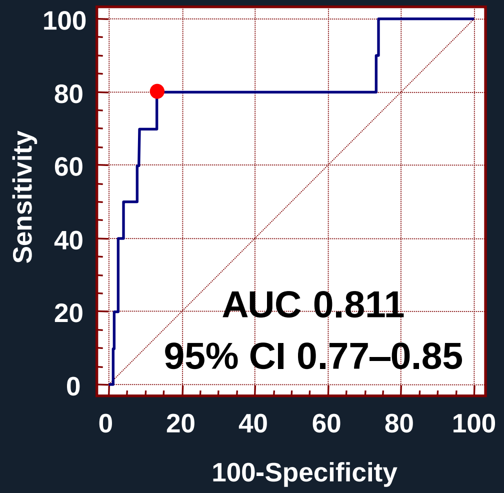


PB 56.3%

Sensitivity 67%

Specificity 86%

422 R-ZES

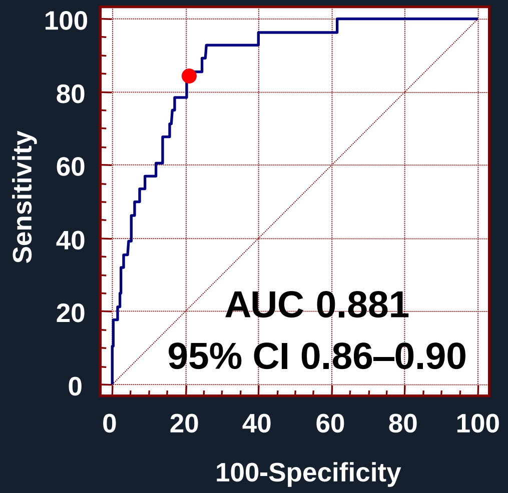


PB 57.3%

Sensitivity 80%

Specificity 87%

813 EES



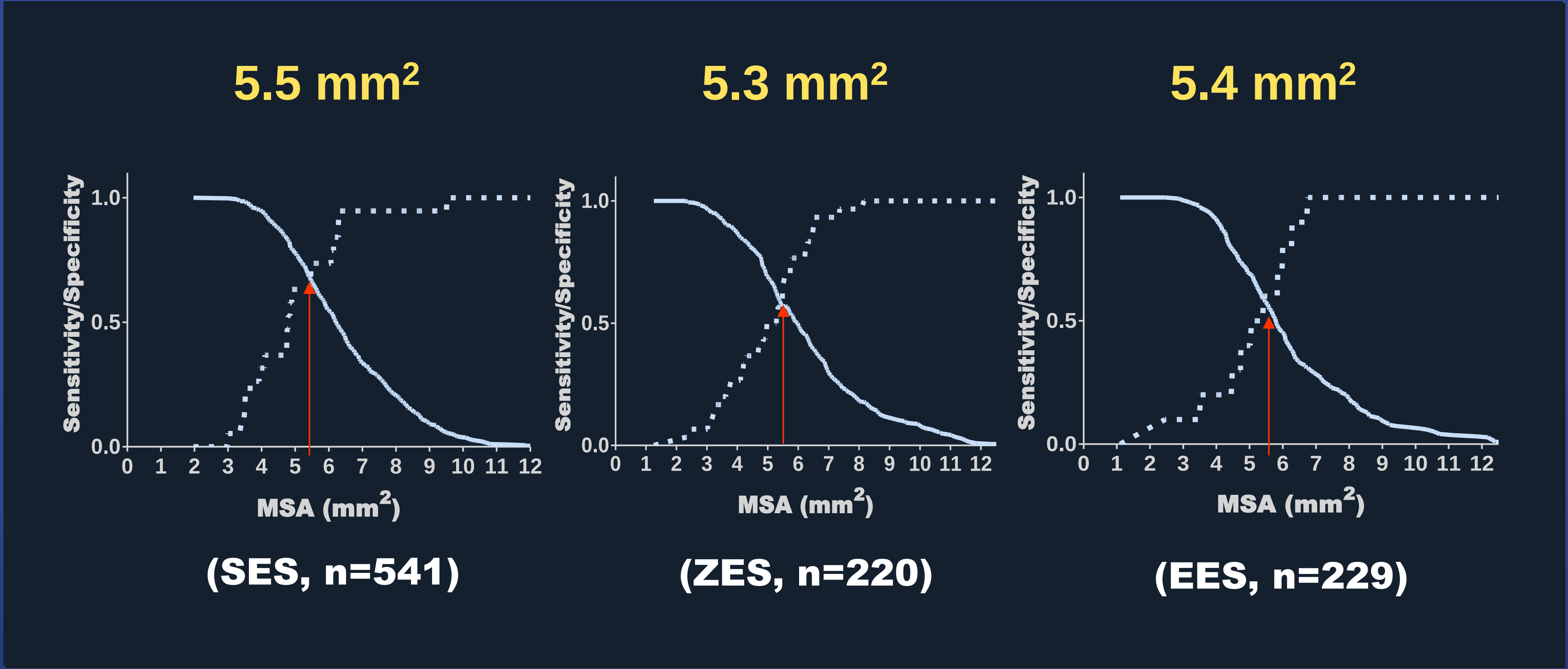
PB 54.2%

Sensitivity 86%

Specificity 80%

Kang SJ et al. Am J Cardiol 2013

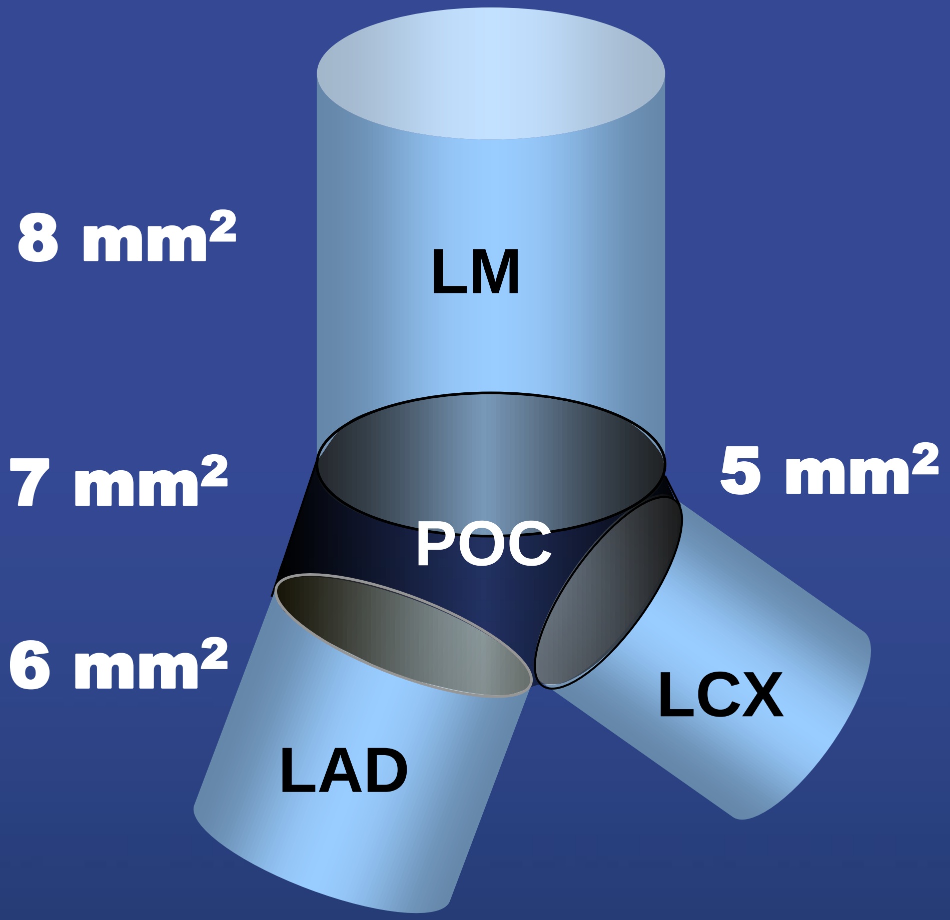
Effective Stent Area (> 5.0 mm²),
Can Lower TLR <2%

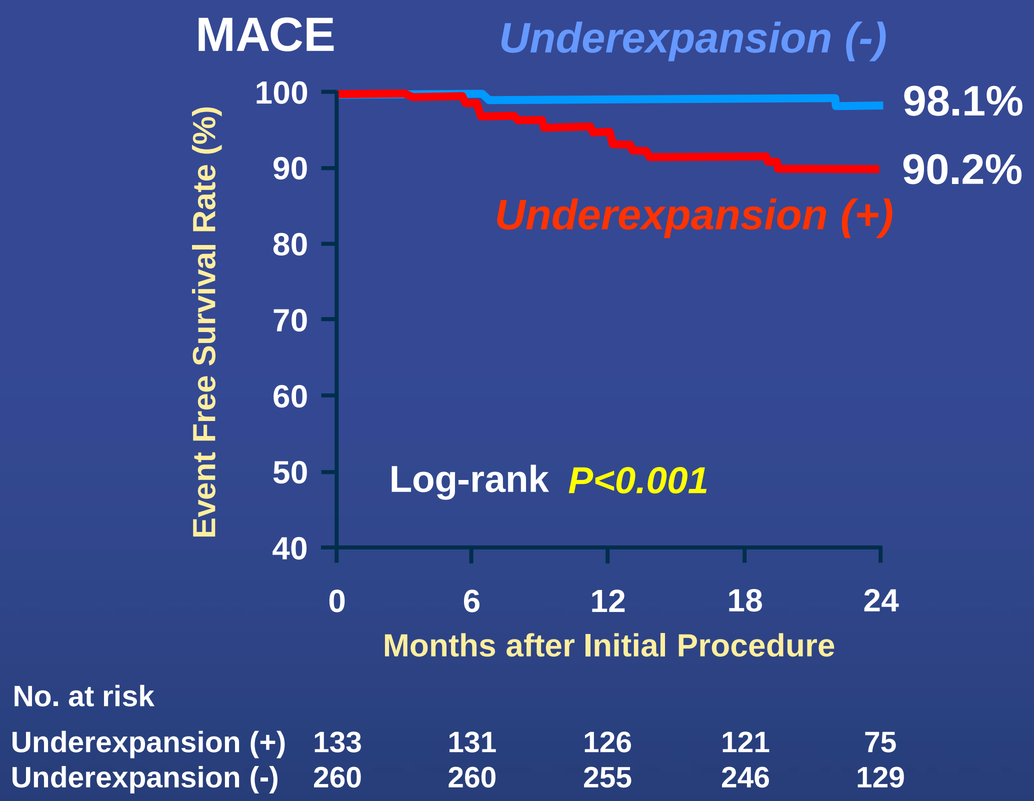


Song HG et al, Catheterization and Cardiovascular Interventions. 2012.

Stent Area after LM Bifurcation PCI : the Bigger the Better

Rule of 5, 6, 7, 8



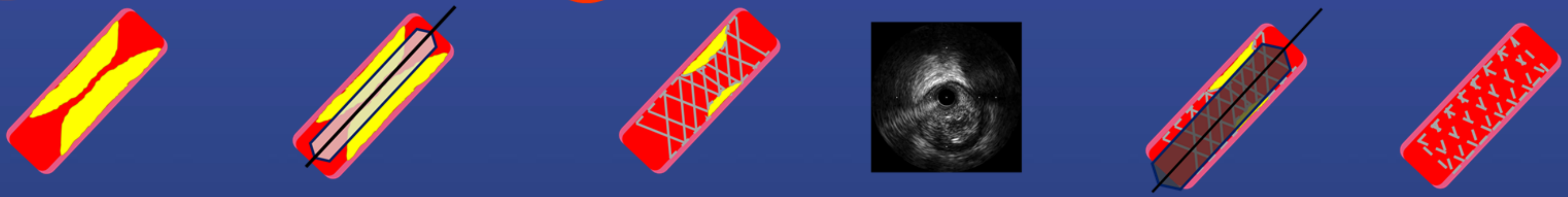


Kang SJ et al. Circ Cardiovasc Interv 2011;4:562-9.

Imaging-Guided PSP

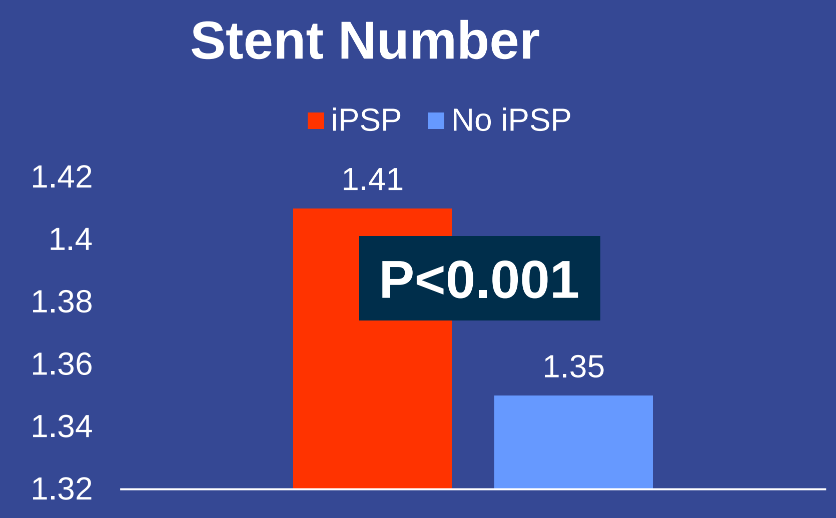
Under the Intracoronary Imaging Guidance

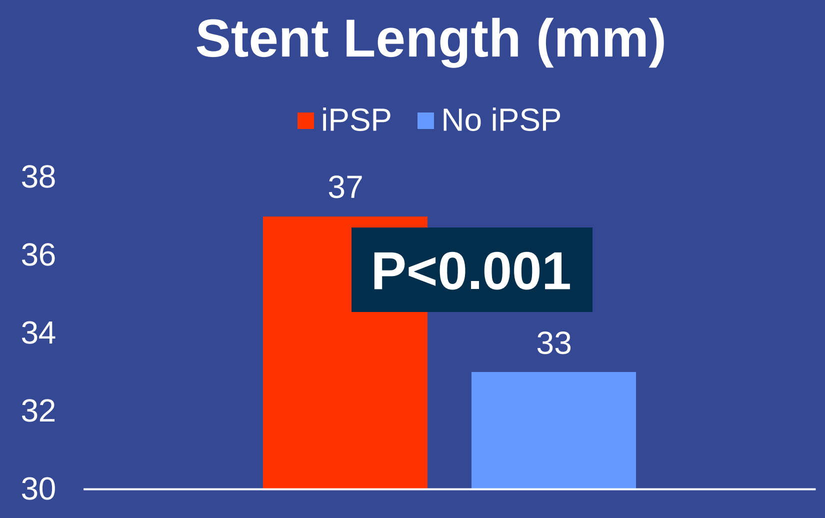
Inspection of lesion characteristic by IVUS	Selection of stent size and length by IVUS	Surveillance of stent outcomes
Calcification Plaque burden and configuration Opening of side branch	Stent landing zone configuration Lesion length Reference vessel size	Stent apposition Stent area Procedural complications
P Pre-dilation	**S** Stent Sizing	**P** Post-dilation
Lesion pre-modification for stent delivery and expansion: High pressure balloon Cutting or scoring balloon Rota-ablation	Full lesion coverage Adequate stent size	Complete stent apposition Sufficient stent area No geographic miss No procedural complications

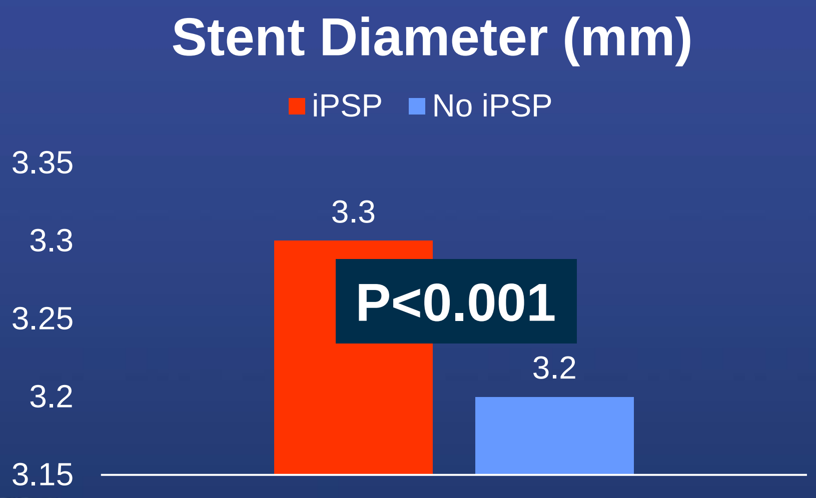


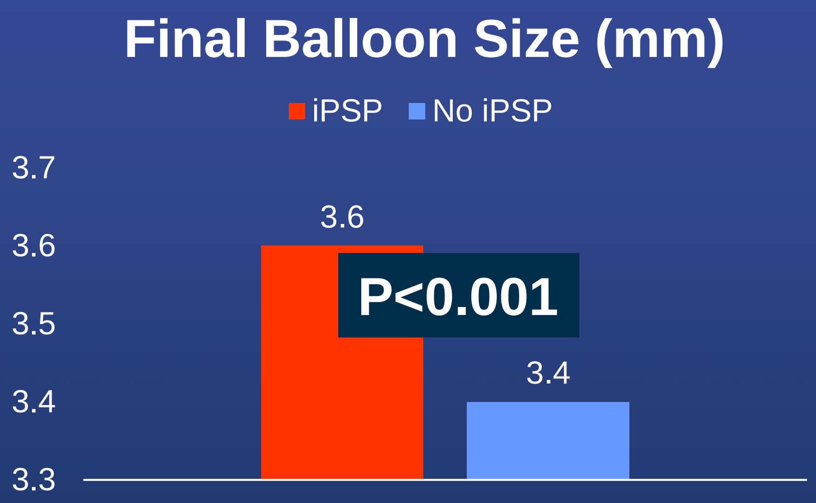
Park HB, Ahn JM, Park SJ et al. JACC Cardiovasc Interv. 2020;13:1403-1413.

Imaging-Guided PSP, What Is Different?









Park HB et al. JACC Cardiovasc Interv. 2020;13:1403-1413.

Imaging-Guided Complex PCI – Better Clinical Outcome

	Crude cumulative incidence (%)			Multivariate analysis		PS matching		IPTW	
	iPSP	No iPSP	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Primary outcome	**5.7**	**8.0**	**0.001**	**0.74 (0.61-0.90)**	**0.003**	**0.71 (0.56-0.90)**	**0.005**	**0.71 (0.63-0.81)**	**<0.001**
Cardiac death	2.3	3.6	0.003	0.73 (0.53-0.99)	0.047	0.78 (0.53-1.15)	0.20	0.62 (0.51-0.75)	0.003
Target vessel MI	0.2	0.5	0.19	0.68 (0.30-1.55)	0.36	0.78 (0.29-2.09)	0.62	0.65 (0.38-1.10)	0.10
TVR	3.4	4.6	0.02	0.73 (0.57-0.94)	0.02	0.68 (0.50-0.92)	0.01	0.74 (0.63-0.87)	<0.001

Park HB et al. JACC Cardiovasc Interv. 2020;13:1403-1413.

Post-dilation was the Most Significant Event Predictor Among 3 Components of iPSP

	Univariate analysis		Multivariate analysis*	
	HR (95% CI)	P value	HR (95% CI)	P value
Pre-dilation	0.89 (0.69-1.15)	0.374	0.84 (0.64-1.11)	0.216
Stent-sizing	0.79 (0.67-0.93)	0.004	0.89 (0.74-1.07)	0.219
Post-dilation	**0.79 (0.67-0.94)**	**0.006**	**0.80 (0.67-0.96)**	**0.016**

Park HB et al. JACC Cardiovasc Interv. 2020;13:1403-1413.

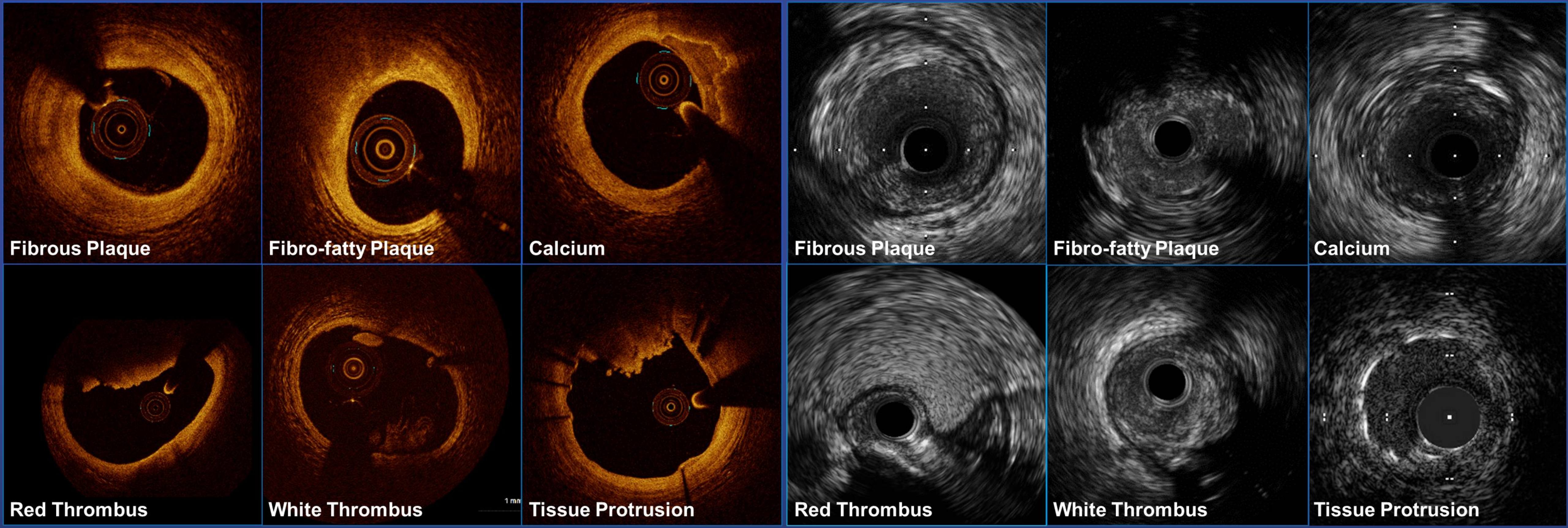
Post-Balloon Size was Larger With IVUS

Pre-dilation	IVUS	Post-dilation	No. of patients (%)	Stent diameter (mm)	Post balloon size (mm)	Annualized event rate	Adjusted HR (95% CI)	P value
No	No	Yes	129 (1.4)	3.04 ± 0.41	3.10 ± 0.81	3.04 %	0.81 (0.35-1.85)	0.613
				Δ +0.05 (P=0.550)				
Yes	No	Yes	1719 (18.0)	3.08 ± 0.38	3.12 ± 0.86	3.07 %	0.80 (0.53-1.21)	0.297
				Δ +0.04 (P=0.104)				
No	Yes	Yes	309 (3.2)	3.43 ± 0.41	3.79 ± 0.70	2.04%	0.72 (0.39-1.35)	0.306
				Δ +0.35 (P<0.001)				
Yes	Yes	Yes	3374 (35.4)	3.26 ± 0.39	3.58 ± 0.60	1.98%	0.63 (0.42-0.93)	0.022
				Δ +0.32 (P<0.001)				

Park HB et al. JACC Cardiovasc Interv. 2020;13:1403-1413.

OCT vs. IVUS

OCT vs. IVUS



Fibrous Plaque
Fibro-fatty Plaque
Calcium
Fibrous Plaque
Fibro-fatty Plaque
Calcium
Red Thrombus
White Thrombus
Tissue Protrusion
Red Thrombus
White Thrombus
Tissue Protrusion

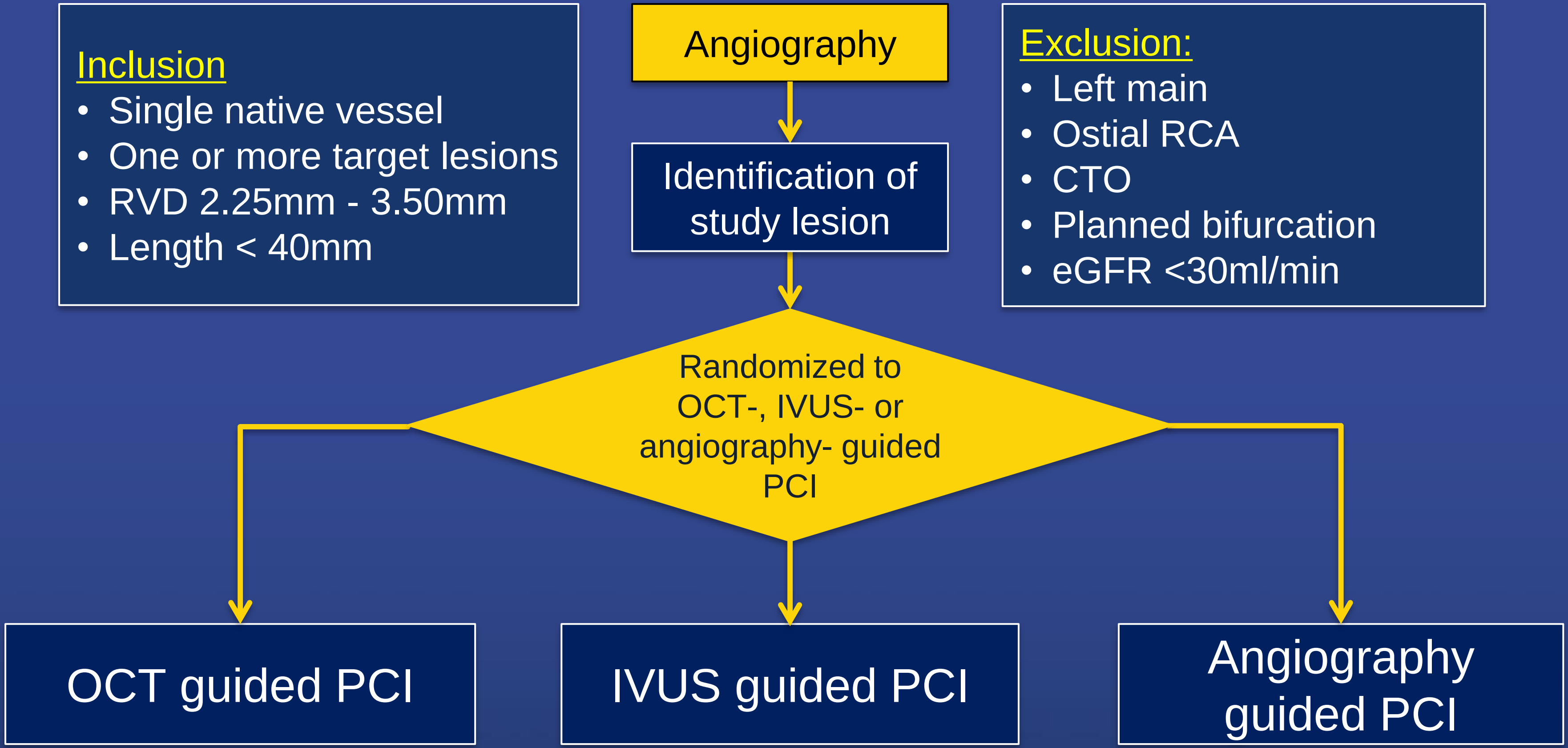
OCT vs. IVUS

	OCT	IVUS
Wave source	Near-infrared light	Ultrasound
Axial resolution, µm	1-2	38-46
Penetration depth in soft tissue, mm	1-2	>5
Blood clearance	Needs Contrast	Not required
Plaque burden at lesion	-	+
Aorto-ostial visualization	-	+
Cross-sectional calcium evaluation	Thickness, angle	Angle only
Lipidic plaque evaluation	Lipidic plaque, cap thickness	Attenuated plaque

Maehara A et al., J Am Coll Cardiol Img 2017;10:1487-503
Koganti S et al., Interv Cardiol 2016;11:11-16

ILUMIEN III – OPTIMIZE PCI

Randomized OCT vs. IVUS vs. Angiography



Ali ZA et al. Lancet 2016:388;2618-28

ILUMIEN III – OPTIMIZE PCI

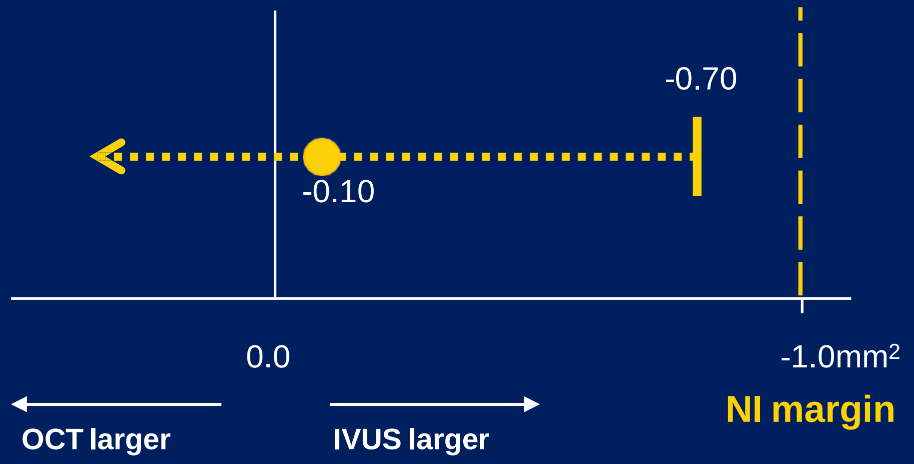
Randomized OCT vs. IVUS vs. Angiography

Primary endpoint: Final post-PCI MSA by OCT

OCT 5.79 mm^2 [4.54, 7.34]

IVUS 5.89 mm^2 [4.67, 7.80]

97.5% one-sided CI: [-0.70, -]



$P_{noninferiority} = 0.001$

Ali ZA et al. Lancet 2016:388;2618-28

IVUS vs OCT vs Angiography : ILUMIEN III

Outcomes of optical coherence tomography compared with intravascular ultrasound and with angiography to guide coronary stent implantation: one-year results from the ILUMIEN III: OPTIMIZE PCI trial

EuroIntervention 2021;16:1085-1091. DOI: 10.4244/EIJ-D-20-00498

- **450 patients (1:1:1 randomization)**
- **Non complex lesions**
- Primary outcome

→ TLF

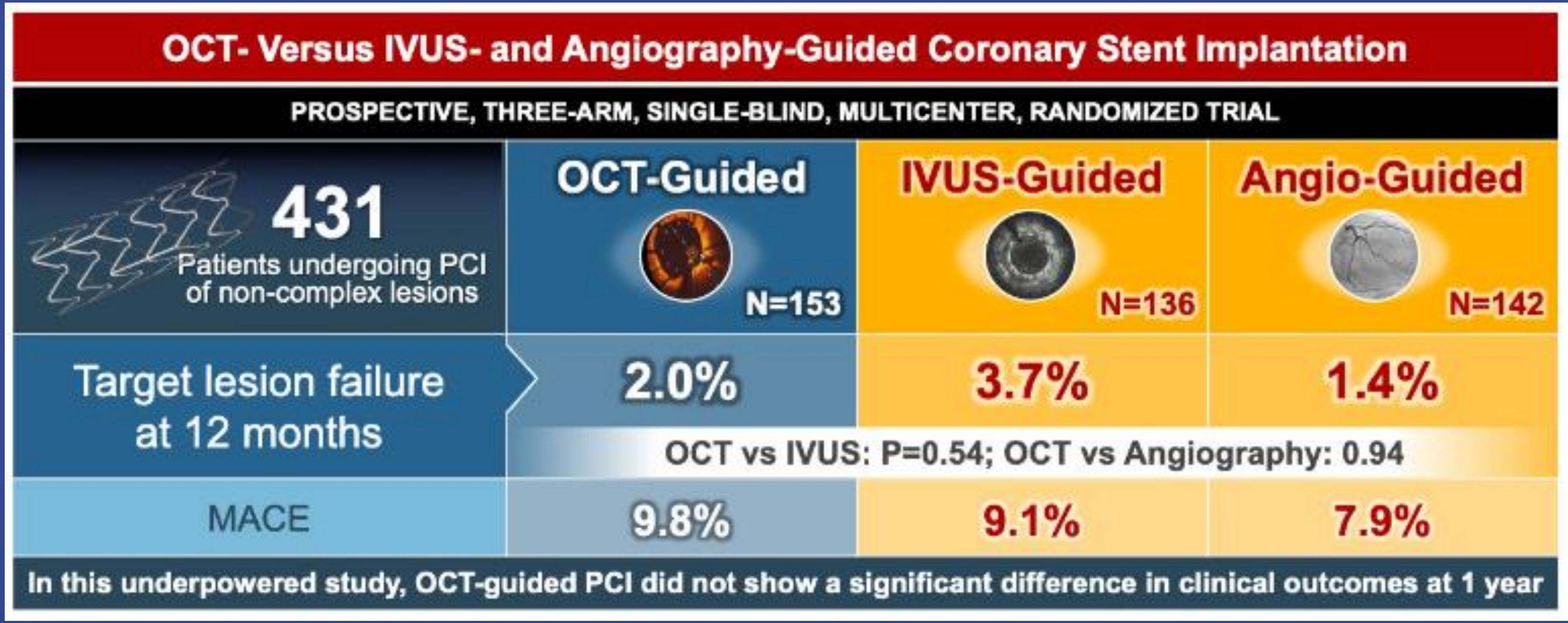
Composite of death from cardiac causes,

target-vessel-related MI

clinical driven target-vessel revascularization

Ali ZA, Stone GW et al. EuroIntervention. 2021 Jan 20;16(13):1085-1091.

IVUS vs OCT vs Angiography : ILUMIEN III



OCT- Versus IVUS- and Angiography-Guided Coronary Stent Implantation

PROSPECTIVE, THREE-ARM, SINGLE-BLIND, MULTICENTER, RANDOMIZED TRIAL

431 Patients undergoing PCI of non-complex lesions	OCT-Guided N=153	IVUS-Guided N=136	Angio-Guided N=142
Target lesion failure at 12 months	2.0%	3.7%	1.4%
	OCT vs IVUS: P=0.54; OCT vs Angiography: 0.94		
MACE	9.8%	9.1%	7.9%

In this underpowered study, OCT-guided PCI did not show a significant difference in clinical outcomes at 1 year

No Significant difference

Ali ZA, Stone GW et al. EuroIntervention. 2021 Jan 20;16(13):1085-1091.

The OPINION RCT: Design

Prospective, multi-center (n=42), randomized (1:1), non-inferiority trial comparing OCT-guided PCI with IVUS-guided PCI

Patients scheduled for PCI using DES*
n = 800

1:1

OCT-guided PCI		**IVUS-guided PCI**
n = 400	*DES: NOBORI biolimus-eluting stent	**n = 400**

8 months: Follow-up coronary angiography

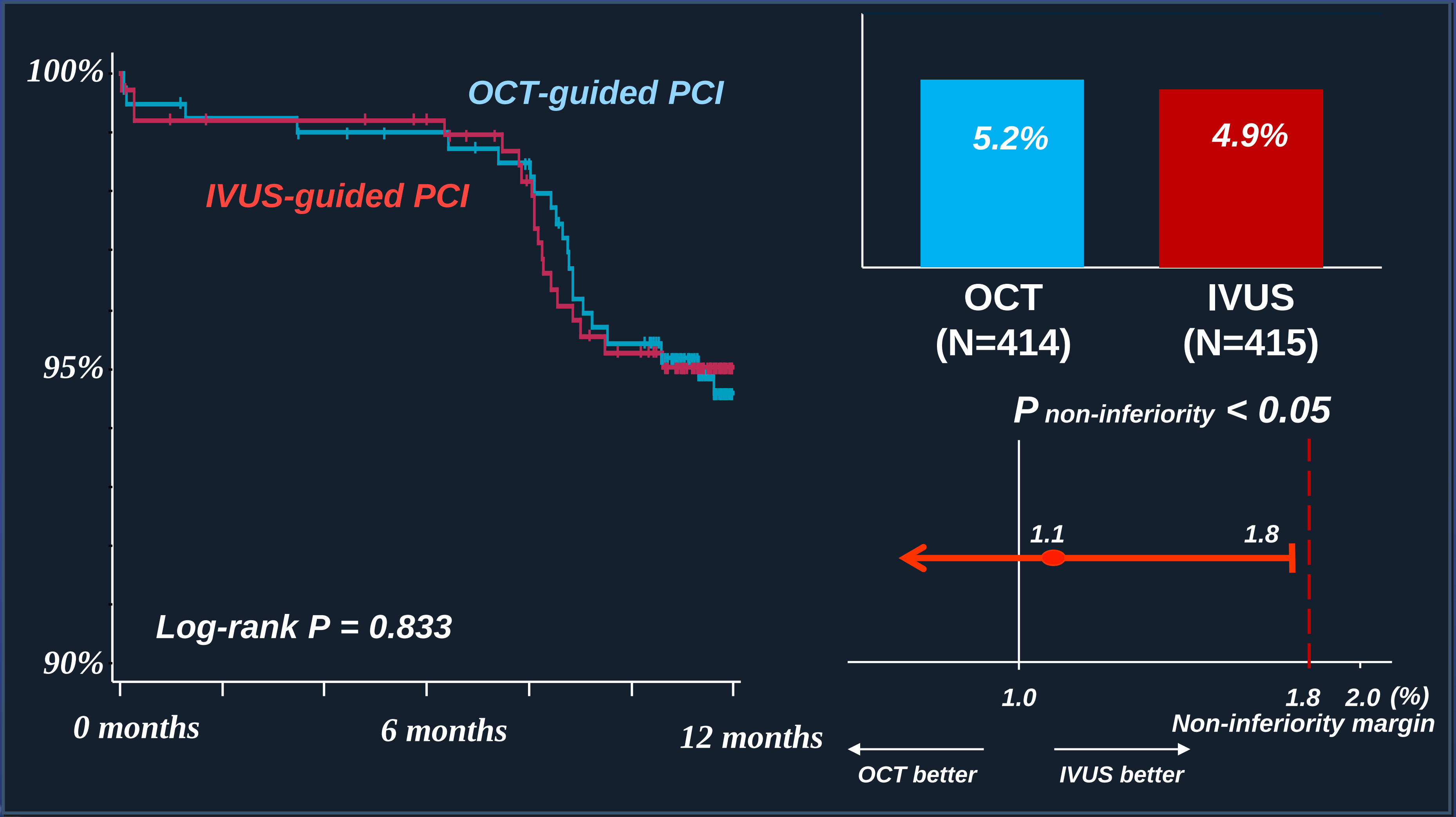
12 months: Clinical follow-up

Primary Endpoint: Target Vessel Failure (TVF) at 12 months after PCI

Kubo T et al., Eur Heart J 2017:38;3139-47

RCT: OPINION Trial: OCT vs. IVUS

1-Year TVF (Cardiac Death, TV-MI, or ID-TVR)



Kubo T et al., Eur Heart J 2017:38;3139-47

MISTIC-1 RCT: Design

Exclusion:
- ACS within 7 days
- Lesion Length >28mm
- LM disease
- CTO
- Bifurcation requiring SB treatment
- Severely calcified lesion
- In-stent restenosis
- LV EF <30%
- eGFR <45ml/min

Prospective, multi-center, randomized (1:1), non-inferiority trial comparing OCT-guided PCI with IVUS-guided PCI

Patients scheduled for PCI using DES*
Jun 2014 – Aug 2016, n = 109

1:1

OCT-guided PCI
n = 54

*DES: NOBORI biolimus-eluting stent

IVUS-guided PCI
n = 55

8 months: Follow-up coronary angiography

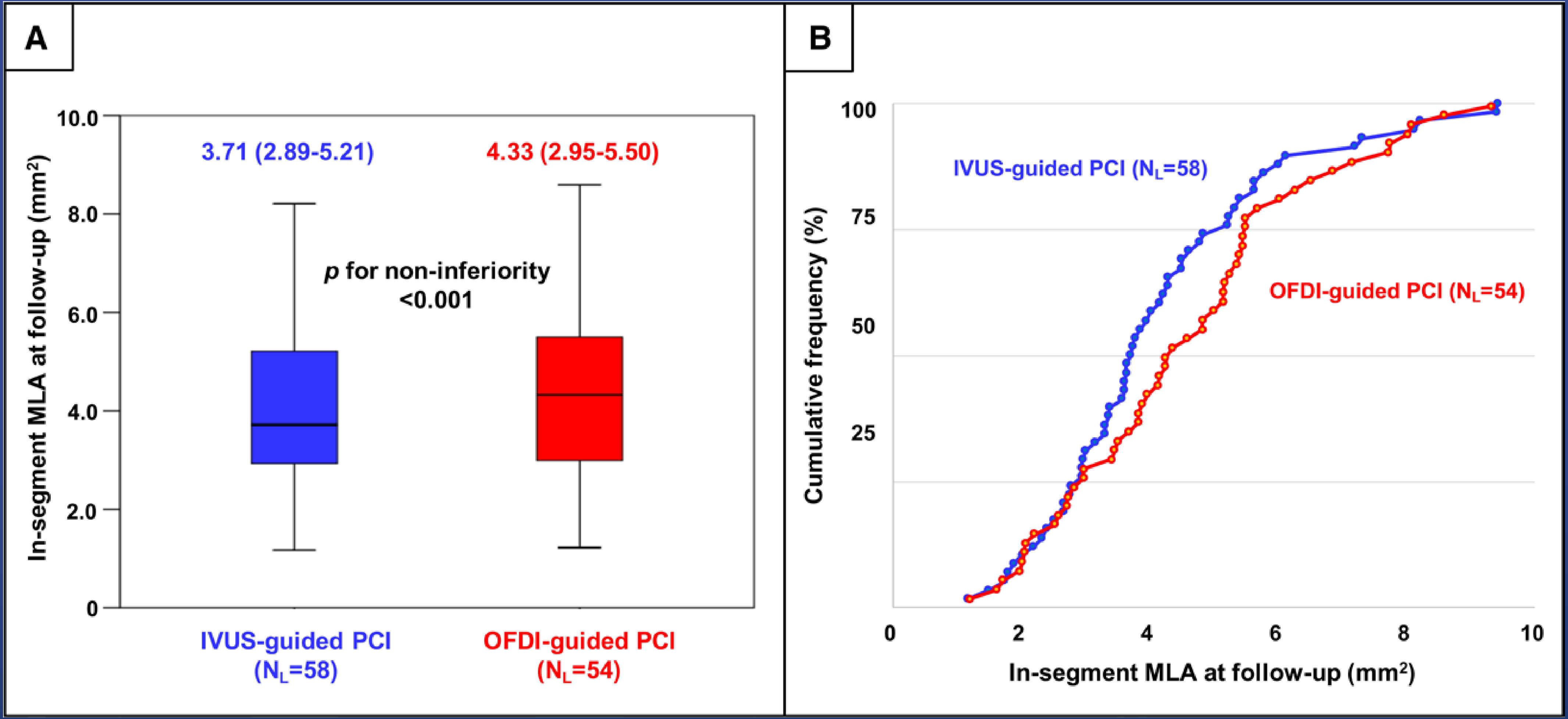
36 months: Clinical follow-up

Primary Endpoint: In-segment MLA by OCT at 8 months

Muramatsu T et al., Circ CV Interv 2020:13;e009314

RCT: MISTIC-1: OCT vs. IVUS

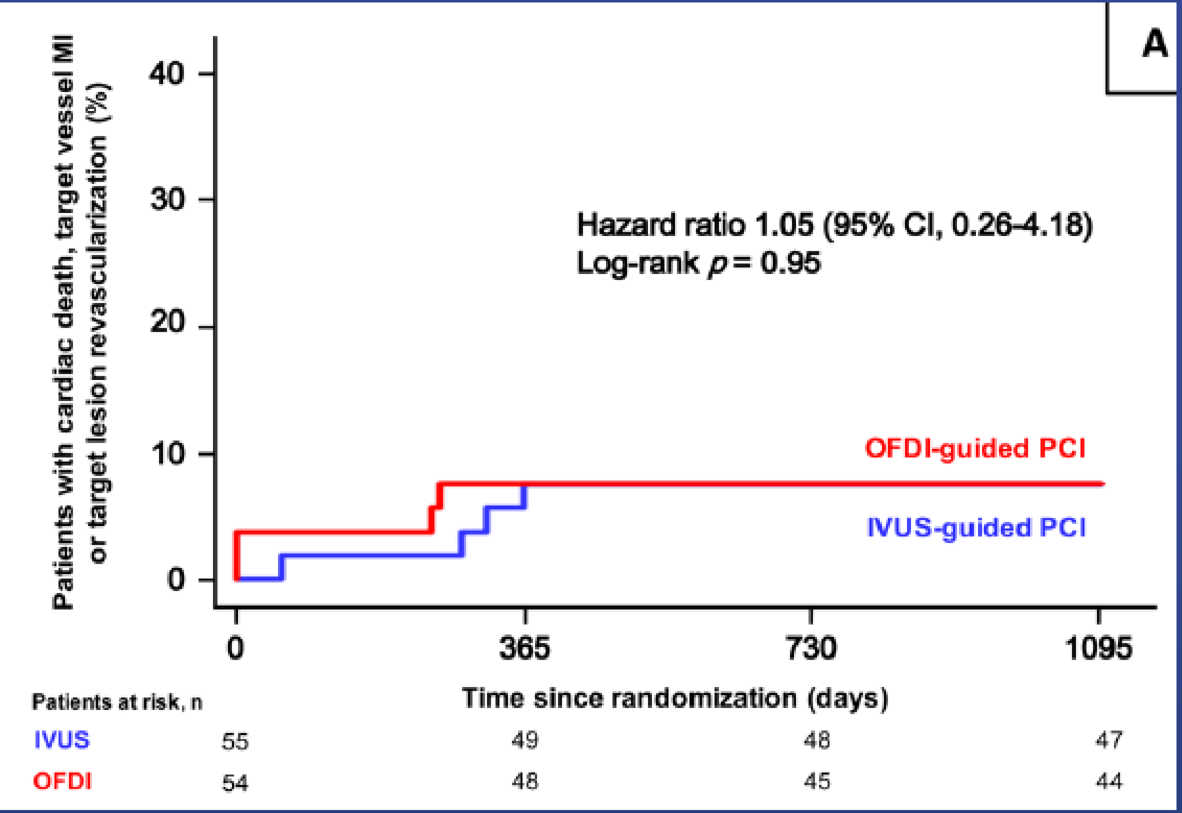
8-month In-segment MLA

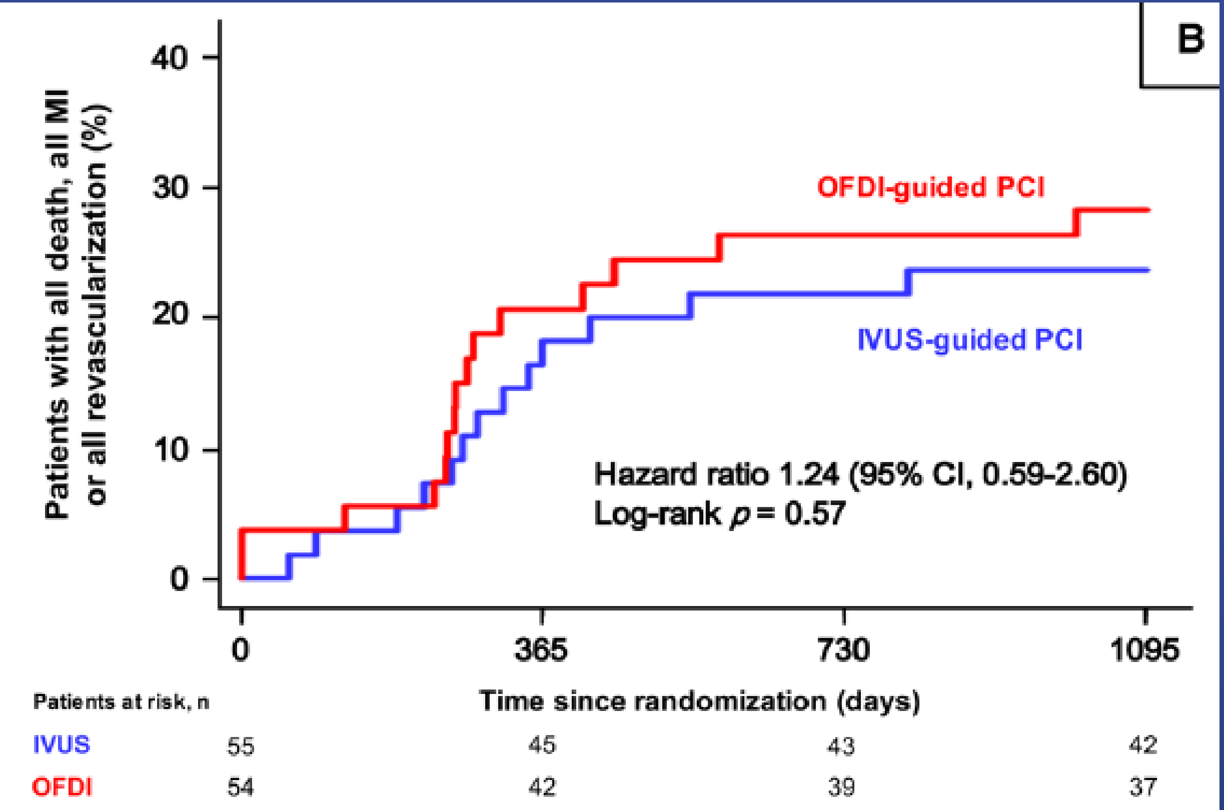


Muramatsu T et al., Circ CV Interv 2020:13;e009314

RCT: MISTIC-1: OCT vs. IVUS

36-month Clinical Outcomes





Muramatsu T et al., Circ CV Interv 2020:13;e009314

Limitations of Prior RCTs

- **ILUMIEN III**
  - Not powered to detect clinical endpoint
  - Vessel diameter limited to 2.25-3.5 mm, length <40mm
  - Complex lesions excluded
    (LM, RCA os, graft, CTO, ISR, planned 2-stent bifurcation)

- **OPINION**
  - Complex lesions excluded
    (LM or 3VD, ostial lesion, CTO, ISR, bypass graft)

OCTIVUS Trial

Pragmatic RCT Comparing OCT vs. IVUS-guided PCI

Optical Coherence Tomography versus Intravascular Ultrasound Guided Percutaneous Coronary Intervention

OCTIVUS Trial

Patients with CAD undergoing PCI (N=2,000)

R

OCT-guided PCI (N=1,000)

IVUS-guided PCI (N=1,000)

Primary Endpoint: Target Vessel Failure at 1 year
(Composite of cardiac death, target-vessel MI and ischemia-driven TVR)

Clinical follow-up at 1, 6, 12 months, then 3 and 5 years

PI:
Seung-Jung Park ,MD.
Duk-Woo Park, MD.

Kang DY et al. Am Heart J. 2020 Oct;228:72-80.

Study Participants

- Inclusion Criteria

- Patients at least 19 years of age
- Subjects with coronary artery disease undergoing PCI

- Exclusion Criteria

- ST-elevation myocardial infarction
- Acute or chronic kidney disease (eGFR <30 ml/min/1.73 m^2) without hemodialysis
- Cardiogenic shock or decompensated HF c severe LV dysfunction (LV EF<30%)
- Life expectancy < 1 year

Kang DY et al. Am Heart J. 2020 Oct;228:72-80.

Primary Endpoint

- Target Vessel Failure at 1 year
  - A composite of Cardiac Death, Target Vessel-related MI, and Ischemia-driven Target Vessel Revascularization

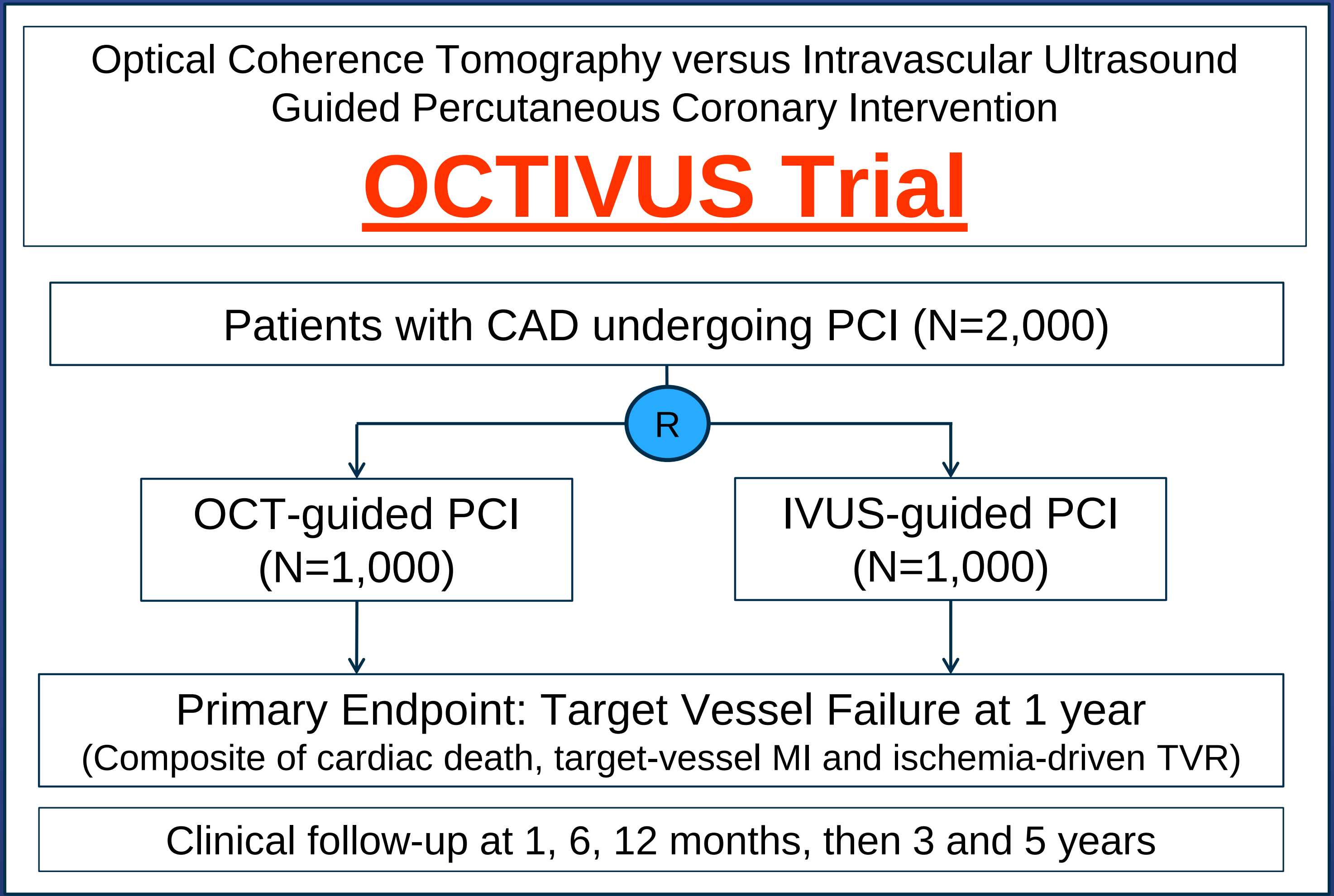
  - Periprocedural MI by SCAI definition

- Hypothesis: OCT would be non-inferior to IVUS

Kang DY et al. Am Heart J. 2020 Oct;228:72-80.

OCTIVUS Trial

Pragmatic RCT Comparing OCT vs. IVUS-guided PCI



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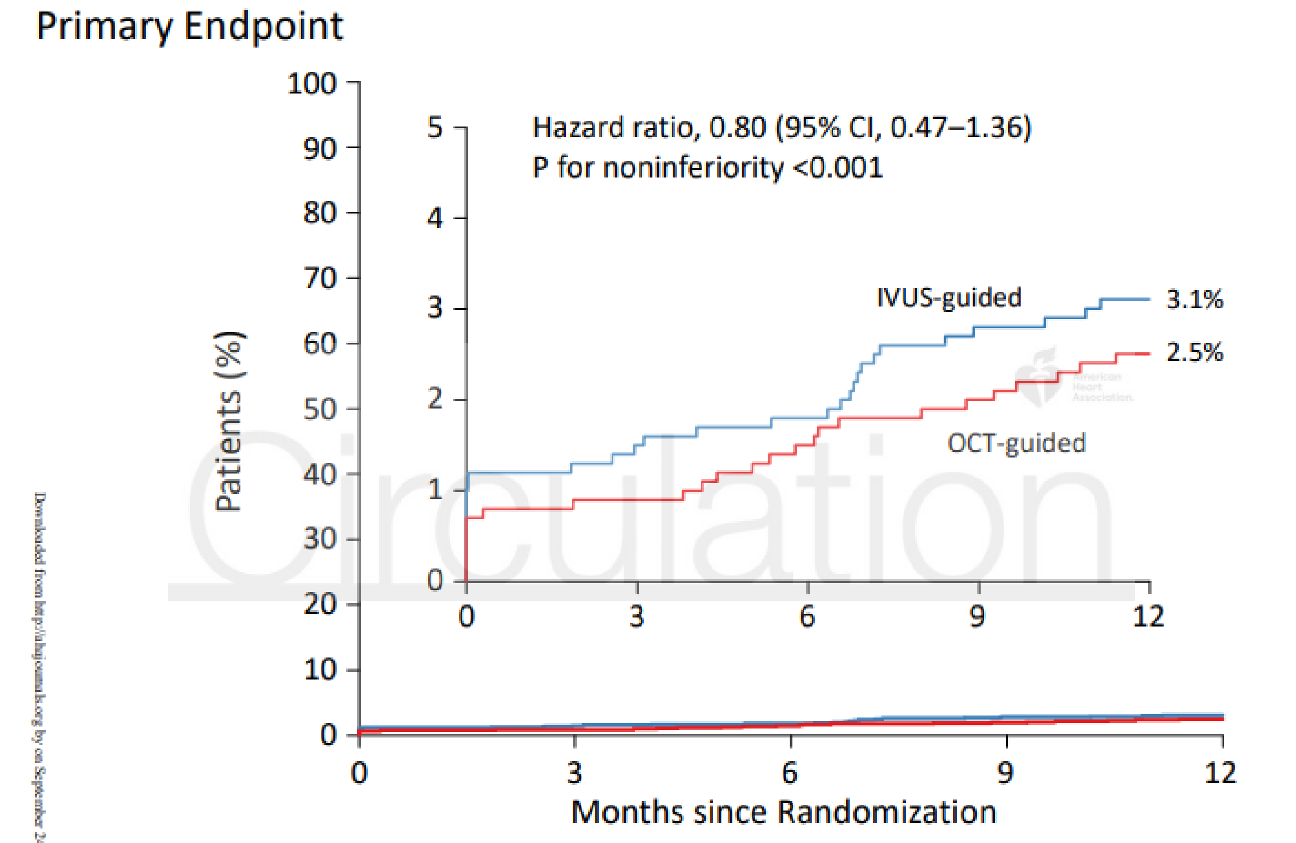
OCTIVUS Trial

Pragmatic RCT Comparing OCT vs. IVUS-guided PCI



No. at Risk	0	3	6	9	12
OCT-guided PCI	1005	990	984	979	912
IVUS-guided PCI	1003	985	981	969	893

- **2008 patients**
- **OCT-guided PCI vs IVUS-guided PCI**
- **DES implantation**

Primary outcome

→ TVF at 1 years

(cardiac death, TVMI, ischemia-driven TLR)

Kang DY, Ahn JM, Park SJ et al., Circulation. 2023 Aug 27.

OCT

Optical coherence tomography imaging during percutaneous coronary intervention impacts physician decision-making: ILUMIEN I study

William Wijns[1]*, Junya Shite[2], Michael R. Jones[3], Stephen W.-L. Lee[4], Matthew J. Price[5], Franco Fabbiocchi[6], Emanuele Barbato[1], Takashi Akasaka[7], Hiram Bezerra[8], and David Holmes[9]

A prospective, non-randomized study to see the impact of OCT on physician decision-making, post-PCI residual ischemia, and clinical outcomes

418 patients with 467 lesions

Mandatory use of FFR and plan PCI strategy

OCT (411 pts, 459 lesions)

↓

Plan changed in 230 (55%) pts, 264 (57%) lesions

Perform PCI

FFR and OCT

- Satisfactory result – No optimization in 75% of pts, 73% of lesions
- Unsatisfactory result – Optimization in 25% of pts, 27% of lesions
  - 14.5% malapposition
  - 7.6% under-expansion
  - 2.7% edge dissection

Follow-up at discharge and at 30 days (401 pts)

Eur Heart J 2015 in press

ILUMIEN I study

	PCI optimiz, without change	PCI optimiz based on pre-PCI OCT	PCI optimiz, based on post-PCI OCT	PCI optimiz, based on pre- and post-PCI OCT	p
Pre-PCI FFR	0.72±0.14	0.73±0.14	0.72±0.14	0.72±0.14	0.93
Post-PCI FFR	0.89±0.07	0.89±0.07	0.89±0.08	0.86±0.09	0.003
Final FFR			0.90±0.10	0.90±0.10	0.24
In-hos MACE	8.8%	6.7%	12.2%	1.5%	0.118
1-mo MACE	8.8%	8%	12.5%	1.5%	0.127

- Following OCT-guided PCI, the rates of MACEs at 30 days were very low (death 0.25%, MI 7.7%, TLR 1.7%, ST 0.25%)
- Physician decision-making was affected by OCT imaging prior to PCI in 57% and post-PCI in 27% of all cases

Wijins et al. *Eur heart j*, 2015

ILUMIEN II study

Comparison of Stent Expansion Guided by Optical Coherence Tomography Versus Intravascular Ultrasound

The ILUMIEN II Study (Observational Study of Optical Coherence Tomography [OCT] in Patients Undergoing Fractional Flow Reserve [FFR] and Percutaneous Coronary Intervention)

Akiko Maehara, MD,*† Ori Ben-Yehuda, MD,*† Ziad Ali, MD,*† William Wijns, MD, PhD,‡ Hiram G. Bezerra, MD,§ Junya Shite, MD,|| Philippe Généreux, MD,*†¶ Melissa Nichols, MS,† Paul Jenkins, PhD,† Bernhard Witzenbichler, MD,# Gary S. Mintz, MD,† Gregg W. Stone, MD*†

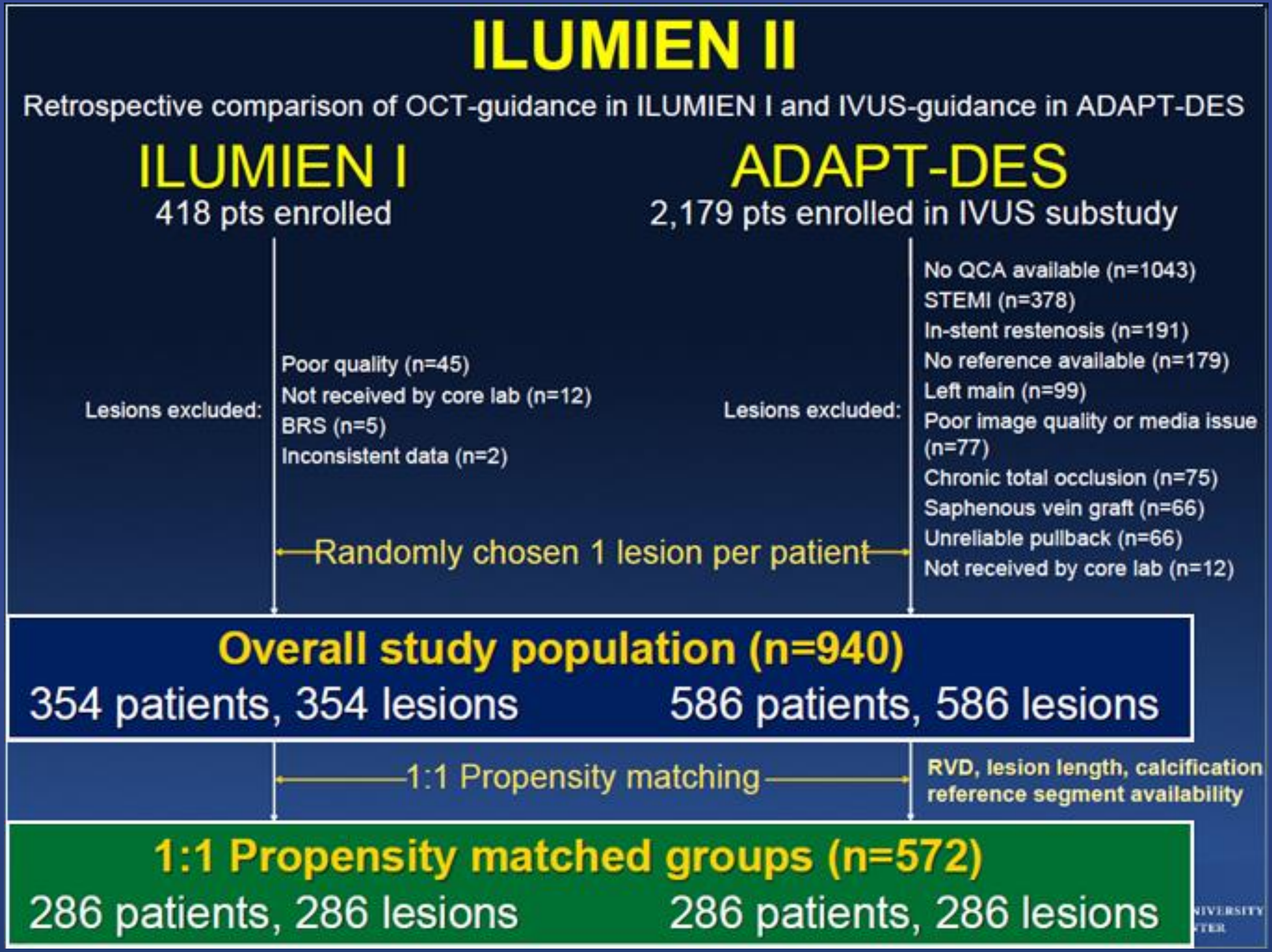
Design: A post-hoc analysis of the outcome of OCT- vs. IVUS-guided PCI from the ILUMIEN I and ADAPT-DES

Aim: To compare a degree of stent expansion achieved by OCT- vs. IVUS-guidance

Primary endpoint: Final post-PCI stent expansion defined as the MSA divided by the mean of the proximal and distal RLA

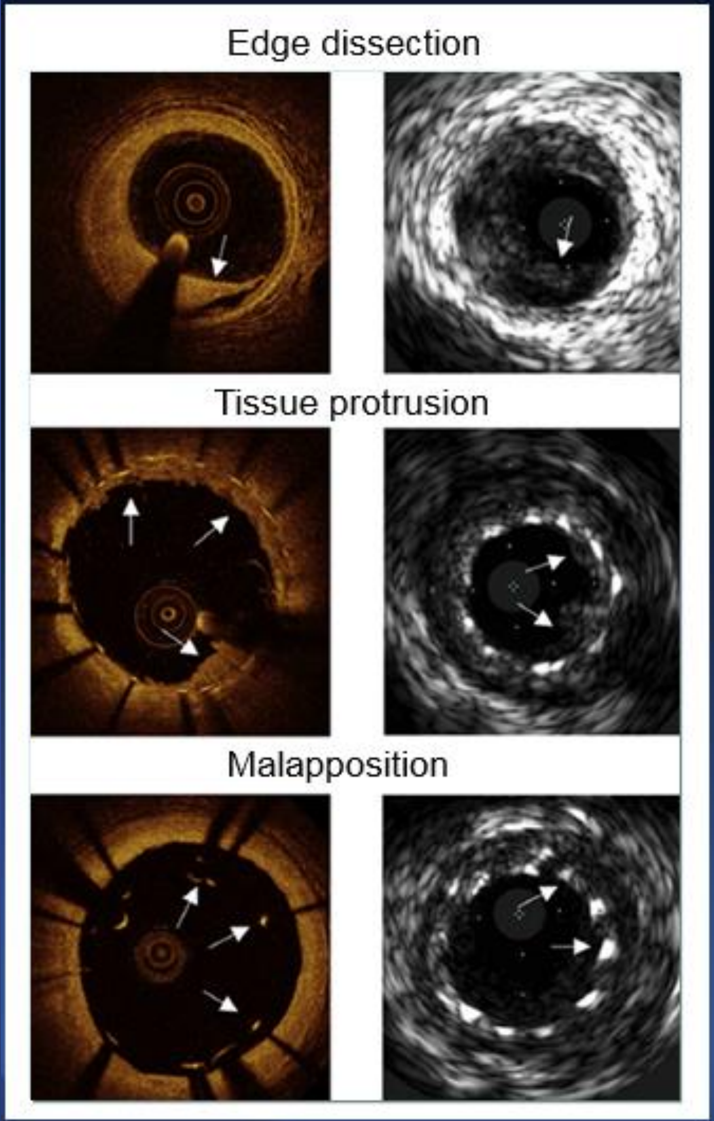
Meahara A. J Am Coll Cardiol Intv 2015;8:1704–14

ILUMIEN II study



Meahara A. J Am Coll Cardiol Intv 2015;8:1704–14

ILUMIEN II study



Qualitative Data in the Propensity-Matched Groups

	OCT	IVUS	p
Any malapposition	27%	14%	0.002
distance/MLD>20%	1%	1%	0.69
Any tissue protrusion	64%	27%	<0.001
protrusion CSA>10%	12%	8%	0.17
Any edge dissection	23%	5%	<0.001
dissec length ≥3mm	2%	1%	0.29

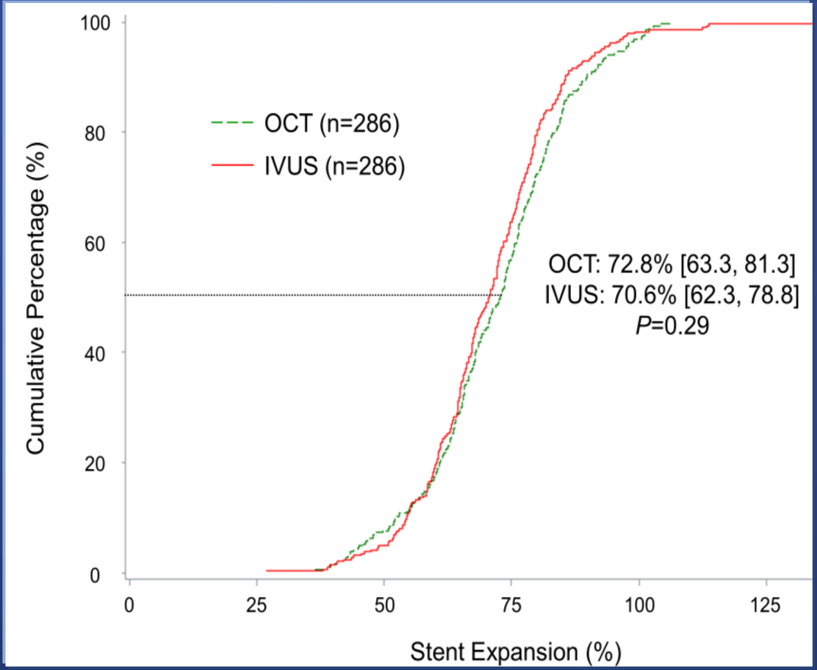
Meahara A. J Am Coll Cardiol Intv 2015;8:1704–14

Meahara A. J Am Coll Cardiol Intv 2015;8:1704–14

ILUMIEN II study

TABLE 5 Multivariable Analysis in the Entire Study Population (N = 940)

	Endpoints			
	Stent Expansion, %	Mean Stent Expansion, %	Diameter Stenosis In-Stent, %	Diameter Stenosis In-Segment, %
Measurement by OCT (N = 354)	72.6 (63.5, 81.4)	89.6 (79.2, 98.5)	6.4 (2.7, 9.9)	13.3 (8.9, 20.2)
Measurement by IVUS (n = 586)	70.5 (62.1, 79.5)	86.8 (77.1, 96.8)	6.4 (3.0, 10.7)	11.2 (7.6, 17.2)
	Adjusted p Values			
OCT vs. IVUS	0.84	0.30	0.19	0.009



Conclusion

OCT-guidance was related to comparable stent expansion, and similar rates of major edge dissection, stent malapposition, and tissue protrusion as compared to IVUS-guidance

Meahara A. J Am Coll Cardiol Intv 2015;8:1704–14

ILUMIEN III : OPTIMIZE PCI

OCT-Guided vs IVUS-Guided vs Angio-Guided PCI

- Randomly allocated 450 patients (1:1:1)
  - OCT guidance ; 158 [35%]
  - IVUS guidance ; 146 [32%]
  - Angiography guidance ; 146 [32%]
- All patients underwent final OCT imaging
- Primary efficacy endpoint ; post-PCI minimum stent area
- Primary safety endpoint ; procedural MACE

Ali ZA et al. The Lancet 2016, Vol 388; 2618-28

ILUMIEN III : OPTIMIZE PCI

OCT-Guided vs IVUS-Guided vs Angio-Guided PCI

Efficacy Endpoints

	OCT (n=140)	IVUS (n=135)	Angio (n=140)	P (OCT vs IVUS)	P (OCT vs Angio)
Minimal stent area(mm²)	5.79 [4.54-7.34]	5.89 [4.67-7.80]	5.49 [4.39-6.59]	0.42	0.12
Minimum stent expansion(%)	88±17	87±16	83±13	0.77	0.02
Mean stent expansion(%)	106 [98-120]	106 [97-117]	101 [92-110]	0.63	0.001

OCT guidance was non-inferior to IVUS guidance (one-sided 97.5% lower CI −0.70 mm2; p=0.001), but not superior (p=0.42).
OCT guidance was also not superior to angiography guidance (p=0.12).

Ali ZA et al. The Lancet 2016, Vol 388; 2618-28

ILUMIEN III : OPTIMIZE PCI

OCT-Guided vs IVUS-Guided vs Angio-Guided PCI

Primary Safety Endpoints

	OCT (n=158)	IVUS (n=146)	Angio (n=146)	P (OCT vs IVUS)	P (OCT vs Angio)
Procedural MACE(%)	2.5	0.7	0.7	0.37	0.37
Complication					
Dissection(%)	1.3	0.0	0.7	0.50	1.00
Perforation	0.0	0.7	0.0	0.48	-
Thrombus	1.3	0.0	0.0	0.50	0.50
Acute closure	0.6	0.0	0.0	1.00	1.00

Procedural MACE was infrequent and not significantly different between the three groups.

Ali ZA et al. The Lancet 2016, Vol 388; 2618-28

ILUMIEN III : OPTIMIZE PCI

OCT-Guided vs IVUS-Guided vs Angio-Guided PCI

Postprocedure OCT measure

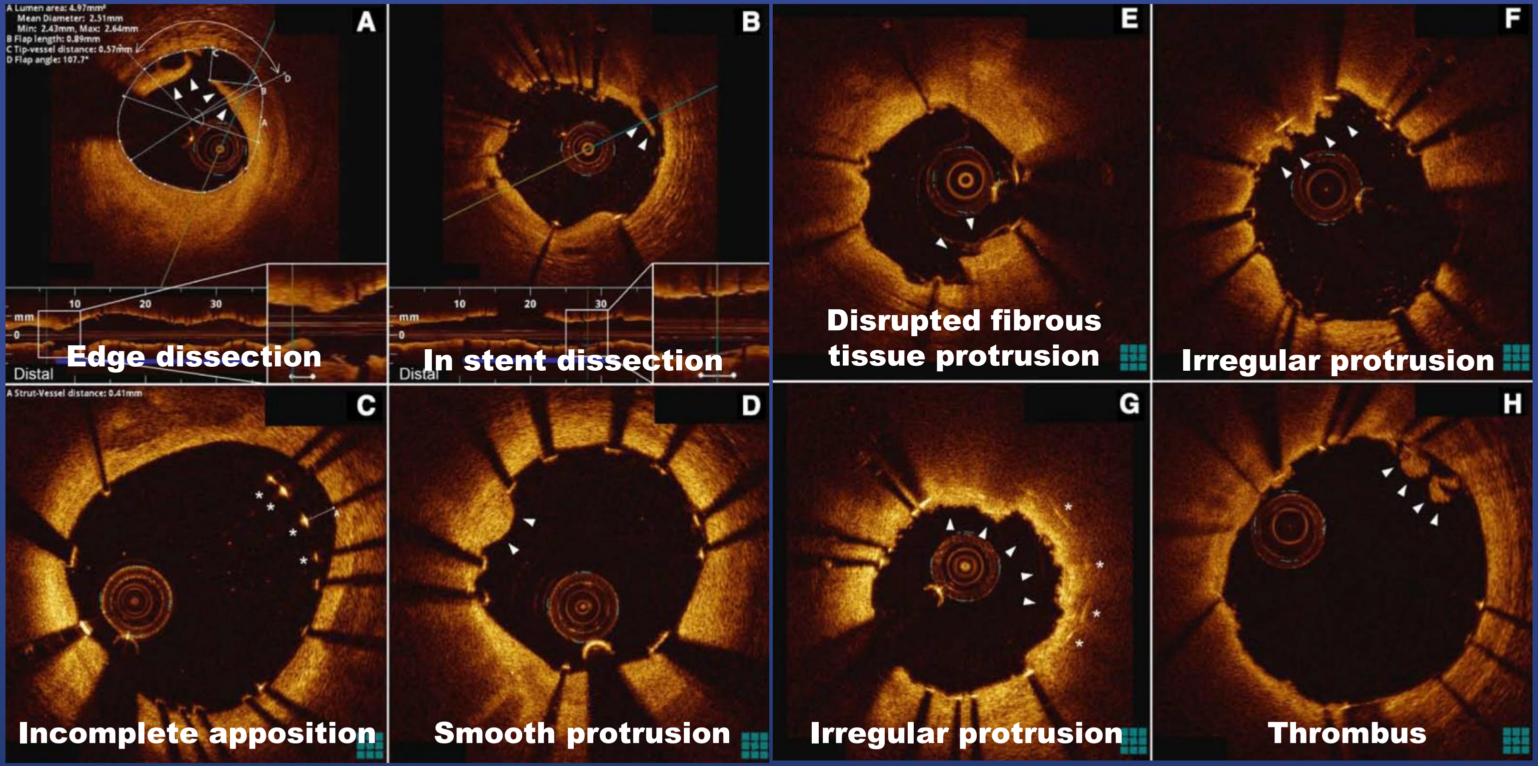
	OCT (n=140)	IVUS (n=135)	Angio (n=140)	P (OCT vs IVUS)	P (OCT vs Angio)
Any dissection(%)	39(28)	53(40)	64(44)	0.04	0.006
Major(%)	19(14)	35(26)	26(19)	0.009	0.25
Minor(%)	20(14)	18(13)	35(25)	0.84	0.02
Any malposition(%)	58(41)	52(39)	83(59)	0.62	0.003
Major(%)	15(11)	28(21)	44(31)	0.02	<0.001
Minor(%)	43(31)	24(18)	39(28)	0.01	0.60

OCT-guided PCI resulted in the fewest untreated major dissection and areas of major stent malapposition.

Ali ZA et al. The Lancet 2016, Vol 388; 2618-28

Post-stent OCT Findings

From MGH OCT registry, 900 lesions in 786 patients with post-stenting OCT were analyzed to identify the OCT predictors for device-oriented clinical end points (cardiac death, target vessel-related MI, TLR and stent thrombosis)



Soeda T, Jang IK et al. Circulation 2015;132:1020-9

Post-stent OCT Findings

Incidence of Post-stent Qualitative and Quantitative OCT Findings (Lesion-Level)

	No MACE	MACE	p
N	795	39	
Edge dissection	29%	31%	0.78
Malapposition	38%	36%	0.76
Tissue protrusion	97%	100%	0.63
Irregular protrusion	52%	74%	0.003
Thrombus	38%	51%	0.13
Small MSA*	40%	59%	0.039

*Small MSA : <5.0 mm^2 for DES and <5.6 mm^2 for BMS

Soeda T, Jang IK et al. Circulation 2015;132:1020-9

Post-stent OCT Findings

Multivariable Predictors of
Device-oriented MACE and TLR

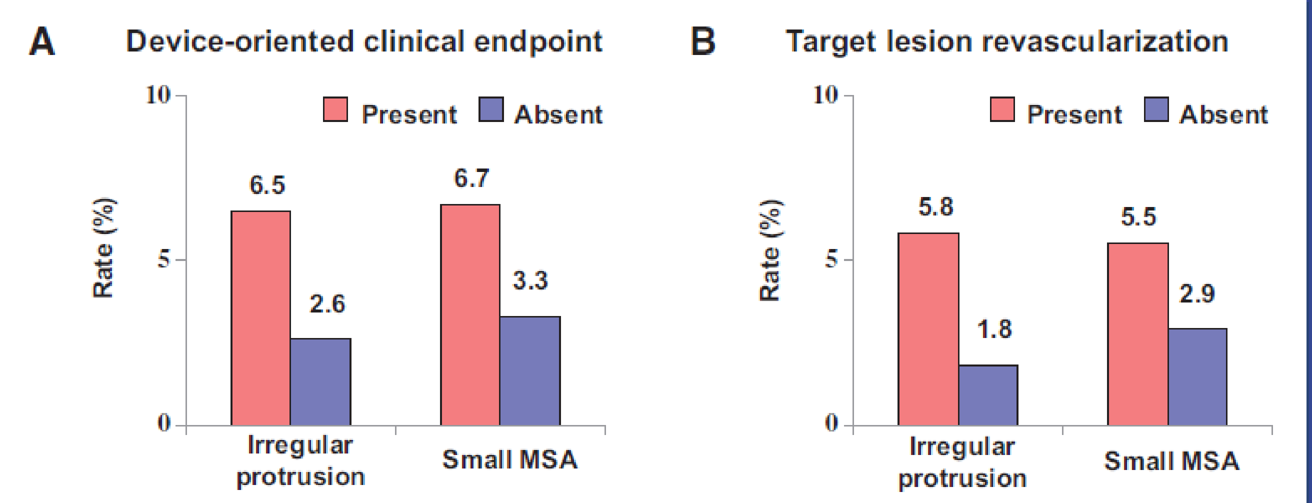
	MACE		TLR	
	OR (95% CI)	p	OR (95% CI)	p
Age, year	NA		0.98 (0.95-1.02)	
Male	3.13 (0.92-10.69)	0.068	NA	
BMS	1.75 (1.19-2.58)	0.005	1.80 (1.23-2.63)	0.002
Irregular protrusion	2.64 (1.40-5.01)	0.003	2.66 (1.40-5.05)	0.003
Small MSA*	2.54 (1.23-5.25)	0.012	2.54 (1.24-5.21)	0.011

*Small MSA : <5.0 mm^2 for DES and <5.6 mm^2 for BMS
Patient-level analysis

Soeda T, Jang IK et al. Circulation 2015;132:1020-9

Post-stent OCT Findings

Rates of Device-oriented MACE and TLR
from multivariable models



	A: Irregular protrusion	A: Small MSA	B: Irregular protrusion	B: Small MSA
Odds ratio (95%CI)	2.64 (1.40 – 5.01)	2.54 (1.23 – 5.25)	2.66 (1.40 – 5.05)	2.57 (1.24 – 5.24)
P-value	0.003	0.012	0.003	0.011
Sensitivity, %	74.4	59.0	78.8	57.6
Specificity, %	47.7	59.6	47.7	59.4
PPV, %	6.5	6.7	5.8	5.5
NPV, %	97.4	96.7	98.2	97.1

Irregular protrusion and small MSA were the independent OCT predictors of MACE, which were primarily driven by TLR

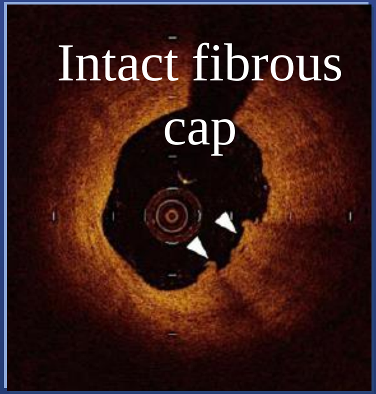
Soeda T, Jang IK et al. Circulation 2015;132:1020-9

Plaque rupture and prognosis in ACS

Plaque rupture and intact fibrous cap assessed by optical coherence tomography portend different outcomes in patients with acute coronary syndrome

Giampaolo Niccoli[1*], Rocco A. Montone[1], Luca Di Vito[2,3], Mario Gramegna[1], Hesham Refaat[1,4], Giancarla Scalone[1], Antonio M. Leone[1], Carlo Trani[1], Francesco Burzotta[1], Italo Porto[1], Cristina Aurigemma[1], Francesco Prati[2,3], and Filippo Crea[1]

- To evaluate the prognostic value of plaque rupture vs. intact fibrous cap in 139 ACS patients undergoing PCI
- No differences in clinical, angiographic, or procedural data

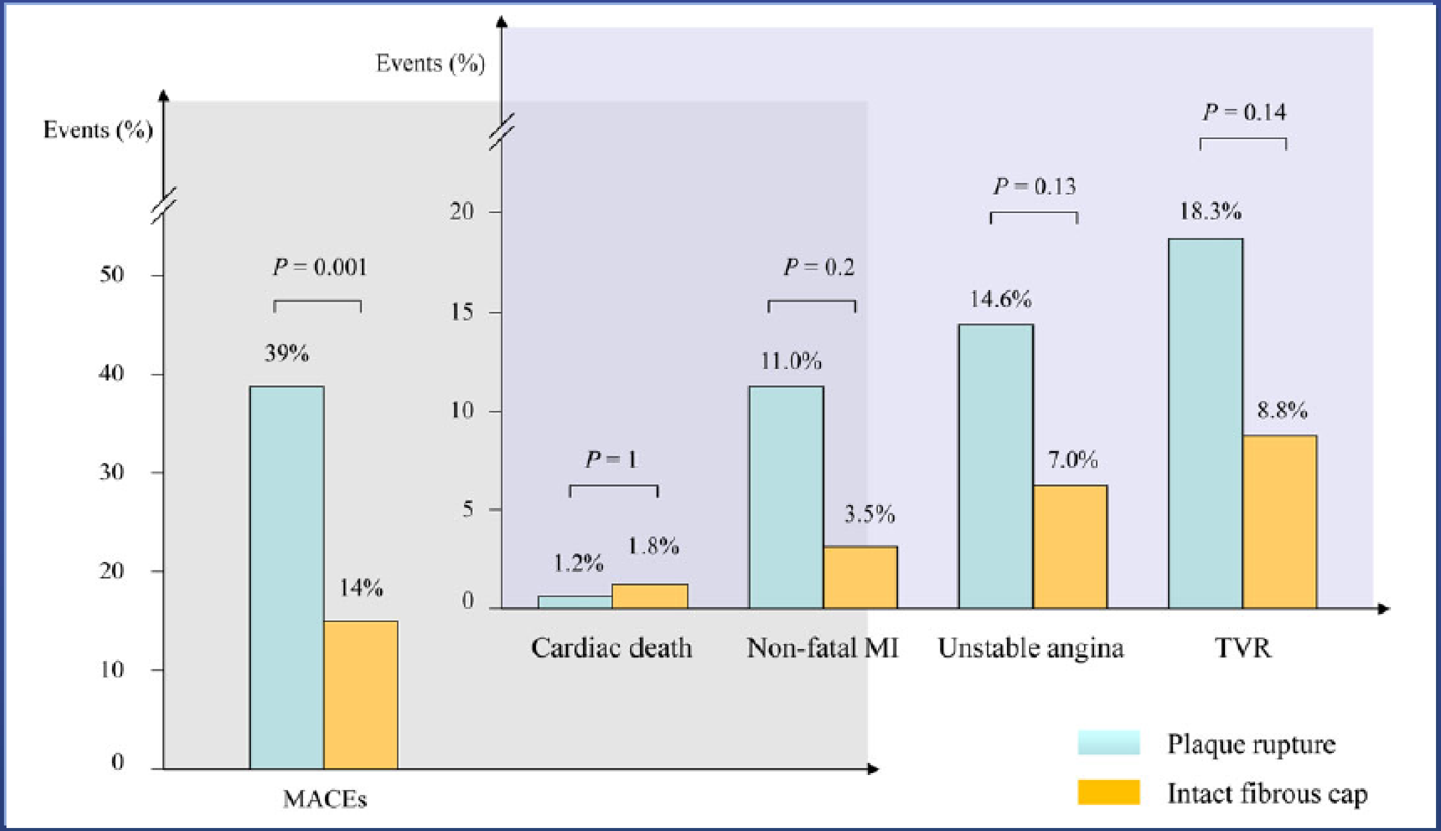


Niccoli et al. Eur Heart J 2015;36:1377-84

Plaque rupture and prognosis in ACS

MACE rates

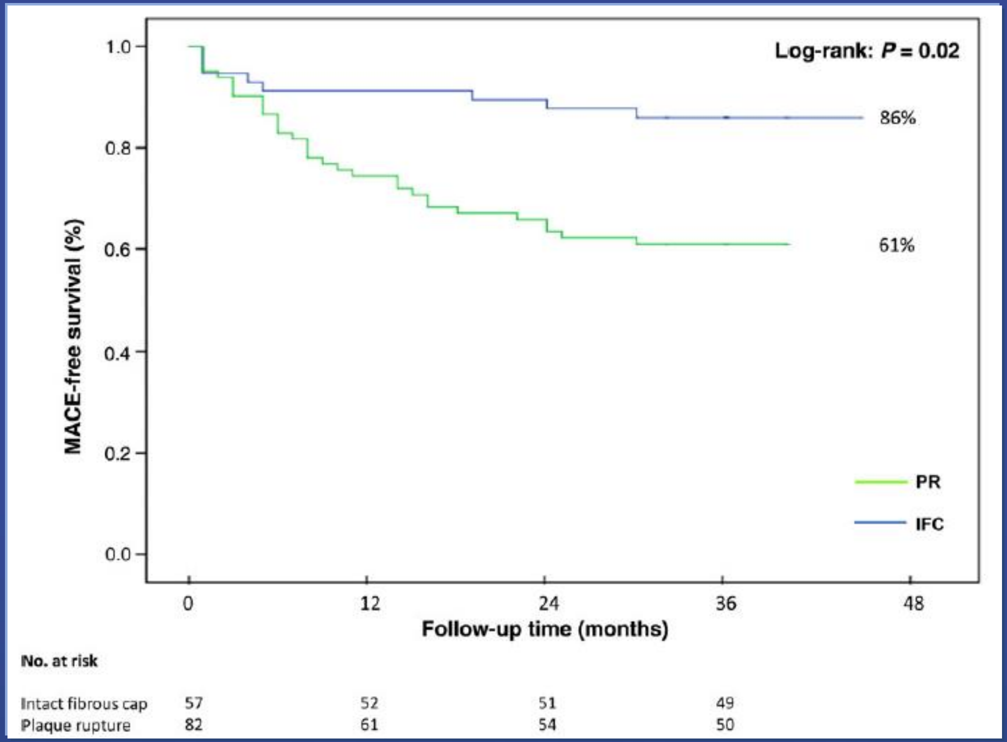
Patients with plaque rupture vs. with intact fibrous cap



Niccoli et al. Eur Heart J 2015;36:1377-84

Plaque rupture and prognosis in ACS

Kaplan–Meier Analysis



Conclusion

Patients with plaque rupture had a worse MACE-free survival (61% vs. 86%) compared with those having an intact fibrous cap

Niccoli et al. Eur Heart J 2015;36:1377-84

Plaque rupture and prognosis in ACS

Predictors of 3-year MACEs
Multivariable Cox regression analysis

	HR	95% CI	p
Obesity (BMI >35)	1.688	0.822-3.845	0.15
Plaque rupture	3.735	1.358-9.735	0.010
Previous PCI	1.449	0.610-4.146	0.34
Stent length	1.028	0.980-1.081	0.26
Age	1.005	0.977-1.034	0.73
Male	1.36	0.335-1.591	0.76

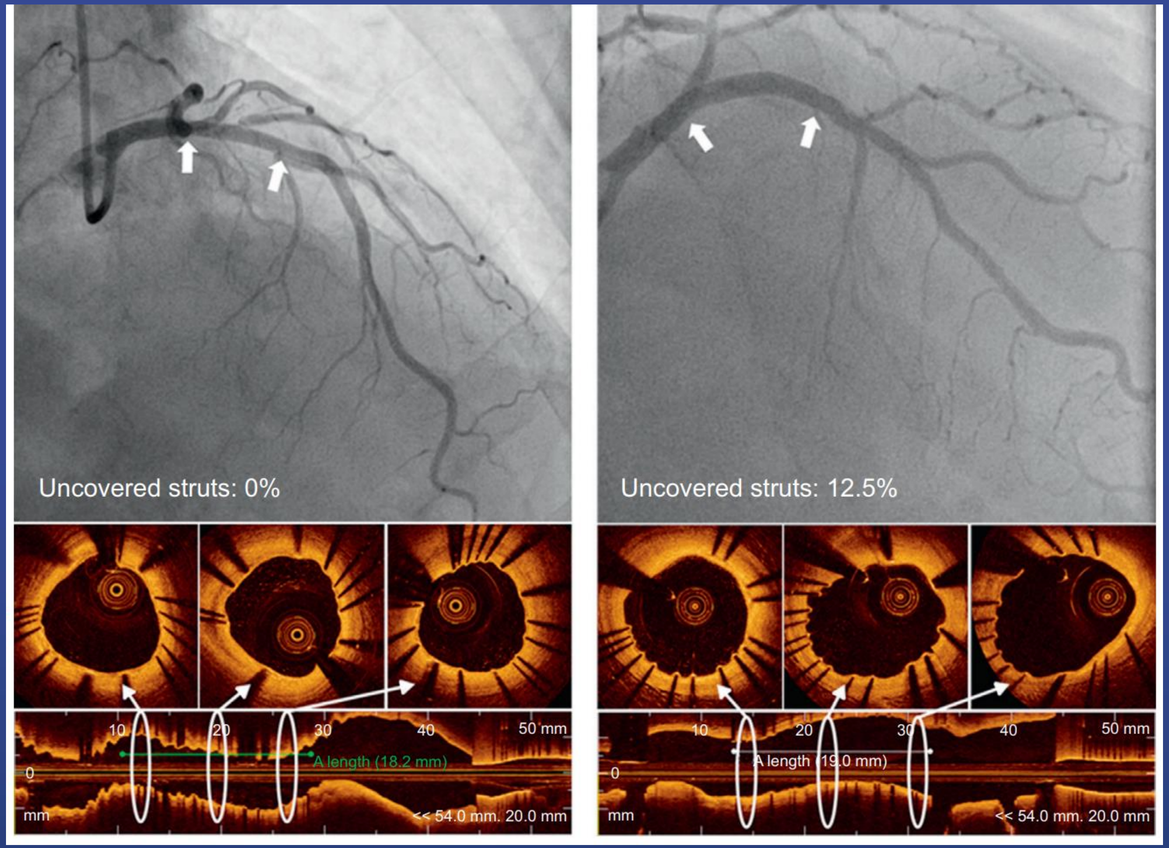
Conclusion

ACS patients with plaque rupture in culprit lesion have a worse prognosis compared to those with IFC, which should be taken into account in risk stratification and management of ACS

Niccoli et al. Eur Heart J 2015;36:1377-84

Stent coverage following OCT vs angio-guided PCI

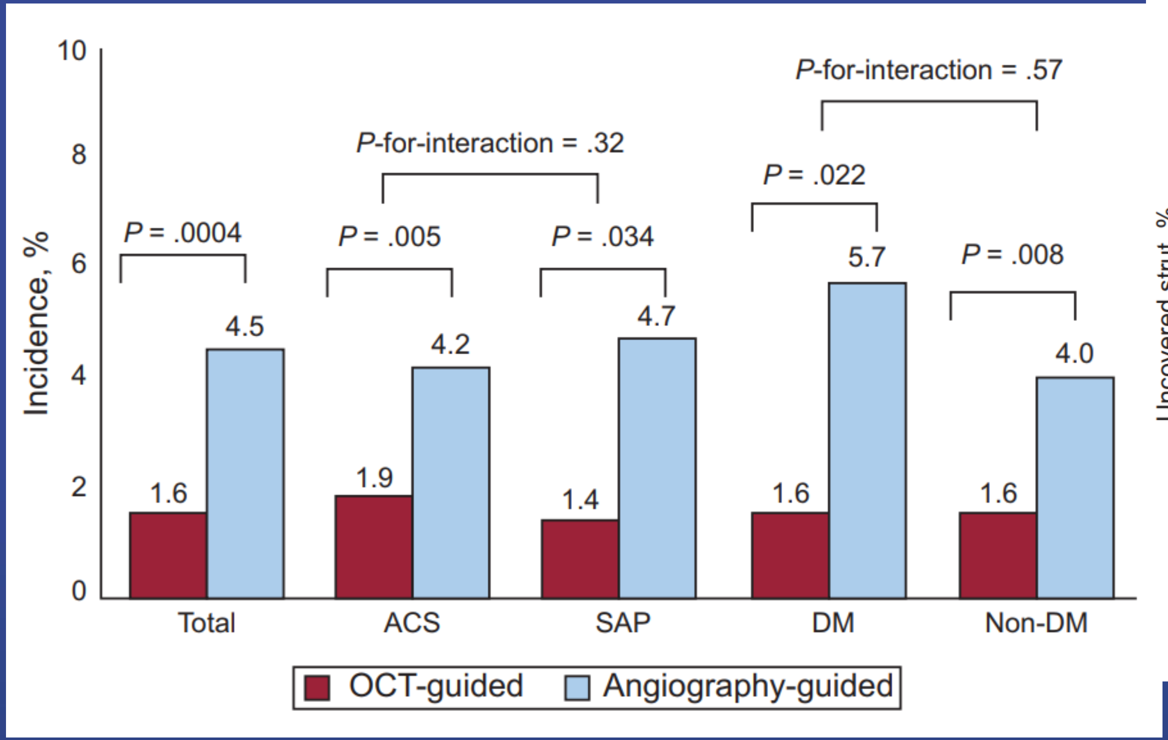
- RCT
- 101 patients (105 lesions)
- OCT guided PCI (n=51) vs angio-guided PCI (n=54)
- 6 months follow-up OCT
- Primary endpoint : incidence of uncovered struts

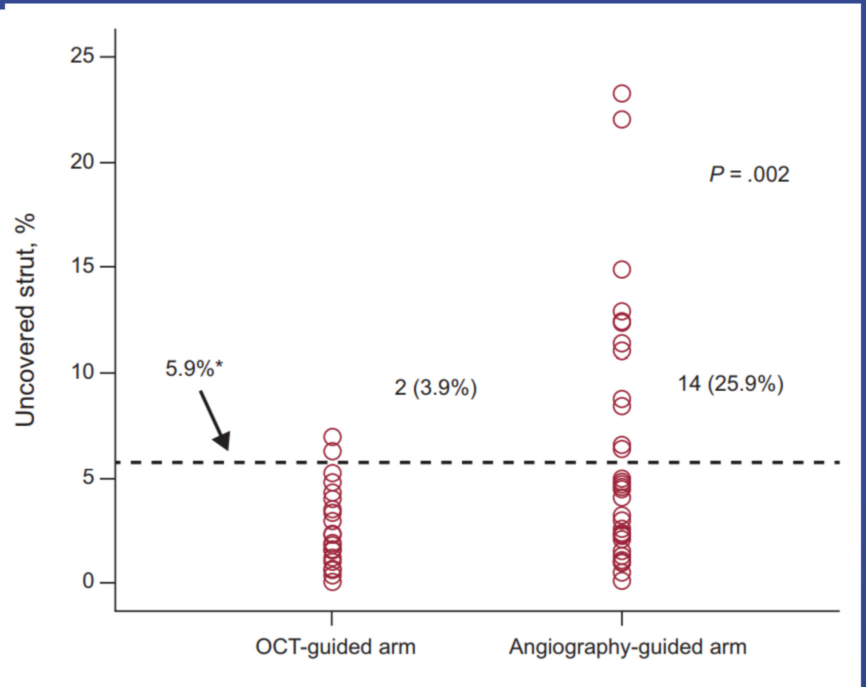


OCT-guided Angio-guided

Hong et al. Rev Esp Cardiol (Engl Ed). 2015 Mar;68(3):190-7

Stent coverage following OCT vs angio





Hong et al. Rev Esp Cardiol (Engl Ed). 2015 Mar;68(3):190-7

OCT guidance vs angiographic guidance

CLI-OPCI study

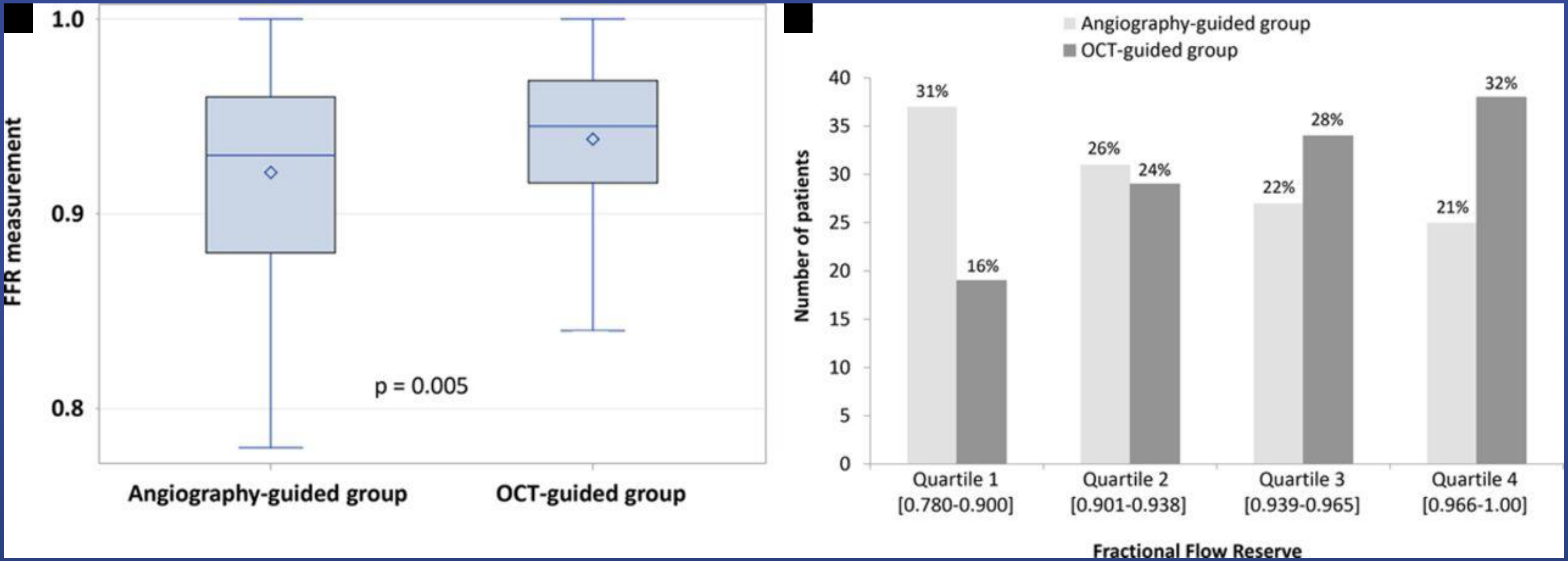
One year outcome	OCT (n=335)	CAG (n=335)	P
Death	3.3%	6.9%	0.035
Cardiac death	1.2%	4.5%	0.010
MI	5.4%	8.7%	0.096
TLR	3.3%	3.3%	1
Definite ST	0.3%	0.6%	0.6
Cardiac death/MI	6.6%	13.0%	0.006
Cardiac death/MI or repeat revascularization*	9.6%	15.1%	0.034

***Even after accounting for baseline and procedural differences (OR=0.49, p=0.037)**

Prati et al. Eurointervention 2012;8:823-9

OCT guidance vs angiographic guidance
DOCTORS study

N=240 (120 vs 120)
Multicenter, prospective, randomized trial



FFR after PCI in the angio vs OCT guided group

Meneveau et al. Circulation. 2016;134:906–917

OCT guidance vs angiographic guidance

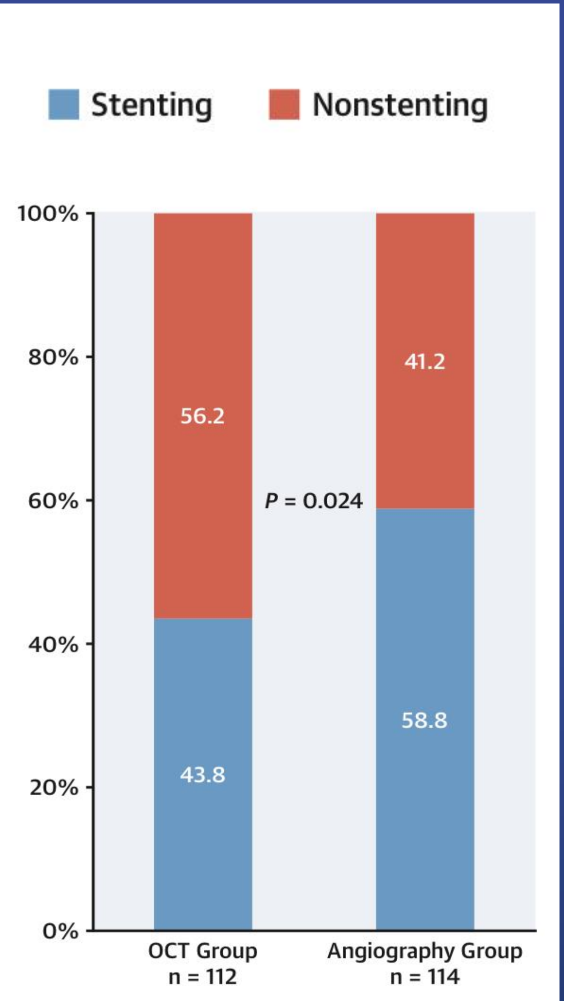
DOCTORS study

Variable	Pre-stenting	Immediately poststenting	Post-OCT optimization	p-value
Reference diameter, mm	2.92±0.53	3.10±0.45	3.11±0.48	0.27
MLD, mm	1.21±0.33	2.79±0.46	2.84±0.43	0.001
Diameter stenosis, %	58.4±10.9	9.5±6.1	8.4±3.9	<0.0001
Reference area, mm	7.0±2.23	7.62±2.42	7.72±2.43	0.10
MLA, mm2	1.28±0.71	5.99±2.11	6.41±1.99	<0.0001
Area stenosis, %	81.1±9.82	21.1±12.4	15.9±7.3	<0.0001

Meneveau et al. Circulation. 2016;134:906–917

OCT vs Angiographic guidance

EROSION III



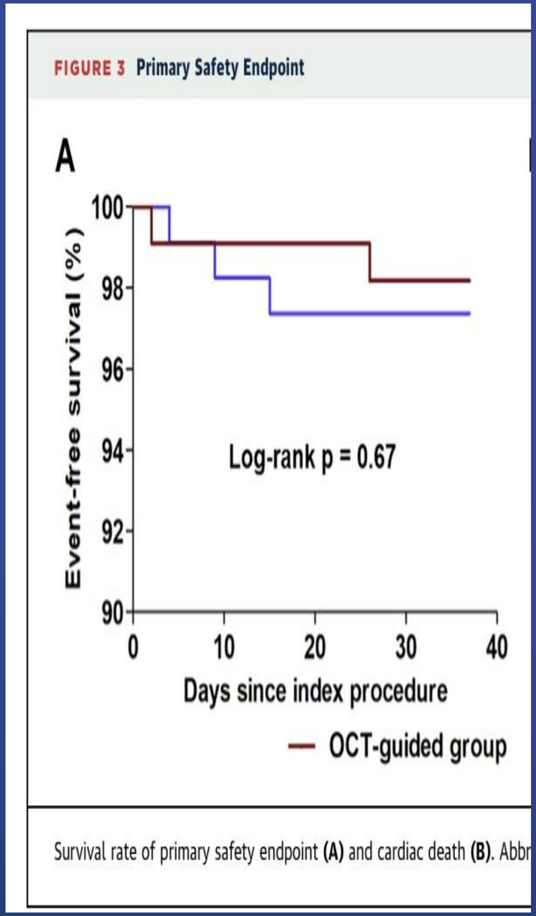
226 STEMI Patient with early infarct patency

R
1:1

OCT Guided (n=112)

Angio Guided (n=114)

OCT guided reperfusion was associated with less stent implantation during primary PCI



Jia et al., JACC APRIL 25, 2022:846–856

OCT guidance vs Angiographic guidance
EROSION III

One year outcome	OCT (n=335)	CAG (n=335)	P
Death	3.3%	6.9%	0.035
Cardiac death	1.2%	4.5%	0.010
MI	5.4%	8.7%	0.096
TLR	3.3%	3.3%	1
Definite ST	0.3%	0.6%	0.6
Cardiac death/MI	6.6%	13.0%	0.006
Cardiac death/MI or repeat revascularization*	9.6%	15.1%	0.034

***Even after accounting for baseline and procedural differences (OR=0.49, p=0.037)**

Prati et al. Eurointervention 2012;8:823-9

OCT guidance vs Angiographic guidance
ILUMIEN IV

ORIGINAL ARTICLE

Optical Coherence Tomography–Guided versus Angiography-Guided PCI

- **2487patients (80 sites in 18 countries)**
- **OCT-guided PCI vs angiography-guided PCI**

Primary outcome

→ minimum stent area after PCI

→ Target vessel failure

(composite of cardiac cause, TVMI, or ischemia-driven TVR)

Ali ZA, Landmesser U, Maehara A, et al. N Engl J Med. 2023;10.1056/NEJMoa2305861

ILUMIEN IV : OPTIMIZE PCI

OCT-Guided vs Angio-Guided PCI

Prospective, randomized, single-blind trial
comparing OCT-guided PCI with Angio-guided PCI

Inclusion:
- DM
- Lesion Length >28mm
- MV
- CTO
- Bifurcation requiring SB treatment
- Severely calcified lesion
- In-stent restenosis

Patients scheduled for PCI

1:1

OCT-guided PCI	Angio-guided PCI
n = 1233	n = 1254

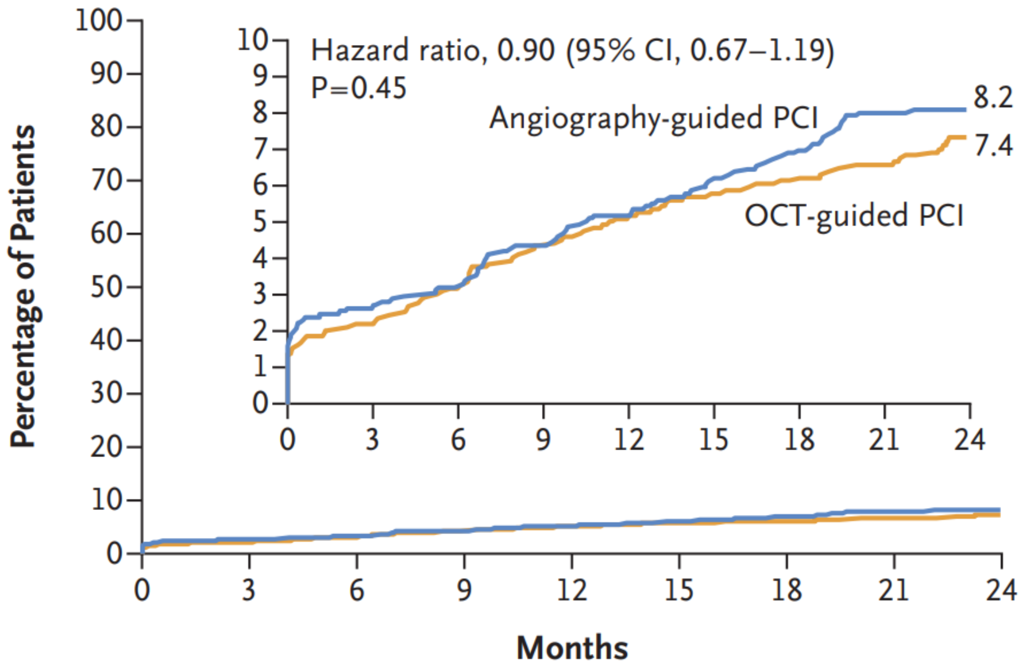
2-yr follow-up

Primary Endpoint:
Minimum stent area after PCI
Target vessel failure (composite of cardiac cause, TVMI, or ischemia-driven TVR)

Ali ZA, Landmesser U, Maehara A, et al. N Engl J Med. 2023;10.1056/NEJMoa2305861

ILUMIEN IV : OPTIMIZE PCI

OCT-Guided vs Angio-Guided PCI



No. at Risk

	0	3	6	9	12	15	18	21	24
Angiography-guided PCI	1254	1195	1184	1168	1143	1108	1092	1070	573
OCT-guided PCI	1233	1187	1174	1157	1127	1096	1085	1077	560

Figure 2. **Patients with Target-Vessel Failure.**

No Significant difference

Ali ZA, Landmesser U, Maehara A, et al. N Engl J Med. 2023;10.1056/NEJMoa2305861

OCT guidance vs Angiographic guidance
RENOVATE-COMPLEX

- 1639 patients (2:1 randomization)
- Complex coronary anatomy

  : true bifurcation lesions, CTO, LM disease, long lesions with more than 38 mm length, MV, ISR, severely calcified lesion; or ostial lesions of a major epicardial coronary artery

- Primary outcome

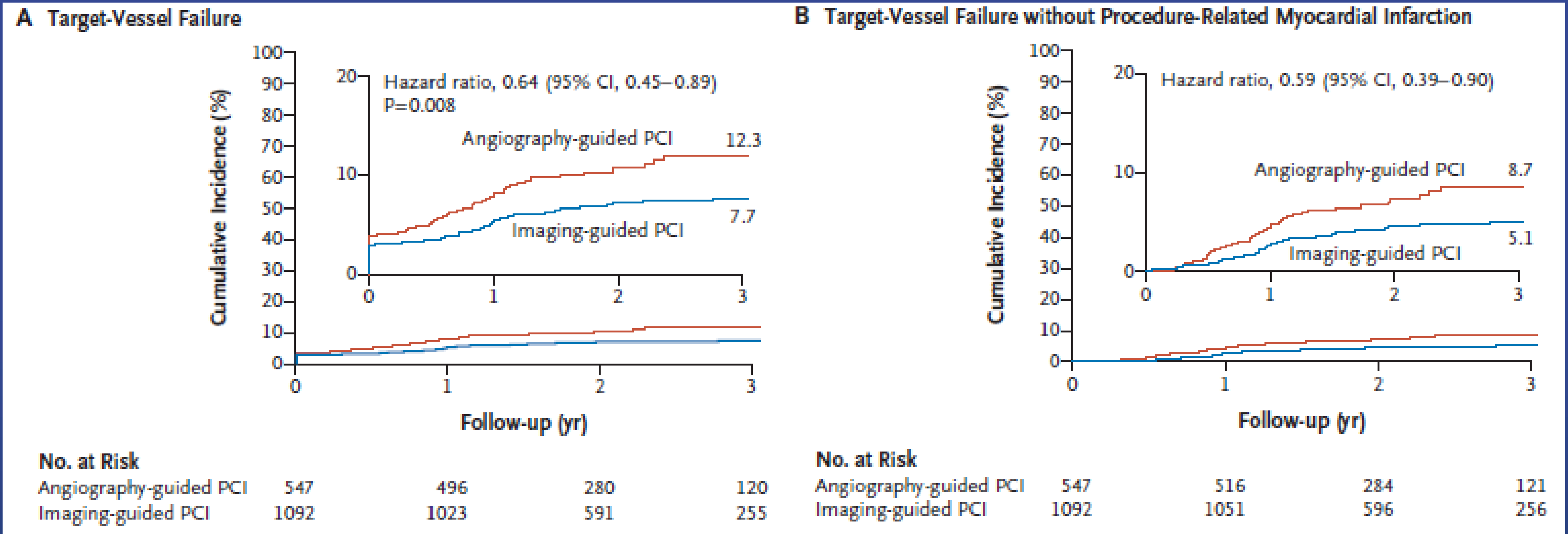
  → Composite of death from cardiac causes,

  target-vessel-related MI

  clinical driven target-vessel revascularization

JM Lee et al., N Engl J Med. 2023 May 4;388(18):1668-1679

OCT guidance vs Angiographic guidance
RENOVATE-COMPLEX



JM Lee et al., N Engl J Med. 2023 May 4;388(18):1668-1679

OCT guidance vs Angiographic guidance
OCTOBER

ORIGINAL ARTICLE

OCT or Angiography Guidance for PCI in Complex Bifurcation Lesions

- **1201 patients (38 centers in Europe)**
- **OCT-guided PCI vs angiography-guided PCI**
- **PCI and complex bifurcation lesion**

Primary outcome

→ MACE at 2 years

(cardiac death, TLMI, ischemia-driven TLR)

Holm NR, Andreasen LN, Neghabat O, et al. N Engl J Med. 2023;10.1056/NEJMoa2307770.

OCT guidance vs Angiographic guidance
OCTOBER

1201 patients with SA, UA, NSTEMI

R
1:1

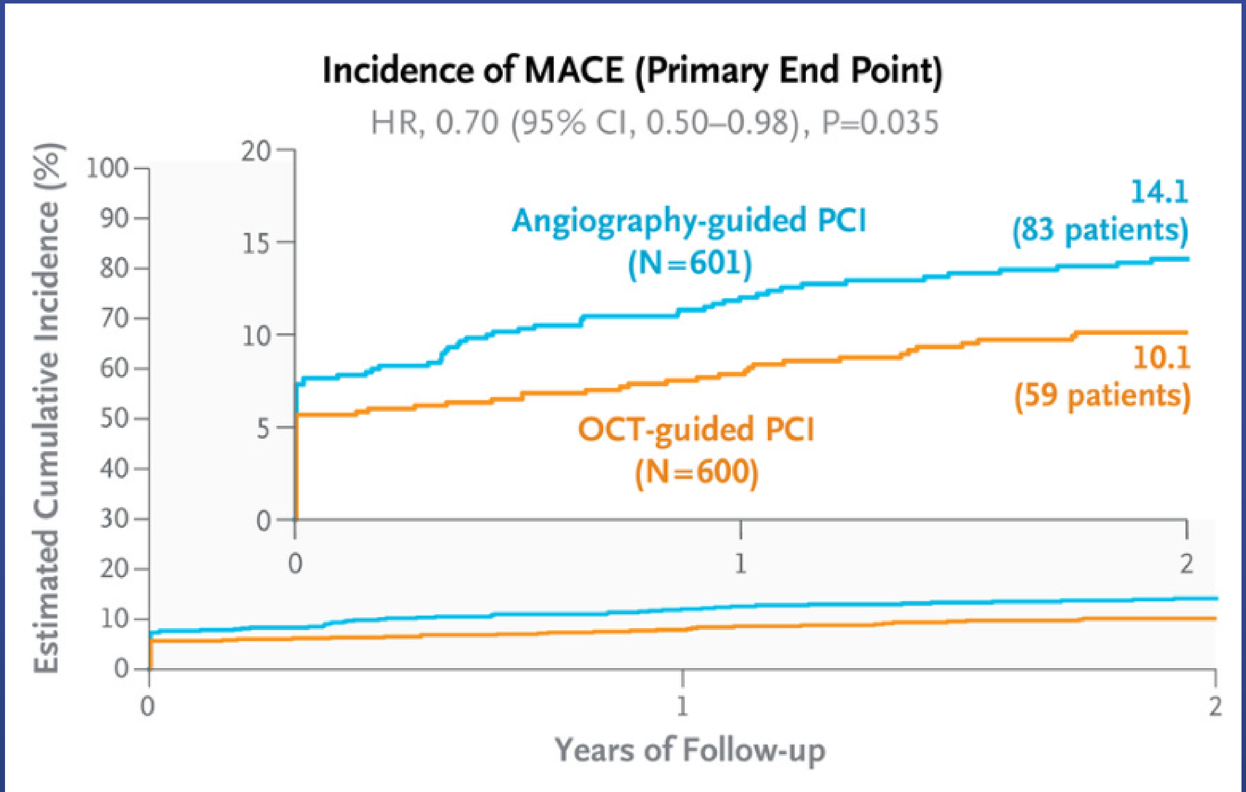
OCT Guided (n=600)

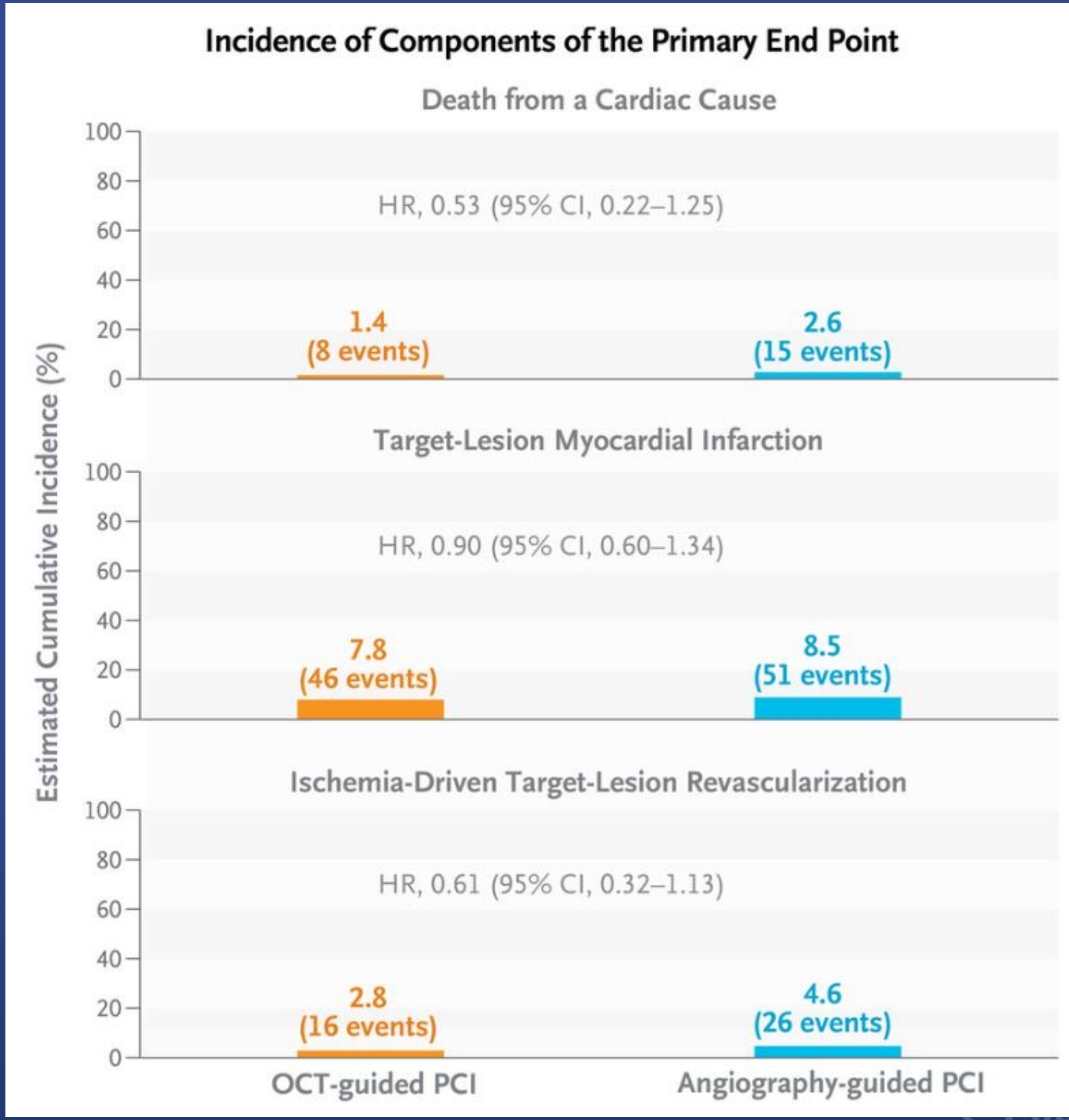
Angio Guided (n=601)

Primary outcome
MACE (death from cardiac cause, TLMI, TVR) at a median follow-up of 2 years

Holm NR, Andreasen LN, Neghabat O, et al. N Engl J Med. 2023;10.1056/NEJMoa2307770.

OCT guidance vs Angiographic guidance
OCTOBER





Holm NR, Andreasen LN, Neghabat O, et al. N Engl J Med. 2023;10.1056/NEJMoa2307770.

OCT guidance vs Angiographic guidance

OCTOBER

	OCT (n=600)	CAG (n=601)	HR (95% CI)
Primary end point: MACE	10.1%	14.1%	0.70 (0.50-0.98)
Clinical secondary end points			
Patient-oriented composite end point	13.6%	17.7%	0.76 (0.56-1.01)
Death from any cause	2.4%	4.0%	0.56 (0.28-1.10)
Death from a cardiac cause	1.4%	2.6%	0.53 (0.22-1.25)
Target-lesion myocardial infarction	7.8%	8.5%	0.90 (0.60-1.34)
Ischemia-driven target-lesion revascuLARIZATION	2.8%	4.6%	0.61 (0.32-1.13)
Stent thrombosis	2.1%	3.0%	0.70 (0.34-1.47)

Holm NR, Andreasen LN, Neghabat O, et al. N Engl J Med. 2023;10.1056/NEJMoa2307770.

OCT guided PCI

Stent underexpansion

PLUS…

(Minor) findings not seen on IVUS

- Malapposition
- Tissue protrusion
- Edge dissection

Stent underexpansion

PLUS…

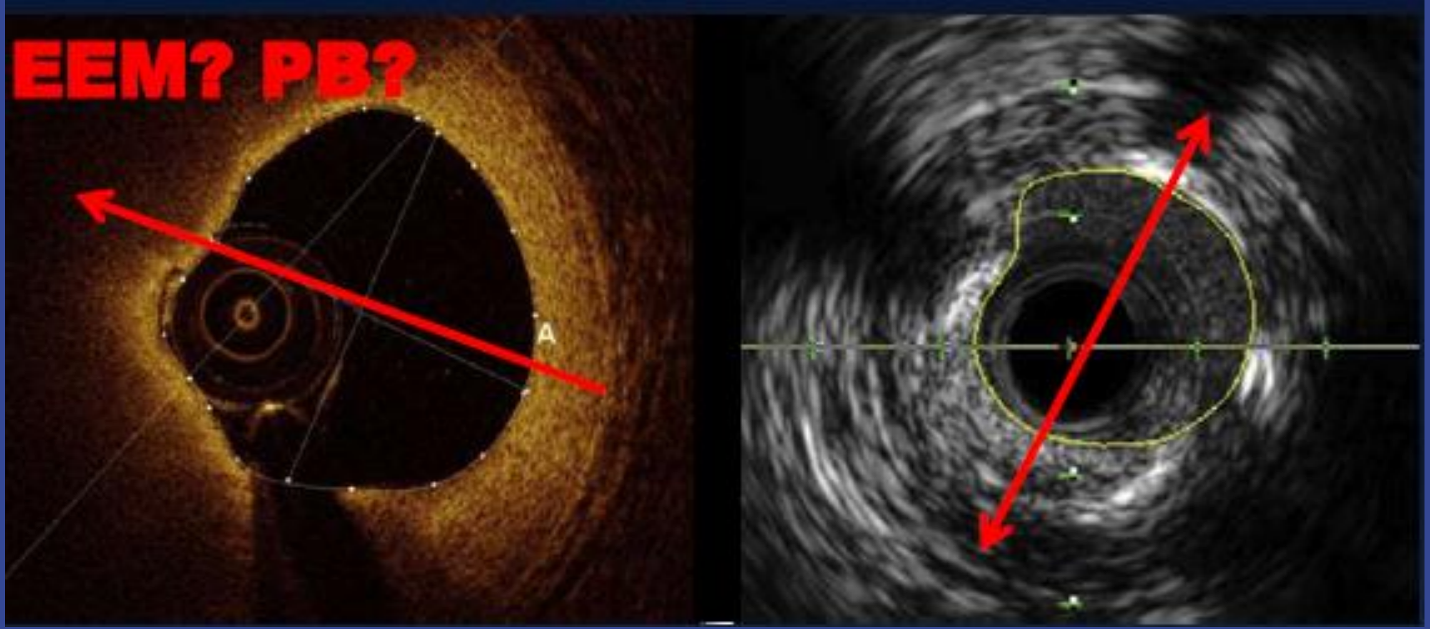
Geographical miss

(major edge dissections,

Plaque burden >50%)

Characteristics of devices

	IVUS	OCT
Energy source	US	NIR laser
Resolution	100-200 um	10-20 um
Frame rate	30 fps	160 fps
Pullback velocity	0.5-2.0 mm/sec	0.5-40 mm/sec
Catheter type	RX 2.4 Fr	RX 2.4 Fr
Penetration depth	5 mm	1-2 mm
Scan diameter	20 mm	10 mm
Blood evacuation	-	Lactate Ringer and/or Contrast medium flush



Ability to Detect Suboptimal Findings (OPUS-CLASS)

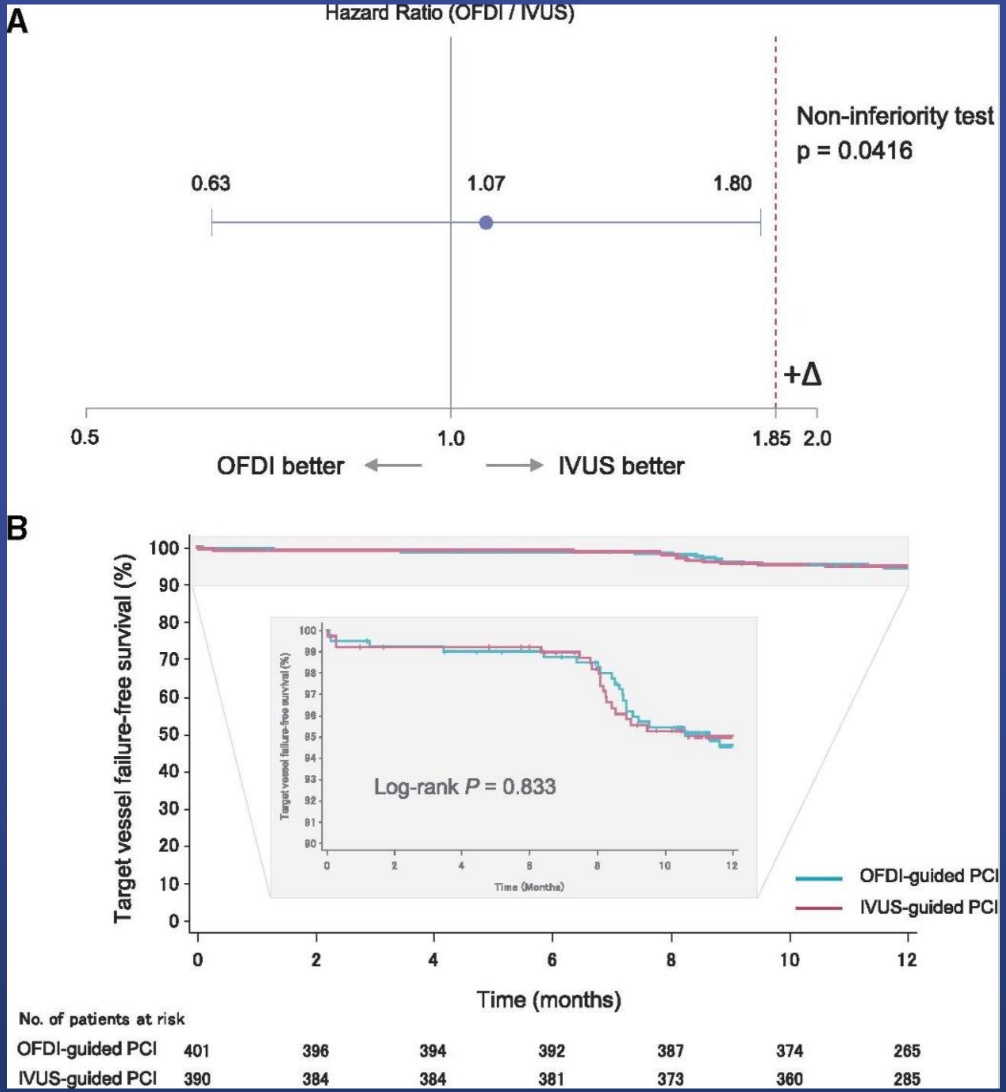
Post-PCI	IVUS	OCT	P
Malapposition	14%	39%	< 0.001
Tissue protrusion	18%	95%	< 0.001
Dissection	0%	13%	0.013
Thrombus	0%	13%	0.013

Kubo et al. JACC imaging 2013;6:1095-104

IVUS vs OCT guided PCI

OPINION Trial

- Multicenter, Prospective, Randomized trial
- Optical frequency domain imaging (OFDI) vs IVUS
- Primary endpoint
  : target vessel failure within 12 months



Kubo T et al. Eur Heart J. 2017 Nov 7; 38(42): 3139–3147.

IVUS vs OCT guided PCI

OPINION Trial

	OFDI-guided PCI (n = 412)	IVUS-guided PCI (n = 405)	P-value
Stent diameter (mm)	2.92 ± 0.39	2.99 ± 0.39	0.005
Total stent length (mm)	25.9 ± 13.2	24.8 ± 13.2	0.06
Multiple stenting	68 (16.5)	59 (14.6)	0.50
Pre-dilatation	316 (76.7)	316 (78.0)	0.67
Post-dilatation	316 (76.7)	304 (75.1)	0.62
Balloon dilatation of side-branch	39 (9.5%)	41 (10.1%)	0.81
Maximum balloon diameter (mm)	3.1 ± 0.8	3.3 ± 1.2	0.06
Maximum inflation pressure, atmosphere	16.0 ± 4.2	16.0 ± 4.2	0.70
No. of OFDI/IVUS procedure	3.0 ± 1.1	3.0 ± 1.1	0.14
Total amount of contrast	164 ± 66	138 ± 56	<0.001

Kubo T et al. Eur Heart J. 2017 Nov 7; 38(42): 3139–3147.

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Intravascular Ultrasound Versus Optical Coherence Tomography Guidance

Ron Waksman, MD, Hironori Kitabata, MD, Francesco Prati, MD, Mario Albertucci, MD, Gary S. Mintz, MD

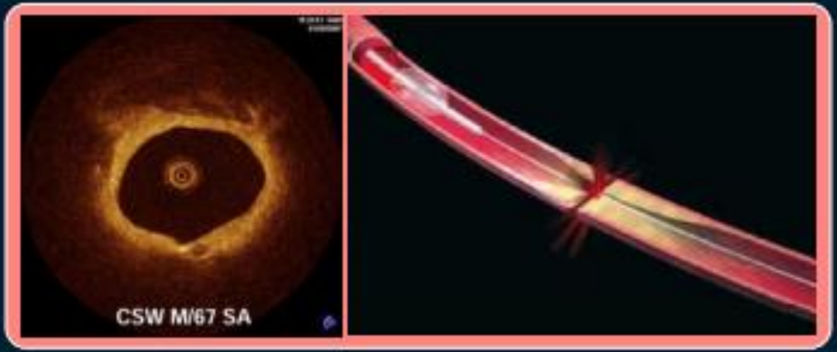
IVUS remains the more trusted modality for stent sizing and optimization until OCT own criteria are validated with clinical outcomes

High frequency OCT for pre-intervention coronary imaging : First in- Human Results

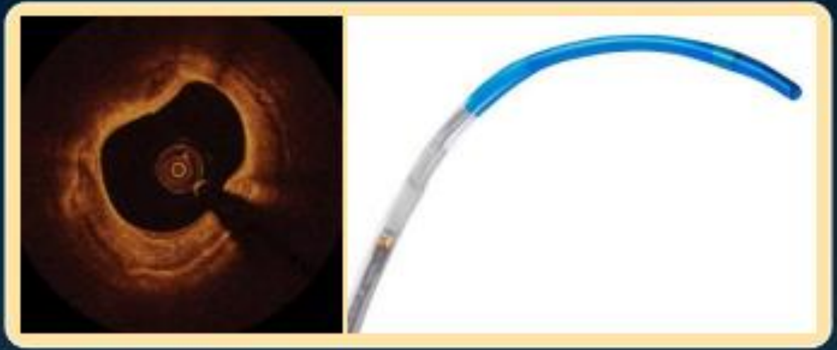
- To investigate the ability of HF-OCT to image pre intervention coronary arteries. (Prior to any vessel preparation)

- Clear Image Length (CIL); cross-sectional images were identified as 'clear image" when > 270 degrees of the lumen and vessel contour were free of blood or any artifact.
- To understand the impact of lesion severity on image quality; MLA was calculated, and quartiles were compared.

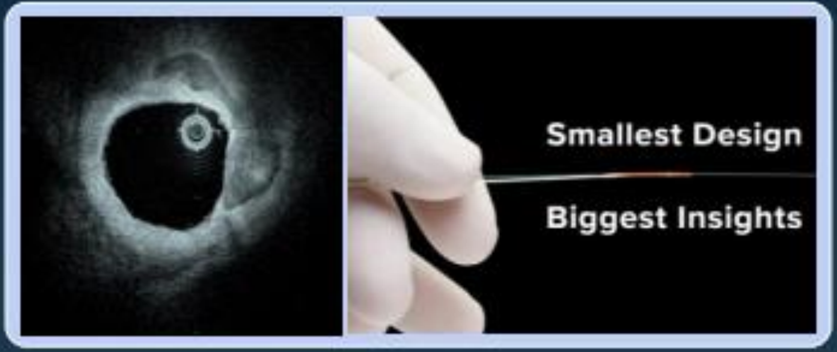
2022 TCT



1st Generation: TD-OCT (2001)
- 250 A-Lines/frame
- Balloon Occlusion of the vessel
- Pullback speed 1-3mm/sec



2nd Generation: FD-OCT (2007)
- 2.7F RX catheter
- Swept Laser (90 K), 500 lines /frame
- FOV ~ 5mm
- Up to 36mm/sec (2.5 second – 75mm)

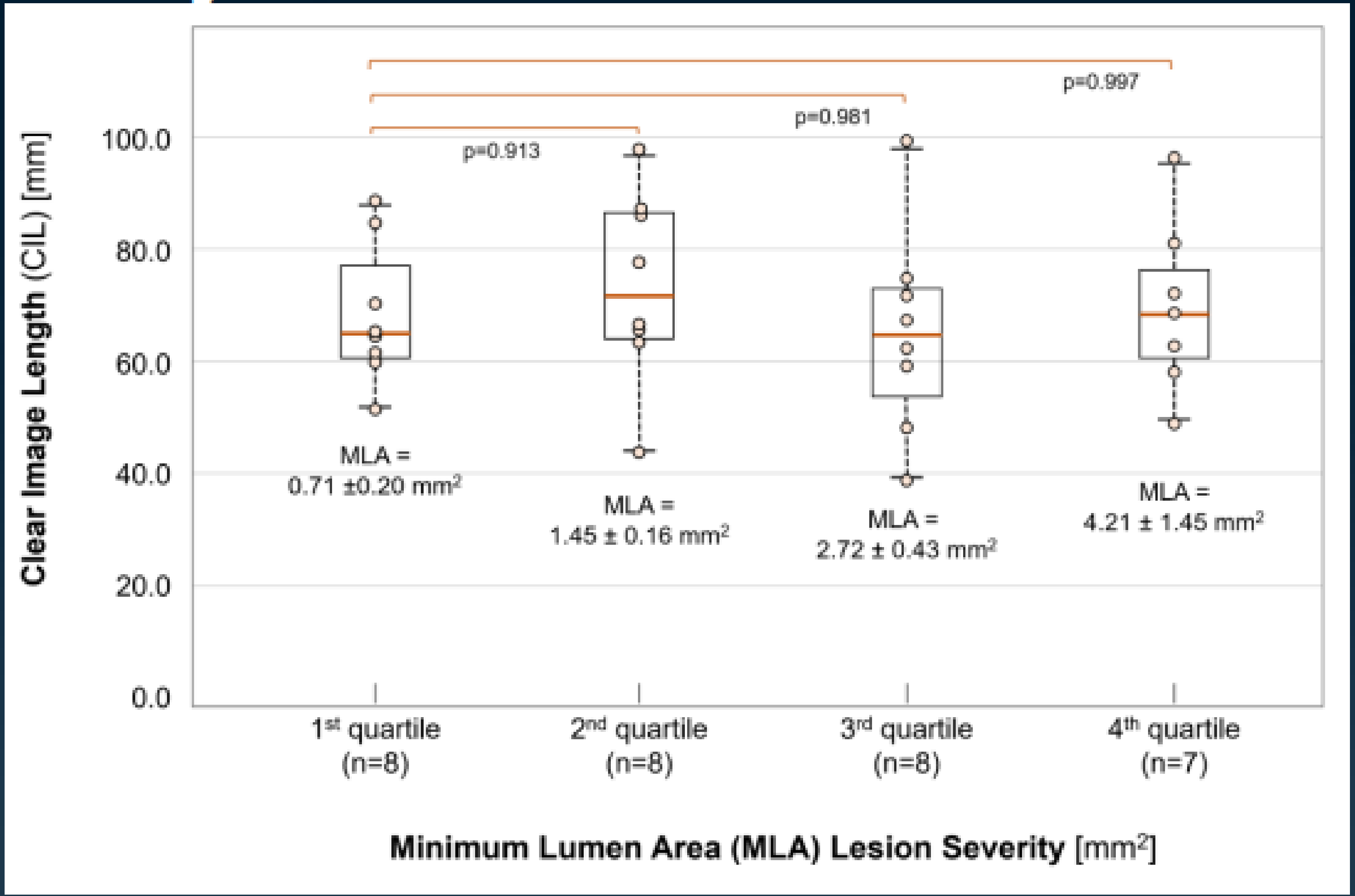


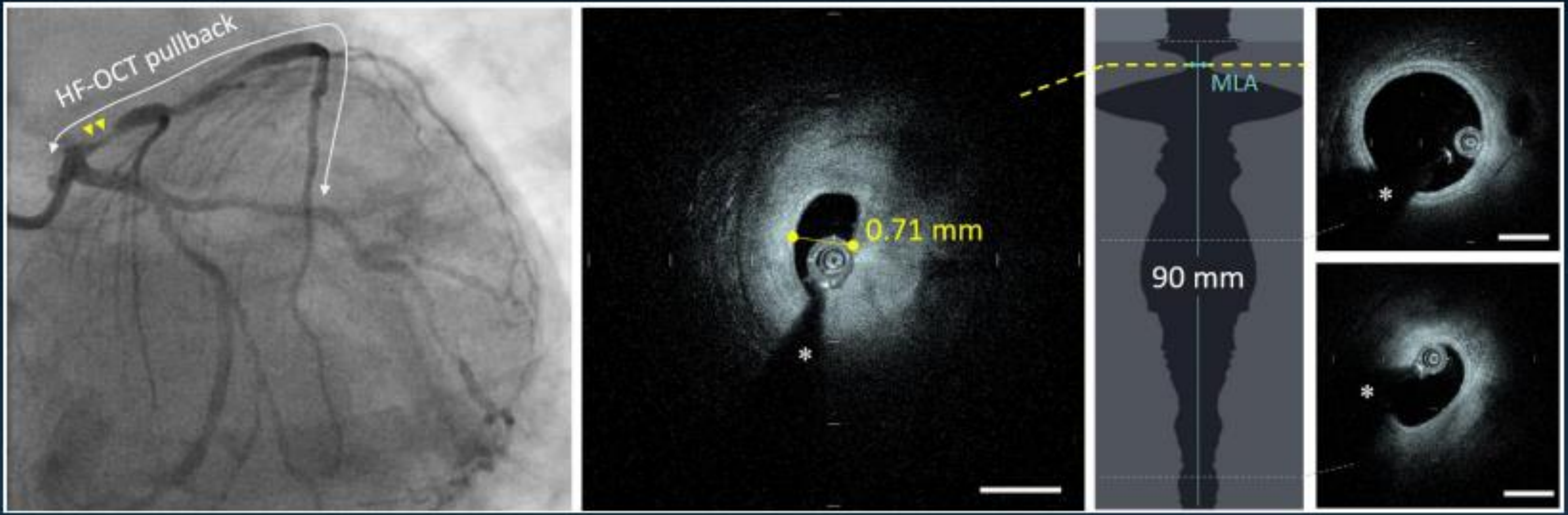
3rd Generation: HF-OCT (02/22/2021)
- 1.8F RX catheter
- VCSEL laser (200 K), 800 lines / frame
- FOV > 7mm
- Up to 100 mm/sec (1 second pullback – 100mm)

Results - Impact of Lesion Severity on Image Quality - MLA

We demonstrate the ability to image severe lesions with excellent clarity.

a. *25% of lesions in the study were below MLA 1.0 (which is the nominal size of most catheters)*
b. *ANOVA testing for difference in CIL across different lesion severity by MLA.*
   i. *We separate MLA severity into quartiles*
   ii. *Levene statistic confirms homogeneity among the groups*
   iii. *ANOVA test demonstrates no statistical difference among the 4 quartiles for CIL*
   iv. *Tukey HSD post hoc analysis demonstrates no statistical difference in CIL between pullbacks of lesions with MLA <1.0 compared to all other groups.*





Results, clinical HF-OCT Imaging

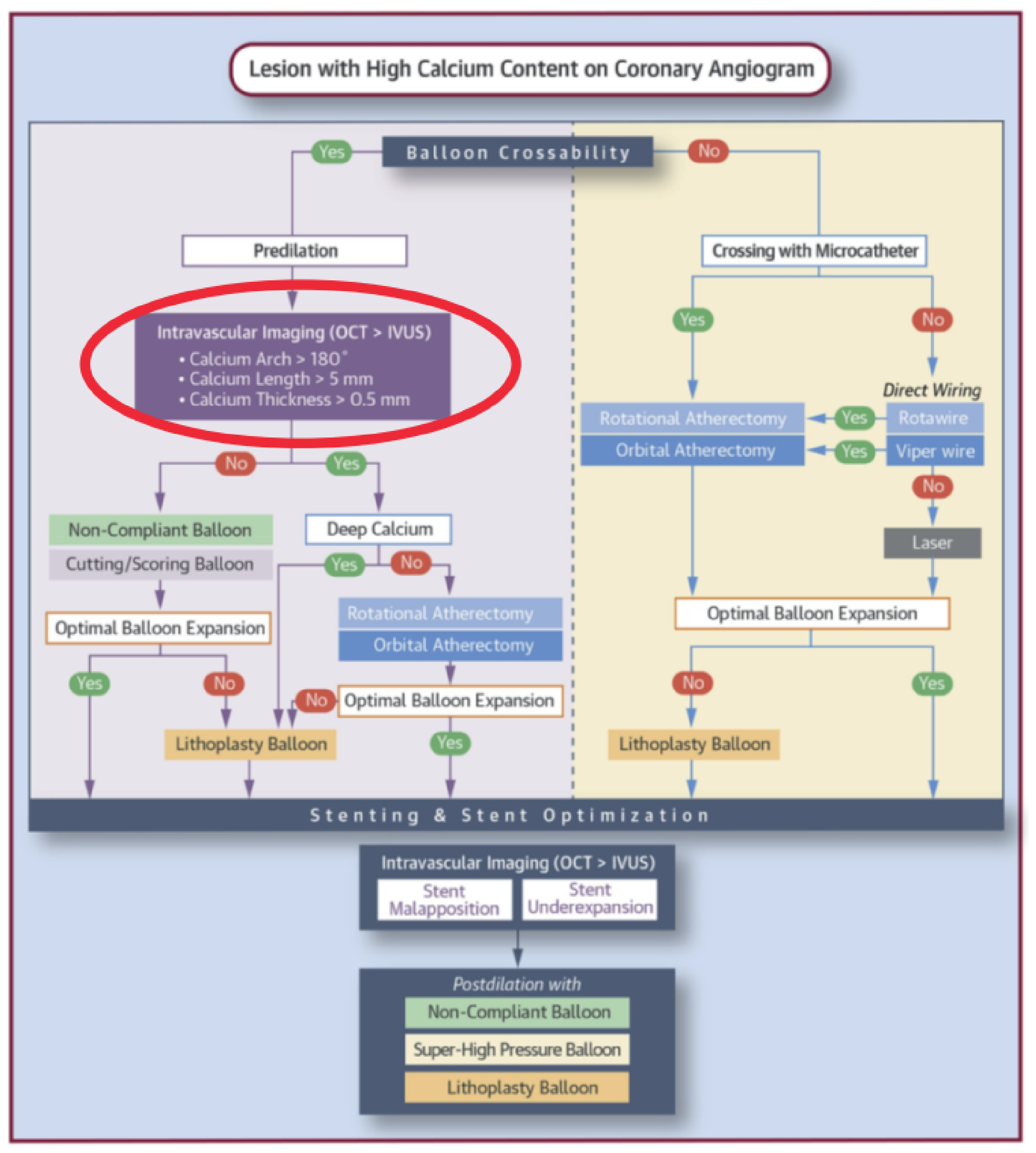
- Pullback length outside the guide catheter = 90 mm
- Clear image length (CIL) = 88 mm (or 98% of the pullback length)

Conclusion

- Results from this study show the efficacy of HF-OCT for the imaging of pre-intervention coronary lesions without any predilatation or vessel instrumentation.

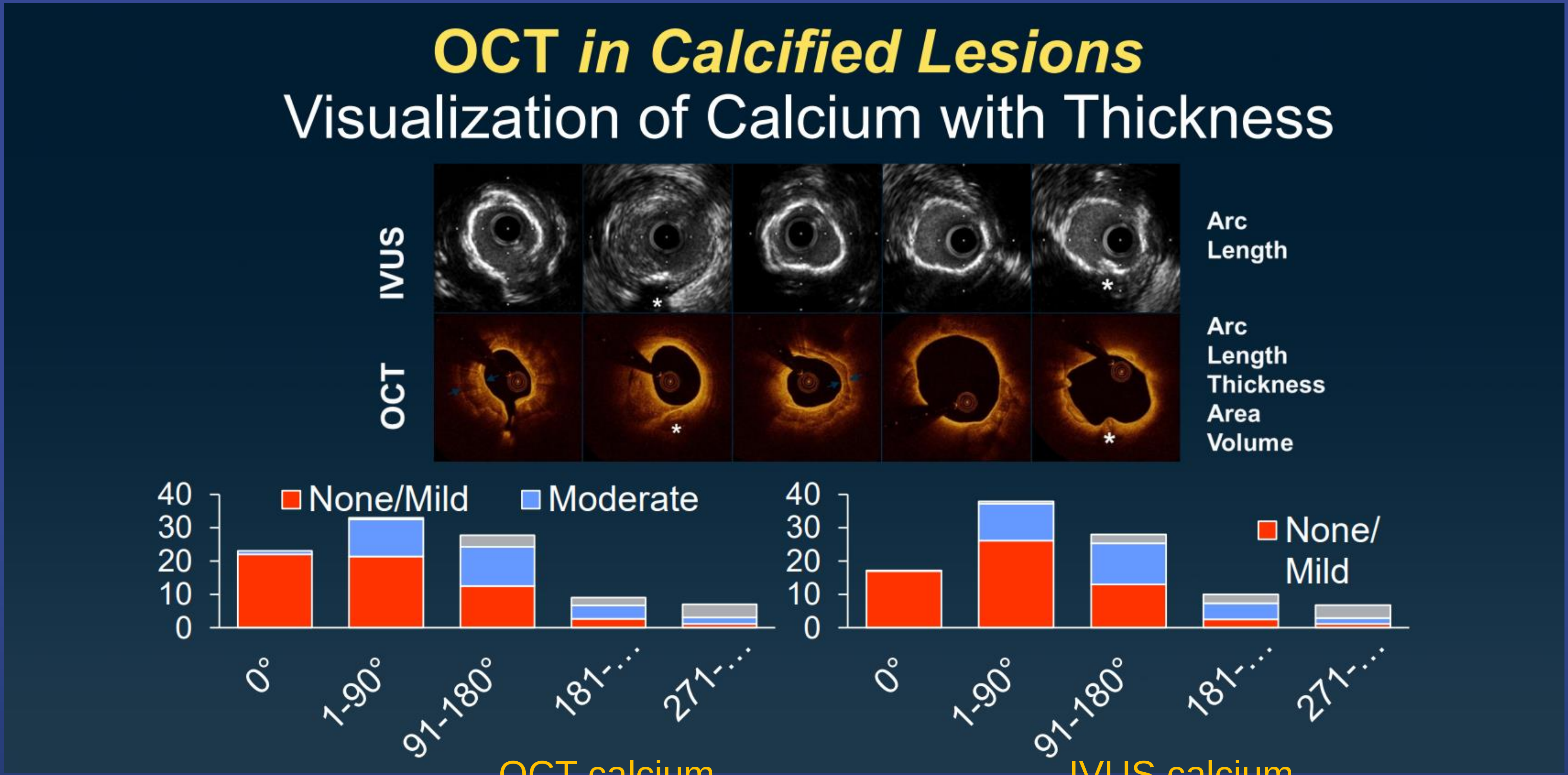
- This may be an ideal platform to explore pre-intervention planning including deriving vessel physiology from fluid dynamic analysis.

OCT for calcified lesion



De Maria et al, JACC CV Intv 2019

OCT in Calcified Lesions
Visualization of Calcium with Thickness



OCT calcium

IVUS calcium

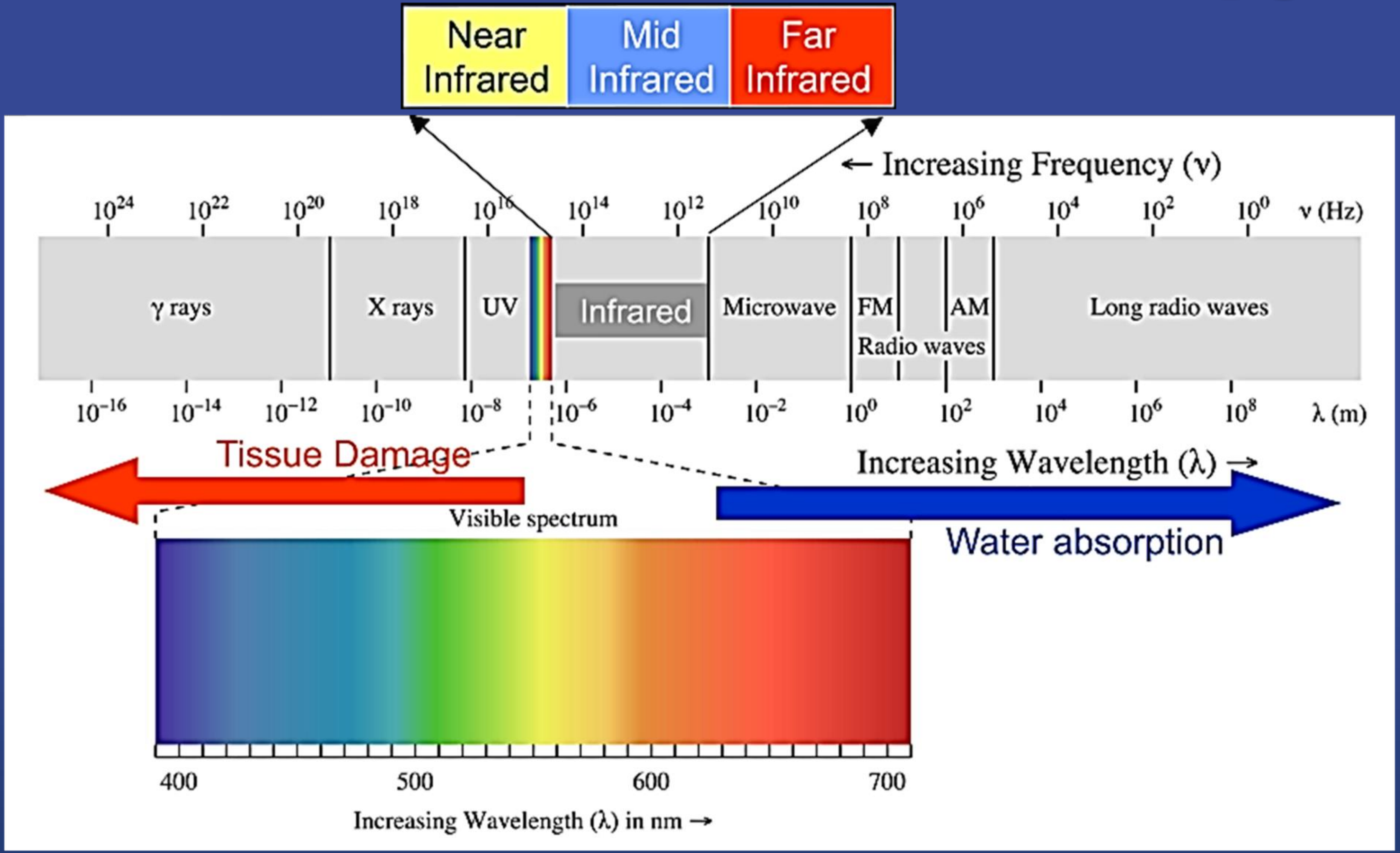
Wang et al. JACC Cardiovasc Imaging 2017;10:869-79

Mintz and Guagliumi. Lancet 2017;390:793-809

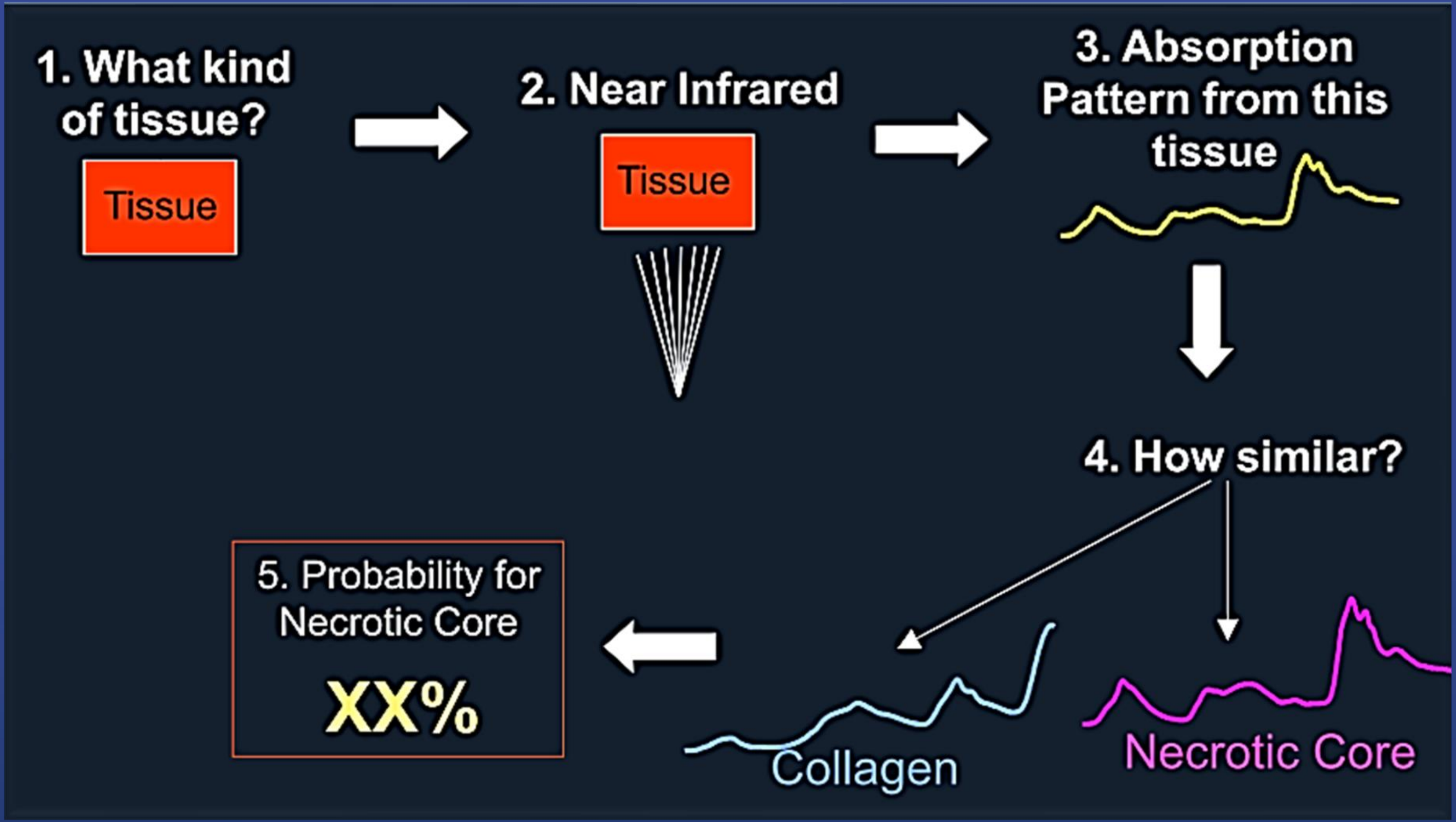
NIRS

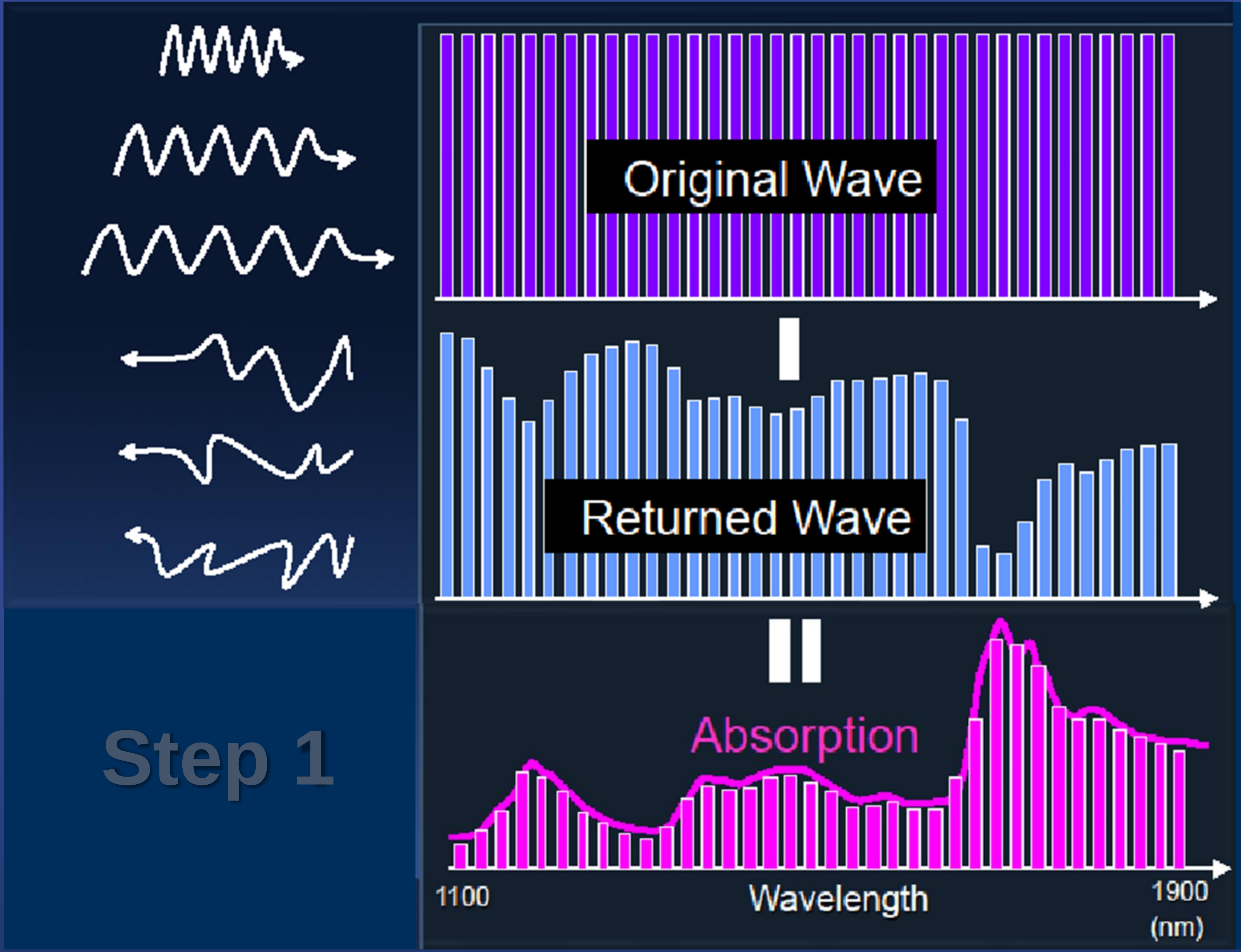
Near-infrared Spectroscopy

Near-infrared Spectroscopy

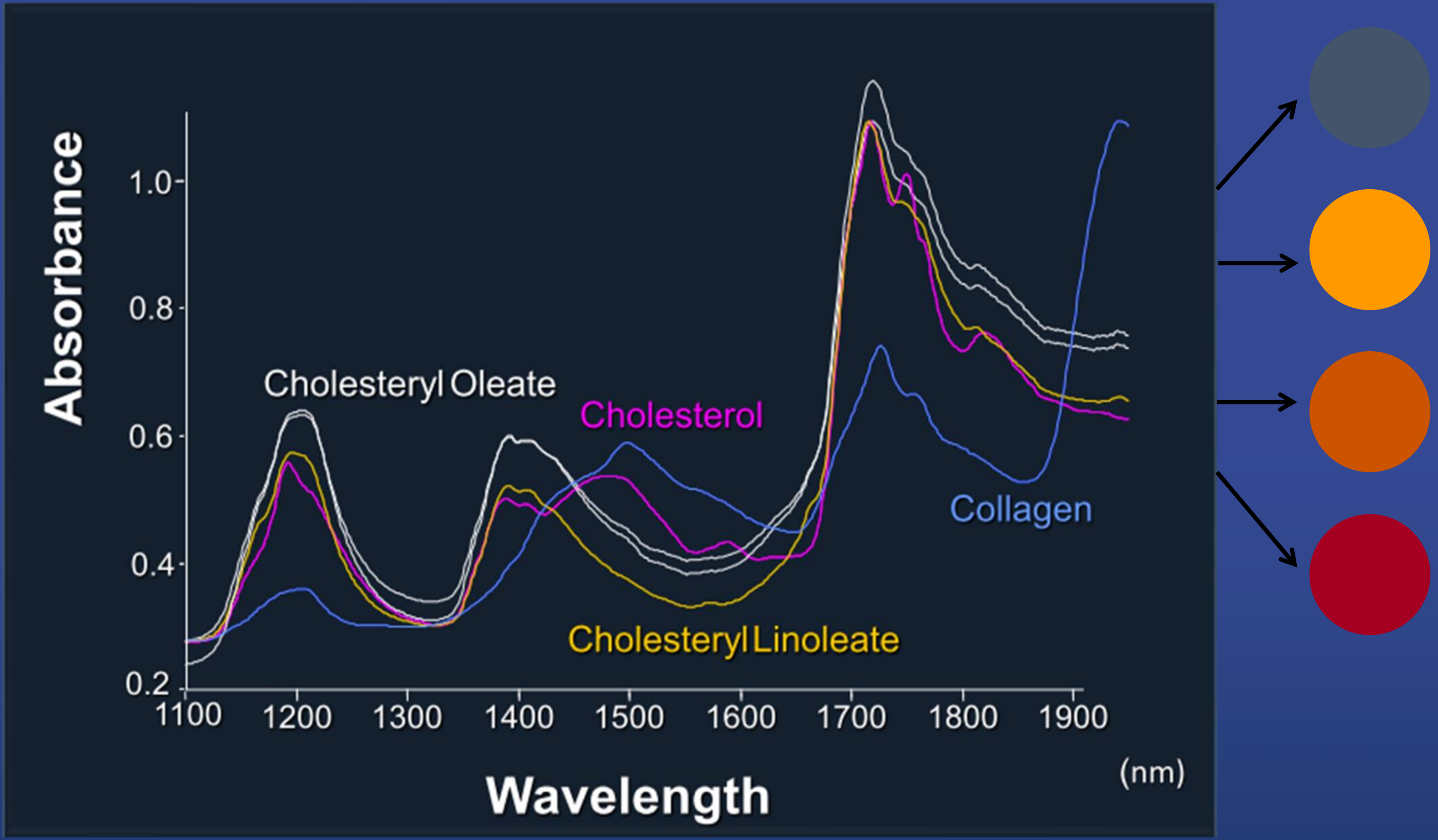


Process of NIR Spectroscopy



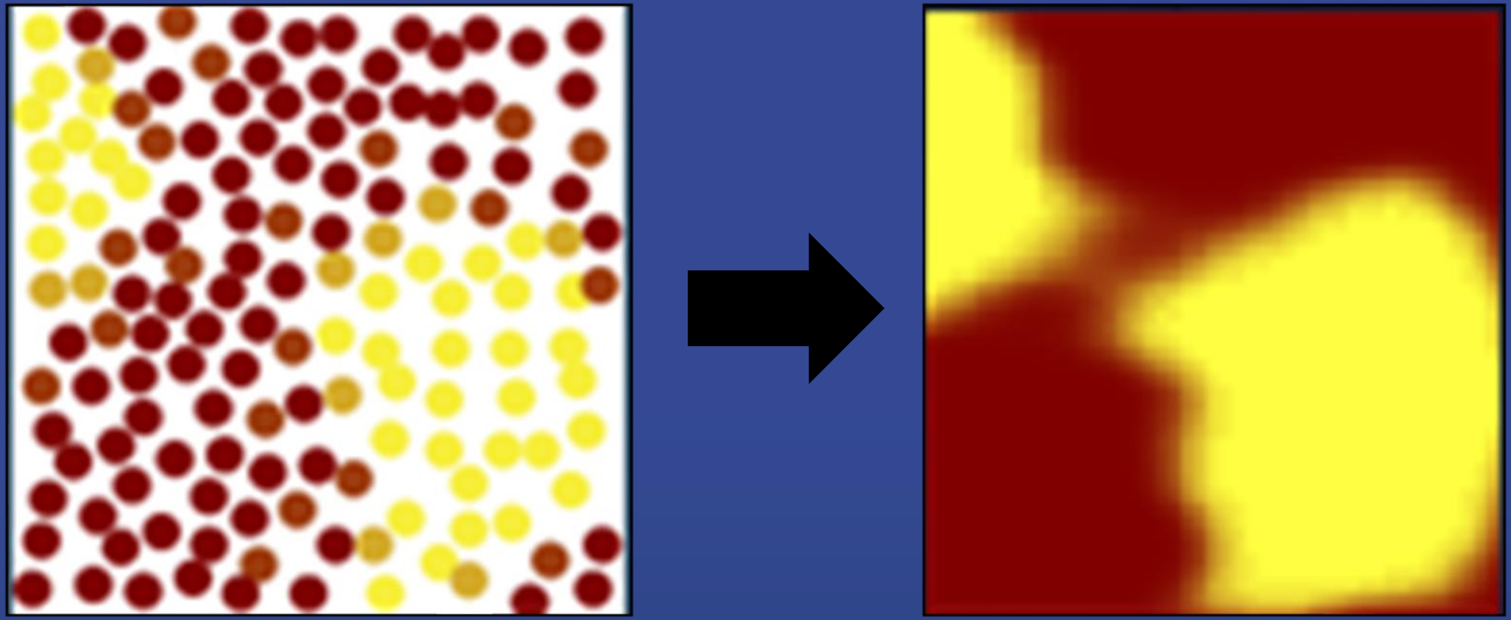

Original Wave
Returned Wave
Absorption
Step 1
1100
Wavelength
1900
(nm)

Step 2



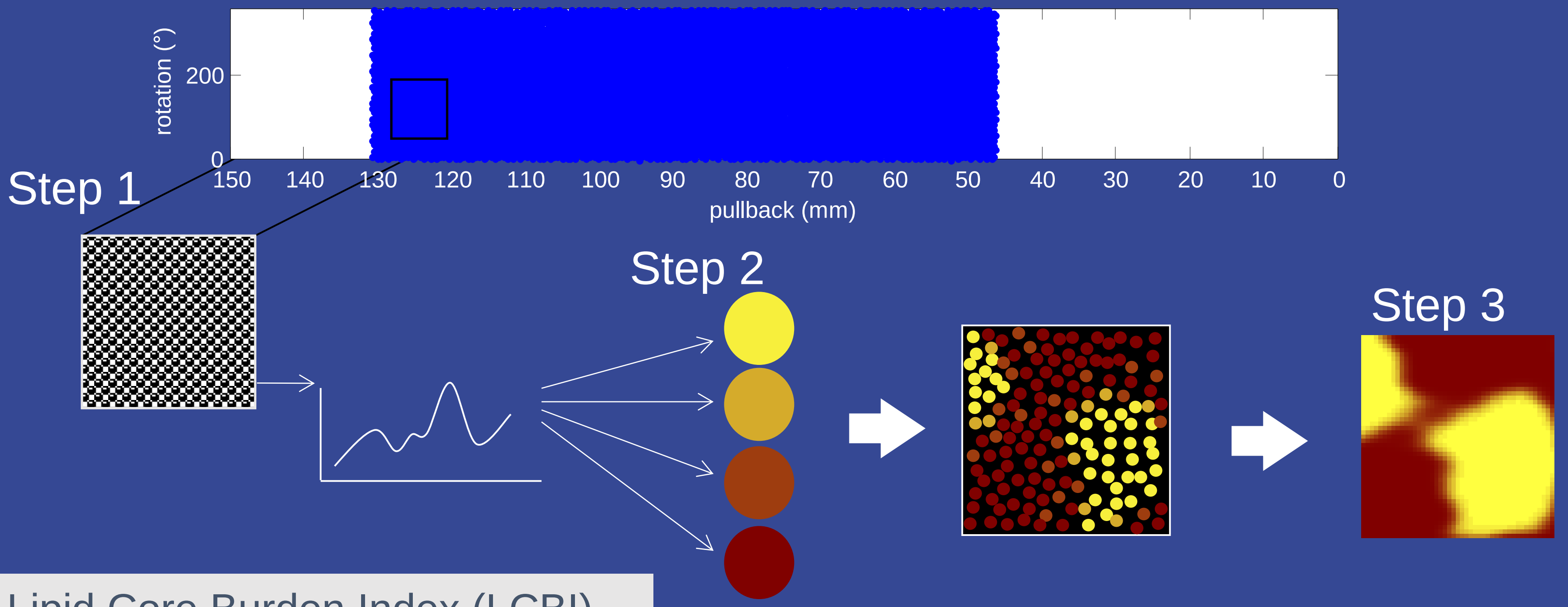
Absorbance
1.0
0.8
0.6
0.4
0.2
Cholesteryl Oleate
Cholesterol
Collagen
Cholesteryl Linoleate
1100
1200
1300
1400
1500
1600
1700
1800
1900
(nm)
Wavelength

Step 3

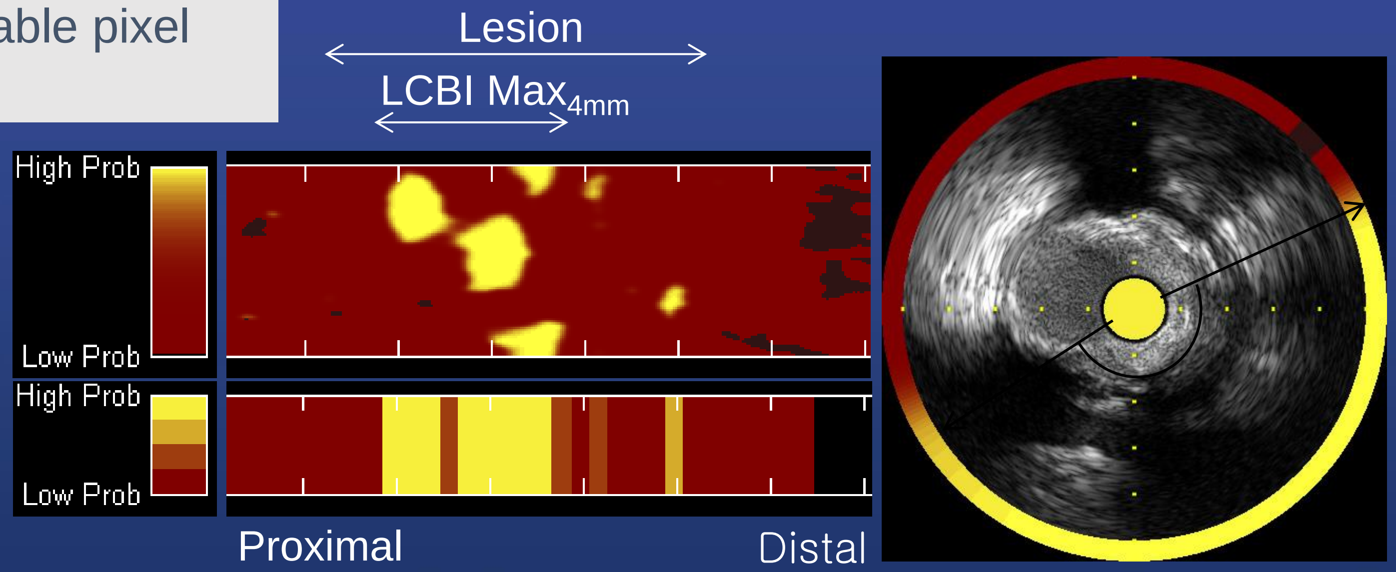


Lipid Core Burden Index (LCBI)
= Yellow pixel / All variable pixel x 1000

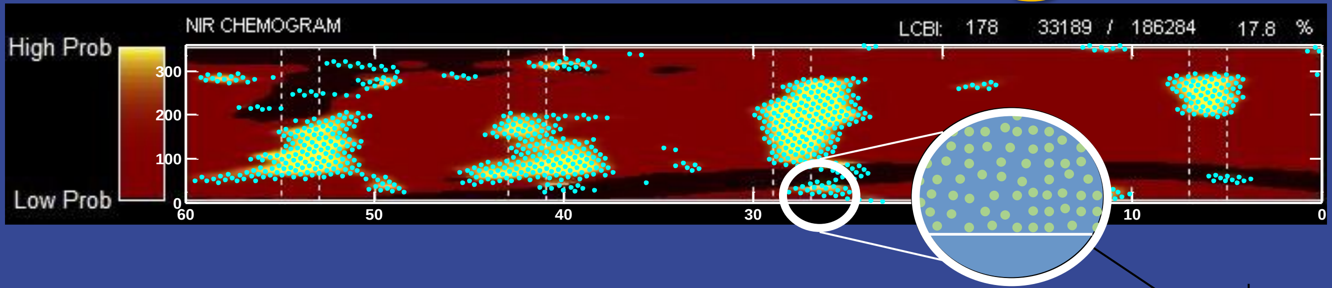
Near Infrared Spectroscopy



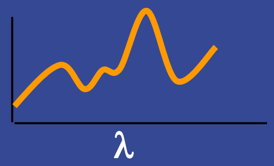
Lipid Core Burden Index (LCBI)
=Yellow pixel /All variable pixel
×1000



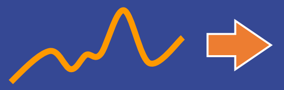
Formation of the Cap Thickness Prediction Image



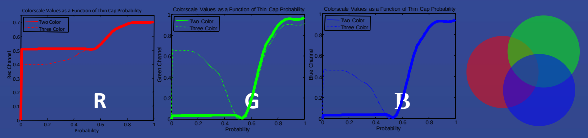
Spectra acquired at discrete pullback and rotation positions



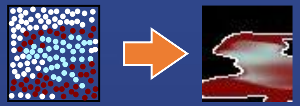
LCP Spectra transformed into posterior probability of thin cap presence



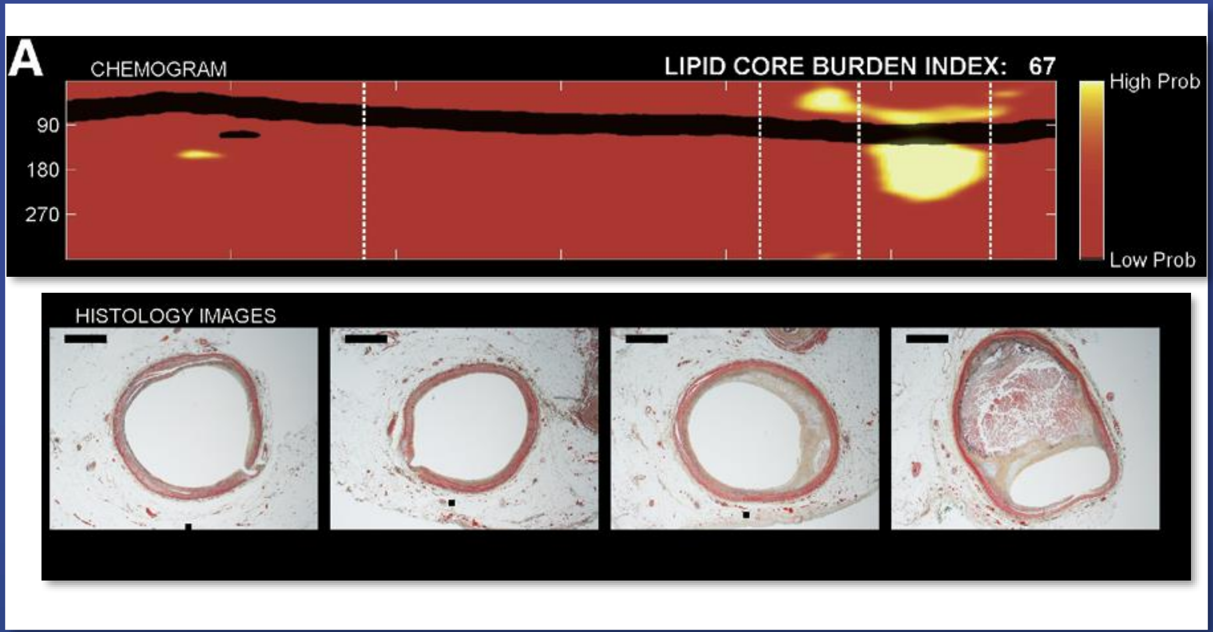
Probability mapped to a color



Pixels formed into an image



Quantification with Lipid Core Burden Index



LCBI = Lipid Core Burden Index (% yellow pixels of ROI x 10)

maxLCBI = the 4 mm segment with highest lipid content

Chemogram Color	Indication
Red	Low probability of LCP
Yellow	High probability of LCP
Black overlay	Indeterminate

Possible causes:
- Guide wire
- Thrombus
- Flow disturbance

Combination NIRS-IVUS Instrument

TVC Imaging System™

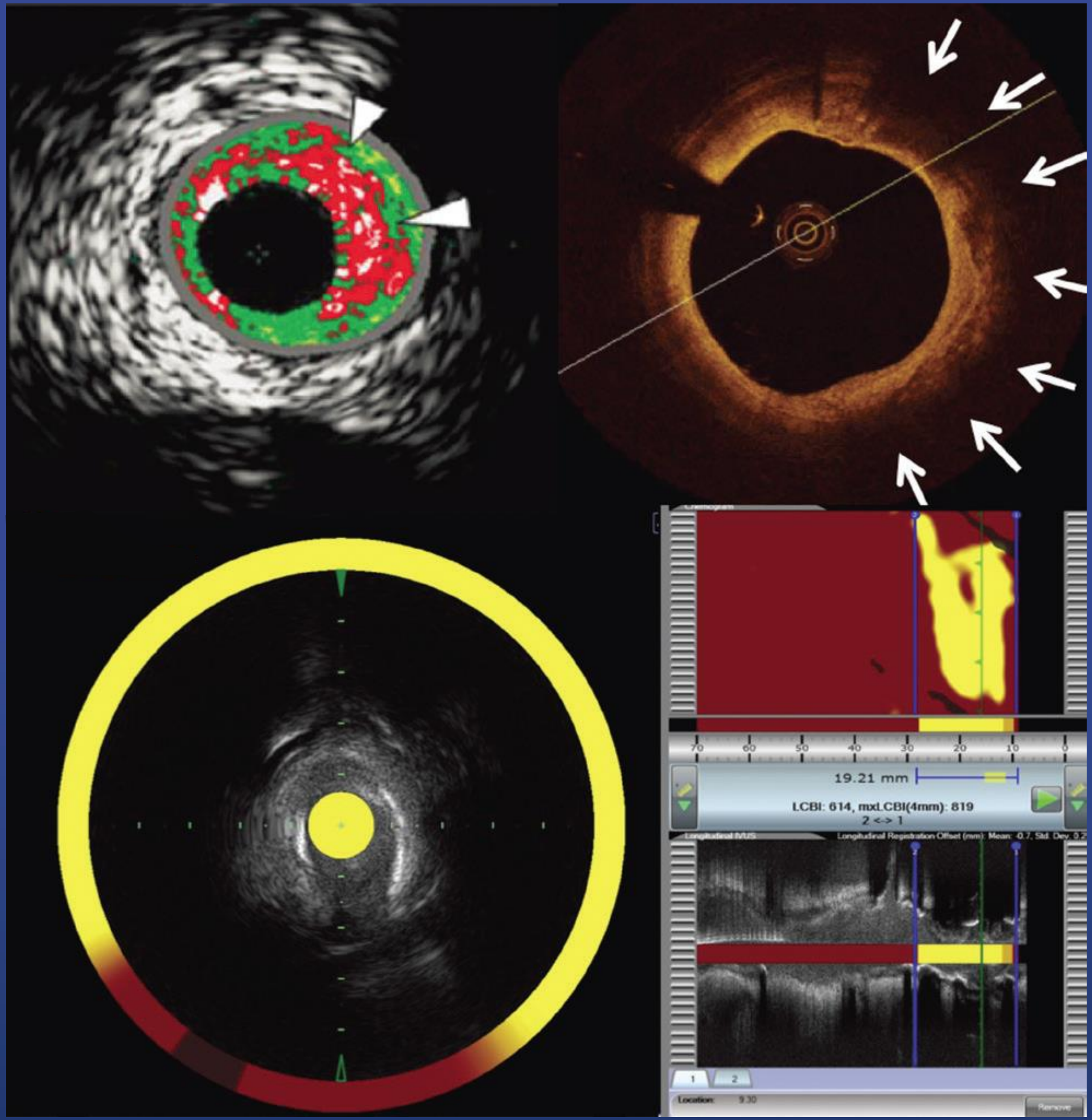
- Laser
- Dual monitors, touchscreen interface
- Pull-back and rotation device

TVC Insight™ Catheter

- Single use, 3.2 Fr
- Dual modality
    - Spectroscopy detects lipid core plaqu
    - IVUS detects vessel structure

Lipid Core Plaque Imaging

VH-IVUS vs. OCT vs. NIRS-IVUS

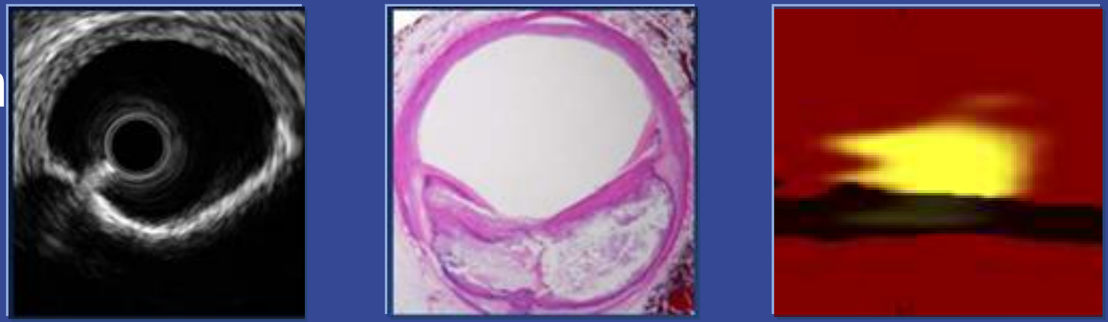


Fuh et al JIC Supplement 2013

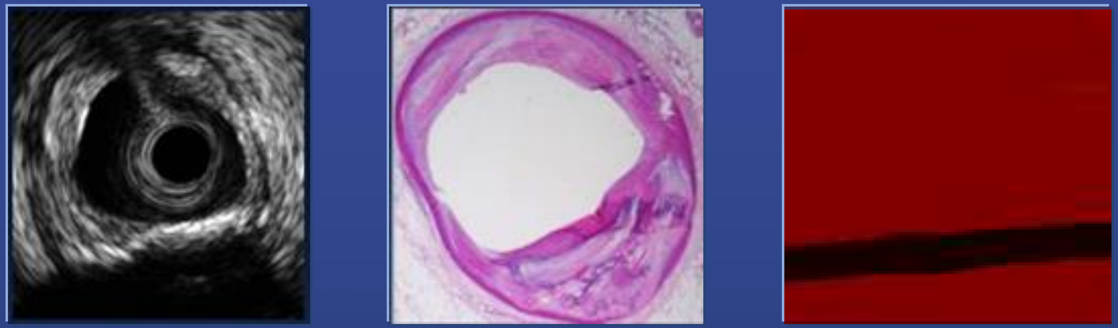
Different type of Calcified Plaque

Necrotic core

Behind Calcium

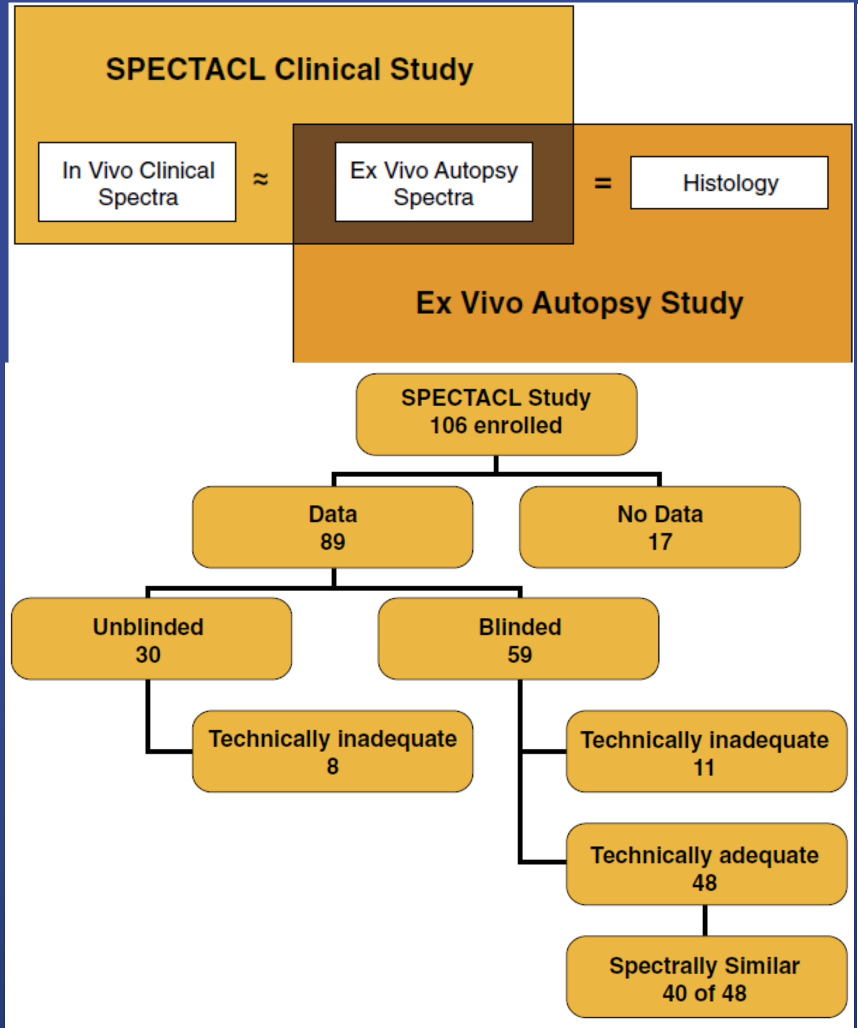


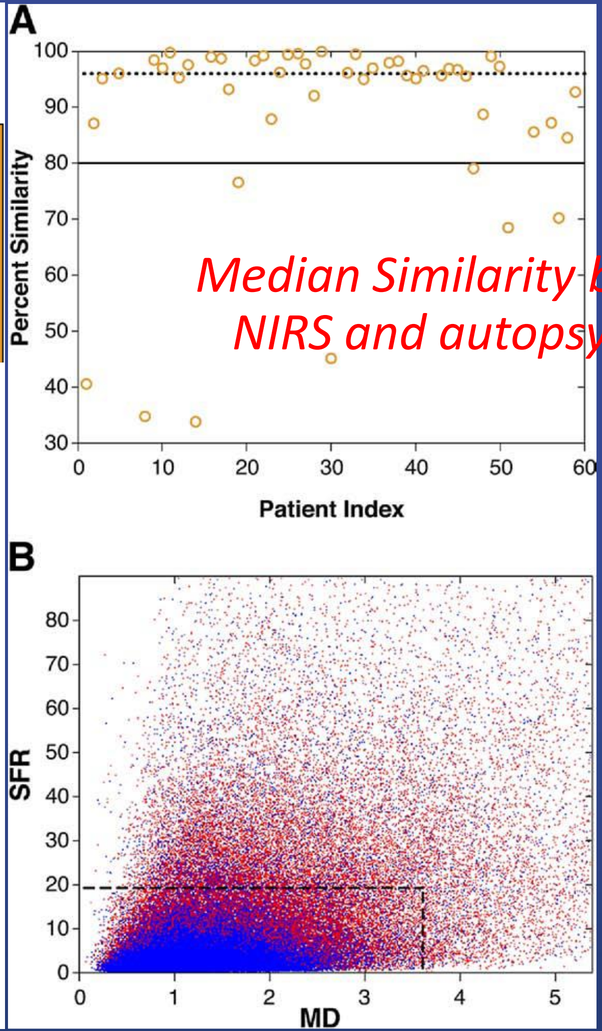
Calcium only



SPECTACL Study

In vivo Validation of NIRS for Detection of Lipid Core Coronary Plaques





Sergio et al. *J Am Coll Cardiol Img*, 2009

The Applications of NIRS-IVUS

- Identifying lesions possessing both architectural features and compositional data characteristic of vulnerable plaques

- Identifying large volume lipid-core plaque (LCP), which may be at greater risk for distal embolization during PCI

- Using IVUS to determine the length of vessel having significant plaque burden and delineating by NIRS the extent of the plaque burden occupied by LCP, data which may influence stent length selection

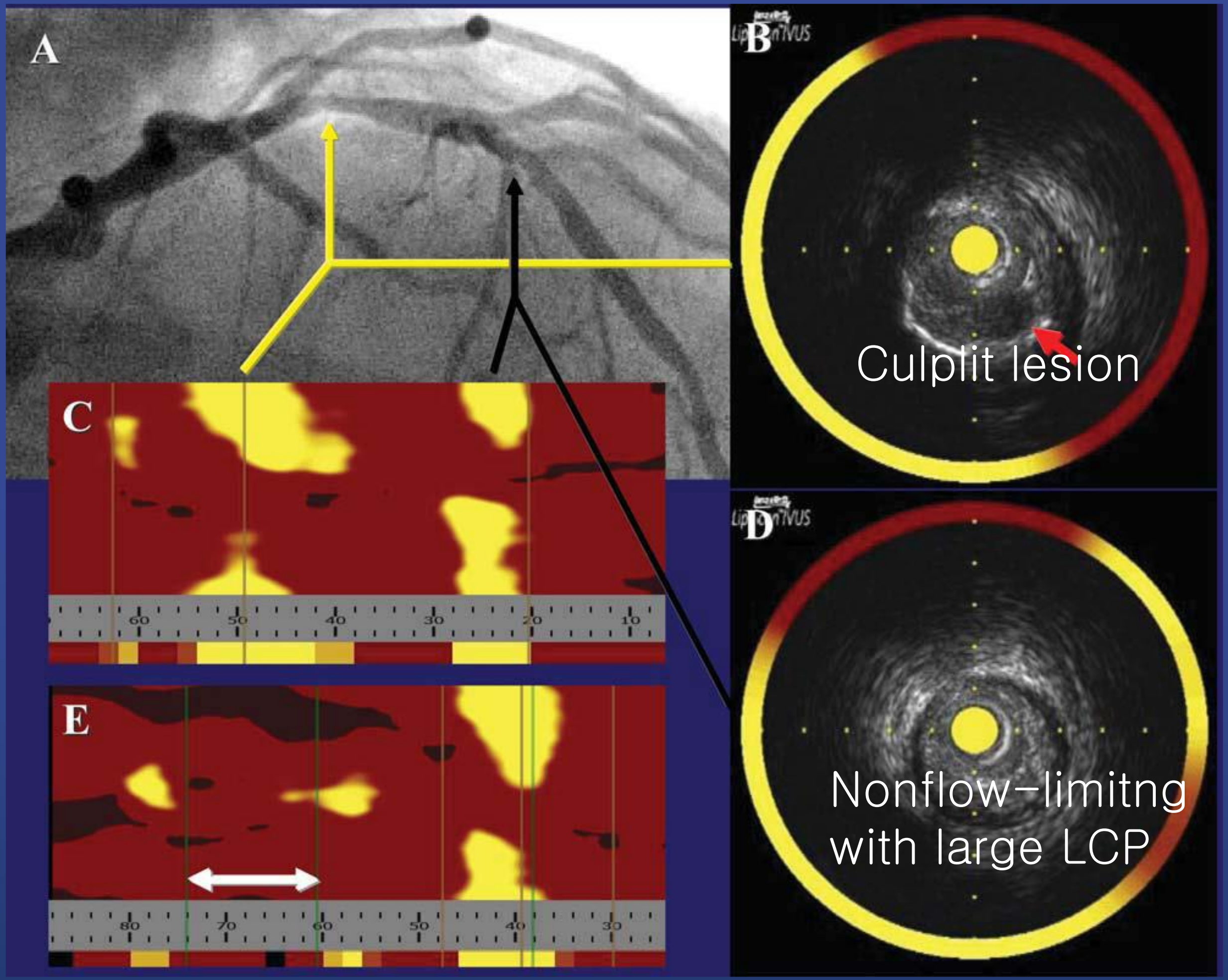
- Localizing nonculprit lesions with morphologic and compositional characteristics of "vulnerable plaque"

- Analyzing plaque composition in heavily calcified segments, a setting in which other imaging modalities have limited utility

RD Madder et al. Catheterization and Cardiovascular Interventions, 2013

The Applications of NIRS-IVUS

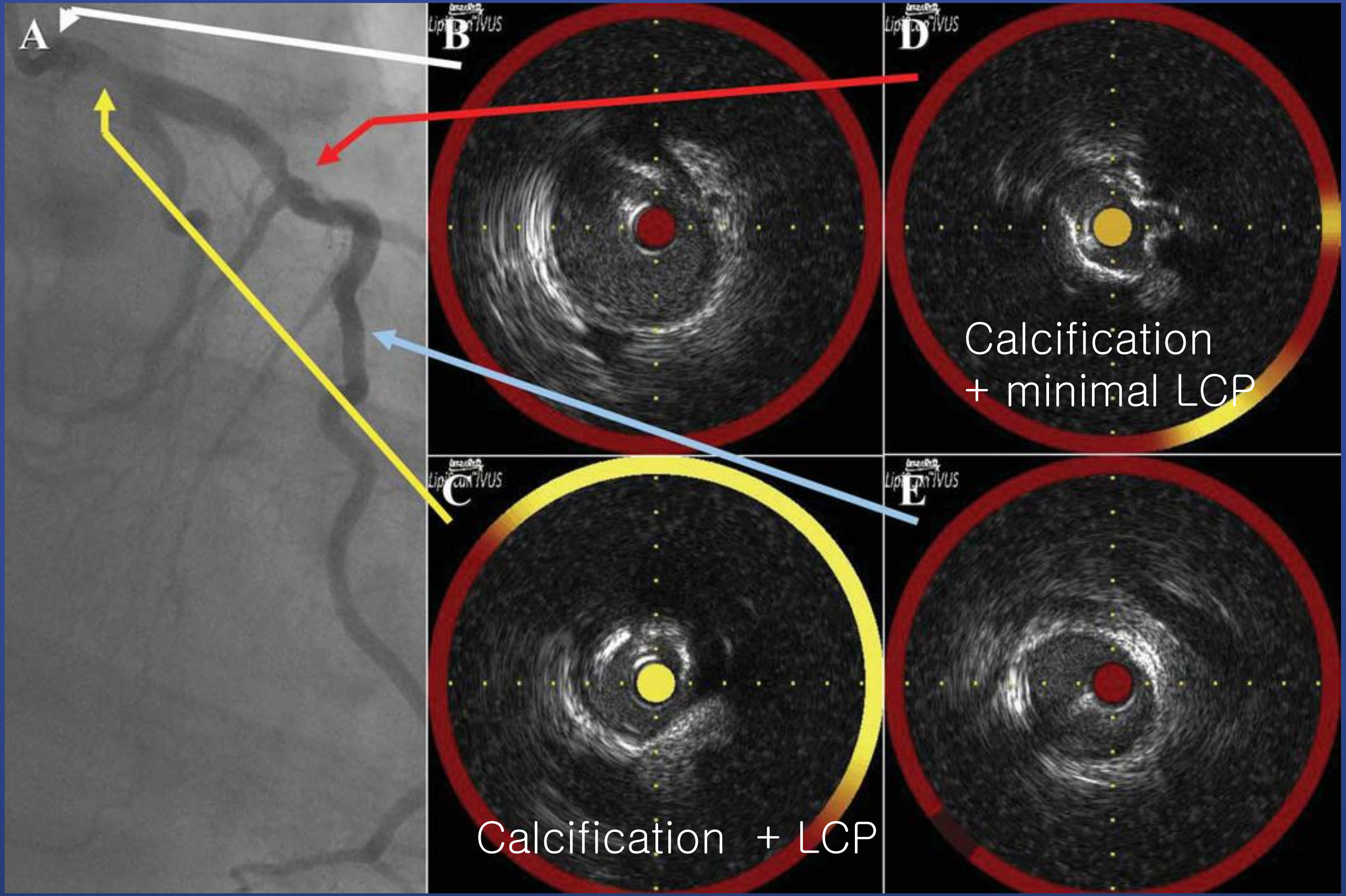
Detection of Potentially Vulnerable Nonflow-Limiting Plaque



RD Madder et al. Catheterization and Cardiovascular Interventions, 2013

The Applications of NIRS-IVUS

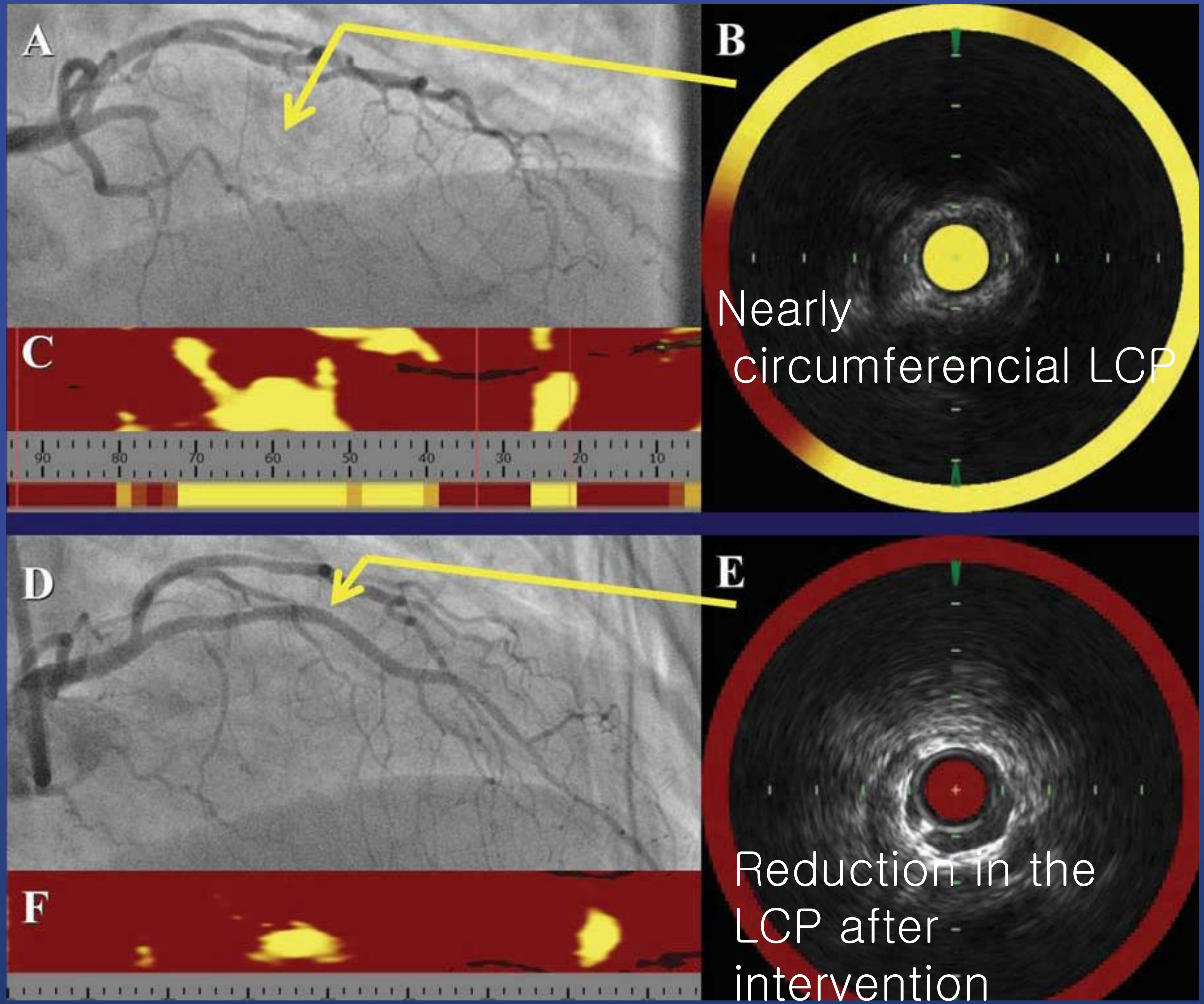
Detection of LCP despite Extensive Calcification



RD Madder et al. Catheterization and Cardiovascular Interventions, 2013

The Applications of NIRS-IVUS

Characterization of a Lesion Causing Chronic Total Occlusion

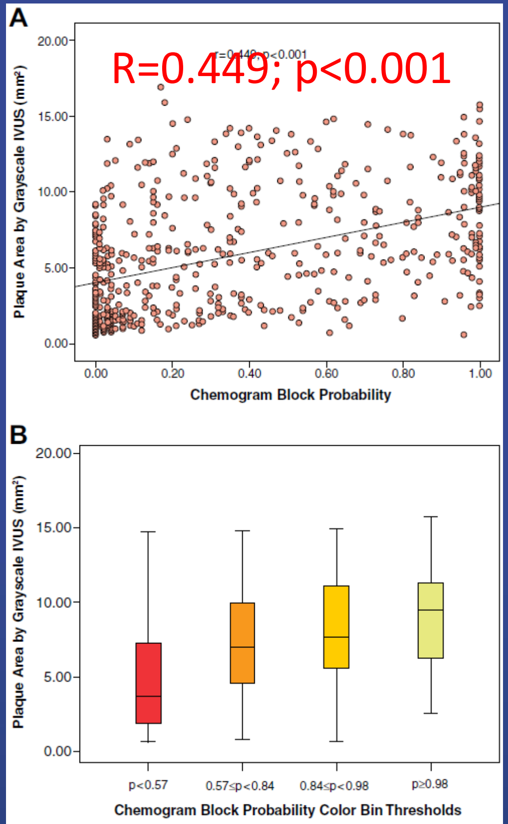


RD Madder et al. Catheterization and Cardiovascular Interventions, 2013

Characterization of Atherosclerosis

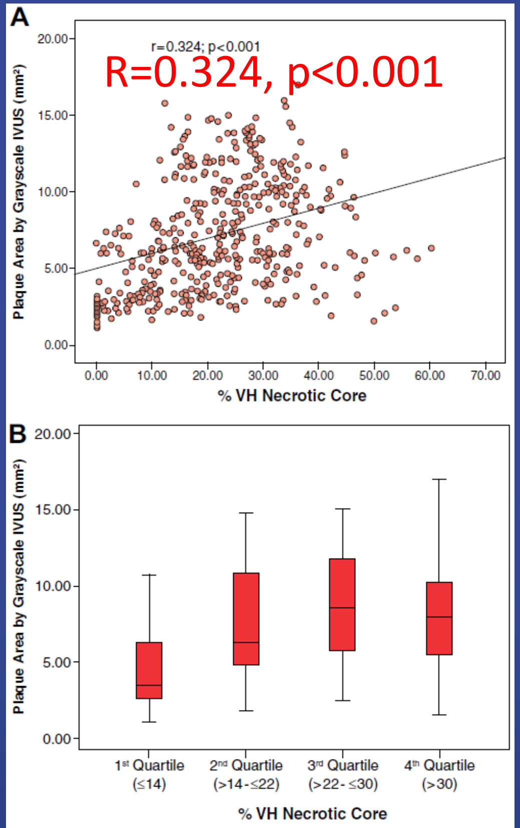
correlation among IVUS,NIRS and VH-NC

IVUS and NIRS



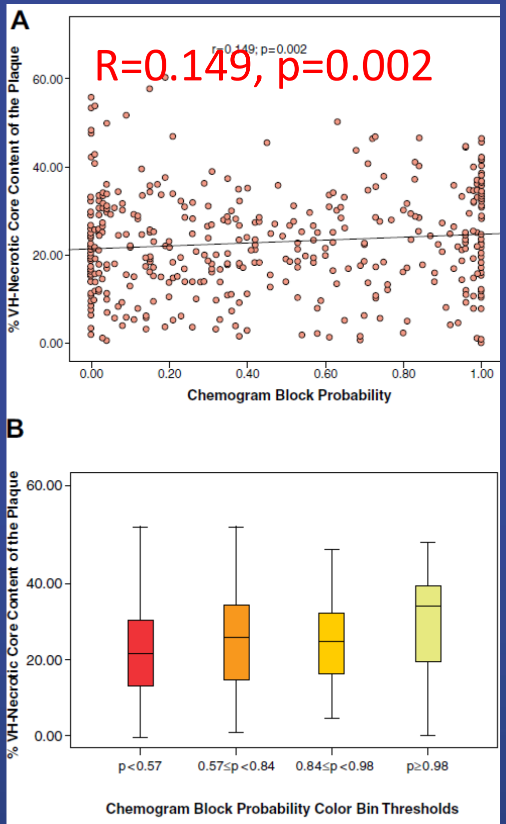
	0.57≤p<0.84	0.84≤p<0.98	p≥0.98
p<0.57	p<0.001	p<0.001	p<0.001
0.57≤p<0.84		p=0.186	p=0.188
0.84≤p<0.98			p=0.968

IVUS and VH-NC



	2nd quartile	3rd quartile	4th quartile
1st quartile	p<0.001	p<0.001	p<0.001
2nd quartile		p=0.091	p=0.775
3rd quartile			p=0.772

NIRS and VH-NC



	0.57≤p<0.84	0.84≤p<0.98	p≥0.98
p<0.57	p=0.552	p=0.788	p=0.002
0.57≤p<0.84		p=1.000	p=0.499
0.84≤p<0.98			p=0.367

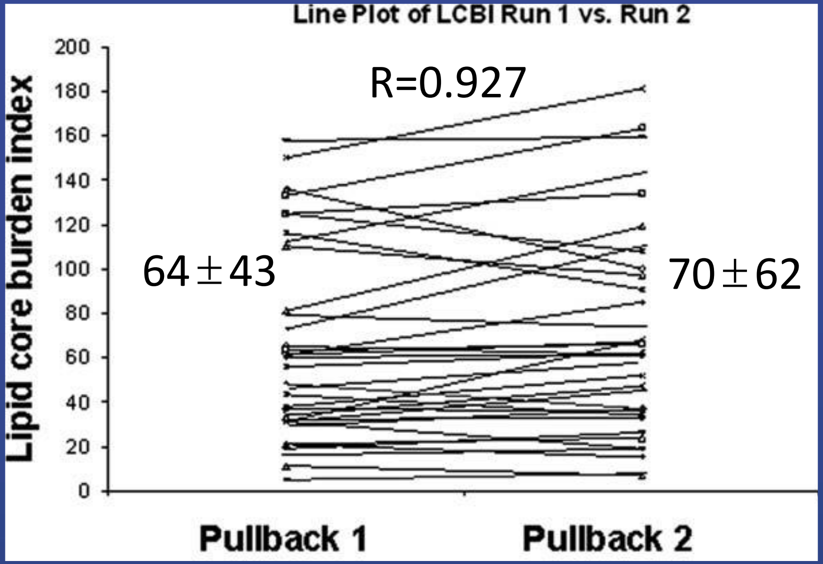
**31 patients with a common region of interest between 2 side branches*

**IVUS : graysclae plaque area *NIRS : chemogram block *VH-NC : necrotic core percentage*

Brugaletta et al. JACC: Cardiovascular Imaging, 2011

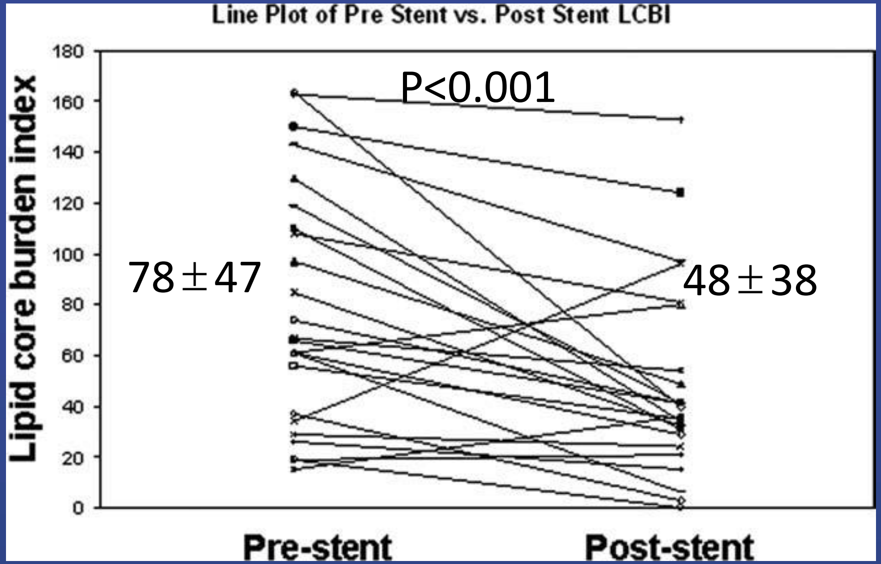
Reproducibility of NIRS

Automated pullback catheter performed in duplicate in 36 vessels in 31 patients



Excellent correlation

The changes in LCBI after stenting in 25 vessels in 22 patients

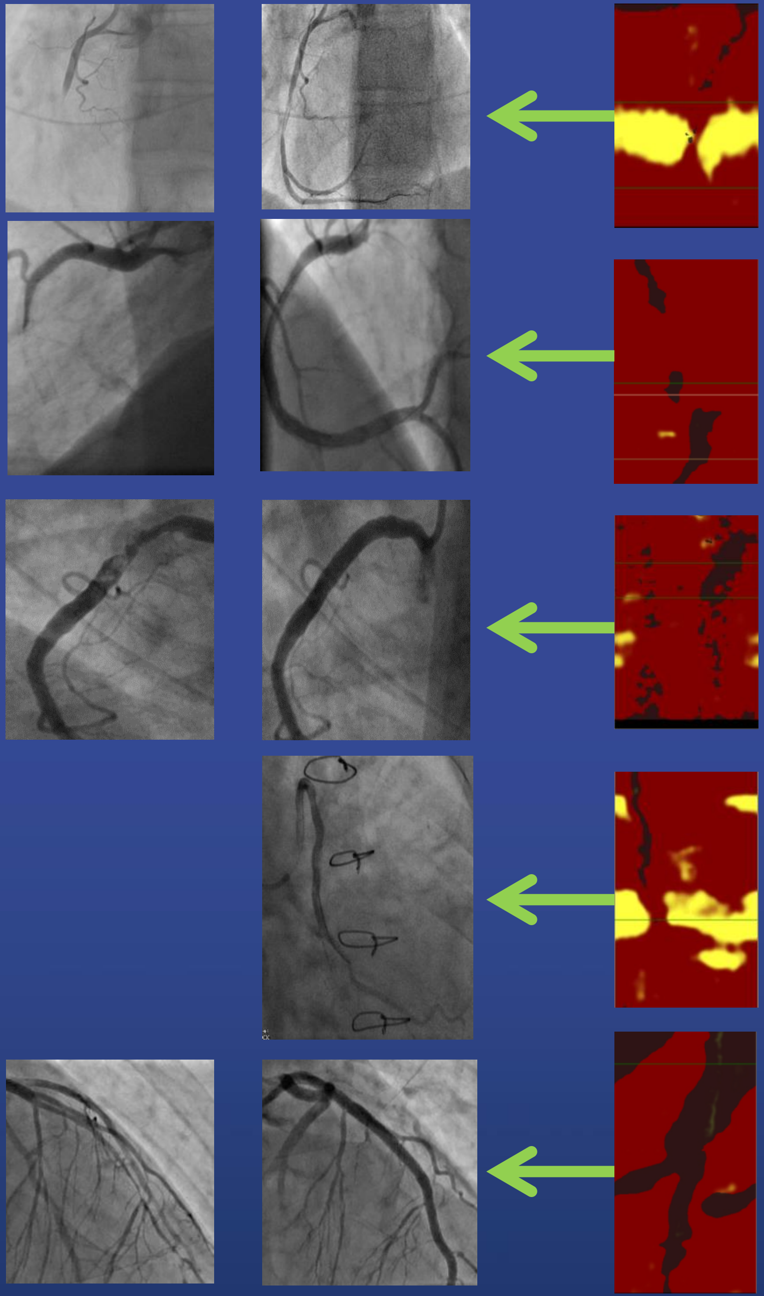


The mean LCBI decreased by 40%

BA Garcia et al. Catheterization and Cardiovascular Interventions, 2010

Five Different STEMIs

NIRS-IVUS Reveals Five Different Causes



Lipid Core Plaque

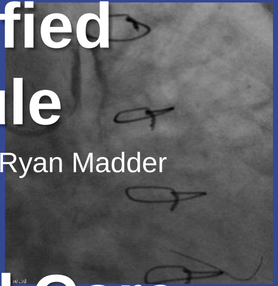
Courtesy Dr. Ryan Madder

Stent Thrombosis

Courtesy Dr. David Erlinge

Calcified Nodule

Courtesy Dr. Ryan Madder



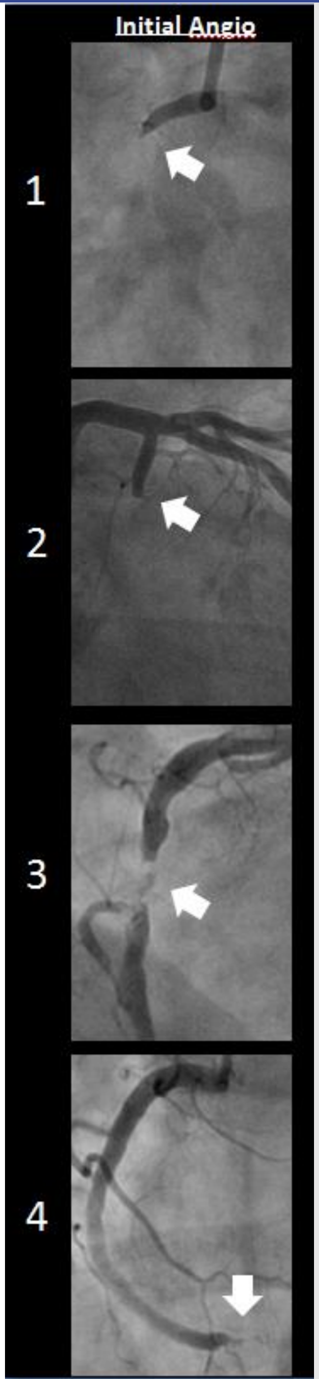
Lipid Core In SVG

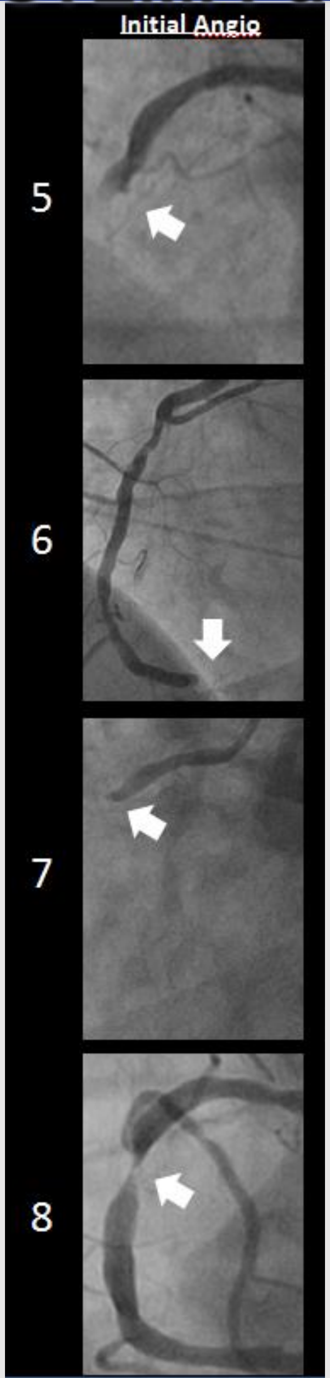
Courtesy Dr. David Erlinge

Dissection

Courtesy Dr. David Erlinge

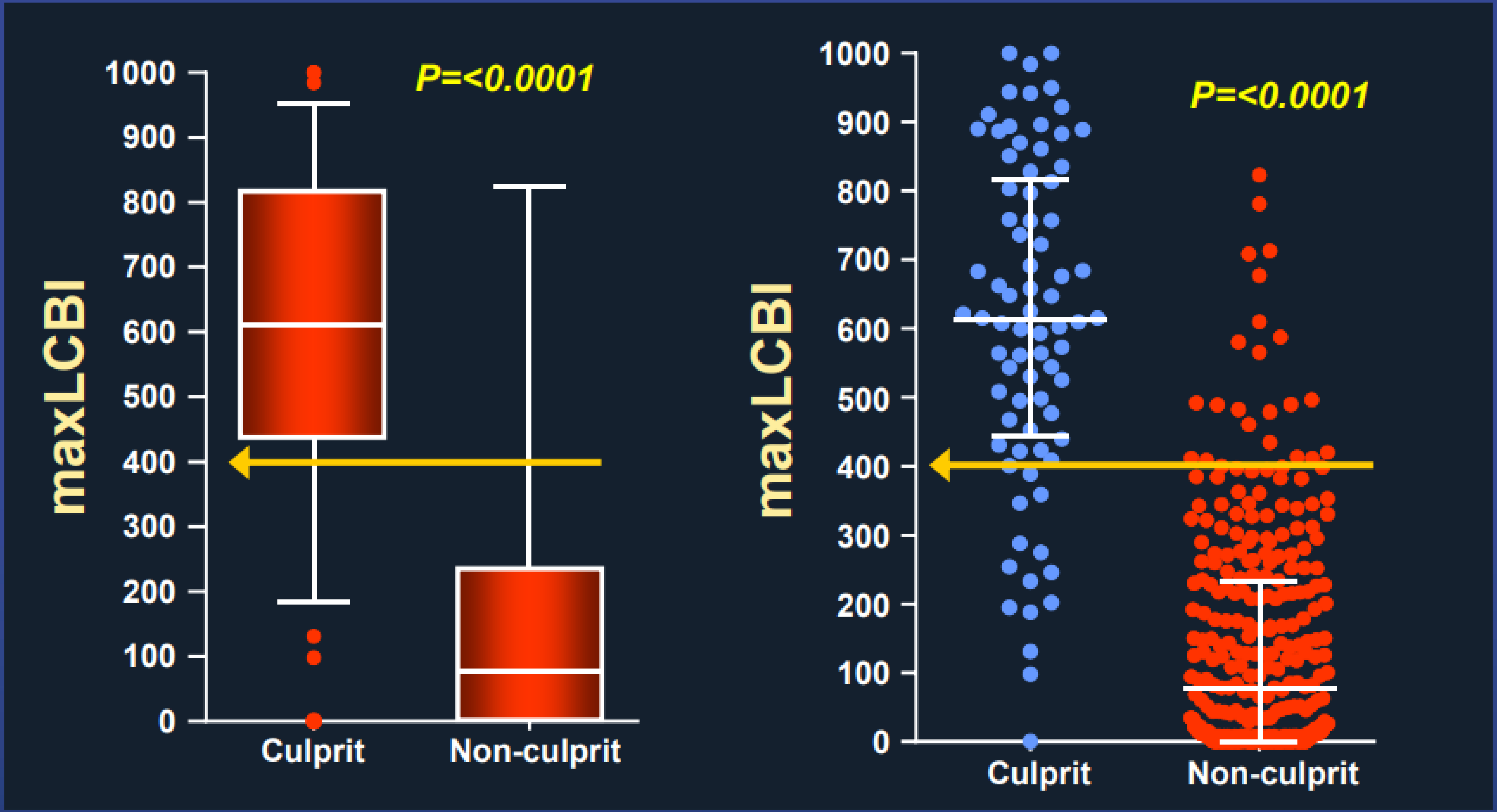
NIRS Findings in STEMI Patients





Culprit vs. non-culprit in STEMI

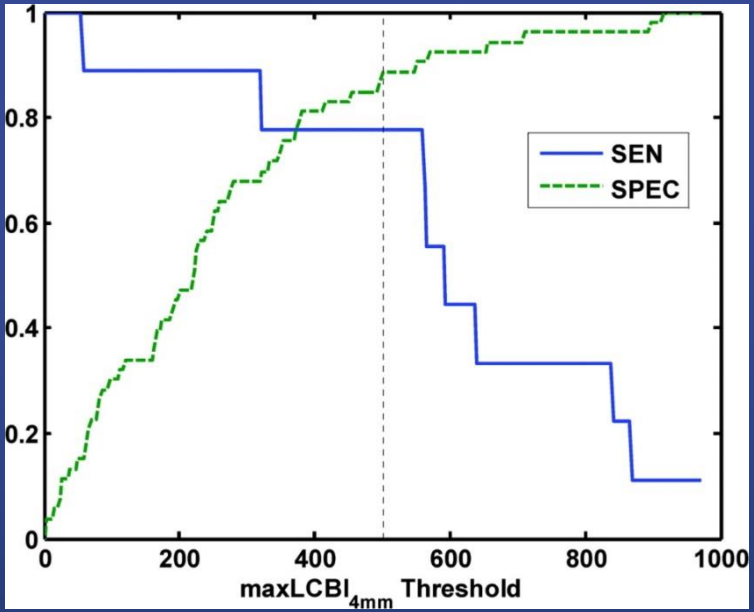
The characteristic of NIRS

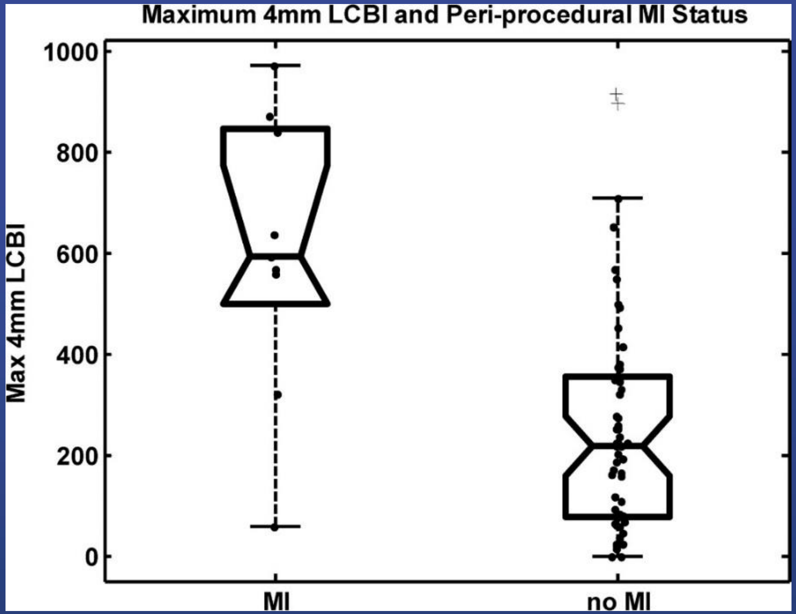


Erlinge D et al. ICI 2013

Lipidic Plaque detected by NIRS and Periprocedural MI

Parameter*	Threshold††	Relative risk of peri-procedural MI (95% CI)	p‡
$maxLCBI_{4mm}$	≥*500*	12 (3.3 to 48)	0.0002
LDL – mg/dL	>*100*	5.4 (1.4 to 23)	0.03§
Complex Plaque	*Y*	3.5 (0.91 to 14)	0.15
Degree Stenosis – %	>*75*	3.1 (0.92 to 11)	0.14**





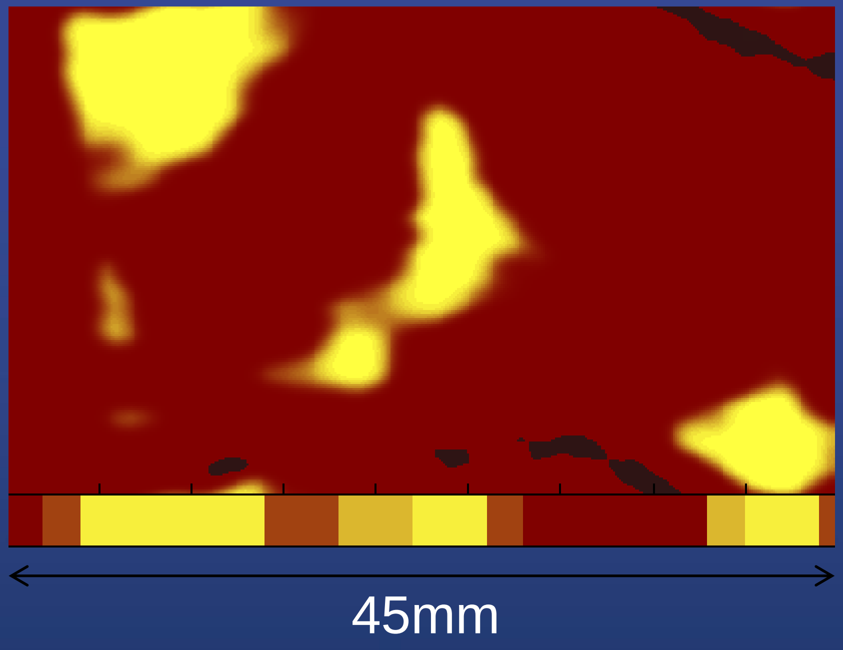
LCBI > 500 associated with 50% risk of periprocedural MI (95% CI, 28–62)

Goldstein, JA, et al. Circulation: Cardiovascular Interventions. 2011; 4: 429-437

Relationship between Lipidic Plaque detected by NIRS and Outcomes

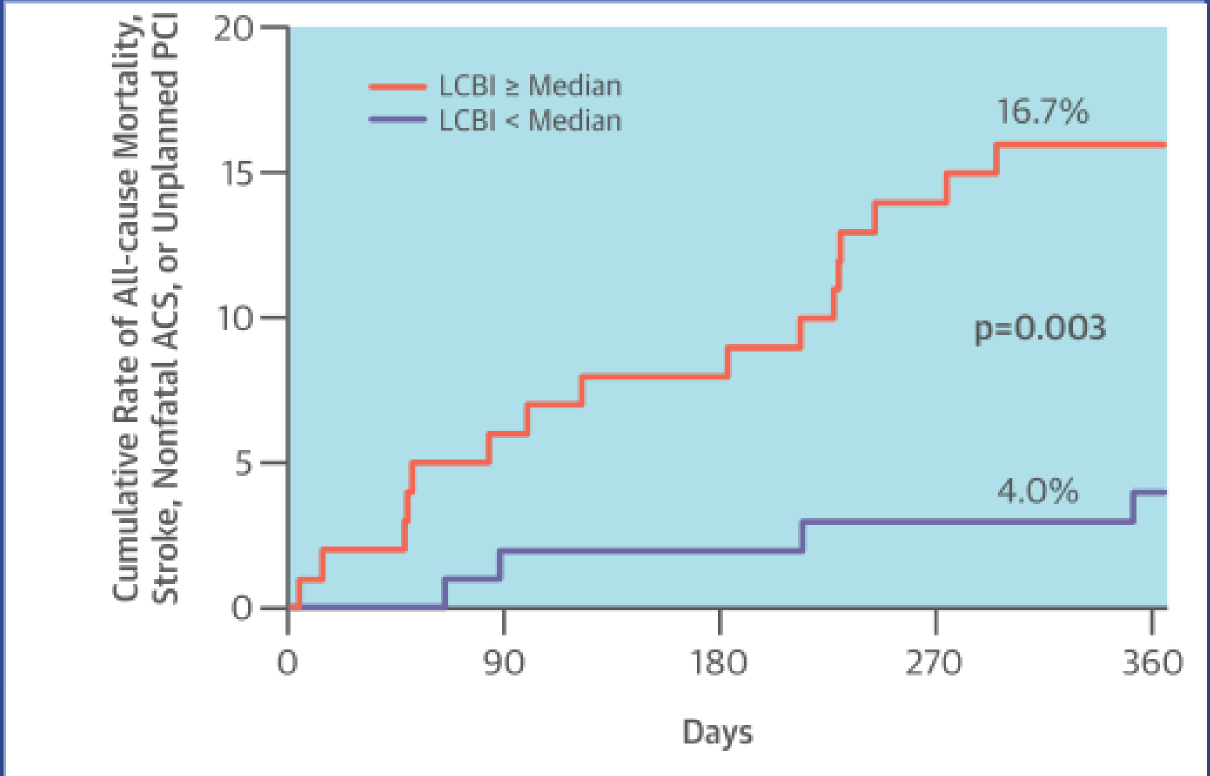
- Prospective Single Center Study, 206 patients (ACS 47%)
- Primary Endpoint: Composite of all-cause mortality, non-fatal ACS, stroke and unplanned PCI during one-year FU
- >40mm non culprit segment of NIRS

Lipid Core Burden Index (LCBI)=188

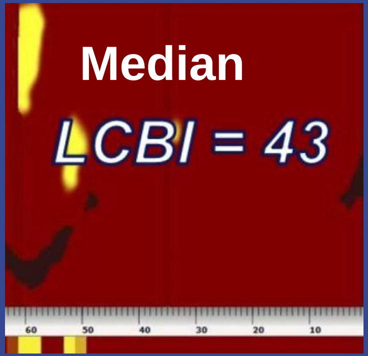


Oemrawsingh RM et al, ESC2003

Relationship between Lipidic Plaque detected by NIRS and Outcomes



No. at Risk					
LCBI < Median	101	99	99	97	91
LCBI ≥ Median	102	94	92	86	83

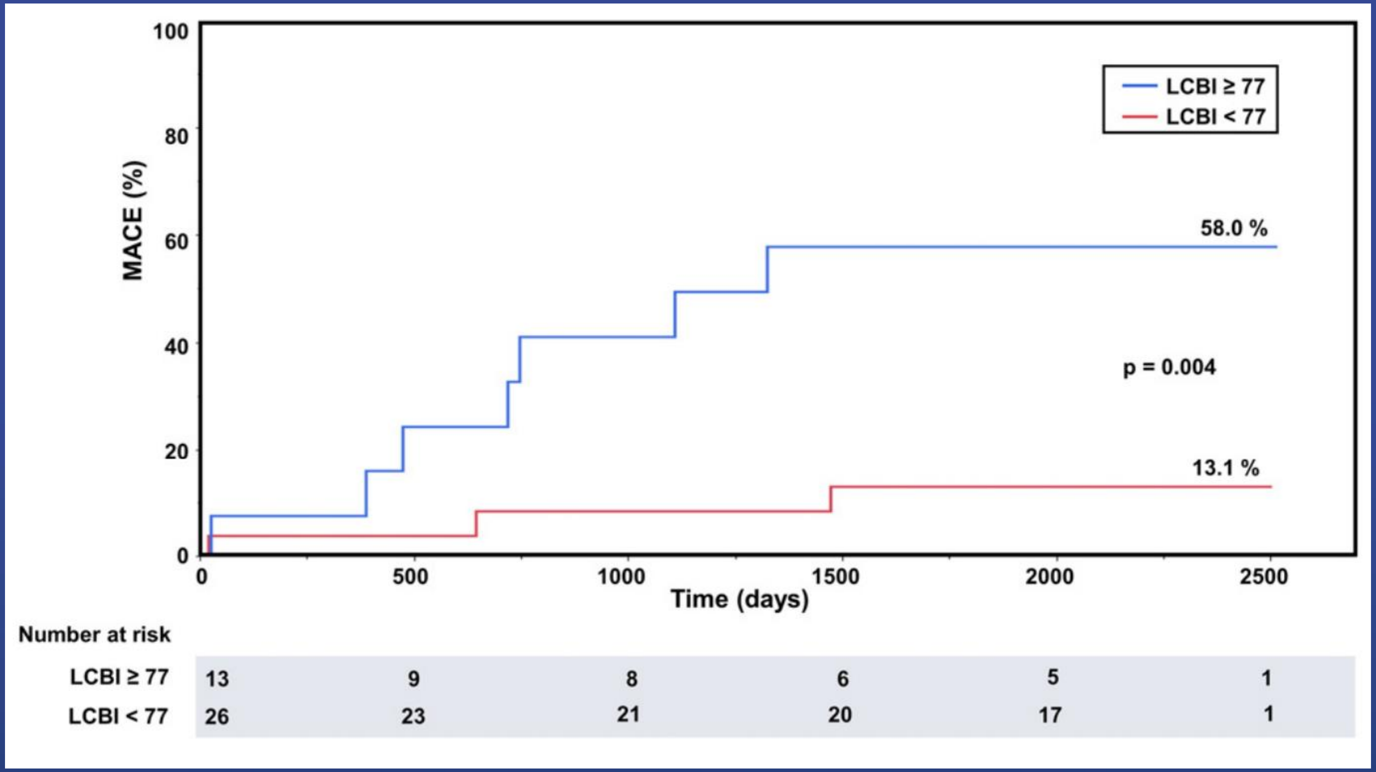


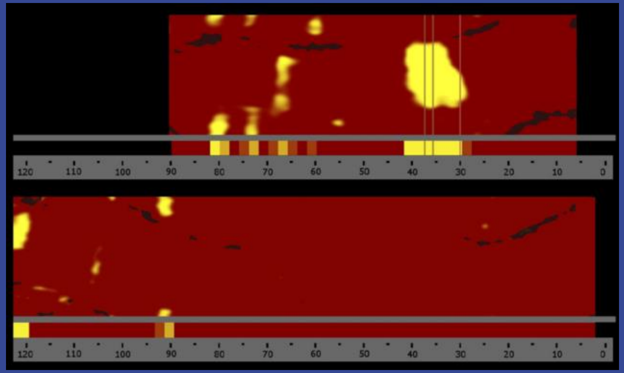
Adjusted HR 4.04 95% CI:1.3-12.3 p=0.01

Oemrawsingh RM et al, JACC 2014;64:2510-8

Relationship between Lipidic Plaque detected by NIRS and Outcomes

ORACLE-NIRS registry





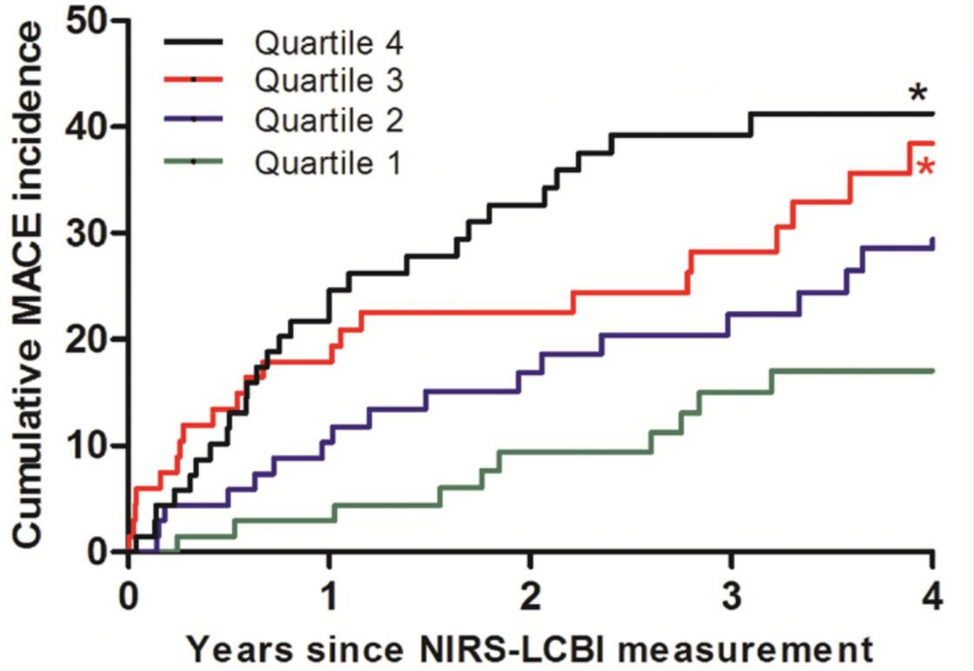
Danek BA et al. Cardiovasc Revasc Med. 2017 Apr - May;18(3):177-181

Relationship between Lipidic Plaque detected by NIRS and Outcomes

ATHEROREMO-NIRS and IBIS-3-NIRS substudy

- ATHEROREMO-NIRS
  n= 203 (Apr 2009 – Jan 2011)
- IBIS-3-NIRS
  n= 131 (Jan 2010 – Jun 2013)

- Diagnostic CAG or PCI for ACS and SAP
- Median follow-up : 4.1 yrs



No. at risk					
LCBI Q1(<83.0)	68	66	52	43	29
LCBI Q2 (≥83.0-227.0)	68	61	47	40	31
LCBI Q3 (≥227.0-360.0)	67	55	42	35	22
LCBI Q4 (≥360.0)	70	53	41	30	25

*p<0.01 as compared to first quartile (reference).

Schumann et al Eur Heart J. 2018 Jan 21;39(4):295-302.

Capabilities of Coronary Imaging Techniques

	CAG	Angioscopy*	OCT*	IVUS	NIRS
Lipid Core		◉	◉	◉	●
Expansive Remodeling				●	
Plaque Burden				●	
Calcification	◉		◉	●	
Lumen Dimension	◉		●	●	
Stent Apposition/Expansion	◉		●	●	
Thin Cap		◉	●	◉	◉
Thrombus	◉	●	●	◉	◉

● Direct, robust, and/or validated

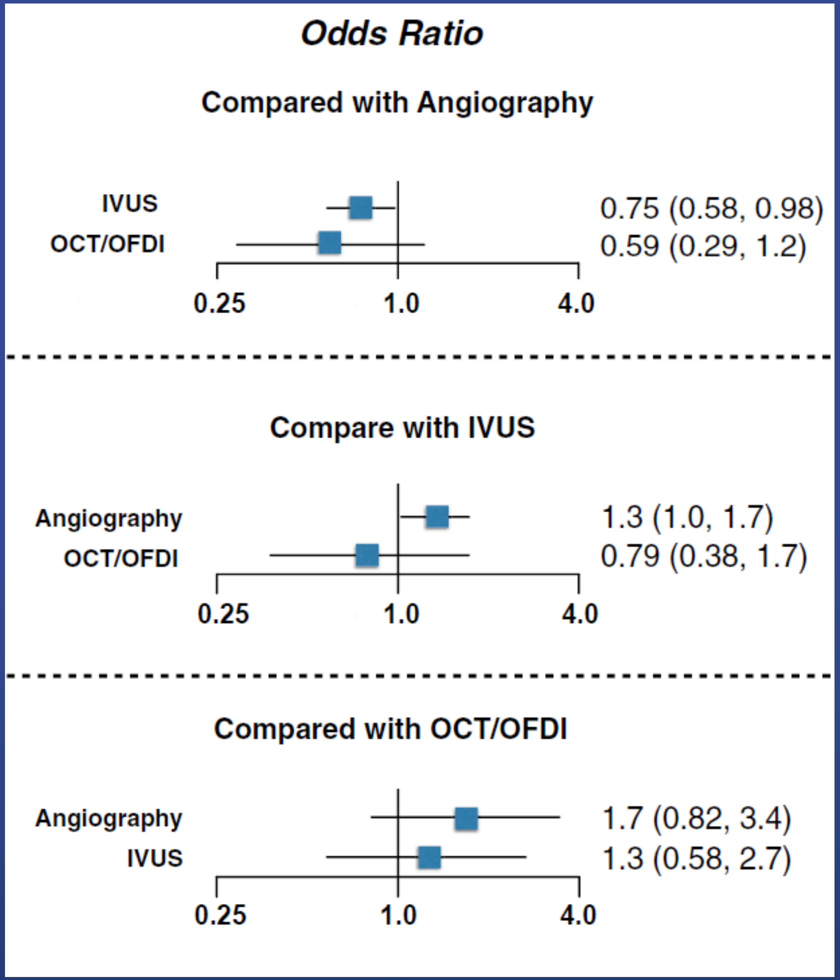
◉ Indirect, inferred from signal dropout, debated and/or unvalidated

** Require blood-free field of view*

Angio vs. IVUS vs. OCT/OFDI

Meta analysis

All cause mortality



	Angiography	IVUS	OCT/OFDI
MACE			
Angiography	-	0.79 (0.67-0.91)	0.68 (0.49-0.97)
IVUS	1.30 (1.10-1.50)	-	0.87 (0.61-1.30)
OCT/OFDI	1.50 (1.00-2.00)	1.10 (0.78-1.60)	-
Cardiovascular death			
Angiography	-	0.47 (0.32-0.66)	0.31 (0.13-0.66)
IVUS	2.10 (1.50-3.10)	-	0.66 (0.27-1.50)
OCT/OFDI	3.20 (1.50-7.60)	1.50 (0.66-3.70)	-
MI			
Angiography	-	0.74 (0.58-0.90)	0.66 (0.35-1.20)
IVUS	1.40 (1.10-1.90)	-	1.10 (0.60-2.10)
OCT/OFDI	1.30 (0.72-2.30)	0.90 (0.47-1.70)	-
TLR			
Angiography	-	0.74 (0.58-0.90)	0.66 (0.35-1.20)
IVUS	1.40 (1.10-1.70)	-	0.88 (0.47-1.60)
OCT/OFDI	1.50 (0.83-2.90)	1.10 (0.61-2.10)	-
Stent thrombosis			
Angiography	-	0.42 (0.20-0.72)	0.39 (0.10-1.20)
IVUS	2.40 (1.40-5.10)	-	0.93 (0.24-3.40)
OCT/OFDI	2.60 (0.80-10.0)	1.10 (0.29-4.20)	

Buccheri et al.JACC: cardiovascular interventions vol.10, no. 24, 2017

Optical Coherence Tomography Versus Intravascular Ultrasound and Angiography to Guide Percutaneous Coronary Interventions

The iSIGHT Randomized Trial

	Angio-Guided PCI	IVUS-Guided PCI	OCT-Guided PCI
Step 01. Selection of vessel references (landing zones)	Regions with **largest lumen diameters** proximal and distal the stenosis. Aim to cover from **"shoulder-to-shoulder"**.	Regions with **largest lumen areas** proximal and distal to the stenoses with **plaque burden <50%**.	Regions with **largest lumen areas** proximal and distal to the stenosis; should be **lipid-free** regions
Step 02. Quantify proximal and distal vessel reference diameters	Visual estimation of maximum lumen diameter at each reference.	• **EEM ≥ 180º + plaque burden <50%:** mean EEM diameter; • **EEM <180º and/or plaque burden >50%:** maximum lumen diameter.	• **EEM ≥ 180º:** mean EEM diameter; • **EEM <180º:** maximum lumen diameter

Step 03. Selection of stent diameter

Discrepancy > 0.5 mm between proximal and distal reference diameters?

- Yes → Use diameter of **smaller** reference
- No → Use diameter of **larger** reference

Step 04. Selection of stent length

Distance between distal and proximal references

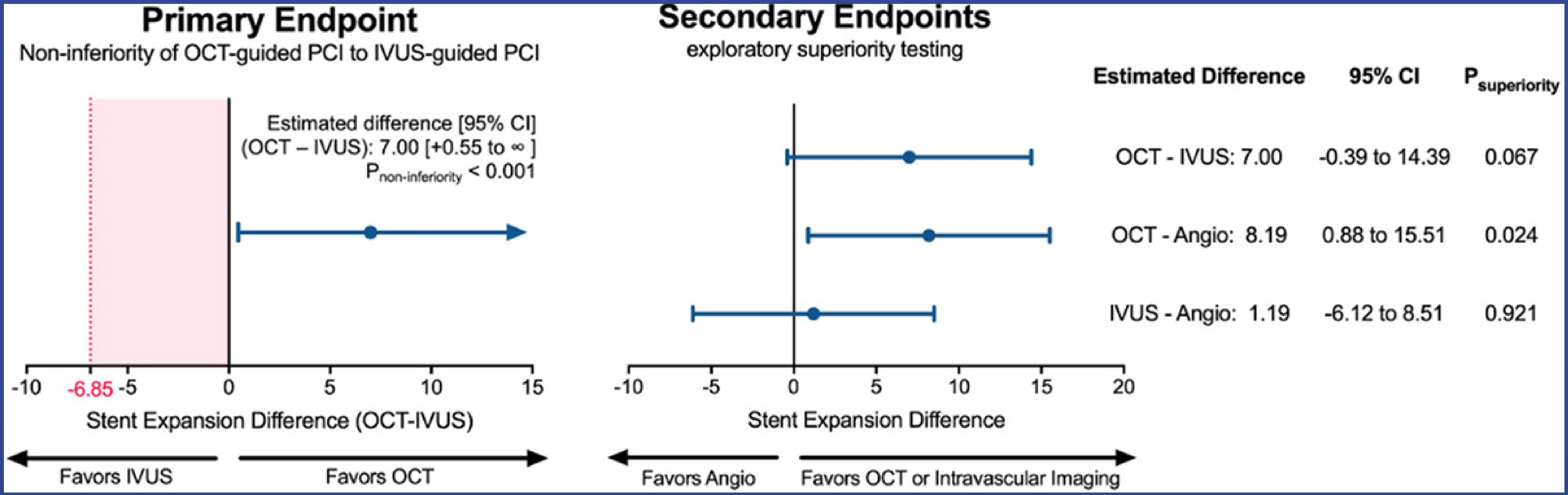
Step 05. Post-dilation

- Discrepancy **> 0.5 mm** between proximal and distal reference diameters: use NC balloons sized to each reference diameter;
- Discrepancy **< 0.5 mm** between proximal and distal reference diameters: use NC balloon sized to the largest reference diameter.

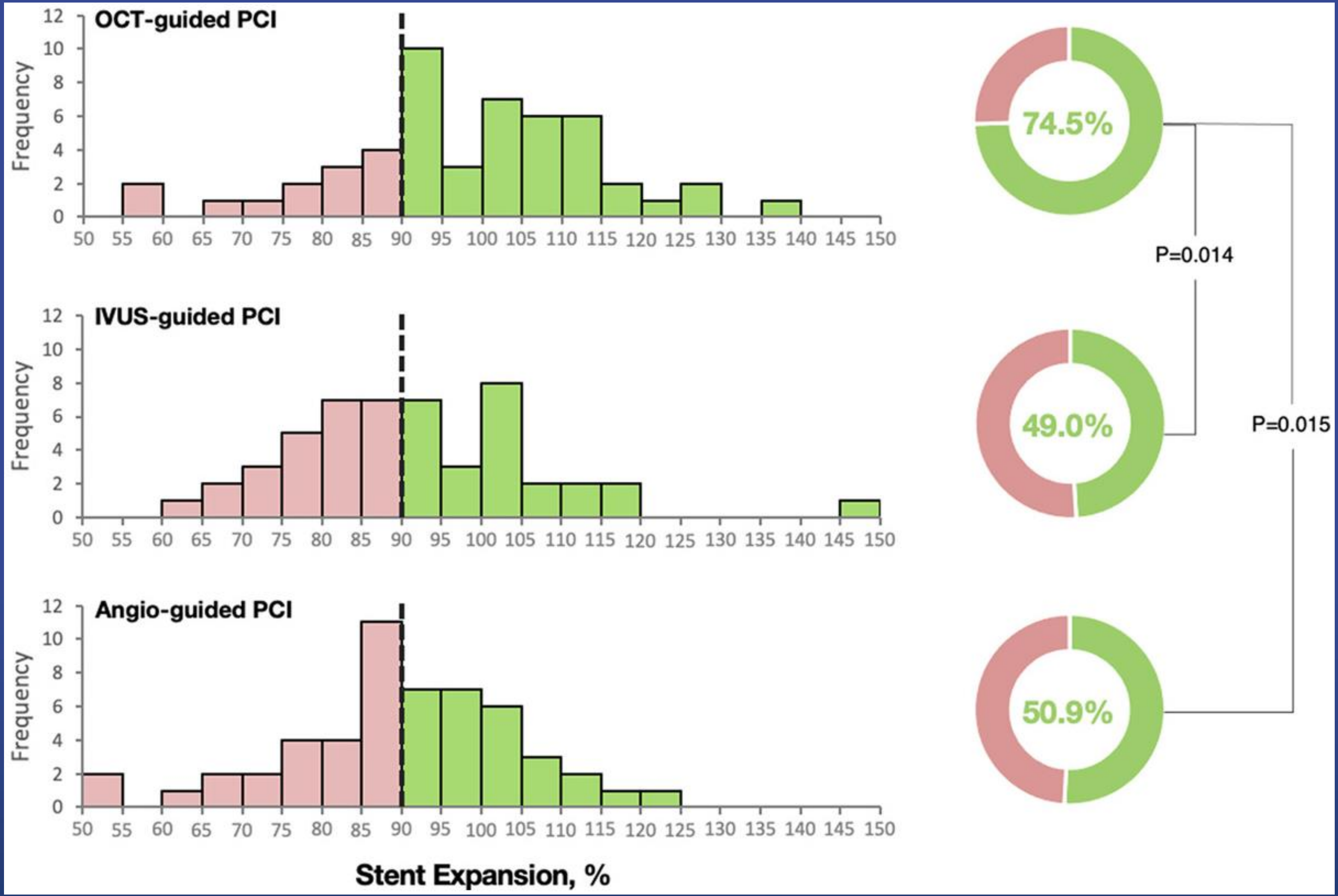
Step 06. Expansion criteria

Residual stenosis **<10%**	Minimum stent area **≥ 90%** average reference lumen area

Circulation: Cardiovascular Interventions, 2021;14:e009452



Circulation: Cardiovascular Interventions, 2021;14:e009452



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