

Lessons from EXCEL IVUS Substudy

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Disclosure Statement of Financial Interest

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

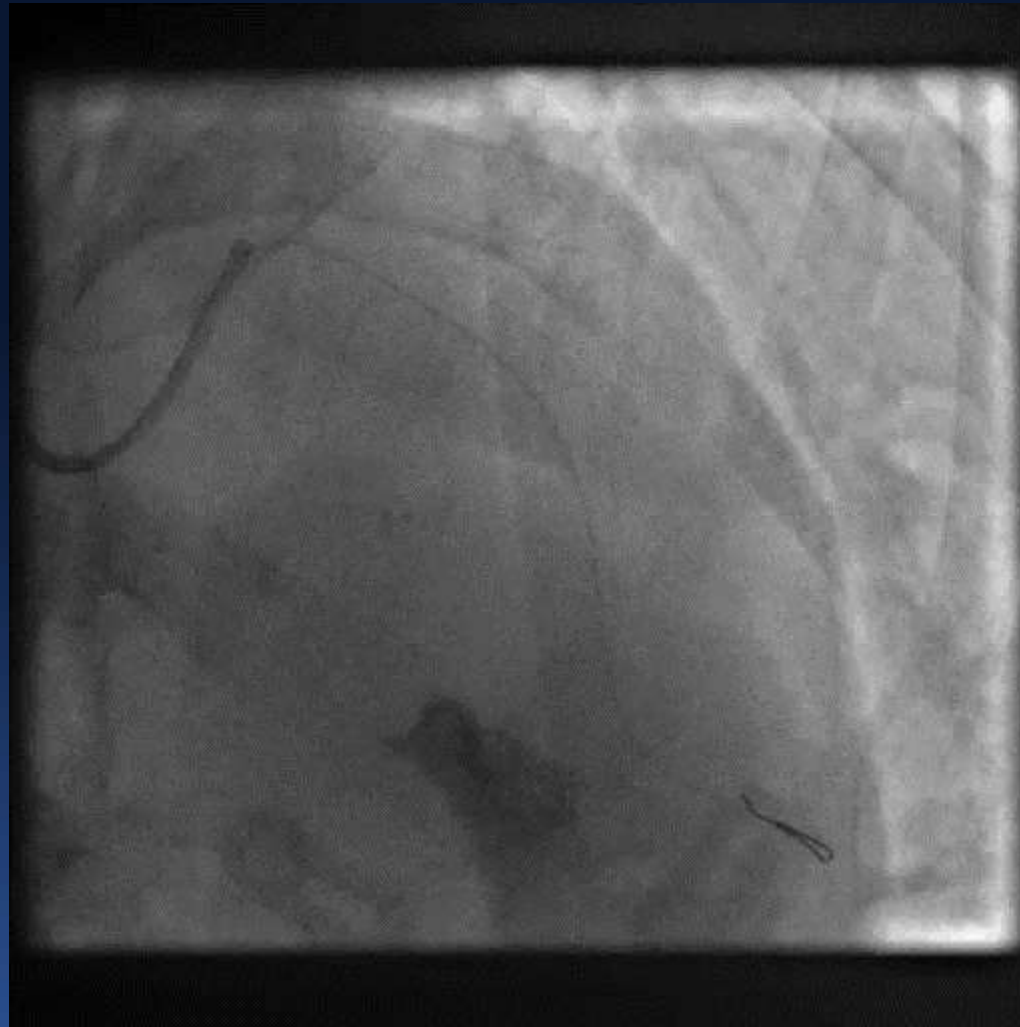
Affiliation/Financial Relationship

- Grant/Research Support
- Consulting Fees/Honoraria

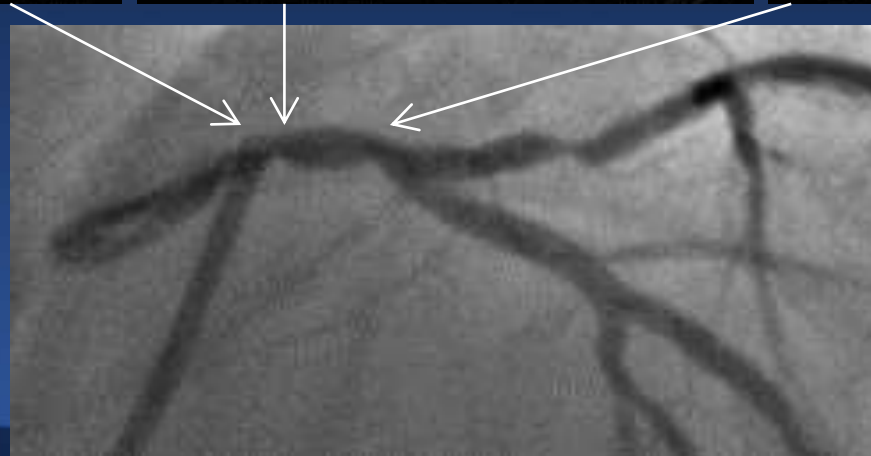
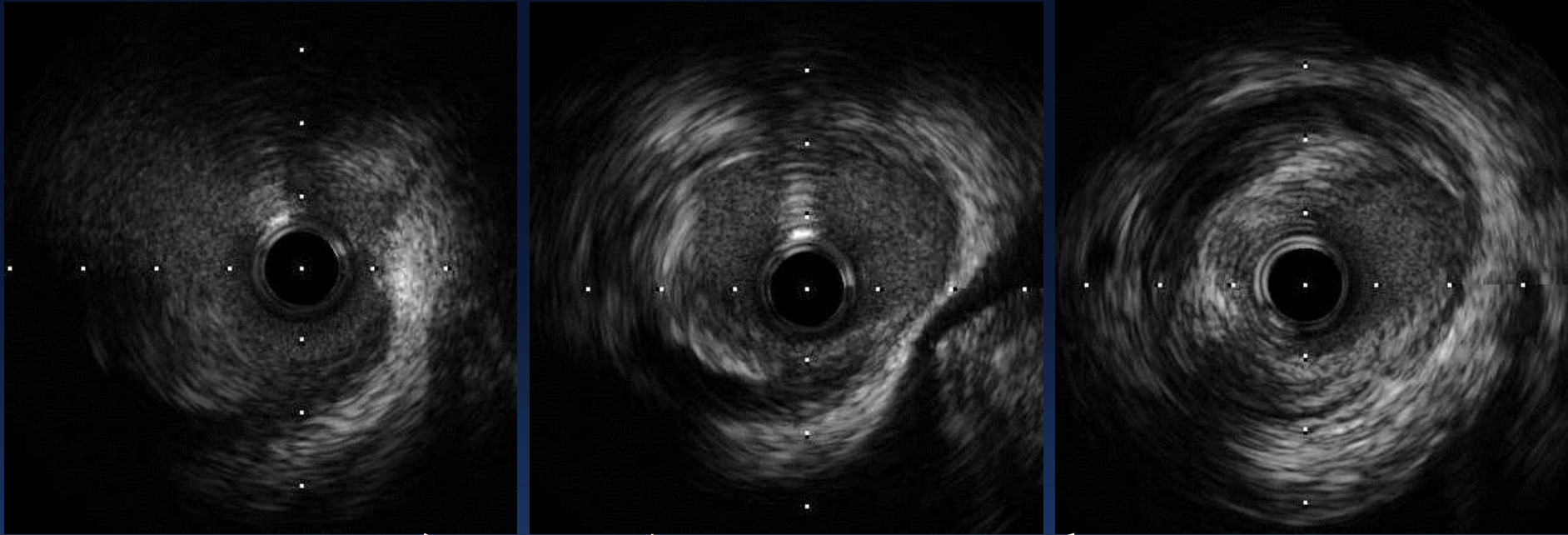
Company

- Boston Scientific, St Jude Medical
- Boston Scientific, OCT Medical Imaging Inc.

Diagnosis of LMCA Disease



Diagnosis of LMCA Disease



Diagnosis of LMCA Disease

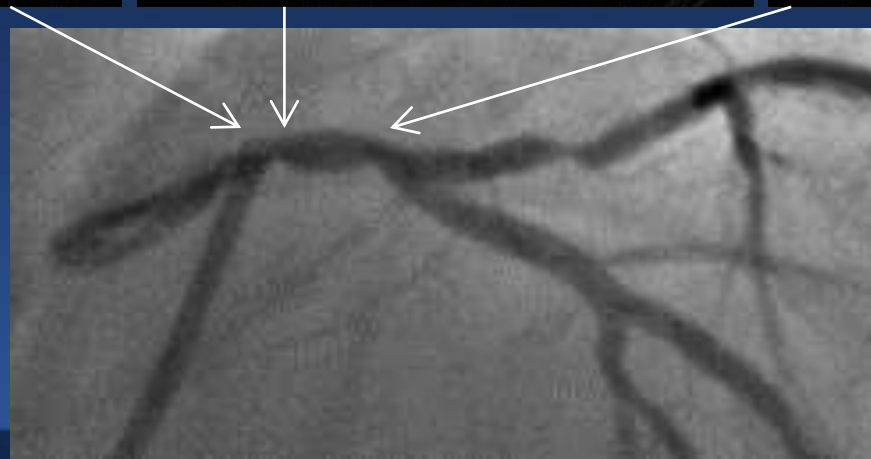
Guiding Catheter

Lumen

Plaque at Ostium

Lumen Area: 7.2mm^2

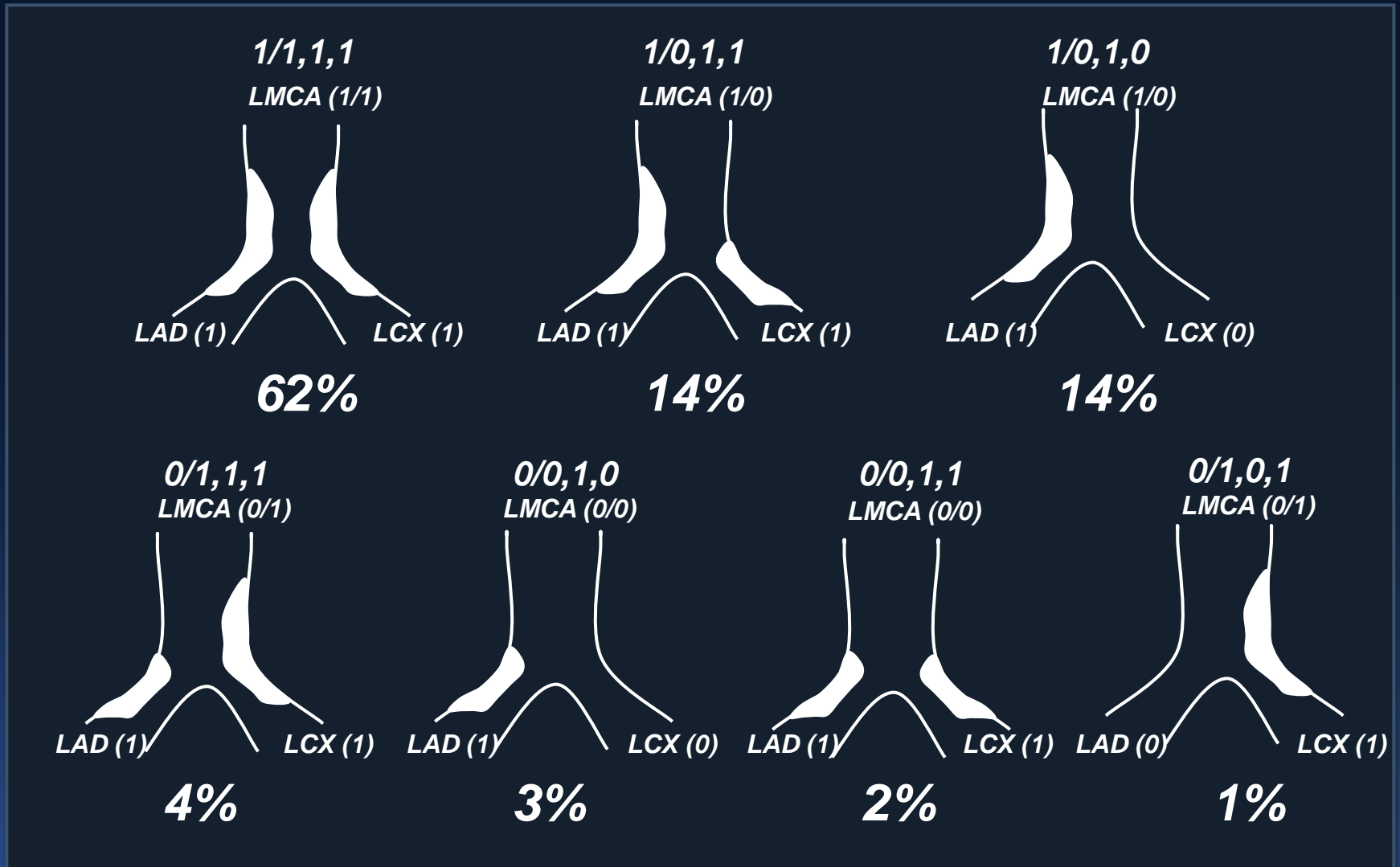
Lumen Area: 4.3mm^2



Plaque Formation in Left Main

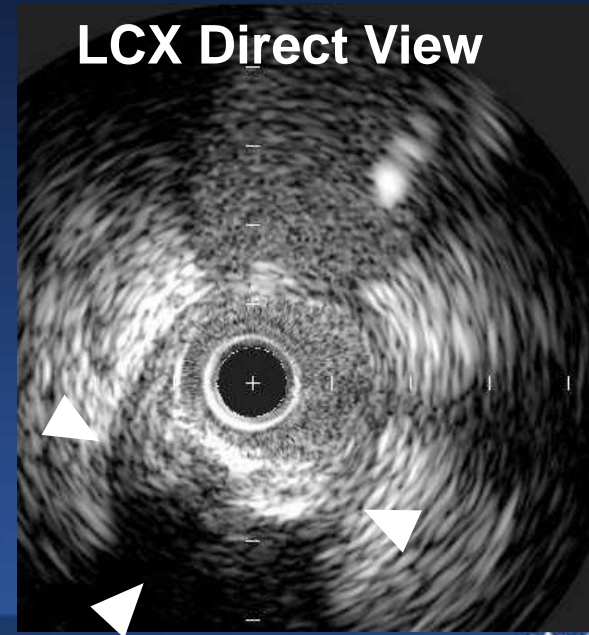
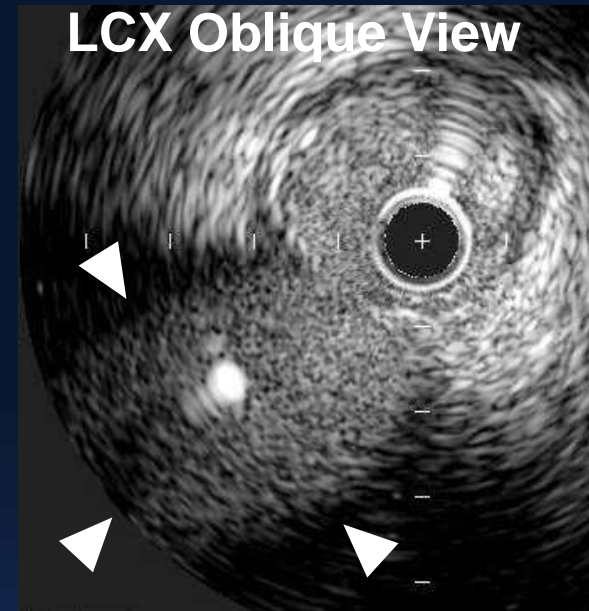


Plaque Distribution by IVUS (n=140)



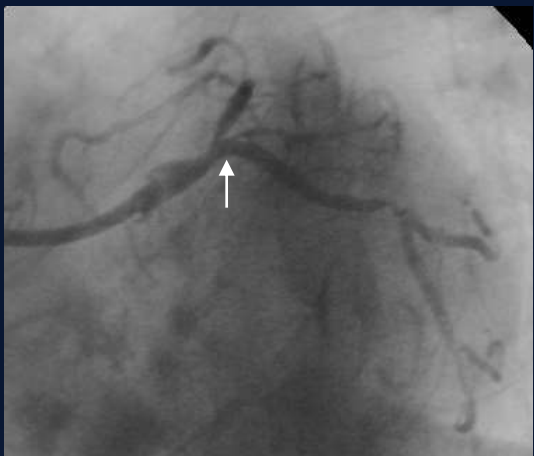
In 90% plaque extends from LMCA-LAD

- Though you don't see anything, this is not true.
- If you see something, this may be true.

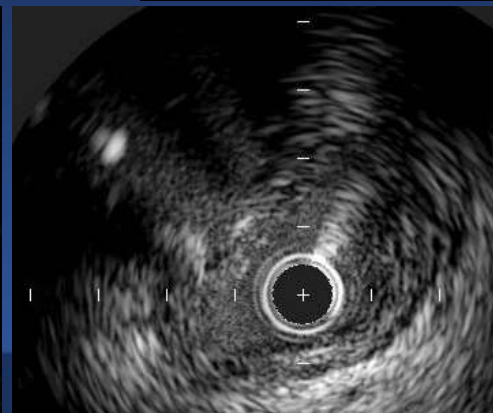
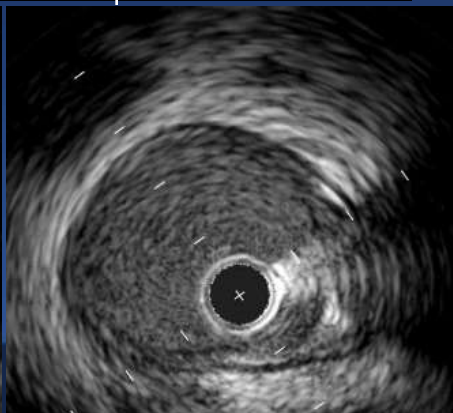
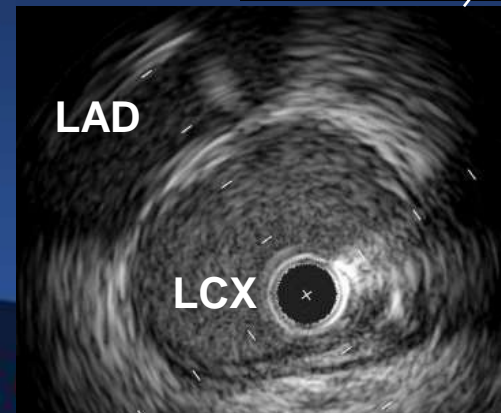
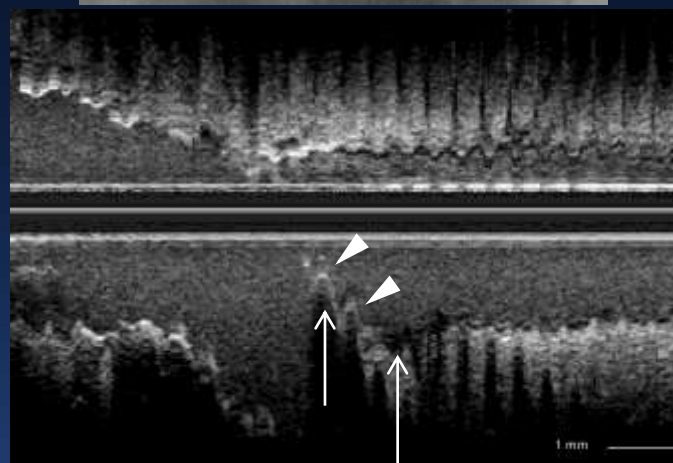
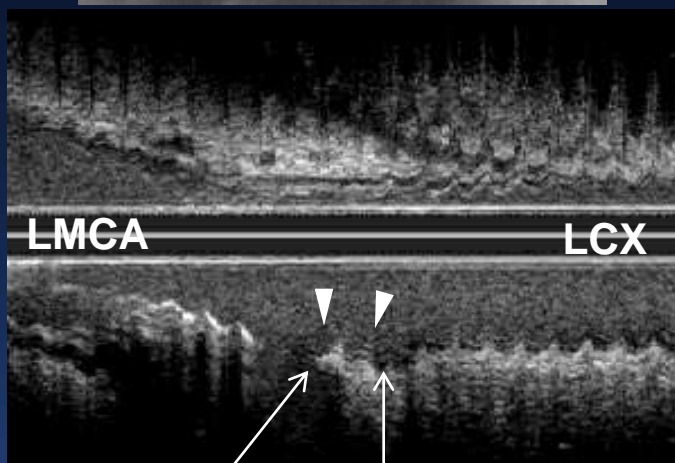
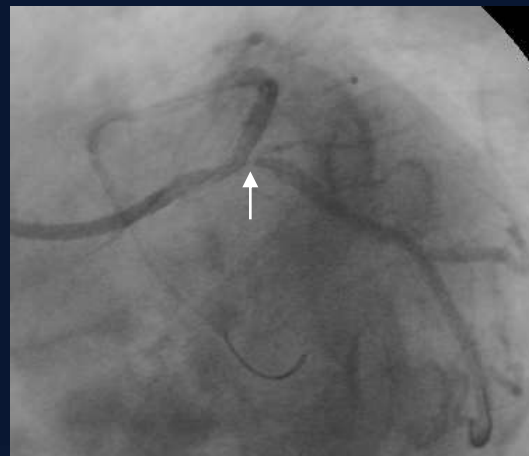


Carina Shift

Pre -PCI



Final



Outcome of LCX after Cross-Over Stenting

43 Patients with distal LMCA lesions without LCX disease ($DS < 50\%$)

LAD-LMCA Cross-Over Stenting

LCX $DS > 50\%$
N=18 (42%)

LCX $DS \leq 50\%$
N=25

FFR < 0.8
N=3 (7%)

FFR ≥ 0.8
N=40

KBT
N=2

KBT
N=4

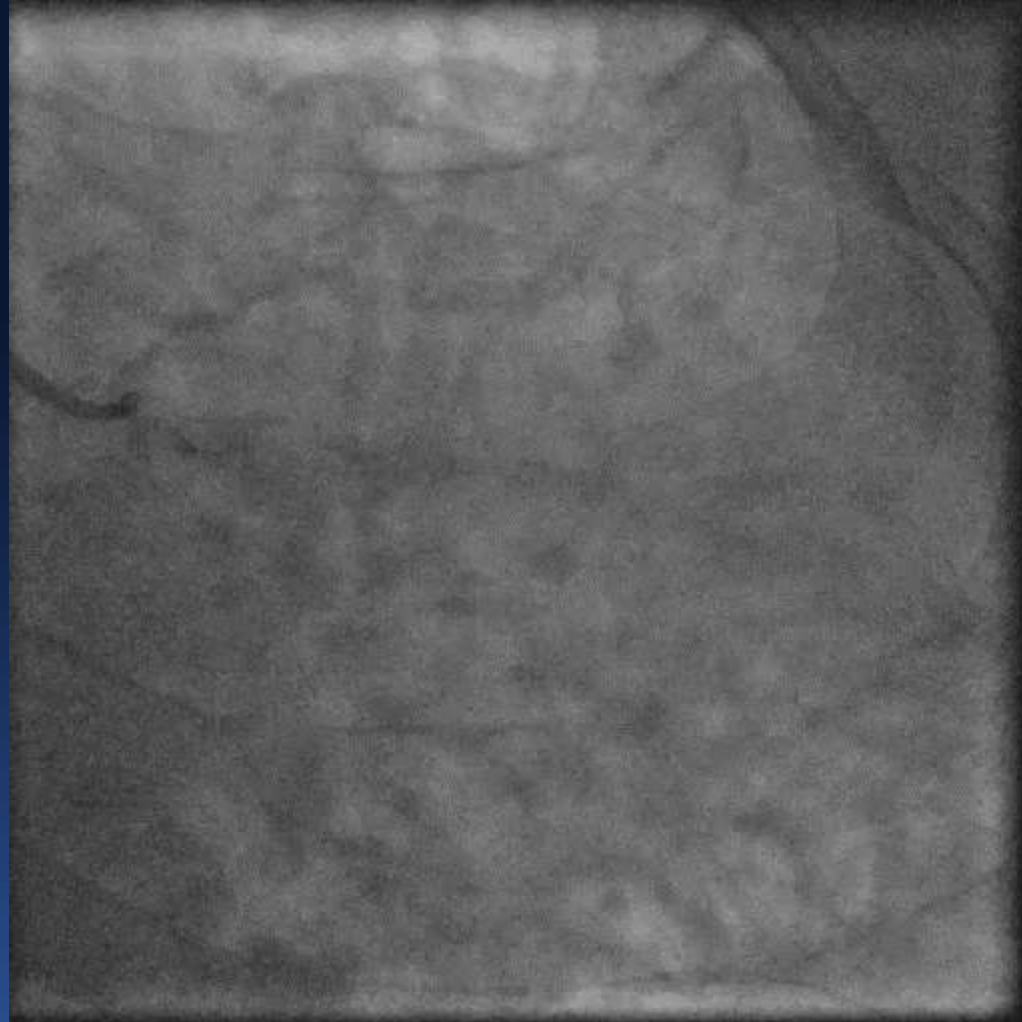
No KBT
N=37

1 Unknown death
in 83 yo patient

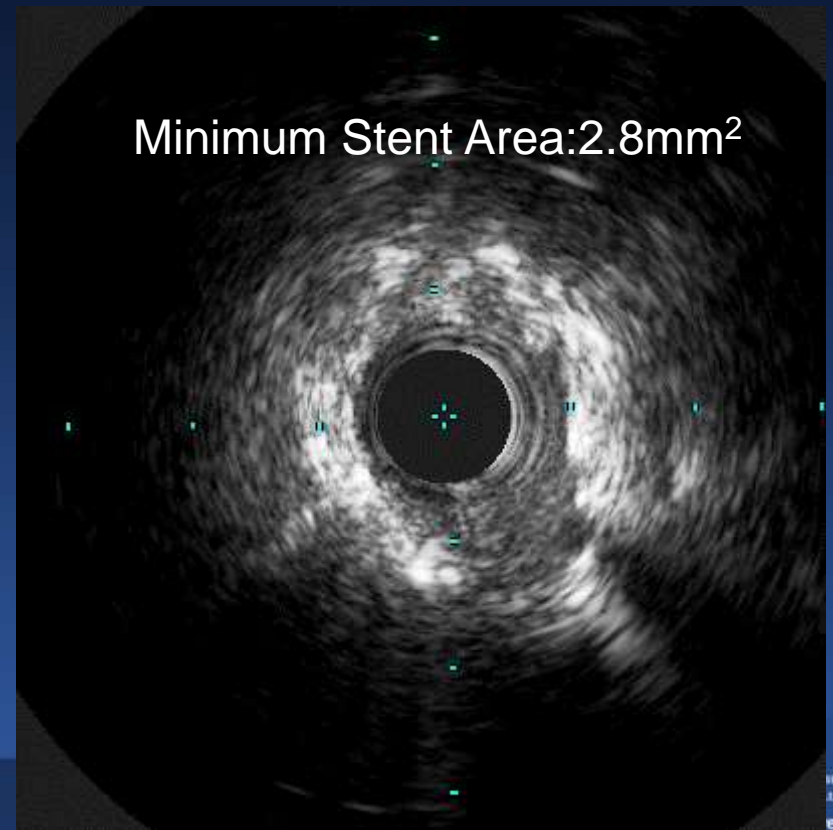
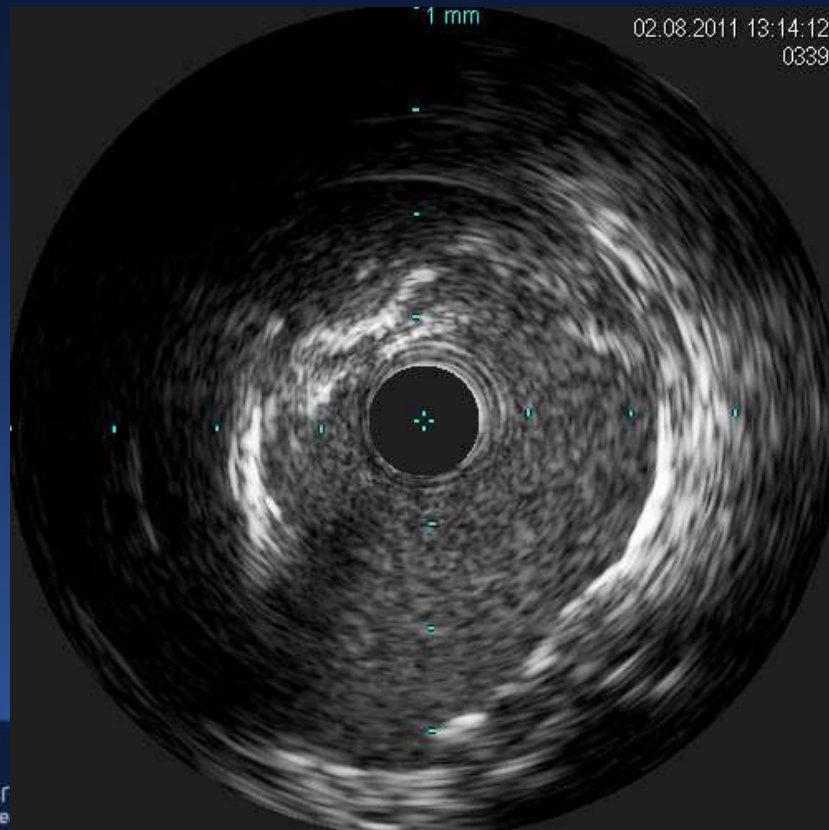
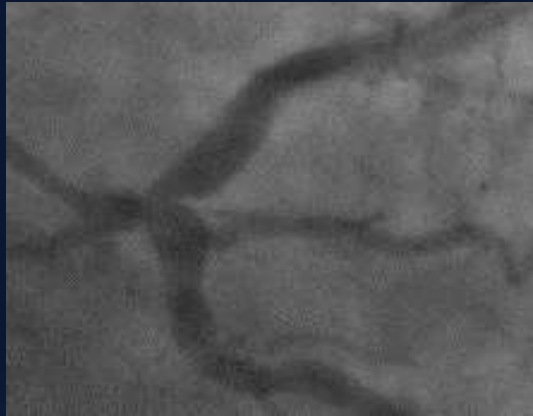
1 Unknown death
in 85 yo patient

- Overall MACE = 4.7% (2/43)
- No Ischemic TLR, MI

Optimization of LMCA Stenting



Optimization of LMCA Stenting



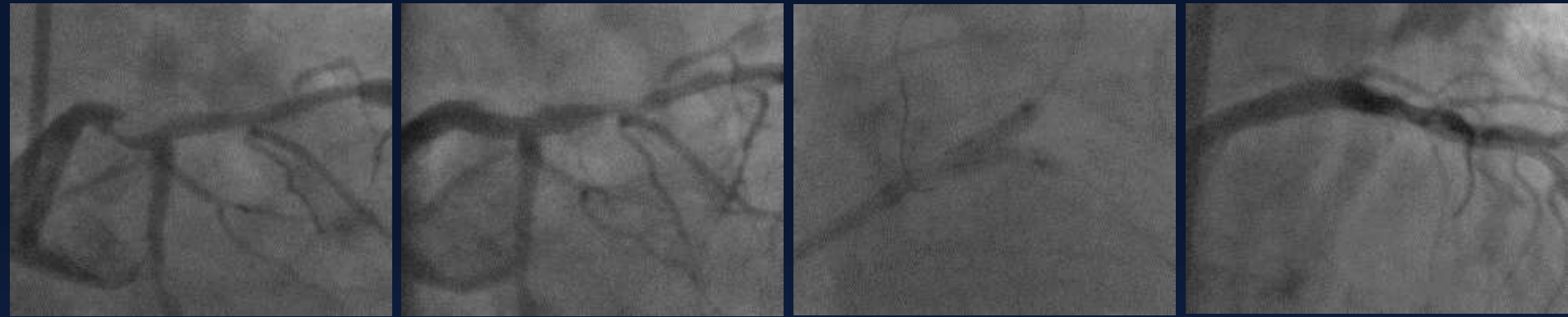
Complication of LMCA Stenting

Pre

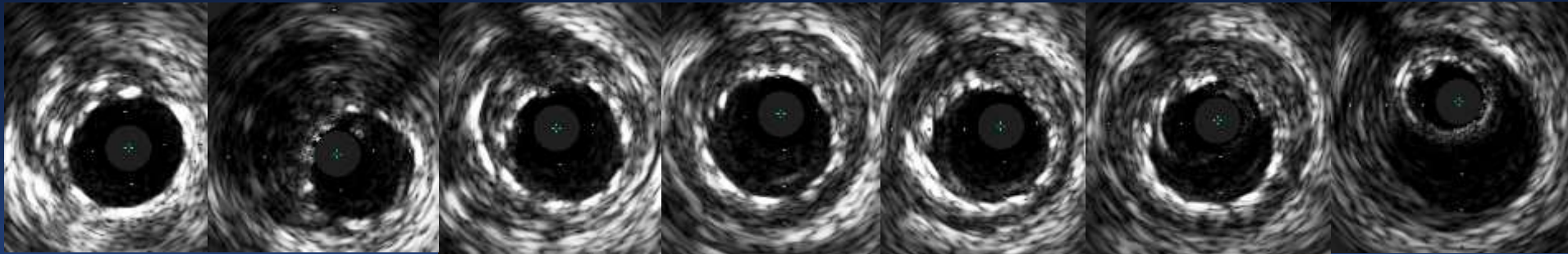
Post-Stent LAD-LMCA

KBT

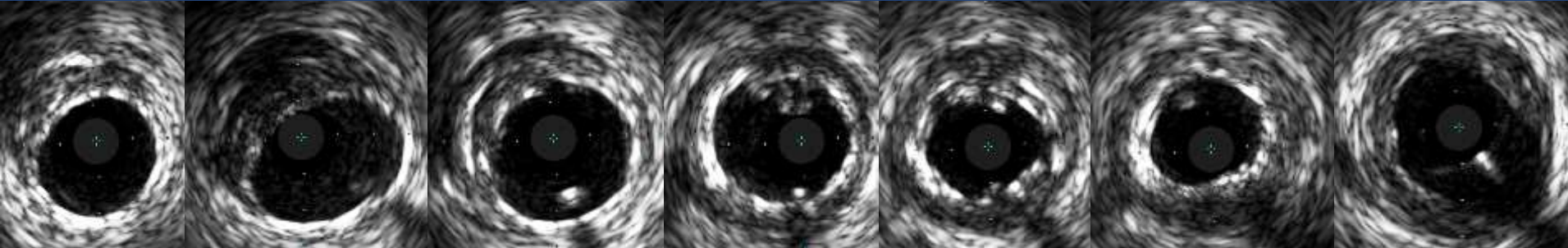
Final



Post-Stent LAD-LMCA



Final



Complication of LMCA Stenting

Pre

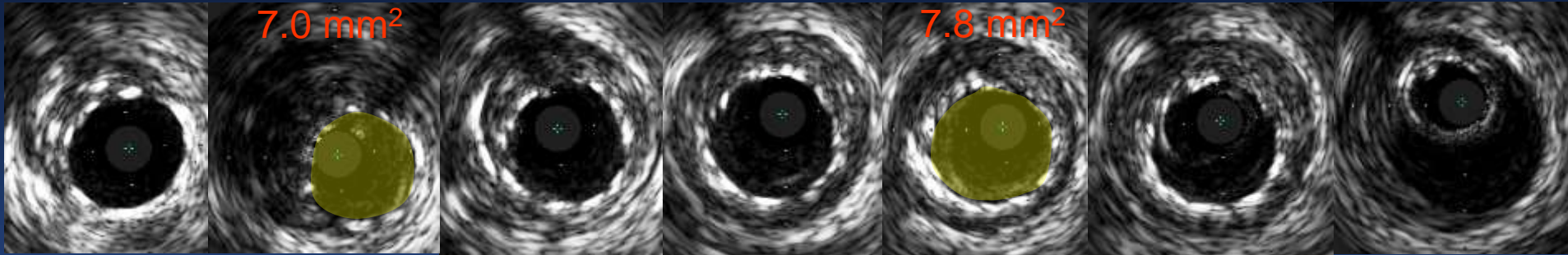
Post-Stent LAD-LMCA

KBT

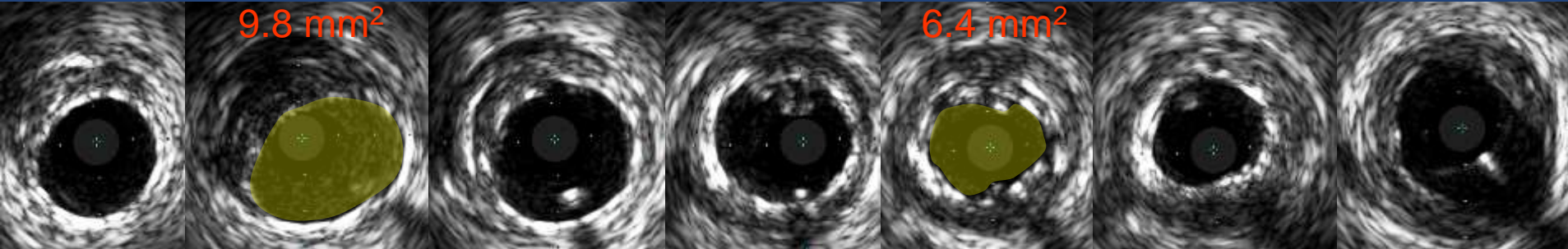
Final



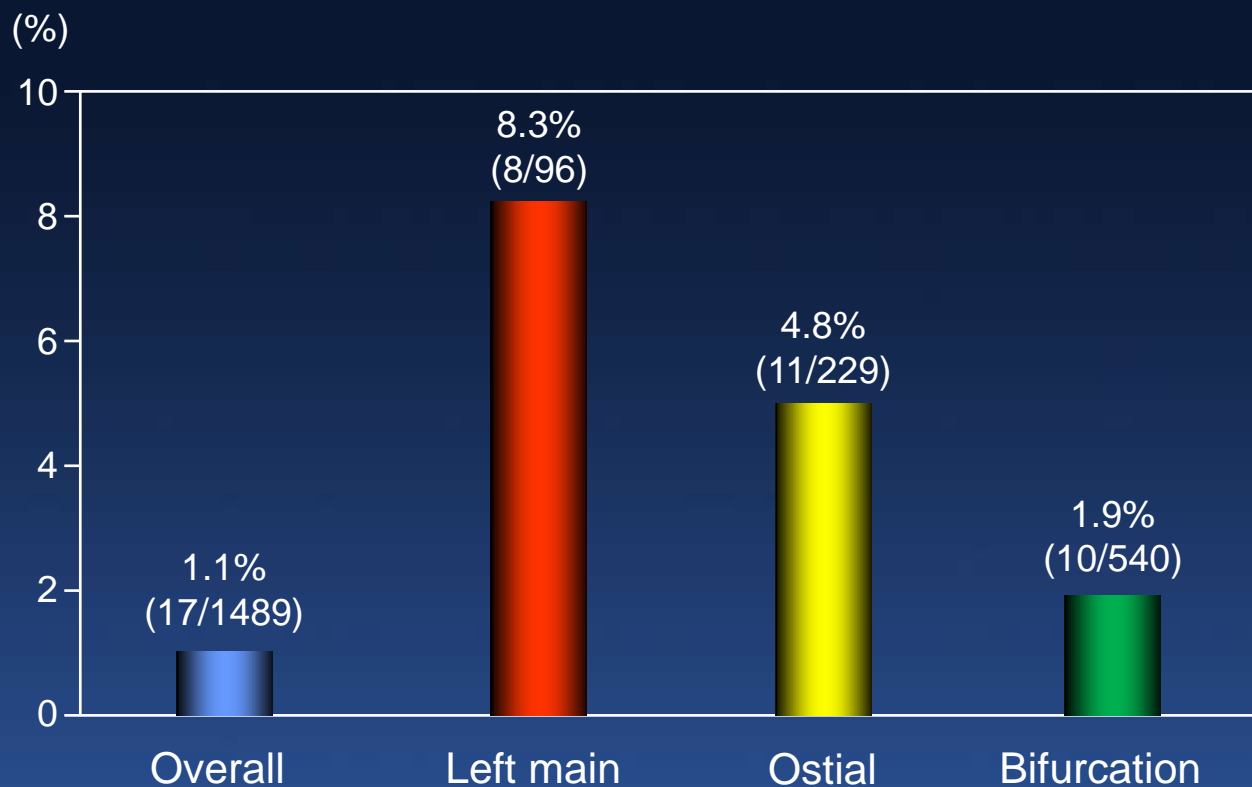
Post-Stent LAD-LMCA



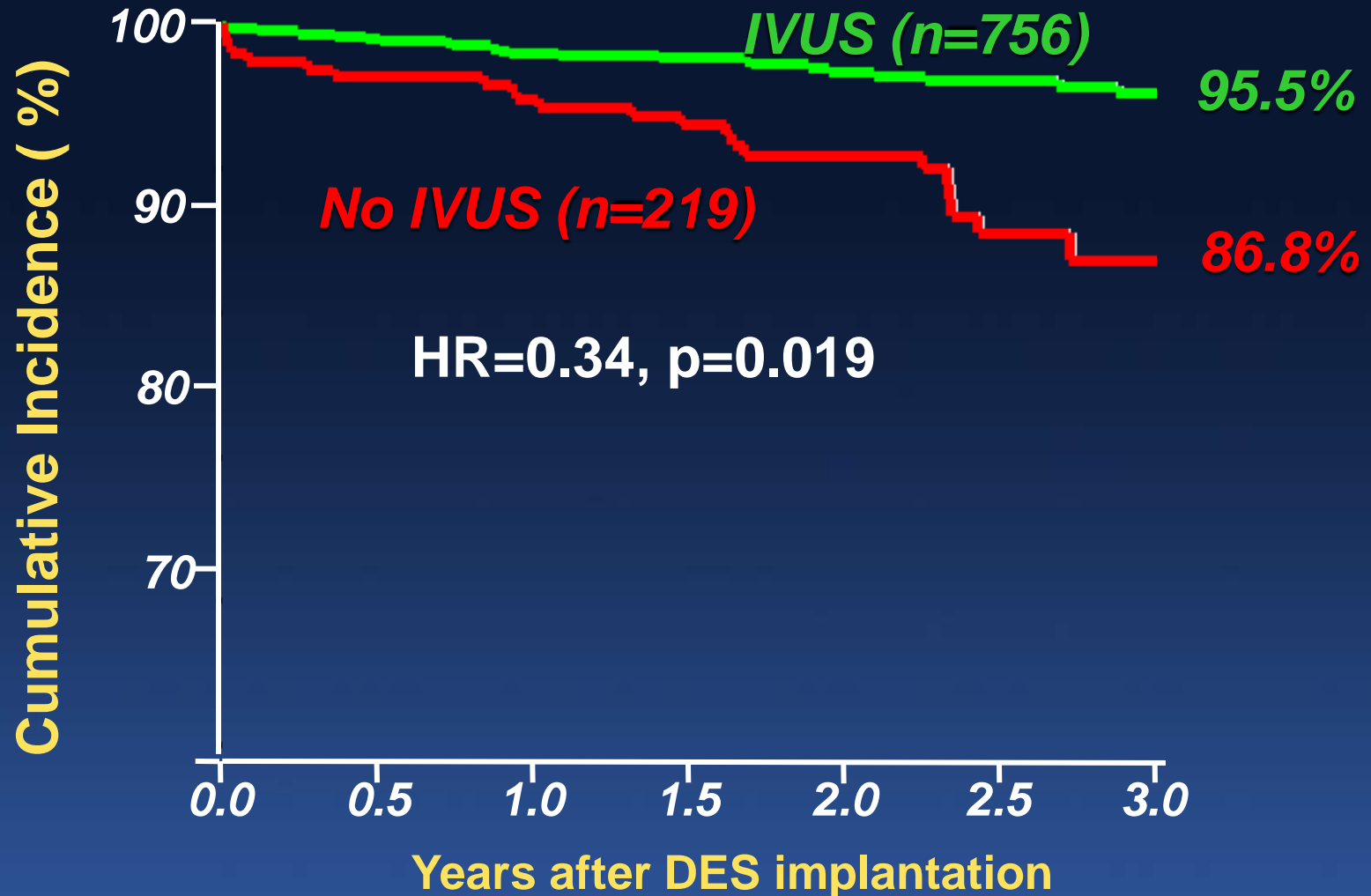
Final



Prevalence of Stent Deformation

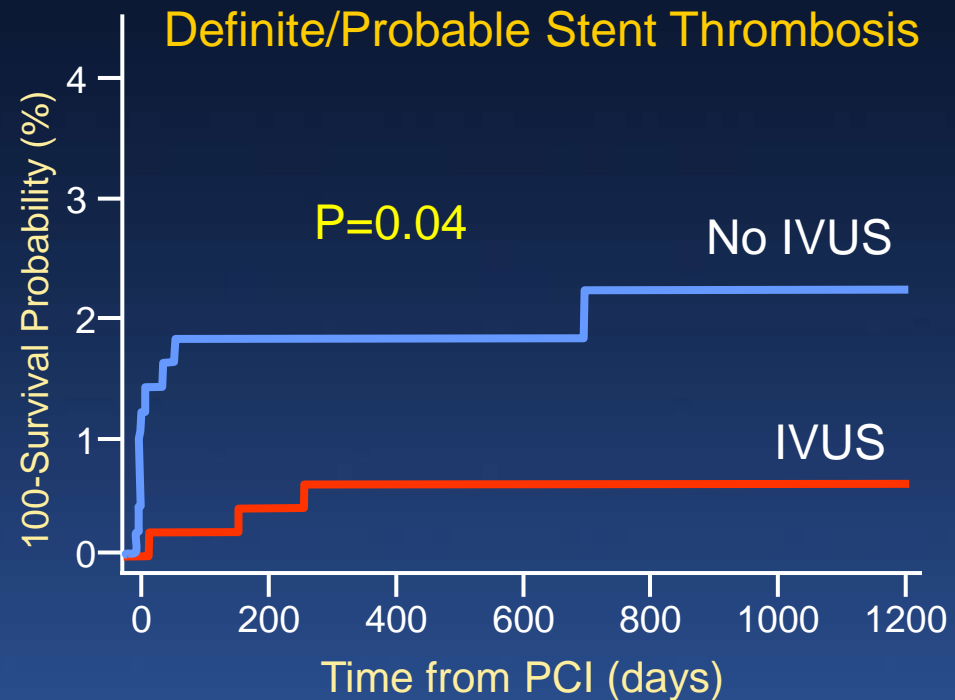
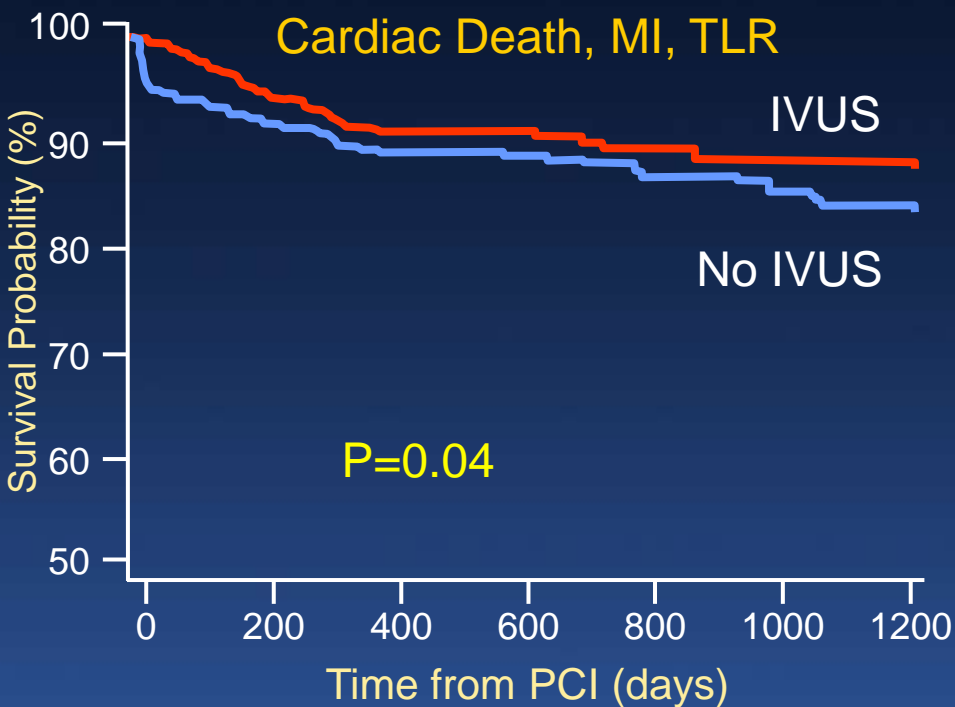


All-cause Mortality after LMCA DES Implantation: Impact of IVUS Guidance



Impact of IVUS Guidance of Unprotected LM Propensity Matched 1010 pts from 4 Registries

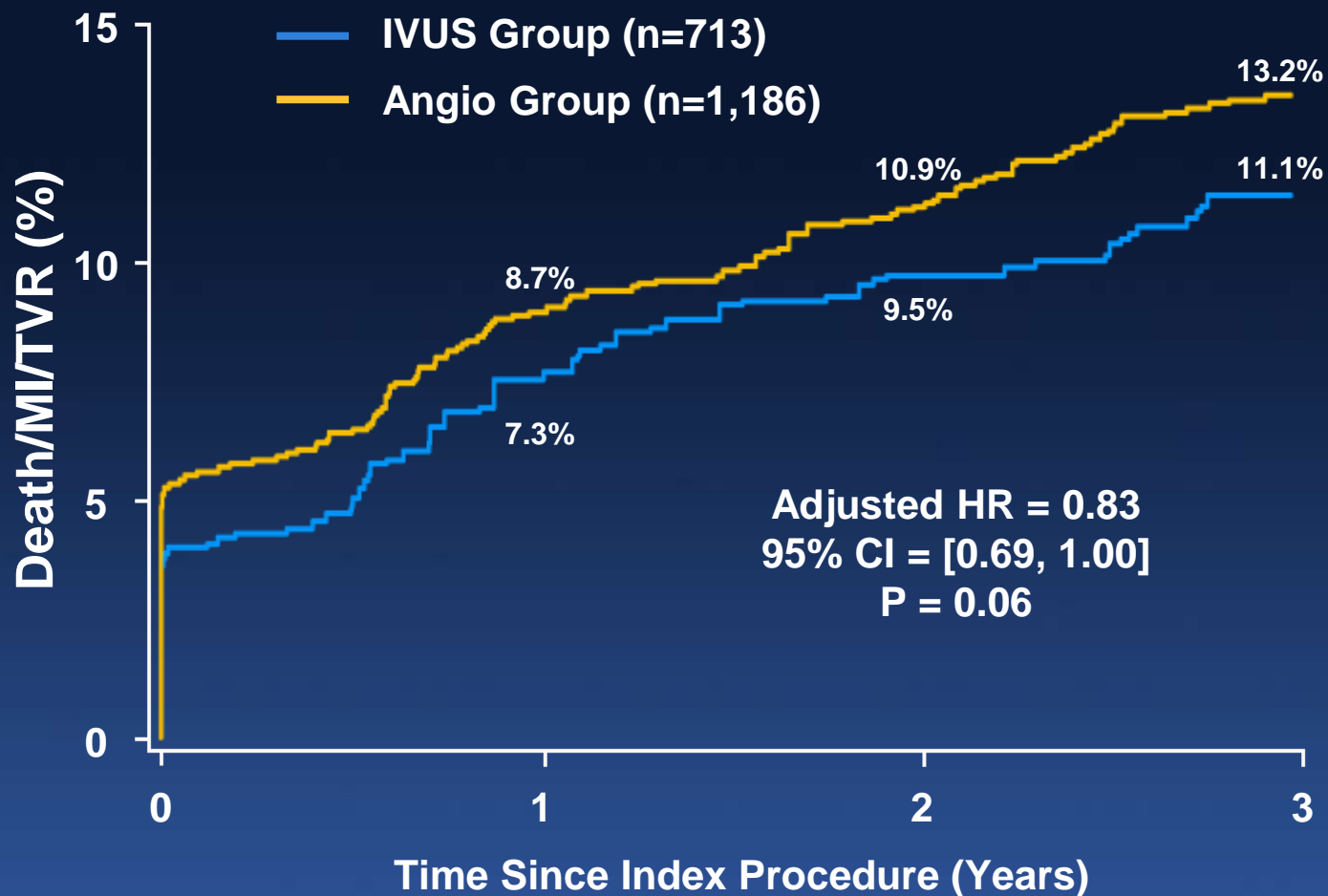
- Distal LM lesion ~60%, 2 stent technique ~13%
- IVUS guidance was an independent predictor of MACE

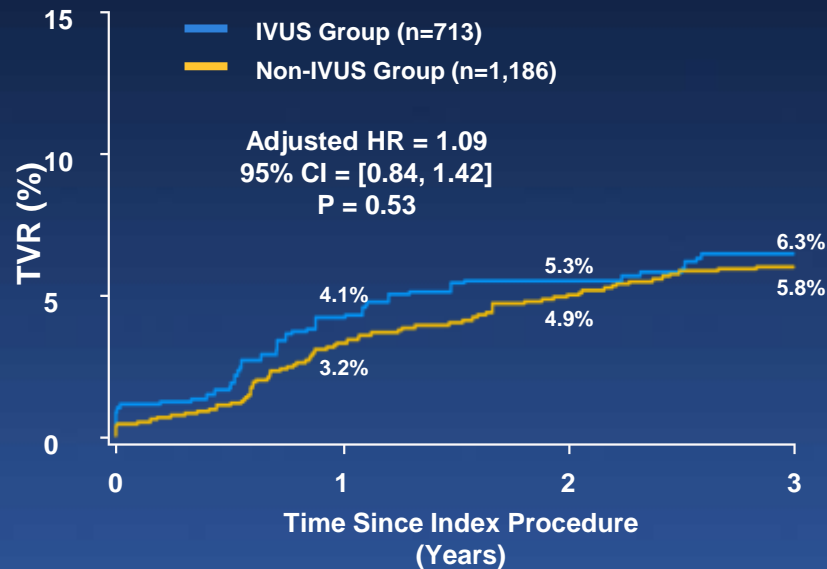
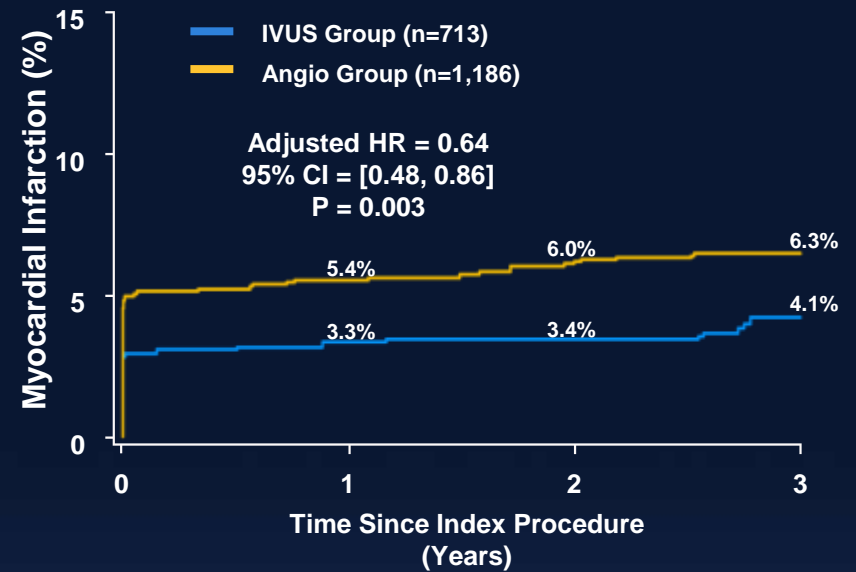
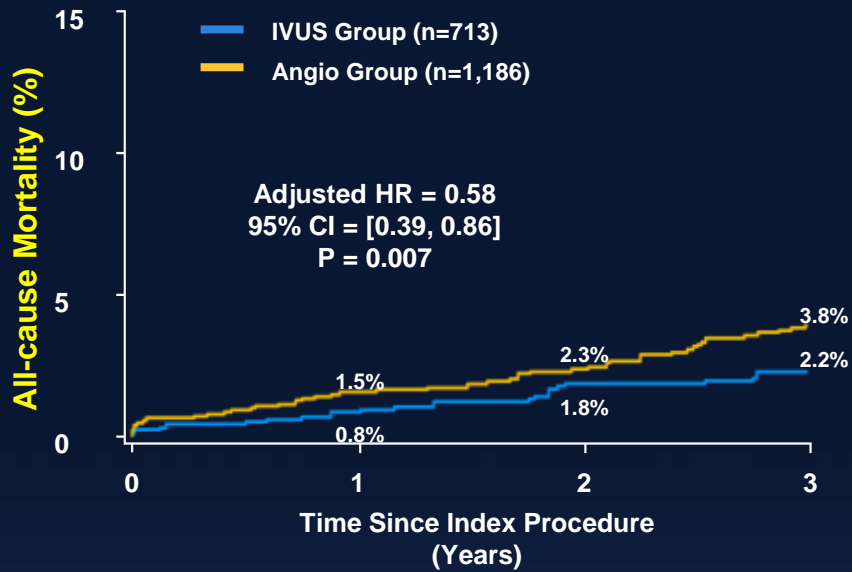


IVUS-guided LM PCI with DES vs a propensity score-matched group of pts treated without IVUS guidance from 4 Spanish registries

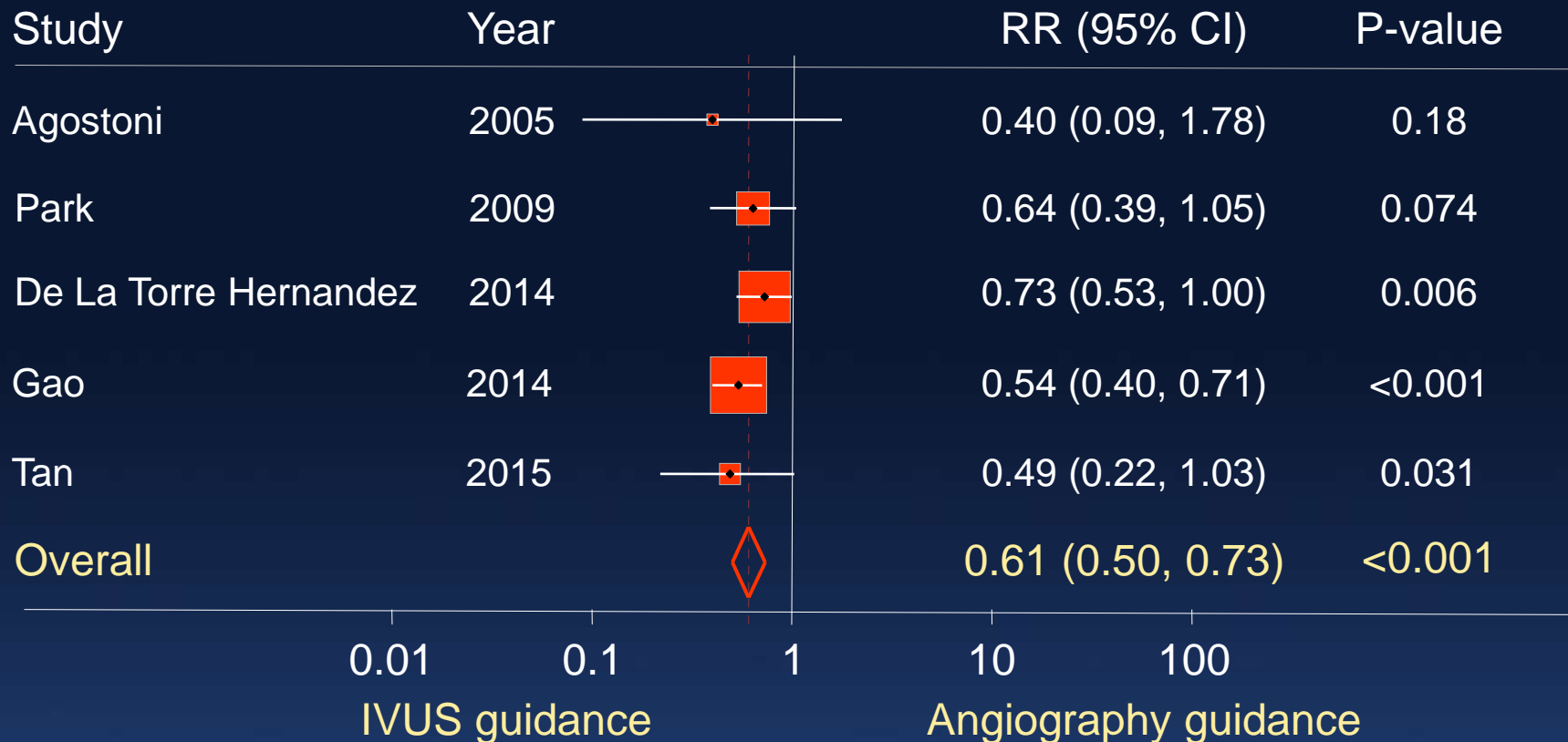
	IVUS	No IVUS	P
<u>All lesions</u>	505	505	
Cardiac death	3.3%	6.0%	0.07
MI	4.5%	6.5%	0.4
TLR	7.7%	6.3%	0.7
Definite/probable ST	0.6%	2.2%	0.04
Cardiac death+MI+TLR	11.7%	16.0%	0.04
<u>Distal lesions</u>	221	226	
Cardiac death+MI+TLR	11.0%	19.0%	0.03
<u>Distal lesions - 2 stents</u>	63	62	
Cardiac death+MI+TLR	16.7%	41.0%	0.02

IVUS vs angiography-guided LMCA PCI at FuWai Hospital (N=1,899)



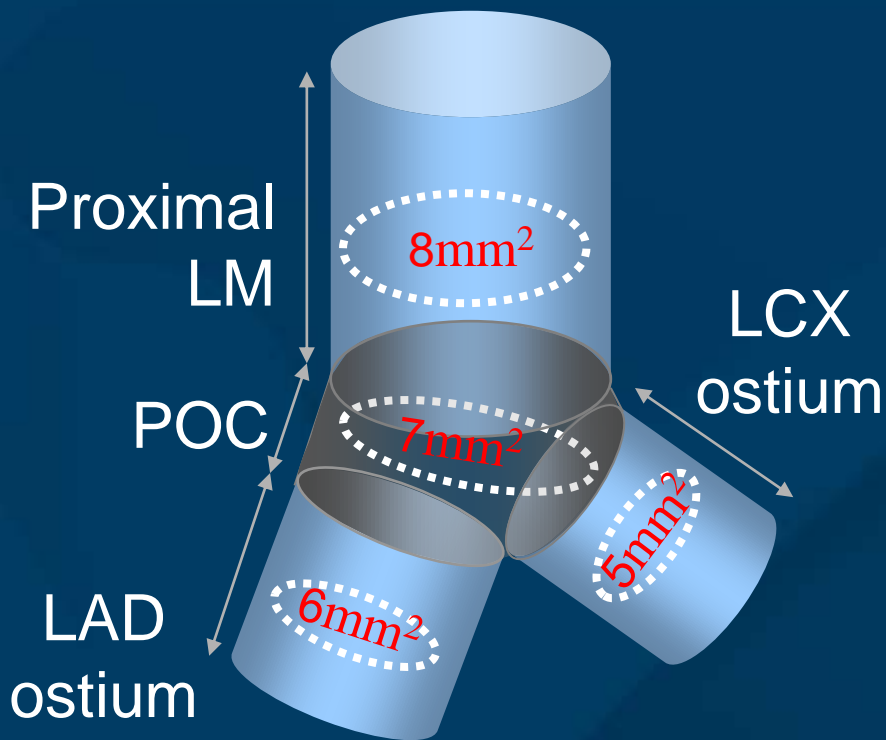


Meta-Analysis of MACE in 5 published studies

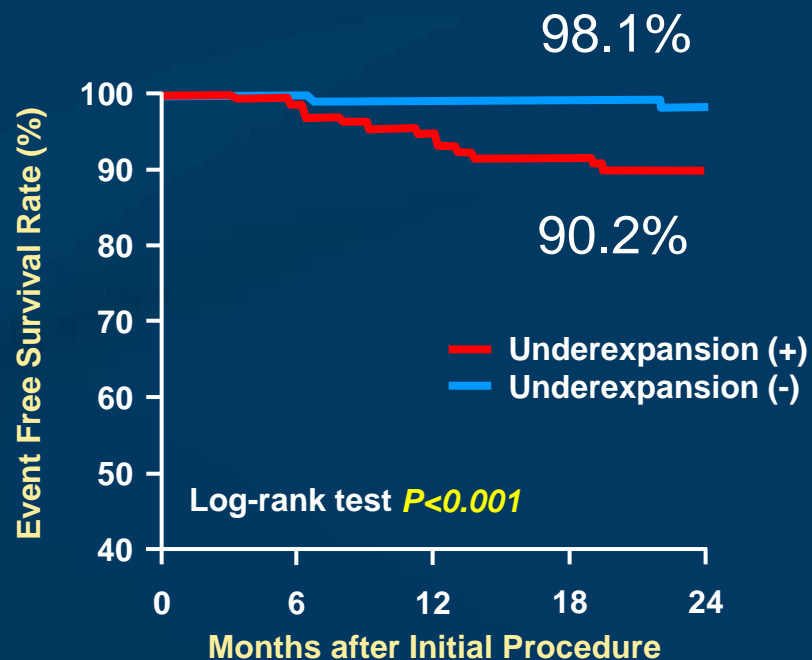


- IVUS-guided DES implantation into LMCA lesions was associated with a significant reduction in
 - MACE (RR: 0.61, 95% CI: 0.50 to 0.73, $p < 0.001$)
 - All-cause Death (RR: 0.53, 95% CI: 0.37 to 0.76, $p = 0.001$)
 - Cardiac Death (RR: 0.40, 95% CI: 0.24 to 0.64, $p < 0.001$)
 - Myocardial Infarction (RR: 0.69, 95% CI: 0.53 to 0.89, $p < 0.001$)
 - Stent Thrombosis (RR: 0.27, 95% CI: 0.11 to 0.65, $p = 0.004$).
- However, there was no significant statistical difference regarding TLR (RR: 0.41, 95% CI: 0.09 to 1.91, $p = 0.255$) and only a trend to reduced TVR (RR: 0.45, 95% CI: 0.16 to 1.27, $p = 0.132$).

MACE-free Survival in LMCA Lesions



MACE



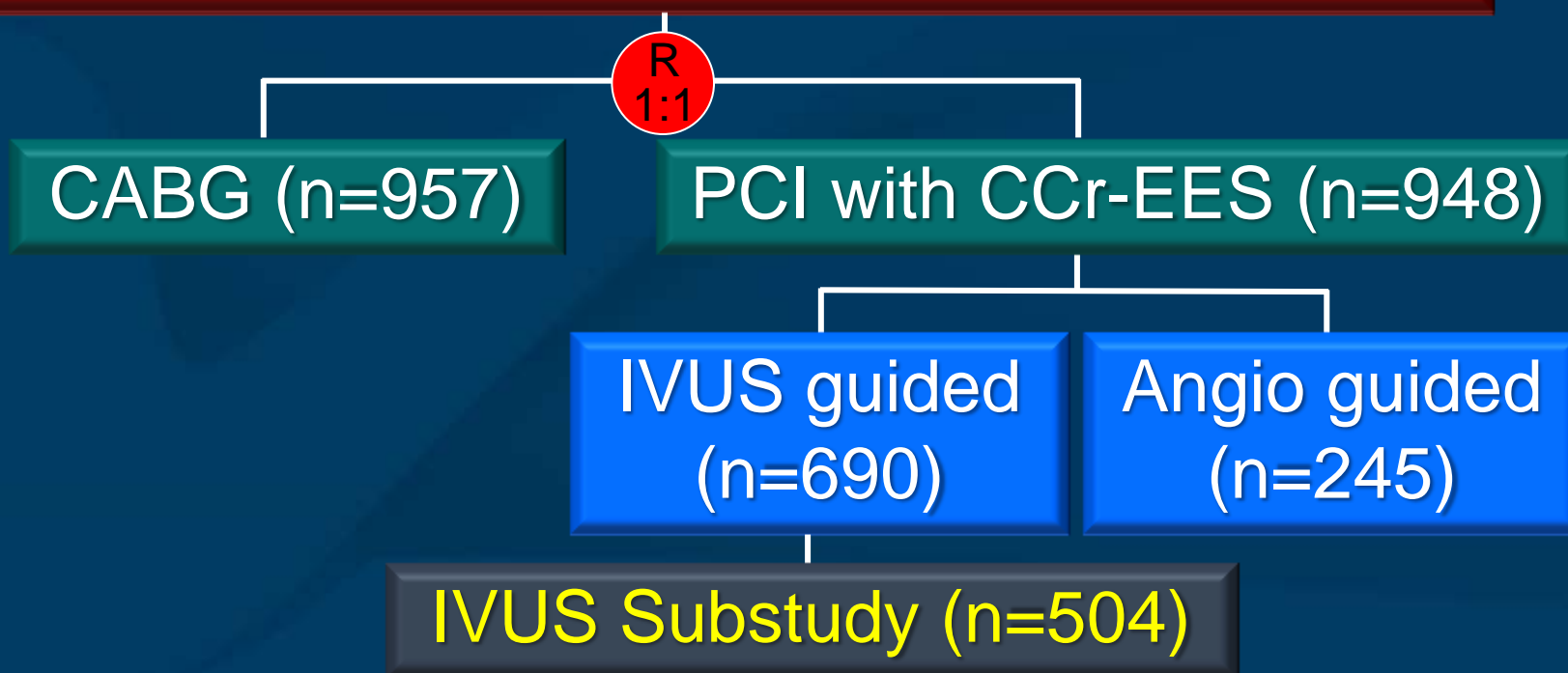
No. at risk

	0	6	12	18	24
Underexpansion (+)	133	131	126	121	75
Underexpansion (-)	260	260	255	246	129

EXCEL Trial

Evaluation of **X**ience versus **C**oronary Artery Bypass Surgery for
Effectiveness of **L**eft Main Revascularization

1,905 pts with unprotected LMCAD at 126 sites in
17 countries were prospectively enrolled



Clinical FU at 30 days, 1 year, 2 years, 3 years

Major Inclusion Criteria

- Unprotected LM CAD with $\geq 70\%$ DS, *or* $\geq 50\%$ - $< 70\%$ with either i) non-invasive evidence of LM ischemia, ii) IVUS MLA $\leq 6.0 \text{ mm}^2$, *or* iii) FFR ≤ 0.80

PCI recommendations

- Complete revascularization of all ischemic territories with EES
- Provisional LM bifurcation treatment preferred
- IVUS guidance strongly recommended
- Routine angiographic follow-up not permitted

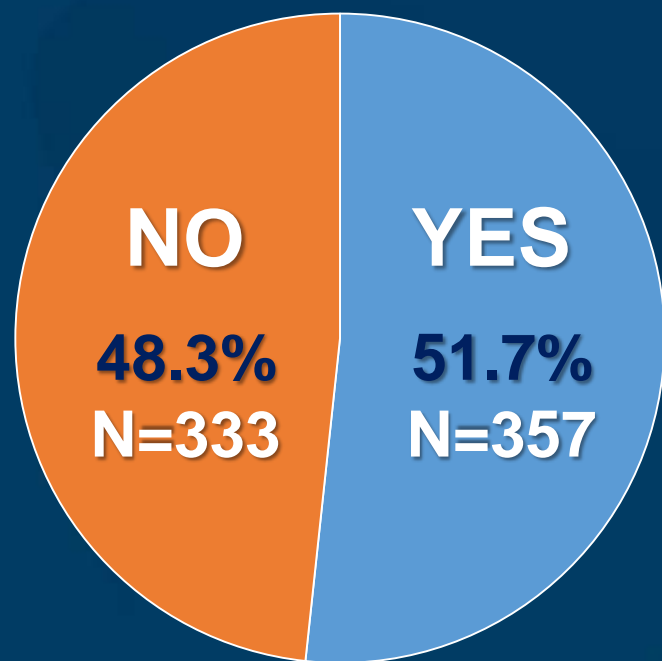
Primary and Secondary Endpoints

Tested hierarchically to preserve alpha

Endpoint	Timing of follow-up	Powered for
Primary endpoint: Death, stroke or MI	Median 3 years, minimum 2 years	Non-inferiority
Secondary endpoint #1: Death, stroke or MI	30 days	Non-inferiority
Secondary endpoint #2a: Death, stroke, MI or IDR	Median 3 years, minimum 2 years	Non-inferiority
Secondary endpoint #2b: Death, stroke or MI	Median 3 years, minimum 2 years	Superiority
Post-hoc endpoint: Cardiac death, MI/stent thrombosis/IDR relates to LM lesion	Median 3 years, minimum 2 years	NA

If the primary endpoint and secondary endpoint #1 both pass, secondary endpoints #2a and #2b are tested simultaneously
IDR = ischemia-driven revascularization

Change in LMCAD stenting by IVUS



Any IVUS usage for LM lesion (n=690)

- Used larger balloon: 30% (107)
- Post-dilated: 29% (102)
- Used higher pressure: 17% (62)
- Treated stent under-expansion: 16% (57)
- Led to provisional 1 stent strategy rather than planned 2 stents: 11% (41)
- Led to planned 2 stent strategy rather than provisional 1 stent: 9% (33)

Patient Characteristics

IVUS MSA tertiles (range)	Low: 4.4-8.7 (n=172)	Inter: 8.8-10.9 (n=169)	High: 11.0-17.8 (n=163)	P Value
Age (years)	65.5±9.8	65.3±9.2	65.7±9.7	0.94
Female	32.0%	22.5%	24.5%	0.11
Diabetes mellitus	33.7%	29.0%	24.5%	0.18
Insulin treated	9.9%	7.7%	4.3%	0.14
Hyperlipidemia	76.6%	68.7%	73.6%	0.26
Hypertension	76.5%	77.4%	67.5%	0.08
Current smoking	25.7%	27.9%	23.6%	0.68
Renal insufficiency*	18.0%	15.5%	14.9%	0.72
Prior MI	16.5%	22.3%	16.3%	0.27
Prior PCI	17.4%	17.9%	21.5%	0.59

*Defined as Cockcroft-Gault equation <60ml/min

Angio and Procedural Characteristics

	Low:	Inter:	High:	P Value
IVUS MSA tertiles (range)	4.4-8.7 (n=172)	8.8-10.9 (n=169)	11.0-17.8 (n=163)	
Distal left main lesion	81.7%	77.4%	78.4%	0.60
Ostial LAD \geq 50%	45.3%	44.4%	47.9%	0.81
Ostial LCX \geq 50%	44.8%	35.5%	37.4%	0.18
LM + 2 vessel disease	36.0%	32.0%	25.8%	0.13
LM + 3 vessel disease	16.3%	20.7%	15.3%	0.39
Syntax score baseline	26.8 \pm 8.4	26.9 \pm 8.4	26.5 \pm 9.0	0.92
>32	21.8%	26.1%	23.9%	0.67
Residual Syntax score	6.1 \pm 5.8	6.3 \pm 6.0	6.3 \pm 6.5	0.96
Total LM stent length (mm)	27.3 \pm 15.2	27.8 \pm 15.6	27.3 \pm 16.4	0.96
LM stent diameter (mm)	3.3 \pm 0.4	3.5 \pm 0.4	3.7 \pm 0.4	<0.01
PCI for non-LM lesions	54.7%	53.8%	52.1%	0.90
Total non-LM stent length (mm)	35.6 \pm 25.1	40.7 \pm 28.7	36.2 \pm 26.5	0.40

IVUS Characteristics

IVUS MSA tertiles (range)	Low: 4.4-8.7 (n=172)	Inter: 8.8-10.9 (n=169)	High: 11.0-17.8 (n=163)	P Value
<u>Left main segment</u>				
Distal bifurcation location	84.3%	81.7%	78.5%	0.52
MSA, mm ²	7.5±1.0	9.9±0.7	12.5±1.4	<0.01
Vessel area at MSA, mm ²	19.3±4.0	21.8±3.7	24.8±4.2	<0.01
Mean stent area, mm ³ /mm	8.9±1.5	11.2±1.2	13.6±1.6	<0.01
Mean vessel area, mm ³ /mm	19.0±3.5	22.1±3.7	25.1±4.1	<0.01
<u>Any target lesion segment</u>				
Attenuated plaque	75.6%	76.3%	69.9%	0.35
Tissue protrusion	8.1%	10.1%	11.7%	0.56
Stent malapposition	18.6%	21.3%	23.3%	0.57
Stent deformation/fracture	9.4%	4.7%	5.6%	0.18
Edge dissection	13.4%	12.4%	12.3%	0.95

Overall 3-Year Outcomes

IVUS MSA tertiles (range)	Low: 4.4-8.7 (n=172)	Inter: 8.8-10.9 (n=169)	High: 11.0-17.8 (n=163)	P L vs I	P L vs H
Death/MI/stroke	19.4% (32)	16.1% (26)	9.6% (15)	0.45	0.01
Death/MI/stroke/IDR*	26.6% (44)	23.8% (39)	18.3% (29)	0.66	0.08
All cause death	13.8% (22)	10.0% (16)	5.2% (8)	0.34	0.01
Cardiovascular death	7.4% (12)	4.8% (8)	4.0% (6)	0.39	0.16
MI	10.5% (17)	8.2% (13)	3.7% (6)	0.49	0.02
Stroke	1.8% (3)	1.2% (2)	2.1% (3)	0.66	0.98
Stent thrombosis (D/P)	3.1% (5)	1.2% (2)	0.0% (0)	0.26	0.03
Target lesion IDR	12.0% (19)	8.3% (13)	8.8% (14)	0.30	0.41
Target vessel IDR	12.0% (19)	10.8% (17)	9.4% (15)	0.79	0.52

*IDR: ischemia driven revascularization

3-Year Left Main Related Outcomes

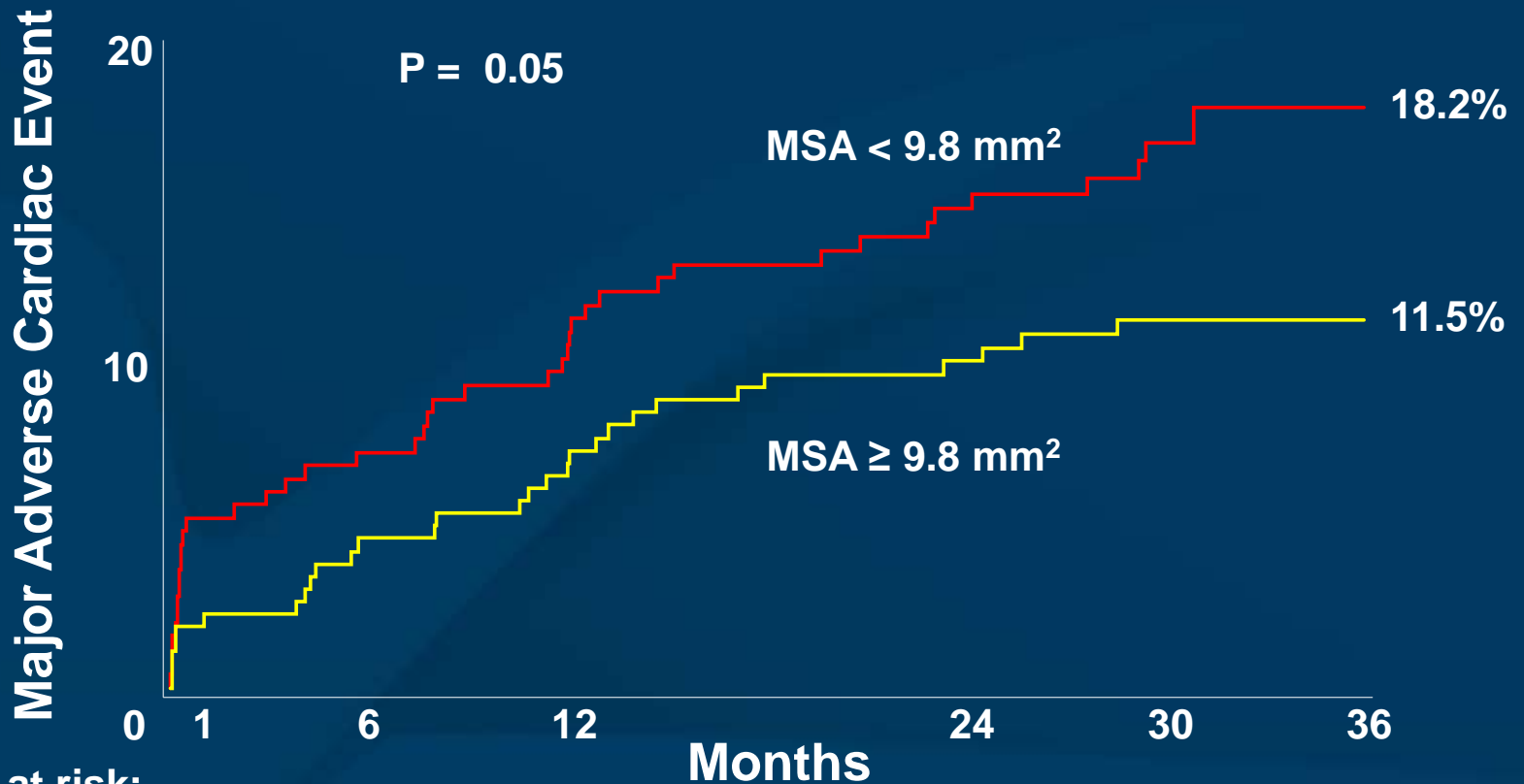
IVUS MSA tertiles (range)	Low: 4.4-8.7 (n=172)	Inter: 8.8-10.9 (n=169)	High: 11.0-17.8 (n=163)	P L vs I	P L vs H
Cardiac death, MI/ST/IDR of LM	19.7 (32)	12.9% (21)	11.3% (18)	0.14	0.05
Cardiac death	6.8% (11)	3.0% (5)	1.9% (3)	0.14	0.03
MI of LM	9.4% (15)	4.3% (7)	3.1% (5)	0.09	0.03
Peri-procedural	4.1% (7)	2.4% (4)	1.8% (3)	0.38	0.23
Spontaneous	4.5% (7)	1.2% (2)	0.6% (1)	0.10	0.03
Stent thrombosis (D/P)	3.1% (5)	0.6% (1)	0% (0)	0.11	0.03
LM ischemia driven TLR	10.2% (16)	8.3% (13)	7.6% (12)	0.61	0.47
LM ischemia driven TVR	10.2% (16)	10.2% (16)	8.2% (13)	0.94	0.61

LM MSA to predict LM related Events

	Adjusted Hazard Ratio (95% CI)	P-value
Final IVUS LM MSA (mm²)	0.89 (0.80-0.99)	0.03
Distal left main lesion location	2.10 (1.0-5.33)	0.05
Diabetes mellitus	1.63 (1.0-2.64)	0.049
Acute coronary syndrome presentation	0.60 (0.36-0.99)	0.045
Male	0.69 (0.41-1.12)	0.16
Age (years)	1.01 (0.99-1.04)	0.32
History of heart failure (NYHA III/ IV)	1.23 (0.38-3.99)	0.73
Left main with 3 vessel disease	1.21 (0.67-2.20)	0.53

Cut off of LM MSA= 9.8 mm² (AUC:0.58)

KM-Curve stratified by MSA Cut-off



Number at risk:

$MSA < 9.8$	245	232	224	212	188	97
$MSA \geq 9.8$	259	252	244	235	220	139

Conclusions

1. IVUS is useful for the diagnosis of severity and distribution of left main disease, optimization of stent, and evaluation of complication.
2. In the EXCEL trial, 68% of PCI cases were performed using IVUS guidance. In the half of IVUS guidance cases, the procedure was changed by the IVUS findings.
3. After treatment with CoCr-EES, a small final MSA of the left main coronary artery measured by IVUS was strongly associated with cardiac death, MI, stent thrombosis, and TLR related LM during 3 year follow-up.