Intravascular Imaging for Guidance of PCI for In-stent Restenosis

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Conflict of Interest Statement

I have nothing to disclose.

Mechanisms of In-stent Restenosis

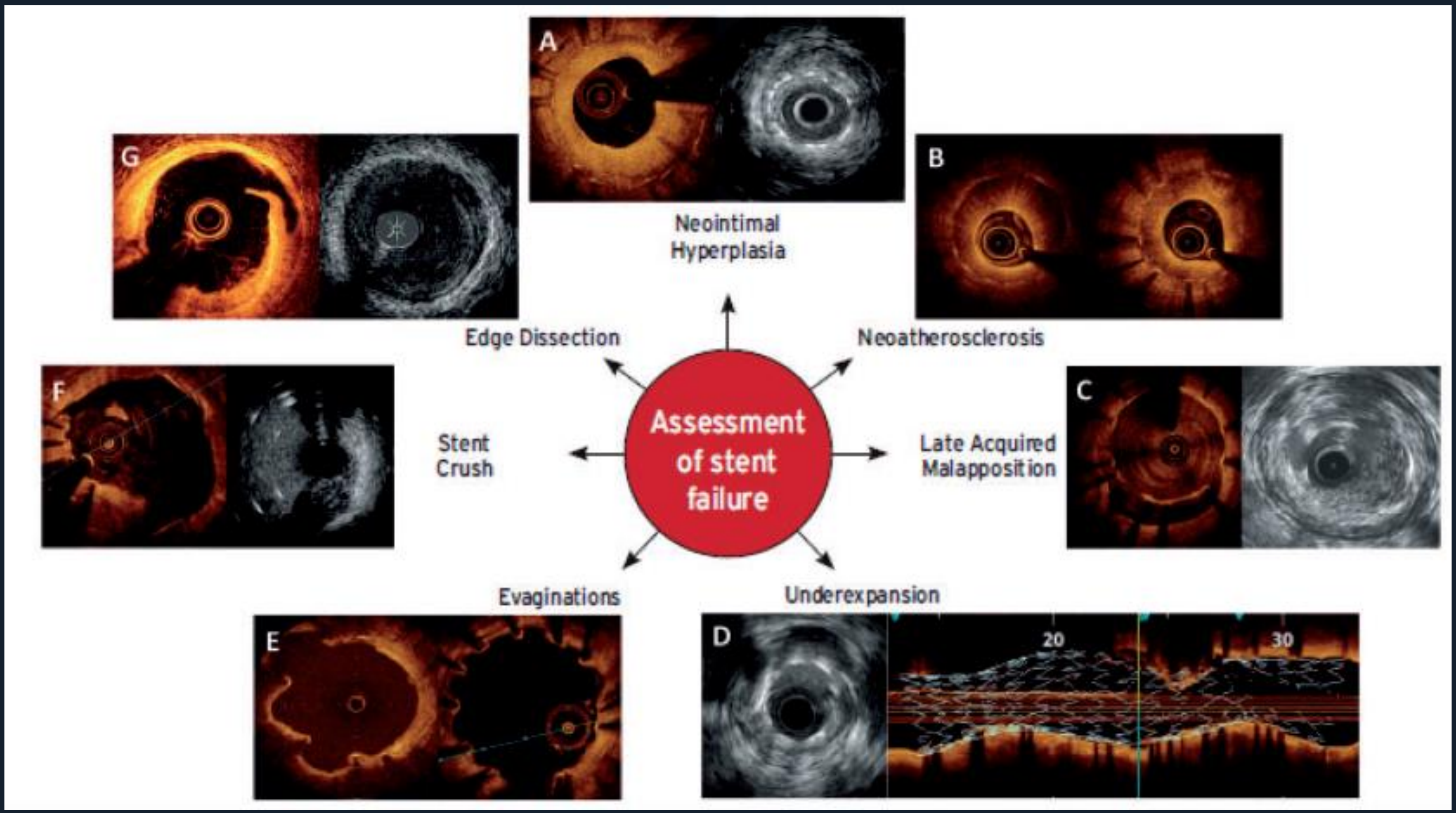
Mechanical Factors

- Chronic stent under-expansion
  - Undersized stents
  - Peri-stent heavy calcification
- Stent fracture
- Gap (missing the lesion)

Tissue re-growth

- Neointimal hyperplasia
- Neoatherosclerosis

Intravascular Imaging for ISR provides Information of underlying mechanisms



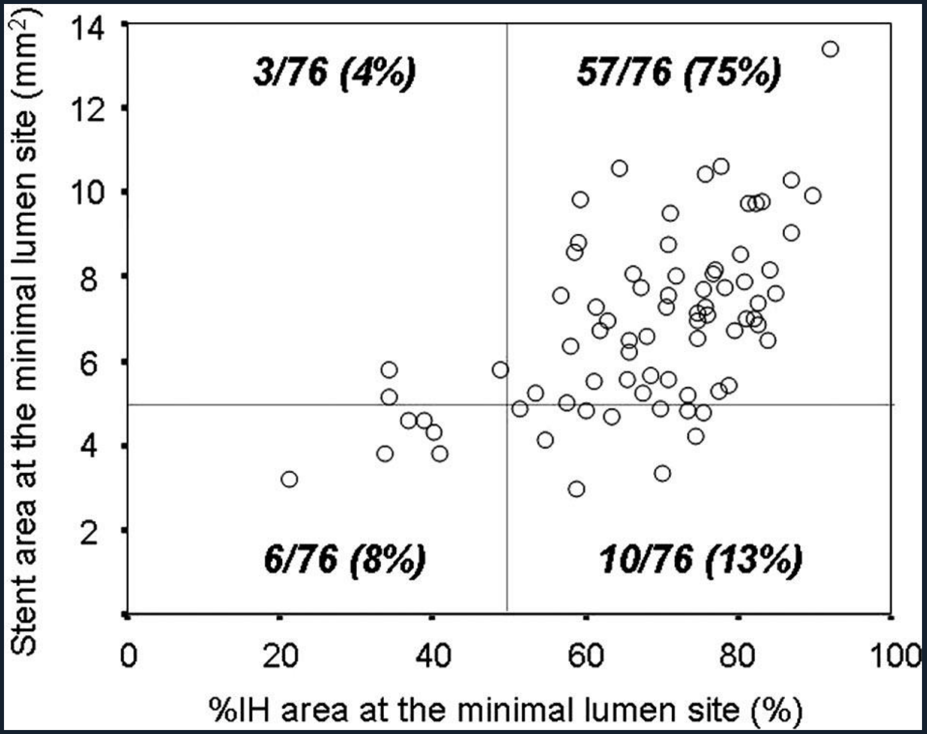
Neumann FJ et al., Eur Heart J. 2019;40:87-165.

IVUS can detect Underlying mechanism

Analysis of 76 ISR lesions at AMC

	Angiographic Restenosis	No Angiographic Restenosis	*P* Value
n	82	312	
Follow-up duration	12.9±10.4	13.5±8.7	0.615
MSA, mm^2	5.7±1.8	6.4±1.9	0.003
MLA, mm^2	2.2±1.0	5.4±1.9	<0.001
IH area at the narrowest lumen, %	4.7±2.2	1.4±1.2	<0.001
%IH area at the narrowest lumen, %	65.9±16.1	19.8±14.7	<0.001
MLA <4 mm^2, n (%)	76 (93%)	83 (27%)	<0.001
%IH area >50%, n (%)	69 (84%)	14 (5%)	<0.001
MSA <5 mm^2, n (%)	32 (39%)	75 (24%)	0.008
Normalized stent volume, mm^2	7.5±1.7	8.1±2.0	0.027
Normalized lumen volume, mm^2	5.2±1.4	7.1±2.0	0.001
Normalized IH volume, mm^2	2.3±1.1	1.0±0.7	0.002
Normalized EEM volume, mm^2	14.6±3.4	16.1±4.0	0.004
Normalized P+M volume, mm^2	7.0±2.4	8.0±3.1	0.021
%IH volume, %	31.0±12.5	12.1±8.5	<0.001

Logistic regression was performed using generalized estimating equations.



Kang SJ, Park SJ et al., Circ Cardiovasc Interv. 2011;4:9-14.

IVUS can detect Under-expansion

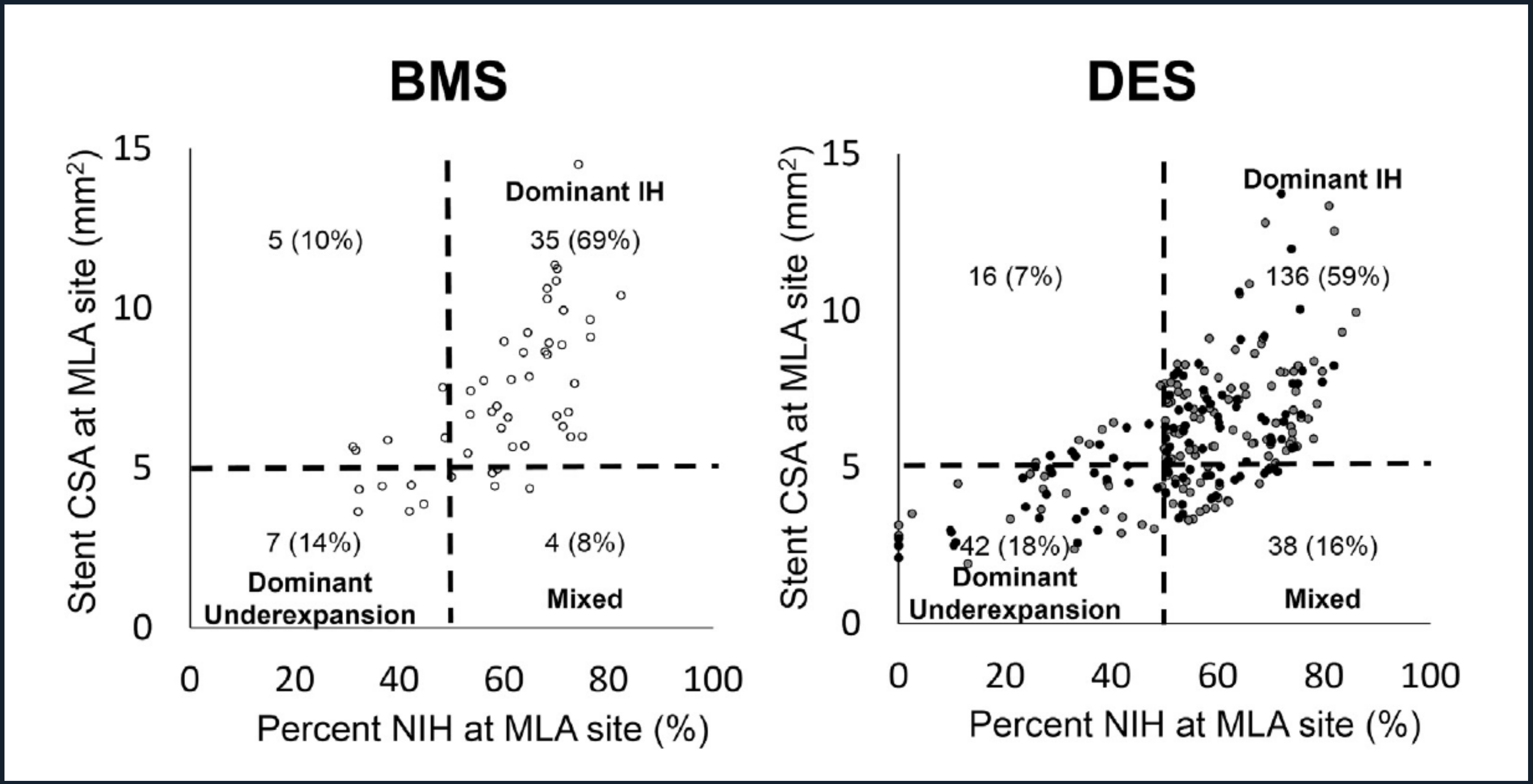
Analysis of 298 ISR lesions at NYPH

	BMS (N=52)	1st generation DES (N=215)	2nd generation DES (N=121)	p-value
Diabetes mellitus	19 (36.5%)	68 (48.9%)	57 (53.3%)	0.14
ACS presentation	28 (53.9%)	81 (58.3%)	56 (52.8%)	0.7
Total stent length (mm)	21.8±13.5	29.4±16.1	32.2±18.7	0.001
Average reference lumen area (mm^2)	**6.3±2.3**	**6.3±1.8**	**6.4±1.9**	**1.0**
Minimum stent area (MSA)	**6.4±2.2**	**4.9±1.6**	**4.7±1.6**	**<0.001**
MSA <5 mm^2	**28.8%**	**56.8%**	**69.2%**	**<0.001**
%NIH at MLA site	**60.9±12.8**	**56.1±16.0**	**52.3±16.9**	**0.006**
Diffuse ISR	28.8%	30.2%	28.0%	1.0
Neointimal calcification (%)	19.2%	13.0%	18.5%	0.41
Stent fracture, n (%)	0.0%	5.8%	6.5%	0.18
Stent malapposition, n (%)	7.7%	10.1%	10.3%	0.9

Goto K, Maehara A et al., Am J Cardiol 2015;116:1351-7.

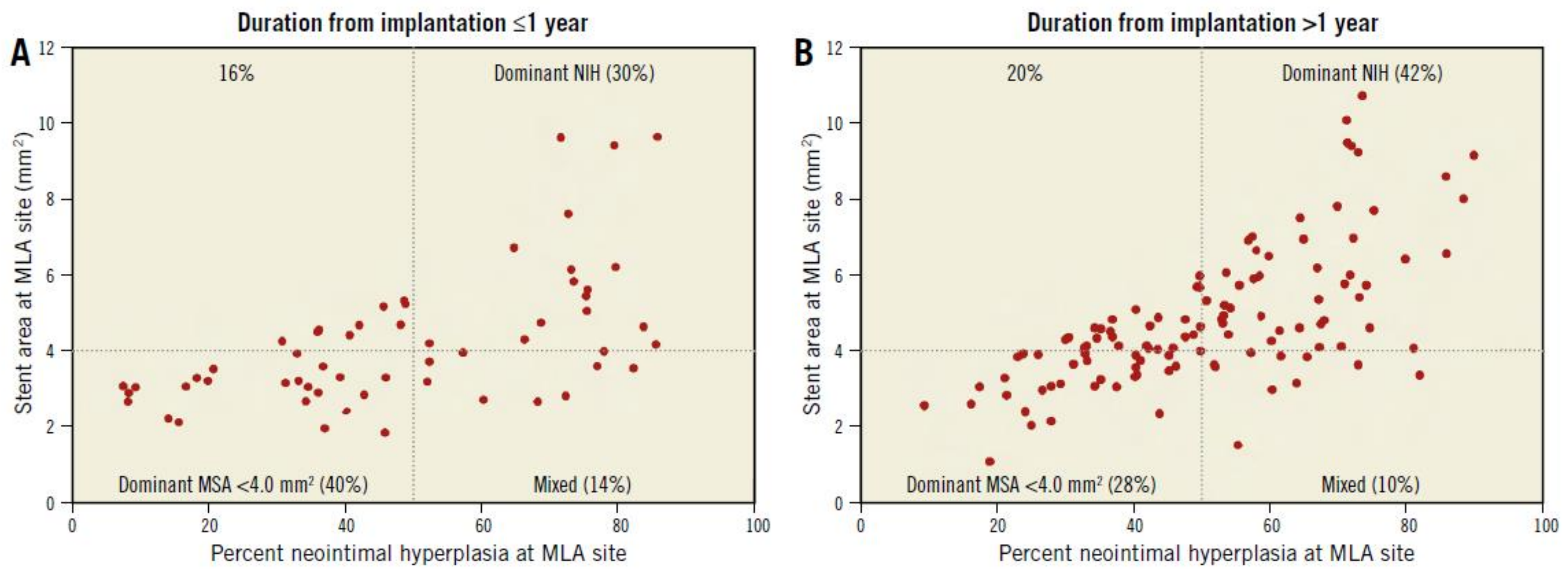
IVUS can detect Underlying mechanism

Analysis of 298 ISR lesions at NYPH



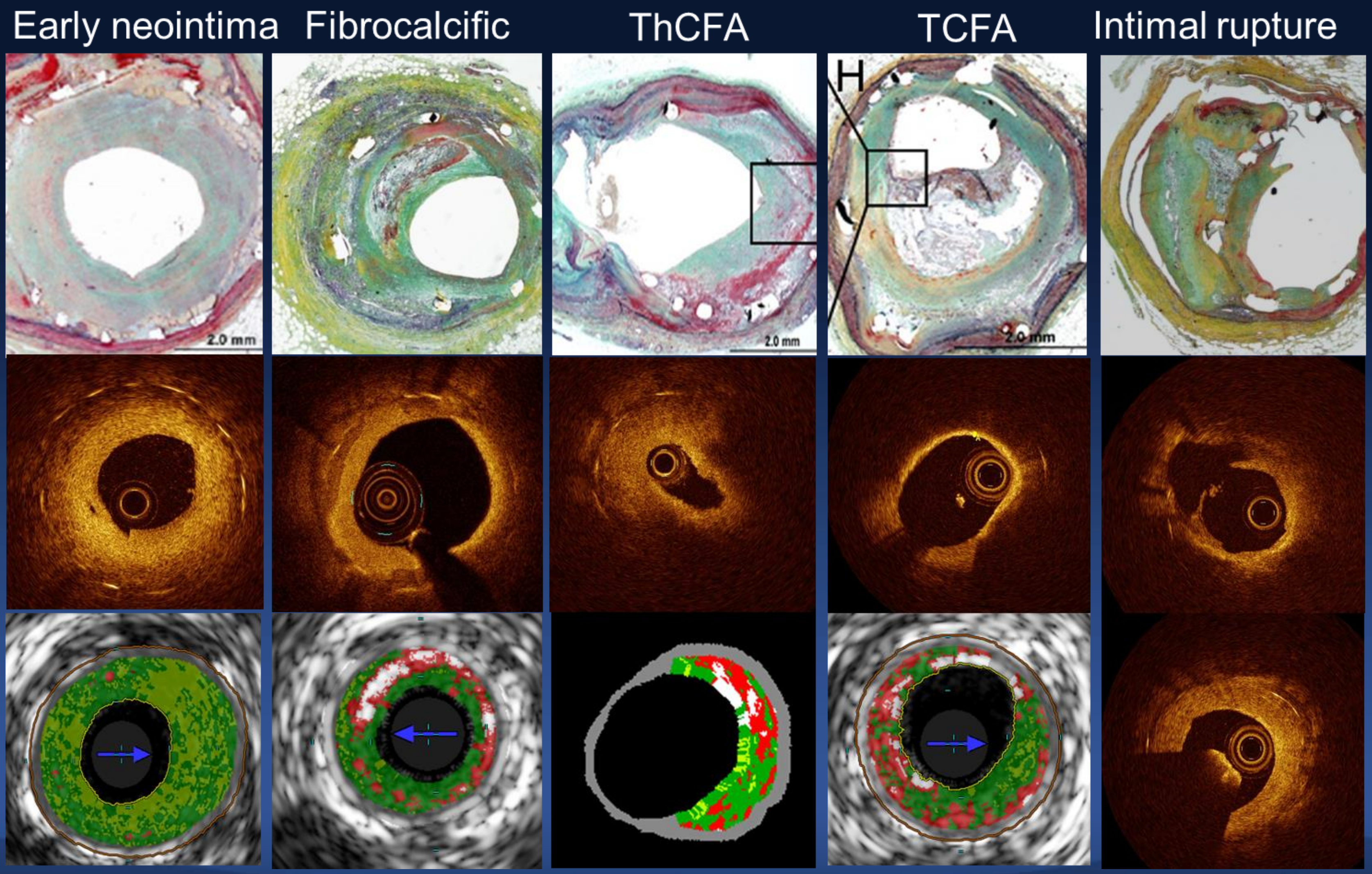
Goto K, Maehara A et al., Am J Cardiol 2015;116:1351-7.

OCT for ISR also provides Information of underlying mechanisms



Song L, Maehara A et al., EuroIntervention 2017;13:294-302.

OCT can detect in-stent Neoatherosclerosis
With lipid-rich plaque or calcification



Nakazawa et al. JACC Cariovasc Imaging 2009;2:625-8

OCT can detect in-stent Neoatherosclerosis
Mechanism of stent failure in AMC data

	DES-ISR[1]	BMS-ISR[2]	VLST[3]	
Lesion	50 DES	51 BMS	6 BMS	27 DES
Median F/U	32 Mo	132 Mo	109 Mo	62 Mo
Lipid or NC	90%	100%	100%	100%
OCT-TCFA	**52%**	**68%**	**100%**	**56%**
OCT-rupture	**58%**	**59%**	**100%**	**63%**
TLR	98%	all	all	all

1. Kang et al. Circulation 2011;123:2954-63
2. Kang et al. JACC Cardiovasc Imaging 2012;5:1267-8
3. Kang et al. JACC Cardiovasc Imaging 2013;6:695-703

Intravascular Imaging in ISR PCI can help to

- Prove the mechanism of restenosis
- Select the optimal treatment modality
  - High-pressure balloon for underexpansion
  - another DES for fracture or gap
  - DEB/DES for neointimal hyperplasia
  - Debulking some undilatable neoatherosclerosis
- Optimize the acute post-ISR PCI results
- Feedback to the operator

2018 ESC Guideline for ISR Treatment

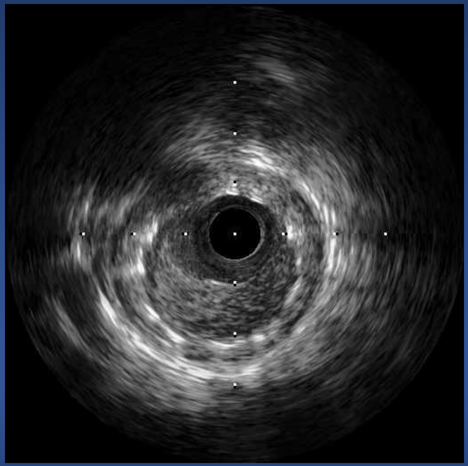
Recommendation	COR	LOE
➢ DES are recommended for the treatment of in-stent restenosis of BMS or DES.	I	A
➢ Drug-coated balloons are recommended for the treatment of in-stent restenosis of BMS or DES	I	A
➢ IVUS and/or OCT should be considered to detect stent-related mechanical problems leading to restenosis	IIa	C

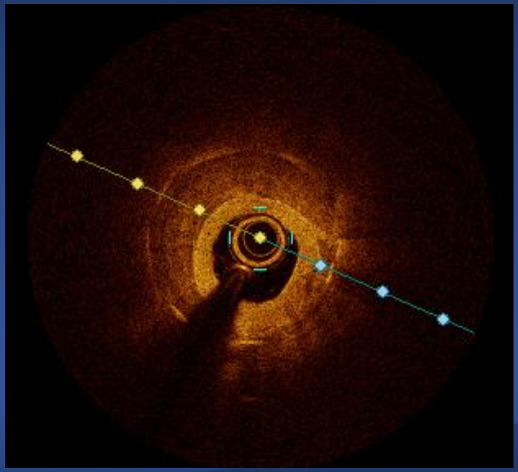
Eur Heart J 2019:40;87-165

OCT vs. IVUS for ISR Imaging

OCT can visualize
- stent strut coverage,
- presence of thrombus,
- calcified neoatherosclerosis

more accurately than angiography or IVUS



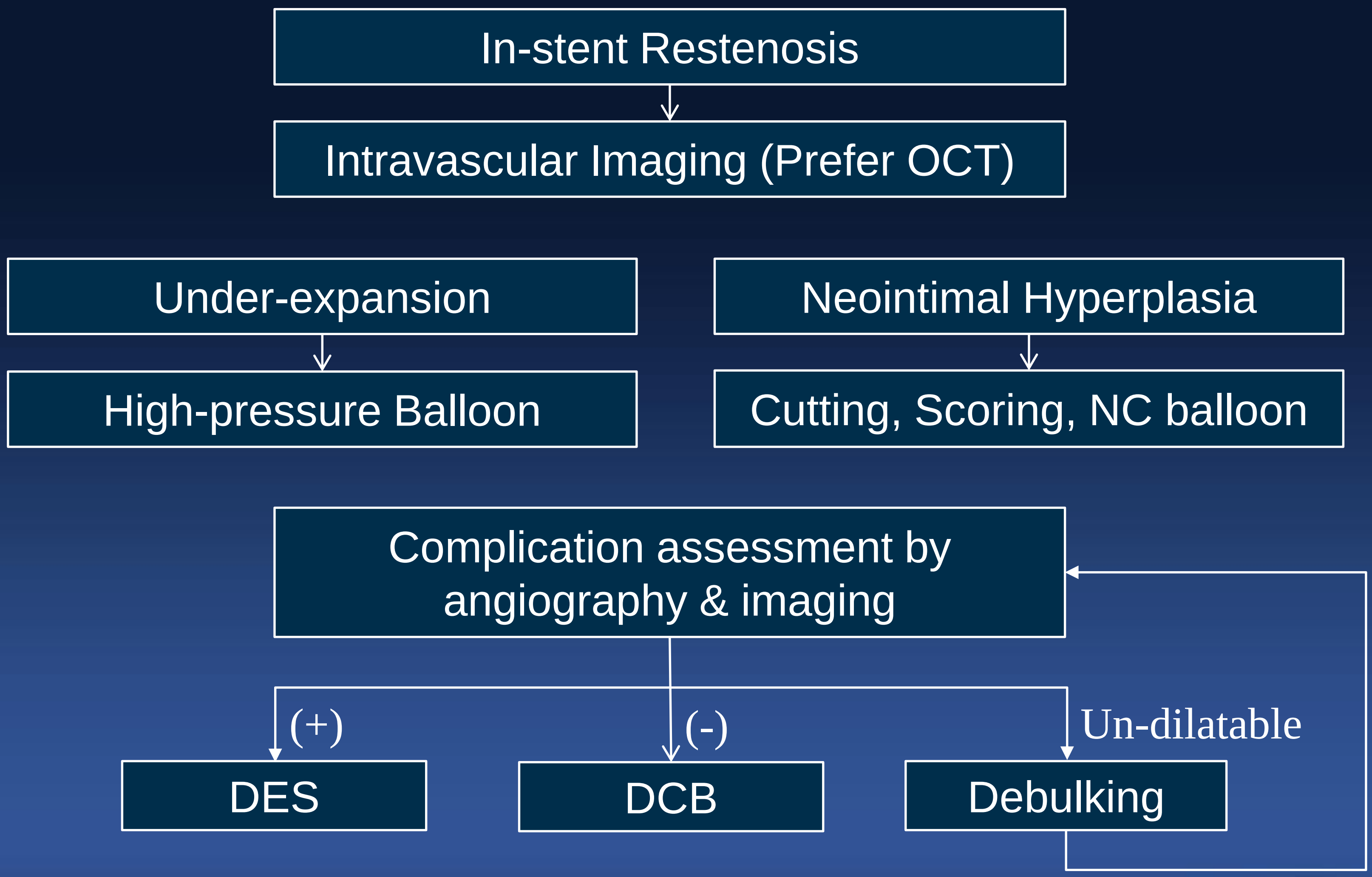


OCT vs. IVUS for Morphologic Evaluation

	Morphologic Evaluation	OCT	IVUS
Pre-PCI	Severity of Calcium	★★★	★★
	Stent Sizing by Vessel Wall	★★	★★★
	Stent length by Normal Vessel	★★★	★★★
Post-PCI	Stent Expansion	★★★	★★★
	Stent Malapposition	★★★	★★
	Stent Deformation at Ostium	★★	★★
	Edge Dissection	★★★	★★
	Residual Disease at Edge	★★★	★★★
At follow-up	Old Stent Expansion	★★★	★★★
	Neointimal Hyperplasia	★★★	★★★
	Neoatherosclerosis	★★★	★★
	Stent Fracture	★★	★★
	Positive Remodeling of Vessel Wall	★	★★★

Maehara A et al., J Am Coll Cardiol Img 2017;10:1487–503

My Treatment Strategy for ISR



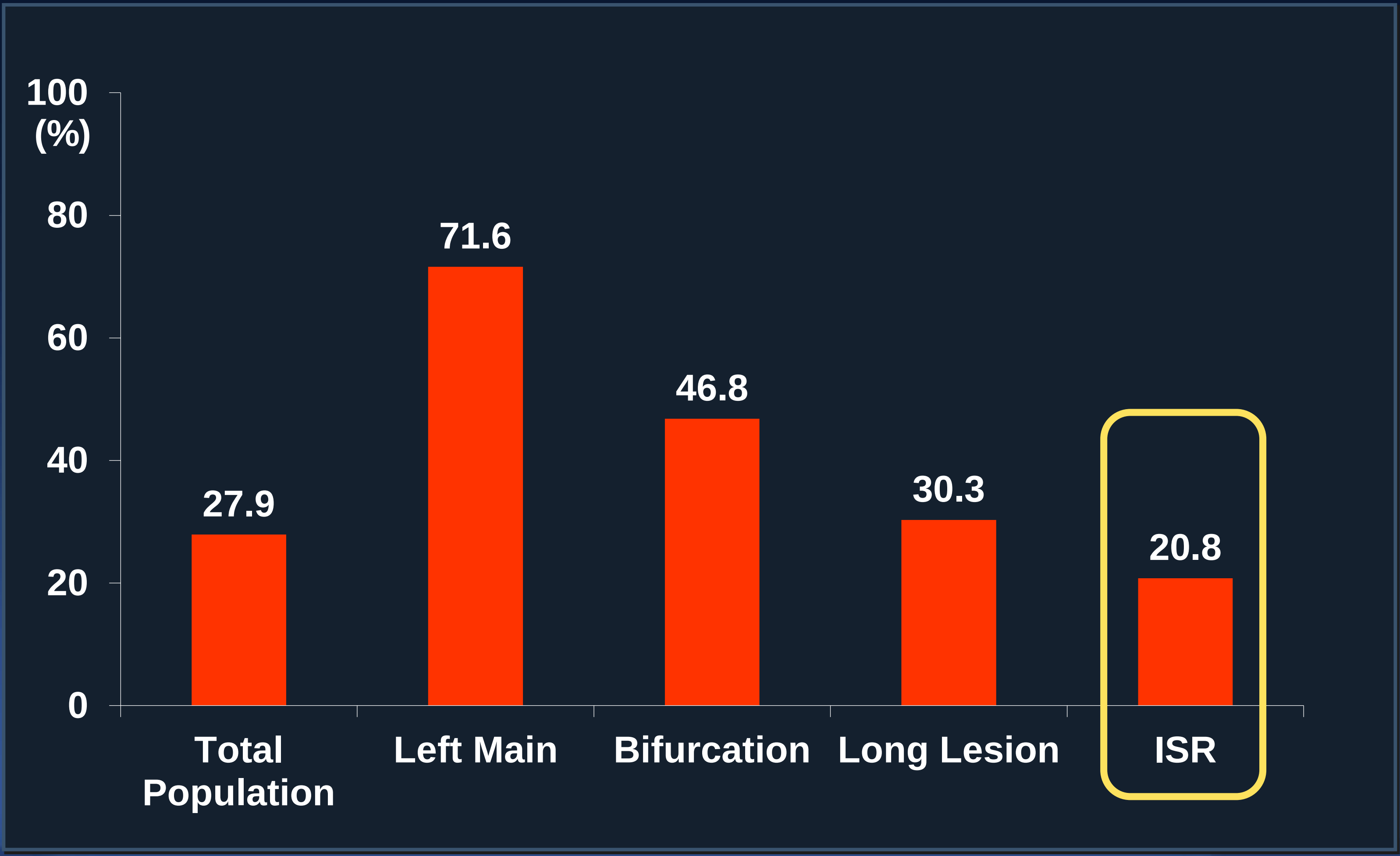
Does the IVUS-guidance Improve Clinical Outcome compared with Angiography-guidance in ISR Treatment?

IVUS vs. Angio-guided ISR PCI
Data from RCTs

No RCT Data

The Use of IVUS on Complex PCI

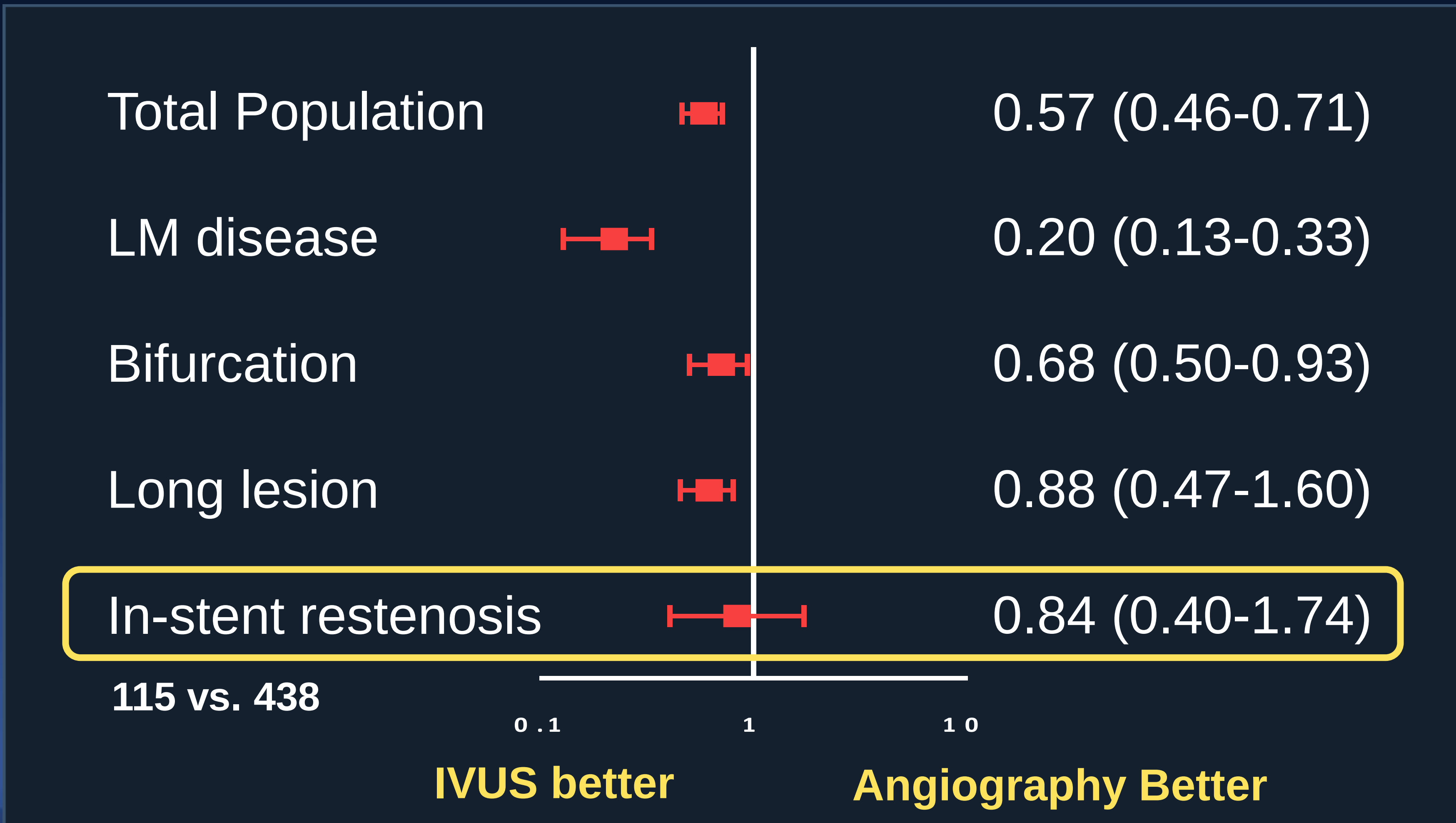
Samsung Medical Center Registry (2003-2015)



Choi KH et al., JACC CV Interv. 2019;12:607-620.

Clinical Impact of IVUS on ISR PCI

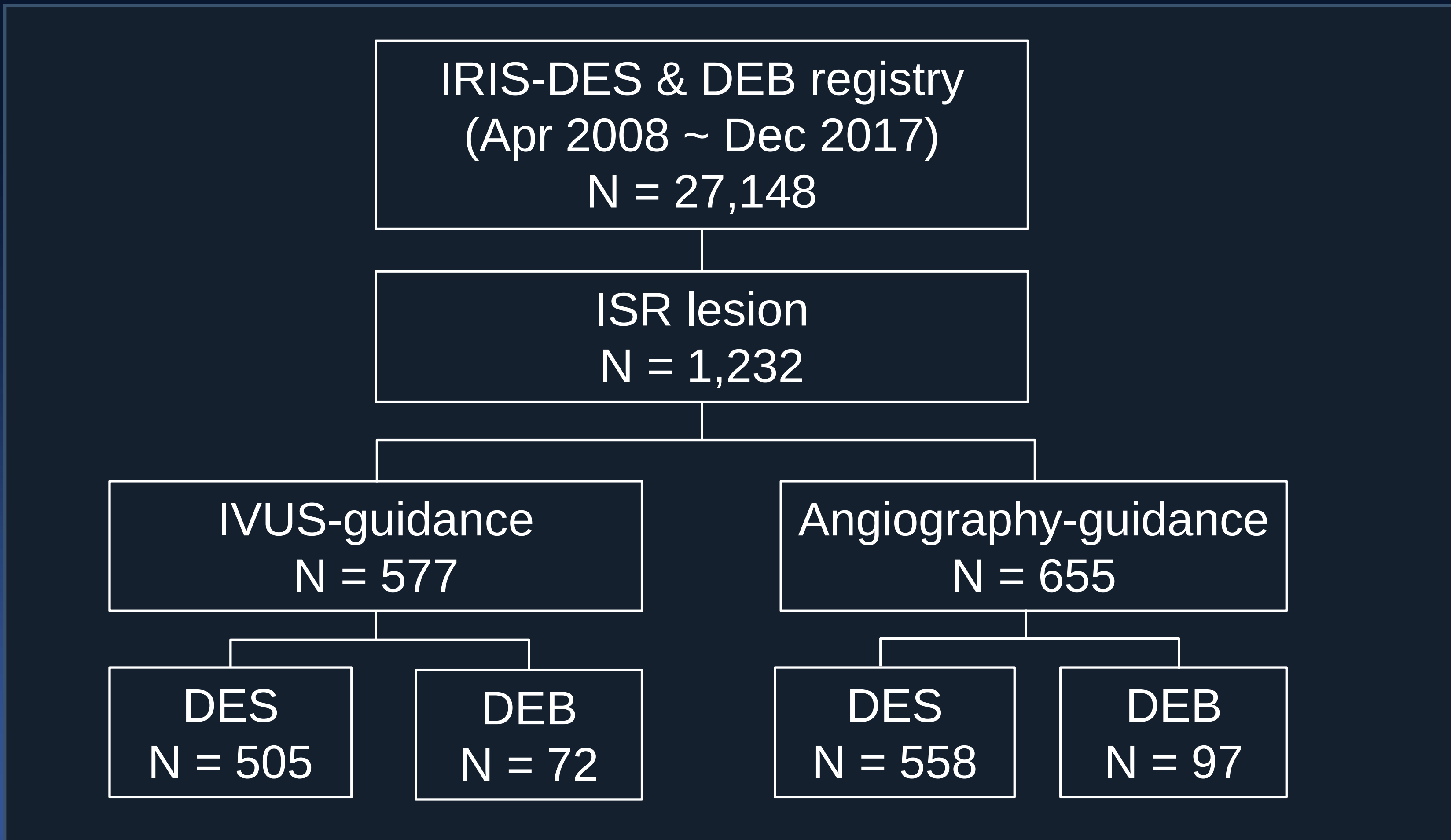
Samsung Medical Center Registry (2003-2015)



Choi KH et al., JACC CV Interv. 2019;12:607-620.

Clinical Impact of IVUS on ISR PCI

From IRIS-DES & DEB registry



IRIS-DES, IRIS-DEB Registry, Preliminary data

Clinical Impact of IVUS on ISR PCI

From IRIS-DES registry

	IVUS-guided (N=577)	Angio-guided (N=655)	P value
Age, years	64 ± 10	66 ± 10	0.002
Male, N (%)	433 (75.0)	480 (73.3)	0.523
BMI, kg/m2	24.8 ± 3.0	24.9 ± 3.4	0.633
Hypertension, N (%)	387 (67.1)	463 (70.7)	0.191
Diabetes, N (%)	216 (37.4)	284 (43.4)	0.04
Current smoker, N (%)	119 (20.6)	149 (22.7)	0.405
Hyperlipidemia, N (%)	379 (65.7)	345 (52.7)	<0.001
Previous HF, N (%)	24 (4.2)	25 (3.8)	0.872
Previous Stroke, N (%)	46 (8.0)	50 (7.6)	0.909
Peripheral a. disease, N(%)	16 (2.8)	17 (2.6)	0.987

IRIS-DES Registry, Preliminary data

Clinical Impact of IVUS on ISR PCI

From IRIS-DES registry

	IVUS-guided (N=577)	Angio-guided (N=655)	P value
Chronic kidney disease, N (%)	27 (4.7)	43 (6.6)	0.192
Chronic lung disease, N (%)	18 (3.1)	11 (1.7)	0.14
ACS at index procedure, N (%)	259 (44.9)	347 (53.0)	0.005
LV ejection fraction, %	57 ± 11	57 ± 11	0.925
Extents of disease, N (%)			0.507
One vessel disease	332 (57.5)	357 (54.5)	
Two vessel disease	164 (28.4)	205 (31.3)	
Three vessel disease	55 (9.5)	27 (4.1)	
Involvement of Left Main, N (%)	55 (9.5)	27 (4.1)	<0.001

IRIS-DES Registry, Preliminary data

Clinical Impact of IVUS on ISR PCI

From IRIS-DES registry

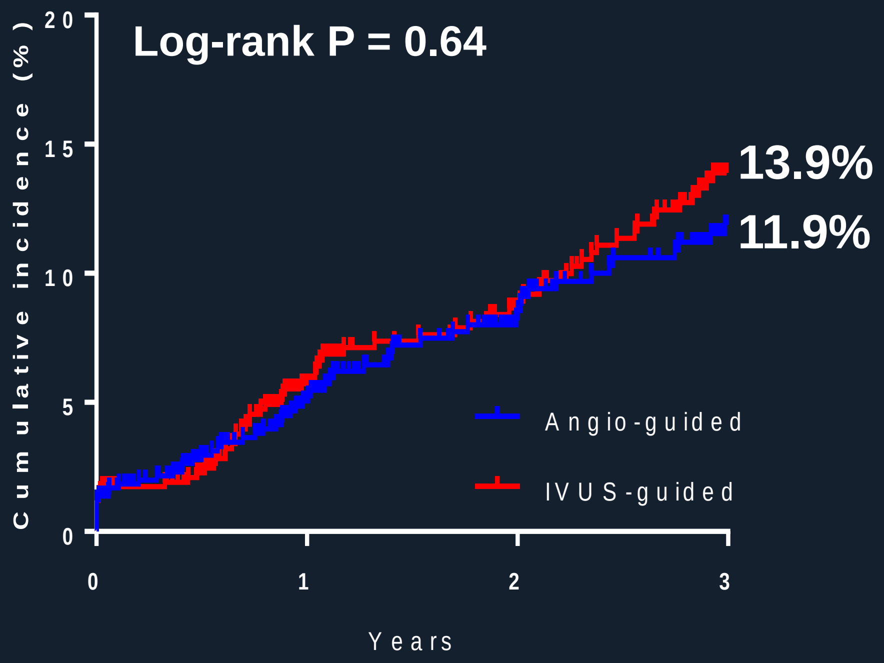
	IVUS-guided (N=577)	Angio-guided (N=655)	P value
Drug-eluting stents, N (%)	505 (87.5)	558 (85.2)	0.27
2nd generation DES, N (%)	390 (77.2)	435 (78.0)	0.825
Drug-eluting balloon, N (%)	72 (12.5)	97 (14.8)	0.27
Total Stent Length, mm	33 ± 19	28 ± 14	<0.001
Average Stent Diameter, mm	3.3 ± 0.4	3.1 ± 0.4	<0.001

IRIS-DES Registry, Preliminary data

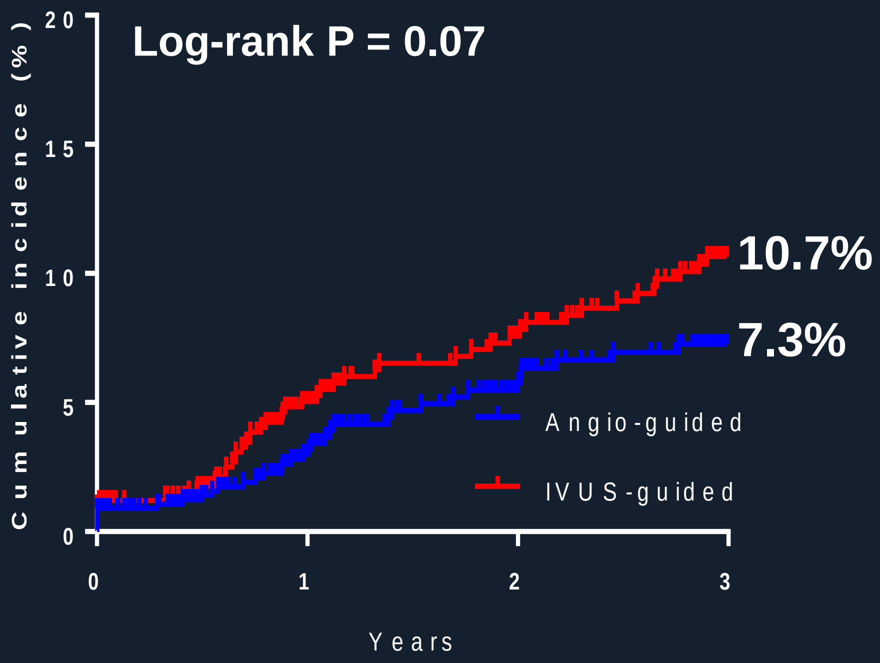
Clinical Impact of IVUS on ISR PCI

From IRIS-DES registry

Target vessel failure



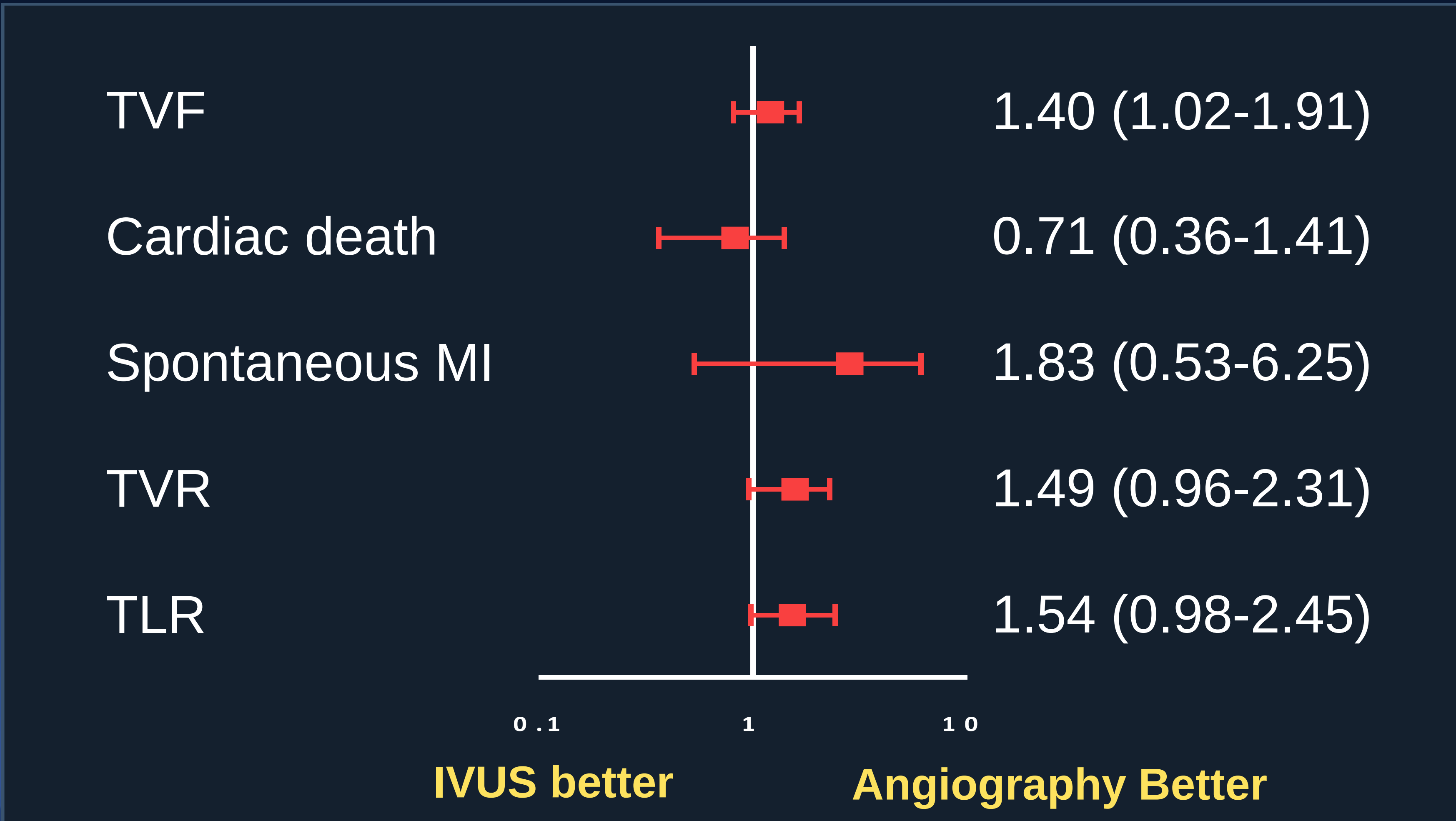
Target vessel Revascularization



IRIS-DES Registry, Preliminary data

Clinical Impact of IVUS on ISR PCI

Unadjusted Hazard Ratio at 3 years



IRIS-DES Registry, Preliminary data

Clinical Impact of IVUS on ISR PCI at 3 year

	Univariate		Multivariate		PS matching	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
TVF	1.16 (0.81-1.66)	0.434	1.14 (0.79-1.65)	0.496	1.14 (0.77-1.69)	0.526
Cardiac death	0.71 (0.36-1.41)	0.434	0.71 (0.34-1.49)	0.362	0.64 (0.29-1.45)	0.289
Target-vessel MI	1.83 (0.53-6.25)	0.336	1.58 (0.45-5.52)	0.477	1.62 (0.48-5.55)	0.44
TVR	1.49 (0.96-2.31)	0.076	1.51 (0.97-2.34)	0.069	1.46 (0.91-2.32)	0.116
TLR	1.54 (0.98-1.54)	0.064	1.56 (0.98-2.47)	0.059	1.53 (0.94-2.49)	0.089

*TVF: a composite of cardiac death, target-vessel spontaneous MI or TVR

IRIS-DES Registry, Preliminary data

IVUS-guidance was not associated with better long-term outcome in registry data,

Why?

- Selected patients (probably with high-risk lesions like LM ISR, recurrent ISR, undilatable ISR, ISR with complications after balloon) would underwent IVUS-guided PCI.

- Treatment strategy (High-pressure balloon + DEB or DES) would not differ with the findings of IVUS findings.
  Fracture / gaps can be visualized with angiography.

Conclusions
Imaging-guidance for ISR Treatment

- Intravascular Imaging (IVUS or OCT) in ISR patients can identify underlying mechanism and help to select optimal treatment modalities.
- Whether routing intravascular imaging for ISR treatment can improve outcome is not clear.

  A randomized controlled study is needed.