Effect of Intravascular Ultrasound-Guided vs. Angiography-Guided Everolimus-Eluting Stent Implantation: the IVUS-XPL Randomized Clinical Trial

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Hong SJ, Kim BK, Hong MK (corresponding author). *JAMA* 2015;314:2155-63 and 2015 AHA Late Breaking Clinical Trials

IVUS usage during PCI

- **Pre-intervention assessment**
  - ✓ Plaque morphology and calcium
  - ✓ Device selection

- **Post-intervention assessment**
  - ✓ Post-stent optimization
  - ✓ Immediate complications

Hong MK, Mintz GS, et al. Eur Heart J. 2006;27:1305-1310
Fujii K, Mintz GS, et al. Circulation. 2004;109:1085-1088
Mintz GS, J Am Coll Cardiol. 2014;64:207-22

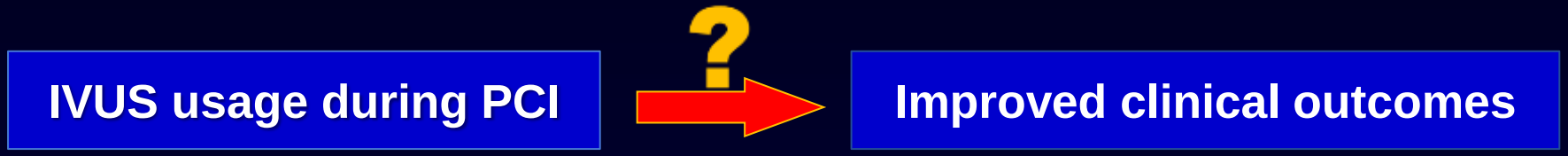
2014 ESC/EACTS Guidelines on myocardial revascularization

Recommendations	Class[a]	Level[b]	Ref.[c]
FFR to identify haemodynamically relevant coronary lesion(s) in stable patients when evidence of ischaemia is not available.	I	A	
FFR-guided PCI in patients with multivessel disease.	IIa	B	
IVUS in selected patients to optimize stent implantation.	IIa	B	702,703,706
IVUS to assess severity and optimize treatment of unprotected left main lesions.	IIa	B	705
IVUS or OCT to assess mechanisms of stent failure.	IIa	C	
OCT in selected patients to optimize stent implantation.	IIb	C	

Level of Evidence is B

Background

- **Clinical usefulness of IVUS**



  - There are no adequately powered randomized clinical trials to prove the clinical usefulness of IVUS for second-generation DESs.

- **Hypothesis**
  - The clinical outcomes of IVUS-guided second-generation DES implantation would be superior to those of angiography-guided DES implantation in a subset of patients with long coronary lesions.

Study Design

- A prospective, randomized, multi-center trial
- At 20 centers in Korea
- Enrollment period: Oct 2010 and July 2014

- Key inclusion criteria
  - Age 20 years or older
  - Patients with typical chest pain or evidence of myocardial ischemia
  - Non-emergent conditions
  - Stent length ≥ 28 mm based on angiographic estimation
  - Significant coronary artery stenosis (>50% based on visual estimate) considered for coronary revascularization with stent implantation

- Key exclusion criteria
  - Acute ST-segment elevation or MI within 48 hours
  - Age >80 years
  - Cardiogenic shock
  - Left ventricular ejection fraction <40%
  - Left main disease requiring PCI
  - Bifurcation lesion with 2-stent technique
  - Chronic total occlusion
  - Presence of previously implanted DES within 6 months
  - In-stent restenosis lesion

Study Design

Patients with long coronary lesions
(Implanted EES ≥28 mm in length)
N = 1400

EES implantation with IVUS guidance
n = 700

EES implantation with angiography guidance
n = 700

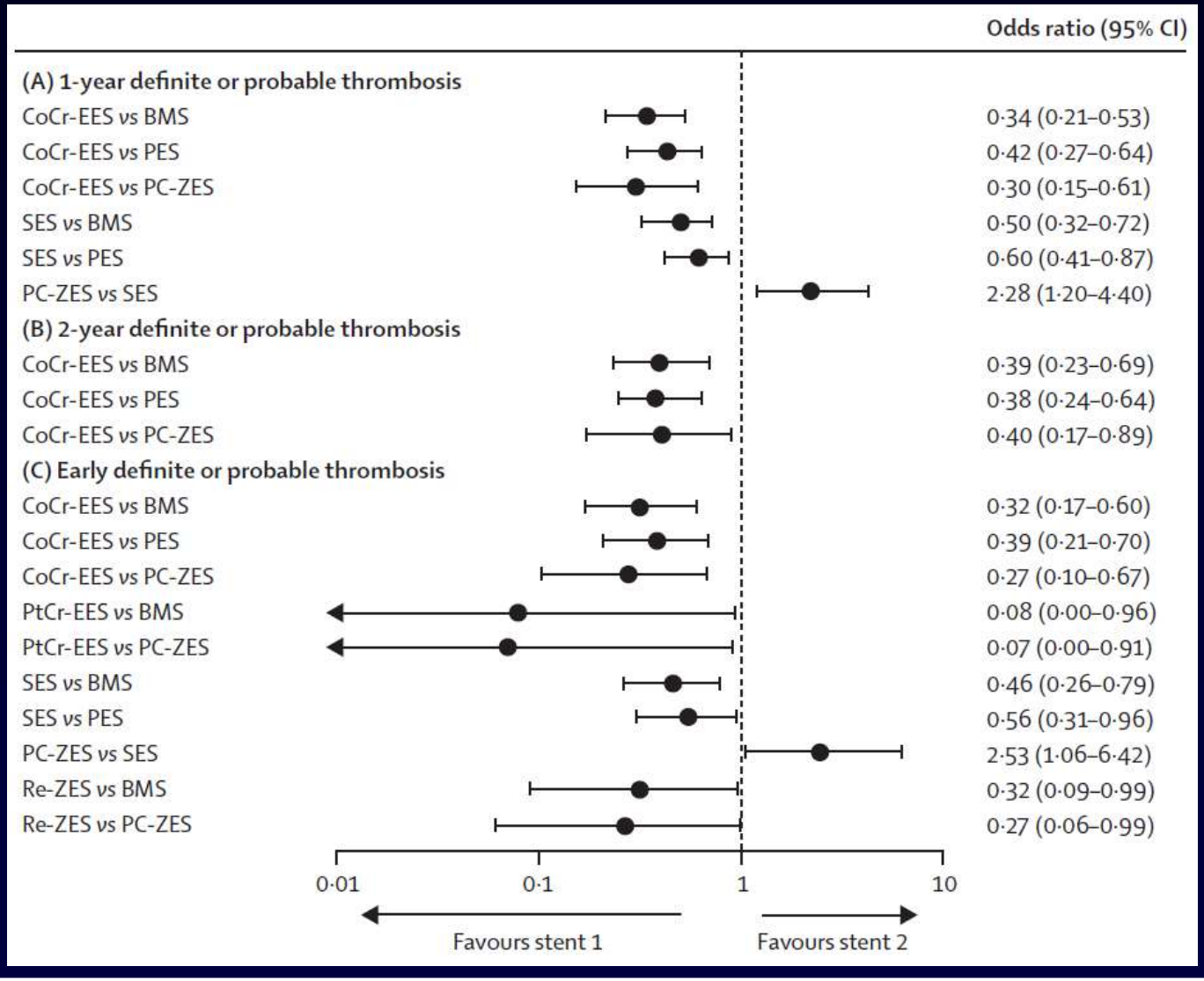
Clinical follow-up at 12 months

Primary end point: MACE

Cardiac death, target-lesion related MI, and ischemia-driven TLR

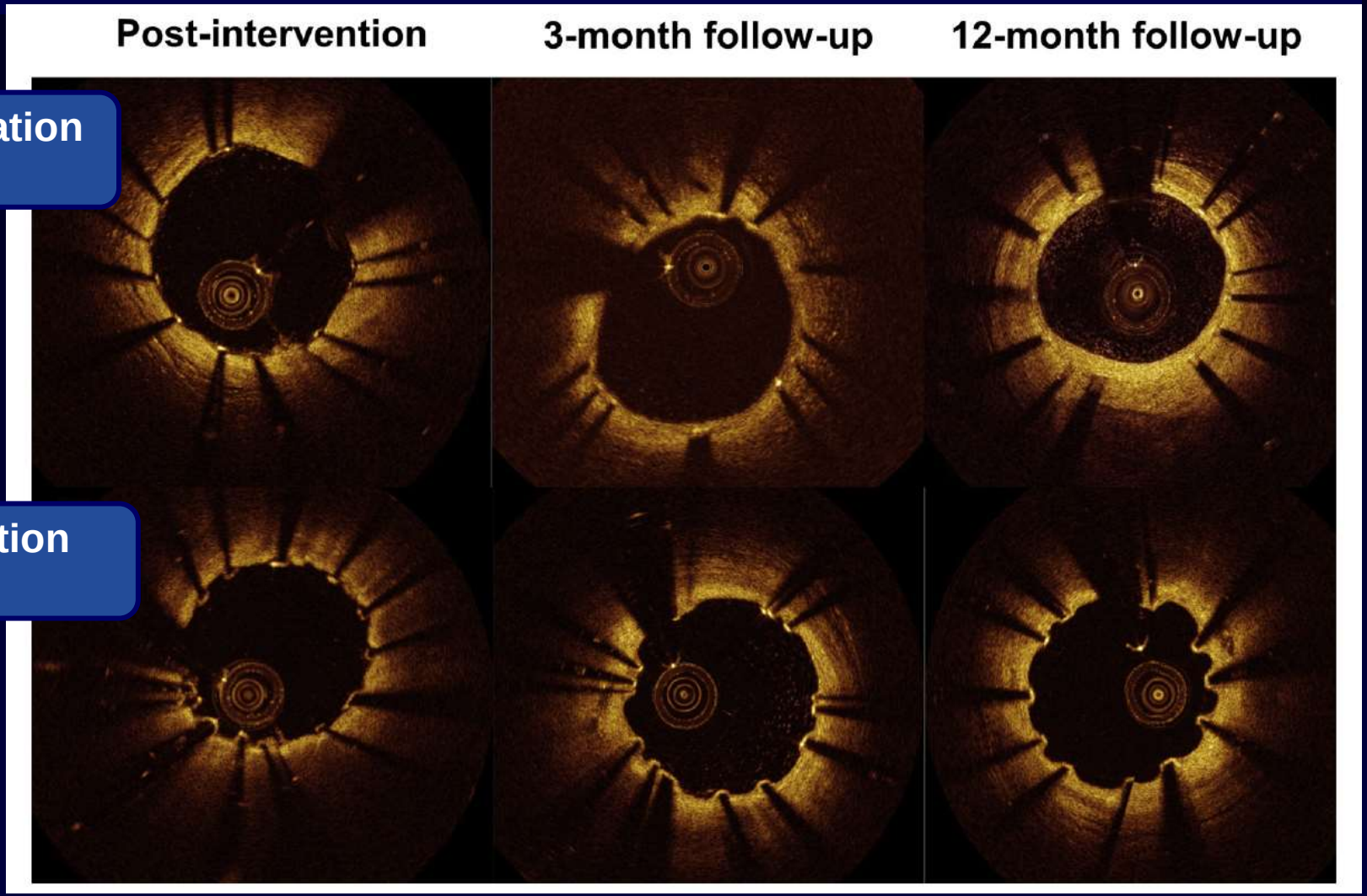
Trial Registration: clinicaltrial.gov Identifier: NCT01308281

Stent thrombosis (network meta-analysis) : EES is better



Palmerini T, et al. Lancet 2012;379:1393-1402

Different vascular healing pattern



Kim JS, Hong MK, et al. *Can J Cardiol*, 2015;31:723-730

Statistical Analysis

- **Sample size calculation**
  - Assumption the overall incidence of MACE to be 7% at the 1-year in the angiography-guidance arm.
  - Superiority comparison with an expected risk reduction of 50% in the IVUS-guidance arm (α=0.05, β=0.8, drop-out=5-10%)

  → Each 700 patients in the IVUS guidance arm and in the angiography guidance arm.

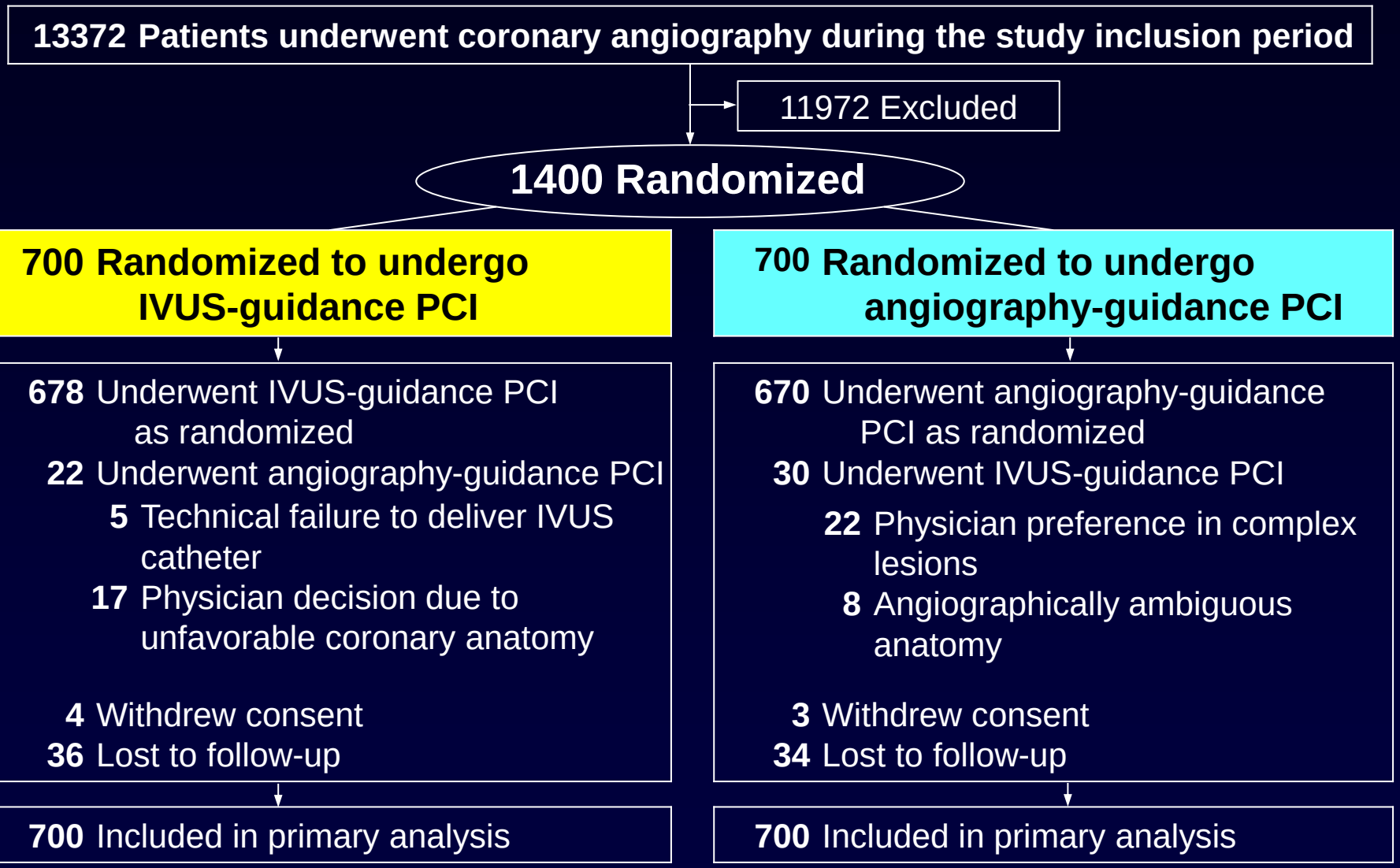
Turco MA, et al. *JACC Cardiovasc Interv.* 2008;1:699-709
Kim YH, et al. *Circulation.* 2006;114:2148-2153

- **Primary analysis**
  - Intention-to-treat analysis with cumulative incidences of MACE at 1 year using the Kaplan-Meier estimates.
  - Comparison using the log-rank test.

Procedure

- Criteria for stent optimization
  - ✓ IVUS-guidance arm
    - Minimal lumen CSA > lumen CSA at distal reference segments
  - ✓ Angiography-guidance arm
    - Angiographic residual diameter stenosis <30% and the absence of angiographically detected dissection

Study Flow


13372 Patients underwent coronary angiography during the study inclusion period
11972 Excluded
1400 Randomized
700 Randomized to undergo IVUS-guidance PCI
700 Randomized to undergo angiography-guidance PCI
678 Underwent IVUS-guidance PCI as randomized
22 Underwent angiography-guidance PCI
5 Technical failure to deliver IVUS catheter
17 Physician decision due to unfavorable coronary anatomy
4 Withdrew consent
36 Lost to follow-up
670 Underwent angiography-guidance PCI as randomized
30 Underwent IVUS-guidance PCI
22 Physician preference in complex lesions
8 Angiographically ambiguous anatomy
3 Withdrew consent
34 Lost to follow-up
700 Included in primary analysis
700 Included in primary analysis

Baseline Characteristics

Characteristics	IVUS-guidance	Angiography-guidance	*P* value
No. of patients	700	700	
Age, y	64 (9)	64 (9)	.54
Male sex	483 (69)	481 (69)	.91
Hypertension	454 (65)	444 (63)	.58
Diabetes mellitus	250 (36)	256 (37)	.74
Left ventricular ejection fraction, %	62.9 ± 9.8	62.4 ± 10.2	.33
Clinical presentation			.36
Stable angina	358 (51)	356 (51)	
Unstable angina	242 (35)	226 (32)	
Acute myocardial infarction	100 (14)	118 (17)	
No. of treated lesions per patients	1.34 (0.56)	1.36 (0.57)	.57
Duration of DAPT, days	365 (180, 365)	365 (180, 365)	.15
Coronary arteries			.14
Left anterior descending artery	455 (65)	419 (60)	
Left circumflex artery	96 (14)	108 (15)	
Right coronary artery	149 (21)	173 (25)	
Baseline QCA data			
Reference vessel diameter, mm	2.89 ± 0.45	2.85 ± 0.45	.13
Minimum lumen diameter, mm	0.83 ± 0.42	0.82 ± 0.43	.56
Diameter stenosis, %	71.1 ± 14.3	71.4 ± 14.4	.70
Lesion length, mm	34.7 ± 10.8	35.2 ± 10.5	.41
Stent length, mm	39.3 ± 13.1	39.2 ± 12.3	.90

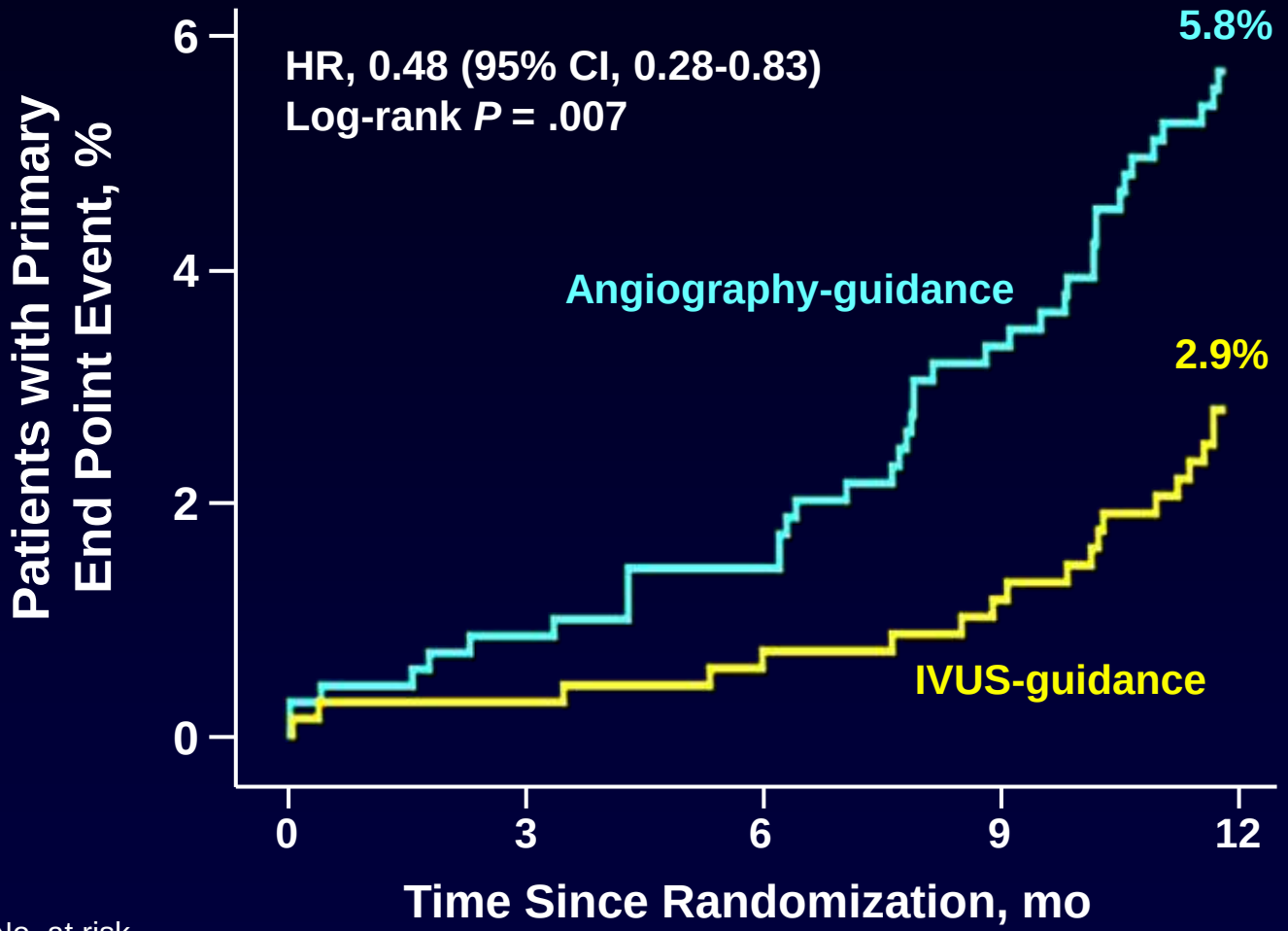
Angiographic and Procedural Characteristics

Characteristics	IVUS-guidance	Angiography-guidance	*P* value
Adjunct post-dilatation	534 (76)	402 (57)	<.001
Final balloon size, mm	3.14 ± 0.43	3.04 ± 0.42	<.001
Overlapping stent	145 (21)	138 (20)	.64
No. of stents per lesions	1.3 (0.5)	1.3 (0.5)	.48
Stent edge dissections	15 (2)	13 (2)	.70
Coronary perforation	0	0	1.00
Maximal inflation pressure, atm	16.5 ± 4.1	15.9 ± 4.1	.052
Post-intervention QCA data			
Reference vessel diameter, mm	3.03 ± 0.44	2.97 ± 0.43	.01
Minimum lumen diameter, mm	2.64 ± 0.42	2.56 ± 0.39	<.001
Diameter stenosis, %	12.79 ± 8.66	13.74 ± 8.05	.04

Clinical outcomes at 1 year

	IVUS-guidance (n=700)	Angiography-guidance (n=700)	Hazard ratio (95% CI)	Log-Rank *P* value
Primary End Point				
MACE	19 (2.9%)	39 (5.8%)	0.48 (0.28–0.83)	.007
Secondary End Point				
Cardiac death	3 (0.4%)	5 (0.7%)	0.60 (0.14-2.52)	.48
Target lesion related MI	0	1 (0.1%)	-	.32
Ischemia-driven TLR	17 (2.5%)	33 (5.0%)	0.51 (0.28-0.91)	.02
Stent thrombosis	2 (0.3%)	2 (0.3%)	1.00 (0.14-7.10)	1.00
Acute	1 (0.1%)	1 (0.1%)	-	-
Sub-acute	1 (0.1%)	0	-	-
Late	0	1 (0.1%)	-	-

Primary End Point



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

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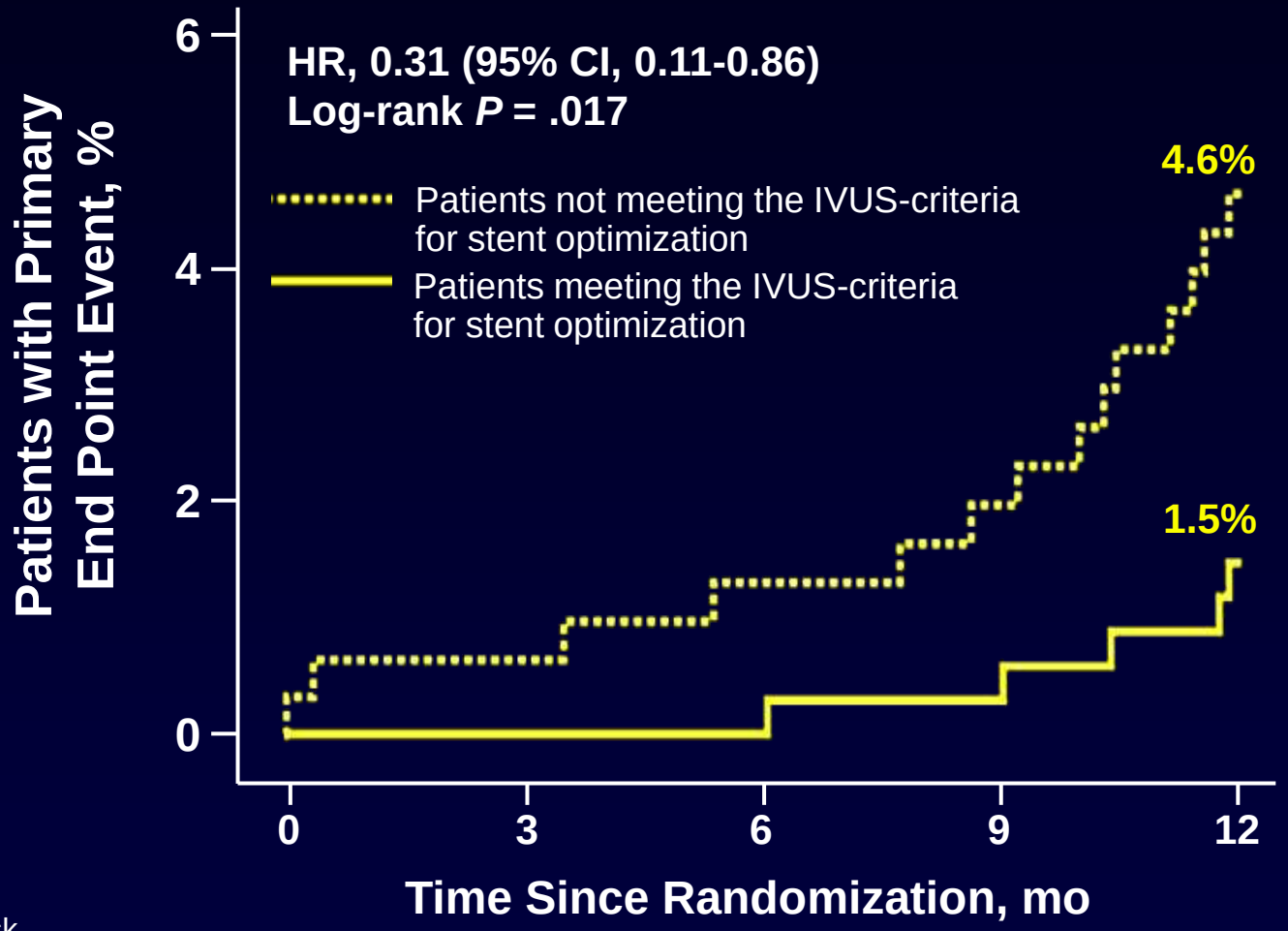
Post-intervention IVUS analysis in subgroup of IVUS guidance

Procedural and IVUS Characteristics	Patients meeting the IVUS criteria	Patients not meeting the IVUS criteria	*P* value
No. of patients	363	315	
Adjunct post-dilatation	282 (78)	237 (75)	.34
Final balloon size, mm	3.15 ± 0.45)	3.13 ± 0.42	.52
Maximal inflation pressure, atm	16.5 ± 3.9	16.4 ± 4.4	.87
Proximal reference EEM area, mm^2	17.52 ± 5.34	17.27 ± 5.04	.56
Proximal reference lumen area, mm^2	9.02 ± 3.51	8.86 ± 3.27	.57
Minimal lumen area, mm^2	6.09 ± 1.91	5.71 ± 1.71	.008
Distal reference EEM area, mm^2	9.44 ± 3.98	10.94 ± 3.83	<.001
Distal reference lumen area, mm^2	5.55 ± 1.82	6.83 ± 1.68	<.001

Primary End Point



No. at risk

Not meeting the criteria	315	299	297	394	285
Meeting the criteria	363	362	345	338	334

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Conclusions

- Among patients requiring long coronary stent implantation, the use of IVUS-guidance for DES implantation was associated with a significant 2.9% absolute reduction and 48% relative reduction in the risk of MACE at 1 year, compared with angiography-guidance.

- Our findings suggest better clinical outcomes of MACE with IVUS-guidance compared to angiography-guidance for DES implantation, particularly for diffuse long lesions.