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

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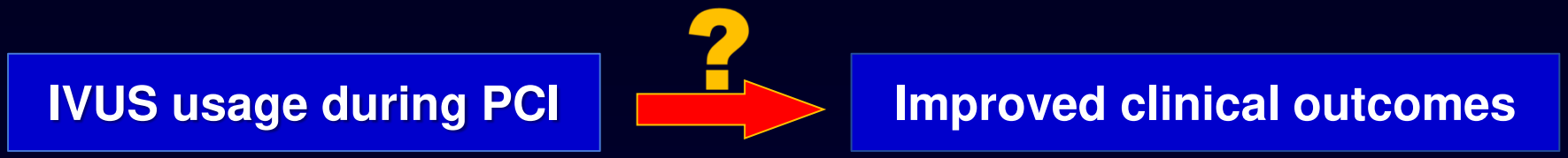
Background

- **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 stent ≥28 mm in length)
N = 1400

DES implantation with IVUS guidance
n = 700

DES 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

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	**670** Underwent angiography-guidance PCI as randomized
22 Underwent angiography-guidance PCI	**30** Underwent IVUS-guidance PCI
5 Technical failure to deliver IVUS catheter	**22** Physician preference in complex lesions
17 Physician decision due to unfavorable coronary anatomy	**8** Angiographically ambiguous anatomy
4 Withdrew consent	**3** Withdrew consent
36 Lost to follow-up	**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

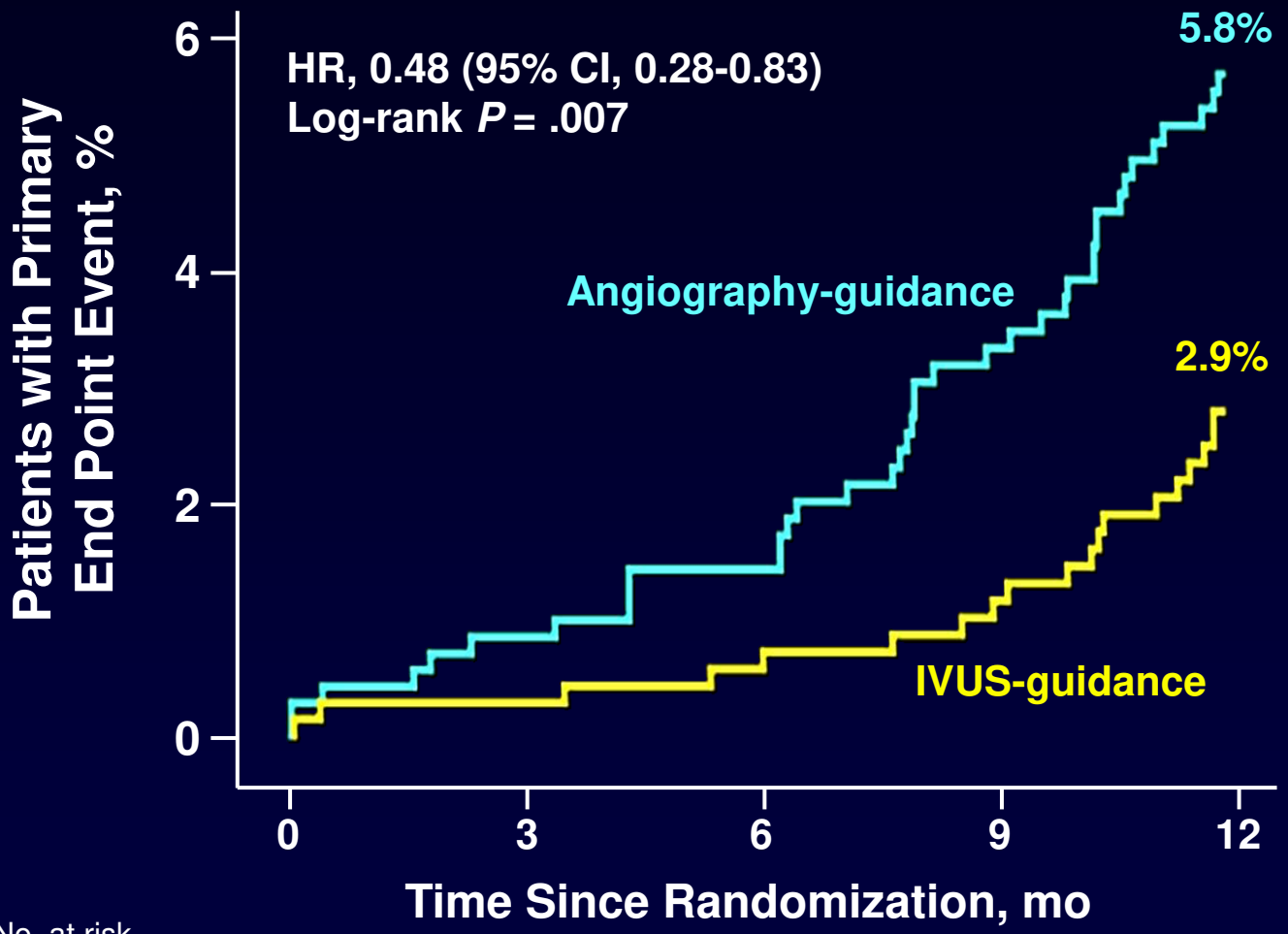
Angiographic and Procedural Characteristics

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

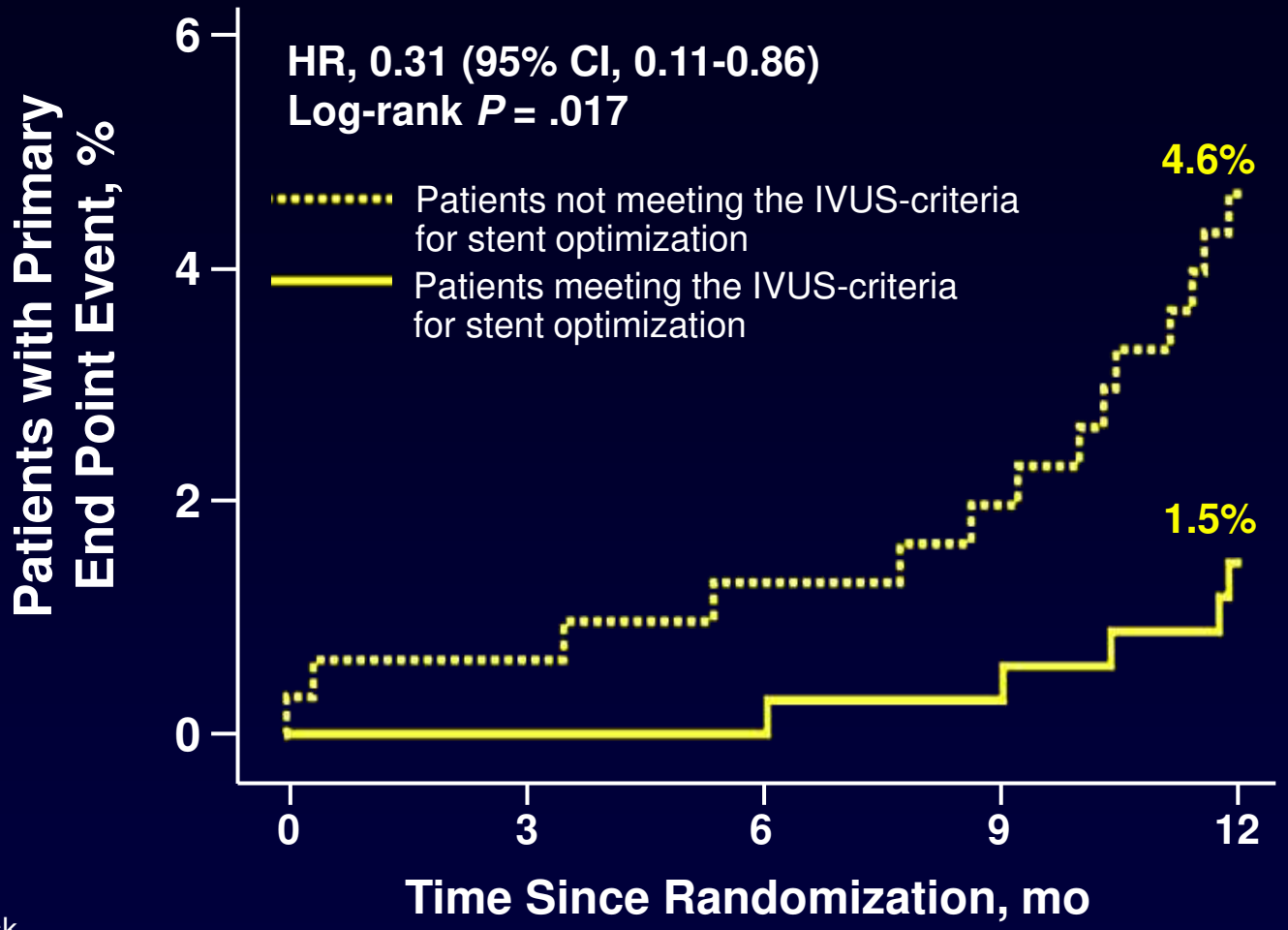


No. at risk					
Angiography arm	700	673	660	643	624
IVUS arm	700	671	665	654	641

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



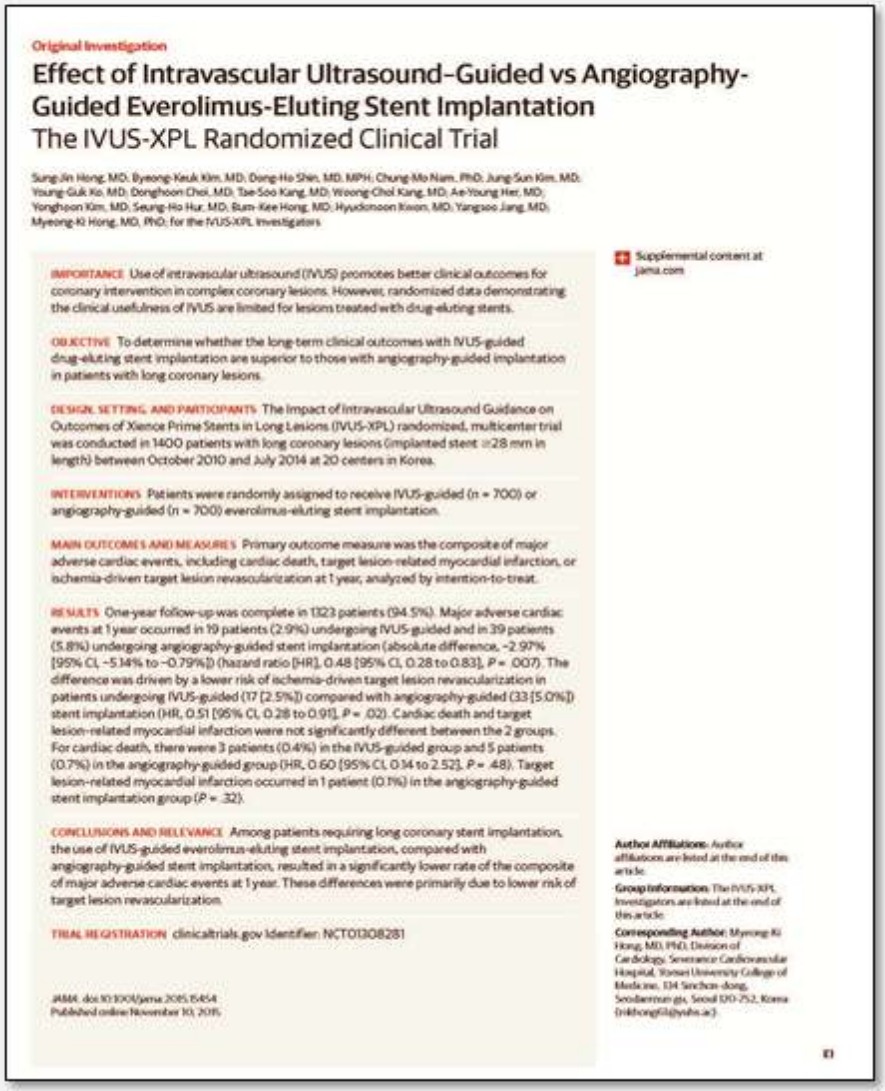
No. at risk

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

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.



Original Investigation

Effect of Intravascular Ultrasound–Guided vs Angiography-Guided Everolimus-Eluting Stent Implantation

The IVUS-XPL Randomized Clinical Trial

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Supplemental content at jama.com

IMPORTANCE Use of intravascular ultrasound (IVUS) promotes better clinical outcomes for coronary intervention in complex coronary lesions. However, randomized data demonstrating the clinical usefulness of IVUS are limited for lesions treated with drug-eluting stents.

OBJECTIVE To determine whether the long-term clinical outcomes with IVUS-guided drug-eluting stent implantation are superior to those with angiography-guided implantation in patients with long coronary lesions.

DESIGN, SETTING, AND PARTICIPANTS The Impact of Intravascular Ultrasound Guidance on Outcomes of Xience Prime Stents in Long Lesions (IVUS-XPL) randomized, multicenter trial was conducted in 1400 patients with long coronary lesions (implanted stent ≥28 mm in length) between October 2010 and July 2014 at 20 centers in Korea.

INTERVENTIONS Patients were randomly assigned to receive IVUS-guided (n = 700) or angiography-guided (n = 700) everolimus-eluting stent implantation.

MAIN OUTCOMES AND MEASURES Primary outcome measure was the composite of major adverse cardiac events, including cardiac death, target lesion-related myocardial infarction, or ischemia-driven target lesion revascularization at 1 year, analyzed by intention-to-treat.

RESULTS One-year follow-up was complete in 1323 patients (94.5%). Major adverse cardiac events at 1 year occurred in 19 patients (2.9%) undergoing IVUS-guided and in 39 patients (5.8%) undergoing angiography-guided stent implantation (absolute difference, −2.97% [95% CI, −5.14% to −0.79%]) (hazard ratio [HR], 0.48 [95% CI, 0.28 to 0.83], *P* = .007). The difference was driven by a lower risk of ischemia-driven target lesion revascularization in patients undergoing IVUS-guided (17 [2.5%]) compared with angiography-guided (33 [5.0%]) stent implantation (HR, 0.51 [95% CI, 0.28 to 0.91], *P* = .02). Cardiac death and target lesion-related myocardial infarction were not significantly different between the 2 groups. For cardiac death, there were 3 patients (0.4%) in the IVUS-guided group and 5 patients (0.7%) in the angiography-guided group (HR, 0.60 [95% CI, 0.14 to 2.52], *P* = .48). Target lesion-related myocardial infarction occurred in 1 patient (0.1%) in the angiography-guided stent implantation group (*P* = .32).

CONCLUSIONS AND RELEVANCE Among patients requiring long coronary stent implantation, the use of IVUS-guided everolimus-eluting stent implantation, compared with angiography-guided stent implantation, resulted in a significantly lower rate of the composite of major adverse cardiac events at 1 year. These differences were primarily due to lower risk of target lesion revascularization.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT01308281

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