Optical Coherence Tomography-Guided or Intravascular Ultrasound-Guided PCI : The OCTIVUS Randomized Clinical Trial

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Background

- Intracoronary imaging-guided PCI with intravascular ultrasound (IVUS) and optical coherence tomography (OCT) showed superior clinical outcomes compared to angiography-guided PCI.[1-4]
- Each intracoronary imaging modality has different imaging technologies, lesion applications, advantages, or limitations.[5]
- However, data on the comparative effectiveness of OCT or IVUS for PCI guidance for broad-range of patients with respect to relevant clinical outcomes are still limited.[6-7]

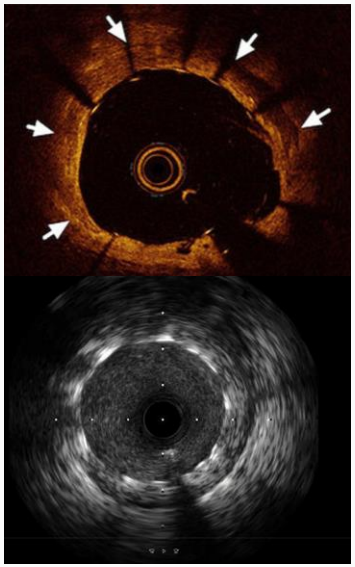
PCI, percutaneous coronary intervention

[1]Hong SJ, et al. *JAMA* 2015;314:2155-63. [2]Kim BK, et al. *Circ Cardiovasc Interv* 2015;8. [3]Zhang J, et al. *J Am Coll Cardiol* 2018;72:3126-37. [4]Lee JM, et al. *New Engl J Med* 2023;388:1668-79. [5]Schlofmitz E, et al. *Circ Cardiovasc Interv* 2020;13. [6]Ali ZA, et al. *Lancet* 2016;388. [7]Kubo T, et al. *Eur Heart J* 2017;38.

Background: Current Guidelines

- Recommendations for intravascular imaging for PCI optimization

Recommendations	Class[a]	Level[b]
IVUS or OCT should be considered in selected patients to optimize stent implantation.[603,612,651–653]	IIa	B
IVUS should be considered to optimize treatment of unprotected left main lesions.[35]	IIa	B



OCT

IVUS

IVUS, intravascular ultrasound; OCT, optical coherence tomography

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

Objective

- To *compare the clinical efficacy and safety of OCT-guided and IVUS-guided strategies* in patients who underwent PCI for significant CAD.

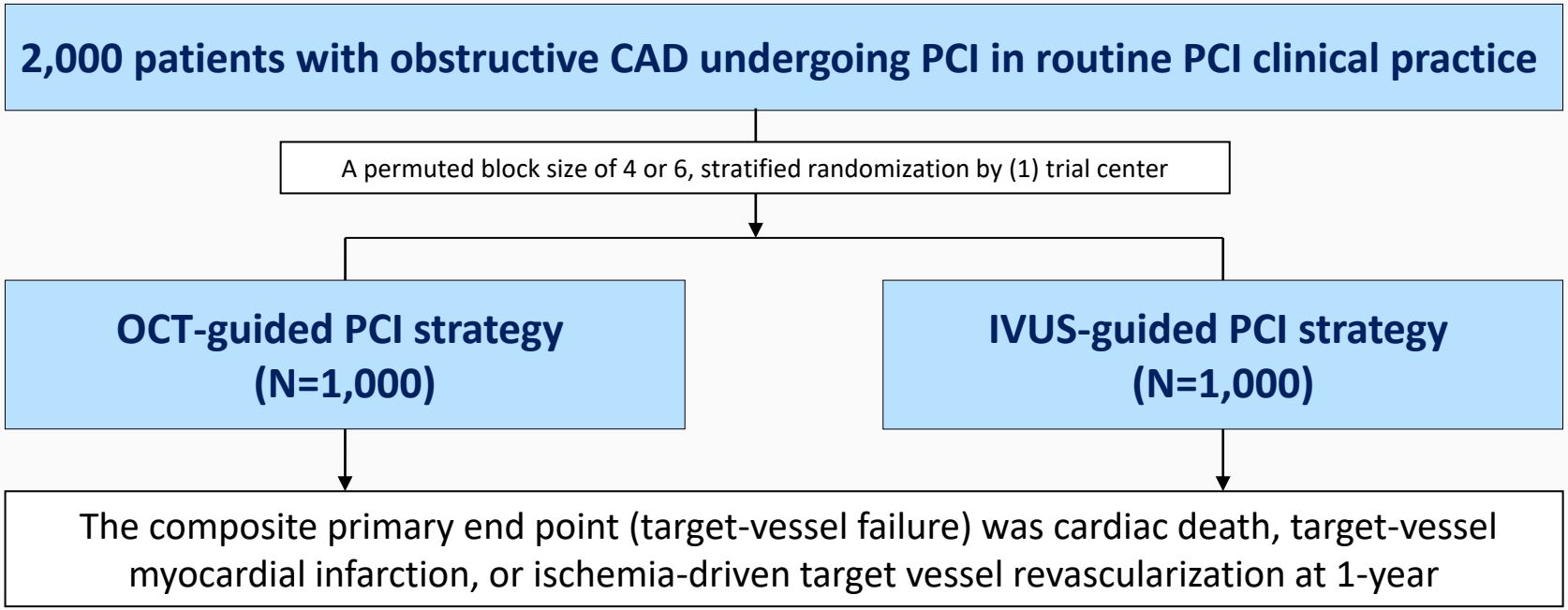
- We hypothesize that *OCT-guided PCI is noninferior to IVUS-guided PCI* with respect to target-vessel failure at 1 year.

Kang DY, Park DW et al. *Am Heart J* 2020;228:72-80

Pragmatic Trial Design

Optical Coherence Tomography–guided versus IntraVascular UltraSound–guided percutaneous coronary intervention

OCTIVUS Trial



Kang DY, Park DW et al. *Am Heart J* 2020;228:72-80

Inclusion and Exclusion Criteria

INCLUSION

1. Men or women at least age ≥ 19 years.
2. Patients with obstructive coronary artery disease (native or restenotic) undergoing PCI with contemporary drug-eluting stents or drug-coated balloons (only for in-stent restenotic lesion) under intracoronary imaging guidance.
3. The patient or guardian agreed to the study protocol and the schedule for clinical follow-up, and provided informed written consent, as approved by the appropriate Institutional Review Board/Ethical Committee of the respective clinical site.

EXCLUSION

1. ST-elevation myocardial infarction.
2. Severe renal dysfunction (eGFR <30 mL/min/1.73 m^2), unless patient is on renal replacement therapy.
3. Cardiogenic shock or decompensated heart failure with severe left ventricular dysfunction (left ventricular ejection fraction < 30%).
4. Life expectancy < 1 years for any non-cardiac or cardiac causes.
5. Any lesion characteristics resulting in the expected inability to deliver the intracoronary imaging catheter during PCI (e.g., severe vessel calcification or tortuosity).

PCI, percutaneous coronary intervention

Kang DY, Park DW et al. *Am Heart J* 2020;228:72-80

Imaging-guided PCI

- PCI procedure was performed using standard techniques.
- In each group, either IVUS (Opticross™ or Opticross™ HD, Boston Scientific, CA) or OCT (C7-XR™ and OPTIS™, Abbott, CA) was used before, during, and immediately after PCI; *a final imaging assessment for PCI optimization was mandated.*
- Stent size, length, and optimization of the stented segment was determined with the use of a predefined common algorithm for IVUS or OCT on the basis of EAPCI expert consensus.[1]
- A distal lumen or external elastic membrane reference-based stent sizing strategy was used and a sufficient stent expansion of more than 80% of the mean reference lumen area with avoiding major stent malapposition or edge dissection was achieved.
- All intravascular imaging data were measured by the independent imaging core laboratories (the Asan Medical Center, Core-lab).

[1]Raber L, et al. *Eur Heart J* 2018;39:3281-3300.

Endpoints

Primary endpoint

- Target-vessel failure (a composite of death from cardiac cause, target vessel-MI, or ischemia-driven target-vessel revascularization) at 1 year after randomization

Secondary endpoints

- Individual components of the primary composite outcome
- Target-lesion failure*
- Stent thrombosis
- Stroke
- Repeat revascularization
- Rehospitalization
- Bleeding events
- Contrast-induced acute kidney injury
- Procedural complications requiring active intervention

MI, myocardial infarction

*Target-lesion failure was a composite of death from cardiac causes, target-vessel MI, or ischemia-driven target-lesion revascularization.

Statistical Considerations

Power Calculation (N = 2,000)

- Assuming a 1-year event rate of 8.0% in the IVUS-guided PCI group
- Statistical power of 80% to detect noninferiority of OCT-guided PCI group with 3.1% of noninferiority margin in primary endpoint (which represented 39% of the expected percentage of patients with an event)
- Calculated with the likelihood-score method by Farrington and Manning at a one-sided type I error of 0.05

Pre-Specified Statistical Analysis

- Primary intention-to-treat analysis
- Kaplan-Meier estimates for calculating cumulative event rates
- Cox proportional hazard models
  - Estimate the relative risks if proportional hazards assumption is not violated
- Sensitivity analysis
  - Sensitivity analyses in the per-protocol and as-treated populations
  - The interaction term between randomized groups and key subgroups was evaluated for primary outcome.

Participating Investigators and Trial Organization

Participating Investigators (9 Sites in South Korea)

Do-Yoon Kang, Jung-Min Ahn, Sung-Cheol Yun, Hoyun Kim, Yeonwoo Choi, Jinho Lee, Duk-Woo Park, Seung-Jung Park (Asan Medical Centers); Seung-Ho Hur, Yun-Kyeong Cho, Cheol Hyun Lee (Keimyung University Dongsan Hospital); Soon Jun Hong, Subin Lim (Korea University Anam Hospital); Sang-Wook Kim, Hoyoun Won (Chung-Ang University Hospital); Jun-Hyok Oh, Jeong Cheon Choe (Pusan National University Hospital); Young Joon Hong (Chonnam National University Hospital); Young Won Yoon (Gangnam Severance Hospital); Soo-Joong Kim (Kyunghee University College of Medicine); Jang-Ho Bae (Konyang University Hospital).

Executive Committee

Duk-Woo Park (Trial PI) Seung-Jung Park (Trial Co-PI) Do-Yoon Kang Jung-Min Ahn

Additional Steering Committee

Seung-Ho Hur Cheol Hyun Lee Soon Jun Hong Sang-Wook Kim

Event Adjudication Committee

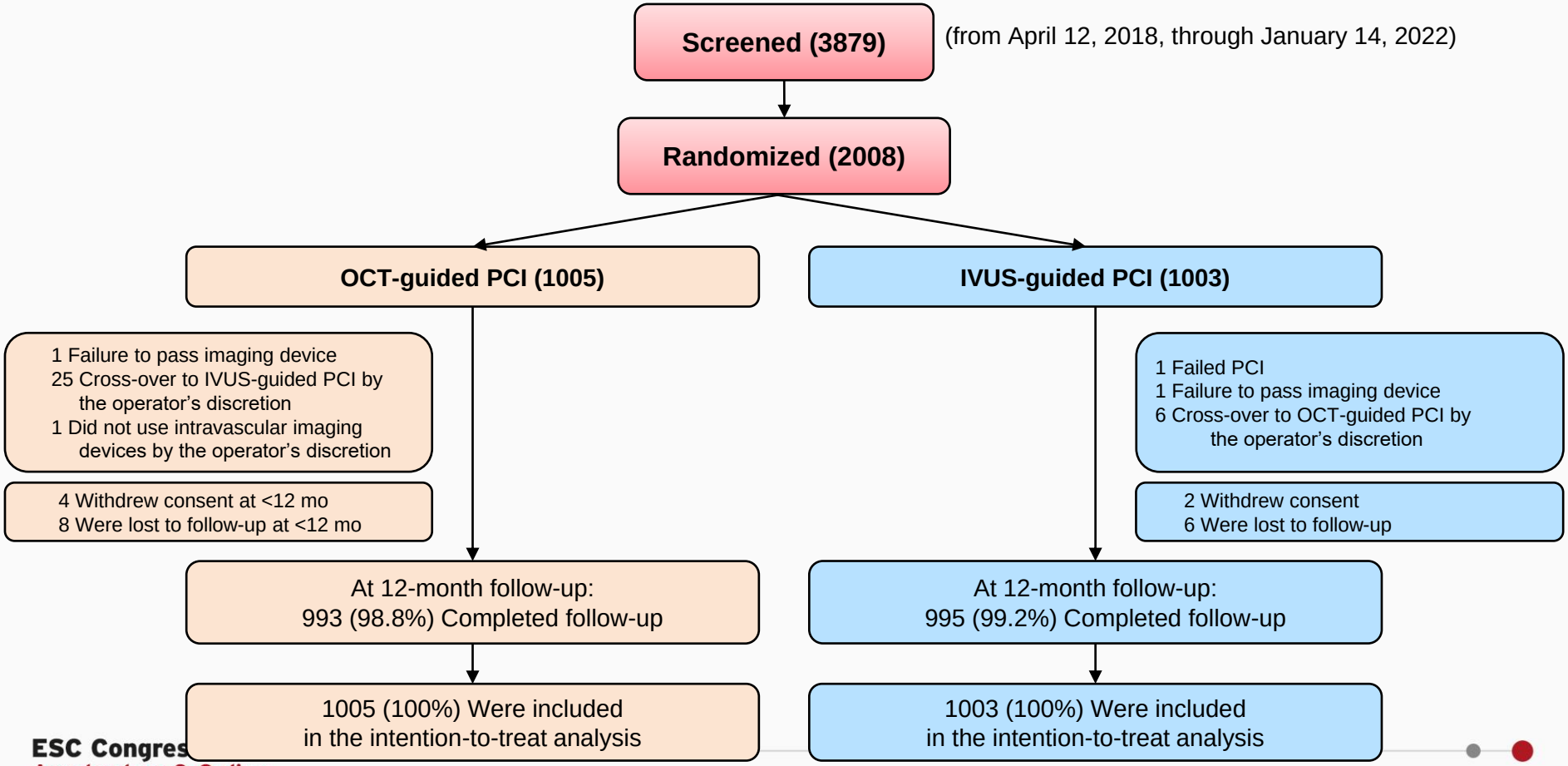
Hanbit Park Junghoon Lee Ju Hyeon Kim
Ha Hye Jo Joong Min Lee Do-Hyeon Kim

Data & Safety Monitoring Board

Jong-Min Song So-Yeon Choi Byeong-Keuk Kim
Mineok Jang Elly Jeong-youn Bae

Trial Funding CardioVascular Research Foundation (CVRF) Abbott Vascular Medtronic

Patient Flow and Follow-Up



Key Baseline Characteristics

	OCT-Guided PCI (N = 1005)	IVUS-Guided PCI (N = 1003)
Age [yrs], mean (SD)	64.3 (10.3)	65.1 (10.5)
Female sex	215 (21.4)	218 (21.7)
Body-mass index	24.9±3.2	25.0±3.1
Diabetes mellitus — no. (%)	325 (32.3)	345 (34.4)
Hypertension — no. (%)	647 (64.4)	639 (63.7)
Dyslipidemia — no. (%)	840 (83.6)	841 (83.9)
Current smoking — no. (%)	217 (21.6)	189 (18.8)
Previous PCI — no. (%)	226 (22.5)	202 (20.1)
Previous CABG — no. (%)	33 (3.3)	18 (1.8)
Previous stroke — no. (%)	66 (6.6)	73 (7.3)
Atrial fibrillation — no. (%)	28 (2.8)	38 (3.8)
End-stage renal disease on dialysis — no. (%)	20 (2.0)	26 (2.6)
Left ventricular ejection fraction [%], mean (SD)	58.8 (9.1)	58.3 (10.1)
Clinical indication for index PCI — no. (%)		
Silent ischemia	106 (10.6)	115 (11.5)
Stable angina	663 (66.0)	654 (65.2)
Acute coronary syndrome	236 (23.5)	234 (23.3)
Unstable angina	137 (13.6)	135 (13.5)
NSTEMI	99 (9.9)	99 (9.9)

Anatomical Characteristics

	OCT-Guided PCI (N = 1005)	IVUS-Guided PCI (N = 1003)
Multivessel disease — no. (%)	608 (60.5)	629 (62.7)
Treated complex coronary lesions — no. (%)		
Left main disease	116 (11.5)	148 (14.8)
Any bifurcation disease — no. (%)	516 (51.3)	540 (53.8)
Ostial lesion — no. (%)	96 (9.6)	99 (9.9)
Chronic total occlusion — no. (%)	56 (5.6)	52 (5.2)
Severely calcified lesion — no. (%)†	76 (7.6)	76 (7.6)
In-stent restenotic lesion — no. (%)	87 (8.7)	77 (7.7)
Diffuse long lesion — no. (%)‡	575 (57.2)	594 (59.2)
Bypass graft disease — no. (%)	3 (0.3)	0 (0.0)
SYNTAX score		
Mean	15.1±8.9	15.8±9.5
Category — no./total no. (%)		
Low, 0 to 22	813 (80.9)	773 (77.1)
Intermediate, 23 to 32	141 (14.0)	173 (17.3)
High, >32	51 (5.1)	57 (5.7)

† Those with encircling calcium seen on angiography ‡ Lesion length ≥28 mm or stent length ≥32 mm of treated segment
SYNTAX, Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery.

Procedural Characteristics

	OCT-Guided PCI (N = 1005)	IVUS-Guided PCI (N = 1003)	P Value
PCI approach			0.99
Radial access	639 (63.6)	638 (63.6)	
Femoral access	366 (36.4)	365 (36.4)	
PCI modality			
Use of drug-eluting stents	970 (96.5)	973 (97.1)	0.45
Used of drug-coated balloons (only for ISR lesion)	35 (3.5)	29 (2.9)	
Mean number of stents per patient	1.6±1.0	1.6±1.0	0.38
Total stent length per patient — mm	47.2±32.4	47.8±32.2	0.69
Post-dilatation with larger or high-pressure balloon — no. (%)	931 (92.6)	917 (91.5)	0.35
Total amount of contrast media used — mL	238.3±112.4	199.8±109.7	<0.001
Total PCI time — min	46.1±23.6	48.9±25.1	<0.001

ISR, In-stent restenosis.

Procedural Outcomes

	OCT-Guided PCI (N = 1005)	IVUS-Guided PCI (N = 1003)	P Value
Procedural success — no. (%)			
Angiography-based‖	993 (98.8)	990 (98.7)	0.84
Imaging-based†	476 / 986 (48.3)	546 / 995 (54.9)	0.003
Procedural complications requiring active intervention — no. (%)‡			
Any	22 (2.2)	37 (3.7)	0.047
IVUS or OCT procedure related complications	0 (0)	0 (0)	

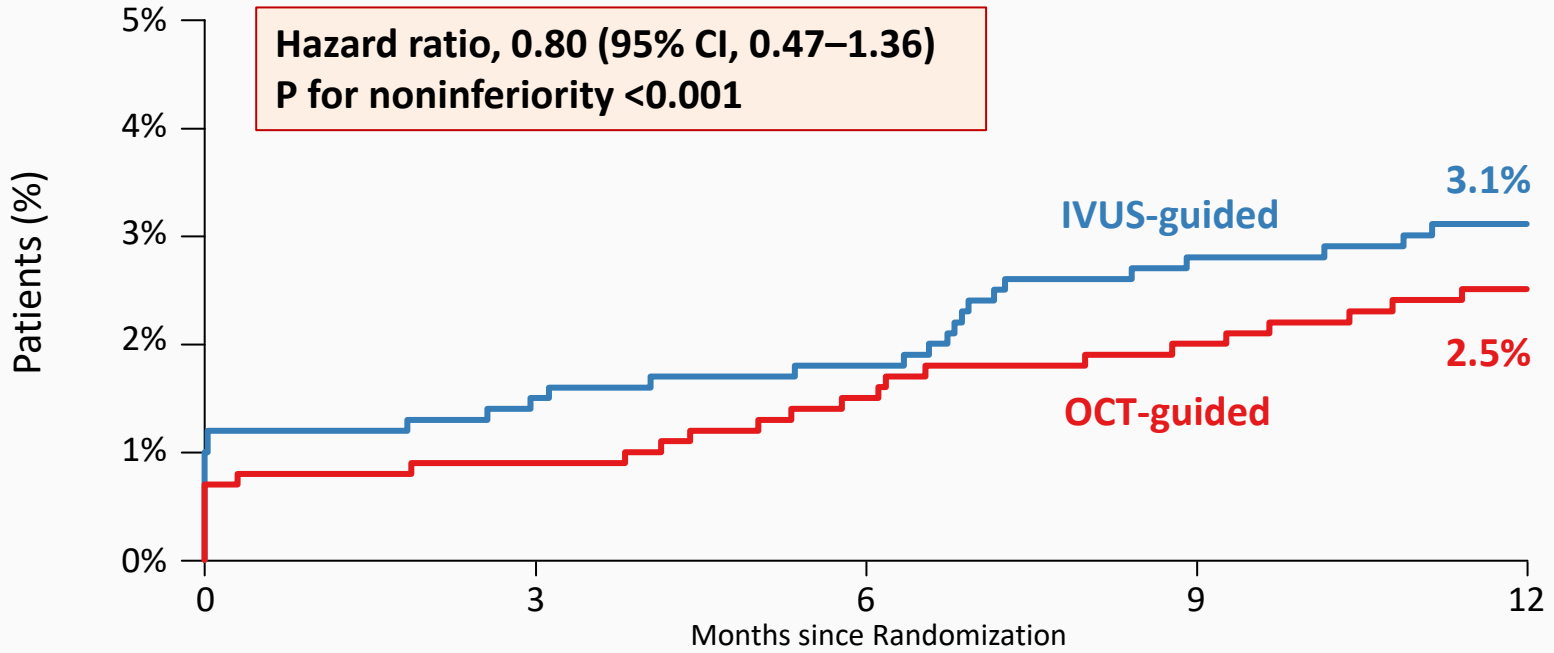
‖ Angiographic device success is defined as successful PCI at the intended target lesion with final in-stent residual stenosis of less than 30% by quantitative coronary angiography.
† By patient-level analyses: imaging-based device success is defined as successful PCI at the intended target lesion, which fulfills all optimal criteria for stent implantation by IVUS or OCT. Among patients with multivessel interventions, all treated lesions should be met for optimization criteria.
‡ Procedural complications requiring active intervention, which were related to PCI or use of intravascular imaging (i.e., procedural safety outcomes).

Core Lab-Imaging Analysis : Lesion-Level Analysis

	OCT-Guided PCI (N = 1005 Patients) (N = 1279 Lesions)	IVUS-Guided PCI (N = 1003 Patients) (N = 1271 Lesions)	P Value
Core Lab Imaging analysis – final post-PCI			
Minimum stent area — mm^2	5.60 ± 2.01	6.70 ± 2.37	<0.001
Minimum stent expansion — %	85.36 ± 17.49	91.37 ± 22.31	<0.001
Minimum stent area by distal reference lumen area — %	134.81 ± 47.75	126.04 ± 39.12	<0.001
Optimization Imaging-Guided PCI Criteria			
All stent-optimization criteria met — no./total no. (%)	613 / 1148 (53.4%)	743 / 1236 (60.1%)	0.001
Optimal stent expansion†	712 / 1148 (62.0%)	860 / 1236 (69.6%)	<0.001
Plaque burden at stent landing zone < 50%	708 / 800 (88.5%)	1016 / 1186 (85.7%)	0.07
No major malapposition§	1059 / 1147 (92.3%)	1209 / 1235 (97.9%)	<0.001
No large dissection¶	1114 / 1141 (97.6%)	1222 / 1231 (99.3%)	0.001

†Optimal stent expansion was defined as a relative stent expansion of >80% (an in-stent minimum stent area divided by average reference lumen area). In lesions with non-evaluable reference lumen area, optimal stent expansion was defined as an absolute in-stent minimum stent area of >5.5 mm^2 by IVUS and >4.5 mm^2 by OCT.
§ Extensive stent malapposition was defined as an acute stent malapposition of ≥0.4 mm with longitudinal extension >1 mm of the stent over its entire length against the vessel wall.
¶ Large dissection was defined as a dissection that occurred 5mm from the edge of the stent, extended to extensive lateral >60º, longitudinal extension >2mm, and flap extending to media or adventitia.

Primary Endpoint of TVF: Cardiac Death, TV-MI, or TVR



No. at Risk					
OCT-guided PCI	1005	990	984	979	912
IVUS-guided PCI	1003	985	981	969	893

CI, confidence interval; TV-MI, target-vessel myocardial infarction; TVR, target-vessel revascularization

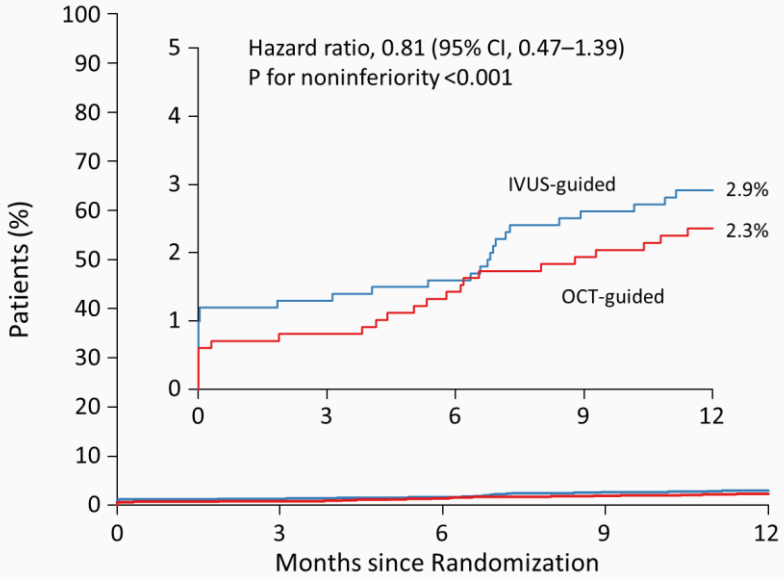
Types of CV Outcomes

Outcome*	OCT-Guided PCI (N = 1005)	IVUS-Guided PCI (N = 1003)	Risk Difference (95% CI)	HR (95% CI)†
Primary composite outcome‡	25 (2.5%)	31 (3.1%)	−0.6 (−2.0 to 0.8)	0.80 (0.47 to 1.36)
Secondary outcomes				
Target-lesion failure§	22 (2.2%)	29 (2.9%)	−0.7 (−2.1 to 0.7)	0.76 (0.43 to 1.31)
Death	10 (1.0%)	14 (1.4%)	−0.4 (−1.4 to 0.6)	0.71 (0.32 to 1.60)
From cardiac cause	3 (0.3%)	6 (0.6%)	−0.3 (−0.9 to 0.3)	0.71 (0.32 to 1.60)
From noncardiac cause	7 (0.7%)	8 (0.8%)	−0.1 (−0.9 to 0.6)	0.87 (0.32 to 2.40)
Target-vessel myocardial infarction	9 (0.9%)	14 (1.4%)	−0.5 (−1.4 to 0.4)	0.64 (0.28 to 1.48)
Periprocedural	7 (0.7%)	11 (1.1%)	−0.4 (−1.2 to 0.4)	0.64 (0.25 to 1.64)
Spontaneous	2 (0.2%)	3 (0.3%)	−0.1 (−0.5 to 0.3)	0.67 (0.11 to 3.98)
Target-lesion revascularization	11 (1.1%)	14 (1.4%)	−0.3 (−1.3 to 0.7)	0.78 (0.36 to 1.72)
Target-vessel revascularization	14 (1.4%)	16 (1.6%)	−0.2 (−1.3 to 0.9)	0.87 (0.43 to 1.79)
Contrast-induced nephropathy — no. (%)**	14 (1.4%)	15 (1.5%)	−0.1 (−1.1 to 0.9)	0.93 (0.45 to 1.91)
Stent thrombosis (ARC definite or probable)	0	2 (0.2%)	NA	NA

*The percentages were estimated by the Kaplan–Meier estimates. †Hazard ratios are for the OCT-guided PCI group, as compared with the IVUS-guided PCI group by use of Cox proportional hazard models. ‡The primary composite outcome was death from cardiac cause, target-vessel myocardial infarction, or target vessel revascularization. §Target-lesion failure was a composite of death from cardiac causes, target-vessel MI, or ischemia-driven target-lesion revascularization. ** Contrast-induced nephropathy was defined as either a greater than 25% increase of serum creatinine or an absolute increase in serum creatinine of 0.5 mg/dL from baseline within 72 h after the index PCI procedure.
CI, confidence interval; HR, hazard ratio; NA, not available; PCI, percutaneous coronary intervention

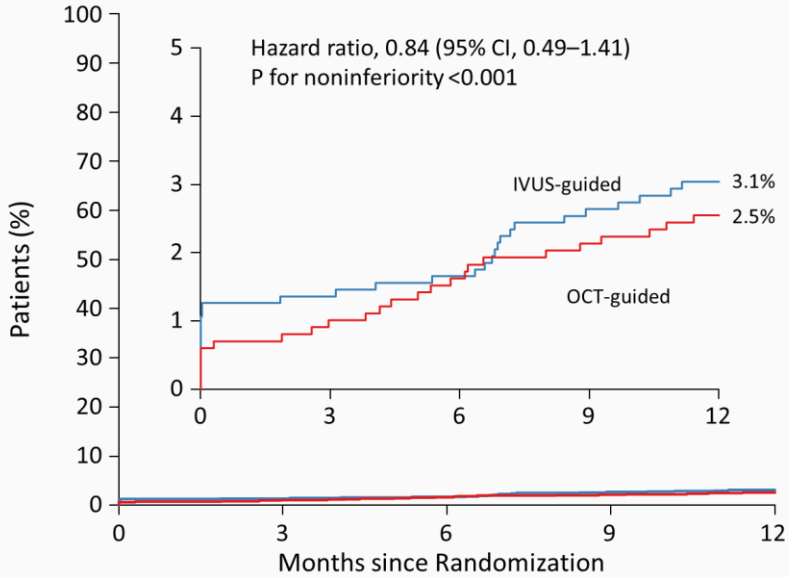
Sensitivity Analysis

Primary Endpoint in the Per-Protocol Population



No. at Risk					
OCT-guided PCI	980	966	960	955	889
IVUS-guided PCI	997	981	977	965	889

Primary Endpoint in the As-Treated Population

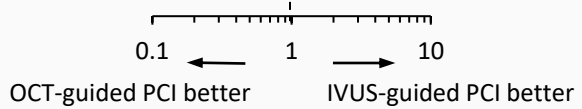


No. at Risk					
OCT-guided PCI	986	970	964	959	893
IVUS-guided PCI	1022	1005	1001	989	912

Prespecified Key Subgroups Analysis:

by Clinical Factors

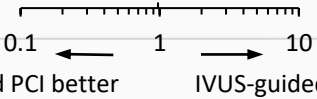
Subgroup	Percent of Patients	Estimated 1-Yr Event Rate (%)		Hazard Ratios (95% CI)	P-for-Interaction
		OCT-guided	IVUS-guided		
Age					0.419
< 65	48.2	2.3	2.1	1.07 (0.45 to 2.51)	
≥ 65	51.8	2.8	4.0	0.68 (0.35 to 1.34)	
Sex					0.212
Female	21.6	2.3	5.1	0.46 (0.16 to 1.31)	
Male	78.4	2.6	2.6	0.99 (0.53 to 1.85)	
Diabetes mellitus					0.222
Yes	33.4	4.4	3.8	1.14 (0.54 to 2.43)	
No	66.6	1.6	2.8	0.59 (0.28 to 1.25)	
Acute coronary syndrome					0.710
Yes	23.4	3.0	4.3	0.69 (0.26 to 1.81)	
No	76.6	2.4	2.7	0.86 (0.46 to 1.61)	
Left ventricular ejection fraction					0.847
≤ 50%	11.2	6.3	8.1	0.78 (0.26 to 2.38)	
> 50%	88.8	2.0	2.9	0.69 (0.35 to 1.34)	



Prespecified Key Subgroups Analysis:

by Anatomical Factors

Subgroup	Percent of Patients	Estimated 1-Yr Event Rate (%)		Hazard Ratios (95% CI)	P-for-Interaction
		OCT-guided	IVUS-guided		
Left main disease					0.868
Yes	13.2	5.3	6.8	0.78 (0.28 to 2.16)	
No	86.9	2.2	2.5	0.87 (0.47 to 1.61)	
Bifurcation disease					0.901
Yes	52.6	3.1	3.7	0.83 (0.43 to 1.61)	
No	47.4	1.9	2.4	0.78 (0.32 to 1.87)	
Diffuse long coronary artery lesion					0.077
Yes	58.2	3.3	2.9	1.15 (0.60 to 2.22)	
No	41.8	1.4	3.4	0.41 (0.16 to 1.05)	
Severely calcified lesion					0.149
Yes	7.6	7.9	8.1	1.36 (0.60 to 3.07)	
No	92.4	2.1	2.7	0.61 (0.31 to 1.23)	
Multivessel disease					0.547
Yes	61.6	3.2	4.2	0.75 (0.42 to 1.36)	
No	38.4	1.5	1.4	1.13 (0.35 to 3.71)	
SYNTAX score					0.096
Low	79.0	1.5	2.9	0.52 (0.26 to 1.04)	
Intermediate	15.6	5.7	3.5	1.63 (0.57 to 4.70)	
High	5.4	9.9	5.3	1.93 (0.46 to 8.06)	



CV Outcomes during the Entire Follow-up Period (Median 2.0 years; range 1.0-4.8 years)

Outcome*	OCT-Guided PCI (N = 1005)	IVUS-Guided PCI (N = 1003)	HR (95% CI)†
Primary composite outcome‡	**58 (5.8%)**	**61 (6.1%)**	**0.91 (0.63 to 1.30)**
Secondary outcomes			
Target-lesion failure§	50 (5.0%)	56 (5.6%)	0.85 (0.58 to 1.25)
Death	28 (2.8%)	27 (2.7%)	0.99 (0.58 to 1.69)
From cardiac cause	11 (1.1%)	11 (1.1%)	0.93 (0.39 to 2.18)
From noncardiac cause	17 (1.7%)	16 (1.6%)	1.03 (0.52 to 2.05)
Target-vessel myocardial infarction	9 (0.9%)	20 (2.0%)	0.45 (0.21 to 0.99)
Periprocedural	7 (0.7%)	11 (1.1%)	0.64 (0.25 to 1.64)
Spontaneous	2 (0.2%)	9 (0.9%)	0.22 (0.05 to 1.04)
Repeat revascularization	52 (5.2%)	50 (5.0%)	1.01 (0.68 to 1.49)
Target-lesion revascularization	31 (3.1%)	33 (3.3%)	0.90 (0.55 to 1.48)
Target-vessel revascularization	39 (3.9%)	38 (3.8%)	0.98 (0.63 to 1.54)

*The listed percentages were estimated as the ratio of the numerator and denominator.
†Hazard ratios are for the OCT-guided PCI group, as compared with the IVUS-guided PCI group by use of Cox proportional hazard models.
‡The primary composite outcome was death from cardiac cause, target-vessel myocardial infarction, or target vessel revascularization.
§Target-lesion failure was a composite of death from cardiac causes, target-vessel MI, or ischemia-driven target-lesion revascularization.

Study Limitations

- It was not possible to mask the imaging modalities from the patients and investigators (the possibility of ascertainment or selection bias).
- The observed number of primary-outcome events was lower than expected (several explanations would be possible).
- There would be the possibility of discrepancy on site-determined and core-laboratory measured imaging interpretation.
- The generalizability and reproducibility of our trial findings may be potentially limited due to the geographic variability in the use of intravascular imaging in the daily PCI practice.
- Our trial did not include an angiography-guided arm.

Summary for the OCTIVUS Key Findings

- In this large-scale, pragmatic RCT comparing OCT and IVUS for PCI guidance in patients with diverse anatomical or clinical characteristics, we found that OCT-guided PCI was noninferior to IVUS-guided PCI with respect to a primary endpoint of target-vessel failure at 1 year.
- The incidence of primary-outcome events was lower than expected, possibly due to improvements in the methods/techniques to perform PCI and general improvements in cardiovascular care during the past few years.
- The amount of contrast dye used during the procedures was higher in the OCT group than in the IVUS group, but it was not related to an increase of contrast-induced nephropathy.

Conclusions

In this OCTIVUS trial involving patients who are undergoing PCI for diverse coronary-artery lesions,

1. **OCT-guided PCI was noninferior to IVUS-guided PCI with respect to a composite of death from cardiac causes, target-vessel myocardial infarction, or ischemia-driven target-vessel revascularization at 1 year.**
2. **However, the selected study population and lower than expected event rates should be considered in interpreting the trial.**