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ORIGINAL RESEARCH ARTICLE

Optical Coherence Tomography–Guided or Intravascular Ultrasound–Guided Percutaneous Coronary Intervention: The OCTIVUS Randomized Clinical Trial

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BACKGROUND: Intravascular imaging–guided percutaneous coronary intervention (PCI) with intravascular ultrasound (IVUS) or optical coherence tomography (OCT) showed superior clinical outcomes compared with angiography-guided PCI. However, the comparative effectiveness of OCT-guided and IVUS-guided PCI regarding clinical outcomes is unknown.

METHODS: In this prospective, multicenter, open-label, pragmatic trial, we randomly assigned 2008 patients with significant coronary artery lesions undergoing PCI in a 1:1 ratio to undergo either an OCT-guided or IVUS-guided PCI. The primary end point was a composite of death from cardiac causes, target vessel–related myocardial infarction, or ischemia-driven target-vessel revascularization at 1 year, which was powered for noninferiority of the OCT group compared with the IVUS group. Safety outcomes were also assessed.

RESULTS: At 1 year, primary end point events occurred in 25 of 1005 patients (Kaplan-Meier estimate, 2.5%) in the OCT group and in 31 of 1003 patients (Kaplan-Meier estimate, 3.1%) in the IVUS group (absolute difference, −0.6 percentage points; upper boundary of one-sided 97.5% CI, 0.97 percentage points; $P<0.001$ for noninferiority). The incidence of contrast-induced nephropathy was similar (14 patients [1.4%] in the OCT group versus 15 patients [1.5%] in the IVUS group; $P=0.85$). The incidence of major procedural complications was lower in the OCT group than in the IVUS group (22 [2.2%] versus 37 [3.7%]; $P=0.047$), although imaging procedure-related complications were not observed.

CONCLUSIONS: In patients with significant coronary artery lesions, OCT-guided PCI was noninferior to IVUS-guided PCI with respect to the incidence of a composite of death from cardiac causes, target vessel–related myocardial infarction, or ischemia-driven target-vessel revascularization at 1 year. The selected study population and lower-than-expected event rates should be considered in interpreting the trial.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique number: NCT03394079.

Key Words: cardiac imaging techniques ■ percutaneous coronary intervention ■ tomography, optical coherence ■ ultrasonography, interventional

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Clinical Perspective

What Is New?

- The OCTIVUS trial (Optical Coherence Tomography versus Intravascular Ultrasound-Guided Percutaneous Coronary Intervention) is a large-scale, randomized controlled, pragmatic trial comparing 2 contemporary imaging strategies of optical coherence tomography (OCT) and intravascular ultrasound (IVUS) for percutaneous coronary intervention (PCI) guidance in patients with diverse coronary artery lesions.
- For 2008 randomly assigned patients, OCT-guided PCI was noninferior to IVUS-guided PCI procedures with respect to a primary composite of death from cardiac causes, target-vessel myocardial infarction, or ischemia-driven target-vessel revascularization at 1 year. There were no apparent between-group differences in the incidence of contrast-induced nephropathy and procedure-related safety events directly associated with use of imaging devices.

What Are the Clinical Implications?

- The primary results of OCTIVUS provide valuable insights into the comparative effectiveness of OCT-guided and IVUS-guided PCI.
- Both OCT and IVUS can be used safely and effectively in the vast majority of procedures, demonstrating comparable acute and long-term outcomes.
- Further research is necessary to provide better identification of which patients or lesions in general can merit imaging-guided PCI, given that the best strategy may be no imaging guidance necessary in low-risk populations with low event rates.

Nonstandard Abbreviations and Acronyms

ILUMIEN IV	Optical Coherence Tomography Guided Coronary Stent Implantation Compared to Angiography: a Multicenter Randomized Trial in PCI
IVUS	intravascular ultrasound
OCT	optical coherence tomography
OCTIVUS	Optical Coherence Tomography versus Intravascular Ultrasound-Guided Percutaneous Coronary Intervention
OPINION	Optical Frequency Domain Imaging vs. Intravascular Ultrasound in Percutaneous Coronary Intervention
PCI	percutaneous coronary intervention
RENOVATE-COMPLEX-PCI	Randomized Controlled Trial of Intravascular Imaging Guidance versus Angiography-Guidance on Clinical Outcomes after Complex Percutaneous Coronary Intervention
SYNTAX	Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery

Although coronary angiography is the standard method to assess the severity of obstructive coronary artery disease and to guide percutaneous coronary intervention (PCI), it has several inherent limitations.[1] To overcome such limitations, there has been an increased interest in the adjunctive role of intracoronary imaging to guide and optimize PCI.[2] Intracoronary imaging with intravascular ultrasound (IVUS) and optical coherence tomography (OCT) has been increasingly used to guide PCI procedures; it can be used to assess target-lesion characteristics, optimize stent implantation, and minimize stent-related problems.[3–5] Current European and US guidelines recommend that IVUS or OCT be considered in selected patients to optimize stent implantation (class IIa recommendation).[6,7]

Several randomized clinical trials demonstrated the superiority of intravascular imaging–guided PCI over angiography-guided PCI for improving clinical outcomes in high-risk or complex lesions and patients.[8–12] In particular, the RENOVATE-COMPLEX-PCI trial (Randomized Controlled Trial of Intravascular Imaging Guidance versus Angiography-Guidance on Clinical Outcomes after Complex Percutaneous Coronary Intervention) showed that imaging-guided PCI (74% of patients with IVUS and 26% with OCT) led to a lower risk of a primary composite of death from cardiac causes, target vessel–related myocardial infarction, or clinically driven target-vessel revascularization than angiography-guided PCI in patients with complex coronary artery lesions.[12]

However, given that each imaging modality of IVUS or OCT has different imaging technologies, lesion applications, advantages, or limitations,[13] data on the comparative effectiveness of these 2 contemporary imaging strategies for PCI guidance are limited. Therefore, we designed the OCTIVUS trial (Optical Coherence Tomography versus Intravascular Ultrasound-Guided Percutaneous Coronary Intervention) to perform a head-to-head comparison of OCT- and IVUS-guided PCI with regard to clinical outcomes in patients with a broad range of coronary artery lesions.

METHODS

The data that support the findings of this study are available from the corresponding authors on reasonable request.

Trial Design and Oversight

The trial was an investigator-initiated, prospective, multicenter, randomized, open-label pragmatic trial conducted at 9 sites in

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South Korea. The trial design and methods have been published previously.[14] All the participating center and trial personnel are listed in the Supplemental Material (section A). The trial protocol (available in the Supplemental Material) was approved by the institutional review board and ethics committees at each participating site. All patients provided written informed consent before randomization.

This investigator-initiated trial was funded by the CardioVascular Research Foundation, Abbott Vascular, and Medtronic. The funders had no role in the trial design; in data collection, analysis, or interpretation; or in the writing of the manuscript. An independent data and safety monitoring board provided oversight by periodically reviewing all reported serious adverse events, and an independent clinical-event adjudication committee adjudicated all clinical outcomes in a blinded manner. Data monitoring, quality checks, and data analyses were conducted by the Clinical Research Center of Cardiology in Asan Medical Center (Seoul, Korea) and were executed under the academic leadership of the investigators. Additional information about trial organization is provided in the Supplemental Material (section B). The executive committee and all authors vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol.

Trial Population and Randomization

Patients ≥19 years of age who were undergoing PCI with contemporary drug-eluting stents or drug-coated balloons (only for in-stent restenosis) for significant coronary artery lesions were eligible for enrollment. OCTIVUS was constructed as a pragmatic comparative effectiveness design[14] (Supplemental Material, section C). To reflect the pragmatic features of trial design, enrollment criteria were designed to capture a broad range of patients with various anatomical or clinical characteristics. Patients were excluded if they had: ST-segment–elevation myocardial infarction at hospital admission: severe renal dysfunction; unstable hemodynamics or decompensated heart failure; severely calcified or tortuous lesions that were expected to not allow a delivery of intracoronary imaging catheter; or inability to be safely randomly assigned to either arm. Details regarding inclusion and exclusion criteria are provided in the Supplemental Material (section D).

After providing written informed consent, eligible patients were randomly assigned in a 1:1 ratio to undergo either OCT-guided PCI or IVUS-guided PCI after diagnostic coronary angiography. Randomization was performed by means of an interactive Web-based response system using a computer-generated randomization sequence in a permuted block size of 4 or 6, stratified according to enrollment site.

Imaging-Guided PCI

PCI procedure was performed using standard techniques. Lesion preparation using a balloon catheter, atherectomy, or other devices, and the choice of a specific drug-eluting stent were left to the discretion of the operators. Detailed protocols for imaging evaluation and acquisition are provided in the Supplemental Material (section E). In each group, either IVUS with rotational transducer (Opticross or Opticross HD, Boston Scientific Corporation, San Jose, CA) or OCT (C7-XR and OPTIS, Abbott, Santa Clara, CA) was used before, during, and immediately after stent implantation. 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 expert consensus.[3] Detailed information on imaging-guided PCI optimization criteria is described in the Supplemental Material (section F). In brief, a distal lumen or external elastic membrane reference-based stent-sizing strategy was used, and a sufficient stent expansion of >80% of the mean reference lumen area with avoidance of major stent malapposition or edge dissection was achieved. If imaging criteria for optimization were not met, additional procedures with a high-pressure balloon or additional stent implantation were performed according to the operators' discretion; a repeat imaging evaluation for final PCI optimization was mandated. In patients with multivessel disease undergoing staged procedures, the initially allocated imaging tool was used in staged PCI procedures. All measurements of quantitative coronary angiography and intravascular imaging data were performed by the independent angiographic and imaging core laboratories at the Asan Medical Center (Supplemental Material, section B).

Procedural anticoagulation was achieved with unfractionated heparin according to the local site protocols. After PCI, all patients were prescribed lifelong aspirin, and a P2Y12 inhibitor (clopidogrel, prasugrel, or ticagrelor) was prescribed for at least 6 to 12 months at the physician's discretion according to the clinical indication and procedural complexity.

Trial End Points and Follow-Up

The primary end point was target-vessel failure, which was defined as a composite of death from cardiac causes, target vessel–related myocardial infarction, or ischemia-driven target-vessel revascularization at 1 year after randomization. Key secondary end points included the individual components of the primary end point, target-lesion failure (a composite of death from cardiac causes, target-vessel myocardial infarction, or ischemia-driven target-lesion revascularization), stent thrombosis, stroke, repeat revascularization, rehospitalization, and bleeding events. Other secondary end points included contrast-induced acute kidney injury, procedural complications requiring active intervention, which were related to PCI or intravascular imaging (ie, procedural safety outcomes), and angiographic or imaging-based device success. Standard definitions were used for clinical outcome assessment,[15–19] and a detailed list of trial outcomes and their definitions is provided in the Supplemental Material (sections G and H). All components of clinical end points were adjudicated by a clinical events committee whose members were unaware of the trial group assignments.

Follow-up was performed at hospital discharge and at 1, 6, and 12 months and then yearly thereafter. Patients who were unable to attend outpatient clinic visits were contacted by telephone interview. During follow-up, guideline-directed medical therapy and management of risk factors for intensive secondary prevention according to contemporary clinical guidelines were highly recommended. At each visit, all information regarding clinical events and cardiovascular medications were systematically collected. Survival status was reconfirmed through the national death registry of the Korean National Health Insurance Service database.[20]

Statistical Analysis

The study was designed to test the hypothesis that OCT-guided PCI would be noninferior to IVUS-guided PCI with respect to

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the primary end point. On the basis of the results of previous studies using IVUS-guided PCI,[21–23] we assumed that the event rate of the primary end point at 12 months would be 8.0% in the IVUS-guided PCI group. A noninferiority margin of 3.1 percentage points was chosen, which represented 39% of the expected percentage of patients with an event. We determined that enrollment of 964 patients in each group would provide the trial with a power of 80% to show noninferiority on the basis of the likelihood-score method by Farrington and Manning at a one-sided type I error of 0.05.[24] Under an assumption that ≈3% of the patients would be lost to follow-up, a final sample of 2000 patients was deemed to be sufficient to evaluate the primary end point. We report primary results for the assessment of noninferiority with a one-sided 97.5% CI. The *P* value and CI for noninferiority was one-sided and was calculated by the Farrington-Manning test. Additional details regarding the sample-size estimation are provided in the Supplemental Material (section I).

All principal analyses were performed on an intention-to-treat basis. Sensitivity analyses were performed in the per-protocol and as-treated populations. Details regarding the statistical methods are provided in the Supplemental Material (section J). Cumulative-event probabilities were estimated with the use of the Kaplan-Meier methods. In time-to-first-event analyses, hazard ratios and 95% CIs were generated with Cox proportional hazards models. Data from patients who did not have primary outcome events between randomization and at 1 year were censored at the time of death, the time of last known contact, or 365 days, whichever occurred first. The proportional hazards assumption was evaluated with a 2-sided score test of the scaled Schoenfeld residuals at the 0.05 level. Absolute differences and 95% CI for trial outcomes at 1 year were also calculated with Kaplan-Meier estimates and Greenwood standard errors.[25] Prespecified subgroup analyses according to clinical or anatomical factors were performed; the interaction term between randomized groups and key subgroups was evaluated for primary end point. Post hoc subgroup analyses were also performed with the components of imaging criteria for PCI optimization.

No interim analyses of the trial end points were planned. The 95% CI for secondary outcomes were not adjusted for multiple comparisons; therefore, the intervals should not be used to infer definitive treatment effects. All statistical analyses were performed with SAS software, version 9.4 (SAS Institute), and R software, version 4.0 (R Foundation for Statistical Computing).

RESULTS

Study Population and Baseline Characteristics

From April 12, 2018, through January 14, 2022, a total of 3879 patients were assessed for eligibility. Finally, 2008 patients underwent randomization, 1005 patients were assigned to undergo OCT-guided PCI, and 1003 were assigned to undergo IVUS-guided PCI (Figure 1). OCT imaging devices were not used in 26 patients in the OCT-guided group owing to failure to pass the imaging device or protocol violations (cross-over to IVUS-assisted PCI by the operator's discretion), and IVUS imaging devices were not used in 8 patients in the IVUS-guided group owing to failed PCI, failure to pass the imaging device, or protocol violations (cross-over to OCT-assisted PCI by the operator's discretion).

Baseline characteristics of the patients were well balanced between the 2 randomized groups (Table 1). The mean±SD age was 64.7±10.4 years, and 21.6% of the patients were women. Overall, 33.4% of patients had diabetes, 76.6% presented with stable ischemic heart disease, and 23.4% presented with an acute coronary syndrome.

Anatomical and Procedural Characteristics

In general, the characteristics of treated lesions were similar in both groups, with the exception of a lower percentage of patients with left main disease in the OCT group compared with the IVUS group (Table 2). Overall, a substantial proportion of patients had diverse types of coronary artery lesions; 61.6% had multivessel disease, 13.1% had left main disease, 52.6% had bifurcation disease, and 58.2% had diffuse long coronary artery lesion. The mean SYNTAX score (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) was similar in both groups.

Procedural characteristics appeared to be similar between the 2 groups, including PCI approach and modality, number or length of stented segment, and use of adjunctive balloon dilation (Table 2; Table S1). The total amount of contrast dye used was higher in the OCT-guided PCI group than in the IVUS-guided PCI group; however, the total PCI time was shorter in the OCT group. Core-laboratory measurement of quantitative coronary angiography and intravascular imaging data are shown in Table S2. By lesion-level analyses, among treated lesions that were available and of sufficient image quality to allow assessment of stent optimization, 53.4% of treated lesions met all stent-optimization criteria in the OCT-guided PCI group, and 60.1% of treated lesions met all stent-optimization criteria in the IVUS-guided PCI group. The incidence of procedure-related complications during the index PCI was lower in the OCT group than in the IVUS group (2.2% versus. 3.7%), although imaging procedure-related complications were not observed (Table 2; Table S3).

Primary and Secondary Outcomes

Ascertainment of the primary and secondary outcomes at 1 year was completed in 99.0% of the patients (98.8% of the OCT group and 99.2% of the IVUS group), and data on vital status were obtained for all patients (Figure 1). Medication use at baseline and during follow-up was similar in both groups (Table S4).

At 1 year after randomization, the primary end point, a composite of death from cardiac causes, target vessel–related myocardial infarction, or ischemia-driven

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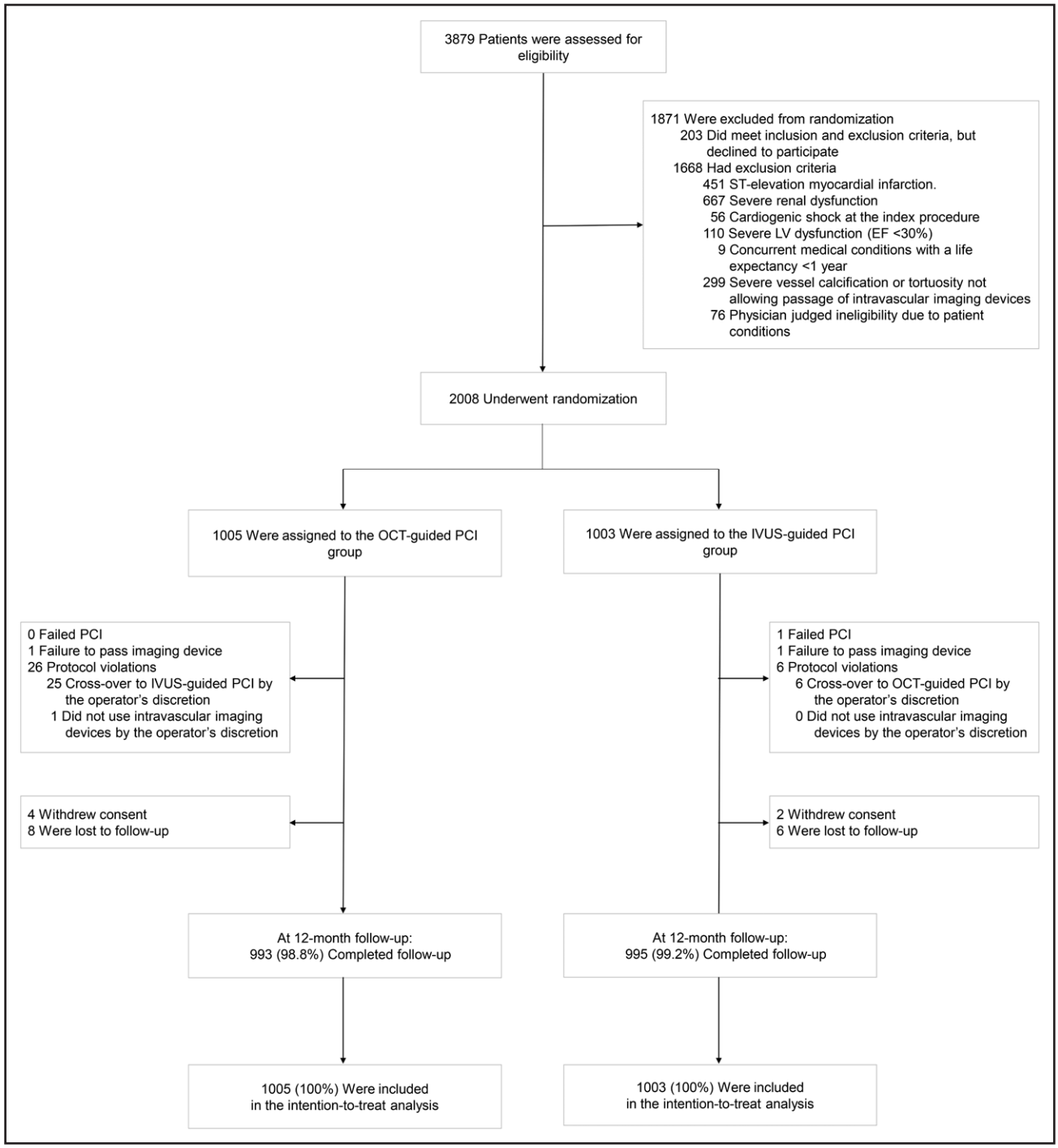

Figure 1. Trial profile.
Assessment of eligibility, randomization, and follow-up of the patients in this trial. EF indicates ejection fraction; IVUS, intravascular ultrasound; LV, left ventricular; OCT, optical coherence tomography; and PCI, percutaneous coronary intervention.

target-vessel revascularization, had occurred in 25 of 1005 patients (2.5%) in the OCT-guided PCI group and in 31 of 1003 patients (3.1%) in the IVUS-guided PCI group (risk difference, −0.6 percentage points; upper boundary of the one-sided 97.5% CI, 0.97; $P<0.001$ for noninferiority; Table 3). The cumulative-incidence curve for the primary end point is shown in Figure 2. Such a finding for primary end point was similar using the alternative definition of myocardial infarction (Figure S1). In a competing-risk analysis, the risk for primary end point was also consistent (hazard ratio, 0.80 [95% CI, 0.47–1.36]). The incidence of key secondary end points of target-lesion failure, death from any cause, stent thrombosis, or repeat revascularization were similar in both groups (Table 3; Figure S2). The incidence of contrast-induced nephropathy was similar in both groups

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Table 1. Baseline Characteristics of the Patients

Characteristic	OCT-guided PCI (n=1005)	IVUS-guided PCI (n=1003)
Age, y	64.3±10.3	65.1±10.5
Female sex, n (%)	215 (21.4)	218 (21.7)
Body mass index*	24.9±3.2	25.0±3.1
Diabetes, n (%)	325 (32.3)	345 (34.4)
Insulin-treated diabetes, n (%)	32 (3.2)	35 (3.5)
Hypertension, n (%)	647 (64.4)	639 (63.7)
Dyslipidemia, n (%)	840 (83.6)	841 (83.9)
Current smoking, n (%)	217 (21.6)	189 (18.8)
Family history of premature coronary artery disease, n (%)†	55 (5.5)	53 (5.3)
Previous myocardial infarction, n (%)	78 (7.8)	63 (6.3)
Previous PCI, n (%)	226 (22.5)	202 (20.1)
Previous coronary artery bypass grafting, n (%)	33 (3.3)	18 (1.8)
Previous stroke, n (%)	66 (6.6)	73 (7.3)
Congestive heart failure, n (%)	30 (3.0)	16 (1.6)
Chronic pulmonary disease, n (%)	28 (2.8)	26 (2.6)
Peripheral vascular disease, n (%)	29 (2.9)	31 (3.1)
Atrial fibrillation, n (%)	28 (2.8)	38 (3.8)
End-stage renal disease on dialysis, n (%)	20 (2.0)	26 (2.6)
Left ventricular ejection fraction, %‡	60.5±7.2	60.1±7.5
Clinical indication for index PCI, n (%)		
Silent ischemia	106 (10.6)	115 (11.5)
Chronic coronary syndrome	663 (66.0)	654 (65.2)
Acute coronary syndrome	236 (23.5)	234 (23.3)
Unstable angina	137 (13.6)	135 (13.5)
Non–ST-segment–elevation myocardial infarction	99 (9.9)	99 (9.9)

Plus–minus values are means±SD. Percentages may not total 100 because of rounding. IVUS indicates intravascular ultrasound; OCT, optical coherence tomography; and PCI, percutaneous coronary intervention.

*The body mass index is the weight in kilograms divided by the square of the height in meters. Data were missing for 5 patients in the IVUS-guided PCI group.

†A family history of premature coronary artery disease was defined as diagnosis of the disease in a male first-degree relative before 55 years of age or in a female first-degree relative before 65 years of age.

‡Data were available for 1621 patients (80.7%) of total patients: 831 patients (82.7%) in the OCT-guided PCI group and 790 (78.8%) in the IVUS-guided PCI group.

(1.4% in the OCT group and 1.5% in the IVUS group). During the entire follow-up period (median, 2.0 years; range, 1.0–4.8 years), overall findings were consistently maintained (Table S5).

Sensitivity and Subgroup Analyses

Primary and secondary end points in the per-protocol and as-treated populations are summarized in Table S6, Table S7, and Figure S3. Noninferiority for primary end

Table 2. Anatomical and Procedural Characteristics

Characteristic	OCT-guided PCI (n=1005)	IVUS-guided PCI (n=1003)	*P* value
Anatomical or lesion characteristics			
Multivessel disease, n (%)	608 (60.5)	629 (62.7)	0.31
No. of diseased vessels, n (%)			0.39
1	397 (39.5)	374 (37.3)	
2	350 (34.8)	346 (34.5)	
3	258 (25.7)	283 (28.2)	
Treated complex coronary lesions, n (%)			
Left main disease	116 (11.5)	148 (14.8)	0.03
Any bifurcation disease	516 (51.3)	540 (53.8)	0.26
Ostial lesion	96 (9.6)	99 (9.9)	0.81
Chronic total occlusion	56 (5.6)	52 (5.2)	0.70
Severely calcified lesion*	76 (7.6)	76 (7.6)	0.99
In-stent restenotic lesion	87 (8.7)	77 (7.7)	0.42
Diffuse long lesion†	575 (57.2)	594 (59.2)	0.36
Bypass graft disease	3 (0.3)	0 (0.0)	0.25
SYNTAX score‡			
Mean	15.1±8.9	15.8±9.5	0.07
Category, n/N (%)			0.10
Low, 0–22	813 (80.9)	773 (77.1)	
Intermediate, 23–32	141 (14.0)	173 (17.3)	
High, >32	51 (5.1)	57 (5.7)	
Procedural characteristics			
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
Use of drug-coated balloons (only for in-stent restenotic lesion)	35 (3.5)	29 (2.9)	
Total No. of lesions treated per patient	1.3±0.6	1.4±0.6	0.36
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
Postdilatation with larger balloon or high-pressure balloon use, n (%)§	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

(*Continued*)

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Table 2. Continued

Characteristic	OCT-guided PCI (n=1005)	IVUS-guided PCI (n=1003)	*P* value
Procedural success, n (%)			
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, n (%)#			
Any	22 (2.2)	37 (3.7)	0.047
IVUS or OCT procedure-related complications	0 (0)	0 (0)	

Plus–minus values are means±SD. Percentages may not total 100 because of rounding. IVUS indicates intravascular ultrasound, OCT, optical coherence tomography; and PCI, percutaneous coronary intervention.

*Severely calcified lesions were those with encircling calcium seen on angiography.

†Diffuse long coronary artery lesion was defined as lesion length ≥28 mm or stent length ≥32 mm of the treated segment.

‡The SYNTAX score (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) reflects a comprehensive angiographic assessment of the coronary vasculature. A higher score denotes higher anatomical complexity. Scores were calculated by the core laboratory.

§Additional post-stent larger balloon or high-pressure balloon was used to resolve incomplete stent expansion or incomplete stent apposition.

‖Angiographic device success is defined as successful PCI at the intended target lesion with final in-stent residual stenosis of <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 (eg, major dissection, coronary perforation, vasospasm, thrombus formation, air embolization, slow flow or no reflow, distal embolization, acute closure, ventricular arrhythmia, cardiac tamponade, or cardiogenic shock) requiring active intervention (prolonged balloon inflations, additional stenting required, thrombus aspiration, pericardiocentesis, cardioversion, or use of mechanical circulatory support devices), which were related to PCI or use of intravascular imaging.

point was also confirmed in the per-protocol and as-treated analyses.

Figure 3 shows the results of the prespecified subgroup analysis; results appeared consistent across various clinical or anatomical subgroups. Post hoc analyses for the primary end point according to the component of imaging-guided optimization criteria are illustrated in Figure S4; overall findings were consistent in each subgroup.

DISCUSSION

In this large-scale, pragmatic, randomized trial comparing 2 contemporary imaging strategies of 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 procedures with respect to a primary composite of death from cardiac causes, target-vessel myocardial infarction, or ischemia-driven target-vessel revascularization at 1 year.

The added clinical benefit of intracoronary imaging for PCI guidance over angiography alone has been confirmed through several randomized clinical trials, in which IVUS was predominantly used.[8–12] Although clinical guidelines and expert consensus support that both IVUS and OCT may be equivalently effective for guiding and optimizing most PCI procedures,[3,6,7] data on clinical outcomes after OCT-guided PCI are still lacking. Previous small-sized trials suggested that OCT-guided PCI was associated with a larger post-PCI minimum stent area and better functional results compared with angiography-guided PCI.[26,27] Despite this, the clinical benefit of OCT-guided PCI should be confirmed in the large-scale trials, such as ILUMIEN IV (Optical Coherence Tomography Guided Coronary Stent Implantation Compared to Angiography: a Multicenter Randomized Trial in PCI; NCT03507777).[28]

Each imaging modality of OCT and IVUS has similarities and differences in imaging technologies; thus, each imaging tool may have the relative benefits or limitations.[29,30] Until recently, there have been limited data on head-to-head comparison between OCT-guided and IVUS-guided PCI with respect to relevant clinical outcomes. In the ILUMIEN III, the minimum stent area and stent expansion with OCT-guided PCI were comparable to IVUS-guided PCI and were larger than angiography-guided PCI, without differences in major clinical events.[26] The OPINION trial (Optical Frequency Domain Imaging vs. Intravascular Ultrasound in Percutaneous Coronary Intervention) showed that OCT-guided PCI was noninferior to IVUS-guided PCI with respect to target-vessel failure at 1 year.[31] However, these trials were not sufficiently powered to detect clinically relevant outcomes and were not tested for a broad range of patients involving high-risk lesion subsets. Therefore, the current pragmatic comparative-effectiveness trial can provide the relevant clinical evidence on the relative efficacy and safety of OCT-guided and IVUS-guided PCI in a large and potentially representative population of the daily practice.

As expected, 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 in the OCT group. However, it should be noted that patients at high risk of contrast-induced nephropathy (ie, severe renal dysfunction at baseline) were not included in the study. By contrast, because OCT pullback speed was faster than IVUS pullback speed, and a real-time angiographic co-registration and automatic measurements with OCT can facilitate a rapid comprehensive evaluation of a long segment of treated vessels, OCT guidance was associated with a shorter PCI time. The incidence of major procedural complications requiring active intervention was lower in the OCT group than in the IVUS group. Although exact reasons for such differences remain unclear, this could have been related to a more aggressive interventional approach in the IVUS arm. In the practical viewpoint, although the common optimization approach was recommended for both OCT and IVUS in the present trial,

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Table 3. Primary and Secondary Outcomes (Intention-to-Treat Population) at 12 Months After Randomization

End points	OCT-guided PCI group (n=1005), n (%)	IVUS-guided PCI group (n=1003), n (%)	Risk difference (95% CI), percentage points	Hazard ratio (95% CI)	$P_{noninferiority}$
Primary end point					
Target-vessel failure (a composite of death from cardiac causes, target-vessel myocardial infarction, or ischemia-driven target-vessel revascularization)	25 (2.5)	31 (3.1)	−0.6 (−2.0 to 0.8)	0.80 (0.47 to 1.36)	<0.001*
Secondary end points					
Target-lesion failure†	22 (2.2)	29 (2.9)	−0.7 (−2.1 to 0.7)	0.76 (0.43 to 1.31)	
Death					
From any causes	10 (1.0)	14 (1.4)	−0.4 (−1.4 to 0.6)	0.71 (0.32 to 1.60)	
From cardiac causes	3 (0.3)	6 (0.6)	−0.3 (−0.9 to 0.3)	0.50 (0.13 to 2.00)	
From noncardiac causes	7 (0.7)	8 (0.8)	−0.1 (−0.9 to 0.6)	0.87 (0.32 to 2.40)	
Target-vessel myocardial infarction‡					
By protocol definition	9 (0.9)	14 (1.4)	−0.5 (−1.4 to 0.4)	0.64 (0.28 to 1.48)	
By 4th universal definition	4 (0.4)	8 (0.8)	−0.4 (−1.1 to 0.3)	0.50 (0.15 to 1.66)	
By Academic Research Consortium-2 definition	4 (0.4)	8 (0.8)	−0.4 (−1.1 to 0.3)	0.50 (0.15 to 1.66)	
Any 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)	
Q wave	0 (0.0)	0 (0.0)	NA	NA	
Non–Q wave	9 (0.9)	14 (1.4)	−0.5 (−1.4 to 0.4)	0.64 (0.28 to 1.48)	
Stent thrombosis§	0	2 (0.2)	NA	NA	
Stroke	7 (0.7)	5 (0.5)	0.2 (−0.5 to 0.9)	1.40 (0.45 to 4.42)	
Any repeat revascularization	16 (1.6)	19 (1.9)	−0.3 (−1.5 to 0.8)	0.84 (0.43 to 1.63)	
PCI	15	17			
Coronary artery bypass grafting	1	2			
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)	
Rehospitalization	75 (7.6)	96 (9.7)	−2.1 (−4.6 to 0.3)	0.77 (0.57 to 1.04)	
Rehospitalization from cardiac causes	27 (2.7)	35 (3.5)	−0.8 (−2.3 to 0.7)	0.77 (0.46 to 1.27)	
Bleeding event, according to BARC type‖					
BARC type 2–5	16 (1.6)	17 (1.7)	−0.1 (−1.2 to 1.0)	0.94 (0.48 to 1.86)	
BARC type 3–5	10 (1.0)	13 (1.3)	−0.3 (−1.2 to 0.6)	0.77 (0.34 to 1.75)	
Contrast-induced nephropathy¶	14 (1.4)	15 (1.5)	−0.1 (−1.1 to 0.9)	0.93 (0.45 to 1.91)	

Clinical follow-up was conducted at 1 month, 6 months, and 12 months and then yearly thereafter. Primary analyses were conducted in the intention-to-treat population 12 months after randomization. In addition, clinical end points were also evaluated during the entire follow-up period (ie, from time of randomization to the day of the first occurrence of a primary end point event, the day of the last office or telephone visit, or the day of death during follow-up; Supplemental Material, Table S5). The listed percentages were estimated with the use of the Kaplan-Meier method; thus, the rate is not the same as the ratio of the numerator and denominator. Hazard ratios are for the OCT-guided PCI group compared with the IVUS-guided PCI group. Because CIs for secondary outcomes have not been adjusted for multiple comparisons, inferences drawn from these intervals may not be reproducible and should not be used to infer definitive treatment effects for secondary end points. BARC indicates Bleeding Academic Research Consortium; IVUS intravascular ultrasound; NA, not available; OCT, optical coherence tomography; and PCI percutaneous coronary intervention.

*This *P* value was obtained from a test of noninferiority with respect to the primary end point. The upper boundary of the one-sided 97.5% CI was 0.97 percentage points (*P*<0.001 for noninferiority). The *P* value and CI for noninferiority was one-sided and was calculated by the Farrington-Manning test.

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

‡Myocardial infarction was assessed according to the protocol definition (Study Endpoint Definitions, Supplemental Material, section H). Myocardial infarction events were also evaluated according to the 4th universal definition of myocardial infarction[17] and the Academic Research Consortium-2 definition of myocardial infarction.[18]

§Stent thrombosis was defined as definite or probable stent thrombosis according to the Academic Research Consortium.[18] Only 2 definite thromboses were observed in the IVUS-guided PCI group at 1 day and 95 days after the procedure.

‖Bleeding events are assessed according to the BARC criteria.[19] BARC type 3–5 indicates severe bleeding.

¶Contrast-induced nephropathy was defined as either a >25% increase of serum creatinine or an absolute increase in serum creatinine of 0.5 mg/dL from baseline within 72 hours after the index PCI procedure. Event rates (%) of contrast-induced nephropathy are presented as calculated percentages.

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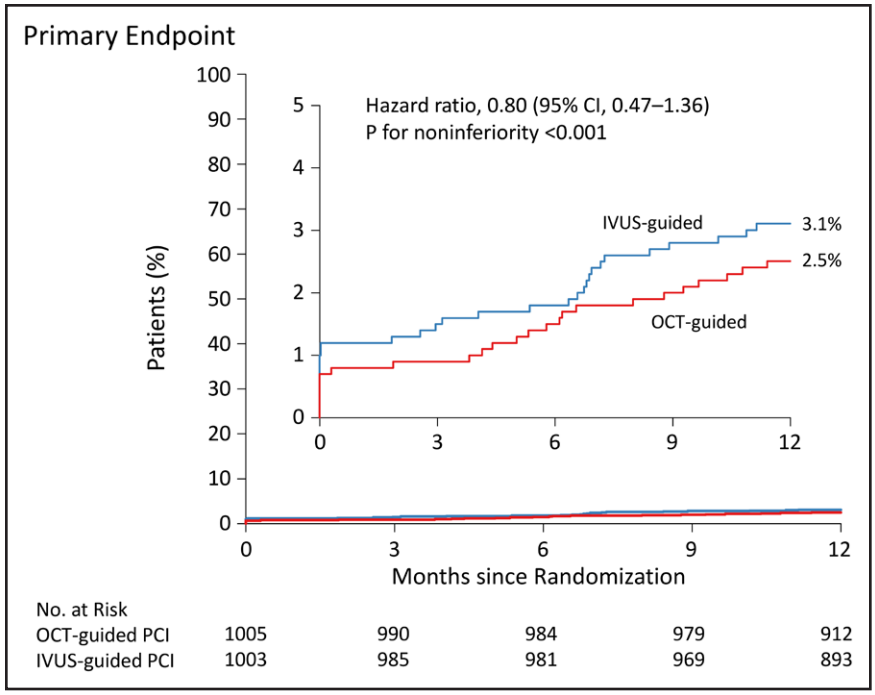

Figure 2. Time-to-event curves for the primary end point.
The primary end point was a composite of death from cardiac causes, target vessel–related myocardial infarction, or ischemia-driven target-vessel revascularization at 12 months after randomization among patients who were undergoing optical coherence tomography (OCT)-guided percutaneous coronary intervention (PCI) or intravascular ultrasonography (IVUS)-guided PCI. The inset shows the same data on an enlarged *y* axis.

a lumen-based approach was commonly used for OCT-guided PCI and a vessel-based (ie, external elastic lamina-based) strategy was usually used for IVUS-guided PCI; thus, maximal stent and balloon size was larger in the IVUS group than in the OCT group.

At the time of trial design, there were no randomized clinical trials evaluating IVUS-guided PCI in a broad range of patients with various anatomical or clinical characteristics reflecting an "all-comer" PCI population; most of available trials had focused on specific lesion criteria or simple coronary artery lesions.[8–10,31] Therefore, our sample-size assumption was determined on the basis of previous observational studies using IVUS-guided PCI in a real-world setting.[21–23] However, the observed number of primary outcome events was lower than expected in our trial. This discrepancy might be explained in part by differences between clinical or lesion characteristics (ie, low-risk nature of the study population who were angiographically relatively simple: mean SYNTAX score, 15.5), and rapidly evolving interventional practice or medical care, including improved stent technology, more effective adjunctive pharmacological therapy, high levels of adherence to recommended medical therapy, and combined use of physiology (ie, fractional flow reserve)-guided PCI. These explanations are congruent with recent trials that used contemporary PCI devices and technologies.[20,32] Given that a cumulative incidence of target-vessel failure at 3 years was 7.7% in the imaging-guided group of the RENOVATE-COMPLEX-PCI trial targeting complex coronary lesions, the observed rate of primary outcome events (≈2.8% at 1 year) in our trial would be reasonably expected. However, we acknowledged that there could be concern for the assessment of noninferiority in the context of using an absolute-risk noninferiority margin. Nevertheless, a trend of lower event rates in the OCT group than in the IVUS group (5.5% versus 6.1%, respectively; hazard ratio, 0.91 [95% CI, 0.63–1.30]) was consistently maintained in the entire follow-up period (Table S5). Given that the observed rates of primary outcome events were lower than expected, an extremely large study sample (approximately >7500 patients) would be required to detect a clinically relevant difference in primary outcome.

Several limitations of the trial should be considered. First, blinding of the patients and investigators to the assignments of imaging modalities was not possible; some degree of ascertainment or selection bias cannot be excluded. Second, because the benefits of intracoronary imaging depend largely on the operators' interpretation and reaction to the imaging findings, there would be the possibility of discrepancy on a site-determined and core laboratory–measured imaging interpretation, by which full optimization of PCI results was only achieved in approximately half of patients. Further studies are required to confirm the validity of the predefined optimization criteria on the basis of expert consensus.[3] Third, geographic variability in the use of intravascular imaging in daily PCI practice may be substantial.[33] Therefore, the generalizability and reproducibility of our trial findings may be potentially limited. Finally, our trial did not include an angiography-guided arm, which might have allowed confirmation of RENOVATE-COMPLEX-PCI, but, more importantly, it could facilitate a cost-effectiveness analysis of imaging-guided PCI versus angiography-guided PCI, as the cost and the reimbursement of OCT and IVUS may be a notable

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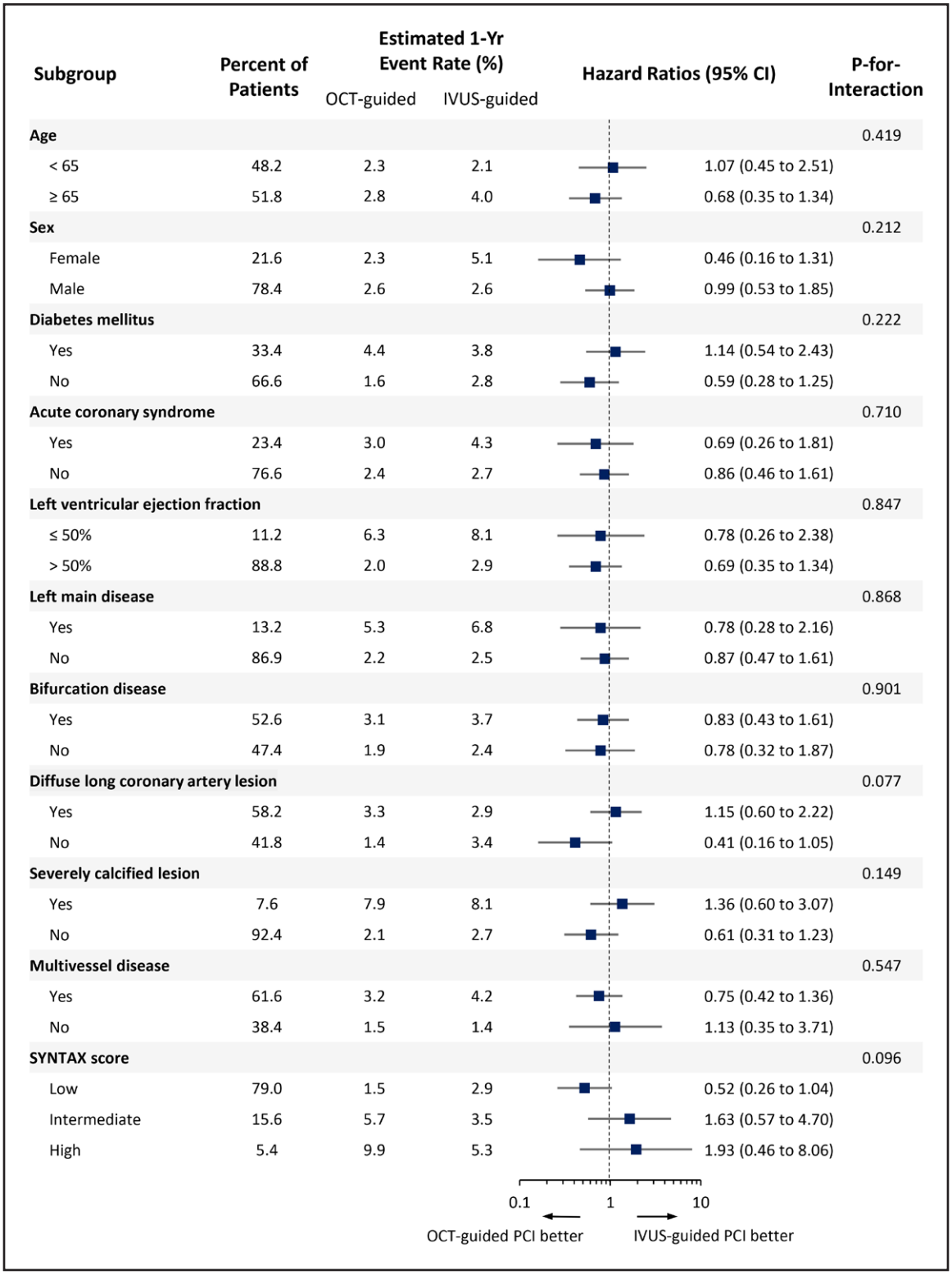

Figure 3. Prespecified subgroup analysis of the primary end point.
Data are shown as the number of primary end point events per total number of patients in that subgroup and the event rate. Event rates were based on Kaplan-Meier estimates in time-to-first-event analyses. Hazard ratios are for the primary composite end point of death from cardiac causes, target vessel–related myocardial infarction, or ischemia-driven target-vessel revascularization at 12 months. The *P* value for interaction represents the likelihood of interaction between variable and treatment. Because the statistical analysis plan did not include a provision for correcting for multiple testing, results are reported as point estimates with 95% CIs. The widths of the CIs have not been adjusted for multiplicity, so they should not be used to infer definitive treatment effects. The SYNTAX score (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) reflects a comprehensive angiographic assessment of the coronary vasculature. A higher score denotes higher anatomical complexity. Scores were calculated by the core laboratory. IVUS indicates intravascular ultrasound; OCT, optical coherence tomography; and PCI, percutaneous coronary intervention.

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consideration and one of the major reasons for low utilization among overall PCI procedures. Further innovation and quality metrics are necessary to realize the full potential of imaging-guided PCI and future ways to overcome the present barriers to use.

Conclusions

Among patients who are undergoing PCI for diverse coronary artery lesions, 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 12 months after the index procedure. However, the study had insufficient statistical power to allow for a firm conclusion owing to lower-than-expected event rates; hence, further research is needed in this area.

ARTICLE INFORMATION

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Supplemental Material

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REFERENCES

1. Mintz GS, Popma JJ, Pichard AD, Kent KM, Satler LF, Chuang YC, DeFalco RA, Leon MB. Limitations of angiography in the assessment of plaque distribution in coronary artery disease. *Circulation*. 1996;93:924–931. doi: 10.1161/01.cir.93.5.924
2. Mintz GS, Guagliumi G. Intravascular imaging in coronary artery disease. *Lancet*. 2017;390:793–809. doi: 10.1016/S0140-6736(17)31957-8
3. Raber L, Mintz GS, Koskinas KC, Johnson TW, Holm NR, Onuma Y, Radu MD, Joner M, Yu B, Jia H, et al; ESC Scientific Document Group. Clinical use of intracoronary imaging. Part 1: Guidance and optimization of coronary interventions. An expert consensus document of the European Association of Percutaneous Cardiovascular Interventions. *Eur Heart J*. 2018;39:3281–3300. doi: 10.1093/eurheartj/ehy285
4. Mintz GS, Matsumura M, Ali Z, Maehara A. Clinical utility of intravascular imaging: Past, present, and future. *JACC Cardiovasc Imaging*. 2022;15:1799–1820. doi: 10.1016/j.jcmg.2022.04.026
5. Truesdell AG, Alasnag MA, Kaul P, Rab ST, Riley RF, Young MN, Batchelor WB, Maehara A, Welt FG, Kirtane AJ; ACC Interventional Council. Intravascular imaging during percutaneous coronary intervention: JACC state-of-the-art review. *J Am Coll Cardiol*. 2023;81:590–605. doi: 10.1016/j.jacc.2022.11.045
6. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, Byrne RA, Collet JP, Falk V, Head SJ, et al; ESC Scientific Document Group. 2018 ESC/EACTS guidelines on myocardial revascularization. *Eur Heart J*. 2019;40:87–165. doi: 10.1093/eurheartj/ehy394
7. Lawton JS, Tamis-Holland JE, Bangalore S, Bates ER, Beckie TM, Bischoff JM, Bittl JA, Cohen MG, DiMaio JM, Don CW, et al. 2021 ACC/AHA/SCAI guideline for coronary artery revascularization: A report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022;145:e18–e114. doi: 10.1161/CIR.0000000000001038
8. Kim JS, Kang TS, Mintz GS, Park BE, Shin DH, Kim BK, Ko YG, Choi D, Jang Y, Hong MK. Randomized comparison of clinical outcomes between intravascular ultrasound and angiography-guided drug-eluting stent implantation for long coronary artery stenoses. *JACC Cardiovasc Interv*. 2013;6:369–376. doi: 10.1016/j.jcin.2012.11.009
9. Hong SJ, Kim BK, Shin DH, Nam CM, Kim JS, Ko YG, Choi D, Kang TS, Kang WC, Her AY, et al; IVUS-XPL Investigators. Effect of intravascular ultrasound-guided vs angiography-guided everolimus-eluting stent implantation: The IVUS-XPL randomized clinical trial. *JAMA*. 2015;314:2155–2163. doi: 10.1001/jama.2015.15454
10. Kim BK, Shin DH, Hong MK, Park HS, Rha SW, Mintz GS, Kim JS, Kim JS, Lee SJ, Kim HY, et al; CTO-IVUS Study Investigators. Clinical impact of intravascular ultrasound-guided chronic total occlusion intervention with zotarolimus-eluting versus biolimus-eluting stent implantation: Randomized study. *Circ Cardiovasc Interv*. 2015;8:e002592. doi: 10.1161/CIRCINTERVENTIONS.115.002592
11. Zhang J, Gao X, Kan J, Ge Z, Han L, Lu S, Tian N, Lin S, Lu Q, Wu X, et al. Intravascular ultrasound versus angiography-guided drug-eluting stent implantation: The ultimate trial. *J Am Coll Cardiol*. 2018;72:3126–3137. doi: 10.1016/j.jacc.2018.09.013
12. Lee JM, Choi KH, Song YB, Lee JY, Lee SJ, Lee SY, Kim SM, Yun KH, Cho JY, Kim CJ, et al; RENOVATE-COMPLEX-PCI Investigators. Intravascular imaging-guided or angiography-guided complex PCI. *N Engl J Med*. 2023;388:1668–1679. doi: 10.1056/NEJMoa2216607
13. Maehara A, Matsumura M, Ali ZA, Mintz GS, Stone GW. IVUS-guided versus OCT-guided coronary stent implantation: a critical appraisal. *JACC Cardiovasc Imaging*. 2017;10:1487–1503. doi: 10.1016/j.jcmg.2017.09.008
14. Kang DY, Ahn JM, Park H, Lee PH, Kang SJ, Lee SW, Kim YH, Park SW, Kim SW, Hur SH, et al. Comparison of optical coherence tomography-guided versus intravascular ultrasound-guided percutaneous coronary intervention: rationale and design of a randomized, controlled OCTIVUS trial. *Am Heart J*. 2020;228:72–80. doi: 10.1016/j.ahj.2020.08.003
15. Hicks KA, Tcheng JE, Bozkurt B, Chaitman BR, Cutlip DE, Farb A, Fonarow GC, Jacobs JP, Jaff MR, Lichtman JH, et al. 2014 ACC/AHA key data elements and definitions for cardiovascular endpoint events in clinical trials: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Data Standards (Writing Committee to

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Develop Cardiovascular Endpoints Data Standards). *J Am Coll Cardiol.* 2015;66:403–469. doi: 10.1016/j.jacc.2014.12.018
16. Moussa ID, Klein LW, Shah B, Mehran R, Mack MJ, Brilakis ES, Reilly JP, Zoghbi G, Holper E, Stone GW. Consideration of a new definition of clinically relevant myocardial infarction after coronary revascularization: an expert consensus document from the Society for Cardiovascular Angiography and Interventions (SCAI). *J Am Coll Cardiol.* 2013;62:1563–1570. doi: 10.1016/j.jacc.2013.08.720
17. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, White HD; Executive Group on behalf of the Joint European Society of Cardiology (ESC)/American College of Cardiology (ACC)/American Heart Association (AHA)/World Heart Federation (WHF) Task Force for the Universal Definition of Myocardial Infarction. Fourth universal definition of myocardial infarction (2018). *J Am Coll Cardiol.* 2018;72:2231–2264. doi: 10.1016/j.jacc.2018.08.1038
18. Garcia-Garcia HM, McFadden EP, Farb A, Mehran R, Stone GW, Spertus J, Onuma Y, Morel M-a, Es G-A, Zuckerman B, et al. Standardized end point definitions for coronary intervention trials: the Academic Research Consortium-2 consensus document. *Circulation.* 2018;137:2635–2650. doi: 10.1161/CIRCULATIONAHA.117.029289
19. Mehran R, Rao SV, Bhatt DL, Gibson CM, Caixeta A, Eikelboom J, Kaul S, Wiviott SD, Menon V, Nikolsky E, et al. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the bleeding academic research consortium. *Circulation.* 2011;123:2736–2747. doi: 10.1161/CIRCULATIONAHA.110.009449
20. Park DW, Kang DY, Ahn JM, Yun SC, Yoon YH, Hur SH, Lee CH, Kim WJ, Kang SH, Park CS, et al; POST-PCI Investigators. Routine functional testing or standard care in high-risk patients after PCI. *N Engl J Med.* 2022;387:905–915. doi: 10.1056/NEJMoa2208335
21. Park DW, Kim YH, Song HG, Ahn JM, Kim WJ, Lee JY, Kang SJ, Lee SW, Lee CW, Park SW, et al; IRIS-DES Investigators. Outcomes after unrestricted use of everolimus-eluting and sirolimus-eluting stents in routine clinical practice: a multicenter, prospective cohort study. *Circ Cardiovasc Interv.* 2012;5:365–371. doi: 10.1161/CIRCINTERVENTIONS.111.966549
22. Lee PH, Kwon O, Ahn JM, Lee CH, Kang DY, Lee JB, Kang SJ, Lee SW, Kim YH, Lee CW, et al. Safety and effectiveness of second-generation drug-eluting stents in patients with left main coronary artery disease. *J Am Coll Cardiol.* 2018;71:832–841. doi: 10.1016/j.jacc.2017.12.032
23. Kwon O, Kang SH, Lee JB, Ahn JM, Lee CH, Kang DY, Lee PH, Kang SJ, Lee SW, Kim YH, et al; IRIS-DES Registry Investigators. Comparative effectiveness of different contemporary drug-eluting stents in routine clinical practice: a multigroup propensity score analysis using data from the stent-specific, multicenter, prospective registries. *Coron Artery Dis.* 2019;30:255–262. doi: 10.1097/MCA.0000000000000730
24. Farrington CP, Manning G. Test statistics and sample size formulae for comparative binomial trials with null hypothesis of non-zero risk difference or non-unity relative risk. *Stat Med.* 1990;9:1447–1454. doi: 10.1002/sim.4780091208
25. Com-Nougue C, Rodary C, Patte C. How to establish equivalence when data are censored: A randomized trial of treatments for B non-Hodgkin lymphoma. *Stat Med.* 1993;12:1353–1364. doi: 10.1002/sim.4780121407
26. Ali ZA, Maehara A, Genereux P, Shlofmitz RA, Fabbiocchi F, Nazif TM, Guagliumi G, Meraj PM, Alfonso F, Samady H, et al; ILUMIEN III: OPTIMIZE PCI Investigators. Optical coherence tomography compared with intravascular ultrasound and with angiography to guide coronary stent implantation (ILUMIEN III: OPTIMIZE PCI): a randomised controlled trial. *Lancet.* 2016;388:2618–2628. doi: 10.1016/S0140-6736(16)31922-5
27. Meneveau N, Souteyrand G, Motreff P, Caussin C, Amabile N, Ohlmann P, Morel O, Lefrancois Y, Descotes-Genon V, Silvain J, et al. Optical coherence tomography to optimize results of percutaneous coronary intervention in patients with non-ST-elevation acute coronary syndrome: results of the multicenter, randomized doctors study (does optical coherence tomography optimize results of stenting). *Circulation.* 2016;134:906–917. doi: 10.1161/CIRCULATIONAHA.116.024393
28. Ali Z, Landmesser U, Karimi Galougahi K, Maehara A, Matsumura M, Shlofmitz RA, Guagliumi G, Price MJ, Hill JM, Akasaka T, et al. Optical coherence tomography-guided coronary stent implantation compared to angiography: a multicentre randomised trial in PCI: design and rationale of ILUMIEN IV: OPTIMAL PCI. *EuroIntervention.* 2021;16:1092–1099. doi: 10.4244/EIJ-D-20-00501
29. Maehara A, Matsumura M, Ali ZA, Mintz GS, Stone GW. IVUS-guided versus OCT-guided coronary stent implantation: a critical appraisal. *JACC Cardiovasc Imaging.* 2017;10:1487–1503. doi: 10.1016/j.jcmg.2017.09.008
30. Shlofmitz E, Ali ZA, Maehara A, Mintz GS, Shlofmitz R, Jeremias A. Intravascular imaging-guided percutaneous coronary intervention: a universal approach for optimization of stent implantation. *Circ Cardiovasc Interv.* 2020;13:e008686. doi: 10.1161/CIRCINTERVENTIONS.120.008686
31. Kubo T, Shinke T, Okamura T, Hibi K, Nakazawa G, Morino Y, Shite J, Fusazaki T, Otake H, Kozuma K, et al; OPINION Investigators. Optical frequency domain imaging vs. Intravascular ultrasound in percutaneous coronary intervention (OPINION trial): one-year angiographic and clinical results. *Eur Heart J.* 2017;38:3139–3147. doi: 10.1093/eurheartj/ehx351
32. Fearon WF, Zimmermann FM, De Bruyne B, Piroth Z, van Straten AHM, Szekely L, Davidavičius G, Kalinauskas G, Mansour S, Kharbanda R, et al; FAME 3 Investigators. Fractional flow reserve-guided PCI as compared with coronary bypass surgery. *N Engl J Med.* 2022;386:128–137. doi: 10.1056/NEJMoa2112299
33. Koskinas KC, Nakamura M, Raber L, Colleran R, Kadota K, Capodanno D, Wijns W, Akasaka T, Valgimigli M, Guagliumi G, et al. Current use of intracoronary imaging in interventional practice: results of a European Association of Percutaneous Cardiovascular Interventions (EAPCI) and Japanese Association of Cardiovascular Interventions and Therapeutics (CVIT) clinical practice survey. *EuroIntervention.* 2018;14:e475–e484. doi: 10.4244/EIJY18M03_01
34. Ford I, Norrie J. Pragmatic trials. *N Engl J Med.* 2016;375:454–463. doi: 10.1056/NEJMra1510059
35. Mintz GS, Nissen SE, Anderson WD, Bailey SR, Erbel R, Fitzgerald PJ, Pinto FJ, Rosenfield K, Siegel RJ, Tuzcu EM, et al. American College of cardiology clinical expert consensus document on standards for acquisition, measurement and reporting of intravascular ultrasound studies (IVUS). A report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol.* 2001;37:1478–1492. doi: 10.1016/s0735-1097(01)01175-5
36. Tearney GJ, Regar E, Akasaka T, Adriaenssens T, Barlis P, Bezerra HG, Bouma B, Bruining N, Cho JM, Chowdhary S, et al; International Working Group for Intravascular Optical Coherence Tomography (IWG-IVOCT). Consensus standards for acquisition, measurement, and reporting of intravascular optical coherence tomography studies: a report from the International Working Group for Intravascular Optical Coherence Tomography Standardization and Validation. *J Am Coll Cardiol.* 2012;59:1058–1072. doi: 10.1016/j.jacc.2011.09.079
37. Mauri L, D'Agostino RB Sr. Challenges in the design and interpretation of noninferiority trials. *N Engl J Med.* 2017;377:1357–1367. doi: 10.1056/NEJMra1510063

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