



Optical coherence tomography–guided PCI in left anterior descending versus non–left anterior descending lesions: a prespecified substudy of the OCCUPI trial

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Received: 9 March 2026 / Accepted: 15 May 2026
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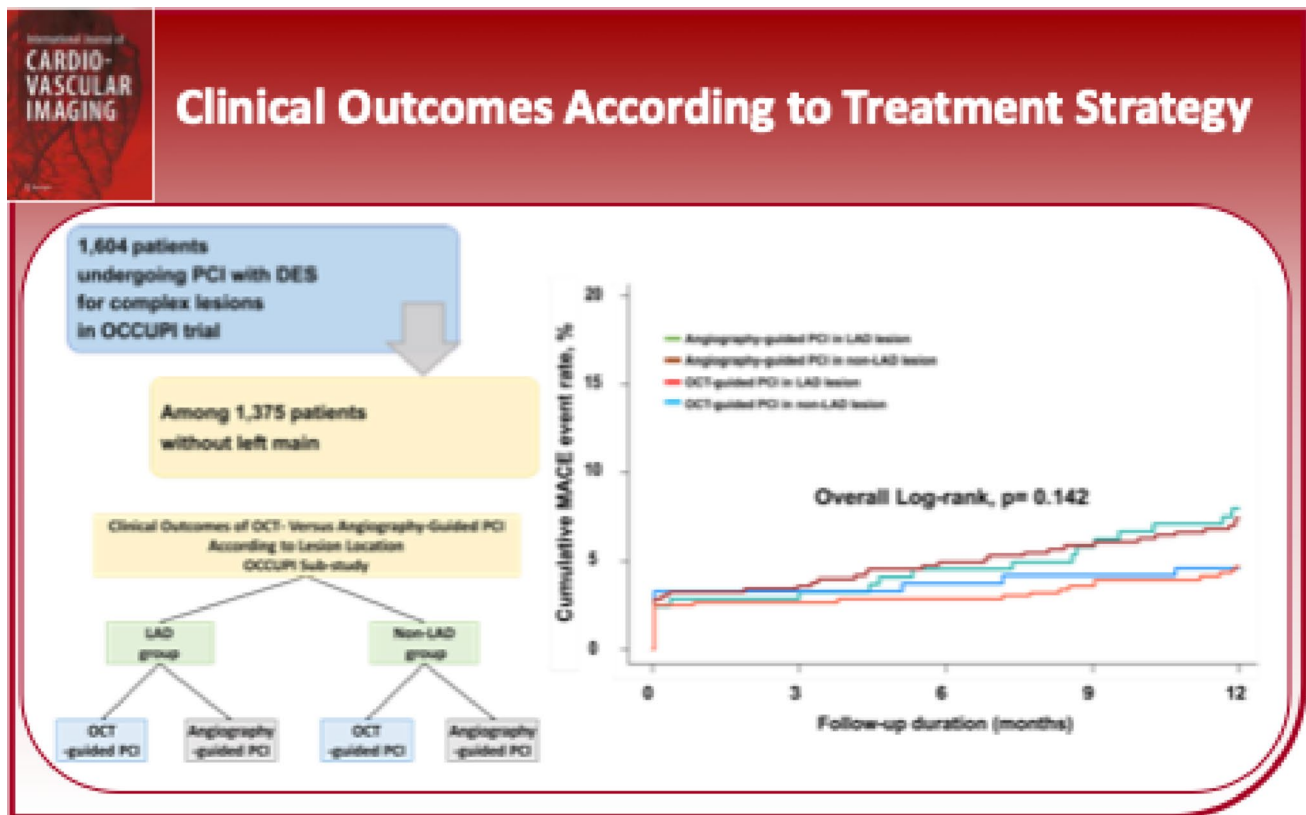
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Abstract

The OCCUPI trial demonstrated the clinical benefit of optical coherence tomography (OCT)–guided percutaneous coronary intervention (PCI). However, whether the effect of OCT guidance differs according to diseased coronary vessel remains unclear. This prespecified substudy evaluated the consistency of clinical outcomes with OCT-guided PCI in left anterior descending (LAD) versus non-LAD lesions. Among 1,375 patients without left main disease, 888 had LAD lesions and 487 had non-LAD lesions. Patients were randomized to undergo PCI guided by either OCT or conventional angiography. The primary endpoint was 1-year major adverse cardiovascular events (MACE), defined as a composite of cardiac death, myocardial infarction, stent thrombosis, or ischemia-driven target-vessel revascularization (TVR). Outcomes were assessed by time-to-event analysis. In the LAD group, 1-year MACE occurred in 4.5% of patients treated with OCT-guided PCI and 5.5% treated with angiography-guided PCI, with no statistically significant difference ($p=0.456$). In the non-LAD group, corresponding MACE rates were 4.6% and 7.7%, respectively ($p=0.099$). There was no significant interaction between diseased vessel and PCI guidance strategy (p for interaction=0.351). Ischemia-driven TVR occurred less frequently with OCT-guided PCI in both LAD and non-LAD lesions, without significant heterogeneity (p for interaction=0.872). In complex coronary lesions, the clinical effect of OCT-guided PCI was consistent between LAD and non-LAD vessels, with fewer repeat revascularizations observed across diseased-vessel subgroups.

Graphical abstract



Clinical Outcomes According to Treatment Strategy Among 1,375 OCCUPI patients without left main disease, 1-year MACE did not significantly differ across OCT- vs angiography-guided PCI in LAD and non-LAD lesions (log-rank $p=0.229$).

Keywords Coronary artery disease · Percutaneous coronary intervention · Optical coherence tomography · Left anterior descending coronary artery

Abbreviations

MACE Major Adverse Cardiovascular Events
 MLD Minimal Lumen Diameter
 OCCUPI Optical Coherence Tomography–Guided

Versus Angiography-Guided PCI for Complex Coronary Lesions
 OCT Optical Coherence Tomography
 QCA Quantitative Coronary Angiography

TLR Target-Lesion Revascularization
TVR Target-Vessel Revascularization

evaluate whether the effect of OCT guidance varies according to diseased vessel.

Introduction

The prognostic importance of coronary diseased vessel has long been recognized, with the left anterior descending artery (LAD) traditionally regarded as a critical coronary vessel because it supplies a large proportion of the left ventricular myocardium. Earlier observational studies consistently reported worse outcomes associated with LAD lesions, largely attributed to the greater myocardial territory at risk and the higher likelihood of left ventricular dysfunction following ischemic injury [1–3].

However, in the contemporary era of percutaneous coronary intervention (PCI) with drug-eluting stents, advances in stent technology, procedural techniques, and adjunctive medical therapy have challenged the concept that LAD location alone confers an intrinsically worse long-term prognosis. Several randomized trials and large registries have demonstrated comparable mortality and major adverse cardiac events (MACE) between LAD and non-LAD lesions after PCI, suggesting that vessel location may no longer be the dominant determinant of outcome [4–8]. Importantly, the diminished prognostic importance of diseased vessel in the modern PCI era highlights that post-PCI outcomes are increasingly determined by lesion complexity and procedural quality rather than by vessel location alone. All major epicardial coronary arteries—including the left anterior descending, left circumflex, and right coronary arteries—supply large myocardial territories; therefore, procedural imperfections may translate into clinically significant adverse events irrespective of diseased vessel.

In complex coronary lesions, inadequate stent expansion, malapposition, or edge-related pathology can translate into residual ischemia and adverse clinical events across all vessels [9, 10]. These considerations highlight the importance of intravascular imaging guidance to ensure optimal stent deployment and lesion coverage. Optical coherence tomography (OCT), with its high spatial resolution, enables precise assessment and correction of procedural imperfections, thereby providing a mechanistic basis for improved PCI outcomes [11–16]. From this perspective, the potential benefit of OCT-guided PCI should be considered broadly applicable across epicardial vessels, rather than confined to specific coronary territories. To address this unresolved issue, we conducted a prespecified substudy of the OCCUPI trial. We compared procedural characteristics and clinical outcomes between LAD and non-LAD lesions, excluding unprotected left main disease, stratified by PCI guidance strategy (OCT-guided vs. angiography-guided PCI), to

Methods

Study design and population

This prespecified substudy derives from the OCCUPI trial—a multicenter, randomized, open-label study conducted at 20 hospitals in South Korea (ClinicalTrials.gov NCT03625908). The main trial enrolled 1,604 patients undergoing PCI with drug-eluting stents for angiographically defined complex lesions between 9 January 2019 and 22 September 2022. In OCCUPI, a “complex lesion” was defined as the presence of at least one of the following after diagnostic angiography: acute myocardial infarction, chronic total occlusion, long lesion (anticipated stent length ≥ 28 mm), severely calcified lesion, bifurcation lesion, small-vessel disease (reference diameter < 2.5 mm), angiographically visible intracoronary thrombus, stent thrombosis, in-stent restenosis, or a bypass-graft lesion [16]. For the present substudy, we excluded patients with unprotected left main (LM) disease ($n=229$; 113 in the OCT group and 116 in the angiography group), yielding an analytic cohort of 1,375. Patients were then stratified by diseased vessel into two groups: LAD (target lesion in the left anterior descending artery) and non-LAD (target lesions in other coronary territories such as the left circumflex or right coronary artery). Within each group, comparisons of clinical and procedural outcomes were performed according to PCI guidance modality, including OCT-guided and angiography-guided PCI. The overall study flow and subgroup stratification are shown in Fig. 1. The OCCUPI trial was conducted in accordance with the Declaration of Helsinki and approved by the institutional review board at each participating center. All participants provided written informed consent. The present analysis was a prespecified substudy of the OCCUPI trial, and additional institutional review board approval was waived.

Randomization and intervention

In the OCCUPI trial, patients were randomized in a 1:1 ratio to undergo OCT-guided PCI or angiography-guided PCI. OCT guidance was performed according to the trial protocol, including pre- and/or post-stenting imaging for device sizing, stent landing zone selection, and optimization assessment (expansion, apposition, and edge dissection). Stent optimization criteria were identical to those prespecified in the OCCUPI trial and have been described previously [16]. Briefly, optimization aimed to achieve adequate

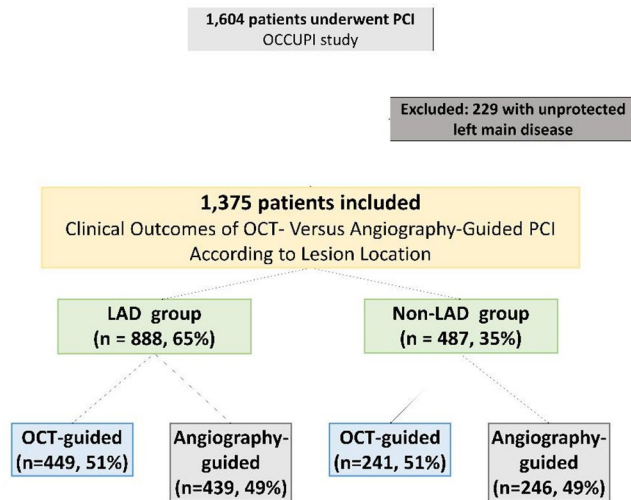


Fig. 1 Study flow Flow diagram of the prespecified OCCUPI substudy, illustrating patient inclusion, exclusion of unprotected left main disease, stratification by diseased vessel (LAD vs. non-LAD), and allocation to OCT-guided or angiography-guided PCI

stent expansion relative to the reference vessel, appropriate stent apposition, and the absence of major edge dissection requiring additional intervention. Detailed OCT acquisition, analysis procedures, and prespecified criteria for stent optimization are provided in the Supplementary Methods. Angiography-guided PCI was performed using standard quantitative angiographic assessment without intravascular imaging. Everolimus-eluting stents (XIENCE series, Abbott Vascular) were used in all patients. Procedural anticoagulation and antiplatelet therapy were administered according to contemporary guideline recommendations and institutional practice. The detailed imaging acquisition protocol and procedural criteria have been described previously [16].

Quantitative coronary angiography and procedural assessment

Quantitative coronary angiographic (QCA) analyses were performed using standard validated software by experienced analysts who were blinded to PCI guidance modality. QCA measurements included minimal lumen diameter (MLD), percent diameter stenosis, reference vessel diameter, stent diameter, and total stent length.

In the OCT-guided group, post-stenting OCT imaging was used to assess procedural optimization. Optimal stent deployment was defined by fulfillment of prespecified criteria for adequate expansion, appropriate apposition, and the absence of major edge dissection, consistent with the main trial protocol. Additional details regarding OCT analysis, stent optimization criteria, and quantitative coronary angiographic methodology are provided in the Supplementary Methods.

Study endpoints

The primary endpoint of this substudy was the occurrence of MACE, defined as a composite of cardiac death, myocardial infarction, stent thrombosis, or ischemia-driven target-vessel revascularization at 1 year after PCI.

Secondary endpoints comprised the individual components of MACE, ischemia-driven target-vessel revascularization (TVR), target-lesion revascularization (TLR), any revascularization, and adverse events such as stroke, major bleeding and contrast-induced nephropathy. A post hoc composite endpoint was defined as the composite of cardiac death, spontaneous myocardial infarction, stent thrombosis, or ischemia-driven target-vessel revascularization.

Procedural outcomes included quantitative coronary angiographic measures such as minimal lumen diameter (MLD), percent diameter stenosis, stent diameter, and stent length. In the OCT-guided group, rates of stent optimization—defined by adequate expansion, apposition, and the absence of major edge dissection—were additionally assessed.

Statistical analysis

Baseline characteristics and procedural outcomes were compared between the LAD and non-LAD groups, stratified by PCI guidance modality (OCT-guided vs. angiography-guided). Categorical variables were expressed as numbers and percentages, and compared using the χ^2 or Fisher's exact test. Continuous variables were presented as mean $\pm$ SD or median with interquartile range, and compared using Student's t-test or the Mann–Whitney U test, as appropriate.

Time-to-event outcomes were estimated using Kaplan–Meier survival analysis and compared by the log-rank test. Hazard ratios (HR) and 95% confidence intervals (CIs) were calculated using Cox proportional hazards regression models. To test whether the treatment effect differed according to diseased vessel, an interaction analysis was performed between PCI guidance modality (OCT vs. angiography) and lesion group (LAD vs. non-LAD).

Multivariable Cox regression analyses were conducted to adjust for potential confounders, including age, sex, body mass index, hypertension, diabetes mellitus, acute coronary syndrome presentation, chronic kidney disease, dyslipidemia, current smoking status, past medical history (previous myocardial infarction, prior percutaneous coronary intervention, prior coronary artery bypass grafting, and previous stroke), as well as discharge medications (aspirin, a P2Y12 inhibitor [clopidogrel, ticagrelor, or prasugrel], a statin, a β -blocker, and an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker). All analyses followed the intention-to-treat principle. A two-sided p value < 0.05 was

considered statistically significant. SAS software, version 9.4 (SAS Institute, Cary, NC, USA) and R version 4.5.0 (R Foundation for Statistical Computing), was used for all the statistical analyses. This trial is registered with ClinicalTrials.gov (NCT03625908) and is completed.

Results

Baseline characteristics

Among 1,375 patients without left main disease, 888 were classified as the LAD group and 487 as the non-LAD group. Median age was similar (LAD 63 [57–70] vs. non-LAD 64 [57–71] years; $p=0.288$) as was BMI (both 25 [23–27] kg/m²; $p=0.082$). The LAD group included fewer men (78% vs. 83%; $p=0.034$) and had lower prevalence of chronic kidney disease (CKD) (6% vs. 9%; $p=0.038$). Prior revascularization was less common in the LAD group: previous PCI 16% vs. 27% ($p<0.0001$) and previous CABG 1% vs. 2% ($p=0.011$). Prevalence of hypertension, diabetes mellitus, dyslipidemia, current smoking, prior myocardial infarction and prior stroke were comparable between groups. Regarding clinical presentation, the distribution of stable angina and acute coronary syndrome was similar (stable angina: 49% vs. 51%, $p=0.428$; ACS: 51% vs. 49%). The prevalence of acute myocardial infarction as the index event was not significantly different between the non-LAD and LAD groups (24% vs. 21%, $p=0.302$). Left ventricular ejection fraction was similar (59.6% [SD 9.7] vs. 59.1% [SD 9.3], $p=0.340$) (Table S1).

Lesion characteristics are summarized in Table S2. The distribution of the PCI guidance strategy was similar between the groups ($p=0.138$), with OCT-guided PCI performed in 49% of LAD lesions and 47% of non-LAD lesions (optimal optimization: 33% vs. 35%, sub-optimal: 16% vs. 12%, respectively). Chronic total occlusion was significantly more frequent in the non-LAD group (11% vs. 6%, $p=0.001$). In contrast, bifurcation lesions (26% vs. 10%, $p<0.0001$) and small vessel disease (21% vs. 13%, $p<0.001$) were significantly more common in the LAD group. The prevalence of calcified lesions (9% vs. 8%, $p=0.661$) and intracoronary thrombus (9% vs. 10%, $p=0.477$) was comparable between the two groups.

Baseline characteristics according to imaging guidance and diseased vessel

Baseline clinical characteristics were generally well balanced across imaging guidance modalities and diseased vessel (Table 1). Apart from a higher prevalence of prior percutaneous coronary intervention in the non-LAD group,

baseline characteristics were otherwise clinically comparable between groups. Median age and sex distribution were similar (63–65 years; $p=0.767$), and the prevalence of hypertension, diabetes, dyslipidemia, and current smoking did not differ significantly. Chronic kidney disease was more frequent in the non-LAD/OCT group (10.8%; $p=0.028$), whereas histories of myocardial infarction, coronary artery bypass grafting, and stroke were comparable. Clinical presentation, left ventricular ejection fraction, and discharge medications were also similar across all subgroups.

Clinical outcomes

During a median follow-up of 351 days, the incidence of major adverse cardiovascular events (MACE) was 5.0% in the LAD group and 6.2% in the non-LAD group ($p=0.345$) (Fig. S1), and a numerically lower event rate was observed with OCT-guided PCI compared with angiography-guided PCI (4.5% vs. 6.3%, $p=0.145$). Across diseased vessel categories (LAD and non-LAD), MACE occurred numerically less frequently in patients undergoing OCT-guided PCI than in those undergoing angiography-guided PCI (Fig. 2). In the LAD group, MACE was observed in 4.5% of patients treated with OCT guidance compared with 5.5% of those treated with angiography guidance (adjusted hazard ratio [HR] 0.78; 95% confidence interval [CI] 0.41–1.49; $p=0.456$). A similar trend was observed in the non-LAD group (4.6% vs. 7.7%; adjusted HR 0.48; 95% CI 0.21–1.15; $p=0.099$). There was no significant interaction between diseased vessel and imaging guidance strategy for MACE (p for interaction=0.351) (Fig. 3). For the composite endpoint of cardiac death, spontaneous myocardial infarction, stent thrombosis, or ischemia-driven target-vessel revascularization, OCT-guided PCI was associated with numerically lower event rates compared with angiography-guided PCI in both LAD and non-LAD vessels. In the LAD cohort, the adjusted hazard ratio was 0.59 (95% CI, 0.22–1.61; $p=0.301$), while in the non-LAD cohort, the adjusted hazard ratio was 0.21 (95% CI, 0.05–0.83; $p=0.026$). There was no significant interaction between diseased vessel and imaging strategy (p for interaction=0.315) (Table 2).

Secondary ischemic outcomes consistently favored OCT-guided PCI. Ischemia-driven target-vessel revascularization (ID-TVR) occurred numerically less frequently in the OCT-guided group, particularly among patients with LAD lesions (0.9% vs. 2.1%; adjusted HR 0.40; 95% CI 0.12–1.33; $p=0.135$). In the non-LAD subgroup, ID-TVR was numerically lower with OCT guidance (1.2% vs. 4.5%; adjusted HR 0.26; 95% CI 0.07–1.06; $p=0.061$), without evidence of effect modification by diseased vessel (p for interaction=0.872) (Table 3).

Table 1 Baseline Characteristics of OCT-Guided Versus Angiography-Guided PCI in LAD and Non-LAD Lesions

Variable	LAD			Non-LAD		
	OCT guidance (n=449)	Angiography guidance (n=439)	p value	OCT guidance (n=241)	Angiography guidance (n=246)	p value
Age, years	63 (56–70)	63 (57–69)	0.961	64 (56–71)	65 (58–71)	0.910
Male sex, n (%)	357 (79.5%)	335 (76.3%)	0.250	196 (81.3%)	207 (84.1%)	0.410
Body mass index, kg/m ²	25 (23–27)	25 (23–26)	0.020	25 (23–27)	25 (23–27)	0.016
Hypertension, n (%)	258 (57.5%)	237 (54.0%)	0.297	142 (58.9%)	144 (58.5%)	0.931
Diabetes mellitus, n (%)	139 (31.0%)	146 (33.3%)	0.463	86 (35.7%)	79 (32.1%)	0.405
Chronic kidney disease, n (%)	21 (4.7%)	31 (7.1%)	0.130	26 (10.8%)	17 (6.9%)	0.132
Dyslipidemia, n (%)	379 (84.4%)	357 (81.3%)	0.222	202 (83.8%)	208 (84.6%)	0.824
Current smoker, n (%)	83 (18.5%)	93 (21.2%)	0.313	52 (21.6%)	47 (19.1%)	0.498
Previous myocardial infarction, n (%)	20 (4.5%)	21 (4.8%)	0.815	13 (5.4%)	18 (7.3%)	0.385
Previous percutaneous coronary intervention, n (%)	81 (18.0%)	63 (14.4%)	0.136	60 (24.9%)	71 (28.9%)	0.324
Previous coronary artery bypass grafting, n (%)	2 (0.4%)	4 (0.9%)	0.397	5 (2.1%)	6 (2.4%)	0.787
Previous stroke, n (%)	18 (4.0%)	21 (4.8%)	0.573	14 (5.8%)	17 (6.9%)	0.619
Clinical presentation						
Stable angina, n (%)	212 (47.2%)	224 (51.0%)	0.256	121 (50.2%)	129 (52.4%)	0.622
Acute coronary syndrome, n (%)	237 (52.8%)	215 (49.0%)	—	120 (49.8%)	117 (47.6%)	—
Unstable angina	139 (31.0%)	123 (28.0%)	—	68 (28.2%)	53 (21.5%)	—
Non-ST-elevation myocardial infarction	68 (15.1%)	61 (13.9%)	—	38 (15.8%)	38 (15.4%)	—
ST-elevation myocardial infarction	30 (6.7%)	31 (7.1%)	—	14 (5.8%)	26 (10.6%)	—
Left ventricular ejection fraction, %	59.4 (SD 8.6)	59.9 (SD 10.7)	0.467	59.4 (SD 8.8)	58.8 (SD 9.8)	0.441
Medication at discharge						
Aspirin, n (%)	440 (98.0%)	433 (98.6%)	0.461	233 (96.7%)	241 (98.0%)	0.378
P2Y12 inhibitor, n (%)	443 (98.7%)	433 (98.6%)	0.969	235 (97.5%)	243 (98.8%)	0.298
Statin, n (%)	435 (96.9%)	422 (96.1%)	0.540	227 (94.2%)	239 (97.2%)	0.108

Values are median (interquartile range) unless otherwise indicated. Continuous variables with normal distribution are presented as mean (standard deviation). Percentages are presented as n (%)

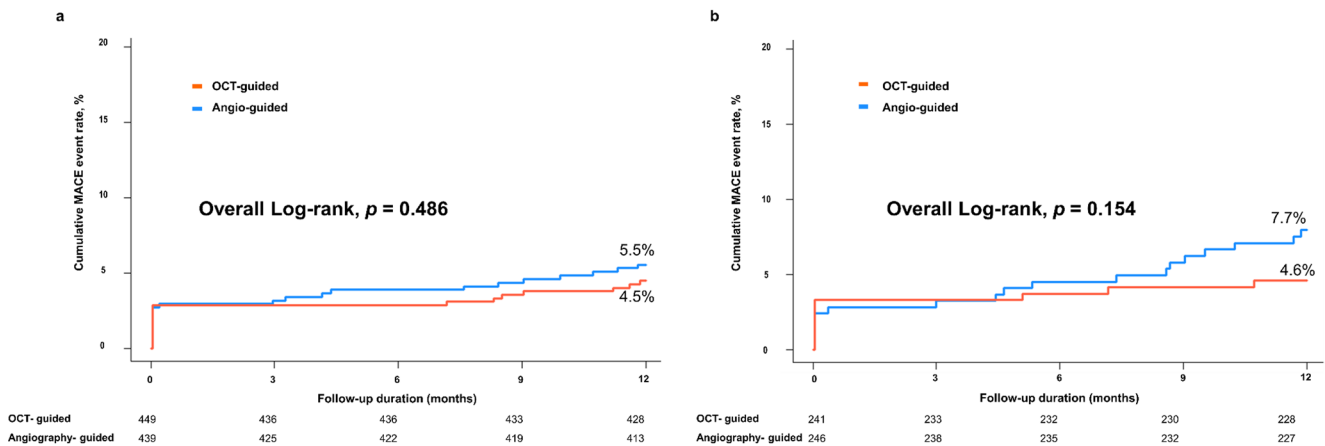


Fig. 2 One-year MACE according to diseased vessel and PCI guidance strategy Kaplan–Meier curves showing the cumulative incidence of major adverse cardiac events (MACE) at 1 year in patients undergoing OCT-guided PCI versus angiography-guided PCI, stratified by target vessel. (a) Lesions involving the left anterior descending artery (LAD)

In the non-LAD subgroup, OCT-guided PCI was associated with a significantly lower risk of target-lesion revascularization (adjusted HR 0.10; 95% CI 0.01–0.90; $p=0.040$) and any revascularization (adjusted HR 0.22; 95% CI 0.08–0.62; $p=0.004$). However, there was no significant

and (b) lesions involving non-LAD vessels. MACE was defined as a composite of cardiac death, myocardial infarction, stent thrombosis, or ischemia-driven target-vessel revascularization. Numbers at risk are shown below each panel. p values were calculated using the log-rank test

interaction between diseased vessel and imaging strategy for these endpoints (p for interaction=0.330 and 0.309, respectively) (Table 3). Rates of stroke, major bleeding events, and contrast nephropathy were low and showed no apparent differences between imaging strategies within either subgroup.

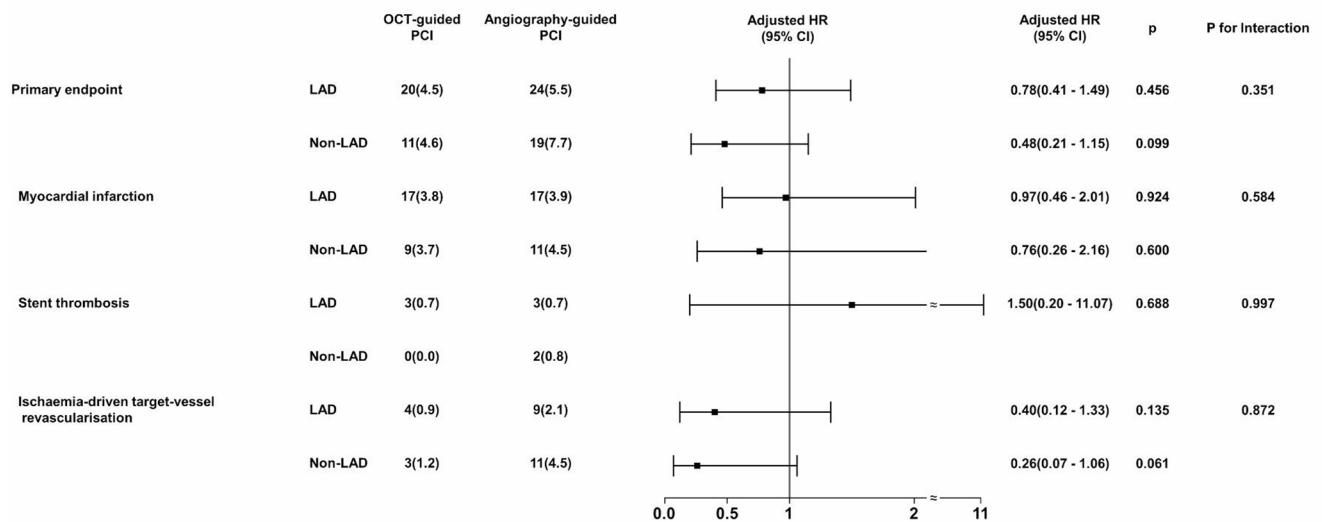


Fig. 3 Association between diseased vessel and OCT-guided versus angiography-guided PCI and clinical outcomes Forest plot of univariate and adjusted hazard ratios for clinical outcomes comparing OCT-guided versus angiography-guided PCI according to diseased vessel (LAD vs. non-LAD). *p* values for interaction assess effect modification by diseased vessel

Table 2 Lesion and Procedural Characteristics by Imaging Strategy and Diseased Vessel

Variable	LAD			Non-LAD		
	OCT-guidance (N=449)	Angiography-guidance (N=439)	<i>p</i> value	OCT-guidance (N=241)	Angiography-guidance (N=246)	<i>p</i> value
Procedural characteristics						
Number of target lesions per patient	1 (1–1)	1 (1–2)	0.014	1 (1–2)	1 (1–1)	<0.001
Number of stents per patient	1 (1–2)	1 (1–2)	0.312	2 (1–2)	1 (1–2)	0.005
Total treated complex lesions, n	527	540	—	264	261	—
Stent diameter, mm	3.3 (3.0–3.5)	3.0 (2.8–3.3)	<0.001	3.3 (3.0–3.5)	3.0 (2.8–3.4)	<0.001
Total stent length, mm	38.0 (29.2–52.2)	35.8 (28.4–50.2)	0.165	41.2 (30.9–58.7)	38.0 (29.5–53.3)	0.044
Adjunct post-dilatation, n (%)	504 (95.6%)	508 (94.1%)	0.310	251 (95.1%)	246 (94.3%)	0.822
High-pressure post-dilatation, n (%)	327 (62.0%)	237 (43.9%)	<0.001	183 (69.3%)	128 (49.0%)	<0.001
Maximal inflation pressure, atm	18.0 (16.0–20.0)	15.0 (12.0–17.0)	<0.001	18.0 (16.0–20.0)	15.0 (12.0–18.0)	<0.001
Final balloon size, mm	3.5 (3.3–4.0)	3.5 (3.0–3.5)	<0.001	3.5 (3.0–4.0)	3.5 (3.0–3.5)	<0.001
Contrast volume per patient, mL	300 (200–380)	200 (170–250)	<0.001	300 (220–370)	205 (180–250)	<0.001
Procedural time per patient, min	51.0 (40.0–69.0)	40.0 (30.0–58.0)	<0.001	50.0 (39.0–65.0)	40.0 (27.0–53.0)	<0.001
Quantitative coronary angiographic analyses						
Reference vessel diameter, mm	2.75 (2.52–3.01)	2.74 (2.46–3.03)	0.396	2.91 (2.56–3.18)	2.90 (2.57–3.26)	0.906
Minimal lumen diameter, mm	0.71 (0.52–0.93)	0.71 (0.47–0.94)	0.865	0.68 (0.38–0.91)	0.61 (0.36–0.91)	0.138
Lesion length, mm	33.0 (24.6–48.1)	30.9 (23.9–45.6)	0.178	36.4 (26.3–53.3)	33.2 (24.7–49.0)	0.042
Post-procedural minimal lumen diameter, mm	2.69 (2.43–2.95)	2.57 (2.35–2.79)	<0.001	2.83 (2.53–3.18)	2.64 (2.39–3.04)	<0.001
Post-procedural diameter stenosis, %	12.0 (7.0–17.0)	14.0 (9.0–19.0)	0.323	12.0 (8.0–17.0)	14.0 (9.0–18.0)	0.009

Values are median (interquartile range) unless otherwise indicated. Percentages are presented as n (%). OCT indicates optical coherence tomography; PCI, percutaneous coronary intervention

Procedural characteristics and quantitative coronary angiographic analyses

Procedural characteristics differed according to PCI guidance modality in both LAD and non-LAD lesions (Table 2). In non-LAD lesions, OCT-guided PCI was associated with a greater number of target lesions treated per patient and a

higher number of stents implanted compared with angiography-guided PCI. Across diseased vessel, OCT-guided PCI consistently employed larger stent diameters than angiography-guided PCI (both $p < 0.001$). Total stent length was modestly longer with OCT guidance in non-LAD lesions but was similar between strategies in LAD lesions.

Table 3 Clinical Outcomes of OCT-Guided Versus Angiography-Guided PCI in LAD and Non-LAD Lesions

Endpoint	LAD (<i>N</i> =888)				Non-LAD (<i>N</i> =487)				<i>p</i> for interaction
	OCT-guided PCI (<i>N</i> =449)	Angiography-guided PCI (<i>N</i> =439)	Adjusted HR (95% CI)	<i>p</i> value	OCT-guided PCI (<i>N</i> =241)	Angiography-guided PCI (<i>N</i> =246)	Adjusted HR (95% CI)	<i>p</i> value	
Primary endpoint									
MACE	20 (4.5%)	24 (5.5%)	0.78 (0.41–1.49)	0.456	11 (4.6%)	19 (7.7%)	0.48 (0.21–1.15)	0.099	0.351
Secondary endpoints									
All-cause death	4 (0.9%)	4 (0.9%)	15.61 (0.12–2073.78)	0.271	0 (0.0%)	1 (0.4%)	Not estimable	—	0.996
Cardiac death	1 (0.2%)	3 (0.7%)	Not estimable	—	0 (0.0%)	1 (0.4%)	Not estimable	—	0.998
MI	17 (3.8%)	17 (3.9%)	0.97 (0.46–2.01)	0.924	9 (3.7%)	11 (4.5%)	0.76 (0.26–2.16)	0.600	0.584
Spontaneous MI	4 (0.9%)	5 (1.1%)	0.86 (0.20–3.83)	0.848	1 (0.4%)	5 (2.0%)	0.28 (0.03–2.63)	0.262	0.370
Target-vessel-related MI	2 (0.4%)	4 (0.9%)	0.39 (0.07–2.29)	0.298	1 (0.4%)	4 (1.6%)	0.23 (0.02–2.89)	0.257	0.971
Non-target-vessel-related MI	2 (0.4%)	1 (0.2%)	Not estimable	—	0 (0.0%)	1 (0.4%)	Not estimable	—	0.998
Periprocedural MI	13 (2.9%)	12 (2.7%)	0.94 (0.40–2.21)	0.878	8 (3.3%)	6 (2.4%)	0.99 (0.25–3.85)	0.986	0.955
Stent thrombosis	3 (0.7%)	3 (0.7%)	1.50 (0.20–11.07)	0.688	0 (0.0%)	2 (0.8%)	Not estimable	—	0.997
Ischemia-driven target-vessel revascularization	4 (0.9%)	9 (2.1%)	0.40 (0.12–1.33)	0.135	3 (1.2%)	11 (4.5%)	0.26 (0.07–1.06)	0.061	0.872
Target-lesion revascularization	4 (0.9%)	8 (1.8%)	0.47 (0.14–1.61)	0.227	1 (0.4%)	9 (3.7%)	0.10 (0.01–0.90)	0.040	0.330
Any revascularization	7 (1.6%)	13 (3.0%)	0.57 (0.22–1.49)	0.250	5 (2.1%)	20 (8.1%)	0.22 (0.08–0.62)	0.004	0.309

Values are *n* (%). Hazard ratios (HRs) were derived from multivariable Cox regression models. CI indicates confidence interval. MACE denotes major adverse cardiovascular events; MI, myocardial infarction

Although adjunct post-dilatation was performed at similarly high rates in all groups, high-pressure post-dilatation was significantly more frequent with OCT guidance in both LAD and non-LAD lesions, accompanied by higher maximal inflation pressures and larger final balloon sizes (all $p < 0.001$). Consistent with these findings, OCT-guided PCI was associated with increased procedural resource utilization, including greater contrast volume use and longer procedural duration, irrespective of diseased vessel (all $p < 0.001$).

Baseline quantitative coronary angiographic characteristics were largely comparable between OCT-guided and angiography-guided PCI in both LAD and non-LAD lesions, including reference vessel diameter, pre-procedural minimal lumen diameter, and lesion length. Post-procedurally, OCT-guided PCI achieved superior angiographic results, with a larger final minimal lumen diameter in both LAD and non-LAD lesions (both $p < 0.001$). Residual diameter stenosis was significantly lower with OCT guidance in non-LAD lesions, while a similar numerical trend was observed in LAD lesions.

Discussion

In this prespecified substudy of the OCCUPI trial excluding left main disease, OCT-guided PCI was associated with more intensive stent optimization and improved

angiographic outcomes compared with angiography-guided PCI, irrespective of diseased vessel (LAD versus non-LAD). Although the magnitude of clinical benefit did not significantly differ between LAD and non-LAD vessels, OCT guidance was consistently associated with lower rates of repeat revascularization and more favorable composite ischemic outcomes across diseased vessel.

Historically, the LAD has been regarded as the most prognostically important coronary artery because it supplies a large myocardial territory, and LAD lesions—particularly in the proximal segment—have been associated with worse outcomes in earlier observational studies and acute myocardial infarction cohorts. This clinical relevance of the LAD should not be underestimated [1–3]. However, contemporary PCI data increasingly challenge the notion that coronary location alone is the dominant determinant of long-term prognosis [4–6]. Our findings further suggest that, in the setting of complex coronary intervention with contemporary drug-eluting stents, procedural quality—particularly when guided by intravascular imaging—may be more influential than coronary artery location per se in determining clinical outcomes.

Previous studies have consistently demonstrated the clinical benefit of intravascular ultrasound (IVUS)-guided percutaneous coronary intervention (PCI). In the randomized ULTIMATE trial, IVUS-guided drug-eluting stent implantation significantly reduced target vessel failure compared with angiography-guided PCI, supporting the role of IVUS

in procedural optimization and outcome improvement. Although prior randomized and registry studies, including the ULTIMATE trial and the ADAPT-DES IVUS substudy, have established the overall benefit of IVUS-guided PCI, none specifically examined whether these benefits differ according to diseased vessel, particularly between LAD and non-LAD arteries [17, 18]. Our study extends these prior findings by evaluating whether the clinical benefit of intravascular imaging-guided PCI differs according to diseased vessel (LAD versus non-LAD).

Although recent trials—ILUMIEN IV, OCTOBER, and OCTIVUS [12, 13, 19]—have firmly established the role of OCT in complex PCI, none have prespecified a comparison of treatment effect by diseased coronary territory. ILUMIEN IV included a heterogeneous high-risk lesion cohort but did not stratify by vessel; OCTOBER was restricted exclusively to complex bifurcations; and OCTIVUS compared OCT with IVUS rather than angiography. Our analysis fills this gap by demonstrating, within a prespecified randomized framework, that the clinical and procedural benefit of OCT-guided PCI is consistent across coronary territories. This finding has direct practice implications: it supports the uniform application of imaging-guided optimization across all major epicardial vessels in complex coronary intervention, rather than its restriction to any single territory.

From a theoretical standpoint, anatomical and technical factors could potentially influence the effectiveness of OCT guidance across different vessels. For example, catheter deliverability, vessel tortuosity, and side-branch anatomy—particularly in the LCX or RCA—may affect image acquisition quality and stent optimization. In addition, the need for contrast-based blood clearance during OCT imaging could raise concerns regarding image uniformity in non-LAD vessels with more complex flow patterns [20, 21].

Despite these considerations, our analysis demonstrated consistent benefits of OCT-guided PCI across both LAD and non-LAD vessels, with no significant interaction between diseased vessel and imaging strategy. These findings suggest that, in contemporary practice, advances in OCT technology and procedural expertise may mitigate vessel-specific technical limitations, allowing high-quality stent optimization to be achieved irrespective of coronary artery location. Ultimately, our results underscore that procedural quality facilitated by intravascular imaging, rather than vessel location per se, is a key determinant of clinical outcomes.

The procedural findings provide mechanistic insights into these clinical outcomes. Across both LAD and non-LAD vessels, OCT-guided PCI was associated with the use of larger stent diameters, higher inflation pressures, more frequent high-pressure post-dilatation, and superior post-procedural luminal dimensions. These differences likely

reflect more accurate vessel sizing and systematic identification of suboptimal stent deployment with OCT, reinforcing the concept that procedural optimization enabled by intravascular imaging—rather than vessel identity alone—is a key determinant of outcomes after PCI.

Collectively, these results indicate that while LAD lesions remain clinically important because of the extent of myocardium at risk, intravascular imaging-guided PCI represents a critical strategy to mitigate lesion-related risk and improve outcomes across coronary territories. Our data support a paradigm in which the prognostic impact of coronary anatomy is increasingly modifiable through high-quality, imaging-guided PCI.

Study limitations

This study has several limitations. First, although prespecified within the OCCUPI trial, this analysis represents a subgroup study and was not specifically powered to detect modest effect modification between diseased vessel and PCI guidance strategy. Second, patients with unprotected left main disease were intentionally excluded because left main lesions inherently involve both the left anterior descending and left circumflex arteries, precluding reliable lesion-level classification by coronary territory. Third, baseline lesion characteristics differed between LAD and non-LAD groups, reflecting inherent anatomical features of each coronary territory rather than allocation bias; although multivariable adjustment was performed, residual confounding cannot be fully excluded. Fourth, generalizability may be limited by the exclusively Korean cohort, the use of XIENCE everolimus-eluting stents only, and the substantial OCT expertise of participating centers. Finally, event rates were relatively low and follow-up was limited to 1 year, and the long-term durability of these findings remains uncertain.

Conclusion

In this prespecified substudy of the OCCUPI trial excluding left main disease, we evaluated whether coronary artery location, defined as LAD versus non-LAD vessel involvement, modifies the clinical benefit of OCT-guided PCI compared with angiography-guided PCI. OCT-guided PCI was associated with more intensive stent optimization, superior acute angiographic results, and a consistently lower risk of repeat revascularization compared with angiography-guided PCI, with no significant interaction between vessel category and imaging strategy. Although LAD lesions have traditionally been regarded as higher risk because of the larger myocardial territory at risk and greater anatomical complexity, our findings suggest that the benefit of OCT-guided PCI is

not substantially modified by coronary artery location in the contemporary era. Rather, procedural quality achieved through meticulous stent optimization, facilitated by intravascular imaging, appears to be a key determinant of clinical outcomes irrespective of the diseased vessel.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s10554-026-03734-5>.

Acknowledgements The authors thank Kwang-Min Lee for statistical analysis assistance.

Author contributions All authors contributed to the conception and design of the study. The study was conceived and supervised by Jung Ho Heo and Byeong-Keuk Kim. Material preparation, data collection, data analysis, and interpretation were performed by Soo-Jin Kim and Seung-Jun Lee, who also drafted the first version of the manuscript. All authors enrolled patients, performed clinical follow-up, critically revised the manuscript for important intellectual content, and approved the final version of the manuscript. All authors had full access to the data, verified the accuracy and integrity of the work, and took final responsibility for the decision to submit the manuscript for publication.

Funding This OCCUPI trial was funded by Abbott Vascular (Santa Clara, CA, USA) and supported by the Cardiovascular Research Center (Seoul, South Korea). The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Data availability The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Competing interests The authors declare no competing interests. S-JL reports research grants and speaker fees from Boston Scientific, Medtronic, ChongKunDang, and Sam Jin Pharmaceutical. JHH reports consulting and speaker fees from Abbott Vascular. J-WL reports consulting fees from Genoss; speaker fees from Yuhan, Boryoung, Sam Jin Pharmaceutical, ChongKunDang, Korea United Pharm, HK inno.N, Novartis, Boehringer Ingelheim, AstraZeneca, Medtronic, Abbott Vascular, Amgen, Sanofi, Boston Scientific, Daiichi-Sankyo, Daewoong Pharmaceutical, Biosensors, Dong-A ST, and JW Pharmaceutical; and participation on the data safety monitoring board of the Rescue SHOCK trial. S-JH reports speaker fees from AstraZeneca, Amgen, ChongKunDang, Hanmi, and Viatrix; and participation on the data safety monitoring board of the IVUS-DCB trial. JSK reports grants from Sam Jin Pharmaceutical, Yuhan, Daiichi-Sankyo, Biosensors, and Qualitech Korea and proctoring fees from Abbott Vascular. Y-GK reports research grants from Medtronic, Korea United Pharm, Cook Medical, Boston Scientific, Otsuka Korea, Dong-A ST, Sam Jin Pharmaceutical, Cordis, HK inno.N, and GC Biopharma. M-KH reports research grants, paid to their institution, from Sam Jin Pharmaceutical and ChongKunDang and honoraria for lectures from Medtronic and Edwards Lifesciences. YJ reports research grants, paid to their institution, from Abbott Vascular. YK reports research grants and speaker fees from Abbott Vascular, Medtronic, Boston Scientific, Merit Medical, HK inno.N, ChongKunDang, and Amgen. B-KK reports research grants and speaker or consulting fees from Abbott Vascular, Yuhan, Sam Jin Pharmaceutical, ChongKunDang, Medtronic, Boston Scientific, Biotronik, Genoss, CGBIO, MicroPort, Daewoong Pharmaceu-

tical, Amgen, Bayer Korea, DIO Medical, Hanmi, AstraZeneca, and Novartis. All other authors declare no competing interests

Ethics approval This study was performed in line with the principles of the Declaration of Helsinki. The OCCUPI trial was approved by the institutional review board at each of the 20 participating centers. This prespecified substudy was deemed exempt from additional IRB review.

Author Responsibility All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

Consent to participate Written informed consent was obtained from all individual participants enrolled in the OCCUPI trial.

Consent to publish Not applicable. The manuscript does not contain any individual person's identifying data, images, or videos.

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