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ORIGINAL RESEARCH

CORONARY

Artificial Intelligence–Based Fully Automated Quantitative Coronary Angiography vs Optical Coherence Tomography–Guided PCI

The FLASH Trial

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ABSTRACT

BACKGROUND Recently developed artificial intelligence–based coronary angiography (AI-QCA, fully automated) provides real-time, objective, and reproducible quantitative analysis of coronary angiography without requiring additional time or labor.

OBJECTIVES This study aimed to evaluate the efficacy of AI-QCA–assisted percutaneous coronary intervention (PCI) compared to optical coherence tomography (OCT)–guided PCI in terms of post-PCI results.

METHODS This trial enrolled 400 patients with significant coronary artery disease undergoing PCI from 13 participating centers in South Korea. Patients were randomized in a 1:1 ratio to either AI-QCA–assisted or OCT-guided PCI. The primary endpoint was the post-PCI minimal stent area (MSA) assessed by OCT. The noninferiority of AI-QCA–assisted PCI to OCT-guided PCI regarding the post-PCI MSA was tested with a noninferiority margin of 0.8 mm^2.

RESULTS A total of 395 patients (199 in the AI-QCA group and 196 in the OCT group) were included in the primary endpoint analysis. The post-PCI MSA was 6.3 ± 2.2 mm^2 in the AI-QCA group and 6.2 ± 2.2 mm^2 in the OCT group (difference, −0.16; 95% CI: −0.59 to 0.28; P for noninferiority < 0.001). Other OCT-defined endpoints, such as stent underexpansion (50.8% [101/199] vs 54.6% [107/196]; $P = 0.48$), dissection (15.6% [31/199] vs 12.8% [25/196]; $P = 0.42$), and untreated reference segment disease (15.1% [30/199] vs 13.3% [26/196]; $P = 0.61$), were not significantly different between groups, except for a higher incidence of stent malapposition in the AI-QCA group (13.6% [27/199] vs 5.6% [11/196]; $P = 0.007$).

CONCLUSIONS This study demonstrated the noninferiority of AI-QCA–assisted PCI to OCT-guided PCI in achieving MSA with comparable OCT-defined endpoints. (Fully Automated Quantitative Coronary Angiography Versus Optical Coherence Tomography Guidance for Coronary Stent Implantation [FLASH]; NCT05388357) (JACC Cardiovasc Interv. 2025;18:187–197) © 2025 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

AI-QCA = artificial intelligence–based quantitative coronary angiography

MSA = minimal stent area

OCT = optical coherence tomography

PCI = percutaneous coronary intervention

QCA = quantitative coronary angiography

Randomized trials have shown that intracoronary imaging-guided percutaneous coronary intervention (PCI) improves clinical outcomes compared with angiography-guided PCI, particularly in cases of complex coronary artery disease.[1-7] Recent clinical guidelines recommend the use of intracoronary imaging as a Class 1A indication for left main, true bifurcation, and long lesions.[8] However, its global use is likely to remain limited because of various practical, logistic, and economic constraints.[9,10] Furthermore, in less complex coronary artery disease in which the clinical benefits of intracoronary imaging are less well established, angiography-guided PCI is expected to continue as the de facto strategy. This underscores the importance of refining and standardizing angiography-guided PCI to improve outcomes of a substantial portion of patients undergoing PCI.

As part of ongoing efforts to optimize angiography-guided PCI, the GUIDE-DES (Quantitative Coronary Angiography vs Intravascular Ultrasound Guidance for Drug-Eluting Stent Implantation) trial evaluated the use of quantitative coronary angiography (QCA) instead of operator-driven visual estimation. In this trial, QCA-guided PCI showed comparable clinical outcomes at 1 year with those of intravascular ultrasound-guided PCI.[11] However, the broader application of this approach is limited by its non-real-time nature, time-consuming processes, and reliance on manual QCA data. Recently, an artificial intelligence–based quantitative coronary angiography (AI-QCA) system has been developed.[12-14] This system offers fully automated, real-time quantitative analyses of angiographic images, providing precise measurements of the severity of coronary artery stenosis and the vessel dimensions without additional time and labor. Consequently, AI-QCA has the potential to address the practical limitations of both conventional angiography-guided PCI and manual QCA-guided PCI approaches.

To evaluate the efficacy of this innovative technology, we designed the FLASH (Fully Automated Quantitative Coronary Angiography Versus Optical Coherence Tomography Guidance for Coronary Stent Implantation) trial. This study aimed to demonstrate the noninferiority of AI-QCA–assisted PCI compared with intracoronary imaging–guided PCI using optical coherence tomography (OCT) in terms of post-procedural results.

METHODS

TRIAL DESIGN AND OVERSIGHT. The FLASH trial was an investigator-initiated, multicenter, prospective, randomized, open-label, parallel-group, noninferiority trial conducted at 13 sites in South Korea. The details of the trial design have been described previously.[15] Information on the participating investigators and the trial organization are provided in the Supplemental Appendix. The protocol was approved by the Institutional Review Board and ethics committee at each participating site, and all patients provided written informed consent.

All authors vouch for the accuracy and completeness of the data and the fidelity of the trial to the protocol. The principal investigator had full access to all the data in the study and had final responsibility for the decision to submit for publication. In addition, an independent Data and Safety Monitoring Board approved the original trial protocol and subsequent

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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amendments and monitored patient safety periodically throughout the trial.

PARTICIPANTS. Patients aged 19 years or older undergoing PCI with contemporary drug-eluting stents for significant coronary artery lesions were eligible for enrollment. Patients were excluded if they had left main disease, chronic total occlusion, or graft vascular lesion; required 2-stenting techniques for coronary bifurcation lesions; or had any lesion characteristics resulting in the expected inability to penetrate the OCT catheter into the lesion such as severe tortuous vessel or a severely calcified vessel. Further details on the inclusion and exclusion criteria are provided in the Supplemental Appendix.

RANDOMIZATION AND PROCEDURES. After providing written informed consent, eligible patients were randomly assigned in a 1:1 ratio to undergo either AI-QCA–assisted PCI or OCT-guided PCI following diagnostic coronary angiography. Randomization was performed through an interactive web response system and stratified by enrollment site.

In the AI-QCA group, AI-QCA analysis was conducted using the MPXA-2000 system (Medipixel, Inc). During the procedure, coronary angiography images were automatically uploaded to the software, which immediately generated quantitative analytic data including the minimum lumen diameter, proximal and distal reference lumen diameters, lesion length, and diameter stenosis (Supplemental Figures 1 and 2). The protocol recommended selecting a stent size approximately 20% larger than the distal reference diameter, rounding down to the nearest suitable size. Stent length was chosen to adequately cover the proximal and distal reference segments based on the lesion length provided by AI-QCA. To minimize residual stenosis, high-pressure postdilation with a noncompliant balloon was strongly recommended, with the final balloon size up to 20% larger than the respective proximal and distal reference diameters as measured by AI-QCA. Once the operator considered the AI-QCA–assisted PCI to be successfully completed, a post-PCI OCT evaluation was performed to assess the primary endpoint. Operators in the AI-QCA–assisted PCI group were not blinded to the final OCT images. Although generally discouraged, additional procedures were permitted to correct significant suboptimal stent results detected by OCT (such as severe underexpansion, extensive strut malapposition, or major stent edge dissection) to ensure patient safety. The primary endpoint was assessed by OCT before any such corrections.

In the OCT group, OCT-guided PCI was performed according to a standardized protocol.[16] Stent size and length were determined using on-site OCT measurements. Stent size was primarily selected based on the average diameter of the external elastic lamina, rounded down to the nearest 0.25 mm. If the external elastic lamina was not visualized, stent size was based on the average of the distal reference lumen diameter, rounded up by 0 to 0.25 mm.[16] Poststenting high-pressure dilatation with a noncompliant balloon was also strongly recommended. A final OCT run was obtained after the completion of the procedure.

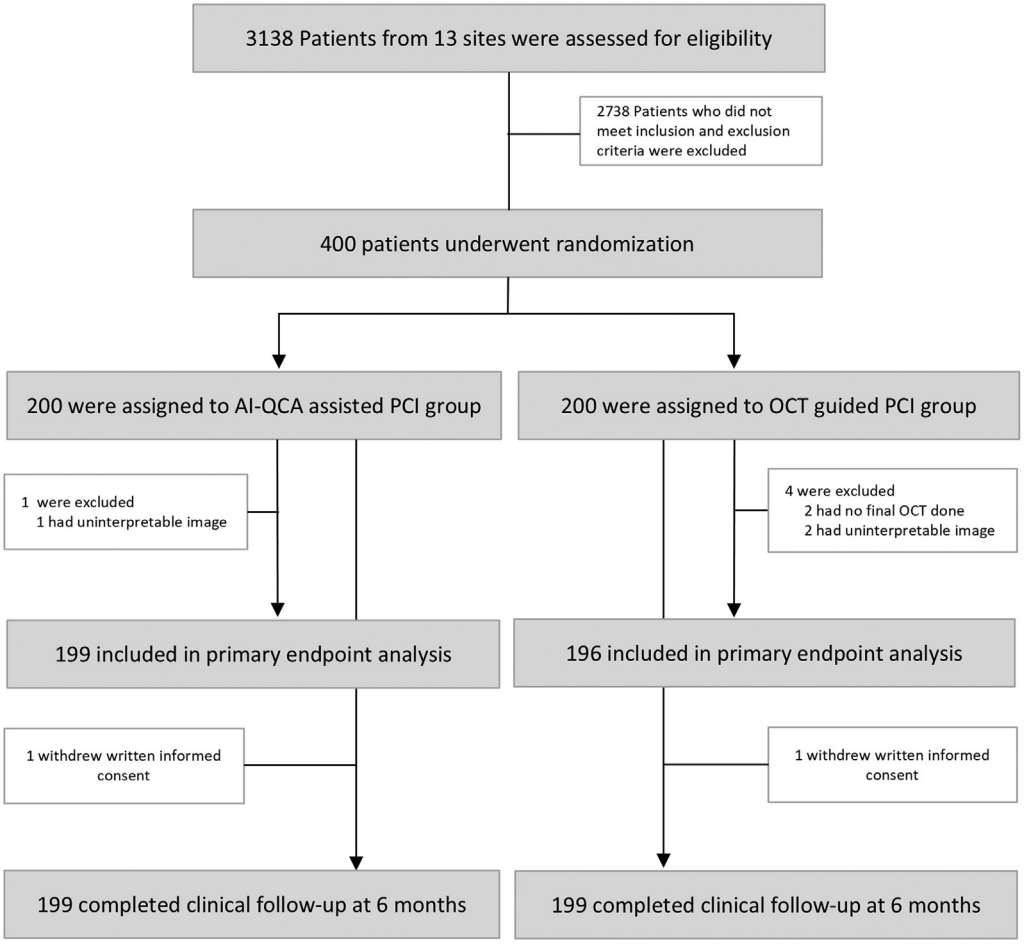
Procedural anticoagulation was achieved with unfractionated heparin according to the local site protocols. After PCI, all patients were prescribed lifelong aspirin and a $P2Y_{12}$ inhibitor (clopidogrel, prasugrel, or ticagrelor) for at least 6 to 12 months at the physician's discretion according to the clinical indication and procedural complexity. Pharmacologic therapy, including statins, antihypertensive, and antidiabetic medications, was optimized in accordance with established practice standards during the study period.

TRIAL ENDPOINTS AND FOLLOW-UP. The primary endpoint was the post-PCI minimal stent area (MSA, mm^2) assessed by an OCT evaluation following the completion of the index PCI. In addition, 2 sensitivity analyses were conducted as follows: 1) MSA measurement for each segment when the stent segment is divided into 2 equal halves; and 2) MSA measurement for each segment when the stent segment was divided by a large side branch (>2 mm) branch point. All OCT imaging analyses were performed by the independent imaging core laboratory at Asan Medical Center blinded to group assignment and clinical data. All imaging data were anonymized in the local research centers and collected at the core laboratory. The secondary safety endpoint was procedural complications, including angiographic dissection, perforation, or acute closure requiring active intervention after stent implantation. Other secondary endpoints were OCT-defined endpoints, angiography-defined endpoints, and clinical outcomes at 6 months. The definition of the endpoint is provided in the Supplemental Appendix.

Follow-up was performed at hospital discharge and at 1 and 6 months. During follow-up, guideline-directed medical therapy, risk factor management, and lifestyle modifications for intensive secondary prevention were strongly recommended in accordance with contemporary clinical guidelines.

STATISTICAL METHODS. The trial was designed to test the hypothesis that AI-QCA–assisted PCI would be noninferior to OCT-guided PCI with respect to the primary endpoint of MSA assessed by final OCT. On

FIGURE 1 Study Flow



AI-QCA = artificial intelligence–based quantitative coronary angiography; OCT = optical coherence tomography; PCI = percutaneous coronary intervention.

the basis of the results of previous studies about post-PCI MSA,[17-20] we assumed the SD of the primary endpoint to be 2.3 mm^2.[21] Considering 5% of cases with an immeasurable minimum stent area, we estimated that a sample of 200 patients in each group would provide the trial with more than 90% power to detect noninferiority using a 1-sided, 2-sample Student's *t*-test. The margin of noninferiority was 0.8 mm^2, and the significance level (alpha) of the test was 0.025.

All principal analyses were performed according to the intention-to-treat principle. Continuous variables were reported as mean ± SD and compared with Student's *t*-tests or Mann-Whitney *U* tests. Baseline and angiographic characteristics were assessed using the Mann-Whitney *U* test. The primary endpoint and other OCT-defined endpoints were assessed using the Student's *t*-test. Categoric variables were reported as frequencies and percentages and compared with the chi-square statistics or Fisher exact test. We reported results for the assessment of noninferiority were presented based on a 1-sided 95% CI. Analyses were performed using SAS software, version 9.4 (SAS Institute).

ROLE OF THE FUNDING SOURCE. This investigator-initiated trial was funded by the Korea Medical Device Development Fund (RS-2022-00141289) and Medipixel, Inc. The funders had no role in the trial design; data collection, analysis, or interpretation; or the writing of the manuscript.

RESULTS

STUDY POPULATION AND BASELINE CHARACTERISTICS. Between October 4, 2022, and February 13, 2024, we randomly assigned 400 participants from 13 hospitals in South Korea to receive AI-QCA-assisted PCI or OCT-guided PCI. The patient assignment and follow-up are shown in Figure 1. All participants underwent the assigned strategy, and final OCT imaging was analyzable in 199 (99.5%) in the AI-QCA group and 196 (98.0%) in the OCT group. Baseline clinical characteristics are presented in Table 1. The mean age was 65.1 ± 9.8 years, 81.8% of patients were men, 29.5% had diabetes, and 40.3% presented as acute coronary syndrome.

PROCEDURAL CHARACTERISTICS. Procedural characteristics are presented in Table 2. Patients received 1 (IQR: 1-1) drug-eluting stent with a diameter of 3.25 mm (IQR: 3.0-3.5 mm) and a length of 26 mm (IQR: 20-34 mm). Additionally, 93.0% (361/388) of the patients underwent postdilation using a high-pressure balloon with 3.7 ± 0.5 mm in maximal balloon diameter and 20.4 ± 4.9 atm in maximal pressure. There were no significant differences between the groups in terms of stent size, balloon size, or postdilation balloon pressure. Procedure duration and contrast volume were not significantly different between groups. Angiographic characteristics are presented in Table 3.

PRIMARY ENDPOINT. A total of 395 patients (199 in the AI-QCA group and 196 in the OCT group) were included in the primary endpoint analysis after excluding 5 patients without evaluable OCT images. The final poststenting OCT evaluation is presented in Table 4. As a primary endpoint, the post-PCI MSA was 6.3 ± 2.2 mm^2 in the AI-QCA group and 6.2 ± 2.2 mm^2 in the OCT group. The MSA in the AI-QCA group was noninferior to the OCT group (difference, −0.16; 95% CI: −0.59 to 0.28; P for noninferiority < 0.001; P for superiority = 0.48) (Figure 2). Sensitivity analysis showed that the MSA in the proximal half segment was 7.2 ± 2.1 mm^2 in the AI-QCA group and 7.1 ± 2.1 mm^2 in the OCT group (difference, −0.07; 95% CI: −0.49 to 0.34; P for noninferiority < 0.001; P for superiority = 0.73), and the MSA in the distal half segment was 6.5 ± 2.3 mm^2 in the AI-QCA group and 6.3 ± 2.3 mm^2 in the OCT group (difference, −0.20; 95% CI: −0.66 to 0.25; P for noninferiority < 0.001; P for superiority = 0.38). Similar results were observed for the MSA in the proximal (8.0 ± 1.9 vs 7.4 ± 2.0 mm^2; difference, −0.59; 95% CI: −1.37 to 0.18; P for noninferiority < 0.001; P for superiority = 0.13) and distal (6.0 ± 1.9 vs 5.8 ± 2.0 mm^2; difference, −0.13; 95% CI, −0.90 to 0.64; P for noninferiority = 0.008; P for superiority = 0.74) stented segments separated by a side branch >2 mm in diameter (Supplemental Figure 3).

TABLE 1 Baseline Characteristics

	AI-QCA (n = 200)	OCT (n = 200)
Age, y	65.0 (58.0-71.8)	61.0 (57.0-64.0)
Male	164 (82.0)	163 (81.5)
Body mass index, kg/m^2	25.1 (23.3-27.1)	24.6 (22.7-26.3)
Diabetes mellitus		
Any	59 (29.5)	59 (29.5)
Requiring insulin	4 (2.0)	5 (2.5)
Hypertension	128 (64.0)	129 (64.5)
Hyperlipidemia	176 (88.0)	175 (87.5)
Current smoker	44 (22.0)	54 (27.0)
Previous myocardial infarction	7 (3.5)	5 (2.5)
Previous coronary intervention	20 (10.0)	24 (12.0)
Previous congestive heart failure	1 (0.5)	0
Left ventricular ejection fraction, %	63 (59-66)	61 (57-64)
Chronic renal insufficiency	8 (4.0)	3 (1.5)
Clinical presentation		
Silent ischemic or stable angina	128 (64.0)	111 (55.5)
Unstable angina	46 (23.0)	59 (29.5)
Acute myocardial infarction	26 (13.0)	30 (15.0)

Values are median (Q1-Q3) or n (%).
AI-QCA = artificial intelligence–based quantitative coronary angiography; OCT = optical coherence tomography.

TABLE 2 Procedural Characteristics

	AI-QCA (n = 200)	OCT (n = 200)	*P* Value
Arterial access			>0.99
Radial	184 (92.0)	184 (92.0)	
Femoral	16 (8.0)	16 (8.0)	
Stent number	1 (1-1)	1 (1-1)	0.36
Total stent length, mm	24 (20-33)	28 (20.0-38)	0.14
Mean stent diameter, mm	3.25 (3.0-3.5)	3.0 (3.0-3.5)	0.025
Postdilation with noncompliance balloon[a]	178 (91.8)	183 (94.3)	0.32
Maximal noncompliance balloon size, mm	3.7 (3.4-4.1)	3.6 (3.3-3.9)	0.040
Maximal noncompliance balloon pressure, atm	20 (16-24)	20 (16-24)	0.31
Procedure duration, min	33 (23-45)	35 (26-46)	0.11
Contrast volume, mL	180 (140-230)	187 (150-220)	0.64
Target vessel			0.10
Left anterior descending	107 (53.5)	128 (64.0)	
Left circumflex	33 (16.5)	27 (13.5)	
Right coronary artery	60 (30.0)	45 (22.5)	

Values are n (%) or median (Q1-Q3). [a]Data were available in 388 patients (194 patients in the AI-QCA group and 194 patients in the OCT group).
Abbreviations as in Table 1.

TABLE 3 Angiographic Characteristics

	AI-QCA (n = 200)	OCT (n = 200)	*P* Value
Quantitative coronary angiography			
Preintervention			
Reference vessel diameter, mm	2.9 (2.6-3.3)	2.9 (2.6-3.2)	0.80
Lesion length, mm	24.7 (19.0-31.8)	25.8 (19.0-34.7)	0.27
Minimal lumen diameter, mm	1.0 (0.7-1.3)	1.0 (0.8-1.2)	0.85
Diameter stenosis, %	66 (55-74)	64 (55-74)	0.57
Postintervention			
Reference vessel diameter, mm	3.0 (2.7-3.5)	3.0 (2.6-3.4)	0.26
Stented length, mm	24.4 (19.6-31.8)	25.8 (19.6-34.5)	0.20
Minimal lumen diameter, mm			
In stent	2.7 (2.4-3.1)	2.7 (2.4-3.0)	0.13
In segment	2.4 (2.0-2.7)	2.4 (2.0-2.7)	0.97
Acute gain, mm			
In stent	1.7 (1.4-2.1)	1.6 (1.3-2.0)	0.14
In segment	1.3 (1.0-1.7)	1.3 (1.0-1.7)	0.91
Diameter stenosis, %			
In stent	12 (5-19)	13 (4-21)	0.52
In segment	21 (12-32)	22 (13-29)	0.56

Values are median (Q1-Q3).
Abbreviations as in Table 1.

SECONDARY ENDPOINT. Among other OCT-defined endpoints, there were no significant differences in overall stent expansion (78.7% ± 14.6% vs 79.2% ± 14.4%; $P = 0.78$), stent underexpansion (50.8% [95% CI: 43.6-57.9] vs 54.6% [95% CI: 47.3-61.7]; $P = 0.48$), dissection (15.6% [95% CI: 10.8-21.4] vs 12.8% [95% CI: 8.4-18.3]; $P = 0.42$), or untreated reference segment disease (15.1% [95% CI: 10.4-20.8] vs 13.3% [95% CI: 8.9-18.8]; $P = 0.61$). However, stent malapposition was more frequent in the AI-QCA group compared with the OCT group (13.6% [95% CI: 9.1-19.1] vs. 5.6% [95% CI: 2.8-9.8]; $P = 0.007$). The mean MSA in the malapposed segment was 8.4 ± 1.9 mm^2, and no malapposed segment had an MSA <5 mm^2. In the AI-QCA group, after poststenting OCT for assessing the primary endpoint, additional procedures were performed in 33 (16.5%) patients to correct the suboptimal results (ie, 2 additional stentings to cover the dissection and 31 additional high-pressure balloon dilatations to correct the malapposition in 5 patients and underexpansion in 26 patients). In the OCT group, 2 additional stentings were performed in 2 patients to cover the dissection (Supplemental Table 1).

Pre- and poststent QCA is presented in Table 3. No significant differences were found between the groups regarding postprocedural stent dimensions or other angiographic secondary outcomes.

Immediate postprocedural safety outcomes were rare and did not differ significantly between the groups. Clinical follow-up at 6 months was completed for 398 patients (99.5%), with 2 patients in each group withdrawing informed consent. The overall clinical event rate was low, with no significant differences between the groups (Table 5).

DISCUSSION

In the FLASH trial, we evaluated the efficacy of artificial intelligence-based fully automated QCA-assisted PCI in patients with less complex coronary artery disease. Our findings demonstrated that AI-QCA-assisted PCI was noninferior to OCT-guided PCI in terms of post-PCI MSA, both overall and in the proximal and distal stent segments separately. In addition, there were no significant differences between the groups in the incidence of stent underexpansion, dissection, untreated reference segment disease, and other procedural safety outcomes, although stent malapposition was more frequent in the AI-QCA-assisted group. Finally, AI-QCA-assisted PCI appeared to be safe, with few procedural and clinical events at 6 months, comparable to the OCT-guided PCI group (Central Illustration). The FLASH trial is the first randomized study to show that AI-QCA technology can be effectively integrated into routine PCI practice, potentially bridging the gap between conventional angiography-guided PCI and state-of-the-art PCI guided by intracoronary imaging.

Conventional angiography-guided PCI has long been the de facto strategy despite its lack of standardization and reliance on operators' subjective visual estimation and experience, which can lead to inaccuracies and interobserver variability.[22] Recently, there were efforts to achieve imaging-guided PCI-like results without actual intracoronary imaging.[23] In this context, the GUIDE-DES trial demonstrated comparable 1-year outcomes between protocolized PCI using on-site manual QCA and intravascular ultrasound-guided PCI. This suggested the potential of manual QCA-based stent and balloon size selection, along with routine high-pressure post-dilatation, to overcome the limitations of conventional angiography-guided PCI.[11] The FLASH study extends these findings by using AI-QCA, which offers a streamlined approach with rapid, automated, and objective analysis of coronary angiograms in real time. This may improve procedural efficiency while reducing the workflow interruptions associated with manual measurements.

Our study protocol recommended selecting stent and final postdilation high-pressure balloon sizes up to 20% larger than the AI-QCA-measured reference vessel diameter. This adjustment aimed to optimize stent expansion while mitigating the risk of procedural risk because a previous study showed that a stent-to-QCA reference vessel diameter ratio of 1.1 to 1.3 was associated with the lowest risk of coronary dissection and 3-year target lesion failure.[23] It also accounted for the fact that QCA lumen diameters are approximately 15% smaller than intravascular ultrasound lumen diameters in vivo.[24,25]

The advantages of imaging-guided PCI are most evident in complex coronary artery disease, which has more significant prognostic implications. However, our study excluded left main lesions, chronic total occlusions, graft vascular lesions, and bifurcation lesions requiring 2-stent techniques because QCA-based assessment for these complex lesions would be less accurate, primarily because of challenges in defining clear reference vessel segments even with current AI technology. Technical advancements including improved coregistration with intracoronary imaging modalities, novel calibration methods, and sophisticated 3-dimensional QCA algorithms could potentially extend the applicability of AI-QCA-assisted PCI to more complex coronary anatomies, a hypothesis that merits further investigation in subsequent studies.

Although stent expansion, dissection, and untreated reference segment disease were not significantly different between groups, malapposition was observed more frequently in the AI-QCA group. This difference likely reflects the capacity of OCT to facilitate precise sizing adjustments and poststenting optimization based on direct geometric measurements. However, previous studies have shown that acute stent malapposition was not significantly associated with long-term adverse clinical events.[26] In addition, in our cohort, the MSA of the malapposed segments was 8.4 mm^2, with no instances <5 mm^2, which is a threshold often associated with increased risk of adverse events. As a result, the higher incidence of malapposition in the AI-QCA group is unlikely to have a significant clinical impact.

STUDY LIMITATIONS. First, this study evaluated the surrogate endpoint, not the clinical endpoint, although the MSA has been considered the strongest surrogate index to best predict long-term stent-related clinical outcomes.[27] In addition, the low rate of procedural complications and clinical outcomes at 6 months limited the determination of definitive conclusions about procedural safety. Second, because of the explanatory nature of the trial and safety considerations, additional procedures were allowed in the AI-QCA group after poststenting OCT for assessing the primary endpoint. This aspect of the protocol, which led to additional procedures in 16.5% of patients in the AI-QCA group, may have influenced clinical outcomes and should be considered when interpreting the 6-month clinical results, although the primary endpoint of the trial was unaffected.

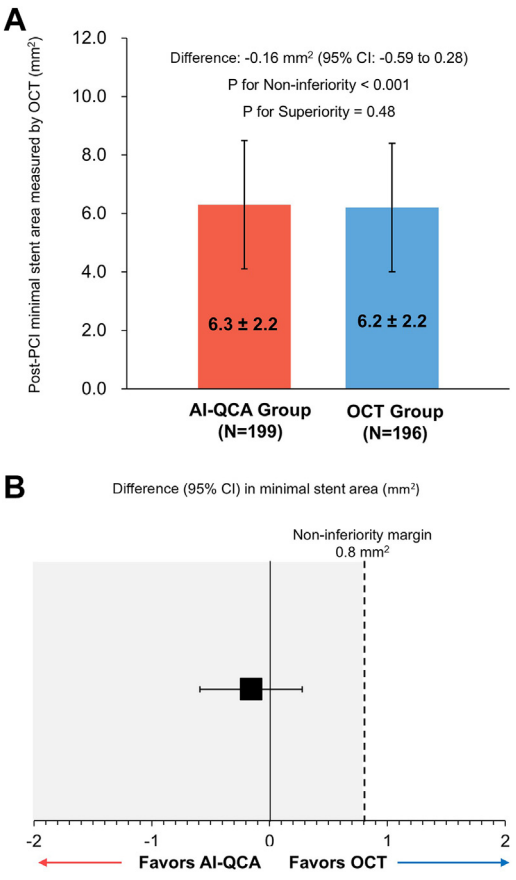
TABLE 4 Poststenting OCT Evaluation

	AI-QCA (n = 199)	OCT (n = 196)	*P* Value
Minimum stent area, mm^2			
Overall stent segment	6.3 ± 2.2	6.2 ± 2.2	0.48
Sensitivity analysis			
2 equal segments			
Proximal stent segment	7.2 ± 2.1	7.1 ± 2.1	0.73
Distal stent segment	6.5 ± 2.3	6.3 ± 2.3	0.38
2 segments separated by a large side branch			
Proximal stent segment	8.0 ± 1.9	7.4 ± 2.0	0.13
Distal stent segment	6.0 ± 1.9	5.8 ± 2.0	0.74
Reference segment			
Proximal lumen area, mm^2	9.4 ± 3.5	9.0 ± 2.9	0.30
Proximal EEM area, mm^2	9.6 ± 8.8	10.0 ± 8.8	0.71
Distal lumen area, mm^2	7.0 ± 2.8	6.7 ± 2.7	0.28
Distal EEM area, mm^2	9.4 ± 5.9	9.3 ± 5.8	0.86
Stent expansion, %			
Overall stent segment	78.7 ± 14.6	79.2 ± 14.4	0.78
Proximal stent segment	80.2 ± 17.9	81.2 ± 16.9	0.58
Distal stent segment	96.1 ± 17.0	96.9 ± 16.8	0.64
Stent underexpansion			
Overall stent segment	101 (50.8)	107 (54.6)	0.48
Proximal stent segment	85 (42.7)	94 (48.0)	0.32
Distal stent segment	28 (14.1)	24 (12.2)	0.59
Stent malapposition			
Any	27 (13.6)	11 (5.6)	0.007
Proximal edge	12 (6.0)	7 (3.6)	0.25
In-stent	15 (7.5)	5 (2.6)	0.024
Distal edge	5 (2.5)	1 (0.5)	0.10
Dissection			
Any[a]	31 (15.6)	25 (12.8)	0.42
Proximal edge	10 (5.0)	7 (3.6)	0.48
In stent	20 (10.1)	15 (7.7)	0.40
Distal edge	7 (3.5)	6 (3.1)	0.80
Untreated reference segment disease			
Any	30 (15.1)	26 (13.3)	0.61
Proximal edge	13 (6.5)	14 (7.1)	0.81
Distal edge	19 (9.5)	16 (8.2)	0.63

Values are mean ± SD or n (%), unless otherwise indicated. [a]The incidence of dissection meeting all 3 criteria (≥60° of the circumference of the vessel at the site of dissection, ≥3 mm in length of the dissection flap, or media or adventitia involvement) was 2.0% (n = 4) in the AI-QCA group and 0.5% (n = 1) in the OCT group (*P* = 0.37).

EEM = external elastic membrane; other abbreviations as in Table 1.

FIGURE 2 Primary Endpoint



(A) The post-PCI minimal stent area of the AI-QCA–assisted PCI group and the OCT-guided PCI group, respectively. Error bars denote SD. (B) The upper limit of the 95% CI for the difference of the post-PCI minimal stent area between groups was lower than the prespecified noninferiority margin of 0.8 mm², which indicates that AI-QCA–assisted PCI was noninferior to OCT-guided PCI. Abbreviations as in Figure 1.

TABLE 5 Immediate Procedural Outcomes and Clinical Outcomes at 6 Months

	AI-QCA	OCT	*P* Value
Procedural safety outcomes	(n = 200)	(n = 200)	>0.99
No reflow[a]	0	0	
Distal embolization	0	0	
Acute closure	0	0	
Dissection of at least type B	1 (0.5)	1 (0.5)	
Side branch flow TIMI flow grade <3[b]	3 (3.9)	4 (4.0)	
Perforation	0	0	
Intraprocedural stent thrombosis	0	0	
Clinical outcomes at 6 mo	(n = 199)	(n = 199)	
Death	1 (0.5)	0	>0.99
Cardiac death	0	0	–
Noncardiac death	1 (0.5)	0	>0.99
Myocardial infarction	0	0	–
Periprocedural	0	0	–
Spontaneous	0	0	–
Any repeated revascularization	1 (0.5)	1 (0.5)	>0.99
Target vessel revascularization	0	1 (0.5)	>0.99
Definite or probable stent thrombosis[c]	0	0	–

Values are n (%), unless otherwise indicated. [a]TIMI <3. [b]A side branch was present in 177 patients. [c]Stent thrombosis according to Academic Research Consortium endpoint definitions.

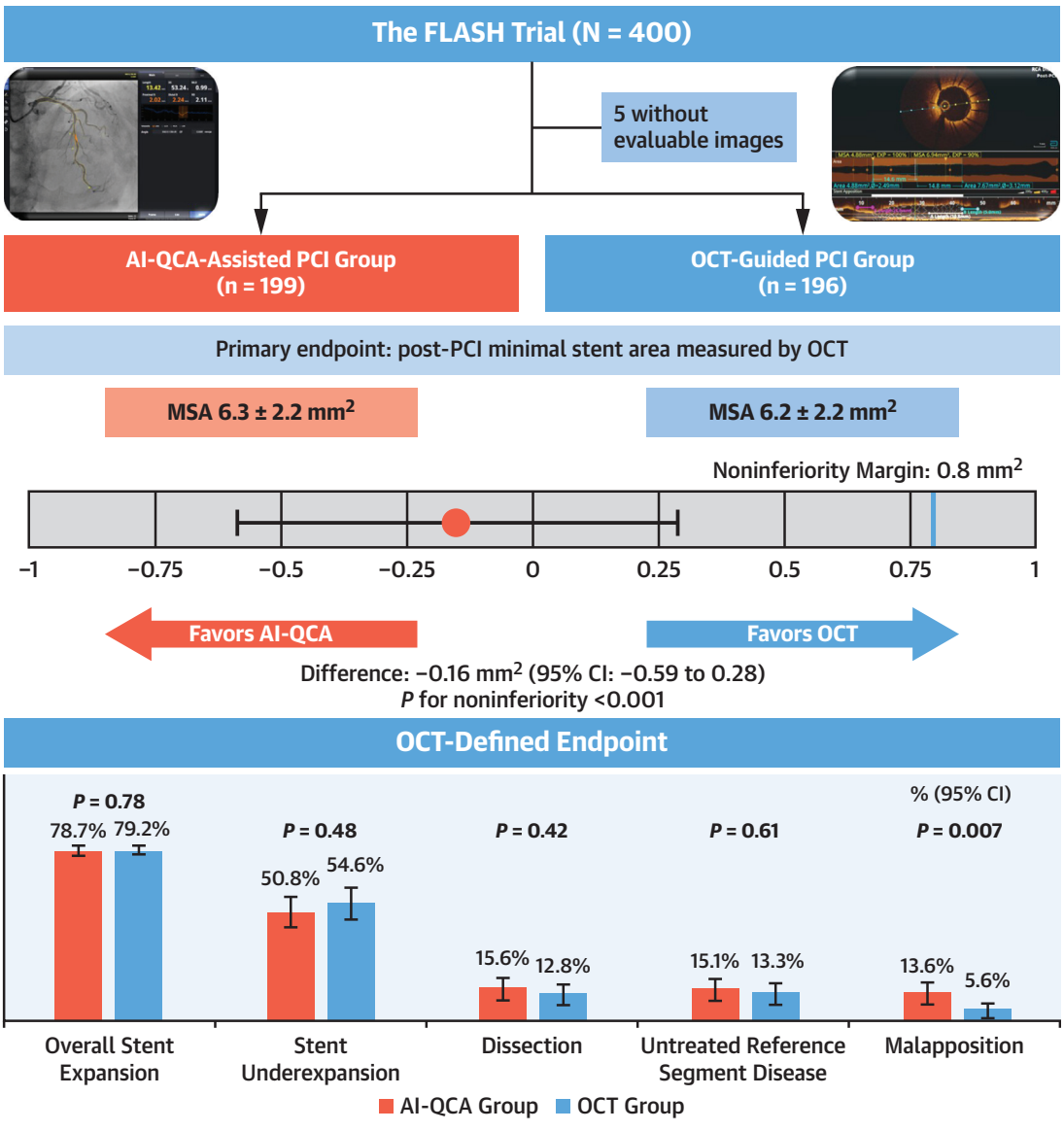
Abbreviations as in Table 1.

Third, although we observed a trend toward shorter procedural duration and reduced contrast volume with AI-QCA guidance, these differences did not reach statistical significance. This may be attributed to the uniform application of postprocedural OCT in both groups and the inclusion of predominantly less complex cases, resulting in a relatively short procedure time. Fourth, although this study focused on AI-QCA-guided stent sizing based on the analysis of native coronary artery before stenting, future research should explore post-stent AI-QCA analysis for optimizing expansion strategies. This could further enhance procedural precision. Fifth, this study was conducted in South Korea, a region where imaging-guided PCI is more frequently performed compared to other areas. To enhance the generalizability of our findings, further validation of this system is necessary in non-Asian regions, particularly in areas where coronary imaging has been underused. Finally, considering the difference of the MSA between angiography-guided PCI and OCT-guided PCI in a recent randomized trial, the noninferiority margin of this study seems to be large.[27]

CONCLUSIONS

This randomized trial demonstrates the noninferiority of AI-QCA–assisted PCI to OCT-guided PCI in achieving the optimal MSA, with comparable procedural complications, OCT-defined endpoints, and 6-month clinical outcomes. The FLASH trial introduces AI-QCA as a promising approach for guiding coronary intervention; it is particularly valuable in resource-limited settings or in less complex coronary artery disease in which the clinical benefits of intravascular imaging are not fully established. Although these findings are encouraging, larger clinical trials focusing on long-term clinical

CENTRAL ILLUSTRATION **AI-QCA-Assisted PCI vs OCT-Guided PCI (The FLASH Trial)**



- AI-QCA-assisted PCI was noninferior to OCT-guided PCI regarding achieving minimal stent area
- Procedural complications were similar between the imaging groups except malapposition occurred more frequently in the AI-QCA group
- While not powered for major clinical outcomes, no differences were observed at 6 months

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The FLASH (Fully Automated Quantitative Coronary Angiography Versus Optical Coherence Tomography Guidance for Coronary Stent Implantation) trial aimed to evaluate the efficacy of artificial intelligence-based quantitative coronary angiography (AI-QCA)-assisted percutaneous coronary intervention (PCI) compared to optical coherence tomography (OCT)-guided PCI in terms of post-PCI results. A total of 400 patients with significant coronary artery disease undergoing PCI were randomized in a 1:1 ratio to either AI-QCA-assisted or OCT-guided PCI. The study found that AI-QCA-assisted PCI was noninferior to OCT-guided PCI in terms of the post-PCI minimal stent area, with comparable procedural complications, OCT-defined endpoints, and 6-month clinical outcomes. However, malapposition occurred more frequently in the AI-QCA group.

outcomes will be crucial to fully establish the role of AI-QCA-assisted PCI in daily interventional cardiology practice.

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PERSPECTIVES

WHAT IS KNOWN? Intracoronary imaging-guided PCI has demonstrated improved clinical outcomes compared to angiography-guided PCI, particularly in complex coronary artery disease. However, its global use remains limited because of various clinical, logistic, and economic constraints.

WHAT IS NEW? This randomized trial demonstrates the noninferiority of AI-QCA–assisted PCI to OCT-guided PCI in achieving optimal the MSA, with comparable procedural complications, OCT-defined endpoints, and 6-month clinical outcomes. The FLASH trial introduces AI-QCA as a promising approach for guiding coronary intervention; it is particularly valuable in resource-limited settings or in less complex coronary artery disease in which the clinical benefits of intravascular imaging are not fully established.

WHAT IS NEXT? Larger clinical trials focusing on long-term clinical outcomes will be necessary to fully establish the role of AI-QCA-assisted PCI in daily interventional cardiology practice.

REFERENCES

1. Hong SJ, Kim BK, Shin DH, et al. Effect of intravascular ultrasound-guided vs angiography-guided everolimus-eluting stent implantation: the IVUS-XPL randomized clinical trial. *JAMA*. 2015;314:2155–2163.

2. Zhang J, Gao X, Kan J, et al. Intravascular ultrasound versus angiography-guided drug-eluting stent implantation: the ULTIMATE trial. *J Am Coll Cardiol*. 2018;72:3126–3137.

3. Lee JM, Choi KH, Song YB, et al. Intravascular imaging-guided or angiography-guided complex PCI. *N Engl J Med*. 2023;388:1668–1679.

4. Holm NR, Andreasen LN, Neghabat O, et al. OCT or angiography guidance for PCI in complex bifurcation lesions. *N Engl J Med*. 2023;389:1477–1487.

5. Stone GW, Christiansen EH, Ali ZA, et al. Intravascular imaging-guided coronary drug-eluting stent implantation: an updated network meta-analysis. *Lancet*. 2024;403:824–837.

6. Li X, Ge Z, Kan J, et al. Intravascular ultrasound-guided versus angiography-guided percutaneous coronary intervention in acute coronary syndromes (IVUS-ACS): a two-stage, multicentre, randomised trial. *Lancet*. 2024;403:1855–1865.

7. Hong SJ, Lee SJ, Lee SH, et al. Optical coherence tomography-guided versus angiography-guided percutaneous coronary intervention for patients with complex lesions (OCCUPI): an investigator-initiated, multicentre, randomised, open-label, superiority trial in South Korea. *Lancet*. 2024;404(10457):1029–1039.

8. Vrints C, Andreotti F, Koskinas KC, et al. 2024 ESC guidelines for the management of chronic coronary syndromes. *Eur Heart J*. 2024;45(36):3415–3537.

9. Fazel R, Yeh RW, Cohen DJ, et al. Intravascular imaging during percutaneous coronary intervention: temporal trends and clinical outcomes in the USA. *Eur Heart J*. 2023;44:3845–3855.

10. Mintz GS. Intravascular imaging, stent implantation, and the elephant in the room. *JACC Cardiovasc Interv*. 2017;10:2499–2501.

11. Lee PH, Hong SJ, Kim HS, et al. Quantitative coronary angiography vs intravascular ultrasonography to guide drug-eluting stent implantation: a randomized clinical trial. *JAMA Cardiol*. 2024;9:428–435.

12. Yang S, Kweon J, Roh JH, et al. Deep learning segmentation of major vessels in X-ray coronary angiography. *Sci Rep*. 2019;9:16897.

13. Park J, Kweon J, Kim YI, et al. Selective ensemble methods for deep learning segmentation of major vessels in invasive coronary angiography. *Med Phys*. 2023;50:7822–7839.

14. Kim Y, Roh JH, Kweon J, et al., eds. Artificial intelligence-based quantitative coronary angiography of major vessels using deep-learning. *Int J Cardiol*. 2024;405:131945.

15. Kim Y, Park H, Yoon H-J, et al. Fully automated quantitative coronary angiography versus optical coherence tomography guidance for coronary stent implantation (FLASH): Study protocol for a randomized controlled noninferiority trial. *Am Heart J*. 2024;275:86–95.

16. Raber L, Mintz GS, Koskinas KC, et al. 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.

17. Doi H, Maehara A, Mintz GS, et al. Impact of post-intervention minimal stent area on 9-month follow-up patency of paclitaxel-eluting stents: an integrated intravascular ultrasound analysis from the TAXUS IV, V, and VI and TAXUS ATLAS Workhorse, Long Lesion, and Direct Stent Trials. *JACC Cardiovasc Interv*. 2009;2:1269–1275.

18. Kang SJ, Ahn JM, Song H, et al. Comprehensive intravascular ultrasound assessment of stent area and its impact on restenosis and adverse cardiac events in 403 patients with unprotected left main disease. *Circ Cardiovasc Interv*. 2011;4:562–569.

19. Prati F, Romagnoli E, Burzotta F, et al. Clinical impact of OCT findings during PCI: the CLI-OPCI II study. *JACC Cardiovasc Imaging*. 2015;8:1297–1305.

20. Soeda T, Uemura S, Park SJ, et al. Incidence and clinical significance of poststent optical

coherence tomography findings: one-year follow-up study from a multicenter registry. *Circulation*. 2015;132:1020–1029.

21. Ali ZA, Maehara A, Généreux P, et al. 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.

22. Campbell PT, Mahmud E, Marshall JJ. Inter-operator and intraoperator (in)accuracy of stent selection based on visual estimation. *Catheter Cardiovasc Interv*. 2015;86:1177–1183.

23. Lee SY, Zhang JJ, Mintz GS, et al. Procedural characteristics of intravascular ultrasound-guided percutaneous coronary intervention and their clinical implications. *J Am Heart Assoc*. 2022;11:e025258.

24. Kubo T, Akasaka T, Shite J, et al. OCT compared with IVUS in a coronary lesion assessment: the OPUS-CLASS study. *JACC Cardiovasc Imaging*. 2013;6:1095–1104.

25. Tu S, Xu L, Ligthart J, et al. In vivo comparison of arterial lumen dimensions assessed by co-registered three-dimensional (3D) quantitative coronary angiography, intravascular ultrasound and optical coherence tomography. *Int J Cardiovasc Imaging*. 2012;28:1315–1327.

26. Lee SY, Mintz GS, Kim JS, Kim BK, Jang Y, Hong MK. Long-term clinical outcomes of drug-eluting stent malapposition. *Korean Circ J*. 2020;50:880–889.

27. Landmesser U, Ali ZA, Maehara A, et al. Optical coherence tomography predictors of clinical outcomes after stent implantation: the ILUMIEN IV trial. *Eur Heart J*. 2024;45(43):4630–4643.

KEY WORDS artificial intelligence, coronary imaging, coronary intervention, quantitative coronary angiography, stent(s)

APPENDIX For a supplemental table and figures, please see the online version of this paper.