ORIGINAL ARTICLE

OCT or Angiography Guidance for PCI in Complex Bifurcation Lesions

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ABSTRACT

BACKGROUND

Imaging-guided percutaneous coronary intervention (PCI) is associated with better clinical outcomes than angiography-guided PCI. Whether routine optical coherence tomography (OCT) guidance in PCI of lesions involving coronary-artery branch points (bifurcations) improves clinical outcomes as compared with angiographic guidance is uncertain.

METHODS

We conducted a multicenter, randomized, open-label trial at 38 centers in Europe. Patients with a clinical indication for PCI and a complex bifurcation lesion identified by means of coronary angiography were randomly assigned in a 1:1 ratio to OCT-guided PCI or angiography-guided PCI. The primary end point was a composite of major adverse cardiac events (MACE), defined as death from a cardiac cause, target-lesion myocardial infarction, or ischemia-driven target-lesion revascularization at a median follow-up of 2 years.

RESULTS

We assigned 1201 patients to OCT-guided PCI (600 patients) or angiography-guided PCI (601 patients). A total of 111 patients (18.5%) in the OCT-guided PCI group and 116 (19.3%) in the angiography-guided PCI group had a bifurcation lesion involving the left main coronary artery. At 2 years, a primary end-point event had occurred in 59 patients (10.1%) in the OCT-guided PCI group and in 83 patients (14.1%) in the angiography-guided PCI group (hazard ratio, 0.70; 95% confidence interval, 0.50 to 0.98; P=0.035). Procedure-related complications occurred in 41 patients (6.8%) in the OCT-guided PCI group and 34 patients (5.7%) in the angiography-guided PCI group.

CONCLUSIONS

Among patients with complex coronary-artery bifurcation lesions, OCT-guided PCI was associated with a lower incidence of MACE at 2 years than angiography-guided PCI. (Funded by Abbott Vascular and others; OCTOBER ClinicalTrials.gov number, NCT03171311.)

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*A full list of the members of the OCTOBER Trial Group is provided in the Supplementary Appendix, available at NEJM.org.

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In 15 to 20% of patients in whom coronary-artery revascularization is indicated, the lesion involves a branch point or bifurcation of the coronary artery.[1] Implantation of stents in lesions that occur at a coronary-artery bifurcation during percutaneous coronary intervention (PCI) is often challenging because one or more stents must be advanced in the atherosclerotic artery and fitted precisely to the branch point.[2] Implantation techniques used in the treatment of more complex bifurcation lesions that involve both the main vessel and the side branch are associated with greater risk of procedural complications and worse clinical outcomes than PCI in less complicated lesions. The incidence of death at 10 years was 30.1% after bifurcation PCI as compared with 19.8% after nonbifurcation PCI in the Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) trial; myocardial infarction, target-lesion revascularization, and stent thrombosis were more frequent with bifurcation PCI in the e-Ultimaster registry (which included 35,839 patients); and the presence of a stenosis in the ostium of the side branch defined a subgroup of patients with bifurcation lesions who were at a higher risk for death (5.0% vs. 3.1%) and repeat revascularization (9.1% vs. 6.7%) than patients with bifurcation lesions with limited side-branch disease.[3-5]

Although the PCI procedure in lesions that occur at a coronary-artery bifurcation is predominantly guided by angiography, angiographic visualization of such lesions is often impeded by ambiguity that may affect the critical steps of stent implantation.[6,7] Optical coherence tomography (OCT) is a light-based, high-resolution, intravascular method of imaging that allows for characterization of plaque components and enables precise measurements of vessel and stent dimensions.[8,9] The use of OCT to guide PCI has been associated with improved procedure results, and treatment-related findings with OCT, including stent underexpansion and residual plaque at the edges of the stent, have predicted coronary events during follow-up.[10,11] The use of intravascular ultrasound (IVUS) to guide PCI has been shown to be superior to angiography-guided PCI in an all-comer population (i.e., a trial population that had minimal exclusion criteria) and in populations with subgroups of patients with complex lesions.[12-14] OCT provides higher-resolution images than IVUS, and mechanistic studies have indicated that OCT could be of particular value in optimizing complex-bifurcation PCI.[15] We conducted the European Trial on Optical Coherence Tomography Optimized Bifurcation Event Reduction (OCTOBER) to investigate whether PCI with routine OCT guidance is superior to standard angiography-guided PCI in revascularization of complex lesions located at a coronary bifurcation.

Methods

Trial Design and Oversight

OCTOBER was a multicenter, open-label, randomized, controlled, superiority trial that assessed clinical outcomes among patients with complex coronary-artery bifurcation lesions who had undergone OCT-guided PCI as compared with those who had undergone angiography-guided PCI. The trial was initiated by the investigators and was conducted at 38 heart centers in Europe (see page 2 in the Supplementary Appendix, available with the full text of this article at NEJM.org). The trial was approved by the Central Jutland Committees on Health Research Ethics and by the national or local ethics committees for the participating sites. All the patients provided written informed consent. The trial was performed in accordance with the principles of the Declaration of Helsinki. Conduct of the trial was overseen by a data safety monitoring board. Members of an independent clinical-end-point committee who were unaware of the trial group assignments adjudicated all definite and possible clinical events. The trial design, treatment protocol, and statistical analysis plan have been published previously,[16] and the protocol is available at NEJM.org. Abbott Vascular and St. Jude Medical provided funding but had no role in the design, conduct, or analysis of the trial or in the interpretation and reporting of the results. The two first authors and the trial statistician performed the statistical analyses and vouch for the completeness and accuracy of the data. The first draft of the manuscript was written by the two first authors. The first author and the trial chairperson (last author) vouch for the overall conduct of the trial and for the fidelity of the trial to the protocol, and all the authors agreed to submit the manuscript for publication.

Patients

Eligible patients were at least 18 years of age and had stable angina, unstable angina, or a non–ST-

segment-elevation myocardial infarction; had a clinical indication for PCI; and had a coronary-artery bifurcation lesion that was revealed on coronary angiography. Eligible bifurcation lesions had a main branch reference diameter of at least 2.75 mm and stenosis of at least 50% by visual estimation. The side branch had to have a reference diameter of at least 2.5 mm and stenosis of at least 50% within 5 mm from the ostium of the side branch by visual estimation. The bifurcation lesion could involve the left main coronary artery. The functional significance of the main-branch stenosis had to have been documented by a standard noninvasive functional test with imaging or a pressure-wire–based method or other objective documentation of ischemia in the myocardial territory that was supplied by the coronary artery that had stenosis. A coronary-artery stenosis of more than 80% of the lumen diameter was considered functionally significant. Patients were excluded if they had had an ST-elevation myocardial infarction within 72 hours before randomization; were in a state of cardiogenic shock; had undergone previous coronary-artery bypass grafting to a target vessel, or the procedure was planned; or had an estimated glomerular filtration rate of less than 50 ml per minute per 1.73 m^2, an expected survival of less than 2 years, a left ventricular ejection fraction of less than 30%, or heart failure symptoms more serious than New York Heart Association class II. Key angiographic exclusion criteria were severe tortuosity of the coronary artery at the target bifurcation lesion, the presence of a chronic total occlusion, or a large thrombus in the left main coronary artery (see page 13 in the Supplementary Appendix for an expanded list of eligibility criteria).

RANDOMIZATION

Randomization was performed during the PCI procedure after placement of a coronary guidewire in both the main vessel and the side branch of the target bifurcation lesion. Patients underwent randomization in a 1:1 ratio to receive OCT-guided PCI or angiography-guided PCI. Randomization was performed with the use of a concealed, external, Web-based randomization service (SkejCard, Department of Clinical Medicine, Aarhus University). The randomization sequence was performed in permuted blocks in random sizes of 4, 6, and 8 and was stratified according to the presence of a lesion located at a bifurcation in the left main coronary artery and whether the physician planned to perform a procedure with implantation of stents in the main branch only (provisional side-branch stent implantation technique) or a two-stent technique (one stent in the main branch and one in the side branch).

INTERVENTION

Patients underwent PCI with the use of conventional PCI bifurcation techniques adapted from the consensus report published by the European Bifurcation Club.[17] The recommendations for the selection of a bifurcation-stent implantation technique are described on page 25 in the Supplementary Appendix. The Xience everolimus-eluting stent (Abbott) was prespecified for implantation, with other newer-generation stents used only when the Xience stent was not available.

In patients who were assigned to OCT-guided PCI, the protocol specified the timing of OCT scans, the checks and measurements to be obtained at each time point, the recommended optimizations, and the treatment goals.[16] The main treatment goals for OCT-guided PCI were optimal coverage of the coronary-artery lesion with a stent, optimal stent expansion, and absence of stent malapposition or accidentally crushed or distorted stents. We considered optimal coronary-artery lesion coverage to be achieved when the 5-mm edge zones adjacent to the stent did not have stenosis of more than 30% of the reference diameter, had no major lipid plaque or plaque rupture, and had no edge dissection that was visible on angiography. We considered optimal stent expansion to be achieved when there was a residual diameter stenosis of less than 10% and there was less than 50% diameter stenosis in the ostium of the side branch when a stent was implanted in the main branch only. We defined the absence of stent malapposition as the entire stent having contact with the vessel wall. We confirmed that the stents were not accidentally crushed or distorted using visual confirmation that the stents were crushed or distorted only where intended by the bifurcation-stent implantation technique (see page 34 and Fig. S1 in the Supplementary Appendix). In patients who underwent angiography-guided PCI, stent implantation was performed according to usual practice, but OCT imaging was not allowed and was con-

sidered a protocol violation; intravascular ultrasonography was not encouraged but was allowed at the operators' discretion if the patient had a lesion located at a left main coronary-artery bifurcation.[18] All cases were reviewed and analyzed by the Interventional Coronary Imaging Core Laboratory at Aarhus University Hospital, Denmark.

END POINTS

The primary end point was a composite of major adverse cardiac events (MACE), defined as death from a cardiac cause, target-lesion myocardial infarction, or ischemia-driven target-lesion revascularization at a median follow-up of 2 years. The database could be closed only after at least 1 year had passed since randomization of the last patient. Key secondary clinical end points included death from a cardiac cause; target-lesion myocardial infarction; target-lesion revascularization; a bifurcation lesion–oriented composite end point of death from a cardiac cause, target lesion myocardial infarction, or target lesion revascularization; and a patient-oriented composite end point of death from any cause, myocardial infarction, any coronary revascularization, or stroke. A complete list of the secondary clinical and procedural end points and their definitions are provided on page 15 in the Supplementary Appendix.

Information about events that occurred during the follow-up period was collected by review of continuous registration of trial-patient admissions at each enrollment site, and by telephone follow-up at 1 month, 1 year, and 2 years after randomization for detection of any unregistered events or possible events. Annual follow-up is specified for 5 years for MACE and for 10 years for death from any cause. Documentation of source data were collected for all events and possible events and were reviewed by the independent Clinical End Point Committee (see page 35 in the Supplementary Appendix).

STATISTICAL ANALYSIS

We estimated that a sample of 984 patients would provide the trial with 80% power at an alpha level of 0.05 to detect an incidence of MACE that was 6 percentage points lower with OCT-guided PCI than with angiography-guided PCI, assuming a 16% 2-year incidence of MACE detected by angiography-guided PCI. The target sample size of 1200 patients was selected to account for uncertainty in the 2-year MACE estimates and loss to follow-up. Details on assumptions for the calculation of the sample size are provided on page 36 in the Supplementary Appendix.

The primary end point and secondary end points were analyzed according to the intention-to-treat principle. Analysis of clinical end points was performed until the date of an event, death, loss to follow-up, or 24 months after the day of randomization, whichever came first. Cox regression analyses were used to calculate the unadjusted hazard ratios for the primary end point and secondary clinical end points and the P value for the primary end point. We considered a two-sided P value of less than 0.05 to be statistically significant with respect to the primary end point. Competing risk analysis was performed to ensure that Kaplan–Meier curves and estimates were valid. Adjusted Cox regression analysis was used to assess whether stratification variables or between-group differences detected at baseline had any effects on the primary end point. Proportional-hazards assumptions in Cox regression models were assessed with the use of log–log plots and plots of observed versus predicted values.

Predefined subgroup analyses were performed with the use of Cox regression analysis. The widths of the confidence intervals of secondary end points have not been adjusted for multiplicity and should not be used to infer treatment effects. All analyses were performed with the use of Stata software, version 17 (StataCorp).

RESULTS

PATIENTS

A total of 1201 patients were enrolled in the trial between July 2017 and March 2022, with 600 patients assigned to receive OCT-guided PCI and 601 patients to receive angiography-guided PCI. One year after randomization, 1190 (99%) of the patients had completed the follow-up or had died, 2 had withdrawn from the trial, and 9 were lost to follow-up. The database for the primary end point was closed before the last 122 of the enrolled patients reached the 2-year follow-up point; 1057 of the remaining 1079 patients (98%) were assessed at the 2-year follow-up or had died (Fig. S2). Three patients who were assigned to OCT-guided PCI were not treated with stent implantation; 2 were reevaluated and admitted for coronary-artery bypass grafting, and 1 received no revas-

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Total (N=1201)	OCT-Guided PCI (N=600)	Angiography-Guided PCI (N=601)
Age — yr	66.3±10.2	66.4±10.5	66.2±9.9
Female sex — no. (%)	253 (21.1)	127 (21.2)	126 (21.0)
Indication for PCI — no. (%)			
Stable angina pectoris	651 (54.2)	330 (55.0)	321 (53.4)
Unstable angina pectoris	111 (9.2)	53 (8.8)	58 (9.7)
NSTEMI	157 (13.1)	79 (13.2)	78 (13.0)
Staged procedure after AMI	282 (23.5)	138 (23.0)	144 (24.0)
Body-mass index†	28.1±0.14	28.0±4.6	28.2±4.9
Median ejection fraction (IQR) — ml	58.0 (50–60)	59.5 (50–60)	58.0 (50–60)
Medical history — no. (%)			
PCI	501 (41.7)	244 (40.7)	257 (42.8)
AMI	350 (29.1)	170 (28.3)	180 (30.0)
Cardiac surgery	16 (1.3)	7 (1.2)	9 (1.5)
Treatment of hypercholesterolemia	927 (77.2)	456 (76.0)	471 (78.4)
Diabetes mellitus	200 (16.7)	103 (17.2)	97 (16.1)
Hypertension	870 (72.4)	422 (70.3)	448 (74.5)
Smoker			
Active	162 (13.5)	77 (12.8)	85 (14.1)
Former	433 (36.1)	228 (38.0)	205 (34.1)
Stroke	29 (2.4)	15 (2.5)	14 (2.3)
Pulmonary hypertension	6 (0.5)	2 (0.3)	4 (0.7)
Other chronic pulmonary disease	57 (4.7)	30 (5.0)	27 (4.5)
Renal failure	26 (2.2)	12 (2.0)	14 (2.3)
Peripheral vascular disease	40 (3.3)	17 (2.8)	23 (3.8)

* Plus–minus values are means ±SD. AMI denotes acute myocardial infarction, IQR interquartile range, NSTEMI non–ST-segment elevation myocardial infarction, and PCI percutaneous coronary intervention.
† The body-mass index is the weight in kilograms divided by the square of the height in meters.

cularization. OCT was performed in 589 patients assigned to the OCT-guided PCI group. Of the patients assigned to angiography-guided PCI, 92 (15%) underwent IVUS-guided PCI, of whom 59 (64%) had a lesion located at a left main coronary-artery bifurcation.

Characteristics of the patients at baseline were well balanced between the two groups (Table 1 and Table S1). The mean (±SD) age of the patients was 66.3±10.2 years, and 253 (21.1%) were women. The indication for PCI was non–ST-segment elevation acute myocardial infarction or secondary lesions requiring revascularization after a recent acute myocardial infarction (in 439 patients [36.6%]).

LESION CHARACTERISTICS AND INTERVENTION

A total of 227 patients (18.9%; 111 patients in the OCT-guided PCI group and 116 in the angiography-guided PCI group) had a lesion located at a left main coronary-artery bifurcation, and 231 patients (19.2%) had multivessel disease with one or more additional target lesions treated either during the index procedure or at a staged procedure. A total of 388 patients in the OCT-guided PCI group and 382 patients in the angiography-guided PCI group were treated with a two-stent implantation technique. Angiographic procedural success was observed in 571 patients (95.8%) in the OCT-guided PCI group and 573 patients (95.7%) in the angiography-guided PCI

Table 2. Procedural Characteristics.*

Characteristic	Total (N=1201)	OCT-Guided PCI (N=600)	Angiography-Guided PCI (N=601)
Median no. of diseased vessels (IQR)	2 (2–2)	2 (2–2)	2 (2–2)
Median no. of lesions to be treated (IQR)	1 (1–1)	1 (1–1)	1 (1–1)
Trial bifurcation vessels — no. of patients (%)			
LMCA–LAD–LCx	227 (18.9)	111 (18.5)	116 (19.3)
LAD-D	847 (70.5)	425 (70.8)	422 (70.2)
LCx–OM	111 (9.2)	55 (9.2)	56 (9.3)
RCA–PDA–PLA	16 (1.3)	9 (1.5)	7 (1.2)
Main-vessel treatment, median total stent length (IQR) — mm	36 (24–50)	38 (28–51)	33 (23–48)
Side-branch treatment			
Side branch stented — no. of patients/total no. (%)	770/1198 (64.3)	388/597 (65.0)	382/601 (63.6)
Median total stent length (IQR) — mm	23 (15–28)	23 (15–28)	23 (15–28)
Median total balloons (IQR) — no.	7 (5–9)	7 (5–10)	6 (5–9)
Largest balloon diameter — mm	4.1±0.02	4.2±0.03	4.0±0.02
Secondary lesions treated — no. of patients (%)	231 (19.2)	106 (17.7)	125 (20.8)

* Plus–minus values are means ±SD. Percentages may not total 100 because of rounding. D denotes diagonal branch, LCx left circumflex artery, LAD left anterior descending artery, LMCA left main coronary artery, OM obtuse marginal branch, PDA posterior descending artery, PLA posterolateral artery, and RCA right coronary artery.

group. Among patients who received OCT-guided PCI, 28 patients (4.7%) had stent expansion of at least 90%, verified by OCT, in all treated segments; final main-vessel OCT showed that 146 of 209 patients (69.9%) with stents implanted only in the main vessel had a side-branch ostial stenosis of less than 50%. Of the 597 patients who underwent OCT-guided PCI, 381 patients (63.8%) had OCT verification of no stent malapposition in all treated segments, 308 patients (51.6%) had OCT verification of no residual edge disease, and 451 patients (75.5%) had verified absence of accidently crushed stent in all treated segments. The median volume of contrast used was 300 ml (interquartile range, 250 to 375) in the OCT-guided PCI group and 200 ml (interquartile range, 160 to 278) in the angiography-guided PCI group. The median procedure time was 113 minutes (interquartile range, 85 to 145) in the OCT-guided PCI group and 80 minutes (interquartile range, 60 to 110) in the angiography-guided PCI group. Additional procedural characteristics are shown in Table 2 and in Tables S2 through S17.

PRIMARY AND SECONDARY END POINTS

MACE (the primary end point) occurred in 59 patients (10.1%) assigned to OCT-guided PCI and in 83 (14.1%) patients assigned to angiography-guided PCI (unadjusted hazard ratio, 0.70; 95% confidence interval [CI], 0.50 to 0.98; P=0.035; adjusted hazard ratio, 0.71; 95% CI, 0.51 to 0.98) (Fig. 1). The 2-year Kaplan–Meier estimates were as follows: for death from any cause, 2.4% among patients in the OCT-guided PCI group as compared with 4.0% in the angiography-guided PCI group (hazard ratio, 0.56; 95% CI, 0.28 to 1.10); for death from a cardiac cause, 1.4% in the OCT-guided PCI group and 2.6% in the angiography-guided PCI group (hazard ratio, 0.53; 95% CI, 0.22 to 1.25); for target-lesion myocardial infarction, 7.8% in the OCT-guided PCI group and 8.5% in the angiography-guided PCI group (hazard ratio, 0.90; 95% CI, 0.60 to 1.34); and for ischemia-driven target-lesion revascularization, 2.8% in the OCT-guided PCI group and 4.6% in the angiography-guided PCI group (hazard ratio, 0.61; 95% CI, 0.32 to 1.13). The 2-year Kaplan–Meier estimates for other secondary end points are

shown in Table 3 and Tables S5 and S6. Subgroup analyses of the primary end point are shown in Figure 2.

SAFETY

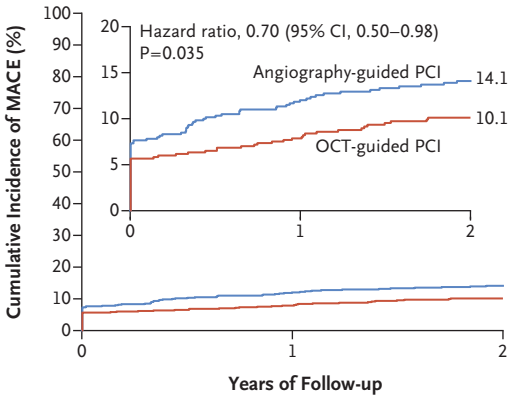
Procedure-related complications were similar between the groups (Table S11). Procedure-related complications occurred in 41 patients (6.8%) in the OCT-guided PCI group and 34 patients (5.7%) in the angiography-guided PCI group. One patient in the OCT-guided PCI group had potential contrast-associated acute kidney injury after PCI, as compared with none in the angiography-guided PCI group.

DISCUSSION

The OCTOBER trial showed that among patients with complex coronary-artery bifurcation lesions, OCT-guided PCI was associated with a lower median 2-year incidence of MACE than angiography-guided PCI. The incidence of procedure-related complications was low, and there was no notable difference between the two groups.

The use of intravascular imaging to guide PCI originated with IVUS, and its clinical usefulness has been confirmed in randomized clinical trials.[12-14] IVUS and OCT have similarities, although OCT has greater image resolution than IVUS, but a lower depth of tissue penetration, except in calcified lesions.[19] In the Optical Frequency Domain Imaging vs. Intravascular Ultrasound in Percutaneous Coronary Intervention (OPINION) trial, OCT-guided PCI was noninferior to IVUS-guided PCI with regard to clinical outcomes in a population that had coronary-artery lesions of differing complexity.[20] This equipoise was achieved despite the use of a treatment protocol for stent expansion that may have favored IVUS. Lesions located at a coronary-artery bifurcation, as compared with other coronary-artery lesions, often require more complex stent-implantation techniques and are associated with a higher risk of death, myocardial infarction, and repeat revascularization.[4,5,21,22] Bifurcation-lesion PCI conducted with angiographic imaging only is also hampered by ambiguity with regard to the evaluation of coronary lesions and stents. Several studies have indicated that OCT may have particular advantages in guiding PCI of lesions located at coronary-artery bifurcations.[6,15,23,24] Our findings confirm those of mechanistic studies that showed OCT could be of particular value in optimizing procedural results in PCI. OCT imaging of lesions located at left main coronary-artery bifurcations was previously shown to be technically feasible, allows for stent optimization, and has appeared beneficial in observational registries.[25-28] We confirmed that OCT guiding of left main coronary-artery lesions was feasible and contributed to the overall results in the OCTOBER trial.

Previous trials that assessed IVUS-guided PCI as compared with angiography-guided PCI have provided few details regarding how these imaging methods should be used to guide bifurcation-lesion PCI.[12,29] The Intravascular Ultrasound Guided Drug Eluting Stents Implantation in "All-Comers" Coronary Lesions (ULTIMATE) trial[29] showed that IVUS-guided bifurcation-lesion PCI, as compared with angiography-guided PCI, was associated with a lower incidence of target-vessel failure, whereas this was not seen in Randomized Controlled Trial of Intravascular Imaging Guidance versus Angiography-Guidance on Clinical Outcomes after Complex Percutaneous Coronary Intervention (RENOVATE-COMPLEX-PCI).[12] The OCTOBER trial specified the timing of OCT imaging during the PCI procedure and set numerous ambitious treatment goals for OCT-guided



No. at Risk

Angiography-guided PCI	601	509	408
OCT-guided PCI	600	537	439

Figure 1. Kaplan–Meier Curves for the Primary End Point.

The primary end point was a composite of major adverse cardiac events (MACE): death from a cardiac cause, target-lesion myocardial infarction, or ischemia-driven target-lesion revascularization. Between-group assessments were made with the use of an unadjusted Cox regression analysis. The inset shows the same data on an enlarged y axis. OCT denotes optical coherence tomography, and PCI percutaneous coronary intervention.

Table 3. Primary and Secondary End Points.*

End Point	Total (N=1201)	OCT-Guided PCI (N=600)	Angiography-Guided PCI (N=601)	Hazard Ratio (95% CI)
	events	*events (estimated percentage)*		
Primary end point: MACE†	142	59 (10.1)	83 (14.1)	0.70 (0.50–0.98)
Clinical secondary end points				
Patient-oriented composite end point‡	182	79 (13.6)	103 (17.7)	0.76 (0.56–1.01)
Death from any cause	36	13 (2.4)	23 (4.0)	0.56 (0.28–1.10)
Death from a cardiac cause	23	8 (1.4)	15 (2.6)	0.53 (0.22–1.25)
Target-lesion myocardial infarction	97	46 (7.8)	51 (8.5)	0.90 (0.60–1.34)
Ischemia-driven target-lesion revascularization§	42	16 (2.8)	26 (4.6)	0.61 (0.32–1.13)
Stent thrombosis	29	12 (2.1)	17 (3.0)	0.70 (0.34–1.47)
Definite	7	3 (0.5)	4 (0.7)	0.75 (0.17–3.34)
Probable	3	2 (0.3)	1 (0.2)	1.99 (0.18–22.0)
Possible	19	7 (1.3)	12 (2.1)	0.58 (0.23–1.47)

* The number of events and estimated percentages were calculated with the use of a Kaplan–Meier survival analysis of data in the intention-to-treat population; therefore, the percentages may not reflect the ratio of the numerator and the denominator. The widths of the confidence intervals have not been adjusted for multiplicity and should not be used to reject or not reject treatment effects.

† Major adverse cardiac event (MACE) is a composite of death from a cardiac cause, target-lesion myocardial infarction, or ischemia-driven target-lesion revascularization. P=0.035 for the between-group comparison of the primary end point.

‡ The patient-oriented composite end point is a composite of death from any cause, any myocardial infarction, any revascularization, or stroke.

§ Ischemia-driven target-lesion revascularization is defined as coronary-artery bypass grafting or PCI with either positive functional ischemic testing or in-stent or edge stenosis and typical angina symptoms.

PCI. Instructions also included safety limits for stent optimization that might have contributed not only to the low incidence of complications but also to the modest fraction of patients in the OCT-guided PCI group who met all treatment goals. However, OCT-guided stent optimization performed according to the OCTOBER protocol still improved clinical outcomes.

Our trial has limitations. Patient eligibility was verified by on-site investigators and not by a centralized core laboratory. Information on race and ethnic group was not collected. The subgroup of patients with lesions located at left main coronary-artery bifurcations who were enrolled in the trial was smaller than planned, which may have reduced the overall population risk. The group assignments were not masked to treating physicians or patients. The trial enrollment period was longer than anticipated and spanned 4 years and 8 months owing to delayed site activation and the coronavirus 2019 (Covid-19) pandemic. We also cannot exclude the possibility that the Covid-19 pandemic had other effects on the trial beyond the prolonged enrollment phase. In a few cases, a final OCT scan was not performed after additional stent-optimization treatments were undertaken. The majority of sites that enrolled patients were university centers, and most investigators had at least moderate experience with OCT guidance for PCI before the start of the trial. The selective use of IVUS in 15% of cases in the angiography-guided PCI group might have improved the results in the control group as compared with a population treated entirely without intravascular imaging and could have led to an underestimation of the true clinical value of OCT-guided PCI for implantation of a stent in a lesion located at a coronary-artery bifurcation.

Among patients with complex lesions located at a coronary-artery bifurcation, at a median fol-

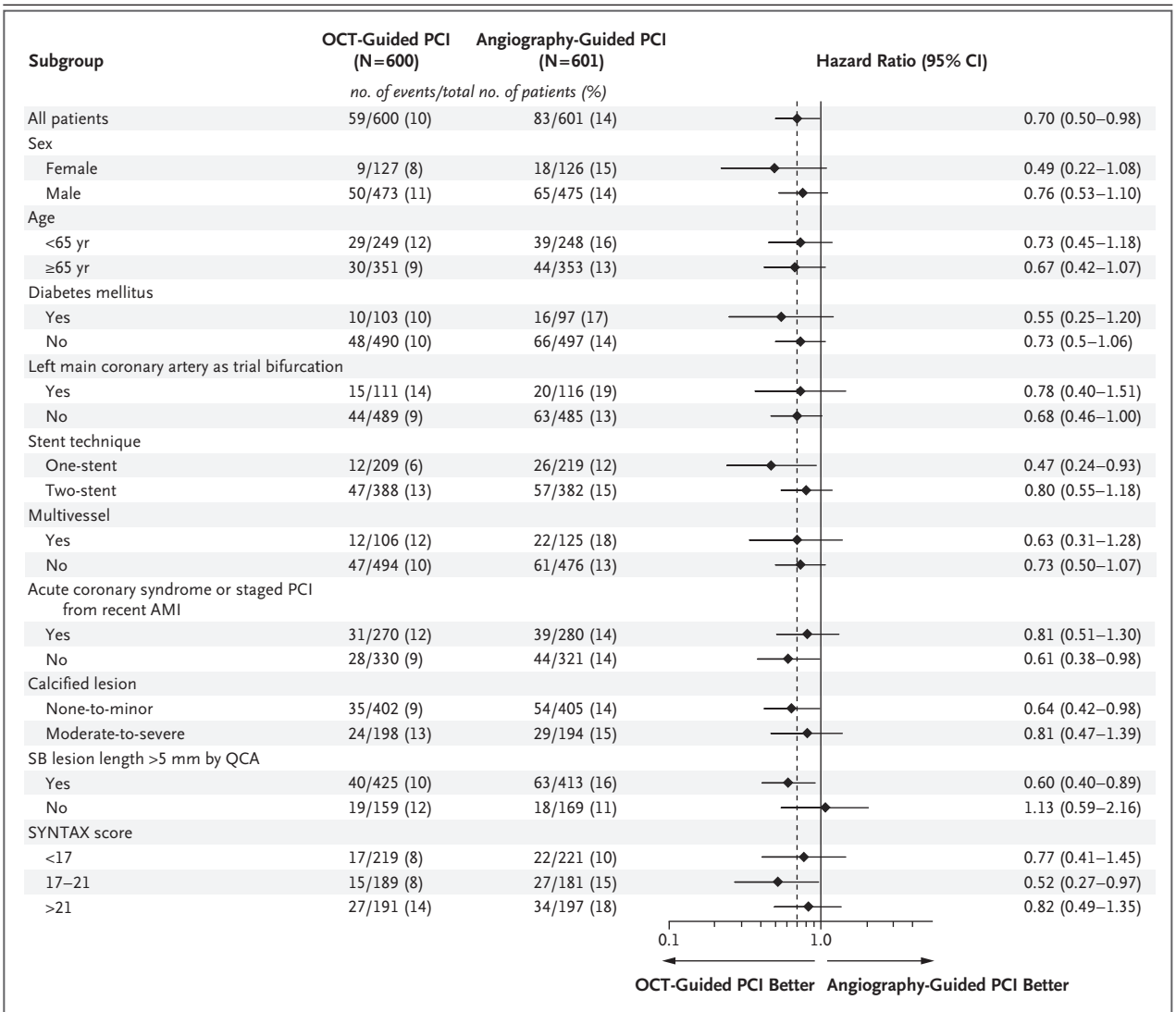


Figure 2. Subgroup Analyses of the Primary End Point.

The primary end point was analyzed with the use of a Cox multivariable regression model. Calcified lesions were assessed as none-to-minor or moderate-to-severe, with moderate defined as radiopacity in the cardiac cycle before contrast injection and severe as radiopacity without cardiac motion before contrast injection. Percentages are Kaplan–Meier estimates. The widths of the confidence intervals have not been adjusted for multiplicity and should not be used to reject or not reject treatment effects. The SYNTAX (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) score is an angiography-based scoring system that estimates the burden and complexity of coronary artery disease. Scores range from 0 to no upper limit; lower scores indicate less complexity of coronary artery disease and predict a better outcome with PCI. SYNTAX subgroups were divided into thirds. AMI denotes acute myocardial infarction, QCA quantitative coronary angiography, and SB side branch.

low-up of 2 years, OCT-guided PCI was associated with a lower incidence of a composite of death from a cardiac cause, target-lesion myocardial infarction, or ischemia-driven target-lesion revascularization (the primary end point) than angiography-guided PCI.

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APPENDIX

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