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Clinical Impact of OCT Findings During PCI

The CLI-OPCI II Study

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ABSTRACT

OBJECTIVES The goal of this study was to assess the clinical impact of optical coherence tomography (OCT) findings during percutaneous coronary intervention (PCI).

BACKGROUND OCT provides unprecedented high-definition visualization of plaque/stent structures during PCI; however, the impact of OCT findings on outcome remains undefined.

METHODS In the context of the multicenter CLI-OPCI (Centro per la Lotta contro l'Infarto-Optimisation of Percutaneous Coronary Intervention) registry, we retrospectively analyzed patients undergoing end-procedural OCT assessment and compared the findings with clinical outcomes.

RESULTS A total of 1,002 lesions (832 patients) were assessed. Appropriate OCT assessment was obtained in 98.2% of cases and revealed suboptimal stent implantation in 31.0% of lesions, with increased incidence in patients experiencing major adverse cardiac events (MACE) during follow-up (59.2% vs. 26.9%; $p < 0.001$). In particular, in-stent minimum lumen area <4.5 mm^2 (hazards ratio [HR]: 1.64; $p = 0.040$), dissection >200 μm at the distal stent edge (HR: 2.54; $p = 0.004$), and reference lumen area <4.5 mm^2 at either distal (HR: 4.65; $p < 0.001$) or proximal (HR: 5.73; $p < 0.001$) stent edges were independent predictors of MACE. Conversely, in-stent minimum lumen area/mean reference lumen area $<70\%$ (HR: 1.21; $p = 0.45$), stent malapposition >200 μm (HR: 1.15; $p = 0.52$), intrastent plaque/thrombus protrusion >500 μm (HR: 1.00; $p = 0.99$), and dissection >200 μm at the proximal stent edge (HR: 0.83; $p = 0.65$) were not associated with worse outcomes. Using multivariable Cox hazard analysis, the presence of at least 1 significant criterion for suboptimal OCT stent deployment was confirmed as an independent predictor of MACE (HR: 3.53; 95% confidence interval: 2.2 to 5.8; $p < 0.001$).

CONCLUSIONS Suboptimal stent deployment defined according to specific quantitative OCT criteria was associated with an increased risk of MACE during follow-up. (J Am Coll Cardiol Img 2015;8:1297–305) © 2015 by the American College of Cardiology Foundation.

Optical coherence tomography (OCT) is the newest intracoronary imaging technique designed for better definition of coronary atherosclerosis and its functional consequences (1–4). The current OCT systems are rapid, with unprecedented spatial resolution allowing high-definition visualization of intraluminal and endothelial structures. Despite the high quality of OCT images, the

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ABBREVIATIONS AND ACRONYMS

BMS = bare-metal stent(s)

CI = confidence interval

DES = drug-eluting stent(s)

HR = hazard ratio

IQR = interquartile range

IVUS = intravascular ultrasound

MACE = major adverse cardiac event(s)

MI = myocardial infarction

MLA = minimum lumen area

MSA = minimal stent area

NSTEMI = non-ST-segment elevation myocardial infarction

OCT = optical coherence tomography

PCI = percutaneous coronary intervention

clinical utility of this technique to improve percutaneous coronary interventions (PCIs) and clinical outcomes remains to be defined (1–3).

Recently, the CLI-OPCI (Centro per la Lotta contro l'Infarto-Optimisation of Percutaneous Coronary Intervention) study compared angiography alone versus angiographic guidance plus OCT guidance for routine PCI (5). The researchers found that OCT can identify nonoptimal stent deployment in approximately one-third of cases, thus providing preliminary evidence of the technique's clinical utility. Importantly, for the first time, the CLIO-PCI study addressed the question of how to interpret OCT findings by setting specific quantitative criteria to identify suboptimal stent deployment (6).

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The aim of the present study was to assess the impact of these pre-specified OCT quantitative criteria on clinical outcomes after PCI. For this purpose, the end-procedural OCT data in a large retrospective study (CLI-OCPI II) were evaluated. The study included 1,002 lesions in 832 patients with a follow-up length of at least 1 year.

METHODS

STUDY DESIGN. This retrospective multicenter PCI registry included cases with frequency domain OCT assessment of stent positioning. All case subjects had at least 1 OCT assessment of the treated vessel, performed at the end of the procedure, with a sufficient acquisition length to address the whole length of the stented segments plus the proximal and distal reference segments (2,6–8). Indications for periprocedural OCT assessment and its practical utilization were left to the operator's discretion; no formal selection criteria or treatment strategies (e.g., routinely stent post-dilation) were prospectively adopted in the enrolled case samples. For the purposes of this study, only OCT findings obtained at the end of the procedure were considered.

All patients provided written informed consent for the index procedure and for telephone/direct visit follow-up. Ethical approval was waived because of the study's observational retrospective design.

As the primary objective of the study, the impact of the presence of an OCT-based suboptimal stent deployment on clinical outcome was explored; the impact of the individual OCT findings on outcome was also appraised. For this purpose, the incidence of major adverse cardiac events (MACE) was a composite of all-cause mortality, myocardial infarction (MI) not clearly attributable to a nontarget vessel (including periprocedural MI defined as creatine kinase-myocardial band level >3 times the upper limit of normal), and target lesion revascularization. All outcomes were defined according to the recommendations of the Academic Research Consortium (9).

Endpoint adjudication was performed by a central clinical event committee in a blinded fashion. No extramural funding was used to support this work, and the authors were solely responsible for the design, conduct, and final contents of the study.

PATIENTS AND PROCEDURES. Overall, 832 consecutive patients in Italy undergoing OCT guidance at 5 experienced and high-volume OCT centers entered the study. Given the retrospective design, treatment choices (including stenting technique, drug-eluting stent [DES] utilization, and additional pharmacological therapy) were according to local practice. In particular, OCT guidance during the procedure was not codified but left to the operator's discretion.

PCIs were performed with standard techniques and catheters by using a femoral or radial approach. All patients received unfractionated heparin (a bolus of 70 IU/kg with additional doses aimed at achieving an intraprocedural activated clotting time of 250 to 300 s). All patients were pretreated with 325 mg of aspirin and a loading dose of clopidogrel 600 mg, prasugrel 60 mg, or ticagrelor 180 mg, if the patient was not already on a maintenance dose. Unless contraindicated, dual antiplatelet therapy was recommended for at least 12 months. During the first year after discharge, patients were followed up by means of scheduled direct visits (generally at 1 and 6 months) and telephone contacts. In case of any adverse event or new hospitalization, source documents were obtained and examined in detail.

OCT MEASUREMENTS AND DEFINITIONS. OCT was acquired by means of the frequency domain C7-XR system or the OPTIS system (both St. Jude Medical, St. Paul, Minnesota) with a nonocclusive technique according to a well-standardized method (2,8). OCT assessment of stent implantation was on the basis of conventional definitions reported in expert consensus OCT documents (2,4,10). The value with maximal predictive accuracy for outcome was used as a cutoff point for each variable (**Figure 1**). In particular, the following factors were considered significant findings:

1. Edge dissection: the presence of a linear rim of tissue with a width ≥200 μm and a clear separation

from the vessel wall or underlying plaque that was adjacent (<5 mm) to a stent edge (2,6).

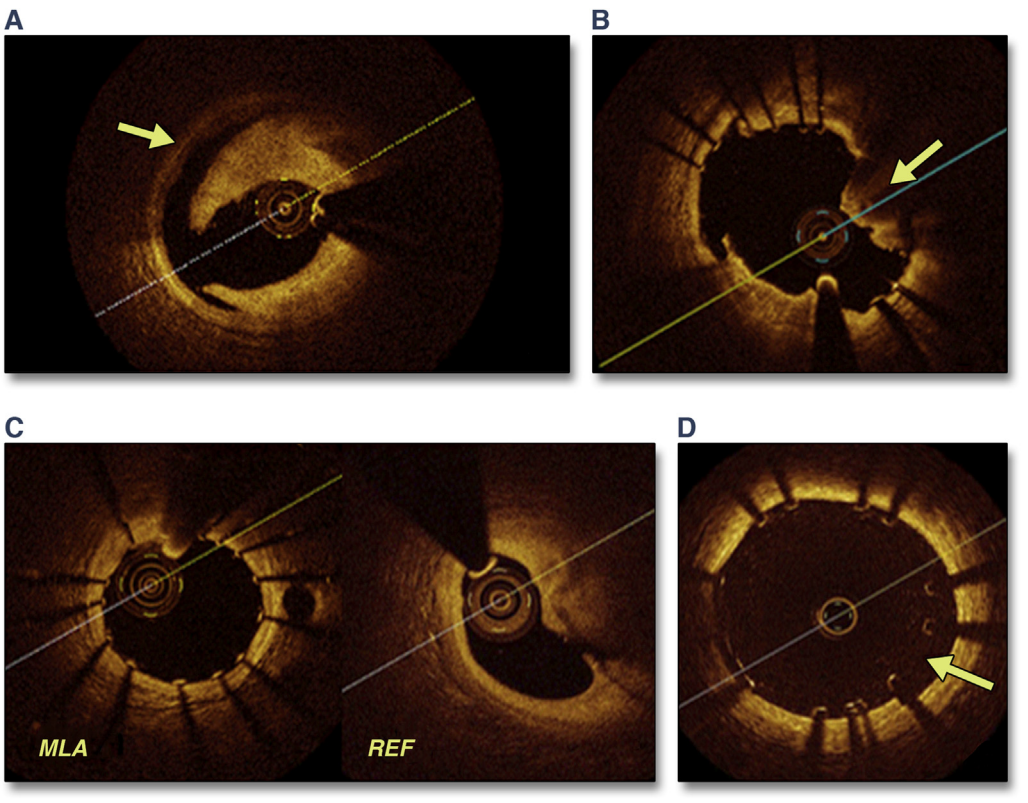
2. Reference lumen narrowing: lumen area <4.5 mm^2 in the presence of significant residual plaque adjacent to stent endings (6);
3. Malapposition: stent-adjacent vessel lumen distance >200 μm (6,10,11);
4. In-stent minimum lumen area (MLA) <4.5 mm^2 (6);
5. In-stent MLA <70% of the average reference lumen area;
6. Intrastent plaque/thrombus protrusion: tissue prolapsing between stent struts extending inside a circular arc connecting adjacent struts or intraluminal mass ≥500 μm in thickness, with no direct continuity with the surface of the vessel wall or highly backscattered luminal protrusion in continuity with the vessel wall and resulting in signal-free shadowing (2,10,12).

Definition of suboptimal OCT stent deployment required the presence of at least 1 of the OCT findings significantly associated with MACE.

By study design, only final OCT images performed at the end of the procedures were analyzed off-line at a certified central core laboratory (Rome Heart Research, Rome, Italy) whose operators were blinded to procedural characteristics and outcomes.

STATISTICAL ANALYSIS. Continuous variables are reported as mean ± SD or median (1st to 3rd quartile) in case of normal or skewed distribution; discrete variables are reported as percentages. The Student *t* test, Mann-Whitney *U* test, chi-square test, and Fisher exact test were applied for bivariate analyses when appropriate. The receiver-operating characteristic curve was used to evaluate the predictive accuracy of each OCT parameter for outcome; the highest Youden index (J statistic) representing the maximum

FIGURE 1 OCT Criteria Applied to Address Suboptimal OCT Stent Deployment



(A) Edge dissection (linear rim of tissue with a width ≥200 μm and a clear separation from the vessel wall or underlying plaque) that was adjacent to a stent edge. **(B)** Intrastent plaque/thrombus protrusion (tissue prolapsing between stent struts extending inside a circular arc connecting adjacent struts or intraluminal mass ≥500 μm in thickness with no direct continuity with the surface of the vessel wall or highly backscattered luminal protrusion in continuity with the vessel wall and resulting in signal-free shadowing). **(C)** Reference (REF) lumen narrowing (lumen area <4.5 mm^2 in the presence of significant plaque adjacent to stent endings). **(D)** Stent malapposition (stent-adjacent vessel lumen distance >200 μm). MLA = minimum lumen area; OCT = optical coherence tomography.

potential effectiveness was used to determine the optimal cutoff (13,14). Combined adverse events were evaluated on a per-patient hierarchical basis; thus, only 1 hard event per patient per event type was summarized as Kaplan-Meier estimates.

All study variables were tested for bivariate association with MACE; if nominally significant ($p < 0.05$), they were simultaneously forced into a Cox regression model to identify independent outcome predictors and to calculate their adjusted hazard ratios (HRs) with associated 95% confidence intervals (CIs). The Cox regression model included the following variables: left ventricular ejection fraction, diabetes mellitus, family history of coronary artery disease, non-ST-segment elevation myocardial infarction (NSTEMI) diagnosis, multivessel disease, left main disease, previous MI, angiographically ambiguous lesion (i.e., intermediate lesion with irregular contour and/or haziness), in-stent restenosis lesion, bare-metal stent (BMS) usage, ostial lesion treatment, and suboptimal final OCT result.

A score quantifying the propensity to incur MACE was computed to adjust for potential confounding factors inherent to the observational nature of the study (15,16). Specifically, the individual score, defined as the conditional probability of experiencing MACE, was estimated with a nonparsimonious logistic regression model, including all available co-variables but excluding those that were OCT related (C-statistic: 0.78; 95% CI: 0.71 to 0.85). Adjusted effect estimates were estimated from models in which the score was entered as covariates. In addition, as a sensitivity analysis, a matched pair analysis was performed on the basis of the propensity to develop MACE.

A 2-tailed, p value <0.05 was established as the level of statistical significance for all tests. All statistical analyses were conducted by using SPSS-PASW version 22.0 (IBM SPSS Statistics, IBM Corporation, Armonk, New York).

TABLE 1 Patient Characteristics

	All Patients (N = 832)	Patients With MACE (n = 105)	Patients Without MACE (n = 727)	p Value
Age, yrs	64 (56–72)	66 (55–75)	64 (56–72)	0.19
Female	243 (29.2)	25 (23.8)	218 (30.0)	0.21
Left ventricular ejection fraction	55 (48–60)	52 (43–60)	55 (48–60)	0.002
Hypertension	587 (70.6)	77 (73.3)	510 (70.2)	0.73
Hypercholesterolemia	510 (61.3)	61 (58.1)	449 (61.8)	0.39
Smoking habit	280 (33.7)	37 (35.2)	243 (33.4)	0.82
Family history of CAD	252 (30.3)	19 (18.1)	233 (32.0)	0.002
Diabetes mellitus	179 (21.5)	27 (25.7)	152 (20.9)	0.31
CKD (GFR <60 ml/min/1.73 m^2)	155 (18.6)	23 (21.9)	132 (18.2)	0.21
Multivessel disease	438 (52.6)	69 (65.7)	369 (50.8)	0.024
Prior MI	164 (19.7)	34 (32.4)	130 (17.9)	<0.001
Prior revascularization	252 (30.3)	29 (27.6)	223 (30.7)	0.50
Prior PCI	238 (28.6)	26 (24.8)	212 (29.2)	0.36
Prior CABG	31 (3.7)	6 (5.7)	25 (3.4)	0.27
Acute coronary syndrome	469 (56.4)	61 (58.1)	408 (56.1)	0.83
STEMI	258 (31.0)	31 (29.5)	227 (31.2)	0.73
NSTEMI	76 (9.2)	20 (19.1)	56 (7.7)	<0.001
Unstable angina	135 (16.2)	10 (9.5)	125 (17.2)	0.05
Stable angina	363 (43.6)	44 (41.9)	319 (43.9)	0.83

Values are median (interquartile range) or n (%).

CABG = coronary artery bypass graft; CAD = coronary artery disease; CKD = chronic kidney disease; GFR = glomerular filtration rate; MI = myocardial infarction; MACE = major adverse cardiac event(s); NSTEMI = non-ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

RESULTS

Between 2008 and 2013, a total of 832 patients with 1,002 lesions undergoing post-stenting OCT assessment were included in the registry. Clinical and procedural features of the study population are summarized in Tables 1 and 2, respectively. The patients' median age was 64 years (interquartile range [IQR]: 56 to 72 years), and the study included 29.2% female subjects. Diagnosis at admission was acute coronary syndrome in 56.4% of patients, including acute ST-segment elevation MI in 31.0%. Most of the patients had a complex lesion profile (Ellis class B2/C 74.8%), with multivessel disease involvement in 52.6%.

Treated lesion location was as follows: left main, 4.8%; left anterior descending artery, 50.7%; left circumflex artery, 21.4%; right coronary artery, 22.7%; and graft conduit, 0.4%. DES implantation occurred in 71.4% of the lesions, and multiple overlapping stents were implanted in 21.4% of cases. Direct stenting and high-pressure stent post-dilation rates were 27.0% and 48.0%, respectively.

All OCT acquisitions were successfully performed; however, during off-line analysis, 1.8% of cases were discarded due to insufficient quality images (e.g., improper acquisition technique) (6). Therefore, OCT assessment was analyzed in 984 stented lesions, and suboptimal stent implantation was noted in 31.0% of cases (Table 3). In particular, OCT disclosed in-stent MLA <4.5 mm^2 in 23.4% of the stented lesions, edge dissection in 12.7%, in-stent lumen underexpansion in 23.7%, malapposition in 49.3%, intrastent plaque/thrombus protrusion in 29.4%, and reference lumen narrowing in 7.5%.

The immediate angiographic success rate (residual stenosis <30% with Thrombolysis In Myocardial Infarction flow grade 3) was 97.6% with a periprocedural MI prevalence of 2.6%. The cumulative MACE rate at a median follow-up of 319 days (IQR: 123 to 576 days) was 12.6%, with 2.9% all-cause mortality, 7.7% nonfatal MI, and 6.7% target lesion revascularization

(Table 4). Notably, 82% of adverse events occurred within the first 12 months after the procedure with a mean time-to-MACE of 26 days (IQR: 1 to 216 days).

MACE PREDICTORS. Compared with patients with event-free survival, patients with MACE during follow-up had a lower left ventricular ejection fraction (52% [IQR: 43% to 60%] vs. 55% [IQR: 48% to 60%]; p = 0.002), more frequent NSTEMI diagnosis (19.1% vs. 7.7%; p < 0.001), more prior MI (32.4% vs. 17.9%; p < 0.001), and more multivessel disease (65.7% vs. 50.8%; p = 0.024) (Table 1). Regarding the procedural aspects, patients with MACE were characterized by higher BMS use (34.4% vs. 20.0%; p = 0.002) and more frequent treatment of a left main (9.6% vs. 4.1%; p = 0.012), ostial (8.8% vs. 4.8%; p = 0.048), angiographically ambiguous (13.6% vs. 8.0%; p = 0.023), or in-stent (7.2% vs. 3.3%; p = 0.045) restenosis lesion (Table 2).

OCT analyses revealed a significantly higher incidence of suboptimal stent deployment in lesions associated with any adverse event during follow-up (59.2% vs. 26.9%; p < 0.001). In particular, patients with lesions and MACE reported more frequent in-stent MLA <4.5 mm^2 (40.8% vs. 20.8%; p < 0.001), dissection >200 μm at the distal stent edge (16.0% vs. 5.7%; p < 0.001), and reference lumen area <4.5 mm^2 in the presence of residual significant plaque at either the distal (22.4% vs. 3.4%; p < 0.001) or proximal (11.2% vs. 1.2%; p < 0.001) stent edges. Conversely, in-stent MLA <70% of the average reference lumen area (30.4% vs. 22.7%; p = 0.07), dissection at the proximal stent edge (6.4% vs. 6.6%; p = 0.92), malapposition (50.4% vs. 49.1%; p = 0.85), or in-stent plaque/thrombus prolapse (30.4% vs. 29.2%; p = 0.83) were not associated with an increased MACE rate (Table 3).

In the multivariable Cox hazard analysis, suboptimal OCT stent deployment was confirmed as an independent predictor of MACE (HR: 3.53; 95% CI: 2.2 to 5.8; p < 0.001), together with impaired left ventricular ejection fraction (HR: 2.12; 95% CI: 1.3 to 3.5; p = 0.003), NSTEMI diagnosis (HR: 1.99; 95% CI: 1.1 to 3.6; p = 0.021), and left main disease (HR: 2.79; 95% CI: 1.3 to 6.2; p = 0.012). Figure 2 presents the relative Kaplan-Meier curves, and Table 5 displays the predictive value of the individual OCT criteria of suboptimal stent deployment. Sensitivity analysis on the basis of 146 patients matched for the propensity to incur MACE confirmed the results stemming from the main analysis in terms of both statistical direction and magnitude.

TABLE 2 Procedural Characteristics

	All Lesions (N = 984)	Lesions With MACE (n = 125)	Lesions Without MACE (n = 859)	p Value
Location of lesion treated				
Left main	47 (4.8)	12 (9.6)	35 (4.1)	0.012
Left anterior descending artery	499 (50.7)	65 (52.0)	434 (50.5)	0.83
Left circumflex artery	211 (21.4)	29 (23.2)	182 (21.2)	0.69
Right coronary artery	223 (22.7)	17 (13.6)	206 (24.0)	0.013
Graft conduit	4 (0.4)	2 (1.6)	2 (0.2)	0.08
Lesion features				
Ellis class B2/C	736 (74.8)	89 (71.2)	647 (75.3)	0.91
Calcified lesion	148 (15.0)	18 (14.4)	130 (15.1)	0.85
Ostial lesion	52 (5.3)	11 (8.8)	41 (4.8)	0.048
Bifurcation lesion	138 (14.0)	23 (18.4)	115 (13.4)	0.17
Chronic total occlusion lesion	24 (2.4)	0 (0.0)	24 (2.8)	0.10
Angiographically ambiguous lesion	86 (8.7)	17 (13.6)	69 (8.0)	0.023
In-stent restenosis lesion	37 (3.8)	9 (7.2)	28 (3.3)	0.045
Stent-thrombosis lesion	28 (2.8)	4 (3.2)	24 (2.8)	0.78
Technical approach				
Direct stenting	266 (27.0)	33 (26.4)	233 (27.1)	0.98
Thrombectomy use	145 (14.7)	17 (13.6)	128 (14.9)	0.89
Post-dilation	472 (48.0)	51 (40.8)	421 (49.0)	0.24
DES	703 (71.4)	79 (63.2)	624 (72.6)	0.048
BMS	215 (21.9)	43 (34.4)	172 (20.0)	0.002
BVS	66 (6.7)	3 (2.4)	63 (7.4)	0.05
Overlapping stent	211 (21.4)	26 (20.8)	185 (21.5)	0.91
Optimal angiographic result*	960 (97.6)	121 (96.8)	839 (97.7)	0.78
Stent diameter, mm	3.0 (2.75-3.5)	3.0 (2.5-3.0)	3.0 (2.75-3.5)	0.07
Stent length, mm	22 (15-28)	18 (15-28)	22 (15-30)	0.18
Max pressure during stent implantation	16 (14-18)	16 (14-18)	16 (14-18)	0.24
Contrast dye	250 (200-300)	230 (200-318)	250 (200-300)	0.46

Values are n (%) or median (interquartile range). *Defined as residual stenosis <30% and final Thrombolysis In Myocardial Infarction 3 flow.

BMS = bare-metal stent; BVS = bioresorbable vascular scaffold; DES = drug-eluting stent; MACE = major adverse cardiac events.

DISCUSSION

The main finding provided by this large multicenter registry was that patients exhibiting suboptimal stent deployment on the basis of specific OCT criteria experienced a higher rate of MACE during follow-up. Indeed, suboptimal stent deployment was significantly more common in the MACE group (59.2% vs. 26.9%; p < 0.001) and was found to be an independent predictor of MACE.

THE NEW ANGLE OF VIEW. Recent intravascular ultrasound (IVUS) data derived from observational studies and large meta-analyses have proven the efficacy of an IVUS-guided approach for reducing adverse clinical outcomes (including death, MI, and stent thrombosis) after PCI (17,18). OCT represents a new angle of view to address the adequacy of stent deployment. Besides enabling measurement of IVUS-validated predictors of MACE (including MLA and inflow/outflow disease), the high resolution of the OCT technique permits detection of features that may be missed by IVUS, such as malapposition, intrastent plaque/thrombus protrusion, or dissections at the stent edges and inside the stents.

TABLE 3 OCT Findings

	All Lesions (N = 984)	Lesion With MACE (n = 125)	Lesion Without MACE (n = 859)	p Value
OCT features				
Minimum in-stent lumen area, mm^2	6.0 ± 2.1	5.6 ± 2.1	6.1 ± 2.1	0.025
Maximum in-stent lumen diameter, mm	3.0 ± 0.5	2.9 ± 0.5	3.0 ± 0.5	0.06
Minimum in-stent lumen diameter, mm	2.4 ± 0.5	2.3 ± 0.5	2.4 ± 0.5	0.029
Lumen symmetry, %	1.2 ± 0.2	1.3 ± 0.2	1.2 ± 0.2	0.12
In-stent lumen expansion, %*	85.6 ± 23.1	85.4 ± 28.9	85.7 ± 22.1	0.91
Distal reference lumen area, mm^2	6.3 ± 2.8	5.6 ± 2.3	6.4 ± 2.9	0.001
Proximal reference lumen area, mm^2	8.2 ± 3.4	7.5 ± 3.2	8.3 ± 3.5	0.016
Malapposition thickness, mm	0.23 ± 0.23	0.25 ± 0.24	0.23 ± 0.22	0.32
Malapposition length, mm	3.4 ± 4.3	3.1 ± 3.7	3.4 ± 4.4	0.45
Intrastent plaque/thrombus protrusion, mm	0.40 ± 0.41	0.46 ± 0.31	0.40 ± 0.42	0.08
Distal edge dissection length, mm	0.23 ± 0.95	0.59 ± 2.09	0.18 ± 0.64	0.05
Distal edge dissection width, mm	0.04 ± 0.13	0.10 ± 0.24	0.03 ± 0.10	0.001
Distal edge dissection arc, °	7.5 ± 25.7	20.3 ± 51.4	5.6 ± 18.8	0.003
Proximal edge dissection length, mm	0.13 ± 0.53	0.20 ± 0.85	0.12 ± 0.47	0.33
Proximal edge dissection width, mm	0.03 ± 0.12	0.04 ± 0.13	0.03 ± 0.12	0.49
Proximal edge dissection arc, °	5.6 ± 18.3	7.5 ± 21.1	5.3 ± 17.9	0.31
Suboptimal OCT criteria				
Minimum in-stent lumen area <4.5 mm^2	230 (23.4)	51 (40.8)	179 (20.8)	<0.001
In-stent lumen underexpansion†	233 (23.7)	38 (30.4)	195 (22.7)	0.07
Malapposition >200 μm	485 (49.3)	63 (50.4)	422 (49.1)	0.85
Intrastent plaque/thrombus protrusion >500 μm	289 (29.4)	38 (30.4)	251 (29.2)	0.83
Edge dissection >200 μm	125 (12.7)	25 (20.0)	100 (11.6)	0.013
Distal dissection	69 (7.0)	20 (16.0)	49 (5.7)	<0.001
Proximal dissection	65 (6.6)	8 (6.4)	57 (6.6)	0.92
Reference narrowing‡	74 (7.5)	38 (30.4)	36 (4.2)	<0.001
Distal narrowing	57 (5.8)	28 (22.4)	29 (3.4)	<0.001
Proximal narrowing	24 (2.4)	14 (11.2)	10 (1.2)	<0.001
At least 1 predictive OCT criterion§	305 (31.0)	74 (59.2)	231 (26.9)	<0.001

Values are mean ± SD or n (%). *Defined as in-stent-to mean reference lumen area. †Defined as in-stent minimum lumen area <70% of the average reference lumen area. ‡Defined as reference lumen area <4.5 mm^2 in the presence of significant residual plaque adjacent to stent endings. §Including only optical coherence tomography (OCT) criteria predictive of major adverse cardiac events (MACE) at multivariable analysis.

The multicenter CLI-OPCI registry (5) showed that OCT could potentially improve the clinical outcomes after coronary intervention in a real-world population. In fact, the 1-year composite of cardiac death or nonfatal MI was significantly lower in the OCT-guided intervention arm. However, the promising conclusions reached by the CLI-OPCI registry should be approached with caution because of its nonrandomized design and relatively small population size (335 patients in the OCT group).

TABLE 4 Clinical Outcomes

	All Patients (N = 832)	Patients With Suboptimal OCT Deployment* (n = 254)	Patients With Optimal OCT Deployment (n = 578)	HR (95% CI)	p Value
MACE	105 (12.6)	64 (25.2)	41 (7.1)	4.41 (2.9–6.8)	0.001
Death	24 (2.9)	11 (4.3)	13 (2.2)	1.97 (0.9–4.5)	0.104
Myocardial infarction	64 (7.7)	42 (16.5)	22 (3.8)	5.01 (2.9–8.6)	0.001
Periprocedural	22 (2.6)	11 (4.3)	11 (1.9)	2.33 (1.0–5.5)	0.050
During follow-up	42 (5.1)	31 (12.2)	11 (1.9)	7.17 (3.5–14.5)	0.001
Target lesion revascularization	56 (6.7)	42 (16.5)	14 (2.4)	7.98 (4.3–14.9)	0.001
Stent thrombosis	30 (3.6)	26 (10.2)	4 (0.7)	16.36 (5.6–47.4)	0.001
Days of follow-up	319 (123–576)	312 (118–584)	324 (129–575)	-	0.536

Values are n (%) or median (interquartile range). *Either in-stent minimum lumen area <4.5 mm^2, dissection >200 μm at the distal stent edge, or distal or proximal reference narrowing.

CI = confidence interval; HR = hazard ratio; other abbreviations as in Table 3.

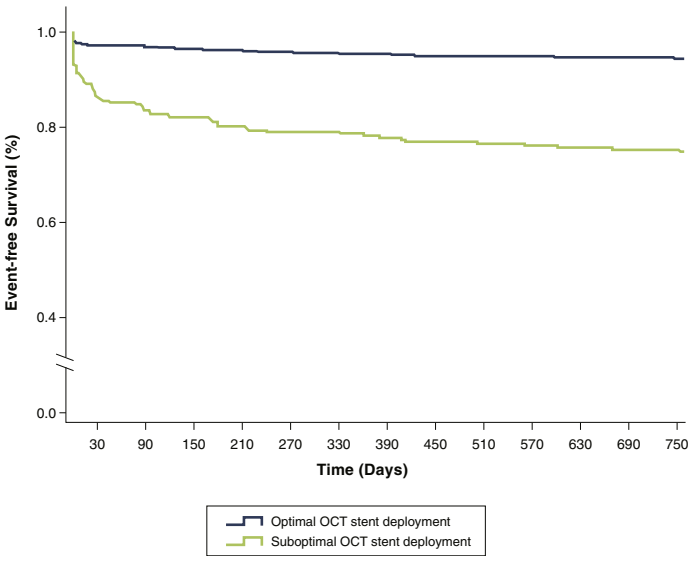
The present study broadens the previous experience of the CLIO-PCI registry by assessing the role of OCT findings after PCI in a much larger population (832 patients and 1,002 lesions; median follow-up 319 days). Consistent with previous data (5), CLI-OPCI II showed that OCT-defined suboptimal stent deployment was a relatively common finding (31.0% of cases), with a significantly higher prevalence in patients experiencing MACE in the first year of follow-up (59.2% vs. 26.9%; $p < 0.001$), and was an independent predictor of worse outcome (HR: 3.53; $p < 0.001$).

SPECIFIC OCT FINDINGS OF SUBOPTIMAL STENTING. Conclusions reached by this study are in line with those emerging from the IVUS substudy of the ADAPT-DES (Assessment of Dual Antiplatelet Therapy with Drug Eluting Stents) trial registry (18). In particular, the CLIO-PCI II highlighted the role of residual reference segment disease. Stented segments exhibiting a narrowing at the reference lumen area <4.5 mm^2 in the presence of significant plaque experienced a worse outcome, with the risk of MACE approximately 5 times higher regardless of the location (proximal or distal reference segment). These data were not unexpected: a large IVUS-identified plaque burden at the stent margins represents a well-known risk factor for late restenosis and thrombosis (19–21).

Dissections >200 μm at the distal stent edge also conveyed a higher risk of MACE (HR: 2.54; $p = 0.004$), whereas proximal dissections had no clinical impact. The relationship between distal dissection and worsened clinical outcome has already been noted in the CLI-OPCI registry (5). This finding was also in line with the ADAPT-DES study confirming the ominous role of distal dissections regardless of the amount of luminal narrowing. The negative impact of stent edge dissection, shown in the present study, was emphasized by the early occurrence of cardiac events. The majority of MACE occurred during the first 3 months after the procedure (**Figure 2**). Importantly, even at the applied 200-μm threshold, significant dissections may be missed by using IVUS (22).

There are 2 general approaches to assessing stent underexpansion. The first is using absolute dimensions that can be expressed as in-stent MLA or minimal stent area (MSA); the second is the relative minimal stent-to-mean reference lumen area percentage. Using IVUS, Ziada et al. (23) and Sonoda et al. (24) showed that the absolute dimension was the strongest predictor of freedom from adverse events after BMS or DES implantation. Similarly, an absolute in-stent MLA <4.5 mm^2 according to OCT in the present study predicted MACE, whereas the relative criterion of stent-to-mean reference lumen area did not. Patients with subsequent MACE had a smaller MLA compared with those with no events; relative stent expansion was virtually identical in the 2 groups. OCT measurements are reportedly smaller than IVUS (22); in keeping with this observation, an in-stent MLA <4.5 mm^2 according to OCT in the present study was

FIGURE 2 Clinical Outcomes



Survival free of major adverse cardiac events according to optimal versus nonoptimal stent deployment assessed using optical coherence tomography (OCT).

TABLE 5 Predictive Value of OCT Criteria

	HR (95% CI)	p Value
Unadjusted		
In-stent minimum lumen area <4.5 mm^2	2.62 (1.8–3.9)	<0.001
Distal dissection >200 μm	3.15 (1.8–5.5)	<0.001
Proximal dissection >200 μm	0.96 (0.4–2.1)	0.92
In-stent lumen underexpansion*	1.49 (1.0–2.3)	0.06
Malapposition >200 μm	1.05 (0.7–1.5)	0.79
Intrastent plaque/thrombus protrusion >500 μm	1.06 (0.7–1.6)	0.79
Distal reference narrowing†	8.26 (4.7–14.5)	<0.001
Proximal reference narrowing†	10.71 (4.6–24.7)	<0.001
Adjusted		
In-stent minimum lumen area <4.5 mm^2	1.64 (1.1–2.6)	0.040
Distal dissection >200 μm	2.54 (1.3–4.8)	0.004
Proximal dissection >200 μm	0.83 (0.4–1.9)	0.65
In-stent lumen underexpansion*	1.21 (0.7–1.9)	0.45
Malapposition >200 μm	1.15 (0.8–1.7)	0.52
Intrastent plaque/thrombus protrusion >500 μm	1.00 (0.6–1.6)	0.99
Distal reference narrowing†	4.65 (2.5–8.8)	<0.001
Proximal reference narrowing†	5.73 (2.2–14.6)	<0.001

*Defined as in-stent minimum lumen area <70% of the average reference lumen area. †Defined as reference lumen area <4.5 mm^2 in the presence of significant plaque.

OCT = optical coherence tomography; other abbreviations as in Table 4.

consistent with the IVUS MSA criterion that has been reported after implantation of second-generation DES (25). Finally, the in-stent MLA reflects both actual stent underexpansion (i.e., the MSA) and in-stent plaque/thrombus prolapse. In the present study, 56.4% of patients presented with acute coronary syndrome, including acute ST-segment elevation MI in 31.0%; this is a patient population in whom in-stent plaque/thrombus prolapse has an important impact on in-stent lumen dimensions, whereas expansion of the metallic scaffold into a thrombus containing lesions is often easier than into a fibrotic lesion in patients with stable angina.

It has been suggested that acute malapposition may be associated with reduced re-endothelialization and increased formation of neointima. However, our data corroborate IVUS findings that failed to relate acute stent vessel wall malapposition with clinical outcome (26,27). Such conclusions were also in line with those recently reported from the CLI-THRO study (28) as well as a report from Im et al. (29). In the CLIO-THRO study (i.e., an OCT prospective registry designed to address the mechanism of stent thrombosis) (28), patients with subacute stent thrombosis more often exhibited stent underexpansion, stent edge dissection, reference lumen narrowing, and smaller MSA but no increased frequency of stent malapposition.

STUDY LIMITATIONS. The main limitation of the present study was its nonrandomized, retrospective design. Thus, some evident clinical imbalances were present in patients experiencing MACE compared with patients with no events during follow-up. However, the presence of nonoptimal OCT criteria for stent deployment was an independent predictor of MACE in the multivariable Cox hazard analysis. This study included patients with different clinical conditions (i.e., patients in stable and acute condition) and treatment approach (i.e., BMS and DES); the role and importance of the described OCT findings could vary among these categories.

Although all the adopted definitions of suboptimal stent deployment were derived from previous IVUS experiences and OCT consensus documents, the proposed "clinical" cutoffs reflect efforts to delineate a practical approach to OCT guidance; these need to be validated in further studies, however. Finally, although some OCT findings are clearly associated with worse outcome, treatment and reformability remain to be investigated.

CONCLUSIONS

The present large multicenter registry showed that suboptimal stent deployment on the basis of specific OCT criteria was frequent in patients experiencing MACE in the first year of follow-up after stent implantation. In particular, suboptimal OCT stent deployment was an independent predictor of worse clinical outcome. These data seem to corroborate the rationale for an OCT-guided strategy during PCI.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE 1: OCT-defined suboptimal stent deployment was a relatively common finding (31.0% of cases), with a significantly higher prevalence in patients experiencing MACE in the first year of follow-up (59.2% vs. 26.9%; $p < 0.001$).

COMPETENCY IN MEDICAL KNOWLEDGE 2: Suboptimal OCT stent deployment, defined according to specific quantitative OCT criteria, was an independent predictor of worse outcome (HR: 3.53; $p < 0.001$).

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: OCT guidance during PCI allowed identification of patients at increased risk of MACE.

TRANSLATIONAL OUTLOOK 1: The management and reformability of OCT-defined suboptimal stent deployment require further investigation.

TRANSLATIONAL OUTLOOK 2: Randomized studies are needed to assess the clinical impact of OCT guidance during PCI.

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