

ORIGINAL STUDIES

Optical coherence tomography, intravascular ultrasound or angiography guidance for distal left main coronary stenting. The ROCK cohort II study

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Abstract

Objectives: to test the safety and efficacy of intravascular imaging and specifically optical coherence tomography (OCT) as a diagnostic tool for left main angioplasty and analyze the mid-term outcome accordingly.

Background: Clinical data and international guidelines recommend the use of intravascular imaging ultrasound (IVUS) to guide left main (LM) angioplasty. Despite early experience using OCT in this setting is encouraging, the evidence supporting its use is still limited.

Methods: ROCK II is a multicenter, investigator-driven, retrospective European study to compare the performance of IVUS and OCT versus angiography in patients undergoing distal-LM stenting. The primary study endpoint was target-lesion failure (TLF) including cardiac death, target-vessel myocardial infarction and target-lesion revascularization. We designed this study hypothesizing the superiority of intravascular imaging over angiographic guidance alone, and the non-inferiority of OCT versus IVUS.

Results: A total of 730 patients, 377 with intravascular-imaging guidance (162 OCT, 215 IVUS) and 353 with angiographic guidance, were analyzed. The one-year rate of TLF was 21.2% with angiography and 12.7% with intravascular-imaging ($p = 0.039$), with no difference between OCT and IVUS ($p = 0.26$). Intravascular-imaging was predictor of freedom from TLF (HR 0.46; 95% CI 0.23–0.93; $p = 0.03$). Propensity-score matching identified three groups of 100 patients each with no significant differences in baseline characteristics. The one-year rate of TLF was 16% in the angiographic, 7% in the OCT and 6% in the IVUS group, respectively ($p = 0.03$ for IVUS or OCT vs.

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angiography). No between-group significant differences in the rate of individual components of TLF were found.

Conclusions: Intravascular imaging was superior to angiography for distal LM stenting, with no difference between OCT and IVUS.

KEYWORDS

intravascular imaging ultrasound, left main coronary artery stenting, optical coherence tomography

1 | INTRODUCTION

After two decades of landmark trials and multiple registries, the European revascularization guidelines finally endorsed percutaneous coronary intervention (PCI) with the new drug-eluting stents (DES) as an alternative to surgery for patients with left main (LM) lesions and low or intermediate anatomic complexity.¹ This important information comes with the long term (> 10 years) follow up of the PRECOMBAT study.²

The most common location of disease in the LM is by far the distal portion with a variable involvement of the left anterior descending and left circumflex arteries at their ostium site.³ Thus, distal LM lesions imply greater complexity for the percutaneous revascularization approach.

The use of intravascular ultrasound (IVUS) to guide PCI in this crucial anatomical setting has been associated to a clinical benefit in terms of mortality, myocardial infarction and thrombosis, with greater benefits if the lesion is located in the distal portion of the left main.^{4–7} For all these reasons, the use of IVUS for this purpose has been granted with a class IIa (B level of evidence) recommendation in the last European guidelines for myocardial revascularization, both for lesion assessment and stent optimization.¹

Optical coherence tomography (OCT) is an attractive alternative to IVUS in assessing LM disease and guiding PCI. Its higher image resolution, faster acquisition and easier interpretation make this imaging technique definitely promising for this purpose. The only exception are lesions located at the ostium of the LM where blood clearance may be challenging.⁸ The use of OCT enhances detection of struts malapposition, tissue protrusion, new thrombus or edge dissections after stenting more accurately and allows a more precise lumen delineation.⁹

Early experience using OCT to evaluate ambiguous LM lesions is encouraging,^{10,11} yet differences in magnitude of lumen areas as compared with IVUS should be taken into consideration.^{12,13}

In the ROCK Cohort I study, OCT guidance of LM PCI was associated with improved midterm angiographic outcome compared to angiographic or IVUS guidance.¹⁴

Nonetheless, though results of this pioneer study appear promising, the evidence of clinical benefit derived from OCT guided LM PCI is far more limited than for IVUS.

Following the aforementioned results of the ROCK I pilot study, the purpose of ROCK II was to evaluate and compare the performance of intravascular imaging versus no imaging, and of OCT versus IVUS as an adjuvant tool for distal LM angioplasty, in terms of clinical endpoints at mid-term follow up.

2 | METHODS

2.1 | Population and procedures

ROCK II is an investigator-driven, international, multicenter, retrospective clinical study in which patients undergoing distal LM angioplasty with one or more of the latest generation DES and at least 12 months of follow up were consecutively included. Patients could be enrolled if they had the sole angiographic guidance or if they had any intravascular imaging guidance (either IVUS or OCT) as an adjunct tool during the procedure.

Distal LM lesion was defined as a lesion limited to the distal portion of the LM stem or extending from other proximal or distal segments. Lesion severity and subsequent indication to PCI, was judged as a stenosis of at least 50% with angiographic criteria.

Exclusion criteria applied were the following: (a) use of a previous generation DES (implantation before January 2012); (b) isolated ostial or proximal involvement of LM lesions; (c) cardiogenic shock.

Patients were grouped for analysis according to the use of angiography alone (ANGIO group) or any intravascular imaging tool during the procedure, either IVUS or OCT. The use of IVUS, OCT or only angiography to guide PCI was decided by the operator (at the time of the procedure), as well as the protocol for IVUS and OCT examination and the corresponding criteria applied to optimize PCI procedures. Likewise, the procedural features such as use of provisional stenting approach, implementation of 2-stent techniques, selection of DES brand and post-PCI antithrombotic therapy were all decided upon by interventional cardiologists performing the procedures. In a prospective fashion, all baseline clinical, angiographic and procedural data (including IVUS and OCT) as well as the follow up information was uploaded into a specifically designed database, then, all data was analyzed retrospectively. For the purpose of data entry in ROCK II study, we shared a common data set which all the investigators fulfilled at the time of study start up.

Clinical events were adjudicated by local investigators following prespecified event definitions; these investigators were blinded to whether intravascular imaging was used or not, and to what type of imaging was used.

All patients underwent office cardiac visits at 12 months and yearly thereafter. Surveillance angiographic follow-up was left at the operator discretion but not required by the protocol.

This study received the institutional review board approval for patient enrollment, for each participating center, beginning from Fatebenefratelli Hospital.

We used the OCT console and probes from Abbott Vascular, (different consoles according to the study period and the center) and IVUS imaging with automated pullback from Volcano Corp.

2.2 | Endpoints and definitions

Primary endpoint was target lesion failure (TLF), defined herein as a composite of cardiac death, target vessel myocardial infarction and

target lesion revascularization (TLR) at 1 year. Secondary endpoints included any single component of the primary outcome, definite or probable stent thrombosis, all-cause mortality and technical success of OCT or IVUS in the relative groups.

Cardiac death was defined as mortality from cardiac etiologies and any sudden death of unknown cause. Target vessel myocardial infarction was defined as a myocardial infarction case with the evidence of myocardial necrosis in the vascular territory of the LM, so involving any segment either of the left anterior descending artery or left circumflex artery.

TLR was always clinically-driven and defined as revascularization for LM restenosis (> 50% angiographic restenosis), also including proximal or distal segments (5 mm) adjacent to the stent or stents used for treatment of the lesion, and including the first 5 mm of the ostial left anterior descending or circumflex arteries. Any surgical revascularization as the result of restenosis as previously defined was also considered a TLR. Definite or probable stent thrombosis was considered according to the definitions by the Academic Research Consortium.

Angiographic success was defined as the attainment at the target site of a final residual diameter stenosis of less than 20 percent with a TIMI III flow and no residual dissection. Procedure success was defined as the attainment of angiographic success at the target site together with the absence of intraprocedural complications leading to MI or death.

Patients and public were not involved in the design and conduction of this study.

2.3 | Statistics

For sample size calculation we designed this study considering the non-inferiority of the OCT group as compared with the IVUS group, and the superiority of any intravascular imaging group over angiographic guidance alone. Assuming a non-inferiority margin value (delta) of 3% for primary endpoint, a power (1-beta) of 90% and a significance 2-sided level (alpha) 5%, to test this hypothesis, we planned to enroll a global population of 730 patients. To take into account the different baseline clinical and technical characteristics, the analysis of events was repeated after propensity matching that proved to be well balanced. This analysis, however, was not powered to detect significant clinical differences in terms of superiority or non-inferiority.

Continuous variables are presented as mean $\pm$ SD or median (interquartile range) and categorical variables as percentages. Distribution was assessed for each variable with the Kolmogorov-Smirnov test. Accordingly, continuous variables were compared with the Student t test if they followed a normal distribution and by Wilcoxon tests when this was not the case. The categorical variables were compared with the chi-square test or Fisher exact test, as required. Kaplan-Meier curves for event-free survival were obtained for each group and compared using the log-rank test and the hazard ratios with 95% confidence interval. Cox proportional hazard multiple regression analysis was used to determine independent predictors of major cardiac adverse events during the follow-up period. The model included

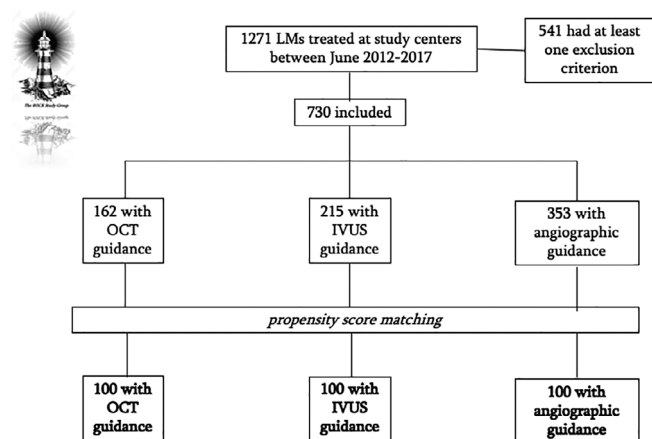


FIGURE 1 3B2 pagROCK II study flow chart. The figure shows the design of the ROCK II study. IVUS, intravascular ultrasound; LM, left main stem; OCT, optical coherence tomography

TABLE 1 Baseline clinical and procedural characteristics of the overall population

	ANGIO	Intravascular imaging	<i>p</i>	OCT	IVUS	<i>p</i>
Number of patients	353	377	—	162	215	—
Male, n (%)	272 (76.7)	286 (76)	0.92	120 (74.3)	166 (77.1)	0.73
Age, years, (mean ± SD)	71 (10)	67 (10)	0.76	69 (10)	69.5 (11)	0.77
Hypertension, n (%)	258 (73.4)	290 (77)	0.40	134 (83.1)	187 (73.7)	0.20
Diabetes, n (%)	120 (34.3)	94 (24.9)	0.03	26 (16.7)	65 (29.9)	0.06
Smoke, n (%)	187 (53.4)	173 (45.8)	0.11	63 (39.2)	107 (50)	0.18
Dyslipidemia, n (%)	170 (48.2)	234 (62)	0.003	112 (68.9)	125 (57.6)	0.13
Previous MI, n (%)	106 (30.5)	113 (30.6)	0.99	42 (25.7)	71 (33.3)	0.27
Previous CABG, n (%)	64 (19)	34 (9.1)	0.003	13 (8.1)	19 (9.4)	0.42
Previous PCI, n (%)	141 (40.2)	151 (40.2)	0.99	52 (32.4)	95 (44.7)	0.10
LVEF, (mean ± SD)	51 (9)	53 (9)	0.11	55 (10)	52 (10)	0.34
Stable angina, n (%)	134 (38)	147 (39.4)	0.46	74 (45.3)	75 (34.6)	0.17
Unstable angina, n (%)	99 (27.7)	90 (24)	0.36	49 (30.8)	43 (20)	0.12
NSTEMI, n (%)	85 (24.3)	83 (22.1)	0.57	44 (27.4)	39 (18.5)	0.21
STEMI, n (%)	42 (12.3)	41 (11.5)	0.33	16 (9.6)	26 (12.4)	0.81
SYNTAX score	26.5 (7.5)	19.9 (7.6)	0.01	19.9 (8.7)	19.9 (7.3)	0.95
LM RVD (mm ± SD)	3.72 ± 0.37	3.86 ± 0.49	0.001	3.84 ± 0.37	3.87 ± 0.49	0.66
Proximal LAD RVD, mm (mean ± SD)	3.25 ± 0.36	3.28 ± 0.46	0.26	3.30 ± 0.41	3.26 ± 0.44	0.36
Proximal LCX RVD, mm (mean ± SD)	2.91 ± 0.45	2.74 ± 0.47	0.001	2.77 ± 0.47	2.72 ± 0.45	0.20
Lesion length-LM to main branch, mm (mean ± SD)	12.3 ± 8.1	9.5 ± 7.9	0.002	9.7 ± 7.1	9.4 ± 7.7	0.25
LM angiographic stenosis, % visual (mean ± SD)	79 ± 12	72 ± 12	<0.001	73 ± 12	71.2 ± 11.5	0.40
Three-vessel disease, n (%)	115 (39.8)	49 (25.9)	0.03	30 (21.9)	33 (28.4)	0.84
Total contrast use (mean ± SD)	220 (100)	220 (105)	0.67	225 (131)	220 (100)	0.46
Total procedural time (mean ± SD)	84 (40)	90 (41)	0.22	92 (45)	88 (50)	0.51
Stent underexpansion	6 (2)	38 (15.4)	0.01	26 (20)	12 (10.5)	0.03
Stent malapposition	2 (0.8)	18 (7.3)	0.02	14 (10)	5 (4)	0.04
Edge dissection	2 (0.8)	19 (7.9)	0.007	13 (9.7)	6 (5.1)	0.04
Predilatation	288 (82)	182 (74.3)	0.09	85 (66.2)	92 (79.5)	0.06
Postdilatation	290 (83.5)	201 (82.8)	0.90	111 (86.2)	95 (80.7)	0.41
LM-LAD stenting	264 (74.9)	180 (72.8)	0.68	98 (76.4)	82 (70.5)	0.40
Two-stent technique, n (%)	64 (18.5)	53 (21.7)	0.42	20 (15.5)	33 (25.7)	0.07
Final kissing balloon, n (%)	220 (61.9)	132 (53.6)	0.08	65 (50.1)	67 (56.1)	0.44
Final POT, n (%)	102 (29.1)	106 (43.6)	0.07	57 (43.9)	49 (43.4)	0.89
Angiographic success, n (%)	340 (98)	243 (98.7)	0.92	128 (99.3)	115 (99)	1.0
Procedural success, n (%)	321 (94.7)	243 (98.7)	0.04	128 (99.3)	115 (99)	1.0

Note: Comparison of baseline and procedural features of the study population according to the use of intravascular imaging, and type of intravascular imaging.

Abbreviations: CABG, coronary artery bypass grafting; LAD, left anterior descending artery; LM, left main stem; LV EF, left ventricular ejection fraction; MI, myocardial infarction; NSTEMI, non-ST elevation MI; PCI, percutaneous coronary intervention; POT, proximal optimization technique; STEMI, ST elevation MI.

all variables that showed association with the primary endpoint in univariate analysis with a *p* value < 0.1. A *p* value < 0.05 was considered as statistically significant.

A propensity score matching was conducted twice. The first was aimed to pair each patient in IVUS group with a patient in OCT group and the second to match each patient in this OCT paired group with a patient in the original ANGIO group. Thus, three comparable groups

of same size could be obtained. In both circumstances the procedure involved two stages:

1. The propensity scores were estimated using logistic regression in which OCT guided PCI was used as the outcome variable and all the baseline clinical and angiographic covariates as predictors.

TABLE 2 Baseline and procedural characteristics of the population after matching

	Angio	IVUS	OCT	p (IVUS vs. OCT)	P (IVUS/OCT vs. Angio)
Number of patients	(n: 100)	(n: 100)	(n: 100)		
Male, n (%)	75 (75)	76 (76)	77 (77)	0.86	0.70
Age, years, (mean $\pm$ SD)	69 $\pm$ 10.3	67.2 $\pm$ 10.9	67.2 $\pm$ 10.3	0.96	0.25
Hypertension, n (%)	72 (72)	79 (79)	73 (73)	0.32	0.25
Diabetes, n (%)	29 (29)	24 (24)	26 (26)	0.74	0.42
Smoke, n (%)	48 (48)	47 (47)	36 (36)	0.11	0.15
Dyslipidemia, n (%)	60 (60)	59 (59)	70 (70)	0.1	0.14
Previous MI, n (%)	29 (29)	23 (23)	26 (26)	0.62	0.33
Previous CABG, n (%)	9 (9)	4 (4)	7 (7)	0.35	0.15
Previous PCI, n (%)	37 (37)	31 (31)	35 (35)	0.54	0.35
LVEF, (mean $\pm$ SD)	51.9 $\pm$ 10	53 $\pm$ 11	52 $\pm$ 8	0.91	0.48
Stable Angina, n (%)	38 (38)	32 (32)	44 (44)	0.12	0.76
Unstable Angina/NSTEMI, n (%)	52 (52)	59 (59)	46 (46)	0.18	0.72
STEMI, n (%)	10 (10)	9 (9)	10 (10)	0.84	0.89
SYNTAX score (mean $\pm$ SD)	19 $\pm$ 7.5	20 $\pm$ 6	17 $\pm$ 7	0.035	0.06
Three-vessel disease, n (%)	28 (28)	24 (24)	23 (23)	0.97	0.45
Calcification, severe, n (%)	12 (12)	9 (9)	11 (11)	0.27	0.20
Thrombotic lesion, n (%)	6 (6)	3 (3)	7 (7)	0.19	0.30
Restenotic lesion, n (%)	8 (8)	5 (5)	9 (9)	0.26	0.39
LM RVD, mm (mean $\pm$ SD)	3.77 $\pm$ 0.40	3.87 $\pm$ 0.53	3.78 $\pm$ 0.64	0.44	0.14
Proximal LAD RVD, mm (mean $\pm$ SD)	3.20 $\pm$ 0.41	3.22 $\pm$ 0.51	3.12 $\pm$ 0.61	0.4	0.27
Proximal LCX RVD, mm (mean $\pm$ SD)	2.82 $\pm$ 0.45	2.75 $\pm$ 0.51	2.79 $\pm$ 0.63	0.76	0.30
Lesion length- LM to main branch, mm (mean $\pm$ SD)	10.5 $\pm$ 7	9.4 $\pm$ 4.9	10.5 $\pm$ 11.9	0.43	0.20
LM angiographic stenosis, % visual (mean $\pm$ SD)	73.2 $\pm$ 13	72 $\pm$ 15	70 $\pm$ 14	0.46	0.10
LM MLD, mm (mean $\pm$ SD)	NA	2.43 $\pm$ 0.26	2.76 $\pm$ 1.4	0.55	NA
LAD MLD, mm (mean $\pm$ SD)	NA	2.43 $\pm$ 0.84	2.43 $\pm$ 0.65	0.99	NA
LCX MLD, mm (mean $\pm$ SD)	NA	2.1 $\pm$ 0.43	2.07 $\pm$ 0.35	0.94	NA
LM MLA, mm ² (mean $\pm$ SD)	NA	4.9 $\pm$ 1.37	5.18 $\pm$ 2.11	0.59	NA
LAD MLA, mm ² (mean $\pm$ SD)	NA	5.45 $\pm$ 2.77	4.86 $\pm$ 2.62	0.56	NA
LCX MLA, mm ² (mean $\pm$ SD)	NA	4.1 $\pm$ 22.35	5 $\pm$ 2.07	0.58	NA
Radial approach	40 (40)	38 (38)	32 (32)	0.43	0.24
PCI on another lesion, n (%)	35 (35)	46 (46)	37 (37)	0.19	0.11
Predilatation, n (%)	70 (70)	84 (84)	50 (50)	<0.001	0.004
Stent diameter (mm $\pm$ SD)	3.4 $\pm$ 0.39	3.58 $\pm$ 0.34	3.51 $\pm$ 0.38	0.18	0.04
Stent length (mm $\pm$ SD)	20.6 $\pm$ 7	18.3 $\pm$ 6.4	22.2 $\pm$ 6.6	<0.001	0.01
Postdilatation, n (%)	78 (78)	81 (81)	57 (57)	<0.001	0.05
Postdilatation balloon diameter (mm $\pm$ SD)	3.82 $\pm$ 0.43	4.02 $\pm$ 0.47	4.17 $\pm$ 0.56	0.08	<0.001
2-stent technique, n (%)	20 (20)	23 (23)	12 (12)	0.04	0.12
Final kissing balloon, n (%)	49 (49)	42 (42)	34 (34)	0.24	0.03
Final POT in LM, n (%)	16 (16)	40 (40)	27 (20)	0.051	<0.001
Edge dissection, n (%)	1 (1)	4 (4)	15 (15)	0.014	<0.001
Plaque prolapse, n (%)	NA	0 (0)	22 (22)	<0.001	-
Final LM MLA, mm ² (mean $\pm$ SD)	NA	11.3 $\pm$ 3.02	10.55 $\pm$ 3.94	0.41	-
Final LAD MLA, mm ² (mean $\pm$ SD)	NA	8.73 $\pm$ 1.81	7.03 $\pm$ 2.91	0.12	-
Final LCX MLA, mm ² (mean $\pm$ SD)	NA	6.05 $\pm$ 0.35	5.53 $\pm$ 0.74	0.41	-

(Continues)

TABLE 2 (Continued)

	Angio	IVUS	OCT	p (IVUS vs. OCT)	P (IVUS/OCT vs. Angio)
Stent malapposition, n (%)	NA	7 (7)	30 (30)	<0.001	-
Major malapposition, n (%)	NA	0 (0)	24 (24)	0.25	-
Stent underexpansion, n (%)	NA	7 (7)	13 (13)	0.15	-
Angiographic success (TIMI 3 and stenosis <20%), n (%)	100 (100)	100 (100)	99 (99)	1	1
Amount of contrast media, (mean ± SD)	225 ± 97	272 ± 107	283 ± 99	0.52	<0.001

Note: Comparison of baseline and procedural features of the study population according to the use of intravascular imaging, and type of intravascular imaging after propensity score matching.

Abbreviations: CABG, coronary artery bypass grafting; LAD, left anterior descending artery; LCX, left circumflex artery; LM, left main stem; LV EF, left ventricular ejection fraction; MI, myocardial infarction; MLA, minimal lumen area; NSTEMI, non-ST elevation MI; PCI, percutaneous coronary intervention; POT, proximal optimization technique; STEMI, ST elevation MI.

TABLE 3 In-hospital course and types of drugs planned at discharge

	Angio (n: 100)	IVUS (n: 100)	OCT (n: 100)	p (IVUS vs. OCT)	p (IVUS + OCT vs. angio)
Access site complications	2% (2)	4% (4)	2% (2)	0.40	0.40
Acute kidney injury	4% (4)	5% (5)	0% (0)	0.06	0.04
Periprocedural MI	6% (6)	1% (1)	0% (0)	0.32	0.05
BARC bleeding (3–5)	2% (2)	2% (2)	1% (1)	0.46	0.45
Procedural success	92% (92)	92% (92)	99% (99)	0.035	0.02
P2Y12 inhibitor				0.26	0.19
Clopidogrel	80% (80)	71% (71)	79% (79)	—	—
Ticagrelor	17% (16)	23% (23)	14% (14)	—	—
Prasugrel	3% (4)	6% (6)	7% (7)	—	—
DAT duration				0.41	0.36
6 months	8% (8)	6% (6)	7% (7)	—	—
12 months	79% (79)	82% (82)	80% (80)	—	—
>12 months	13% (13)	12% (12)	13% (13)	—	—
Oral anticoagulation				0.36	0.51
VKA	6% (6)	4% (4)	4% (4)	—	—
DOAC	0% (0)	2% (2)	0% (0)	—	—

Note: Comparison of in-hospital course and types of drugs prescribed at discharge according to the use of intravascular imaging, and type of intravascular imaging.

Abbreviations: BARC, bleeding Academic Research Consortium; DAT, dual antiplatelet therapy; DOAC, direct oral anticoagulant; VKA, vitamin K antagonist.

2. Patients were matched using simple 1:1 nearest neighbor matching that is based on a “greedy” matching algorithm that sorts the observations in the corresponding group by their estimated propensity score.

Calibration was tested using the Hosmer-Lemeshow test and accuracy was assessed using the area under the ROC curve. The “psmatching” custom dialogue was used in conjunction with SPSS version 24 (IBM, Armonk, New York). The psmatching program performs all analyses in R through the SPSS R-Plugin.

3 | RESULTS

Between June 2012 and June 2017 a total of 1271 patients with LM disease were treated by means of PCI at the study centers. After the exclusion of 541 patients which encountered at least one of the exclusion criteria (use of first generation DES = 95, ostial lesion = 169, cardiogenic shock = 93) or had incomplete clinical data (=184). A total of 730 patients were selected to enter the analysis (Figure 1). The brands and year of DES used is available in Table 5.

TABLE 4 Events at 12 months follow up in original and matched groups. Hazard ratios for IVUS and OCT with respect to angiography

	ANGIO (N = 353)	IVUS (N = 215)	HR 95%CI		OCT (N = 162)	HR 95%CI	
Primary endpoint (TLF)	75 (21.2%)	29 (13.5%)	0.63 (0.42–0.94)	$p = 0.02$	19 (11.7%)	0.55 (0.34–0.88)	$p = 0.01$
Cardiac death	16 (4.5%)	4 (1.9%)	0.41 (0.14–1.21)		2 (1.3%)	0.27 (0.06–1.17)	
Myocardial infarction	15 (4.2%)	7 (3.2%)	0.76 (0.32–1.84)		9 (5.6%)	1.3 (0.58–2.9)	
TLR	39 (11%)	22 (10.2%)	0.92 (0.56–1.51)		7 (4.3%)	0.39 (0.18–0.85)	
All cause death	49 (13.9%)	11 (5%)	0.37 (0.19–0.69)		5 (2.9%)	0.22 (0.09–0.54)	
Stent thrombosis (def/prob)	2 (0.6%)	4 (1.9%)			1 (1%)		
Bleeding (BARC 3,4,5)	5 (1.4%)	0			0		
Matched groups	N = 100	N = 100			N = 100		
Primary endpoint (TLF)	16 (16%)	6 (6%)	0.37 (0.15–0.91)	$p = 0.03$	7 (7%)	0.43 (0.18–1.01)	$p = 0.05$
Cardiac death	4 (4%)	2 (2%)			1 (1%)		
Myocardial infarction	4 (4%)	1 (1%)			2 (2%)		
TLR	9 (9%)	4 (4%)	0.44 (0.14–1.39)		6 (6%)	0.66 (0.25–1.80)	
All cause death	6 (6%)	3 (3%)			2 (2%)		
Stent thrombosis (def/prob)	1 (1%)	1 (1%)			1 (1%)		
Bleeding (BARC 3,4,5)	1 (1%)	0			0		

Note: HRs in the middle column represent unadjusted HRs of IVUS versus ANGIO and HRs in the right column represent unadjusted HRs of OCT versus ANGIO.

Abbreviations: BARC, bleeding academic research consortium; CI, confidence interval; HR, hazard ratio; TLF, target lesion failure; TLR, target lesion revascularization.

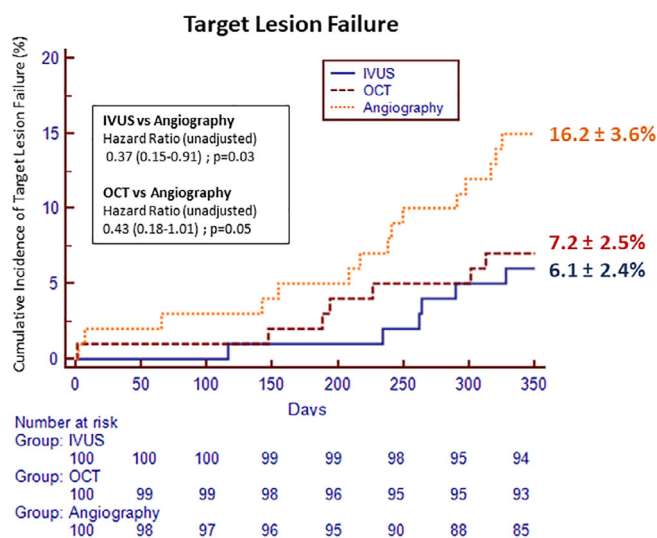


FIGURE 2 Kaplan–Meier curves for target lesion failure. The figure shows Kaplan–Meier curves for the cumulative incidence of the primary endpoint of target lesion failure in the three groups. IVUS, intravascular ultrasound; OCT, optical coherence tomography [Color figure can be viewed at wileyonlinelibrary.com]

A total of 367 had intravascular imaging guidance during index procedure (162 with OCT and 215 with IVUS), and 353 had only angiographic guidance. Baseline and procedural characteristics are presented in Table 1. Patients in the ANGIO group had more extensive coronary artery disease, whereas OCT was able to detect more

periprocedural stent-related complications. Procedural success was significantly higher in the intravascular imaging groups (98.7% vs. 94.7%, $p = 0.04$). After propensity matching we obtained three groups of 100 patients each which did not show significant baseline and procedural differences between the populations (Table 2). In-hospital course and types of drugs at discharge are depicted in Table 3. Despite the use of similar amount of total contrast volume, there was a significant reduction in acute kidney injury and periprocedural MI in the intravascular imaging group, which was also associated to an improved procedural success. On the other hand, there was no difference between OCT and IVUS. Surveillance angiographic follow-up was performed in 18% of the patients, due to clinical indication. We performed an analysis aimed to assess if there was a different outcome between the group of patients with angiographic follow up versus no angiographic follow, but we did not find any significant difference.

In Table 4 are shown the clinical events at 12 months follow up in original and matched groups. Hazard ratios for IVUS and OCT with respect to angiography are presented for the primary endpoint of TLF. The primary endpoint of TLF at 12 months occurred significantly more in the ANGIO than the IVUS/OCT group (21.2% vs. 12.7%, $p = 0.039$), but there was not a significant difference between OCT and IVUS subgroups (11.7% vs. 13.5%, $p = 0.26$).

In the matched groups, TLF occurred in 16% of ANGIO, 6% of IVUS and 7% of OCT groups. The hazard ratio for the primary endpoint of TLF for IVUS with respect to angiography was HR 0.37, 95%CI 0.15–0.91; $p = 0.03$ and for OCT with respect to

TABLE 5 Brands of drug-eluting stent (DES) used and year

Number of patients	ANGIO 353	IVUS 115	OCT 162
Xience, Abbott Vascular	105	75	81
2012	15	10	10
2013	16	15	8
2014	14	18	21
2015	25	12	16
2016	19	10	15
2017	16	10	11
Resolute Onyx, Medtronic	35	20	10
2012	—	—	—
2013	—	—	—
2014	14	5	2
2015	7	8	1
2016	6	2	5
2017	8	5	2
Orsiro, Biotronik, Germany	51	15	8
2012	—	—	—
2013	—	—	—
2014	—	—	—
2015	15	2	1
2016	23	5	1
2017	13	8	6
Cre8, CID, Italy	120	20	31
2012	—	—	—
2013	—	—	—
2014	—	—	—
2015	65	4	1
2016	40	4	12
2017	15	12	18
Other manufacturers	72	8	47
2012	—	1	1
2013	7	2	18
2014	15	1	12
2015	20	2	6
2016	14	2	3
2017	16	—	7

angiography was HR 0.43, 95%CI 0.18–1.01; $p = 0.05$. Figure 2 shows the Kaplan–Meier curves for cumulative incidence of TLF in the three matched groups with the corresponding hazard ratios (Table 5).

4 | DISCUSSION

The main findings of the ROCK II study are: (a) The use of intravascular imaging to guide distal LM stenting provides a prognostic

advantage with respect to the use of angiography alone. (b) IVUS and OCT show comparable benefits on clinical outcomes as compared to angiography alone.

The LM stem shares some anatomical peculiarities that render this subset different from other lesion sites, therefore the risk for stent malapposition or underexpansion is higher than in other settings.^{5,6} Moreover, the clinical consequences of restenosis or thrombosis of the LM or one of its ramifications may have more severe consequences if compared to other anatomical scenarios.

The use of intravascular imaging for LM interventions is a valuable adjuvant tool either for initial lesion analysis, and for to the final assessment after stenting.^{7,8} IVUS is usually performed for this task and the ESC/EACTS Revascularization guidelines strongly suggest to perform LM angioplasty by means of IVUS optimization (Class IIa, level of evidence B).¹ Moreover, the expert consensus of the European Bifurcation Club also recommends the use of intravascular imaging to guide this type of intervention on a routine basis.¹⁵

There are several studies which analyze the role of intravascular imaging as adjuvant for LM stenting. A post hoc analysis of the MAIN-COMPARE study showed a reduction in mortality after LM DES implantation under IVUS guidance.⁷ In a patient-level pooled analysis of four registries, IVUS-guided LM PCI was associated with higher freedom from hard clinical endpoints.⁵ The SCAAR study group showed how IVUS guidance led to a 35% reduced composite endpoint of mortality, TLR and stent thrombosis.⁴ In this regard, the use of specific IVUS guidance protocols with predefined optimization targets could provide an additional advantage with respect to a liberal use of IVUS.¹⁶ We would like to emphasize that a randomized clinical trial comparing head-to-head angiography versus intravascular imaging as guidance for LM stenting is lacking so far.

OCT offers several technical advantages as compared to IVUS. Its higher resolution allows a more precise lumen depiction and a more accurate identification of relevant findings during PCI such as struts malapposition, edge dissection, plaque prolapse or intraprocedural stent thrombosis. OCT has demonstrated a high added value in many PCI settings⁹ (Figure 3).

Therefore, OCT appears as a very attractive alternative to IVUS for LM PCI guidance. Nonetheless, there are few studies which investigate the role of OCT for LM stenting. Dato et al. published the results of a single center study aiming at assessing the feasibility of OCT in terms of detection of the severity of intermediate LM lesions. OCT was shown not only feasible in this setting, but also the therapeutic decisions taken following its interpretation well correlated with a good clinical outcome.¹¹ During our previous experience in ROCK I we assessed the role of OCT guidance versus a “normal” strategy (angiographic guidance +25% of IVUS) for distal LM stenting. In this study we showed how OCT was able to better assess immediate stent deployment as compared to a standard strategy, that included IVUS guidance at the operator's discretion. Moreover, OCT was also associated with superior angiographic results at 6-month angiographic follow up, including improved LLL, binary restenosis and percent diameter stenosis compared to standard practice.¹⁴

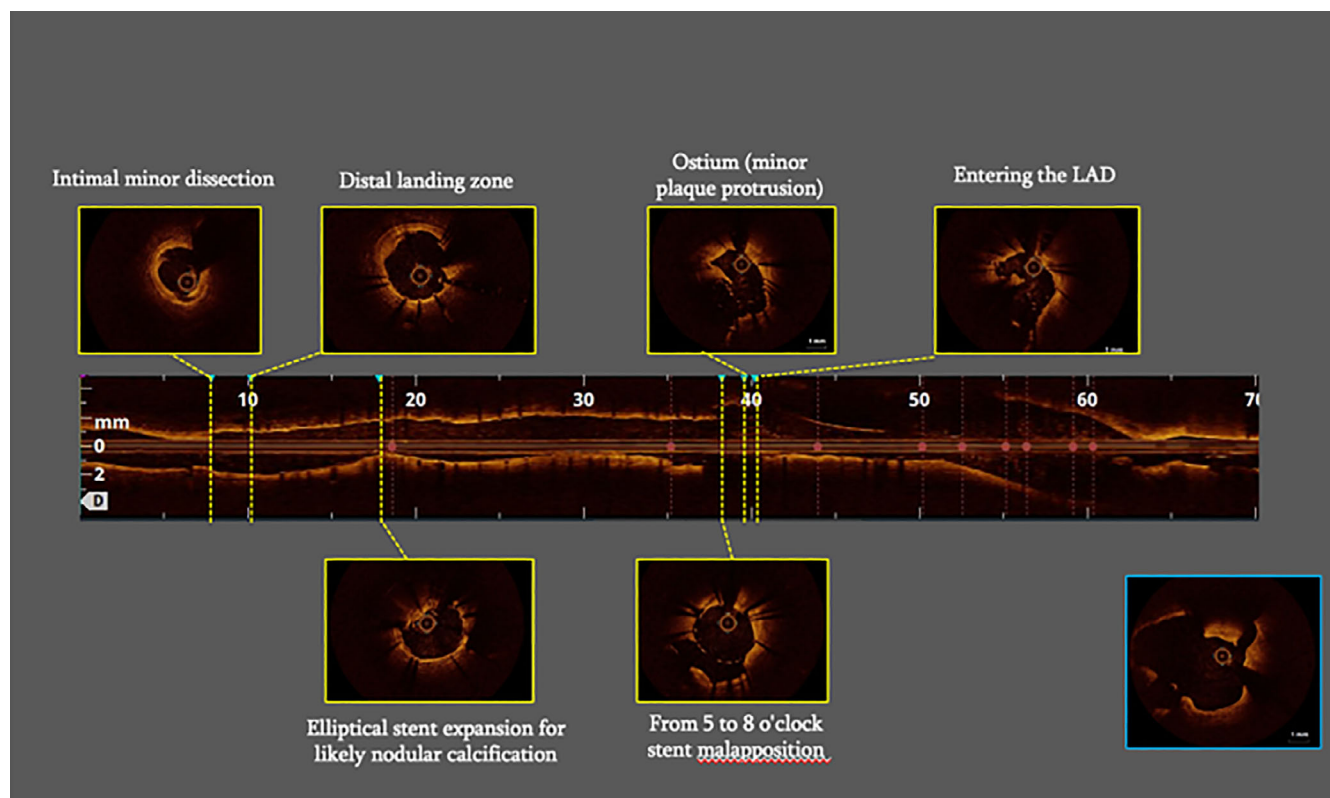


FIGURE 3 Final assessment of LM PCI with double kissing crush stenting by means of OCT, showing some peculiarities which are not easily assessed with angiography alone. LM, left main stem; OCT, optical coherence tomography [Color figure can be viewed at wileyonlinelibrary.com]

Recently, the British Cardiovascular Intervention Society published a report of LM PCI performed between 2007 and 2014 in England and UK showing an increase of intravascular imaging use (from 30% to 50% of the cases), which was associated with a significant reduction in in-hospital major adverse events (OR: 0.470; 95% CI: 0.37–0.590; $p < 0.001$). Intravascular imaging use was also associated with reduction in mortality at 1 year (OR: 0.660; 95% CI: 0.570–0.770; $p < 0.001$). The same study showed an increase in the use of OCT instead of IVUS beginning in year 2012. Unfortunately, a direct comparison between OCT and IVUS has not been previously reported. With ROCK II we were able to provide, for the first time, a head-to-head comparison of OCT and IVUS powered for clinical endpoints (With ROCK II we were able to provide a comparison of OCT to IVUS since the beginning of the study and in terms of clinical outcomes).¹⁷

The improved resolution of superficial structures, the more detailed evaluation of stent apposition and final expansion and the possibility to readily detect distal or proximal stent-related dissections are recognized advantages of OCT over IVUS.^{12,18,19}

Indeed, 3D-OCT reconstruction can in part overcome some limitations of 2D-OCT and has become an important tool for the evaluation of the side branch ostium after LM bifurcation PCI, to assess possible stenosis due to shifting of the carina. This technique can also assess the optimal guidewire recrossing point through the cell strut before the final kissing balloon inflation in case of double stent strategy and finally detect longitudinal deformation of the stent.²⁰

On the other hand, the analysis of deeper wall structures results improved with IVUS. Moreover, an impaired analysis (suboptimal blood clearance, which occurred in 8% of the OCT subgroup) of the more proximal segments render OCT less reliable for this portion of the LM.²⁰ This is the reason why in ROCK II we only enrolled patients with distal LM disease and, despite the possibility to adopt some tips and tricks to overcome the limitations of OCT for proximal LM assessment, we currently suggest to use IVUS for the analysis of this segment.

4.1 | Limitations

There are several limitations regarding this study that we would like to acknowledge. This is an observational comparative registry with baseline differences between groups. Notwithstanding the use of propensity score matching, it still remains possible that some unmeasured confounders could have an effect on clinical outcome. Despite an accurate propensity matching, the angiographic-assistance-alone group might have suffered of a higher risk population/worse immediate outcome, although such differences were not significant. The sample size was powered for clinical outcome for the whole population. Since there were important baseline differences between groups, we did propensity matching confirming the results, but we acknowledge such findings should be considered hypothesis-generating. Another potential limitation is the lack of very long-term clinical outcomes and the eventual impact of OCT guidance as compared to IVUS. In this regard the

extended follow up of ROCK-II (currently ongoing) will hopefully provide this information. Finally, being ROCK II a retrospective analysis, we were not able to standardize the criteria used for intravascular imaging.

5 | CONCLUSIONS

The ROCK II study confirms the superiority of intravascular imaging versus angio guidance for distal LM stenting. ROCK II also confirms the feasibility of OCT assessment for distal LM stenting and for the first time shows that IVUS or OCT-guided stenting resulted in the same results. We believe the time has come, to plan and run RCTs to address the main message of ROCK II study, the equivalence of OCT versus IVUS as guidance for distal LM stenting in terms of hard clinical endpoints.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data available on request due to privacy/ethical restrictions.

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