Long-Term Outcomes of Drug-Eluting Stent Implantation After Rotational Atherectomy for Left Main Coronary Artery Bifurcation Lesions

Yasushi Fuku, MD[a], Kazushige Kadota, MD[a], Mamoru Toyofuku, MD[b], Takeshi Morimoto, MD, MPH[c], Masanobu Ohya, MD[a], Hirooki Higami, MD[d], Kyohei Yamaji, MD[e], Hiromi Muranishi, MD[e], Yuhei Yamaji, MD[e], Koji Nishida, MD[f], Daisuke Furukawa, MD[f], Tomohisa Tada, MD[g], Euihong Ko, MD[b], Kenji Ando, MD[e], Hiroki Sakamoto, MD[g], Takashi Tamura, MD[b], Kazuya Kawai, MD[f], and Takeshi Kimura, MD[d,*], on behalf of the AOI LMCA Stenting Registry Investigators

The clinical outcomes of drug-eluting stent (DES) implantation after rotational atherectomy (RA) for complex left main coronary artery (LMCA) bifurcation lesions remain unclear. Among 1,809 patients retrospectively enrolled in the Assessing Optimal percutaneous coronary Intervention for LMCA Registry, we identified 1,199 patients with LMCA bifurcation lesions treated by crossover stenting with DES for the main vessel. The study population was divided according to the use of RA. The patients in the RA group were further subdivided into the 2 subgroups on the basis of the stenting approach. The rates of periprocedural myocardial infarction and in-hospital death in the RA group were comparable to those in the non-RA group. The cumulative 5-year incidences of all-cause death and target lesion revascularization (TLR) were significantly higher in the RA group than those in the non-RA group. However, after adjusting confounders, the excess risks of the RA group relative to the non-RA group for all-cause death and TLR were no longer significant (hazard ratio 0.95, 95% confidence intervals 0.59 to 1.52, p = 0.83, and hazard ratio 1.46, 95% confidence intervals 0.82 to 2.60, p = 0.20, respectively). In the RA group, the cumulative 5-year incidences of all-cause death and TLR were markedly higher in the 2-stent subgroup than in the 1-stent subgroup (58.1% vs 26.0%, p = 0.001, and 43.0% vs 16.3%, p = 0.001, respectively). In conclusion, DES implantation after RA was a safe and feasible strategy in treating those patients with complex LMCA bifurcation lesions. In this strategy, the 2-stent approach was associated with markedly worse 5-year clinical outcomes than the 1-stent approach. **(Am J Cardiol 2019;123:1796−1805)**

Percutaneous coronary intervention (PCI) for complex left main coronary artery (LMCA) bifurcation lesions remains a technical challenge. Calcified lesions, in particular, were reported to be associated with higher procedural risks and worse clinical outcomes than noncalcified lesions.[1-4] Current guidelines recommend coronary artery bypass grafting as a preferred management option for patients with unfavorable anatomy for PCI.[5] However, PCI is frequently selected as the only option for patients with complex LMCA bifurcation lesions when they are inoperable or have high operative risk and rotational atherectomy (RA) is a treatment option for calcified LMCA lesions in practice.[6] Data on the clinical outcomes after PCI using RA for LMCA bifurcation lesions are sparse[7-11] and little information is available about the differences in the clinical outcomes between the 1- and 2-stent approaches after RA for LMCA bifurcation lesions. Therefore, we sought to compare the long-term clinical outcomes between drug-eluting stent (DES) implantation with or without RA for complex LMCA bifurcation lesions and between the 1- and 2-stent approaches after RA.

Methods

The Assessing Optimal PCI for LMCA (AOI-LMCA) registry is an investigator-initiated multicenter registry conducted in 6 institutions in Japan from 2004 to 2012, in which 1,809 consecutive patients who underwent coronary stent implantation for significant LMCA lesions were retrospectively enrolled. The design and main results of the AOI-LMCA registry were reported previously.[12] Significant

[a]Department of Cardiology, Kurashiki Central Hospital, Kurashiki, Japan; [b]Department of Cardiology, Japanese Red Cross Society Wakayama Medical Center, Wakayama, Japan; [c]Department of Clinical Epidemiology, Hyogo College of Medicine, Nishinomiya, Japan; [d]Department of Cardiovascular Medicine, Graduate School of Medicine, Kyoto University, Kyoto, Japan; [e]Department of Cardiology, Kokura Memorial Hospital, Kokura, Japan; [f]Department of Cardiology, Chikamori Hospital, Kochi, Japan; and [g]Department of Cardiology, Shizuoka General Hospital, Shizuoka, Japan. Manuscript received December 13, 2018; revised manuscript received and accepted March 5, 2019.

Clinical Trial Registration: URL: http://www.umin.ac.jp/ctr/index/htm/ Unique Identifier: UMIN000014706.

See page 1804 for disclosure information.

*Corresponding author: Tel: +81-75-751-4254; fax: +81-75-751-3289.
E-mail address: taketaka@kuhp.kyoto-u.ac.jp (T. Kimura).

0002-9149/
https://doi.org/10.1016/j.amjcard.2019.03.002

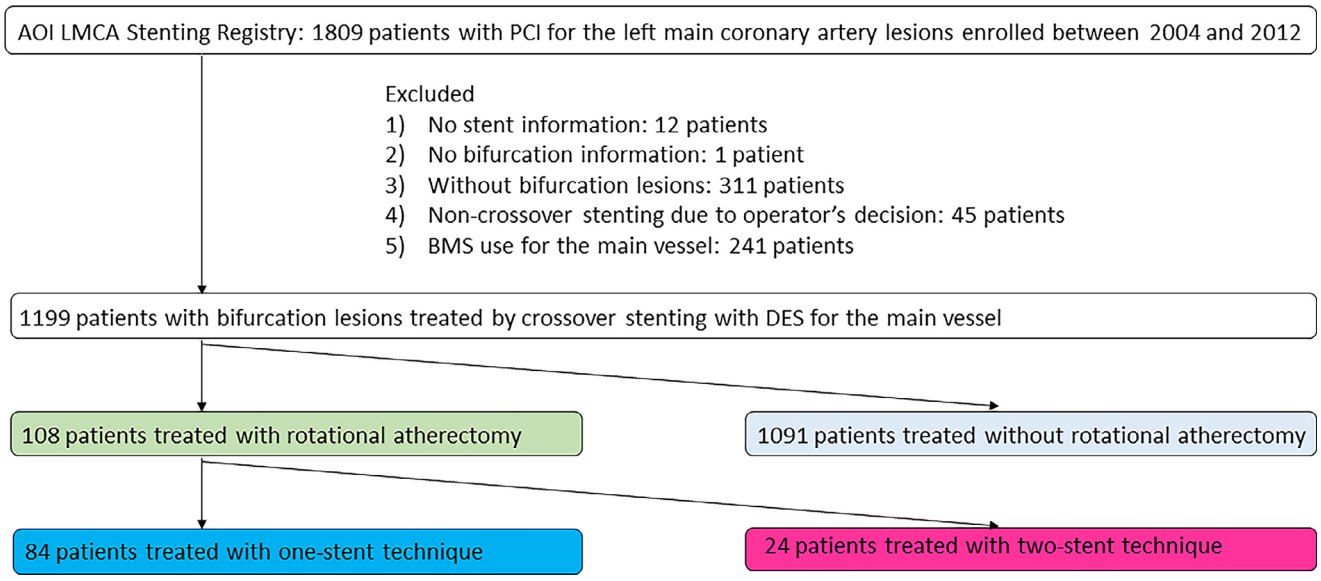

Figure 1. Study flow chart.
BMS = bare-metal stent; DES = drug-eluting stent; LMCA = left main coronary artery; PCI = percutaneous coronary intervention.

LMCA lesions were defined angiographically as at least 50% diameter stenosis in the LMCA by visual estimation. Among the 1,809 patients, we identified 1,199 patients with LMCA bifurcation lesions treated by crossover stenting with DES for the main vessel as the current study population (Figure 1). The study population was divided according to the use of RA (RA group: n = 108, and non-RA group: n = 1,091). The patients in the RA group were further subdivided into the 2 subgroups on the basis of the stenting approach: 84 patients who underwent the 1-stent approach (1-stent subgroup) and 24 patients who underwent the 2-stent approach (2-stent subgroup) (Figure 1).

We took 3 steps to investigate the outcomes. First, we evaluated the procedural and in-hospital outcomes including slow flow and coronary perforation during RA, periprocedural myocardial infarction (MI), and in-hospital death. Second, we compared the 5-year clinical outcomes between the RA and non-RA groups in terms of all-cause death, cardiac death, target lesion revascularization (TLR), target lesion failure (TLF), and definite or probable stent thrombosis. Third, we compared the 5-year clinical outcomes between the 1- and 2-stent subgroups in the RA group in terms of all-cause death, cardiac death, TLR, TLF, and definite or probable stent thrombosis.

Cardiac death included all the death without obvious noncardiac causes. MI was defined as ischemic symptoms and/or ischemic changes of electrocardiogram along with elevated cardiac enzymes (troponin or creatine kinase-MB fraction) greater than the upper limit of normal. Periprocedural MI was defined according to the third universal definition of MI.[13] TLR was defined as repeat PCI or coronary artery bypass grafting for restenosis or thrombosis of the target lesion within the stent or within 5 mm proximal or distal adjacent to the stent including the ostium and/or the treated segment of the side branch. TLF was defined as a composite of cardiac death, MI, and TLR. Stent thrombosis was defined by the Academic Research Consortium criteria.[14] The clinical event committee adjudicated all the clinical events based on the original source documents. The use and technique of RA was left to the discretion of each operator. Planned RA was sometimes performed for complex LMCA bifurcation lesions, although current guidelines recommend RA as a preparatory procedure in the treatment of heavily calcified or fibrotic lesions that cannot be adequately dilated before stenting.

The study was approved by each institutional ethics committee and was conducted in accordance with the provisions of the Declaration of Helsinki and the ethical guidelines for epidemiological studies in Japan. Written informed consent was waived according to the Ethical Guidelines for Medical and Health Research Involving Human Subjects in Japan, whereas no patient refused to participate in the study when being contacted for follow-up.

Continuous variables were presented as mean ± standard deviation or median and interquartile range, and were compared between groups using Student's t test or the Mann-Whitney U test, based on the distribution. Categorical variables were presented as numbers and percentages, and were compared between groups with the chi-square test or the Fisher's exact test, as appropriate. Cumulative incidences of events were estimated by the Kaplan-Meier method, and the difference was assessed by the log-rank test. Multivariable Cox proportional hazard models were constructed to adjust for the potential confounders. We evaluated the risk of the RA group relative to the non-RA group for all-cause death, cardiac death, TLR, and TLF, which are expressed as hazard ratio and 95% confidential interval. A Cox proportional hazard model for definite or probable stent thrombosis was not constructed due to a small number of patients with this event. The risk-adjusting variables in the Cox proportional hazard models included 20 clinically relevant factors listed in Tables 1 and 2, as

Table 1
Baseline patient, lesion, and procedural characteristics and procedural outcomes: RA group versus Non-RA group

Variable	RA group (n = 108)	Non-RA group (n = 1,091)	p value
Age (years)	75.7 ± 10.1	71.6 ± 10.0	<0.001
Age ≥80 years, n (%)*	40 (37)	267 (25)	0.004
BMI (kg/m^2)	22.4 ± 3.5	23.5 ± 3.5	0.002
Men	67 (62%)	831 (76%)	0.001
Hypertension	91 (84%)	811 (74%)	0.02
Diabetes mellitus*	46 (43%)	483 (44%)	0.74
Insulin-treated diabetes	18 (17%)	123 (11%)	0.10
Current smoking	12 (11%)	177 (16%)	0.16
eGFR (ml/min/1.73 m^2)	52.1 ± 24.4	59.4 ± 23.6	0.003
HD*	16 (15%)	59 (5%)	<0.001
eGFR <60 and non-HD*	51 (47%)	455 (42%)	0.27
Clinical presentation*			0.01
Stable CAD	94 (87%)	806 (74%)	
NSTEMI/UA	10 (9%)	207 (19%)	
STEMI	4 (4%)	78 (7%)	
Decompensated HF	5 (5%)	84 (8%)	0.24
Shock vital*	1 (1%)	49 (5%)	0.08
Atrial fibrillation/flutter	5 (5%)	86 (8%)	0.22
Previous PCI*	54 (50%)	503 (46%)	0.44
Previous MI	33 (31%)	341 (31%)	0.88
Previous CABG	27 (25%)	150 (14%)	0.002
Previous HF*	22 (20%)	147 (14%)	0.049
Previous stroke*	16 (15%)	144 (13%)	0.64
Malignancy*	16 (15%)	108 (10%)	0.11
Peripheral vascular disease*	18 (17%)	137 (13%)	0.23
LVEF (%)†	56.7 ± 12.0	56.7 ± 13.5	0.96
EuroSCORE	6.7 ± 3.3	5.6 ± 5.6	0.001
Medications			
Aspirin	107 (99%)	1052 (97%)	0.36
Thienopyridine	107 (99%)	1044 (96%)	0.17
Warfarin	11 (10%)	113 (10%)	0.94
Statins*	66 (61%)	744 (68%)	0.13
β–blockers*	34 (32%)	327 (30%)	0.74
ACE-I/ARB*	60 (56%)	608 (56%)	0.97
PPI	45 (42%)	500 (46%)	0.38
SYNTAX score‡	33.2 ± 10.3	27.4 ± 9.6	<0.001
Moderate-severe calcification*	80 (74%)	121 (11%)	<0.001
LMCA plus multivessel disease*	87 (81%)	731 (67%)	0.004
LMCA true bifurcation	74 (69%)	587 (54%)	0.003
Use of IABP	5 (5%)	113 (10%)	0.06
Use of PCPS	0 (0%)	12 (1%)	0.27
Use of imaging modalities			0.42
IVUS*	71 (66%)	755 (69%)	
OCT	5 (5%)	40 (4%)	
None	33 (31%)	298 (27%)	
RA			
Final burr size, mm, median (range)	1.75 (1.5−2.0)		
RA use for SV	13 (12%)		
Balloon			
POT	11 (10%)	179 (16%)	0.09
Final KBT	74 (69%)	860 (79%)	0.01
Final balloon size (MV) (mm)	3.31 ± 0.53	3.32 ± 0.47	0.84
Final balloon size (SV) (mm)	2.76 ± 0.59	2.77 ± 0.45	0.96
Stent			
Use of G2-DES (MV)*	38 (35%)	444 (41%)	0.27
Stent size (MV) (mm)	3.15 ± 0.37	3.22 ± 0.35	0.046
Stent size (MV) ≥3.5 mm*	50 (46%)	621 (57%)	0.03
Stent length (MV) (mm)	32.4 ± 18.0	26.2 ± 12.2	0.001
Stent length (MV) ≥30 mm*	42 (39%)	254 (23%)	<0.001
Two-stent approach	24 (22%)	245 (23%)	0.96
Procedural outcomes			
Slow/no flow related to RA	1 (1%)		
Coronary perforation related to RA	0 (0%)		
Periprocedural MI§	6 (6.4%)	32 (4.0%)	0.27
In-hospital death	3 (2.8%)	32 (2.9%)	1.0

ACE-I = angiotensin converting enzyme inhibitor; ARB = angiotensin Ⅱ receptor blocker; BMI = body mass index; CABG = coronary artery bypass grafting; CAD = coronary artery disease; eGFR = estimated glomerular filtration rate; G2-DES = second-generation drug-eluting stent; HD = hemodialysis; HF = heart failure; IABP = intra-aortic balloon pumping; IVUS = intravascular ultrasound; KBT = kissing balloon technique; LMCA = left main coronary artery; LVEF = left ventricular ejection fraction; MV = main vessel; NSTEMI = non-ST-segment elevation myocardial infarction; OCT = optical coherence tomography; PCI = percutaneous coronary intervention; PCPS = percutaneous cardiopulmonary support; POT = proximal optimization technique; PPI = proton pump inhibitor; RA = rotational atherectomy; STEMI = ST-segment elevation myocardial infarction; SV = side vessel; SYNTAX = Synergy between PCI with Taxus and Cardiac Surgery; UA = unstable angina.

* Indicates potential independent risk-adjusting variables selected for Cox proportional hazards models.

† Calculated in 81 patients in the RA group and in 846 patients in the non-RA group.

‡ Calculated in 84 patients in the RA group and in 957 patients in the non-RA group.

§ Calculated in 94 patients with stable coronary artery disease in the RA group and in 807 patients with stable coronary artery disease in the non-RA group.

well as the 3 periods based on the types of stents implanted: 2004 to 2006 (bare-metal stent period), 2007 to 2009 (G1-DES period), and 2010 to 2012 (G2-DES period), because treatment strategies and other related factors changed over time. These were consistent with the previous report from the AOI-LMCA registry.[12] Proportional hazard assumptions for the variables were assessed on the plots of log (time) versus log (-log [survival]) stratified by each variable and were verified to be acceptable for all the variables. All statistical analyses were performed by a physician (Y.F.). Statistical analysis was performed with the aid of a commercially available software (IBM SPSS Statistics 23; International Business Machines Corporation, Armonk, New York). A 2-sided probability value less than 0.05 was regarded as statistically significant.

Results

Regarding the baseline patient characteristics, the RA group had older patients, more women, smaller body mass index, and more patients with hypertension, a history of coronary artery bypass grafting, a history of heart failure, impaired renal function including those receiving hemodialysis, or a higher EuroSCORE than the non-RA group. The prevalence of acute coronary syndrome was lower in the RA group than in the non-RA group. Regarding the

Table 2
Clinical outcomes at 5-year: RA group versus Non-RA group

	Number of patients with event (cumulative incidence)		Unadjusted HR (95% CI)	p value	adjusted HR (95% CI)	p value
	RA group	Non-RA group				
All-cause death	29 (34%)	186 (21%)	1.63 (1.10-2.42)	0.01	0.95 (0.59-1.52)	0.83
Cardiac death	12 (14%)	74 (8%)	1.68 (0.91-3.09)	0.10	0.84 (0.40-1.76)	0.65
Target lesion revascularization	20 (22%)	105 (12%)	2.13 (1.32-3.43)	0.002	1.46 (0.82-2.60)	0.20
Target lesion failure	30 (31%)	174 (19%)	1.91 (1.30-2.81)	0.001	1.30 (0.81-2.07)	0.28
Definite or probable ST	1 (1%)	12 (1%)	0.85 (0.11-6.52)	0.87	NA	–

CI = confidence interval; HR = hazard ratio; NA = not applicable; RA= rotational atherectomy; ST = stent thrombosis.

lesion and procedural characteristics, patients in the RA group more often had moderate-severe calcification, true bifurcation, multivessel disease, and higher SYNTAX score than patients in the non-RA group (Table 2). The uses of ≥3.5 mm stent size in the main vessel and final kissing balloon technique were less frequent in the RA group than in the non-RA group. The stent length in the main vessel was significantly longer in the RA group than in the non-RA group. The uses of second-generation DES, imaging modalities, and the 2-stent approach were comparable between the 2 groups. Final burr size in the RA group was median 1.75 (range: 1.5 to 2.0) mm. The use of RA in the side vessels was 12% of patients. Regarding the procedural outcomes in the RA group, slow flow related to RA occurred in 1 patient. No coronary perforation occurred as related to the RA use. The rates of periprocedural MI and in-hospital death were not significantly different between the RA and non-RA groups (Table 1).

The cumulative 5-year incidences of all-cause death, TLR, and TLF were significantly higher in the RA group than those in the non-RA group (Figure 2). The cumulative 5-year incidence of cardiac death also trended to be higher in the RA group than in the non-RA group (Figure 2). However, after adjusting confounders, the excess risks of the RA group relative to the non-RA group for all-cause death, cardiac death, TLR, and TLF were no longer significant (Table 2). The rate of stent thrombosis was low and comparable in both RA and non-RA groups without any very late stent thrombosis (Figure 2).

In the RA group, the baseline patient characteristics were comparable between the 1-stent and 2-stent subgroups. Regarding the lesion and procedural characteristics, patients in the 2-stent subgroup more often had LMCA plus multivessel disease, and LMCA true bifurcation, and more often underwent RA for side vessels and final kissing balloon technique than patients in the 1-stent subgroup. The

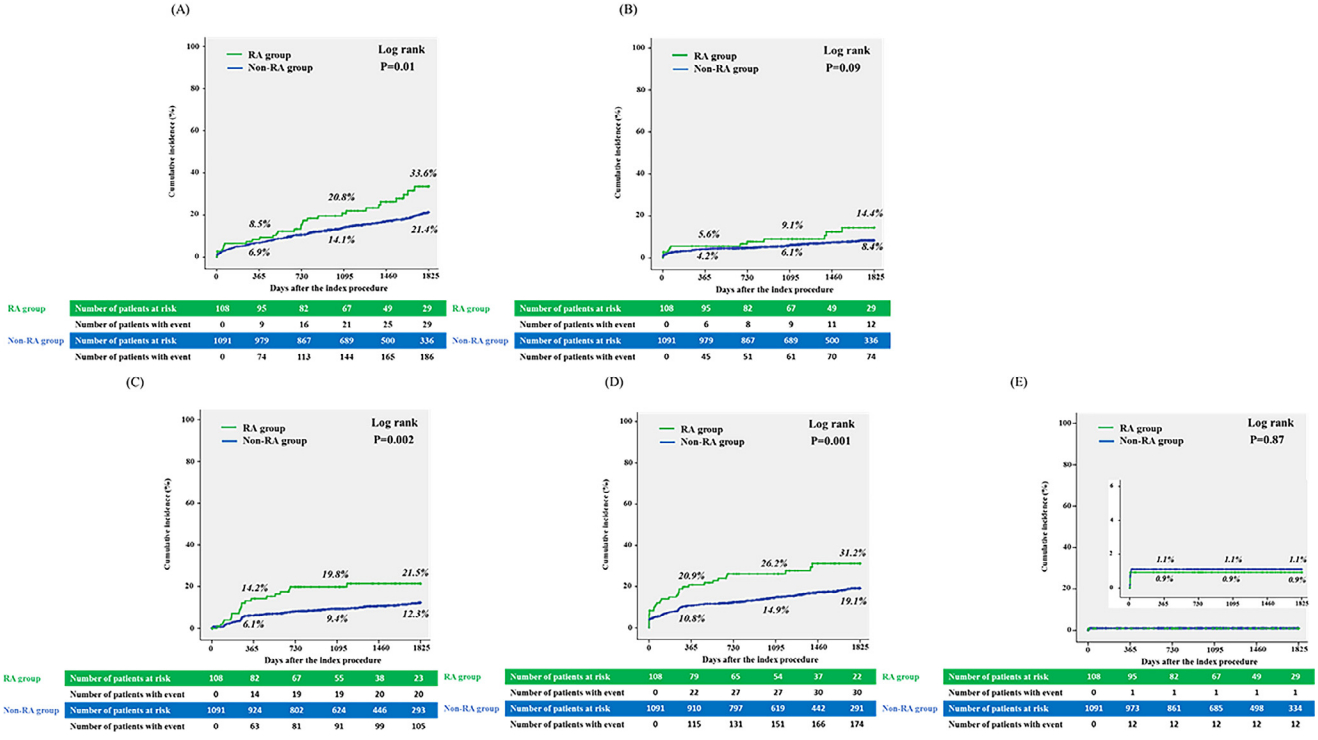

Figure 2. Kaplan-Meier curves for clinical outcomes: RA versus non-RA groups (A) All-cause death, (B) Cardiac death, (C) Target lesion revascularization, (D) Target lesion failure, and (E) Definite or probable stent thrombosis.
RA = rotational atherectomy.

Table 3
Baseline patient, lesion, and procedural characteristics of RA group: 1-stent subgroup versus 2-stent subgroup

Variable	1-stent (n = 84)	2-stent (n = 24)	p value
Age (years)	74.8 ± 10.2	78.8 ± 9.5	0.09
Age ≥80 years	28 (33%)	12 (50%)	0.14
BMI (kg/m^2)	22.4 ± 3.3	22.7 ± 4.0	0.65
Men	55 (66%)	12 (50%)	0.17
Hypertension	73 (87%)	18 (75%)	0.20
Diabetes mellitus	37 (44%)	9 (38%)	0.57
Insulin-treated diabetes	14 (17%)	4 (17%)	1.0
Dyslipidemia	46 (55%)	12 (50%)	0.68
Current smoking	10 (12%)	2 (8%)	1.0
eGFR (ml/min/1.73 m^2)	52.8 ± 24.1	49.8 ± 25.8	0.60
HD	12 (14%)	4 (17%)	0.75
eGFR <60 and non-HD	40 (48%)	11 (46%)	0.88
Clinical presentation			0.22
Stable CAD	74 (88%)	20 (83%)	
NSTEMI/UA	6 (7%)	4 (17%)	
STEMI	4 (5%)	0 (0%)	
Decompensated HF	5 (6%)	0 (0%)	0.59
Shock vital	1 (1%)	0 (0%)	1.0
Atrial fibrillation/flutter	5 (6%)	0 (0%)	0.56
Previous PCI	42 (50%)	12 (50%)	1.0
Previous MI	22 (26%)	11 (46%)	0.07
Previous CABG	23 (27%)	4 (17%)	0.29
Previous HF	15 (18%)	7 (29%)	0.26
Previous stroke	15 (18%)	1 (4%)	0.12
Malignancy	12 (14%)	4 (17%)	0.75
Peripheral vascular disease	14 (17%)	4 (17%)	1.0
LVEF (%)*	56.6 ± 12.4	57.2 ± 10.1	0.87
EuroSCORE	6.7 ± 3.4	6.8 ± 3.0	0.86
Medications			
Aspirin	83 (99%)	24 (100%)	1.0
Thienopyridine	83 (99%)	24 (100%)	1.0
Warfarin	10 (12%)	1 (4%)	0.45
Statins	54 (64%)	12 (50%)	0.21
β-blockers	26 (31%)	8 (33%)	0.83
ACE-I/ARB	49 (58%)	11 (46%)	0.28
PPI	36 (43%)	9 (38%)	0.64
SYNTAX score†	32.7 ± 10.4	34.9 ± 10.0	0.41
Moderate−severe calcification	61 (73%)	19 (79%)	0.52
LMCA plus multivessel disease	64 (76%)	23 (96%)	0.04
LMCA true bifurcation	53 (63%)	21 (88%)	0.02
Use of imaging modalities			0.09
IVUS	57 (68%)	14 (58%)	
OCT	4 (5%)	1 (4%)	
None	23 (27%)	10 (42%)	
RA			
Final burr size, mm, median	1.75	2.0	0.25
RA use for SV	4 (5%)	9 (38%)	<0.001
Balloon			
POT	8 (10%)	3 (13%)	0.71
Final KBT	50 (60%)	24 (100%)	<0.001
Final balloon size (MV) (mm)	3.34 ± 0.52	3.20 ± 0.56	0.26
Final balloon size (SV) (mm)	2.48 ± 0.44	2.96 ± 0.60	0.01
Stent			
Use of G2-DES (MV)	27 (32%)	11 (46%)	0.22
Stent size (MV) (mm)	3.17 ± 0.35	3.08 ± 0.41	0.31
Stent size (MV) ≥3.5 mm	40 (48%)	10 (42%)	0.61
Stent length (MV) (mm)	33.2 ± 19.3	29.6 ± 12.8	0.39
Stent length (MV) ≥30 mm	35 (42%)	7 (29%)	0.27
Use of G2-DES (SV)		13 (54%)	
Stent size (SV) (mm)		2.90 ± 0.44	
Two-stent approach			
Culottes		16 (67%)	
T-stenting		6 (25%)	
Mini-crush		2 (8%)	

ACE-I = angiotensin converting enzyme inhibitor; ARB = angiotensin Ⅱ receptor blocker; BMI = body mass index; CABG = coronary artery bypass grafting; CAD = coronary artery disease; eGFR = estimated glomerular filtration rate; G2-DES = second-generation drug-eluting stent; HD = hemodialysis; HF = heart failure; IVUS = intravascular ultrasound; KBT = kissing balloon technique; LMCA = left main coronary artery; LVEF = left ventricular ejection fraction; MV = main vessel; NSTEMI = non-ST-segment elevation myocardial infarction; OCT = optical coherence tomography; PCI = percutaneous coronary intervention; POT = proximal optimization technique; PPI = proton pump inhibitor; RA = rotational atherectomy; STEMI = ST-segment elevation myocardial infarction; SV = side vessel; SYNTAX = Synergy between PCI with Taxus and Cardiac Surgery; UA = unstable angina.

* Calculated in 66 patients in the 1-stent subgroup and in 15 patients in the 2-stent subgroup.

† Calculated in 64 patients in the 1-stent subgroup and in 20 patients in the 2-stent subgroup.

final balloon size for the side vessels was significantly larger in the 2-stent subgroup than in the 1-stent subgroup. There was no difference in the stent size and length of the main vessel as well as in the use of second-generation DES between the 2 subgroups (Table 3). The cumulative 5-year incidences of all-cause death, cardiac death, TLR, and TLF were much higher in the 2-stent subgroup than in the 1-stent subgroup (Figure 3). Among the 13 patients with all-cause death in the 2-stent subgroup, 6 patients died suddenly (Table 4). In the landmark analyses, the rates of all these events within 1 year were significantly higher in the 2-stent subgroup than in the 1-stent subgroup, whereas those from 1 to 5 years were not significantly different between the 2 groups (Figure 4). There was 1 probable subacute stent thrombosis in the 2-stent subgroup, whereas there was no definite or probable stent thrombosis in the 1-stent subgroup.

In the non-RA group, patient characteristics were comparable between the 2 groups. On the contrary, the 2-stent subgroup, in comparison with the 1-stent subgroup, had more complex lesion characteristics such as multivessel disease, true bifurcation, and higher SYNTAX score (Supplementary Table 1). The cumulative 5-year incidences of TLR and TLF were significantly higher in the 2-stent subgroup than in the 1-stent subgroup, whereas those of all-cause death and cardiac death were comparable between the 2 groups (Figure 5).

Discussion

The principal findings of this study are as follows: (1) The rates of slow flow and coronary perforation related to RA for LMCA bifurcation lesions were very low, and the periprocedural complications of DES implantation after

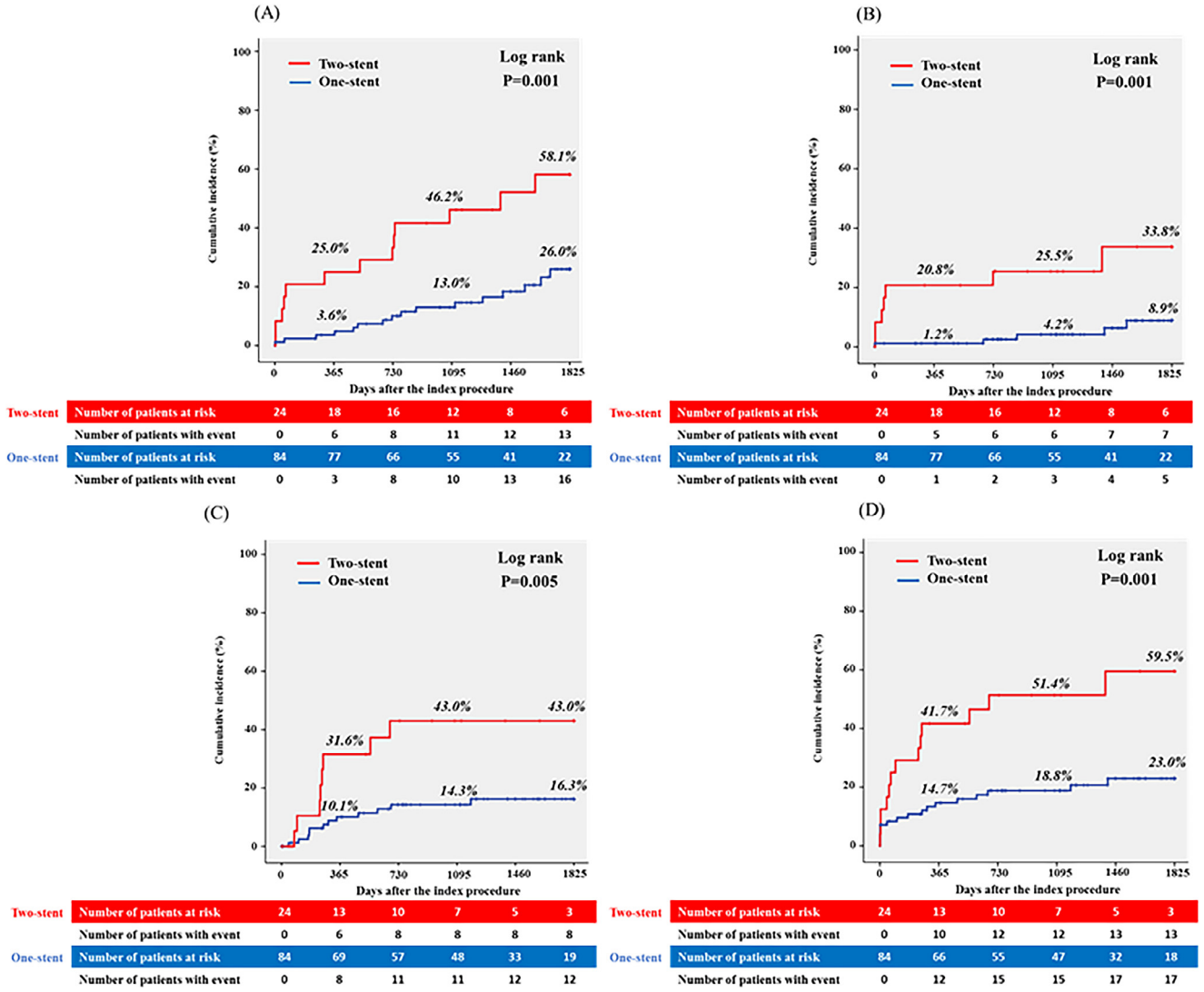

Figure 3. Kaplan-Meier curves for clinical outcomes in the RA group: 1- versus 2-stent subgroups (A) All-cause death, (B) Cardiac death, (C) Target lesion revascularization, and (D) Target lesion failure.
RA = rotational atherectomy.

RA for LMCA bifurcation lesions were not different from those of DES implantation without RA; (2) The long-term outcomes of DES implantation after RA for LMCA bifurcation lesions were not significantly different from those of DES implantation without RA in terms of all-cause death and TLF; (3) In patients undergoing DES implantation after RA for LMCA bifurcation lesions, those undergoing the 2-stent approach had worse 5-year clinical outcomes than those undergoing the 1-stent approach, especially within 1 year postprocedure.

The major concerns on the RA use in PCI for LMCA bifurcation lesions are slow flow and coronary perforation that may cause a sudden hemodynamic deterioration. In our study, slow flow related to RA occurred in only 1 patient and no coronary perforation occurred. It is reported that smaller burr sizing (burr-to-artery ratio <0.7) was associated with lower rates of angiographic complications as compared with aggressive burr sizing (burr-to-artery ratio ≥0.7).[15,16] The median burr size of this study was 1.75 mm. The burr-to-artery ratio was lower than 0.6, if we substitute the average stent size of 3.15 mm for the average vessel size, which was not available. This low burr-to-artery ratio could be 1 of the reasons for low rate of slow flow and no coronary perforation. Also, a large coronary microvasculature area in the LMCA territory might be associated with reduced risk of slow flow. The rates of periprocedural MI and in-hospital death in the RA group were 6.4% and 2.8%, respectively, and were comparable to other series of RA for LMCA disease including nonbifurcation lesions, with the rate of periprocedural MI ranging from 2% to 22.5%[8-11] and that of in-hospital death ranging from 1.2% to 7.7%.[8-10] Therefore, it is reasonable to consider that RA use for LMCA bifurcation lesions before DES implantation is safe and feasible in terms of the immediate clinical outcomes.

Currently randomized clinical trials showed that surgical and percutaneous strategies could be equivalent for the treatment of patients with LMCA lesions and low or intermediate SYTAX scores.[17,18] In practice, however, percutaneous

Table 4
The details of patients with all-cause death in the two-stent group after rotational atherectomy

Case	Age, years	Sex	Clinical presentation	True bifurcation	Stent (MV)	Stent (SV)	Stenting strategy	Days from PCI to death	Event
1	88	F	Stable angina	(+)	SES	SES	Provisional T	4	Sudden death (probable ST)
2	75	M	Stable angina	(+)	SES	BES	Culotte	4	CPA due to coronary artery spasm or arrhythmia (no significant coronary artery stenosis)
3	78	F	Stable angina	(−)	BES	SES	Culotte	44	Sudden death
4	61	M	Stable angina	(+)	BES	BES	Culotte	56	Sudden death
5	59	M	NSTEMI	(+)	SES	SES	Mini crush	67	Sudden death
6	70	M	NSTEMI	(+)	SES	BMS	Culotte	307	Pneaumonia
7	95	F	NSTEMI	(+)	BES	BES	Culotte	526	Renal failure
8	86	F	Stable angina	(+)	BES	BES	Culotte	727	Heart failure
9	78	M	Stable angina	(+)	EES	EES	Culotte	737	Cancer
10	66	F	Stable angina	(+)	BES	BES	Culotte	742	Cancer
11	75	M	Stable angina	(+)	SES	BES	Culotte	1081	Cancer
12	88	M	Stable angina	(+)	SES	BES	Culotte	1396	Sudden death
13	83	M	Stable angina	(+)	SES	SES	Provisional T	1611	Pancreatitis

BES = biolimus-eluting stent; BMS = bare metal stent; CPA = cardiopulmonary arrest; EES = everolimus-eluting stent; MV = main vessel; NSTEMI = non-ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; SES = sirolimus-eluting stent; ST = stent thrombosis; SV = side vessel.

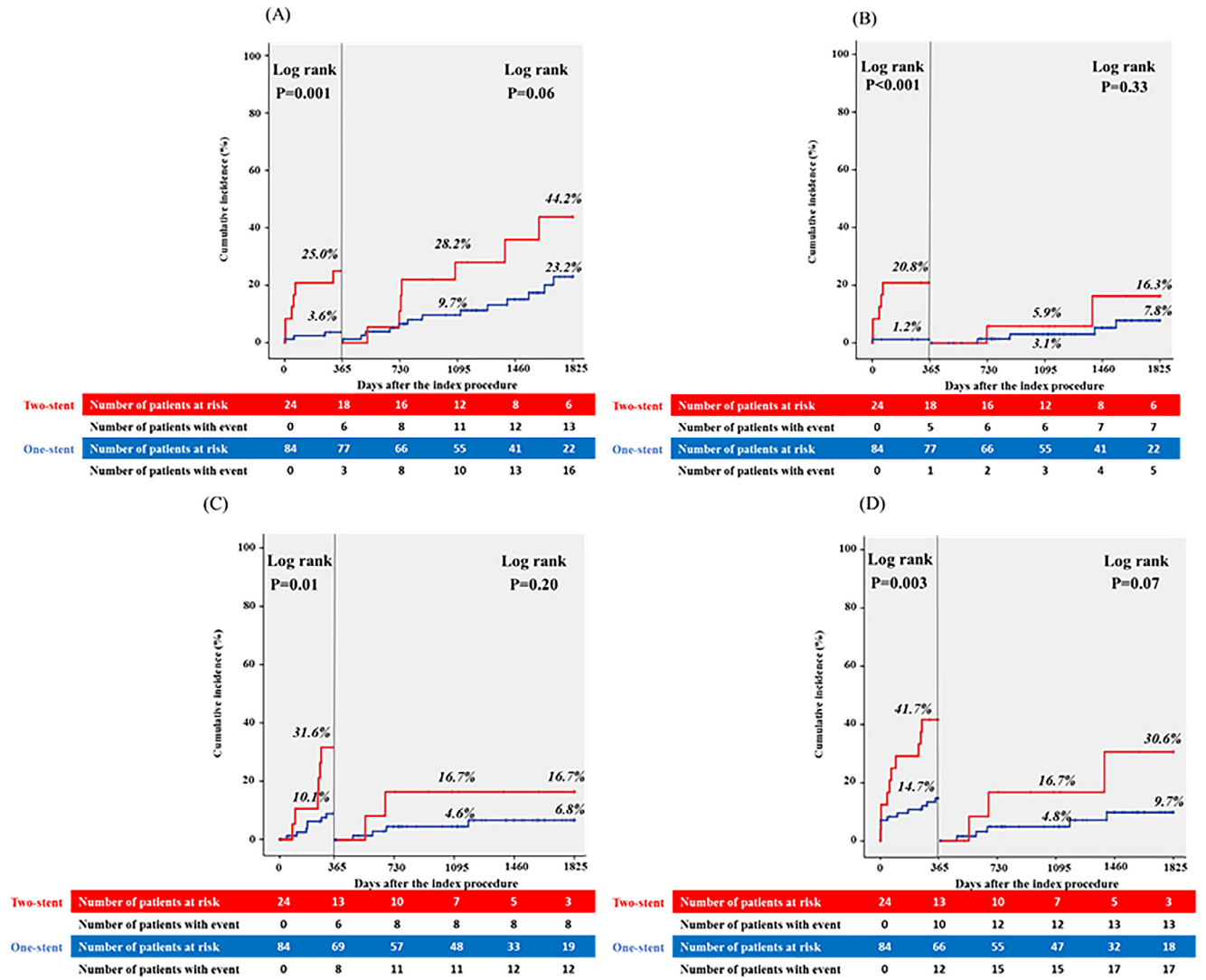

Figure 4. Landmark analyses at 1-year in the RA group: 1- versus 2-stent subgroups (A) All-cause death, (B) Cardiac death, (C) Target lesion revascularization, and (D) Target lesion failure.
RA = rotational atherectomy.

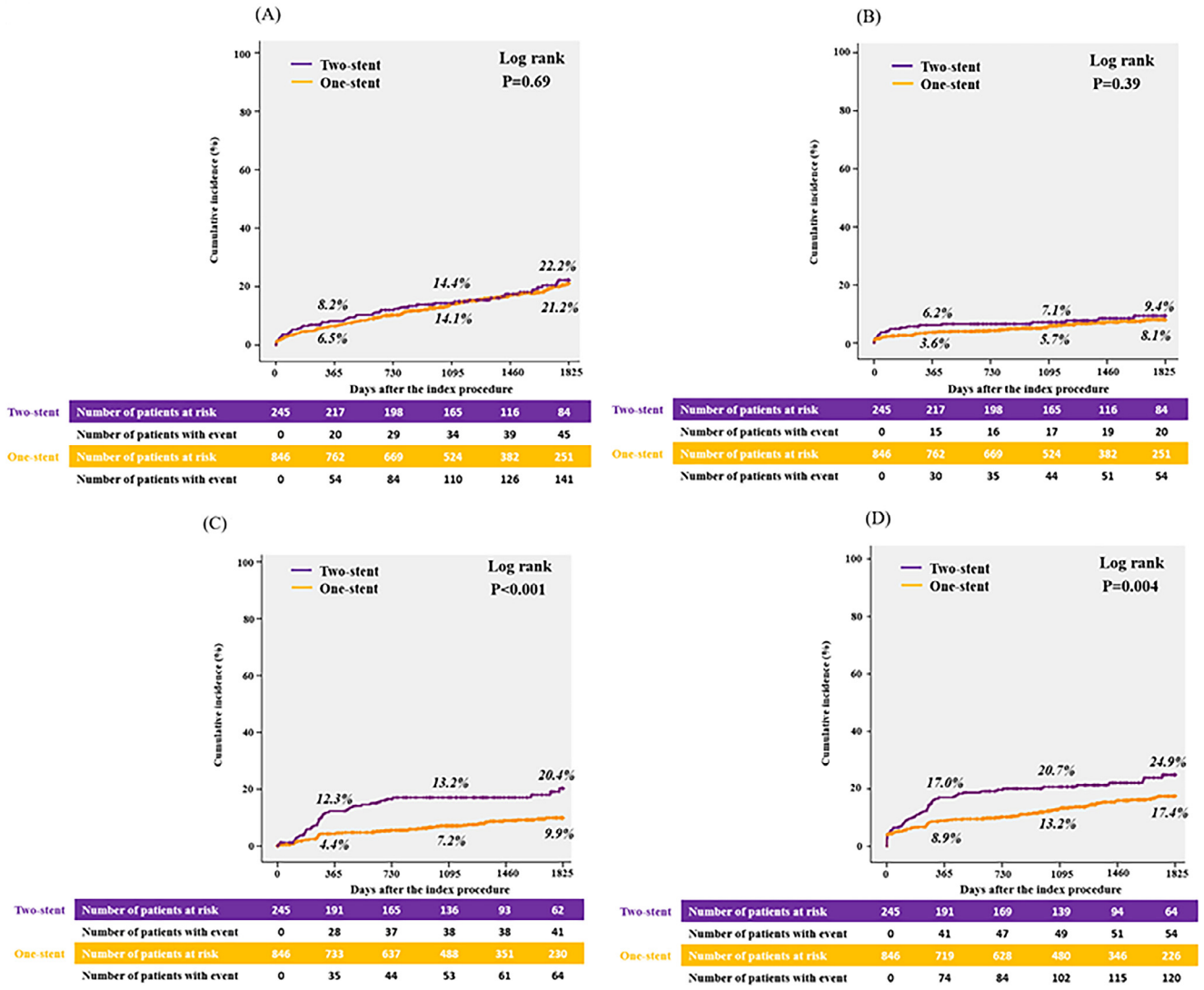

Figure 5. Kaplan-Meier curves for clinical outcomes in the Non-RA group: 1- versus 2-stent subgroups (A) All-cause death, (B) Cardiac death, (C) Target lesion revascularization, and (D) Target lesion failure.
RA = rotational atherectomy.

strategies are frequently selected as the only option for patients with high SYNTAX scores when they are inoperable or have high operative risk and RA can be a treatment option for calcified LMCA lesions. To our knowledge, this is the first report to compare the long-term clinical outcomes with or without RA use before DES implantation or LMCA bifurcation lesions. In this study, the long-term outcomes of DES implantation after RA for LMCA bifurcation lesions were not significantly different from those of DES implantation without RA in terms of all-cause death and TLF. The 1-year rate of stent thrombosis in the RA group was comparable to that in the non-RA group. It is remarkable that no very late stent thrombosis occurred even in calcified LMCA bifurcation lesions. The high flow condition and low shear rate of the LMCA may have a protective effect against very late stent thrombosis.[12] The large vessel diameter of the LMCA might have contributed to the favorable clinical outcomes of DES implantation after RA. Stent underexpansion occurs more frequently in calcified lesions than in noncalcified lesions. The negative impact of stent underexpansion might be less pronounced in large vessels than in small vessels. The high prevalence of intravascular ultrasound (IVUS) use in this study might also have contributed to the favorable clinical outcomes. Indeed, a few observational studies have suggested that IVUS use for LMCA stenting was associated with better clinical outcomes including mortality and TLR.[19-21] These studies also demonstrated that the IVUS use for LMCA stenting was associated with larger stent diameters. The use of IVUS for LMCA stenting would be essential to prevent stent underexpansion, especially in calcified LMCA lesions that are difficult to dilate.

In the present study, patients in the RA group who underwent the 2-stent approach had worse 5-year clinical outcomes than those who underwent the 1-stent approach. Several previous studies also reported that the 2-stent approach for LMCA bifurcation lesions was associated with worse clinical outcomes including cardiac death than the 1-stent approach.[22-24] However, in our previous report from the same registry including both RA and non-RA

patients, the bifurcation 2-stent strategy as compared with bifurcation 1-stent strategy was associated with increased long-term risk for TLR and stent thrombosis, but not for mortality.[12] One of the reasons for the worse outcomes in the 2-stent subgroup may be due to the lesion complexity. Nevertheless, it would be important to note that the cumulative 5-year incidence of all-cause death as well as cardiac death in patients who received RA was markedly higher in the 2-stent subgroup than in the 1-stent subgroup. We should at least be very cautious in selecting PCI in those patients in whom RA and 2-stent approach would be needed. The usage rate of imaging modalities in the 2-stent subgroup tended to be lower than that in the 1-stent group. Imaging modalities should proactively be used when attempting the 2-stent approach after RA in patients with LMCA bifurcation lesions.

Notably, in the present study, the event rates within 1 year were significantly higher for all the outcomes in the 2-stent subgroup than in the 1-stent subgroup. Takagi et al demonstrated that the presence of calcification, true bifurcation, and insulin-treated diabetes were associated with increased risk of in-stent restenosis of major branches, and that the occurrence of in-stent restenosis of major branches within 1 year was associated with cardiac death.[25] Similarly, in our study, the high cardiac death rate within 1 year in the 2-stent subgroup might be explained by the high in-stent restenosis rate within 1 year. Frequent and meticulous observation would be mandatory within 1 year in patients with LMCA bifurcation lesions treated with the 2-stent approach after RA.

This study has 5 major limitations. First and foremost, it is a nonrandomized retrospective observational study. The choices of the RA, stenting strategy, and use of imaging method were left to the discretion of each operator; thus, treatment strategy might differ between institutions and a selection bias could be present affecting clinical outcomes. Second, the number of patients who underwent RA was too small to draw definitive conclusions on the role of RA for LMCA bifurcation lesions. Further, we did not make an adjusted comparison between the 1- and 2-stent subgroups because of a small number of patients. Third, proximal optimization technique (POT) is currently used as standard procedure in the treatment of LMCA bifurcation. However, all patients enrolled in this study underwent PCI from 2004 to 2012 and POT was not a standard procedure at that time. If the use rate of POT had been higher, the clinical outcome might have been different. Fourth, several combinations of DES type and stenting strategy including RA for side vessels were used, and there was no definition for the standard procedure for the 2-stent approach after RA for complex LMCA bifurcation lesions. Finally, this study lacks data on patients treated with coronary artery bypass grafting. The patients who underwent RA were considered to be at high surgical risk or inoperable because of their high EuroSCORE.

In conclusion, DES implantation after RA was a safe and feasible strategy in treating those patients with complex LMCA bifurcation lesions. In patients treated with this strategy, the 2-stent approach was associated with markedly worse 5-year clinical outcomes than the 1-stent approach.

Disclosures

Takeshi Kimura is a member of the Advisory Board of Abbott Vascular Japan. The other authors report no conflicts of interest in regards to this manuscript.

Acknowledgment

The authors appreciate the support and data collection of the co-investigators participating in the AOI LMCA stenting registry.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi:10.1016/j.amjcard.2019.03.002.

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