Comparison of Clinical Characteristics of Stent Thrombosis Between the Right Coronary Artery and the Left Coronary Artery

— A Subanalysis of the REAL-ST Registry —

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Background: Stent thrombosis (ST) remains a severe complication following stent implantation. We previously reported the risk factors for ST after 2nd-generation drug-eluting stent (DES) in the REAL-ST (Retrospective Multicenter Registry of ST After First- and Second-Generation DES Implantation) registry.

Methods and Results: In this subanalysis, we aimed to reveal the difference in ST between right coronary (RCA) and left (LCA) coronary arteries. A total of 307 patients with ST were divided into the RCA-ST group (n=93) and the LCA-ST group (n=214). Multivariate analysis revealed younger age (odds ratio [OR] 0.96, 95% confidence interval [CI] 0.93–0.99, $P=0.01$), ostial lesion at the time of index percutaneous coronary intervention (OR 4.37, 95% CI 1.43–13.33, $P=0.01$), bifurcation lesion at the time of index PCI (OR 0.05, 95% CI 0.02–0.12, $P<0.01$), chronic total occlusion (CTO) lesion at the time of index PCI indication (OR 4.19, 95% CI 1.05–16.71, $P=0.04$), and use of prasugrel at the time of ST (OR 7.30, 95% CI 1.44–36.97, $P=0.02$) were significantly associated with RCA-ST.

Conclusions: Younger age, ostial or CTO lesion, and use of prasugrel at the time of ST were prominent factors in RCA-ST, whereas bifurcation lesion was associated with LCA-ST. We should pay attention to the differences between RCA-ST and LCA-ST to prevent ST.

Key Words: Bifurcation lesion; Chronic total occlusion (CTO) lesion; Ostial lesion; Right coronary artery; Stent thrombosis

Stent thrombosis (ST) is a serious complication following stent implantation, resulting in fatal or nonfatal acute myocardial infarction (AMI).^{1,2} The incidence of late or very late ST was greater with 1st-generation drug-eluting stents (DES) than with bare-metal stents,³ which dampened the enthusiasm for DES. Although several studies have demonstrated better clinical outcomes with 2nd-generation DES compared with 1st-generation DES,^{4,5} ST still occurred with 2nd-generation DES. Recently, our group reported on the REAL-ST (Retrospec-

tive Multicenter Registry of ST After First- and Second-Generation DES Implantation) registry to elucidate the risk factors and long-term outcomes of patients with definite ST after 2nd-generation DES implantation.⁶ The REAL-ST registry revealed that the risk factors for ST were different among early ST, late ST, and very late ST, and the long-term clinical outcomes were worse in patients with ST than in those without ST.⁶ However, we could not provide sufficient data to elucidate the mechanism of ST, which highlighted the need for a detailed subanalysis.

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Table 1. Comparison of Baseline Characteristics of the RCA-ST and LCA-ST Patient Groups

Variables	All patients (n=307)	RCA-ST group (n=93)	LCA-ST group (n=214)	P value
Age (years)	68.1±10.5	66.2±9.7	69.0±10.8	0.02
Male sex	247 (80.5)	73 (78.5)	174 (81.3)	0.57
BMI (kg/m ²)	23.5±3.6 (n=294)	24.0±3.5 (n=89)	23.3±3.6 (n=205)	0.10
Hypertension	244 (79.5)	74 (79.6)	170 (79.4)	0.98
Diabetes mellitus	145 (47.2)	43 (46.2)	102 (47.7)	0.82
Dyslipidemia	252 (82.1)	77 (82.8)	175 (81.8)	0.83
Current smoker	97/306 (31.7)	26/93 (28.0)	71/213 (33.3)	0.35
Hemoglobin (mg/dL)	13.0±2.1 (n=288)	12.8±1.9 (n=86)	13.1±2.2 (n=202)	0.33
eGFR (mL/min/1.73 m ²)	59.1±30.8 (n=288)	52.6±31.4 (n=86)	61.9±30.2 (n=202)	0.07
Hemodialysis	43 (14.0)	21 (22.6)	22 (10.3)	<0.01
Prior myocardial infarction	99 (32.2)	31 (33.3)	68 (31.8)	0.79
Prior PCI	140 (45.6)	48 (51.6)	92 (43.0)	0.16
Prior CABG	13 (4.2)	6 (6.5)	7 (3.3)	0.22
Prior stroke	38 (12.4)	10 (10.8)	28 (13.1)	0.57
Prior PAD	48 (15.6)	19 (20.4)	29 (13.6)	0.13
Prior heart failure	39 (12.7)	9 (9.7)	30 (14.0)	0.29
Multivessel disease	121 (39.4)	32 (34.4)	89 (41.6)	0.24
LVEF (%)	51.9±14.4 (n=294)	53.4±14.0 (n=89)	51.2±14.5 (n=205)	0.29
Clinical presentation at index PCI				0.94
STEMI	92 (30.0)	30 (32.2)	62 (29.0)	
NSTEMI	19 (6.2)	6 (6.5)	13 (6.1)	
Unstable angina	36 (11.7)	10 (10.8)	26 (12.1)	
Stable angina	160 (52.1)	47 (50.5)	113 (52.8)	
Medications at discharge				
Aspirin	303 (98.7)	93 (100)	210 (98.1)	0.32
Ticlopidine	12 (3.9)	5 (5.4)	7 (3.3)	0.52
Clopidogrel	276 (89.9)	79 (84.9)	197 (92.1)	0.06
Prasugrel	14 (4.6)	9 (9.7)	5 (2.3)	0.01
Cilostazol	28 (9.1)	5 (5.4)	23 (10.7)	0.13
Anticoagulation	30 (9.8)	9 (9.7)	21 (9.8)	0.97
ACEI/ARB	194 (63.2)	57 (61.3)	137 (64.0)	0.65
β-blocker	144 (46.9)	44 (47.3)	100 (46.7)	0.93
Calcium-channel blocker	107 (34.9)	36 (38.7)	71 (33.2)	0.35
Statin	215 (70.0)	65 (69.9)	150 (70.1)	0.97
Oral hypoglycemia agent	80 (26.1)	25 (24.2)	55 (25.7)	0.83
Insulin	34 (11.1)	11 (11.8)	23 (10.7)	0.78

Categorical variables are expressed as number and (%). Continuous variables are shown as mean±SD. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker; BMI, body mass index; CABG, coronary artery bypass graft; eGFR, estimated glomerular filtration rate; LCA, left coronary artery; LVEF, left ventricular ejection fraction; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; PAD, peripheral arterial disease; RCA, right coronary artery; ST, stent thrombosis; STEMI, ST-segment elevation myocardial infarction.

The pathophysiology of ST includes patient-, lesion-, procedure-, and stent-related factors.⁷ Because underlying plaques, such as calcified nodules, which are known to be associated with ST,⁸ are significantly different between the right coronary artery (RCA) and left coronary artery (LCA),⁹ the mechanism of ST may differ in the coronary arteries. Furthermore, the long-term outcomes following ST may also differ between the RCA and LCA, because left ventricular function and long-term outcomes are generally worse with LCA-AMI than with RCA-AMI.¹⁰

The aim of this subanalysis of REAL-ST was to compare the clinical characteristics and outcomes between ST in the RCA and ST in the LCA, and to find the clinical factors associated with ST in the RCA.

Methods

The REAL-ST registry was conducted as a retrospective multicenter registry, and the study design of the main analysis has been described elsewhere.⁶ Definite ST was defined according to the Academic Research Consortium criteria.¹¹ The study protocol conformed to the Declaration of Helsinki principles, and was approved by the ethics committee of each participating institution. The present subanalysis has selected patients who had definite ST with 2nd-generation DES as the study population from the REAL-ST registry data, and they were divided into the RCA-ST and LCA-ST groups for comparison of clinical characteristics. We sought the factors that were related to RCA-ST by using a multivariate stepwise logistic regression

Table 2. Comparison of Lesion and Procedural Characteristics at the Index PCI Between the RCA-ST and LCA-ST Groups

Variables	All patients (n=307)	RCA-ST group (n=93)	LCA-ST group (n=214)	P value
De novo lesion	271 (88.3)	76 (81.7)	195 (91.1)	0.02
In-stent restenosis	37 (12.1)	17 (18.3)	20 (9.3)	0.03
Ostial lesion	25 (8.1)	15 (16.1)	10 (4.7)	<0.01
Bifurcation lesion	130 (42.3)	7 (7.5)	123 (57.5)	<0.01
Treated with 1-stent technique	111 (36.2)	6 (6.5)	105 (49.1)	<0.01
Treated with 2-stent technique	19 (6.2)	1 (1.1)	18 (8.4)	0.01
Lesion type				0.92
A	10 (3.3)	4 (4.3)	6 (2.8)	
B1	33 (10.7)	10 (10.8)	23 (10.7)	
B2	82 (26.7)	25 (26.9)	57 (26.6)	
C	182 (59.3)	54 (58.1)	128 (59.8)	
Severe calcification	80 (26.1)	27 (29.0)	53 (24.8)	0.43
Tortuous lesion	64 (20.8)	24 (25.8)	40 (18.7)	0.16
Chronic total occlusion	16 (5.2)	8 (8.6)	8 (3.7)	0.10
Rotational ablation use	46 (15.0)	17 (18.3)	29 (13.6)	0.29
Post-dilatation	219 (71.3)	61 (65.6)	158 (73.8)	0.14
Total stent length (mm)	34.5±20.2 (n=293)	35.5±23.0 (n=89)	34.1±19.0 (n=204)	0.82
Max pressure of stent deployment (atm)	15.1±4.7 (n=293)	15.5±4.8 (n=89)	14.9±4.6 (n=204)	0.40
Stent overlap	111 (36.2)	31 (33.3)	80 (37.4)	0.50
IVUS/OCT use at index PCI	245 (79.8)	72 (77.4)	173 (80.8)	0.49
Stent edge dissection	2 (n=301, 0.7)	0 (n=91, 0.0)	2 (n=210, 1.0)	1.00
Post-diameter stenosis ≥20%	86 (n=301, 28.6)	22 (n=91, 24.2)	64 (n=210, 30.5)	0.20

Categorical variables are expressed as number and (%). Continuous variables are shown as mean ± SD. IVUS, intravascular ultrasound; OCT, optical coherence tomography. Other abbreviations as in Table 1.

model. The incidence of all-cause death and recurrent ST within 4 years after the index ST were compared between the 2 groups.

Data are expressed as mean ± SD or percentage. Categorical variables are presented as numbers (percentage) and compared with a Pearson's χ^2 test or Fisher's exact test. The Kolmogorov-Smirnov test was performed to determine if the continuous variables were normally distributed. Normally distributed continuous variables were compared between the groups using an unpaired Student's t-test. Otherwise, continuous variables were compared using a Mann-Whitney U-test. Multivariate stepwise logistic regression analysis was performed to investigate variables associated with RCA-ST. In this model, RCA-ST was adopted as a dependent variable. Variables that had a marginal association ($P < 0.20$) with RCA-ST in univariate logistic regression analyses were adopted as independent variables. Incidences of all-cause death and recurrent ST after the index ST events were estimated by the Kaplan-Meier method, and the differences between groups were assessed by log-rank test. The odds ratio (OR) and the 95% confidence interval (CI) were calculated. A P-value < 0.05 was considered statistically significant. All analyses were performed using statistical software, SPSS 23.0/Windows (SPSS, Chicago, IL, USA).

Results

A total of 307 patients who had definite ST of native coronary arteries following 2nd-generation DES implantation were analyzed in the present study, and were divided into the RCA-ST group (n=93) and the LCA-ST group (n=214). The comparison of baseline patient characteristics between

the 2 groups is shown in **Table 1**. As compared with the LCA-ST group, the RCA-ST group had the following clinical characteristics: younger age, higher prevalence of hemodialysis, more prasugrel users. General comorbidities such as hypertension, diabetes mellitus, and dyslipidemia were not different between the 2 groups.

The comparison of lesion and procedural characteristics at the time of index PCI between the 2 groups is shown in **Table 2**. An ostial lesion at the index PCI was more frequently observed in the RCA-ST group (16.1%) than in the LCA-ST group (4.7%) ($P < 0.01$). Meanwhile, bifurcation lesion at the index PCI was significantly less frequent in the RCA-ST group (7.5%) than in the LCA-ST group (57.5%) ($P < 0.01$). Total stent length tended to be longer in CTO lesions of the RCA-ST (n=8: 74.8±26.9 mm) than those of the LCA-ST group (n=8: 51.9±27.6 mm) without reaching statistical significance ($P = 0.10$). The comparison of lesion and procedural characteristics at the time of ST is shown in **Table 3**. The use of prasugrel was significantly greater in the RCA-ST group (9.7%) than in the LCA-ST group (1.4%) ($P < 0.01$). ST types, including early ST, late ST and very late ST, were comparable between the RCA-ST and LCA-ST groups ($P = 0.14$). Treatments for ST were comparable between groups; 9 patients in the RCA-ST group used prasugrel at the time of ST and all 9 patients using prasugrel experienced early ST; 3 patients in the LCA-ST used prasugrel at the time of ST and of them 2 cases were early ST and 1 was very late ST.

Table 4 shows the results of univariate logistic regression analysis and multivariate stepwise logistic regression analysis investigating the variables associated with RCA-ST. The multivariate stepwise logistic regression analysis showed that ostial lesion at the time of index PCI (OR

Table 3. Comparison of Patient Characteristics, and Procedural and Lesion Characteristics at Time of ST in the RCA-ST and LCA-ST Groups

	All patients (n=307)	RCA-ST group (n=93)	LCA-ST group (n=214)	P value
Medications at ST				
Aspirin	265 (86.3)	79 (84.9)	186 (86.9)	0.64
Ticlopidine	10 (3.3)	5 (5.4)	5 (2.3)	0.18
Clopidogrel	227 (73.9)	62 (66.7)	165 (77.1)	0.06
Prasugrel	12 (3.9)	9 (9.7)	3 (1.4)	<0.01
Cilostazol	13 (4.2)	3 (3.2)	10 (4.7)	0.76
Non-antiplatelet therapy	31 (10.1)	9 (9.7)	22 (10.3)	0.87
Anticoagulation	27 (8.8)	8 (8.6)	19 (8.9)	0.94
ACEI/ARB	171 (55.7)	45 (48.4)	126 (58.9)	0.09
β -blocker	130 (42.3)	39 (41.9)	91 (42.5)	0.92
Calcium-channel blocker	102 (33.2)	37 (39.8)	65 (30.4)	0.11
Statin	196 (63.8)	61 (65.6)	135 (63.1)	0.67
Oral hypoglycemia agent	73 (23.8)	25 (26.9)	48 (22.4)	0.40
Insulin	38 (12.4)	14 (15.1)	24 (11.2)	0.35
Clinical presentation at ST				
STEMI	217 (70.7)	67 (72.0)	150 (70.1)	0.90
NSTEMI	35 (11.4)	9 (9.7)	26 (12.1)	
Unstable angina	25 (8.1)	7 (7.5)	18 (8.4)	
Cardiac arrest	30 (10.8)	10 (10.8)	20 (9.3)	
Procedural and lesion characteristics				
ST type				0.14
Early ST	176 (57.3)	46 (49.5)	130 (60.7)	
Late ST	64 (20.8)	25 (26.9)	39 (18.2)	
Very late ST	67 (21.8)	22 (23.7)	45 (21.0)	
Stent type at ST				0.35
Biolimus-eluting	68 (22.1)	17 (18.3)	51 (23.8)	
Cobalt-chromium everolimus-eluting	124 (40.4)	36 (38.7)	88 (41.1)	
Platinum-chromium everolimus-eluting	45 (14.7)	14 (15.1)	31 (14.5)	
Zotarolimus-eluting, Resolute	18 (5.9)	9 (9.7)	9 (4.2)	
Zotarolimus-eluting, Endeavor	52 (16.9)	17 (18.3)	35 (18.3)	
Initial TIMI flow grade				0.07
0	224 (73.0)	60 (64.5)	164 (76.6)	
1	16 (5.2)	4 (4.3)	12 (5.6)	
2	40 (13.0)	18 (19.4)	22 (10.3)	
3	27 (8.8)	11 (11.8)	16 (7.5)	
Final TIMI flow grade				0.15
0	3 (1.0)	2 (2.2)	1 (0.5)	
1	10 (3.3)	1 (1.1)	9 (4.2)	
2	33 (10.7)	7 (7.5)	26 (12.1)	
3	261 (85.0)	83 (89.2)	178 (83.2)	
Multivessel ST	10 (3.3)	0 (0.0)	10 (4.7)	0.04
Stent fracture	12 (3.9)	7 (7.5)	5 (2.3)	0.05
Peri-stent staining	5 (1.6)	1 (1.1)	4 (1.9)	1.00
IABP use	131 (42.7)	35 (37.6)	96 (44.9)	0.24
PCPS use	20 (6.5)	6 (6.5)	14 (6.5)	0.98
IVUS/OCT use at ST	228 (74.3)	65 (69.9)	163 (76.2)	0.25
Additional stent implantation	103 (33.6)	32 (34.4)	71 (33.2)	0.83
Thrombus aspiration	103 (33.6)	32 (34.4)	71 (33.2)	0.83
Emergency CABG	12 (3.9)	5 (5.4)	7 (3.3)	0.52

Categorical variables are expressed as number and (%). Continuous variables are shown as mean $\pm$ SD. IABP, intra-aortic balloon pumping; PCPS, percutaneous cardiopulmonary support; TIMI, Thrombolysis in Myocardial Infarction. Other abbreviations as in Tables 1,2.

Table 4. Univariate Logistic Regression Analysis and Multivariate Stepwise Logistic Regression Analysis to Find Associations With RCA-ST

	Univariate			Multivariate		
	OR	95% CI	P value	OR	95% CI	P value
Continuous variables						
Age (per 1 year old)	0.98	0.95–0.99	0.04	0.96	0.93–0.99	0.01
BMI (per 1 kg/m ²)	1.06	0.99–1.14	0.10			
Hemoglobin (per 1 mg/dL)	0.94	0.84–1.06	0.32			
LDL cholesterol (per 1 mg/dL)	1.00	0.99–1.01	0.93			
Hemoglobin A1c (per 1%)	1.12	0.90–1.39	0.30			
eGFR (per 1 mL/min/1.73 m ²)	0.99	0.98–0.99	0.02			
LVEF (per 1%)	1.01	0.99–1.03	0.29			
Total stent length at index PCI (per 1 mm)	1.00	0.99–1.02	0.60			
Categorical variables						
Variables at index PCI						
Hypertension	1.01	0.55–1.84	0.98			
Dyslipidemia	1.07	0.57–2.04	0.83			
Diabetes mellitus	0.94	0.58–1.54	0.35			
Current smoking	0.78	0.46–1.33	0.35			
AMI as clinical presentation	1.34	0.81–2.20	0.25			
Prior PCI	1.41	0.87–2.31	0.16			
Prior PAD	1.64	0.87–3.10	0.13			
Hemodialysis	2.55	1.32–4.91	<0.01			
In-stent restenosis lesion	2.17	1.08–4.36	0.03			
Ostial lesion	3.92	1.69–9.10	<0.01	4.37	1.43–13.33	0.01
Bifurcation lesion	0.06	0.03–0.14	<0.01	0.05	0.02–0.12	<0.01
Bifurcation lesion treated with 2 stents	0.12	0.02–0.90	0.04			
Chronic total occlusion lesion	2.42	0.88–6.67	0.09	4.19	1.05–16.71	0.04
Severely calcified lesion	1.24	0.72–2.14	0.43			
Tortuous lesion	1.51	0.85–2.70	0.16	1.99	0.95–4.18	0.07
Post-dilatation	0.68	0.40–1.14	0.14			
Rotational ablation	1.43	0.74–2.75	0.29			
Stent overlap	0.84	0.50–1.40	0.50			
IVUS/OCT use	0.81	0.45–1.47	0.49			
Clopidogrel	0.49	0.23–1.04	0.06			
Prasugrel	4.48	1.46–13.76	<0.01			
Cilostazol	0.47	0.17–1.28	0.14			
Variables at ST						
Early ST	0.63	0.39–1.03	0.07			
Stent fracture	3.40	1.05–11.02	0.04			
Initial TIMI flow grade 3 (vs. 0, 1 and 2)	2.10	1.20–3.68	0.01	2.04	0.99–4.15	0.05
Final TIMI flow grade 3 (vs. 0, 1 and 2)	1.68	0.80–3.55	0.17			
Emergency CABG	1.68	0.52–5.44	0.39			
IABP use	0.74	0.45–1.22	0.24			
PCPS use	0.99	0.37–2.65	0.98			
Aspirin	0.85	0.43–1.70	0.65			
Ticlopidine	2.38	0.67–8.41	0.18			
Clopidogrel	0.59	0.35–1.02	0.06			
Prasugrel	7.54	1.99–28.52	0.03	7.30	1.44–36.97	0.02
ACEI/ARB	0.66	0.40–1.07	0.09			
Calcium-channel blocker	1.52	0.91–2.52	0.11			

Multivariate stepwise logistic regression analysis model included variables that had an association ($P < 0.2$) with RCA ST in the univariate logistic analysis: ACEI/ARB at the time of ST, age per 1 year old, AMI as clinical presentation at index PCI, BMI per 1 kg/m², bifurcation lesion, bifurcation lesion treated with 2 stents, calcium-channel blocker, chronic total occlusion lesion, cilostazol at index PCI, clopidogrel at index PCI, clopidogrel at the time of ST, early ST, final TIMI flow grade 3 (vs. 0, 1 and 2), hemodialysis, initial TIMI flow grade 3 (vs. 0, 1 and 2), in-stent restenosis lesion, ostial lesion, post-dilatation, prasugrel at index PCI, prasugrel at the time of ST, prior PAD, stent fracture, and tortuous lesion. AMI, acute myocardial infarction; LDL, low-density lipoprotein. Other abbreviations as in Tables 1–3.

4.37, 95% CI 1.43–13.33), CTO lesion at the time of index PCI (OR 4.19, 95% CI 1.05–16.71), and use of prasugrel at the time of ST (OR 7.30, 95% CI 1.44–36.97) were significantly associated with RCA-ST, whereas age (OR 0.96, 95% CI 0.93–0.99) and bifurcation lesion at the time of index PCI (OR 0.05, 95% CI 0.02–0.12) were inversely associated with RCA-ST.

The comparisons of clinical outcomes in the 2 groups are shown in **Figure 1** and **Figure 2**. The median follow-up period was 715 (interquartile range 135–1215) days. The incidence of all-cause death tended to be lower in the RCA-ST group than in the LCA-ST group ($P=0.08$), while the incidence of recurrent ST did not differ between groups ($P=0.34$).

Discussion

The main findings of this study are that younger age, ostial lesion, bifurcation lesion, CTO lesion, and use of prasugrel at the time of ST were significantly associated with definite ST in the RCA. Moreover, the incidence of all-cause death tended to be lower in the RCA-ST group than in the LCA-ST group, whereas the incidence of recurrent ST was not different between the groups. Although several studies have reported risk factors of ST such as AMI, CTO lesion, long lesion, diabetes mellitus, chronic kidney disease and the RCA,^{12,13} the clinical differences between RCA-ST and LCA-ST have not been discussed in the literature. Our results suggest that the mechanism of ST is different between these coronary arteries.

First, we will discuss why ostial lesions were significantly associated with RCA-ST as compared with LCA-ST. It is well known that in-stent restenosis occurs more frequently in ostial RCA lesions than in non-ostial RCA lesions.¹⁴ Recent intravascular imaging studies have revealed the close association between in-stent restenosis and neoatherosclerosis,¹⁵ suggesting the possibility that in-stent plaque rupture caused by neoatherosclerosis is one of the reasons for ST in ostial RCA lesions. The aorto-ostial RCA has lower distensibility and excessive rigidity with a hinge motion,¹⁶ resulting in stent deformation, including recoil and fracture after stent implantation, in ostial lesions.^{16–18} Moreover, calcified nodules are frequently observed in the ostium of the RCA,⁹ which might be an important underlying plaque in ST. Although the literature regarding ST in the ostial LCA (left main ostium) is sparse, multiple mechanisms underlying ostial RCA lesions may be associated with RCA-ST.

Why were bifurcation lesions less frequently observed in the RCA-ST than in the LCA-ST? These lesions, which are a well-known risk factor of ST, occur less in the RCA than in the LCA.^{19,20} Furthermore, variations of bifurcation lesions are wider in the LCA than in the RCA,²¹ because the LCA has several bifurcations such as the left main distal, left anterior descending artery-diagonal branch, left circumflex artery-obtuse marginal branch, and left circumflex artery-posterolateral branch, whereas the RCA has only a few bifurcations such as the posterior descending branch-posterolateral branch. Therefore, the reason why bifurcation lesions were less frequently observed in the RCA-ST group could be less opportunities to treat bifurcation lesions during PCI to the RCA.

We now discuss why CTO lesions were more frequently observed in the RCA-ST than in the LCA-ST. The Canadian Multicenter CTO Registry revealed that CTO

occurred more frequently located in the RCA than in the LCA.²² Furthermore, the total stent length was longer in RCA-CTO lesions than in LCA-CTO lesions.²³ Several studies report that stent deployment to CTO lesions is an important risk factor of ST,^{19,24} and that longer stents are also a risk factor of ST.²⁵ In the present study, total stent length in CTO lesions tended to be longer in the RCA-ST group than in the LCA-ST. The greater incidence of CTO and longer stent length might be the reason why CTO lesions were more frequently observed in the RCA-ST group.

The use of prasugrel was more frequently observed in the RCA-ST than in the LCA-ST group. Because STEMI patients treated with prasugrel are associated with favorable outcomes such as lower ST events as compared with STEMI patients treated with clopidogrel,²⁶ prasugrel is considered to be a more potent thienopyridine than clopidogrel. One possible explanation for our results was that ST in the RCA was associated with mechanical reasons such as stent fracture or stent deformation rather than pharmacological reasons such as drug-non-responders, whereas the cause of ST in the LCA was associated with pharmacological rather than mechanical reasons.

Furthermore, all cases of prasugrel administration at the time of ST in the RCA-ST group were patients with early ST, which is considered to be associated with the PCI procedure rather than with antithrombotic medications.¹ Although efficacy and safety have been confirmed in Japanese patients,²⁷ the lower dose regimen of prasugrel (loading dose: 20 mg in Japan vs. 60 mg in Western countries, maintenance dose: 3.75 mg in Japan vs. 10 mg in Western countries) may be a possible explanation for the association between the use of prasugrel and ST in this study.

The RCA-ST group had relatively better outcomes compared with the LCA-ST in the present study. In general, AMI caused by LCA occlusion has worse clinical outcomes compared with AMI caused by RCA occlusion,^{10,28} partly because left ventricular function is more severely damaged by LCA than by RCA occlusion.¹⁰ Furthermore, because most of the patients with ST presented with acute coronary syndrome,¹¹ LCA-ST might have more cases of fatal AMI than RCA-ST.

Study Limitations

This retrospective subanalysis of the REAL-ST registry has several limitations, which have been described elsewhere.⁶ Furthermore, the present study did not investigate gene polymorphism such as CYP2C19, which is closely associated with nonresponders to clopidogrel.^{29,30} Second, some quantitative coronary angiographic data, including minimal lumen diameter and reference diameter, were not available. Although we discussed the association of RCA-ST with use of prasugrel, the number of prasugrel users was much smaller than the number of clopidogrel users. Because we enrolled patients with ST after implantation of various 2nd-generation DES, it remains unclear whether the differences in ST between RCA and LCA are common across the various DES. Finally, there was a lack of some variables, including peak creatine phosphokinase levels and left ventricular function, at the time of ST events because of the nature of a retrospective registry.

Conclusions

Younger age, ostial lesion, CTO lesion, and use of prasugrel at the time of ST were significantly associated with definite ST in the RCA, whereas bifurcation lesion was significantly associated with definite ST in the LCA. The incidence of all-cause death tended to be lower with RCA-ST than with LCA-ST. We should pay attention to the differences between RCA-ST and LCA-ST to prevent and treat definite ST more effectively.

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Appendix

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