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Severe Acute Stent Malapposition After Drug-Eluting Stent Implantation: Effects on Long-Term Clinical Outcomes

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Background—The effects of severe acute stent malapposition (ASM) after drug-eluting stent implantation on long-term clinical outcomes are not clearly understood. We evaluated long-term clinical outcomes of severe ASM using optical coherence tomography.

Methods and Results—We pooled patient- and lesion-level data from 6 randomized studies. Five studies investigated follow-up drug-eluting stent strut coverage and one investigated ASM. In this data set, a total of 436 patients with 444 lesions underwent postintervention optical coherence tomography examination and these data were included in the analysis. Severe ASM was defined as lesions with ≥400 μm of maximum malapposed distance or ≥1 mm of maximum malapposed length. Composite events (cardiac death, target lesion–related myocardial infarction, target lesion revascularization, and stent thrombosis) were compared between patients with and without severe ASM. The postintervention optical coherence tomography findings indicated that 62 (14.2%) patients had lesions with ≥400 μm of maximum malapposed distance and 186 (42.7%) patients had lesions with ≥1 mm of maximum malapposed length. The 5-year clinical follow-up was completed in 371 (86.1%) of the eligible 431 patients. The cumulative rate of composite events was similar among the patients in each group during 5-year follow-up: 3.3% in patients with ASM ≥400 μm of maximum malapposed distance versus 3.1% in those with no ASM or ASM <400 μm of maximum malapposed distance (*P*=0.89), and 1.2% in patients with ASM ≥1 mm of maximum malapposed length versus 4.6% in those with no ASM or ASM <1 mm of maximum malapposed length (*P*=0.06).

Conclusions—During the 5-year follow-up, ASM severity was not associated with long-term clinical outcomes in patients treated with drug-eluting stents. (*J Am Heart Assoc*. 2019;8:e012800. DOI: 10.1161/JAHA.119.012800.)

Key Words: drug-eluting stent • optical coherence tomography • percutaneous coronary intervention

Acute stent malapposition (ASM) is frequently observed in percutaneous coronary intervention. However, the clinical effects of ASM following drug-eluting stent (DES) implantation remain controversial. Analyses of large multicenter registries of patients who underwent postintervention optical coherence tomography (OCT) assessment suggested

that neither the presence nor the severity of acute malapposition were associated with clinical outcome.[1,2] However, recent analyses of several stent thrombosis registries consistently found that extensively malapposed struts were frequently identified in patients who experienced stent thrombosis.[3–5] Despite current uncertainties regarding the clinical relevance and potential sequelae of ASM, an expert consensus of the European Association of Percutaneous Cardiovascular Interventions recommended avoidance of extensive ASM (ie, maximum malapposed distance ≥400 μm or maximum malapposed length ≥1 mm), and correction when anatomically feasible.[6] This recommendation was based on OCT studies that investigated associations between ASM and subsequent integration by neointimal tissue.[7–9] However, the stent optimization criteria to minimize ASM require further validation.

Based on the European Association of Percutaneous Cardiovascular Interventions' proposed postintervention optimization targets for ASM,[6] the aims of this study were: (1) to evaluate the incidence of severe ASM after DES implantation, (2) to observe serial changes in severe ASM using follow-up

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Clinical Perspective

What Is New?

- Severe acute stent malapposition was not associated with adverse clinical events during the post–drug-eluting stent implantation 5-year follow-up.

What Are the Clinical Implications?

- Additional interventional procedures for severe acute stent malapposition may not be necessary.

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OCT examination, and (3) to compare 5-year clinical outcomes between patients with and without severe ASM.

Methods

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

Study Population

We pooled patient- and lesion-level data from 6 randomized studies that investigated follow-up DES strut coverage (5 studies) and ASM (1 study).[10–15] The study flow diagram is presented in Figure 1. The details of these studies are presented in Tables 1 and 2. The 6 studies had similar characteristics and inclusion/exclusion criteria. These OCT studies included patients who underwent a single or short-length DES implantation for noncomplex lesions and excluded those with complex coronary lesions (eg, diffuse long lesions requiring multiple or long stents, unprotected left main stenosis, bifurcation, chronic total occlusion, and severe calcification). All studies were performed by Severance Cardiovascular Hospital researchers. The angiographic and OCT data from these studies were analyzed at a single core laboratory (Cardiovascular Research Center, Seoul, Korea). Final OCT findings after the completion of study procedures were used for postintervention OCT data. To be consistent with other studies,[10,12–14] the data from earlier follow-ups were used when studies had >1 OCT follow-up.[11,15] From a total of 491 randomized patients, 436 patients with 444 DES-treated lesions underwent postintervention OCT examination. The data from these patients were included in the analysis. Each patient received at least 75 mg of aspirin and a loading dose of 300 mg of clopidogrel at least 12 hours before intervention. During the intervention, unfractionated heparin was administered to maintain an activated clotting time of >250 seconds. Stent implantation was performed according to current standard techniques. If a patient had >1 lesion to treat, all were treated using the assigned study procedures. Patients continued to take 100 mg of aspirin and 75 mg of clopidogrel daily for at least 12 months after stent implantation. The individual study protocols were approved by the institutional review board of our hospital. Written informed consent was obtained from each enrolled patient.

Coronary Angiographic and OCT Analyses

Quantitative coronary angiography analysis was performed using an offline computerized quantitative coronary angiographic system (CAAS, Pie Medical Imaging). Using the guiding catheter for magnification-calibration, minimal lumen diameter and reference vessel diameter of the treated coronary lesions were measured from diastolic frames in a single and matched view showing the smallest minimal lumen diameters. The reference vessel diameter was an average of proximal and distal segment measurements of the reference vessel.

Two types of OCT systems (time-domain M2 or frequency-domain C7-XR; LightLab Imaging, Inc., St. Jude Medical) were used in the present study (Table 1). The detailed OCT imaging methods were described in previous studies.[10–16] The OCT procedure and image acquisition were previously described.[10–15] All OCT images were analyzed using certified offline software (Qlvus, Medis Medical Imaging Systems) at a core laboratory (Cardiovascular Research Center) by analysts who were blinded to patient and procedural information.[16] All cross-sectional images were analyzed at 1-mm intervals. Because OCT findings from 3 studies were measured at 0.2-mm intervals, these data were reanalyzed at 1-mm intervals.[11,12,15] The stent and lumen cross-sectional areas were measured, and neointimal hyperplasia cross-sectional area was calculated as the stent minus lumen cross-sectional area. Lumen, stent, and neointima volumes were estimated using Simpson's rule, and the corresponding volume index was calculated as the volume divided by measured longitudinal length. A malapposed strut was defined as a strut that was detached from the vessel wall as follows: sirolimus-eluting stent ($\geq$160 µm, Cypher, Cordis); zotarolimus-eluting stent ($\geq$110 µm, Endeavor Resolute, Medtronic CardioVascular); everolimus-eluting stent ($\geq$100 µm, Xience, Abbott Vascular and Promus Element, Boston Scientific); and biolimus-eluting stent ($\geq$130 µm Nobori, Terumo Corp. and Biomatrix, Biosensors International).[10–15] If the OCT examination revealed a malapposed strut, maximum malapposed distance and consecutive length were determined per stented lesion. Severe ASM was arbitrarily defined as lesions with $\geq$400 µm of maximum malapposed distance or $\geq$1 mm of maximum malapposed length.[6]

Clinical Outcomes

The clinical data were obtained from medical record reviews. All deaths were considered cardiac deaths unless
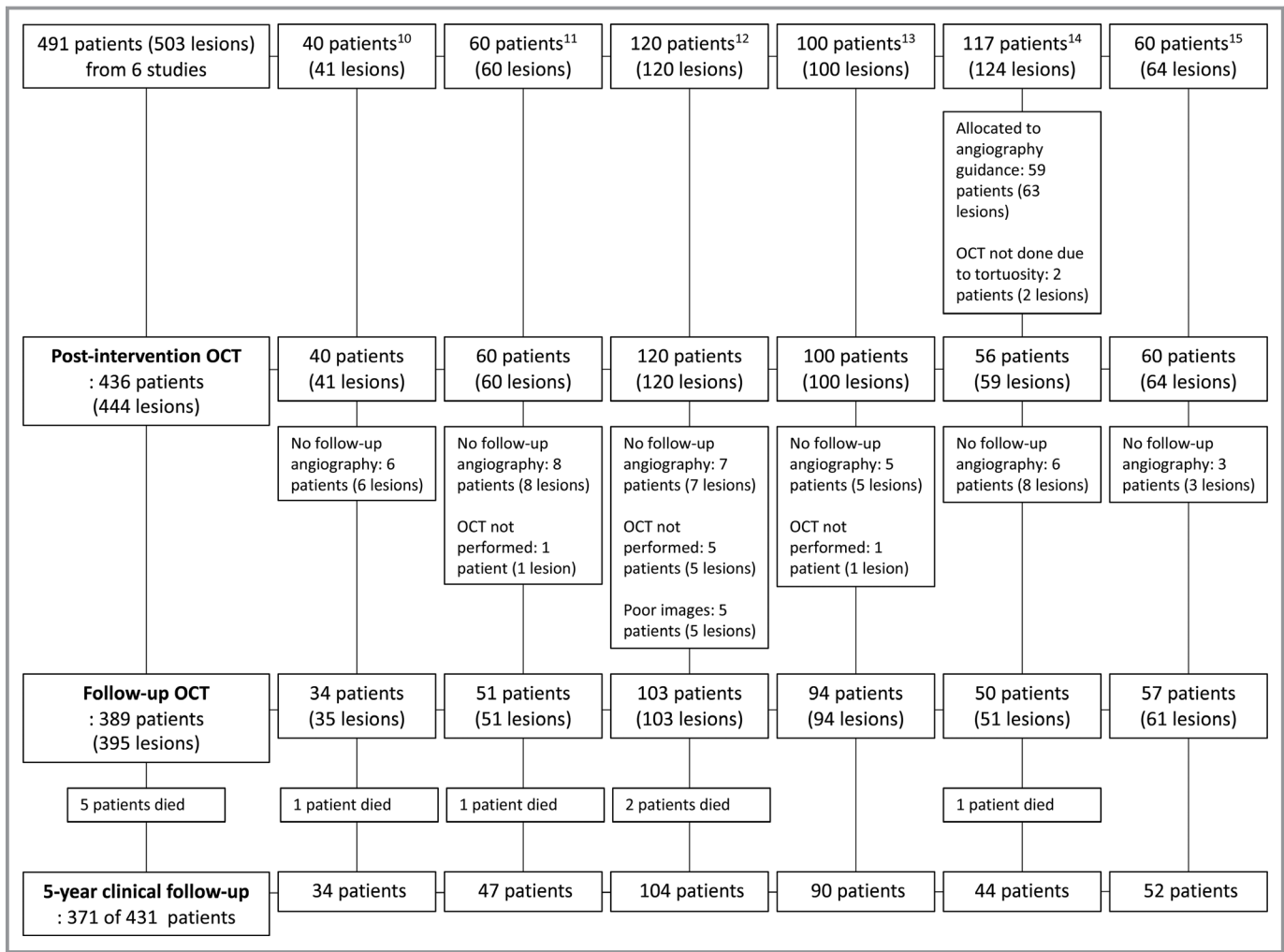
Figure 1. Study flow diagram. OCT indicates optical coherence tomography.

a definite noncardiac cause was established.[17] Myocardial infarction after discharge was defined as the presence of clinical symptoms, electrocardiographic changes, or abnormal echocardiographic findings accompanied by an increase in the creatine kinase myocardial band fraction above the upper limit or an increase in troponin-T or troponin-I levels to greater than the 99th percentile of the upper normal limit. Definite or probable stent thrombosis was defined according to the recommendations of the Academic Research Consortium.[17] Target lesion revascularization was defined as any repeat percutaneous intervention of the target lesion or bypass surgery of the target vessel

Table 1. Main Characteristics of 6 Randomized OCT Studies

Study	Patients (Lesions), No.	Study Procedures	OCT Systems and Examinations	Primary Outcome	Results
Kim et al[10]	40 (41)	ZES-R vs EES	M2; postprocedure, 3 mo	Strut coverage	Comparable
Kim et al[11]	60 (60)	BES vs SES	C7-XR; postprocedure, 3 and 12 mo	Strut coverage	BES better
Kim et al[12]	120 (120)	BES vs SES	C7-XR; postprocedure, 6 mo	Strut coverage	BES better
Kim et al[13]	100 (100)	PtCr-EES vs CoCr-EES	C7-XR; postprocedure, 3 mo	Strut apposition	PtCr-EES possibly better
Kim et al[14]	117 (124)	OCT vs angiography guidance	C7-XR; postprocedure, 6 mo	Strut coverage	OCT guidance better
Kim et al[15]	60 (64)	EES vs SES	C7-XR; postprocedure, 3 and 12 mo	Strut coverage	EES better

BES indicates biolimus-eluting stent; CoCr-EES, cobalt-chromium everolimus-eluting stent; EES, everolimus-eluting stent; OCT, optical coherence tomography; PtCr-EES, platinum-chromium everolimus-eluting stent; SES, sirolimus-eluting stent; ZES-R, Resolute zotarolimus-eluting stent.

Table 2. Inclusion and Exclusion Criteria of 6 Randomized OCT Studies

	Kim et al[10]	Kim et al[11]	Kim et al[12]	Kim et al[13]	Kim et al[14]	Kim et al[15]
Major inclusion criteria	Stable or unstable angina De novo lesions with significant stenosis Vessel size of 2.5 to 3.5 mm by visual estimation that could be covered by a single stent	Stable or unstable angina and non–ST-segment–elevation MI De novo lesions with significant stenosis Vessel size of 2.5 to 3.5 mm and stent length ≤24 mm	Stable angina or acute coronary syndrome De novo lesions with significant stenosis Vessel size of 2.5 to 3.5 mm and lesion length ≤24 mm	Stable or unstable angina De novo lesions with significant stenosis Stent diameter of 2.5 to 3.5 mm and stent length ≤24 mm	De novo lesions with significant stenosis Vessel size of 2.5 to 4.0 mm that could be covered by a single stent	Stable or unstable angina and non–ST-segment–elevation MI De novo lesions with significant stenosis Vessel size of 2.5 to 3.5 mm and stent length ≤24 mm
Major exclusion criteria	Unprotected left main disease Overlapping stents or bifurcated lesions Unsuitable lesions for occlusion technique	ST-segment–elevation MI Complex lesion morphologies	Diffuse long lesions requiring multiple or long (>28 mm) stents Complex lesion morphologies	Acute MI diffuse long (≥28 mm) or implantation of multiple stents Complex lesion morphologies	Presence of an overlapping stent or long stent (>30 mm) Complex lesion morphologies	ST-segment–elevation MI Complex lesion morphologies

MI indicates myocardial infarction; OCT, optical coherence tomography.

performed for restenosis or other complications of the target lesion.[17]

Statistical Analysis

Statistical analysis was performed using SAS (version 9.2; SAS Institute). Continuous variables were reported as mean±SD or median (interquartile range) as appropriate and were compared using Student *t* test or Wilcoxon rank sum test. Categorical variables were reported as number (percentage) and were compared using chi-square test or Fisher exact test. OCT findings per lesion were reported as median (interquartile range) and compared using a hierarchical multilevel regression model including patients and individual studies as random effects. To evaluate independent predictors for severe ASM, the odds ratio (OR) with 95% CI was analyzed using a multivariable analysis. Clinically relevant variables or variables with a $P<0.10$ on univariate analysis were entered into a multivariable model: age, sex, current smoking, clinical presentation of acute myocardial infarction,
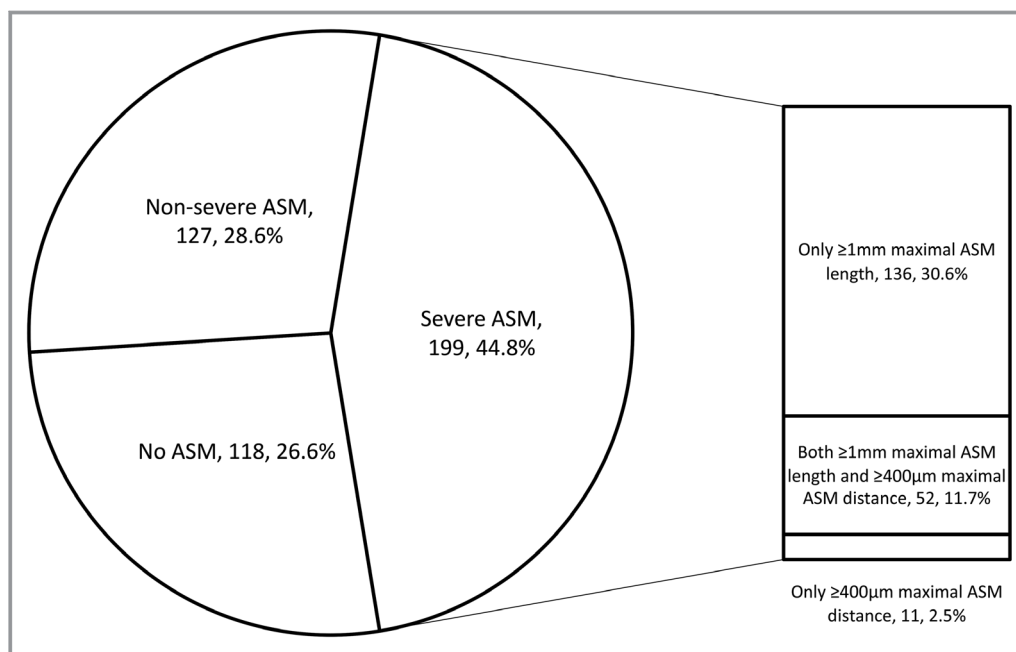

Figure 2. Incidence of acute stent malapposition (ASM) after drug-eluting stent implantation.

Table 3. Baseline Characteristics According to ASM Distance

	Distance of ASM		P Value
	≥400 μm	<400 μm or None	
Patients, No.	62	374	
Age, y	60.7±9.4	61.9±8.9	0.35
Male	49 (79.0)	270 (72.2)	0.26
Diabetes mellitus	20 (32.3)	129 (34.5)	0.73
Hypertension	36 (58.1)	236 (63.1)	0.45
Current smoking	24 (38.7)	95 (25.4)	0.03
Hypercholesterolemia	40 (64.5)	247 (66.0)	0.81
Clinical presentation			0.29
Stable angina	45 (72.6)	257 (68.7)	
Unstable angina	10 (16.1)	89 (23.8)	
Acute myocardial infarction	7 (11.3)	28 (7.5)	
Previous percutaneous coronary intervention	5 (8.1)	41 (11.0)	0.49
Previous myocardial infarction	2 (3.2)	23 (6.2)	0.56
Lesions, No.	63	381	
Treated artery			0.11
Left anterior descending	40 (63.5)	206 (54.1)	
Left circumflex	7 (11.1)	87 (22.8)	
Right	16 (25.4)	88 (23.1)	
Types of implanted stents			0.30
Sirolimus-eluting stent	22 (34.9)	99 (26.0)	
Biolimus-eluting stent	9 (14.3)	82 (21.5)	
Everolimus-eluting stent	23 (36.5)	129 (33.9)	
Zotarolimus-eluting stent	9 (14.3)	71 (18.6)	
No. of implanted stents	1.0±0.2	1.0±0.2	0.80
Stent diameter, mm	3.3±0.4	3.2±0.4	0.011
Stent-to-reference vessel diameter ratio	1.0±0.1	1.1±0.1	<0.001
Total stent length, mm	19.2±5.8	18.8±4.9	0.60
Adjuvant balloon	41 (65.1)	209 (54.9)	0.13
Inflation pressure, atm	16.9±3.9	16.5±3.9	0.62
Preintervention angiography			
Reference vessel diameter, mm	3.3±0.5	3.0±0.5	<0.001
Minimal lumen diameter, mm	1.0±0.5	1.0±0.5	0.64

Continued

Table 3. Continued

	Distance of ASM		P Value
	≥400 μm	<400 μm or None	
Lesion length, mm	16.8±6.1	16.2±5.1	0.48
Postintervention angiography			
Reference vessel diameter, mm	3.4±0.5	3.1±0.4	<0.001
Minimal lumen diameter, mm	3.1±0.5	2.8±0.4	<0.001
Postintervention optical coherence tomography			
Stent volume index, mm³/mm	8.3 (6.9–10.7)	7.3 (6.0–8.6)	0.008
Lumen volume index, mm³/mm	8.0 (6.6–10.4)	7.1 (5.8–8.4)	0.008
Malapposed struts, %	7.1 (4.1–11.6)	1.0 (0–3.1)	<0.001
Maximal strut-to-wall distance, μm	492 (450–607)	161 (120–240)	<0.001
Maximal malapposed length, mm	1.8 (1.0–3.4)	0.2 (0–1.6)	0.003

Results are presented as number (percentage), mean±SD, or median (interquartile range). ASM indicates acute stent malapposition.

types of implanted stents, stent-to-reference vessel diameter ratio, total stent length, and use of adjuvant balloon. Cumulative incidence values for clinical events at 5 years were calculated using the Kaplan–Meier estimate and were compared using a Cox regression model that included individual studies as random effects. Given the different patient enrollment among the individual studies, events beyond 5 years were censored to preserve analysis homogeneity. A $P<0.05$ was considered statistically significant for all analyses.

Results

ASM Distance

Lesions with ≥400 μm of maximal ASM distance were identified in 63 of 444 (14.2%) lesions (Figure 2). The results for baseline characteristics according to malapposed distance are presented in Table 3. Angiography revealed that reference vessel diameter was greater in lesions with ≥400 μm malapposed distance. The stent-to-reference vessel diameter ratio was smaller in these lesions. Using multivariable analysis, the stent-to-reference vessel diameter ratio was an independent predictor for lesions with ≥400 μm malapposed distance (OR, 0.599 per 0.1 increase; 95% CI, 0.444–0.808 [$P=0.0008$]). On postintervention OCT, lesions with ≥400 μm malapposed distance had greater stent and lumen volume indices, higher malapposed strut percentages, and longer

Table 4. Follow-Up OCT Findings According to ASM Distance

	Distance of ASM		
	≥400 µm (n=54)	<400 µm or None (n=341)	*P* Value
Time intervals after stenting, mo	4.5±1.6	4.6±2.0	0.53
Stent volume index, mm³/mm	8.4 (7.0–10.6)	7.4 (6.0–8.7)	0.009
Lumen volume index, mm³/mm	8.0 (6.5–9.8)	6.9 (5.6–8.2)	0.007
Neointimal volume index, mm³/mm	0.4 (0.3–0.5)	0.4 (0.2–0.6)	0.95
Malapposed struts, %	0.9 (0–3.2)	0 (0–0.7)	0.011
Maximal strut-to-wall distance, µm	221 (146–385)	120 (100–190)	0.004
Maximal malapposed length, mm	0.2 (0–1.2)	0 (0–0.2)	0.033

Results are presented as number (percentage), mean±SD, or median (interquartile range). ASM indicates acute stent malapposition; OCT, optical coherence tomography.

Table 5. Five-Year Clinical Outcomes According to ASM Distance

	Distance of ASM			
	≥400 µm (n=62)	<400 µm or None (n=374)	HR (95% CI)	*P* Value
Cardiac death*	1 (1.7)	0	…	0.14
Any MI*	0	8 (2.2)	…	0.61
Target lesion–related MI*	0	2 (0.6)	…	1.00
TLR*	1 (1.7)	11 (3.1)	…	1.00
Definite/probable ST*	0	1 (0.3)	…	1.00
Composite of cardiac death, target lesion–related MI, and definite/probable ST*	1 (1.7)	2 (0.6)	…	0.37
Composite of cardiac death, target lesion–related MI, definite/probable ST and TLR	2 (3.3)	11 (3.1)	1.108 (0.245–5.017)	0.89

Results are presented as number (percentage). ASM indicates acute stent malapposition; HR, hazard ratio; MI, myocardial infarction; OCT, optical coherence tomography; ST, stent thrombosis; TLR, target lesion revascularization.
*Fisher exact test was used because there were few events.

malapposed lengths, compared with those with no ASM or <400 µm of maximal ASM distance. These findings persisted on follow-up OCTs (Table 4). During 5 years of follow-up, cardiac death occurred in 1 patient and noncardiac death in 5 patients. Thus, among the eligible 430 patients, 370 (86.0%) completed the 5-year follow-up and the other 60 (14.0%) were censored during the follow-up. Table 5 presents 5-year clinical outcomes according to malapposed distance. There was no difference in the 5-year composite outcome of cardiac death, target lesion–related myocardial infarction, target lesion revascularization, and definite/probable stent thrombosis, between the 2 groups (Figure 3A) and among the 3 groups with ASM ≥400 µm, ASM <400 µm, and those without ASM (Figure 4A).

ASM Length

Of 444 lesions, 188 (42.3%) lesions showed ≥1 mm of maximum ASM length (Figure 2). The results for baseline characteristics according to malapposed length are presented in Table 6. Angiography revealed that reference vessel diameter was greater and lesion length was longer in lesions with ≥1 mm malapposed length. The stent-to-reference vessel diameter ratio was smaller and the total stent length was longer in lesions with ≥1 mm malapposed length. Using multivariable analysis, the stent-to-reference vessel diameter ratio (OR, 0.740 per 0.1 increase; 95% CI, 0.608–0.901 [*P*=0.0028]), total stent length (OR, 1.048 per 1 mm increase; 95% CI, 1.004–1.094 [*P*=0.0316]), and the usage of adjuvant balloon (OR, 0.539; 95% CI, 0.340–0.855 [*P*=0.0088]) were independent predictors for lesions with ≥1 mm malapposed

length. Postintervention OCT revealed that lesions with ≥1 mm malapposed length had greater stent and lumen volume indices, higher percentages of malapposed struts, and greater strut-to-wall distances, compared with those with no ASM or <1 mm of malapposed length. These characteristics were also present on follow-up OCT (Table 7). Table 8 presents the results for 5-year clinical outcomes, according to malapposed length. There was no distinct between-group difference in 5-year composite outcome (Figure 3B). The risk of composite outcome was not increased in patients with ASM compared with those without ASM (Figure 4B).

Figure 5 represents Kaplan–Meier event curves for the composite outcome between patients with versus those without severe ASM. There was no difference between the 2 groups in the 5-year composite outcome (hazard ratio, 0.636; 95% CI, 0.166–3.472 [*P*=0.66]).

Discussion

In this OCT study, severe ASM characterized by maximal axial distance or consecutive length was not uncommon, even in noncomplex lesions treated using DESs. The stent-to-reference
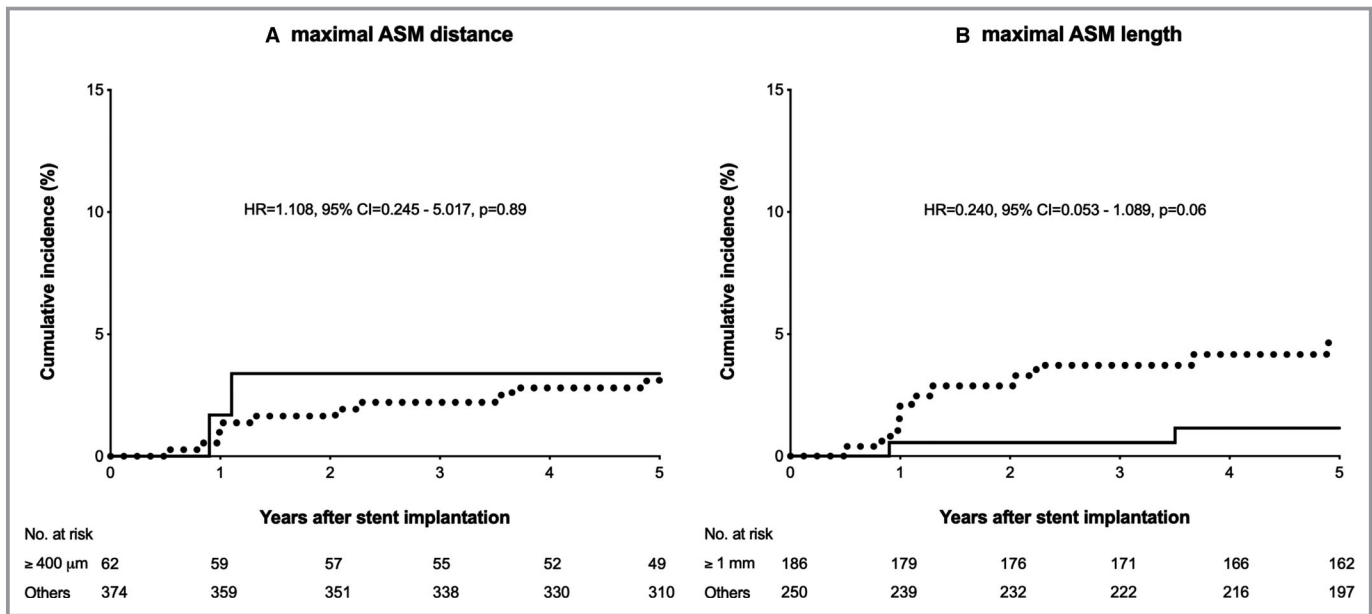
Figure 3. Kaplan–Meier event curves for the composite outcome of cardiac death, target lesion–related myocardial infarction, target lesion revascularization, and stent thrombosis between 2 groups according to the distance and length of acute stent malapposition (ASM). (**A**) Maximal ASM distance, (**B**) maximal ASM length. Line indicates the patients with severe ASM; dotted line indicates the patients without severe ASM. HR indicates hazard ratio.

vessel diameter ratio was consistently smaller in lesions with severe ASM, compared with those without severe ASM. The follow-up OCTs revealed that maximal strut-to-wall distance of late stent malapposition was greater in patients with severe ASM compared with those without

severe ASM. However, severe ASM was not associated with adverse clinical events during the post-DES implantation 5-year follow-up.

This is the first OCT-based analysis to investigate the effects of severe ASM after DES implantation. ASM was found
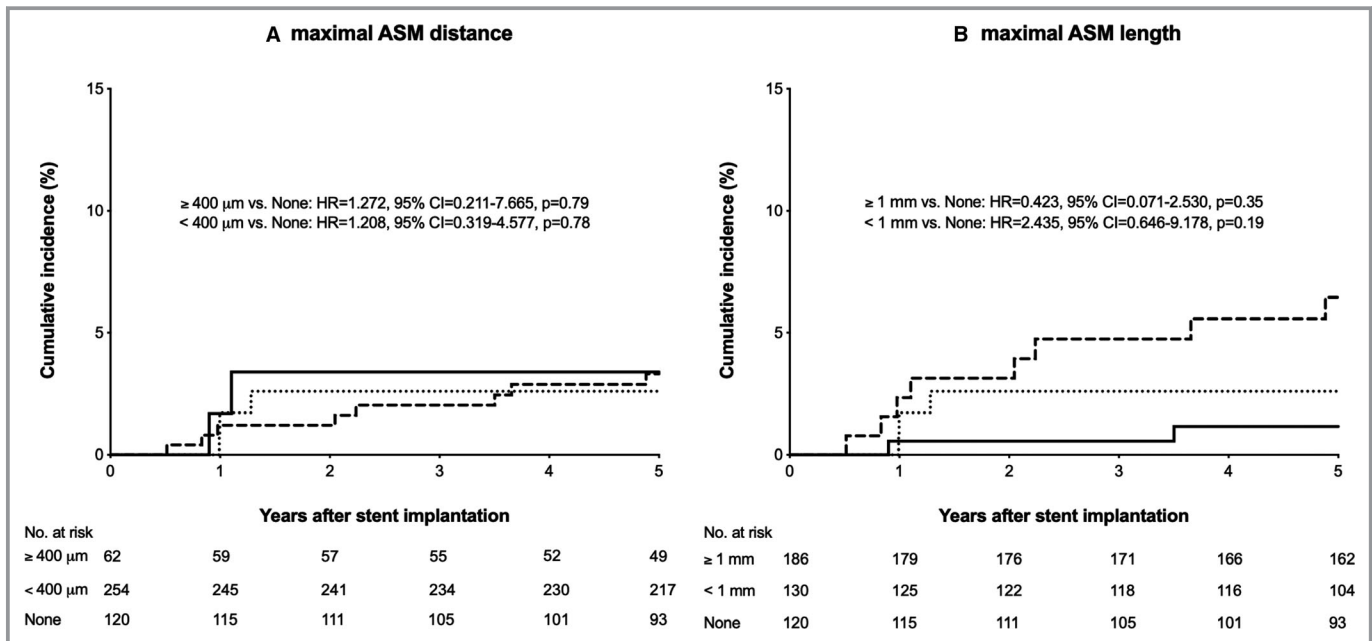

Figure 4. Kaplan–Meier event curves for composite outcome among 3 groups according to the distance and length of acute stent malapposition (ASM). (**A**) Maximal ASM distance, (**B**) maximal ASM length. Line indicates the patients with severe ASM; dashed dotted line indicates the patients with nonsevere ASM; dotted line indicates the patients without ASM. HR indicates hazard ratio.

Table 6. Baseline Characteristics According to the Length of ASM

	Length of ASM		
	≥1 mm	<1 mm or None	P Value
Patients, No.	186	250	
Age, y	62.8±8.9	60.9±8.9	0.026
Men	128 (68.8)	191 (76.4)	0.08
Diabetes mellitus	64 (34.4)	85 (34.0)	0.93
Hypertension	115 (61.8)	157 (62.8)	0.84
Current smoking	54 (29.0)	65 (26.0)	0.48
Hypercholesterolemia	130 (69.9)	157 (62.8)	0.12
Clinical presentation			0.19
Stable angina	137 (73.7)	165 (66.0)	
Unstable angina	34 (18.3)	65 (26.0)	
Acute myocardial infarction	15 (8.1)	20 (8.0)	
Previous percutaneous coronary intervention	21 (11.3)	25 (10.0)	0.66
Previous myocardial infarction	14 (7.5)	11 (4.4)	0.16
Lesions, No.	188	256	
Treated artery			0.13
Left anterior descending	102 (54.3)	144 (56.3)	
Left circumflex	34 (18.1)	60 (23.4)	
Right	52 (27.6)	52 (20.3)	
Types of implanted stents			<0.001
Sirolimus-eluting stent	67 (35.6)	54 (21.1)	
Biolimus-eluting stent	47 (25.0)	44 (17.2)	
Everolimus-eluting stent	48 (25.5)	104 (40.6)	
Zotarolimus-eluting stent	26 (13.8)	54 (21.1)	
No. of implanted stents	1.0±0.2	1.0±0.2	0.60
Stent diameter, mm	3.2±0.3	3.2±0.4	0.85
Stent-to-reference vessel diameter ratio	1.0±0.1	1.1±0.1	<0.001
Total stent length, mm	19.6±5.5	18.4±4.6	0.021
Adjuvant balloon	118 (62.8)	132 (51.6)	0.019
Inflation pressure, atm	16.8±4.0	16.4±3.8	0.39
Preintervention angiography			
Reference vessel diameter, mm	3.2±0.5	3.0±0.4	0.003
Minimal lumen diameter, mm	1.0±0.5	1.0±0.5	0.42

Table 6. Continued

	Length of ASM		
	≥1 mm	<1 mm or None	P Value
Lesion length, mm	17.2±5.8	15.6±4.7	0.003
Postintervention angiography			
Reference vessel diameter, mm	3.3±0.5	2.1±0.4	0.002
Minimal lumen diameter, mm	2.9±0.4	2.8±0.4	0.035
Postintervention optical coherence tomography			
Stent volume index, mm^3/mm	7.8 (6.3–9.1)	7.3 (5.9–8.4)	0.046
Lumen volume index, mm^3/mm	7.6 (6.2–8.9)	7.0 (5.7–8.3)	0.033
Malapposed struts, %	4.9 (2.8–8.4)	0.1 (0–1.2)	<0.001
Maximal strut-to-wall distance, μm	286 (194–416)	149 (100–190)	<0.001
Maximal malapposed length, mm	2.0 (1.3–3.6)	0.2 (0–0.2)	<0.001

Results are presented as number (percentage), mean±SD, or median (interquartile range). ASM indicates acute stent malapposition; OCT, optical coherence tomography.

in 73.4% (326/444) of noncomplex lesions. Severe ASM (≥400 μm of maximum malapposed distance or ≥1 mm of maximum malapposed length) was found in 44.8% (199/444) of the lesions. The ASM incidence was comparable to previous OCT study findings[18–20]; the incidence of severe ASM was higher than expected. The ASM length component accounted for 94.5% of the severe ASM (188/199 lesions) cases. The 82.5% of the 63 lesions with ≥400 μm of maximum ASM distance also had ≥1 mm of maximum malapposed length. In contrast, the 72.3% of the 188 lesions with ≥1 mm of maximum ASM length did not have ≥400 μm of maximum malapposed distance. The factor of ≥1 mm maximum ASM length reflects a wider range of ASM compared with the ASM distance.

The stent-to-reference vessel diameter ratio was an important factor for lesions with ≥400 μm maximum ASM distance and those with ≥1 mm maximum ASM length. The mean ratio for lesions with severe ASM was 1.0, and was 1.1 for lesions without severe ASM. There are 2 possible causes of ASM development: (1) marked mismatch between stent size selection and luminal dimensions, or (2) stent underexpansion caused by factors such as inadequate implantation pressure or plaque-related factors (calcifications), or both, despite an adequate stent-artery ratio.[21] The adjuvant balloon was used for more than one half of all lesions and complex coronary lesions were excluded from the analysis. Therefore, these findings suggested that a stent that is 10% larger than

Table 7. Follow-Up OCT Findings According to the Length of ASM

	Length of ASM		
	≥1 mm (n=173)	<1 mm or None (n=222)	P Value
Time intervals after stenting, mo	4.8±1.7	4.5±2.2	0.06
Stent volume index, mm³/mm	7.7 (6.4–9.1)	7.3 (5.9–8.7)	0.045
Lumen volume index, mm³/mm	7.2 (6.0–8.6)	6.8 (5.5–8.1)	0.016
Neointimal volume index, mm³/mm	0.3 (0.2–0.5)	0.4 (0.3–0.8)	0.012
Malapposed struts, %	0.4 (0–2.8)	0 (0–0.3)	0.001
Maximal distance of strut-to-vessel wall, μm	150 (120–300)	110 (90–157)	0.004
Maximal length of malapposed struts, mm	0.2 (0–1.0)	0 (0–0.2)	0.002

Results are presented as mean±SD or median (interquartile range). ASM indicates acute stent malapposition; OCT, optical coherence tomography.

Table 8. Five-Year Clinical Outcomes According to the Length of ASM

	Length of ASM			
	≥1 mm (n=186)	<1 mm or None (n=250)	HR (95% CI)	P Value
Cardiac death*	0	1 (0.4)	…	1.00
Any MI*	2 (1.2)	6 (2.5)	…	0.48
Target lesion–related MI*	1 (0.6)	1 (0.4)	…	1.00
TLR*	2 (1.2)	10 (4.2)	…	0.08
Definite/probable ST*	1 (0.6)	0	…	0.43
Composite of cardiac death, target lesion–related MI, and definite/probable ST*	1 (0.6)	2 (0.8)	…	1.00
Composite of cardiac death, target lesion–related MI, definite/probable ST and TLR	2 (1.2)	11 (4.6)	0.240 (0.053–1.089)	0.06

Results are presented as number (percentage). ASM indicates acute stent malapposition; HR indicates hazard ratio; MI, myocardial infarction; ST, stent thrombosis; TLR, target lesion revascularization.
*Fisher exact test was used because there were few events.

the reference vessel diameter is appropriate for reducing the risk of severe ASM. Postintervention severe ASM was correlated with severe malapposed status at follow-up. After stent implantation, physiologic vascular healing results in progressive ASM reduction over time.[21] However, this response depends on the degree of ASM. The more severe the stent malapposition, the greater the possibility of persistence at follow-up.[7–9]

The importance of stent size selection was also raised by the study from Kitahara et al, in which >10% of stent oversizing to angiographic reference vessel diameter was associated with a significant reduction in the incidence of stent thrombosis compared with low oversizing in small-sized vessel (<2.75 mm) but not in large-sized vessel (≥2.75 mm).[22] Given the present results that ASM was not associated with adverse cardiac events despite the close relation with stent sizing, it is an interesting finding that the relationship between stent size selection and stent thrombosis depended on reference vessel diameter, suggesting the presence of other links such as *footprint*.[23] Although the larger-sized vessel in lesions with severe ASM might mask the potential risk of stent thrombosis in the present study, the incidence of stent thrombosis in large-sized vessel was not significantly different between oversized stents versus others from the study by Kitahara et al.[22]

Previous intravascular ultrasound or OCT studies have consistently found negative associations between ASM and clinical events.[1,2,24,25] This study provides more information about ASM severity and clinical outcomes, including results from up to 5 years after DES implantation. Nevertheless,
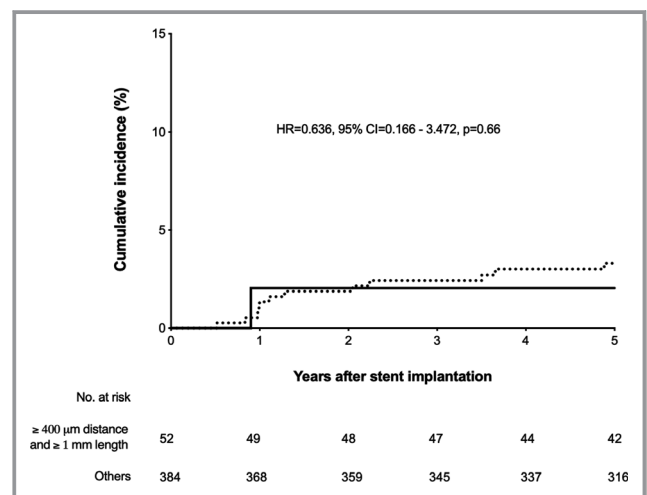
stent malapposition has been identified in patients with stent thrombosis and may be one of the important mechanisms causing stent thrombosis.[3–5] Pathology studies of stent thrombosis may help understand the discordance among OCT study results. An autopsy study by Nakazawa et al[26]

Figure 5. Kaplan–Meier event curves for composite outcome between patients with (line) vs those without severe acute stent malapposition (dotted line).

found that localized strut hypersensitivity was exclusive to late thrombosis associated with sirolimus-eluting stent use, and suggested that the chronic inflammation was related to increased thrombogenicity. Vascular healing was stimulated by the stenting injury of the vessel wall.[27] Therefore, compared with apposed struts, severe ASM will not initiate the wound healing inflammatory cascade because the stent floats in the lumen without touching the vessel wall. The persistent hypersensitivity reactions that are possibly related to the use of polymers or antiproliferative drugs may be attenuated in malapposed struts. The severe ASM found with currently available limus-based DES might alone be insufficient to trigger stent thrombosis. However, late-acquired stent malapposition might be associated with a mechanism different from ASM. With increasing thrombogenicity, chronic inflammation is associated with local release of collagenases that weaken and lead to the expansion of the vessel wall (positive arterial remodeling).[28] Steady changes that result in a local environment where thrombi are easily developed may explain the phenomenon in which stent malapposition is found in patients with late or very late stent thrombosis. Associations between late-acquired stent malapposition and adverse cardiac events remain to be determined.[29,30]

Study Limitations

This study has some limitations. First, differences between the protocols used for the randomized studies might have introduced bias. Second, given the low incidence of adverse clinical events, the statistical power of this study might have been too low to detect between-group differences in clinical outcomes. Thus, there was a potential risk of type II error. Third, the results should not be generalized to populations of patients with complex coronary lesions. These limitations warrant further studies to confirm the clinical impact of severe ASM.

Conclusions

Severe ASM was not uncommon, even in noncomplex coronary lesions treated with DES. However, severe ASM was not associated with poor long-term clinical outcomes in these patients.

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Disclosures

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