Late Stent Malapposition After Drug-Eluting Stent Implantation

An Intravascular Ultrasound Analysis With Long-Term Follow-Up

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Background—Late stent malapposition (LSM) after drug-eluting stent (DES) implantation has not been evaluated sufficiently in real-world practice.

Methods and Results—We evaluated the incidence, mechanisms, predictors, and long-term prognosis of LSM after DES implantation in 557 patients (705 native lesions; sirolimus-eluting stent in 538 lesions and paclitaxel-eluting stent in 167 lesions) in whom intravascular ultrasound was performed at index and 6-month follow-up. LSM occurred in 82 patients with 85 lesions (12.1% overall, 95% CI 9.7% to 14.5%, 71 lesions (13.2%) in sirolimus-eluting stents and 14 lesions [8.4%] in paclitaxel-eluting stents, $P=0.12$]; the incidence was 25.0% (4/16) after directional coronary atherectomy before stenting, 27.5% (14/51) in chronic total occlusion lesions, and 31.8% (7/22) after primary stenting in acute myocardial infarction ($P=0.13$, $P<0.001$, and $P=0.001$, respectively, versus elective stenting with conventional balloon predilation, 9.7% [60/616]). There was an increase of external elastic membrane area (from 17.1 ± 3.6 to 21.4 ± 4.8 mm^2, $P<0.001$) that was greater than the increase in plaque area (from 9.3 ± 2.5 to 10.5 ± 2.7 mm^2, $P<0.001$). Independent predictors of LSM were total stent length, primary stenting in acute myocardial infarction, and chronic total occlusion lesions. Except for 1 death in the non-LSM group, there were no major adverse cardiac events in either LSM or non-LSM patients during a mean 10-month follow-up after detection of LSM.

Conclusions—LSM occurs in 12% of cases after DES implantation. The predictors of LSM are total stent length, primary stenting in acute myocardial infarction, and chronic total occlusion lesions. LSM after DES implantation was not associated with any major adverse cardiac events during a subsequent 10-month (mean) follow-up. **(*Circulation*. 2006; 113:414-419.)**

Key Words: ultrasonics ■ stents ■ coronary disease

Several studies have reported late stent malapposition (LSM) in 4% to 5% of patients after bare-metal stent (BMS) implantation.[1–3] Although drug-eluting stents (DESs) dramatically reduce in-stent restenosis, there may be an increased frequency of LSM on follow-up intravascular ultrasound (IVUS) examination.[4,5] The primary aims of the present study were (1) to determine the incidence of LSM after DES implantation in a large, real-world practice of coronary intervention that included complex lesion subsets and (2) to evaluate the clinical impact of LSM on long-term prognosis (major adverse cardiac events [MACE]). Secondarily, we also sought to identify the mechanisms and the clinical, angiographic, and IVUS predictors of LSM in these patients.

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Methods

Study Population

From the Asan Medical Center clinical and core IVUS laboratory database, we identified 557 patients with 705 native lesions who underwent DES implantation into de novo lesions with IVUS imaging at index and 6-month follow-up (mean interval 6.1 ± 2.1 months). Sirolimus-eluting stents (Cypher stent, Cordis/Johnson and Johnson) and paclitaxel-eluting stents (TAXUS stent, Boston Scientific Corp) were used in 538 and 167 lesions, respectively. All patients undergoing DES implantation at Asan Medical Center were requested to have a 6-month follow-up angiogram; in addition, IVUS

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was performed at 6-month follow-up in patients in whom IVUS had been previously performed at baseline.

Primary stenting of the infarct-related culprit lesion in acute myocardial infarction (MI) patients was performed within 12 hours after symptom onset. Chronic total occlusion (CTO) lesions were defined by the absence of antegrade flow or only minimal flow of contrast distal to the occlusion (Thrombolysis In Myocardial Infarction [TIMI] flow grade 0 or 1)[6]; the duration of the total occlusion as estimated by clinical information, sequential angiographic information, or both was >1 month in all CTO patients.

All patients received a 300-mg loading dose of clopidogrel followed by clopidogrel 75 mg/d for 6 months and aspirin 200 mg/d indefinitely. Cilostazol 200 mg/d for 3 to 6 months after DES implantation was additionally prescribed in 16 patients (20%) with LSM and 74 (16%) without LSM ($P=0.5$).[7] Fifty-one LSM patients (62%) and 283 non-LSM patients (60%; $P=0.8$) continued to receive clopidogrel 75 mg/d for 5.4±4.1 and 5.1±4.2 months, respectively ($P=0.5$), beyond the 6-month angiogram.

Definition of MACE and Clinical Follow-Up

Long-term (ie, beyond 6-month) clinical follow-up data were obtained from outpatient record reviews or telephone interviews. Death was classified as cardiac versus noncardiac. MI was defined as an elevation of the MB fraction of creatinine kinase to a value 3 times the upper limit of the normal range. Target-lesion revascularization was repeat percutaneous or surgical intervention of the stented lesion. MACE was defined as death of cardiac origin, MI, and target-lesion revascularization. All patients were followed up for a minimum of 4.0 months (range 4.0 to 20.3 months) after the 6-month follow-up angiogram and IVUS, except for 1 sudden death in a patient without LSM.

IVUS Imaging and Analysis

Poststenting and 6-month follow-up IVUS imaging were performed after intracoronary administration of 0.2 mg of nitroglycerin with a motorized transducer pullback system (0.5 mm/s) and a commercial scanner (SCIMED) that consisted of a rotating 30- or 40-MHz transducer within a 3.2F or 2.6F imaging sheath.

LSM was defined as separation of at least 1 stent strut from the intimal surface of the arterial wall that was not overlapping a side branch, was not present immediately after stent implantation, and had evidence of blood flow (speckling) behind the strut.[1] Postprocedural incomplete stent apposition was classified into 2 groups: (1) resolved, incomplete apposition present after the procedure but no longer present at 6-month follow-up and (2) persistent, incomplete apposition present both after the procedure and at 6-month follow-up.[5]

Qualitative analysis was performed as follows. First, we reviewed all 705 follow-up IVUS tapes to identify cases of stent malapposition. Second, index (poststenting) and follow-up IVUS tapes were reviewed side-by-side to discriminate cases in which incomplete stent malapposition existed immediately after stent implantation. This included independent review of index and follow-up IVUS studies by 2 of the authors (M.-K.H. and Y.-H.K.).

Using computerized planimetry, we performed quantitative IVUS analysis at (1) LSM sections, (2) postprocedural incomplete stent apposition sections, (3) stented segments with complete late apposition, and (4) reference segments. Quantitative measurements included external elastic membrane (EEM), lumen, and stent cross-sectional areas (CSA) at stented and reference segments; EEM, stent, plaque and media (P&M), intrastent lumen, intimal hyperplasia, and LSM CSA at LSM sections; and incomplete stent apposition CSA at postprocedural incomplete stent apposition sections.[8] LSM CSA was measured every 1 mm within LSM sections; LSM volumes were calculated with Simpson's rule.

Quantitative Coronary Angiographic Analysis

With the guiding catheter for magnification-calibration and an online system (ANCOR version 2.0, Siemens), minimal luminal diameter (MLD) of the lesion and diameters of the reference segments were measured before and after stenting and at 6-month follow-up.

TABLE 1. Baseline Clinical Characteristics

	LSM	Non-LSM	*P*
No. of patients	82	475	
Age, y	57±11	57±9	0.8
Male gender, n (%)	61 (74)	344 (72)	0.7
Hypertension, n (%)	40 (49)	224 (47)	0.9
Diabetes mellitus, n (%)	17 (21)	113 (24)	0.6
Lipid profiles, mg/dL			
Total cholesterol	184±40	180±36	0.3
Triglyceride	148±79	141±105	0.7
HDL cholesterol	44±11	45±18	0.5
Cigarette smoking, n (%)	33 (40)	185 (39)	0.9
No. of diseased vessels, n (%)			0.5
1	36 (44)	200 (42)	
2	31 (38)	159 (34)	
3	15 (18)	116 (24)	
Clinical presentation, n (%)			1.0
Stable angina	40 (49)	234 (49)	
Unstable angina	32 (39)	186 (39)	
Acute MI	10 (12)	55 (12)	

Statistical Analysis

Statistical analysis was performed with the SPSS software program (SPSS Inc). Categorical data are presented as frequencies and compared with χ^2 statistics or Fisher's exact test. Continuous variables are presented as mean±SD and compared with unpaired or paired Student *t* test or Mann-Whitney *U* test and correlation coefficients. Event-free survival was analyzed with the Kaplan-Meier method, and the corresponding probability value was obtained from log-rank test. A probability value <0.05 was considered statistically significant.

A subgroup analysis of electively stented lesions after only conventional balloon predilation was also performed because this represents the typical strategy for the majority of lesions undergoing percutaneous coronary intervention. These lesions were not treated by unusual coronary interventions (ie, directional coronary atherectomy [DCA] before stenting) or in unusual clinical situations (acute MI or CTO lesions). This analysis was similar to our previous BMS study.[2] Sirolimus- versus paclitaxel-eluting stents were also compared.

Multiple stepwise logistic regression analysis was performed to assess independent predictors for LSM. To identify the independent predictors of LSM, the clinical, angiographic, and IVUS variables were entered into per-lesion models. To analyze the impact of LSM on long-term prognosis, only 1 lesion per patient was included: that with LSM for patients who had LSM and that with the most unfavorable characteristics for occurrence of adverse events for patients without LSM.

Results

LSM was documented in 85 lesions in 82 patients (12.1% overall, 95% CI 9.7% to 14.5%): 71 (13.2%, 95% CI 10.3% to 16.1%) of lesions treated with sirolimus-eluting stents and 14 (8.4%, 95% CI 4.2% to 12.6%) of lesions treated with paclitaxel-eluting stents ($P=0.12$). Baseline clinical and angiographic characteristics comparing LSM and non-LSM are shown in Tables 1 and 2, respectively. Preintervention quantitative coro-

TABLE 2. Baseline Angiographic Characteristics and Poststenting IVUS Measurements

	LSM	Non-LSM	*P*
No. of lesions	85	620	
Coronary artery dilated, n (%)			0.2
Left main	...	11 (1)	
Left anterior descending	59 (68)	369 (60)	
Left circumflex	8 (10)	97 (16)	
Right	18 (22)	143 (23)	
Types of DES, n (%)			0.12
Sirolimus-eluting stent	71 (84)	467 (75)	
Paclitaxel-eluting stent	14 (16)	153 (25)	
Total stent length, mm	39.3±20.0	31.5±16.1	<0.001
Reference-vessel diameter, mm	3.0±0.5	2.9±0.9	0.3
MLD, mm			
Preintervention	0.7±0.7	1.0±0.6	<0.001
Postintervention	2.8±0.4	2.8±0.5	0.9
Pressure (atm)	16.3±3.3	16.1±3.4	0.6
Elective stenting with conventional balloon predilation, n (%)	60 (70)	556 (90)	<0.001
DCA before stenting, n (%)	4 (5)	12 (2)	0.115
Primary stenting in acute MI, n (%)	7 (8)	15 (2)	0.004
CTO, n (%)	14 (17)	37 (6)	<0.001
Adjunct high-pressure balloon angioplasty, n (%)	46 (54)	315 (51)	0.6
Poststenting IVUS measurements, mm^2			
Distal reference-segment EEM CSA	11.3±4.1	11.0±3.8	0.5
Distal reference-segment lumen CSA	7.0±2.7	6.8±2.4	0.4
Lesion-segment stent CSA	6.5±1.8	6.5±1.9	1.0
Proximal reference-segment EEM CSA	15.6±3.8	15.0±3.9	0.17
Proximal reference-segment lumen CSA	8.9±2.4	8.7±2.8	0.6

nary angiography (QCA) MLD was significantly smaller and total stent length was significantly longer in the LSM group than in the non-LSM group. Compared with the non-LSM group, there was more primary MI stenting and treatment of CTO lesions in the LSM group and a tendency for more prestenting DCA in the LSM group.

After baseline characteristics (listed in Tables 1 and 2) were adjusted among subgroups, compared with the frequency of LSM in lesions that were treated with conventional balloon predilation and elective stenting (9.7%, 95% CI 7.4% to 12.1%, 60/616), LSM occurred in 7 (31.8%, 95% CI 12.4% to 51.3%) of 22 lesions that underwent primary stenting in acute MI ($P=0.001$), in 14 (27.5%, 95% CI 15.2% to 39.7%) of 51 CTO lesions ($P<0.001$), and in 4 (25.0%, 95% CI 10.3% to 46.2%) of 16 lesions treated with prestenting DCA ($P=0.13$).

Poststenting QCA and IVUS findings comparing lesions with and without LSM are also shown in Table 2. At follow-up, QCA MLD was larger in the LSM group (2.7±0.5 versus 2.5±0.7 mm, $P=0.025$).

In the subgroup of elective stenting after conventional balloon predilation (n=616), angiographic findings and poststenting IVUS measurements comparing lesions with and without LSM are shown in Table 3. Preintervention QCA MLD was also

TABLE 3. Baseline Angiographic Characteristics and Poststenting IVUS Measurements in the Subgroup of Lesions With Stenting After Conventional Balloon Predilation

	LSM	Non-LSM	*P*
No. of lesions	60	556	
Total stent length, mm	38.6±19.7	30.6±15.8	0.003
Reference-vessel diameter, mm	3.0±0.4	2.9±1.0	0.8
MLD, mm			
Preintervention	0.9±0.5	1.1±0.5	0.010
Postintervention	2.8±0.4	2.8±0.5	1.0
Pressure, atm	16.4±3.2	16.1±3.4	0.5
Poststenting IVUS measurements, mm^2			
Distal reference-segment EEM CSA	11.3±4.1	11.1±3.8	0.8
Distal reference-segment lumen CSA	6.8±2.5	6.8±2.4	0.9
Lesion-segment stent CSA	6.3±1.7	6.5±1.9	0.5
Proximal reference-segment EEM CSA	15.5±3.7	14.9±3.9	0.3
Proximal reference-segment lumen CSA	8.9±2.2	8.7±2.8	0.6

significantly smaller and total stent length was significantly longer in the LSM group than in the non-LSM group.

The location of LSM was at the edge (within 5 mm from stent margin) in 14 lesions (16%; 12 proximal and 2 distal; 12 sirolimus-eluting stents and 2 paclitaxel-eluting stents) and within the body of the stent in 71 lesions (84%; 59 sirolimus-eluting stents and 12 paclitaxel-eluting stents). Poststenting and follow-up IVUS measurements at the LSM segment are shown in Table 4. The maximum CSA and arc of LSM measured 3.0±1.9 mm^2 and 130±35°, respectively. The maximum number of stent struts and maximum distance between stent struts and intima/lumen border were 2.9±1.2 and 1.3±0.4 mm, respectively. There was an increase of EEM CSA (from 17.1±3.6 mm^2 after implantation to 21.4±4.8 mm^2 at follow-up, $P<0.001$) and an increase of P&M CSA (from 9.3±2.5 mm^2 after implantation to 10.5±2.7 mm^2 at follow-up, $P<0.001$). The increase in EEM was greater than the increase in P&M ($P<0.001$). LSM CSA correlated directly with the increase in EEM CSA ($r=0.882$, $P<0.001$).

Predictors of LSM

Stepwise multiple logistic regression analysis was performed to determine independent predictors of LSM. The following variables were tested (all with $P<0.2$ in univariate analysis):

TABLE 4. Poststenting and Follow-Up IVUS Measurements at the LSM Segment in the Total Cohort of 85 Patients

	After Stenting	Follow-Up	*P*
EEM CSA, mm^2	17.1±3.6	21.4±4.8	<0.001
Stent CSA, mm^2	7.8±1.7	7.8±1.7	0.4
Plaque and media CSA, mm^2	9.3±2.5	10.5±2.7	<0.001
Intrastent lumen CSA, mm^2	7.8±1.7	6.5±1.6	<0.001
Intimal hyperplasia CSA, mm^2	...	1.3±0.7	NA
LSM CSA, mm^2	...	3.0±1.9	NA
LSM volumes, mm^3	...	10.0±9.3	NA
LSM length, mm	...	3.9±1.4	NA

NA indicates not applicable.

TABLE 5. Baseline Angiographic Characteristics and Poststenting IVUS Measurements Comparing Sirolimus- and Paclitaxel-Eluting Stents With LSM

	Sirolimus-Eluting Stent	Paclitaxel-Eluting Stent	*P*
No. of lesions	71	14	
Total stent length, mm	38.7±19.9	42.4±20.8	0.5
Reference-vessel diameter, mm	3.1±0.5	3.1±0.4	1.0
MLD, mm			
Preintervention	0.7±0.7	0.6±0.6	0.6
Postintervention	2.8±0.4	2.8±0.4	0.6
Pressure, atm	16.3±3.4	16.1±3.0	0.9
DCA before stenting, n (%)	4 (6)	0	1.0
Primary stenting in acute MI, n (%)	7 (10)	0	0.6
CTO, n (%)	11 (16)	3 (21)	0.7
Poststenting IVUS measurements, mm^2			
Distal reference-segment EEM CSA	11.1±3.5	12.4±6.3	0.5
Distal reference-segment lumen CSA	6.8±2.4	7.7±3.7	0.4
Lesion-segment stent CSA	6.5±1.7	6.7±2.5	0.7
Proximal reference-segment EEM CSA	15.7±4.0	15.3±3.2	0.8
Proximal reference-segment lumen CSA	8.9±2.3	8.8±2.9	0.9

lesion location, types of DES (sirolimus- versus paclitaxel-eluting stent), total stent length, preintervention QCA MLD, primary stenting in acute MI, DCA before stenting, CTO lesions, and proximal reference-segment EEM CSA. Independent predictors of LSM were total stent length (P=0.001, OR=1.021, 95% CI=1.009 to 1.034), primary stenting in acute MI (P=0.003, OR=4.263, 95% CI=1.664 to 10.918), and CTO lesions (P=0.007, OR=2.594, 95% CI=1.299 to 5.183). In the subgroup of elective stenting after conventional balloon predilation, the only independent predictor of LSM was total stent length (P=0.001, OR=1.025, 95% CI=1.011 to 1.039).

Comparison Between Sirolimus- and Paclitaxel-Eluting Stents

Baseline angiographic characteristics and IVUS measurements between sirolimus- versus paclitaxel-eluting stents are shown in Table 5; there were no significant differences. At follow-up, there was a tendency for a smaller increase in EEM CSA (P=0.19) and a statistically smaller increase in P&M CSA and intimal hyperplasia CSA in sirolimus-eluting stents (P=0.016 and 0.029, respectively; Table 6).

TABLE 6. Comparison of IVUS LSM Segment Measurements Between Sirolimus- and Paclitaxel-Eluting Stents

	Sirolimus-Eluting Stent	Paclitaxel-Eluting Stent	*P*
No. of lesions	71	14	
Δ EEM CSA, mm^2	4.1±2.2	5.0±2.4	0.19
Δ Plaque and media CSA, mm^2	1.1±1.0	1.8±1.3	0.016
Δ Intrastent lumen CSA, mm^2	−1.2±0.5	−2.0±1.2	0.023
Intimal hyperplasia CSA, mm^2	1.2±0.5	2.0±1.2	0.029
LSM CSA, mm^2	3.0±1.9	3.2±1.9	0.8

Postprocedural Incomplete Stent Apposition

Postprocedure incomplete stent apposition was observed in 51 lesions (7.2%; 47 sirolimus-eluting stents and 4 paclitaxel-eluting stents; 50 proximal stent edge and 1 distal stent edge). Incomplete stent apposition persisted in all 51 lesions at 6-month follow-up. Poststenting and follow-up IVUS measurements at this segment are shown in Table 7. In these lesions, there were consistent increases in both EEM and P&M CSA, although the size of the incomplete apposition segment did not change. There were no MACEs (including target-lesion revascularization) in these patients with postprocedure incomplete stent apposition who had an average follow-up of 16.6±4.0 months after DES implantation.

Long-Term Follow-Up

At 6 months, target-lesion revascularization was necessary in 20 patients with 22 lesions in the non-LSM group but in none of the LSM patients (P=0.095); 5 non-LSM patients also required revascularization of a nontarget lesion. Therefore, 542 patients with 683 lesions were eligible for long-term (beyond 6 months) clinical follow-up. The mean duration of long-term clinical follow-up after the 6-month angiogram was 10.9±4.4 and 10.1±3.9 months in the LSM and non-LSM groups, respectively (P=0.1). One patient in

TABLE 7. Poststenting and Follow-Up IVUS Measurements in Patients With Incomplete Stent Apposition of the Stented Segment at the Time of Stent Implantation

	Poststenting	Follow-Up	*P*
EEM CSA, mm^2	19.3±4.3	20.3±4.3	<0.001
Stent CSA, mm^2	8.6±1.9	8.6±1.9	0.6
Plaque and media CSA, mm^2	8.8±2.7	9.9±2.7	<0.001
Intrastent lumen CSA, mm^2	8.6±1.9	7.4±1.7	<0.001
Intimal hyperplasia CSA, mm^2		1.2±0.5	
Incomplete stent apposition CSA, mm^2	1.9±1.2	1.9±1.2	0.124

the non-LSM group died suddenly 2.6 months after the 6-month follow-up angiogram. Except for this 1 death in a non-LSM patient, there was no other MACE beyond 6 months in either group. There was no significant difference in event-free survival rate between the 2 groups (log-rank probability value=0.67).

Discussion

In this retrospective analysis of 705 native lesions treated with DES implantation and studied with postimplantation and follow-up IVUS, we found 85 lesions (12.1%) with LSM at 6-month follow-up, in 13.2% of sirolimus-eluting stents and 8.4% of paclitaxel-eluting stents. Total stent length, primary stenting in acute MI, and CTO lesions were independent predictors of LSM. Long-term clinical follow-up was available for a mean of 10.2 months after detection of LSM; compared with non-LSM patients, patients with LSM showed similarly favorable outcomes. In particular, LSM was not associated with any subsequent events.

A higher incidence of stent malapposition at follow-up was reported in the sirolimus-eluting stent group than in the BMS group in the RAVEL trial.[4] However, the true incidence of LSM could not be determined because postprocedural IVUS was not performed.[4] A recent IVUS substudy of the TAXUS II trial reported a statistically similar incidence of LSM between paclitaxel-eluting stents (8.0% to 9.5%) and BMS (5.4%).[5] In the TAXUS IV IVUS substudy, however, there was a lower incidence of LSM than in TAXUS II in both groups (1.1% and 2.2%, respectively).[9] Because complex lesions that included very long lesions, CTOs, and thrombotic lesions were excluded in the previous randomized trials, the actual incidence of LSM in a real-world daily practice could not be determined. In the present study of real-world patients, the actual incidence of LSM at a 6-month follow-up after DES implantation appeared to higher than in the randomized trials and appeared to be higher than in BMS-treated patients.

Mechanism of LSM

In the present study, the main cause of LSM was an increase in EEM out of proportion to the increase in peristent P&M; as shown in Table 4, the increase in EEM was greater than the modest increase in P&M CSA (Table 4), and LSM CSA correlated directly with the increase in EEM CSA. These findings are similar to previous studies of LSM after BMS implantation,[1,2,10] although the magnitude of the vascular response appears to be different. However, these findings are somewhat (but not entirely) different from those reported by Tanabe et al.[5] Tanabe et al also reported that the cause of LSM was a significant increase in EEM CSA, but they did not find a difference between P&M CSA at follow-up compared with postimplantation.[5] The present study included 71 sirolimus-eluting and 14 paclitaxel-eluting stents with LSM; the study by Tanabe et al only included paclitaxel-eluting stents. Furthermore, 11 of 19 LSM segments in the study by Tanabe et al were of the moderate-release preparation. However, most importantly, both studies showed that the main cause of LSM was positive remodeling (an increase in EEM), not a decrease in plaque mass. When the sirolimus- and paclitaxel-eluting stents were compared, sirolimus-eluting stents with LSM had a smaller increase in EEM and P&M CSA, which suggests that the mechanism of LSM in sirolimus-eluting stents was a greater suppression of peristent neointimal hyperplasia (supported by the smaller amount of intrastent neointimal hyperplasia), whereas the mechanism of LSM in paclitaxel-eluting stents was a greater amount of peristent positive remodeling (Table 6).

Predictors of LSM

Our previous study showed that primary stenting in acute MI and prestent DCA were independent predictors of LSM after BMS implantation.[2] The IVUS substudy of TAXUS II reported that predictors of LSM after paclitaxel-eluting stent implantation were lesion length, unstable angina, and absence of diabetes.[5] In the present study, independent predictors of LSM after DES implantation were total stent length, primary stenting in acute MI, and CTO lesions. Because very long lesions are typically treated by multiple overlapping DESs, total stent length in the present study and lesion length in the previous study[5] shared similar concepts. The incidence of LSM after primary stenting in acute MI was 11.5% after BMS implantation in the previous study[2] and 31.8% after DES implantation in the present study. Compared with elective DES implantation, a higher incidence of LSM in acute MI patients might be explained by abluminal thrombus resolution[2] after primary stenting in acute MI patients. TAXUS II did not include acute MI patients, but thrombus dissolution may have also been important in unstable angina. The incidence of LSM in CTO lesions was 27.5% in the present study. Subintimal passage of the guidewire, creation of a false lumen, or stenting of the false lumen may result in injury to the adventitial layer during DES implantation of CTO lesions, contributing to LSM. Prestent DCA was an independent predictor of LSM in BMS implantation.[2,3] Although pre-DES DCA did not achieve statistical significance because of the small number of prestent DCA lesions, the incidence of LSM was 25.0% in the present study. Therefore, when a DES is implanted after DCA, a positive synergistic effect of LSM with DCA and DES on LSM should be expected. In the univariate statistical analysis of the present study, preintervention QCA MLD was significantly smaller in the LSM group than in the non-LSM group. This finding was consistent with our previous report of predictors of LSM after BMS implantation.[2] The common denominator may be vessel injury. Larger balloons or higher pressures may be necessary to optimize results after stenting of lesions with smaller or tighter MLDs.[2]

Postprocedural Incomplete Stent Apposition

The incidence of postprocedural incomplete stent apposition after DES was 7.2% in the present study, similar to the previous TAXUS II IVUS substudy.[5] However, unlike the present study, the TAXUS II IVUS substudy showed >50% resolution of postprocedure incomplete stent apposition at follow-up.[5] The reasons for this difference are unclear. In the present study, almost all postprocedural incomplete stent apposition was at the proximal edge of the stent; incomplete stent apposition within the body of the stent was typically resolved before the end of the procedure by additional balloon inflations. In order for incomplete apposition at the proximal edge of the stent to resolve, there would have to be plaque progression or negative remodeling at the proximal edge, something that was not observed in the present study. However, importantly, the long-term prognosis of persistent incomplete stent apposition was favorable in the present study, similar to the TAXUS II IVUS substudy.[5]

Long-Term Follow-Up After Detection of LSM

Previous studies have suggested that compared with non-LSM groups, LSM was not associated with any MACE after BMS

implantation[2] or in the TAXUS II and IV IVUS substudies.[5,9] In a study of 13 patients who received sirolimus-eluting stents and showed LSM at follow-up, there were no changes in IVUS-measured vessel dimensions and magnitude of LSM CSA, and there were favorable long-term clinical outcomes during the subsequent year.[11] The majority of lesions were treated with sirolimus-eluting stents in the present study. As in TAXUS II and IV[5,9] and the previously reported BMS group,[2] the present study showed favorable long-term clinical outcomes in LSM patients after implantation of sirolimus-eluting and paclitaxel-eluting stents.

Study Limitations

This was a retrospective, observational analysis from a single center. The relation between preintervention plaque characteristics and LSM was not evaluated. Sirolimus-eluting stents were used in most lesions in this study. This study was underpowered to show a difference in MACE rates between LSM and non-LAM patients.

Conclusions

In this single-center experience, LSM occurred in 12% of cases after DES implantation. The predictors of LSM were total stent length, primary stenting in acute MI, and CTO lesions. Importantly, LSM after DES implantation was not associated with any MACE during a mean 10-month follow-up after detection of LSM in the present study population.

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Disclosures

None.

References

1. Shah VM, Mintz GS, Apple S, Weissman NJ. Background incidence of late malapposition after bare-metal stent implantation. *Circulation*. 2002; 106:1753–1755.
2. Hong MK, Mintz GS, Lee CW, Kim YH, Lee SW, Song JM, Han KH, Kang DH, Song JK, Kim JJ, Park SW, Park SJ. Incidence, mechanism, predictors, and long-term prognosis of late stent malapposition after bare-metal stent implantation. *Circulation*. 2004;109:881–886.
3. Nakamura M, Kataoka T, Honda Y, Bonneau HN, Hibi K, Kitamura K, Tamai H, Aizawa T, Yock PG, Fitzgerald PJ. Late incomplete stent apposition and focal vessel expansion after bare metal stenting. *Am J Cardiol*. 2003;92:1217–1219.
4. Serruys PW, Degertekin M, Tanabe K, Abizaid A, Sousa JE, Colombo A, Guagliumi G, Wijns W, Lindeboom WK, Ligthart J, de Feyter PJ, Morice MC, for the RAVEL study group. Intravascular ultrasound findings in the multicenter, randomized, double-blind RAVEL (randomized study with the sirolimus-eluting velocity balloon-expandable stent in the treatment of patients with de novo native coronary artery lesions) trial. *Circulation*. 2002; 106:798–803.
5. Tanabe K, Serruys PW, Degertekin M, Grube E, Guagliumi G, Urbaszek W, Bonnier J, Lablanche JM, Siminiak T, Nordrehaug J, Figulla H, Drzewiecki J, Banning A, Hauptmann K, Dudek D, Bruining N, Hamers R, Hoye A, Ligthart JMR, Disco C, Koglin J, Russell ME, Colombo A, for the TAXUS II study group. Incomplete stent apposition after implantation of paclitaxel-eluting stents or bare metal stents: insights from the randomized TAXUS II trial. *Circulation*. 2005;111:900–905.
6. TIMI Study Group. The Thrombolysis and Myocardial Infarction (TIMI) trial: phase I findings. *N Engl J Med*. 1988;318:265–270.
7. Park SW, Hong MK, Moon DH, Oh SJ, Lee CW, Kim JJ, Park SJ. Treatment of diffuse in-stent restenosis with rotational atherectomy followed by radiation therapy with a rhenium-188-mercaptoacetyltriglycine-filled balloon. *J Am Coll Cardiol*. 2001;38:631–637.
8. Mintz GS, Nissen SE, Anderson WD, Bailey SR, Erbel R, Fitzgerald PJ, Pinto FJ, Rosenfield K, Siegel RJ, Tuzcu EM, Yock PG. American College of Cardiology clinical expert consensus document on standards for acquisition, measurement and reporting of intravascular ultrasound studies (IVUS): a report of the American College of Cardiology task force on clinical expert consensus documents. *J Am Coll Cardiol*. 2001;37:1478–1492.
9. Weissman NJ, Koglin J, Cox DA, Hermiller J, O'Shaughnessy C, Mann JT, Turco M, Caputo R, Bergin P, Greenberg J, Kutcher M, Wong SC, Strickland W, Mooney M, Russell ME, Ellis SG, Stone GW. Polymer-based paclitaxel-eluting stents reduce in-stent neointimal tissue proliferation: a serial volumetric intravascular ultrasound analysis from the TAXUS-IV trial. *J Am Coll Cardiol*. 2005;45:1201–1205.
10. Mintz GS, Shah VM, Weissman NJ. Regional remodeling as the cause of late stent malapposition. *Circulation*. 2003;107:2660–2663.
11. Degertekin M, Serruys PW, Tanabe K, Lee CH, Sousa JE, Colombo A, Morice MC, Ligthart JMR, de Feyter PJ. Long-term follow-up of incomplete stent apposition in patients who received sirolimus-eluting stent for de novo coronary lesions: an intravascular ultrasound analysis. *Circulation*. 2003;108: 2747–2750.

CLINICAL PERSPECTIVE

After drug-eluting stent (DES) implantation, late stent malapposition (LSM) has been more frequently observed in follow-up intravascular ultrasound (IVUS) study. The current study comprised 557 patients with 705 native lesions in whom IVUS was performed at index and 6-month follow-up after DES implantation. LSM occurred in 85 lesions (12%). IVUS substudies of the previous randomized SIRIUS and TAXUS trials reported the actual incidence of LSM (8.0% to 9.5%) after DES implantation and showed favorable long-term clinical outcomes of LSM after DES implantation. However, because complex lesions, including very long lesions, chronic total occlusion lesions, and thrombotic lesions, were excluded in the previous randomized trials, the actual incidence of LSM in a real-world daily practice could not be determined. In the present study of real-world patients, the actual incidence of LSM at a 6-month follow-up after DES implantation appeared to higher than in the randomized trials and appeared to be higher than in patients treated with bare-metal stents. As in the SIRIUS and TAXUS randomized trials, development of LSM after DES implantation in real-world patients with more complex lesion subsets was not associated with any major adverse cardiac events during a subsequent 10-month follow-up. Independent predictors of LSM after DES implantation in the present study were longer total stent length, primary stenting in acute myocardial infarction, and chronic total occlusion lesions. In conclusion, LSM occurs in 12% of patients after DES implantation. The long-term clinical outcomes in LSM after DES implantation were favorable in real-world patients.