Comprehensive Intravascular Ultrasound Assessment of Stent Area and Its Impact on Restenosis and Adverse Cardiac Events in 403 Patients With Unprotected Left Main Disease

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Background—We assessed the optimal intravascular ultrasound (IVUS) stent area to predict angiographic in-stent restenosis (ISR) after sirolimus-eluting stent implantation for unprotected left main coronary artery (LM) disease.

Methods and Results—A total of 403 patients treated with single- or 2-stent strategies (crushing and T-stent) had immediate poststenting IVUS and 9-month follow-up angiography. Poststenting minimal stent area (MSA) was measured in each of 4 segments: ostial left anterior descending (LAD), ostial left circumflex (LCX) polygon of confluence (POC, confluence zone of LAD and LCX), and proximal LM above the POC. Overall, 46 (11.4%) showed angiographic restenosis at 9 months: 3 of 67 (4.5%) nonbifurcation lesions treated with a single-stent, 14 of 222 (6.3%) bifurcation lesions treated with single-stent crossover, and 29 of 114 (25.4%) of bifurcation lesions treated with 2 stents. The MSA cutoffs that best predicted ISR on a segmental basis were 5.0 mm^2 (ostial LCX ISR), 6.3 mm^2 (ostial LAD ISR), 7.2 mm^2 (ISR within the POC), and 8.2 mm^2 (ISR within the LM above the POC). Using these criteria, 133 (33.8%) had underexpansion of at least 1 segment. Angiographic ISR (at any location) was more frequent in lesions with underexpansion of at least 1 segment versus lesions with no underexpansion (24.1% versus 5.4%, $P<0.001$). Two-year major adverse coronary event–free survival rate was significantly lower in patients with underexpansion of at least 1 segment versus lesions with no underexpansion ($90\pm3\%$ versus $98\pm1\%$, log-rank $P<0.001$), and poststenting underexpansion was an independent predictor for major adverse cardiac events (adjusted hazard ratio, 5.56; 95% confidence interval, 1.99–15.49; $P=0.001$).

Conclusions—With these criteria, IVUS optimization during LMCA stenting procedures may improve clinical outcomes. (*Circ Cardiovasc Interv*. 2011;4:562-569.)

Key Words: stent ■ imaging ■ diagnostic ■ coronary ■ restenosis

Although a feasible therapeutic alternative to bypass surgery for unprotected left main (LM) coronary artery stenosis,[1–4] percutaneous coronary intervention is still challenging even after in the drug-eluting stent (DES) era. Stent underexpansion has been the most important mechanism of DES failure including restenosis and stent thrombosis with a minimum stent area (MSA) of less than 5.0–5.5 mm^2 as the best intravascular ultrasound (IVUS) predictor for first-generation DES restenosis or early thrombosis.[5–7] However, there are no data suggesting the optimal MSA cutoff to predict restenosis and long-term clinical outcomes after DES treatment of a LM stenosis—especially since in-stent restenosis (ISR) can occur within any of the following 4 segments: the ostium of the left circumflex (LCX: the most common

site), the ostium of the left anterior descending (LAD), the polygon of confluence (POC) of the LAD and LCX, and the LM above the POC. Thus, the aim of this study was to assess (1) the optimal IVUS-MSA to prevent ISR within each of these 4 segments in patients undergoing sirolimus-eluting stent implantation for unprotected LM disease and (2) the impact of these criteria on clinical events.

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Methods

Between March 2003 and May 2009, a total of 450 patients with unprotected LM disease (angiographic diameter stenosis >50%) underwent sirolimus-eluting stent implantation (Cypher stent, Cordis, Johnson & Johnson, Miami Lakes, FL) and 9-month follow-up

WHAT IS KNOWN

- Although proper stent expansion is essential to prevent drug-eluting stent restenosis and thrombosis, the lack of data for the left main (LM) and both side branch ostia has limited the value of intravascular ultrasound optimization for LM stenting.

WHAT THE STUDY ADDS

- A smaller minimal stent area predicted angiographic in-stent restenosis at 9 months after drug-eluting stent implantation to treat LM disease.
- The best minimal stent area criteria that predicted angiographic restenosis on a segmental basis were 5.0 mm^2 for the left circumflex artery ostium, 6.3 mm^2 for the left anterior descending artery ostium, 7.2 mm^2 for the polygon of confluence, and 8.2 mm^2 for the proximal LM above the polygon of confluence.
- Poststenting underexpansion was an independent predictor for 2-year major adverse cardiac events, especially repeat revascularization.
- With the criteria, intravascular ultrasound optimization during LM stenting procedures may improve clinical outcomes.

angiographic surveillance at the Asan Medical Center, Seoul, Korea. Excluding 22 patients with kissing stent, 3 patients with single stent from LM to LCX (side branch crossover) and 22 patients without complete poststenting IVUS, a total of 403 patients treated with single-stent (main branch crossover) or 2-stent (including crushing and T-stent) techniques were included in this current study. All had immediate poststenting IVUS, 9-month angiography, and 2-year clinical follow-up data. Two-year major adverse cardiovascular events (MACE) were defined as death of cardiac cause, target lesion revascularization (TLR), and myocardial infarction. Revascularization was defined as ischemia-driven if there was angiographic diameter stenosis (DS) ≥50%, as documented by a positive functional study, ischemic changes on an ECG, or ischemic symptoms. In addition, the lesions with angiographic DS ≥70% assessed by quantitative coronary analysis were considered to be 'ischemia-driven even in the absence of documented ischemia. Myocardial infarction was diagnosed by the presence of ischemic symptoms or signs plus cardiac enzyme elevation (creatine kinase–myocardial band elevation >3 times or creatine kinase elevation >2 times the upper limit of normal or troponin I >1.5 ng/mL). We obtained written informed consent from all patients, and the ethics committee approved this study.

Coronary Angiography

Qualitative and quantitative angiographic analysis was done by standard techniques with automated edge-detection algorithms (CASS-5, Pie Medical, Maastricht, the Netherlands) in the angiographic analysis center of the CardioVascular Research Foundation, Seoul, Korea.[8–10] Angiographic stenosis was defined as >50% DS. The Medina classification was used to describe the location and distribution of lesions at the LM bifurcation.[11] The 4 prespecified segments—ostial LAD (5 mm-segment distal to the carina), ostial LCX (5 mm-segment distal to the carina), POC (confluence zone of LAD and LCX as described by Ramcharitar et al[12]), and proximal LM above the POC were evaluated poststenting and at follow-up. Angiographic ISR was assessed at each of these 4 segments separately and defined as >50% of DS at follow-up.
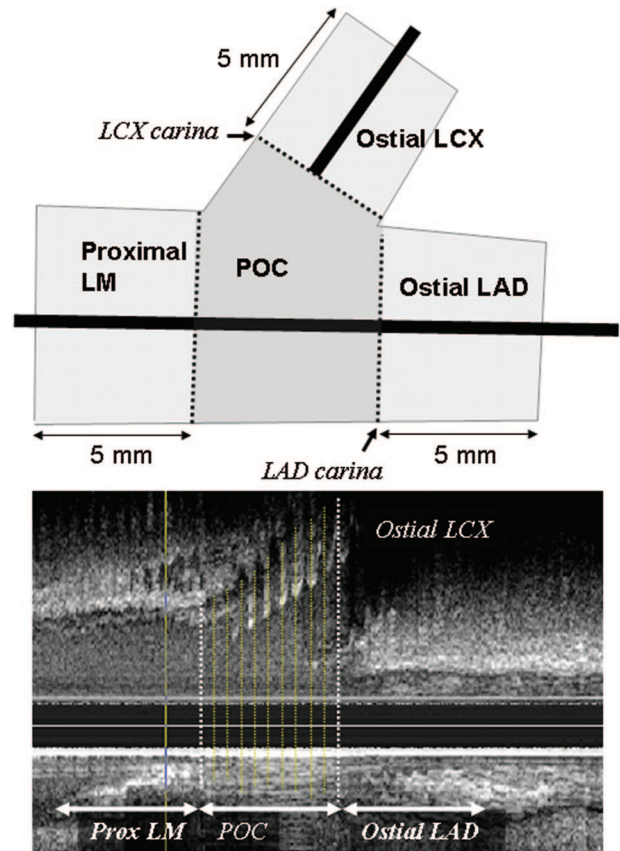

Figure 1. Intravascular ultrasound (IVUS) defined 4 segments within the left main (LM) bifurcation: (1) ostial left anterior descending artery (LAD) (5 mm-segment distal to the carina), (2) polygon of confluence (POC) (confluent zone of the LAD and left circumflex artery (LCX) on longitudinal IVUS image), (3) proximal LM above the POC (5-mm segment just proximal to the POC), all assessed by LAD pullback, and (4) ostial LCX (5-mm segment distal to the carina), assessed by LCX pullback.

Intravascular Ultrasound

Immediate poststenting IVUS imaging was performed after intracoronary administration of 0.2 mg nitroglycerin, using motorized transducer pullback (0.5 mm/s) and a commercial scanner (Boston Scientific/SCIMED, Minneapolis, MN) consisting of a rotating 30 or 40-MHz transducer within a 3.2F imaging sheath. Using computerized planimetry (EchoPlaque 3.0, Indec Systems, MountainView, CA), off-line IVUS analysis was performed.

LAD pullback was performed in all 403 lesions and used to assess the poststenting MSA within 3 of the 4 prespecified segments (Figure 1): ostial LAD (5 mm distal to the carina, defined as the frame immediately distal to the take-off of the side branch[13]), POC (confluence zone of LAD and LCX on longitudinal IVUS image reconstruction in parallel with the QCA-based definition), and proximal LM segment just above the POC (Figure 1 and Figure 2). Among 114 lesions treated with a 2-stent technique, LCX pullback was available in 104 (91%) and was used to assess the poststenting MSA within ostial LCX (5 mm distal to the carina, also defined as the frame immediately distal to the take-off of the side branch[13]). At the site of the MSA, the cross-sectional areas of external elastic membrane and peristent plaque surrounding stent were measured by 2D planimetry. Peristent plaque burden was calculated as plaque/external elastic membrane×100 (%). The IVUS MSA that best predicted angiographic ISR within each of these corresponding segments was then assessed.

Statistical Analysis

All statistical analyses were performed using SAS release 9.1 (SAS Institute Inc, Cary, NC) or SPSS (version 10.0, SPSS Inc, Chicago,
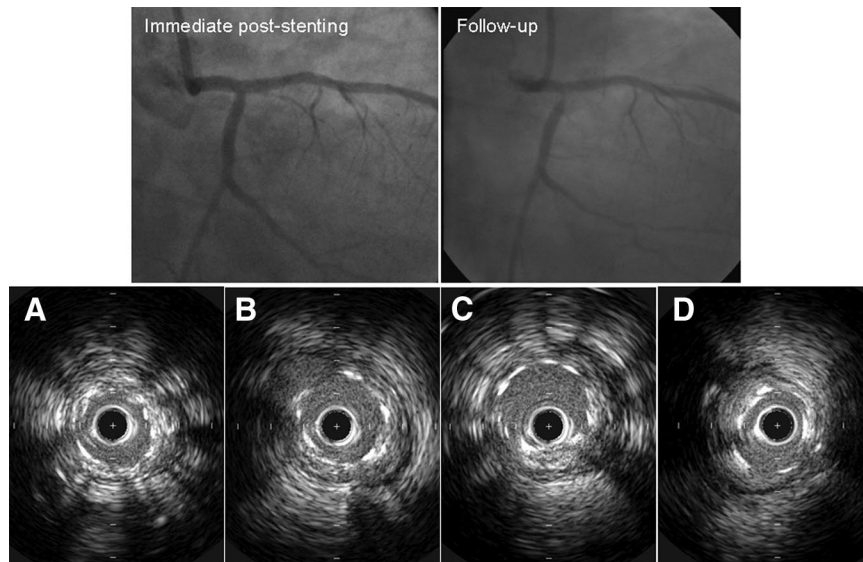
Figure 2. In a 60-year-old man, 2 Cypher stents were implanted at the left main (LM) bifurcation, using the crushing technique. Although immediate poststenting angiography showed a good result (**upper left**), intravascular ultrasound (IVUS) demonstrated underexpansion of all stented segments: **A**, minimal stent area (MSA) within the left anterior descending artery (LAD) ostium=5.0 mm²; **B**, MSA within the polygon of confluence (POC)=6.3 mm²; **C**, MSA within proximal LM=6.8 mm²; **D**, MSA within the left circumflex artery (LCX) ostium=4.0 mm². At 9-month follow-up, angiography revealed in-stent restenosis of the LCX ostium (**upper right**).

IL). All values are expressed as mean±1 SD (continuous variables) or as counts and percentages (categorical variables). Continuous variables were compared by use of the unpaired t test or nonparametric Mann-Whitney test; categorical variables were compared with the χ^2 statistics or Fisher exact test.

To predict angiographic ISR within each of the 4 prespecified segments, a receiver-operating curve was used to identify the optimal IVUS-MSA cutoff value that minimized the distance between the curve and upper the corner, using MedCalc (MedCalc Software, Mariakerke, Belgium). The sensitivity and specificity of each cutoff was obtained.

Cumulative incidence rates of 2-year adverse cardiac events were estimated by the Kaplan-Meier method and compared by the log-rank test. A Cox proportional hazard regression analyses were performed to find the predictors of long-term adverse outcomes. Variables with a probability value ≤0.20 in univariable analyses were candidates for the multivariable Cox proportional hazard regression models. A backward elimination process was used to develop the final multivariable model, and adjusted hazard ratio (HR) with 95% confidence intervals (CI) was calculated. A probability value <0.05 was considered statistically significant.

Results

Clinical, Procedural, and Angiographic Findings

The baseline characteristics and angiographic findings were summarized in Tables 1 and 2. Within the total cohort of 403 patients, 54 (13%) had only ostial and/or shaft LM disease and 349 (87%) had a distal LM stenosis that was classified as Medina (1, 1, 1) in 28%, (1, 1, 0) in 24%, (1, 0, 0) in 14%, (0, 1, 0) in 11%, (1, 0, 1) in 5%, and (0, 1, 1) in 4%. Table 3 summarizes the poststenting IVUS findings.

Angiographic Restenosis at 9-Month Follow-Up

With a follow-up duration of 8.5±3.6 months, 46 (11.4%) of 403 lesions had angiographic restenosis. Excluding 9 lesions with restenosis of a nonstented LCX ostium after crossover stenting, the overall ISR rate was 9.2%.

Figure 3 shows the incidences of angiographic restenosis according to the stent technique. Among 67 nonbifurcation lesions treated with a single stent, only 3 (4.5%) had ISR, and all involved the LM ostium. In 222 LM bifurcation lesions treated with a single-stent crossover, restenosis was observed in 14 (6.3%) lesions that included 15 restenotic segments (2 proximal

LM above the POC [13%], 1 POC [7%], 3 LAD ostium [20%], and 9 nonstented LCX ostium [60%]). In 114 LM bifurcation lesions treated with a 2-stent technique, the ISR rate was 25.4% (29/114), which included 46 ISR segments: 5 proximal LM above the POC (11%), 6 POC (13%), 8 LAD ostium (17%), and 27 LCX ostium (59%). Overall in this patient population, restenosis was more frequent after a 2-stent technique was used to treat a LM bifurcation versus a single-stent technique (25.4% [29/114] versus 6.3% [14/222], P<0.001).

IVUS Predictors for Angiographic ISR

The poststenting MSA within the LAD ostium was significantly smaller in lesions with ISR of the LAD ostium than

Table 1.   Clinical and Procedural Characteristics in 403 Patients

Age, y	59.8±9.9
Male, n (%)	289 (72%)
Hypertension, n (%)	208 (52%)
Diabetes, n (%)	139 (35%)
Smoking, n (%)	54 (32%)
Hyperlipidemia, n (%)	170 (42%)
Clinical manifestation	
Stable angina, n (%)	257 (64%)
Unstable angina, n (%)	123 (30%)
Acute myocardial infarction, n (%)	23 (6%)
Glycoprotein IIbIIIa, n (%)	53 (13%)
Intra-aortic balloon pump, n (%)	24 (6%)
Stent length, mm	40.1±24.0
Stent diameter, mm	3.5±0.3
Max balloon pressure, atm	17.1±3.5
Types of stent technique	
Isolated left main single stent	67 (17%)
Single-stent with main branch crossover	222 (55%)
Two-stent with crushing technique	99 (25%)
Two-stent with T-stent technique	15 (3%)

Table 2.   Angiographic Findings (n=403 Lesions)

	Prestenting	Poststenting	Follow-Up
MLD, LAD ostium, mm	1.7±0.8	2.8±0.5	2.7±0.6
DS, LAD ostium, %	29.9±19.9	8.9±8.8	14.6±13.9
MLD, POC, mm	2.6±8.1	3.5±0.5	3.3±0.5
DS, POC, %	42.2±17.4	8.2±8.3	12.5±12.1
MLD, LM, mm	1.9±0.5	3.4±0.4	3.2±0.6
DS, LM, %	49.4±13.9	7.7±8.3	12.7±12.8
MLD, LCX ostium, mm	2.2±0.7	2.5±0.5	2.3±0.6
DS, LCX ostium, %	29.8±19.9	17.2±12.5	24.6±16.7
Distal carina angle, degree	74.7±28.0	74.7±25.0	
Proximal carina angle, degree	117.6±29.3	114.7±26.9	
TIMI 3 flow in LM-LAD	88%	100%	99%
TIMI 3 flow in LCX	93%	100%	99%

MLD indicates minimum lumen diameter; LAD, left anterior descending artery; DS, diameter stenosis; POC, polygon of confluence; LM, left main; LCX, left circumflex artery; and TIMI, Thrombolysis In Myocardial Infarction grade.

those without (6.1±1.2 mm^2 versus 8.2±1.7 mm^2, $P<0.001$). Using receiver-operating curve analysis, the IVUS-MSA cutoff value that predicted LAD ostial ISR was 6.3 mm^2 (area under the curve [AUC], 0.847; 95% CI, 0.80–0.88; sensitivity, 73%; specificity, 85%).

Lesions with ISR within the POC had a smaller poststenting MSA within the POC compared with those without (6.2±0.8 mm^2 versus 8.8±1.9 mm^2, $P=0.001$). An IVUS-MSA within the POC <7.2 mm^2 best predicted ISR within the POC (AUC, 0.909; 95% CI, 0.87–0.94; sensitivity, 100%; specificity, 78%).

A smaller MSA within the proximal LM was seen in lesions with ISR of the LM proximal to the POC compared with those without ISR (7.3±1.4 mm^2 versus 10.3±2.4 mm^2, $P<0.001$). The IVUS-MSA cutoff within the proximal LM above the POC that best predicted ISR within the POC was 8.2 mm^2 (AUC, 0.868; 95% CI, 0.83–0.90; sensitivity, 80%; specificity, 81%).

Among 104 lesions that were treated with 2-stent technique and had poststenting LCX pullback IVUS images, 26% (27/104) showed ISR at the LCX ostium. Poststenting MSA within the LCX ostium correlated with follow-up angiographic DS of the LCX ostium ($r=-0.47$, $P<0.001$). Compared with non-ISR lesions, lesions with ISR at the LCX ostium had a smaller MSA within the LCX ostium (4.5±0.8 mm^2 versus 6.0±1.3 mm^2, $P<0.001$) as well as a greater peristent plaque burden (58.0±10.7% versus 49.6±7.8%, $P<0.001$). The IVUS-MSA cutoff within the LCX ostium that best predicted ISR of the LCX ostium was 5.0 mm^2 (AUC, 0.852; 95% CI, 0.77–0.91; sensitivity, 78%; specificity, 78%).

Underexpansion and ISR
When underexpansion was defined as a poststentng IVUS-MSA <5.0 mm^2 at the LCX ostium, <6.3 mm^2 at the LAD ostium, <7.2 mm^2 at the POC, or <8.2 mm^2 at the LM above the POC (Figure 4); 56 (54%) of 104 lesions treated with 2 stents had underexpansion in at least 1 of the 4 prespecified segments. Angiographic ISR (at any stented segment) was observed in 26 (46%) of 56 patients with underexpansion of at least 1 segment; conversely, angiographic ISR was seen in only 3 (6%) of 48 patients with adequate expansion at all

Table 3.   Poststenting IVUS Findings

	Total	Single Stent	Two-Stent	P Value
LAD ostium, n†	336	222	114	
MSA, mm^2	8.1±1.8	8.3±1.8	7.8±1.7	0.015
EEM area at the MSA, mm^2	16.6±3.7	16.8±3.8	16.3±3.4	0.172
Peristent plaque burden, %	50.6±8.0	50.0±8.2	51.7±7.4	0.067
MSA <6.3 mm^2	58 (17%)	29 (13%)	29 (25%)	0.004
POC, n†	336	222	114	
MSA, mm^2	8.7±1.9	9.1±1.9	8.1±1.8	<0.001
MSA <7.2 mm^2	77 (23%)	40 (18%)	37 (33%)	0.003
Proximal LM above the POC, n	403	289	114	
MSA, mm^2	10.2±2.4	10.0±2.2	10.5±2.8	0.055
EEM area at the MSA, mm^2	21.8±5.1	21.8±5.2	21.8±4.7	0.936
Peristent plaque burden, %	52.2±9.2	53.0±9.0	50.2±9.3	0.007
MSA <8.2 mm^2	83 (21%)	60 (21%)	23 (20%)	0.896
LCX ostium, by LCX pullback,* n			104	
MSA, mm^2			5.6±1.4	
EEM area at the MSA, mm^2			11.8±2.8	
Peristent plaque burden, %			51.7±9.3	
MSA <5.0 mm^2			38 (37%)	

LAD indicates left anterior descending artery; MSA, minimal stent area; EEM, external elastic membrane; POC, polygon of confluence; LM, left main; and LCX, left circumflex artery.

*LCX pullback was performed in 104 of 114 lesions treated with a 2-stent technique.

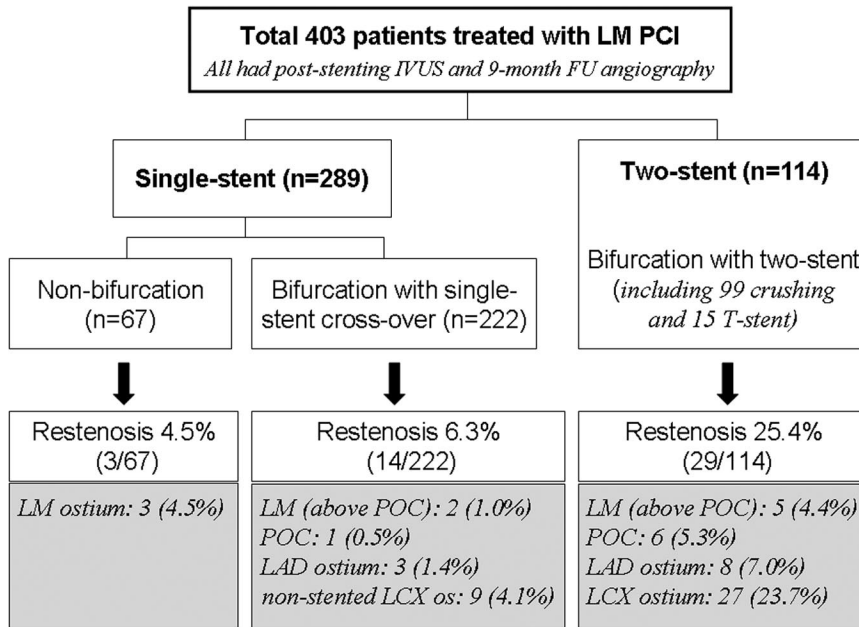†Sixty-seven lesions with stent placement at ostium or shaft were excluded.

Figure 3. Incidence of angiographic restenosis in single- and 2-stent groups. LM indicates left main coronary artery; PCI, percutaneous coronary interventions; POC, polygon of confluence; LAD, left anterior descending artery; LCX, left circumflex artery.

sites. The LCX ostium was the most common site of underexpansion (Figure 3).

On the other hand, in the 289 LM lesions treated with a single-stent (including 67 nonbifurcation lesions and 222 bifurcation lesions with stent crossover), 77 (27%) showed underexpansion in at least 1 of the 3 stented segments: ostial LAD, POC, or LM above the POC. The incidence of angiographic ISR (at any segment) was higher in patients with underexpansion of at least 1 of the 3 segments versus those without underexpansion (6.5% [5/77] versus 1.4% [3/212], $P=0.020$).

Thus, in the overall cohort of 393 patients (104 treated with 1 stent and 289 treated with 2 stents) who complete poststenting IVUS assessment for all stented segments (10 did not have imaging of the LCX ostium), 133 (33.8%) had underexpansion at least 1 stented segment. The rate of ISR (at any

one of the stented segments) was much higher in the presence of underexpansion of at least 1 segment compared with lesions without any underexpansion (24.1% [32/133] versus 5.4% [14/260], $P<0.001$). In addition, any stent underexpansion was more frequent in the 2-stent group than in the single-stent group (54% [56/104] versus 27% [77/289], $P<0.001$).

Figure 5 shows the frequencies of underexpansion and ISR in each of the stented segments. Especially, 37% of the LCX ostia had an MSA <5.0 mm^2, and more than half of those had ISR at the LCX ostium at follow-up.

Underexpansion as a Predictor of Adverse Clinical Outcomes

The mean clinical follow-up duration was 23.8 ± 3.2 months (median, 24.0 months; interquartile range, 21.9–25.8 months). A total of 19 (4.8%) patients had 2-year MACE. TLR was performed in 16 (4.1%) patients (3 coronary artery bypass surgery and 13 percutaneous coronary intervention). Four (1%) patients died of cardiac causes, and 2 (0.5%) patients had an acute myocardial infarction related to very late stent thrombosis. The cumulative MACE-free survival rate was significantly lower in patients with underexpansion of any segment versus patients without any underexpansion ($90.2\pm2.6\%$ versus $98.1\pm0.9\%$ at 2 years, log-rank $P<0.001$, Figure 6), as was TLR-free survival ($90.9\pm2.4\%$ versus $98.5\pm0.7\%$ at 2 years, log-rank $P<0.001$). Using the multivariable Cox model, poststenting underexpansion was an independent predictor for the occurrence of MACE (adjusted HR, 5.56; 95% CI. 1.99–15.49; $P=0.001$) as well as TLR at follow-up (adjusted HR, 6.08; 95% CI, 1.94–19.02; $P=0.002$; Table 4).

Although acute malapposition was observed in 28 lesions (25 malapposition within the LM and 3 malapposition within the LAD ostium), malapposition was related to neither ISR nor MACE at follow-up.
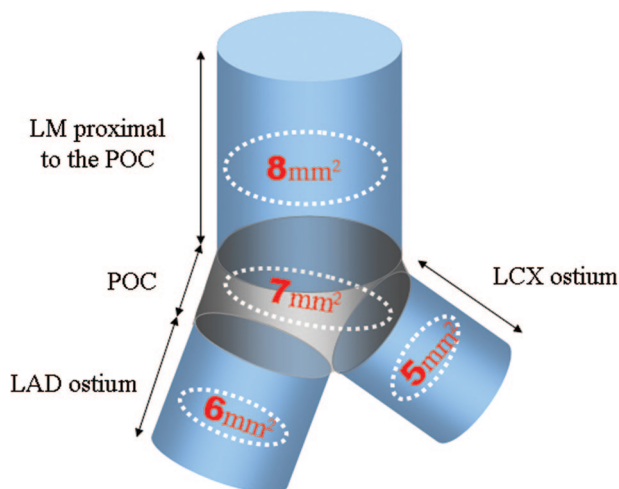

Figure 4. Minimal stent area (MSA) cutoff values for the prediction of angiographic in-stent restenosis (ISR) on a segmental basis. LM indicates left main artery; POC, polygon of confluence; LAD, left anterior descending artery; LCX, left circumflex artery.
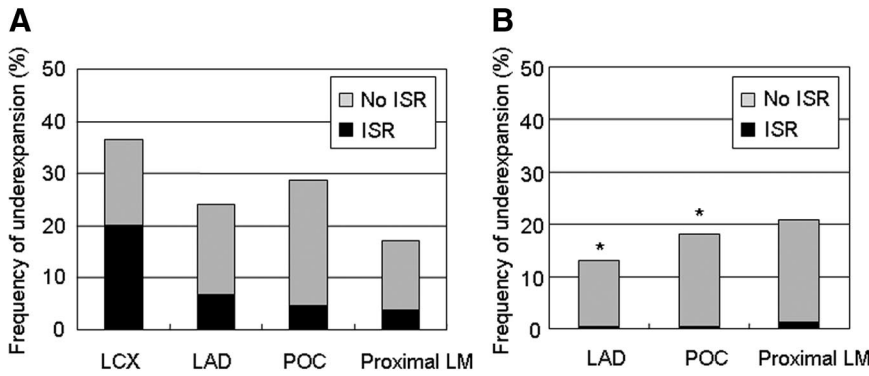
Figure 5. A, Frequency of underexpansion in the 2-stent group (n=104). Left circumflex artery (LCX) ostium was the most common site of underexpansion (37%); and in-stent restenosis (ISR) developed at in 55% of the underexpanded LCX ostia. **B**, Frequency of underexpansion in the single-stent group (n=289 including 67 nonbifurcation stents and 222 bifurcation lesions treated with a 1-stent crossover technique). The rate of underexpansion at the left anterior descending artery (LAD) ostium and polygon of confluence (POC) was significantly lower in the single-stent group versus the 2-stent group, $P<0.05$.

Discussion

The major findings of this study of 403 LM lesions treated with DES implantation and IVUS imaging of both the LAD and LCX were the following. (1) Compared with the high rate of ISR in LM bifurcation lesions with 2 stents (25.4%), bifurcation lesions with a single stent showed a lower restenosis rate (6.3%) that was similar to nonbifurcation lesions (4.5%); (2) A smaller IVUS-MSA predicted angiographic ISR at 9 months after DES implantation to treat LM disease; (3) The best IVUS-MSA criteria that predicted angiographic ISR on a segmental basis were 5.0 mm^2 for the LCX ostium, 6.3 mm^2 for the LAD ostium, 7.2 mm^2 for the POC, and 8.2 mm^2 for the proximal LM above the POC; (4) Poststenting underexpansion was an independent predictor for 2-year MACE, especially repeat revascularization; (5) Stent malapposition did not predict ISR or MACE.

Proper stent expansion is essential to prevent DES restenosis and thrombosis.[14–16] Nevertheless, the lack of data for the LM and ostia of the LAD and LCX has limited the value of IVUS optimization for LM stenting.

The current study may be unique in that LM bifurcation lesions were divided into 4 segments, and each segment was independently assessed. Bifurcation lesions are complex and among the most difficult to evaluate using intravascular imaging. The current approach has been selected to be comprehensive, and we propose that similar methodology be used to assess other bifurcation lesion subsets, especially when defining predictors of restenosis.

Although patients in this current study underwent percutaneous coronary intervention under IVUS guidance, one-third had stent underexpansion within at least 1 stented segment as defined retrospectively by the ROC cut-points. Consequently, the rate of 9-month angiographic ISR was as high as 24% in the presence of underexpansion within at least 1 segment compared with only 5% in lesions with adequate expansion of all segments.

As expected, the frequency of underexpansion in the 2-stent group was twice as high as the 1-stent group. Because LCX ostium has been reported to be the most common site of ISR, the higher frequency of underexpansion, especially at the LCX ostium, can explain the greater risk of ISR when LM bifurcation lesions are treated with a 2-stent strategy.[17]

As an independent predictor for restenosis, poststenting underexpansion contributed to the occurrence of adverse cardiovascular events mainly driven by a statistically significant lower rate of TLR. Because a well-expanded stent can provide more room for intimal hyperplasia, interventionists should focus on correction of stent underexpansion, a preventable mechanism of ISR, using IVUS-guidance during the procedure.

This current study included only lesions treated with sirolimus-eluting stents that have only a minimal amount of intimal hyperplasia. However, the results may be applicable to any DES as long as the late loss is small. Thus, we believe that the suggested MSA criteria may be a practical guideline for optimization of 2-stent procedure in LM bifurcation disease.

Finally, incomplete stent apposition poststenting was related to neither restenosis nor MACE, consistent with previous studies evaluating non-LM lesions treated with stenting.[18–20]
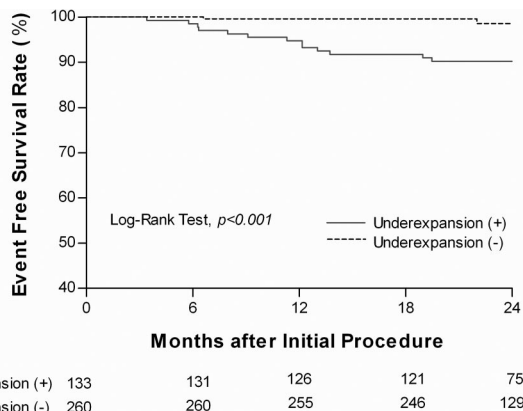
Limitations

Because preintervention IVUS analysis was not performed in all patients, the implication of preprocedural lesion characteristics on the clinical outcomes was not assessed. Although the importance of pullback IVUS images from both the LAD and LCX both prestenting and poststenting has been emphasized, this could not be completed in some patients due to the technical difficulty in passing the guide wire and/or the short-monorail IVUS catheter into the side branch through tight turns, tight lesions, and/or stent struts. Because poststenting LCX pullback was not checked in most single-stent lesions with main branch crossover, IVUS predictors for

Figure 6. Kaplan-Meier curve for major adverse cardiac event (MACE)-free survival.

Table 4. Hazard Ratios of Adverse Cardiac Events for Poststenting Underexpansion Versus Adequate Expansion

	Univariable Analysis			Multivariable Analysis		
	Crude Hazard Ratio	95% CI	P Value	Adjusted Hazard Ratio	95% CI	P Value
Major adverse cardiac events	5.504	1.981–15.290	0.001	5.557*	1.993–15.491	0.001
Target lesion revascularization	5.863	1.889–18.195	0.002	6.080†	1.944–19.015	0.002
Myocardial infarction	NS			NS		
Death of cardiac cause	4.246	0.436–41.315	0.213	3.113‡	0.299–32.443	0.342

CI indicates confidence interval.

*Adjusted by sex, age, and diabetes.

†Adjusted by sex and diabetes.

‡Adjusted by age.

Criteria for underexpansion=at least 1 of the following: minimal stent area <5.0 mm^2 at the left circumflex artery ostium, <6.3 mm^2 at the left anterior descending artery ostium, <7.2 mm^2 at the polygon of confluence, and <8.2 mm^2 at the proximal left main artery.

restenosis of nonstented LCX ostium were not evaluated. The current study included patients who had poststenting IVUS and 9-month follow-up angiography; therefore, the possibility of selection bias was not entirely excluded. Furthermore, the relatively low rates of ISR, except at the LCX ostium, and cardiac events may affect the current data. Finally, further study is necessary for stent optimization considering vessel size and amount of supplied myocardium.

Conclusion

The LM bifurcation was divided into 4 segments to perform a comprehensive analysis of predictors of restenosis. A smaller IVUS-MSA within any one of these segments was responsible for a higher rate of angiographic ISR and clinical MACE. Thus, correcting underexpansion with these optimal IVUS criteria using IVUS guidance during LM stenting procedures may reduce cardiac events after DES treatment for unprotected LM disease.

Disclosures

None.

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