Effect of Intravascular Ultrasound Findings on Long-Term Repeat Revascularization in Patients Undergoing Drug-Eluting Stent Implantation for Severe Unprotected Left Main Bifurcation Narrowing

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We studied the effect of the preprocedural intravascular ultrasound findings on stent expansion and the pre- and postprocedural findings on the long-term clinical outcomes in patients undergoing drug-eluting stent implantation for unprotected left main (LM) bifurcation disease. Using a left anterior descending (LAD) pullback, we evaluated the ostial LAD artery (3 mm distal to the carina), the polygon of confluence (POC; the confluent zone of the LAD artery and left circumflex artery), and the distal LM artery (3 mm just proximal to the POC). The measurements included the minimum lumen area (MLA) and minimum stent area within each segment. In 168 LM bifurcations, the preprocedural MLA and post-stenting minimum stent area within the LM artery were located within the POC in 41% and 70%, respectively. Independent predictors for the post-stent minimum stent area within the distal portion of LM artery above the LAD carina were the preprocedural lumen area of the LAD carina ($\beta = 0.253$, 95% confidence interval [CI] 0.10 to 0.36, $p = 0.001$) and preprocedural MLA within the POC ($\beta = 0.205$, 95% CI 0.04 to 0.23, $p = 0.008$). During the 41.8 ± 18.0-month follow-up period, 26 patients experienced cardiac events. In the multivariate Cox model, female gender (adjusted hazard ratio 2.56, 95% CI 1.173 to 5.594, $p = 0.018$) and preprocedural MLA within the POC (adjusted hazard ratio 0.829, 95% CI 0.708 to 0.971, $p = 0.020$) were independent predictors for the occurrence of events at 3 years of follow-up. In conclusion, as assessed by the LAD pullback, the preprocedural MLA within the POC was a surrogate reflecting the overall severity of LM bifurcation disease, contributed to the post-stent minimum stent area within the distal segment of LM bifurcation, and was a predictor of clinical events during follow-up. © 2011 Published by Elsevier Inc. (Am J Cardiol 2011;107:367–373)

Drug-eluting stent implantation for unprotected left main (LM) coronary artery stenosis has been evolving into a feasible therapeutic alternative to bypass surgery, especially in patients at very high surgical risk.[1–5] However, irrespective of the stent implantation strategy, the LM bifurcation location is a major determinant of adverse outcomes, even in the drug-eluting stent era.[6,7] The intravascular ultrasound (IVUS) examination can provide unique insights into the extent and distribution of coronary atherosclerosis. However, no data are available suggesting the pre- and postprocedural IVUS predictors of adverse events after drug-eluting stent implantation into distal LM bifurcation stenoses. The aims of the present study were to assess the distribution patterns of atherosclerotic plaque and the severity of bifurcation LM stenosis and the effect of the IVUS lesion characteristics on stent expansion and the long-term clinical outcomes in patients undergoing drug-eluting stent implantation for unprotected distal bifurcation LM disease.

Methods

From February 2003 to November 2007, 509 patients with unprotected LM disease (angiographic diameter stenosis >50%) underwent percutaneous coronary intervention with drug-eluting stent implantation at the Asan Medical Center (Seoul, Korea). Of these 509 patients, 168 with distal LM bifurcation lesions underwent preprocedural IVUS obtained by pullback from the left anterior descending artery (LAD) to the LM (LAD pullback). All patients had immediate post-stenting LAD pullback images available.

All patients underwent either routine angiographic surveillance at 6 to 12 months or clinically driven repeat angiography (follow-up period 16.6 ± 15.5 months). After the angiographic follow-up examination, noninvasive stress

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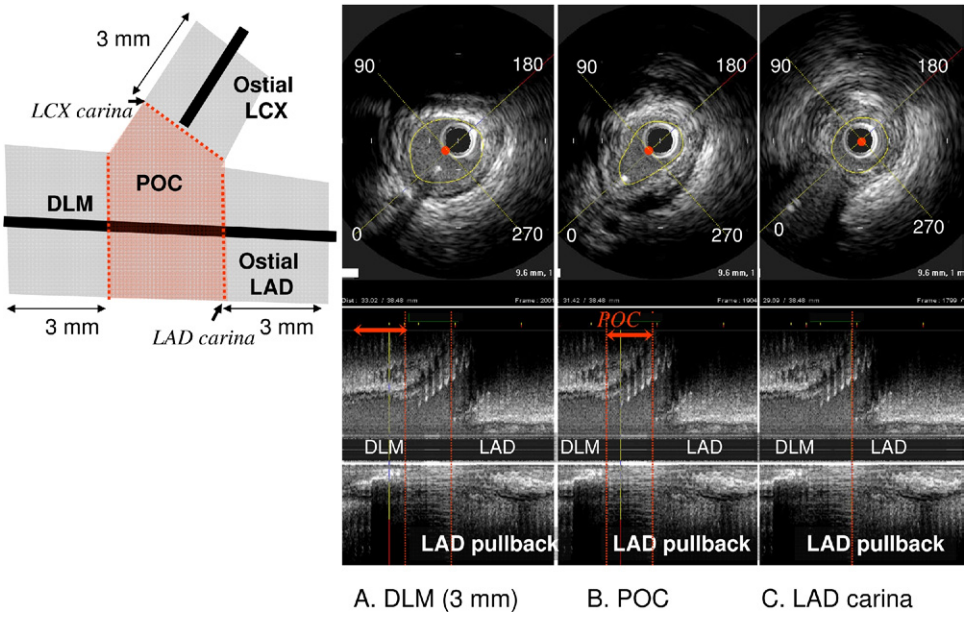

Figure 1. *(Left)* Four segments of LM bifurcation assessed by LAD pullback image. Ostial LAD is 3-mm segment distal to carina; POC is confluence zone of LAD and left circumflex artery (LCX) on longitudinal IVUS image. Distal LM (DLM) is 3-mm segment just proximal to POC. Separately assessed by LCX pullback, ostial LCX defined as 3-mm segment distal to carina. *(Right)* Circumferential distribution of plaque at MLA site of each segment of LM bifurcation by LAD pullback. Using protractor centered on lumen, arc of circumferential distribution of significant plaque (>6-mm thickness) measured in clockwise direction. The direction of the take-off of the side branch was taken as 0°.

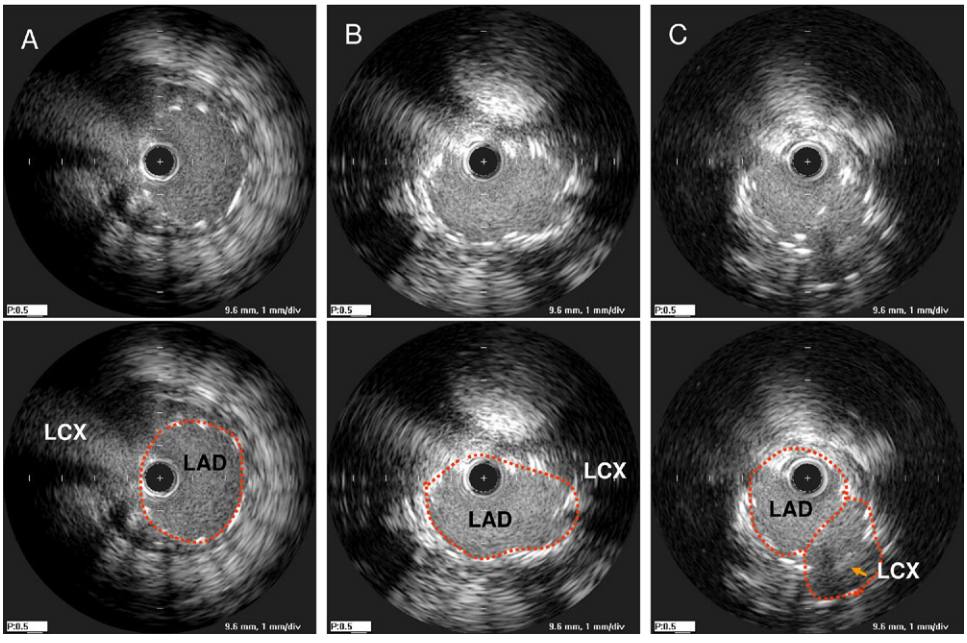

Figure 2. Measurement of minimum stent area (MSA) within POC in LM bifurcation treated with different stent techniques. *(A)* Single-stent technique, *(B)* 2-stent with crushing technique, and *(C)* 2-stent with kissing technique. LCX, left circumflex artery.

testing was performed annually. Inducible ischemia on a stress test (with or without ischemic chest pain) was regarded as a clinical indicator for angiography. The clinical follow-up period was 42.0 ± 17.8 months. Major adverse cardiovascular events were defined as death from cardiac causes, target lesion revascularization, and myocardial infarction. Myocardial infarction was diagnosed by the presence of ischemic symptoms or signs plus cardiac enzyme elevation (creatine kinase-MB elevation >3 times or creatine kinase elevation >2 times the upper limit of normal). All patients provided written informed consent, and the ethics committee approved the present study.

Qualitative and quantitative angiographic analysis was done using standard techniques with automated edge-detection algorithms (CASS-5, Pie-Medical B.V., Maastricht, The Netherlands) in the angiographic analysis center of the

Table 1
Clinical and procedural data in 168 left main (LM) bifurcations

Variable	Bifurcating LM
Age (years)	59.4 ± 10.8
Men	126 (75%)
Hypertension	83 (49%)
Diabetes mellitus	54 (32%)
Smoker	54 (32%)
Hyperlipidemia*	66 (39%)
Clinical manifestation	
Stable angina pectoris	85 (51%)
Unstable angina pectoris	81 (48%)
Acute myocardial infarction	2 (1%)
Glycoprotein IIb/IIIa	21 (13%)
Intra-aortic balloon pump	11 (7%)
Drug-eluting stent type	
Cypher	161 (96%)
Taxus	6 (4%)
Stent length (mm)	40.7 ± 22.0
Stent diameter (mm)	3.4 ± 0.2
Maximum balloon pressure (atm)	17.5 ± 3.1
Types of 2-stenting techniques	
T stenting	10 (15%)
Crush stenting	37 (54%)
Kissing stents	21 (30%)
Culotte technique	1 (1%)

* Defined as total cholesterol >200 mg/dl or taking antilipidemic medication.

Cardiovascular Research Foundation (Seoul, Korea).[8–10] Angiographic stenosis was defined as >50% diameter stenosis. At follow-up, in-stent restenosis was defined as >50% diameter stenosis anywhere within the LM artery or within 5 mm distal to the LAD artery or left circumflex artery ostia. The Medina classification was used to describe the location and distribution of lesions at the LM bifurcation.[11]

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, Minnesota) consisting of a rotating 30- or 40-MHz transducer within a 3.2Fr imaging sheath. Using computerized planimetry (EchoPlaque, version 3.0, Indec Systems, MountainView, California), offline IVUS analysis was performed.

The carina was identified as the frame immediately distal to the take-off of the side branch.[12] In the present study, most patients did not undergo left circumflex artery pullback. Therefore, on the LAD pullback, 3 segments within the LM bifurcation were defined (Figure 1): the ostial LAD (3 mm distal to the carina), the polygon of confluence (POC; confluence zone of the LAD and left circumflex artery on longitudinal IVUS image reconstruction in parallel with the quantitative coronary analysis-based definition suggested by Ramcharitar[13]), and the distal LM (3 mm just proximal to the POC). At the site of the minimum lumen area (MLA) within each of these 3 segments, the cross-section areas of lumen, stent, and external elastic membrane were measured using 2-dimensional planimetry. The plaque burden was calculated as the plaque + media/external elastic membrane × 100%. The IVUS criteria for a significant stenosis was an MLA <4.0 mm^2 at the LAD ostium and an MLA <6.0 mm^2 at the distal LM (including the distal LM and POC).

Table 2
Diagnostic accuracy of angiographic diameter stenosis in left main (LM) bifurcation compared to intravascular ultrasound (IVUS)-measured minimum lumen area (MLA)

Angiographic Diameter Stenosis	IVUS-Defined Minimum Lumen Area (mm^2)	
Distal left main*	≥6.0	<6.0
≤50%	23	4
>50%	33	108
Ostial left anterior descending†	≥4.0	<4.0
≤50%	25	4
>50%	51	89

* Sensitivity 97%, specificity 33%, positive predictive value 64%, and negative predictive value 89%.
† Sensitivity 96%, specificity 41%, positive predictive value 77%, and negative predictive value 85%.

Table 3
Pre- and post-stenting intravascular ultrasound (IVUS) analysis in 168 left main bifurcations

IVUS Findings	Value
Preprocedural	
At minimum lumen area site of ostial left anterior descending artery	
Lumen area (mm^2)	4.0 ± 2.1
External elastic membrane area (mm^2)	12.6 ± 3.5
Plaque burden (%)	66.9 ± 13.9
At carina of LAD	
Lumen area (mm^2)	4.5 ± 2.3
External elastic membrane area (mm^2)	13.4 ± 3.8
Plaque burden (%)	65.7 ± 14.5
Minimum lumen of polygon of confluence (mm^2)	6.4 ± 3.1
At minimum lumen area of distal left main	
Lumen area (mm^2)	5.8 ± 3.0
External elastic membrane area (mm^2)	18.7 ± 5.5
Plaque burden (%)	68.2 ± 13.9
Post-stenting	
Minimal stent area within polygon of confluence (mm^2)	8.5 ± 2.3
Minimal stent area within distal left main (mm^2)	9.8 ± 2.7
Minimal stent area within distal portion of left main above carina (mm^2)	8.1 ± 2.0
Minimal stent area within ostial left anterior descending artery (mm^2)	7.5 ± 1.8
Minimal stent area within ostial left circumflex artery (mm^2)* (n = 66)	6.1 ± 2.1

* Data obtained from left circumflex artery pullback in 66 lesions; minimum lumen area was equivalent to minimum stent area in 2-Stent group.

The circumferential plaque distribution was assessed at the MLA sites of each segment. Using a protractor centered on the lumen, the arc of the circumferential distribution of significant plaque (>0.6-mm plaque thickness) was measured in a clockwise direction using the take-off of the side branch as 0° (Figure 1).[14]

Immediately after stenting, 3 segments (distal LM, POC, and LAD ostium) were identified in parallel with the preprocedural assessments. The minimum stent area was measured within each segment. In addition, the minimum stent

Table 4
Pre- and post-stenting intravascular ultrasound (IVUS) findings according to different stent techniques in 168 left main bifurcation lesions

Techniques	Patients (n)	Preprocedural MLA Within				Post-Stenting MLA Within			
		Distal LM (mm^2)	POC (mm^2)	LAD Ostium (mm^2)	Left Circumflex Artery Ostium (mm^2)*	Distal LM (mm^2)	POC (mm^2)	LAD Ostium (mm^2)	Left Circumflex Artery Ostium (mm^2)†
Single stent	99	6.2 ± 3.2	7.1 ± 3.3	4.4 ± 2.1	6.1 ± 3.1	9.6 ± 2.4	8.5 ± 2.2	7.8 ± 1.9	7.5 ± 2.6
Two stent	69	5.3 ± 2.7	5.3 ± 2.6‡	3.6 ± 2.0‡	3.6 ± 1.4‡	10.0 ± 3.0	8.5 ± 2.6	7.5 ± 2.0	5.7 ± 1.8‡
T-stent	10	5.6 ± 2.4	4.6 ± 2.2‡	3.3 ± 1.1	3.0 ± 1.4‡	10.2 ± 1.9	6.7 ± 1.6‡§	7.8 ± 1.4§	5.0 ± 2.5‡
Crush	37	5.3 ± 2.8	5.4 ± 2.9‡	3.8 ± 2.5‡	3.7 ± 1.8‡	10.1 ± 3.4	7.6 ± 1.6‡§	7.3 ± 1.8	6.1 ± 1.8
Kissing	21	5.1 ± 3.1	5.3 ± 2.1‡	3.5 ± 1.2	3.7 ± 1.5‡	9.8 ± 3.0	11.1 ± 2.5‡	6.4 ± 1.4‡	5.5 ± 1.2‡
Culotte	1	5.7	7.0	2.6	3.20	13.0	6.6	7.5	5.2
Total	168	5.8 ± 3.0	6.4 ± 3.1	4.0 ± 2.1	4.5 ± 2.5	9.8 ± 2.7	8.5 ± 2.3	7.5 ± 1.8	6.1 ± 2.1

* Data obtained using left circumflex artery pullback before stenting in 72 lesions (25 in single-stent group, 7 T-stent, 29 crushing, 10 kissing, and 1 culotte).

† Data obtained by post-stenting left circumferential artery pullback in 66 lesions (post-stenting MLA measured in single-stent group in 13), and minimum stent area (equivalent to MLA) measured in 2-stent group (n = 53; 8 T-stent, 29 crushing, 15 kissing, 1 culotte).

‡ $p < 0.05$ vs single-stent (nonparametric, Mann-Whitney *U* test);§ $p < 0.05$ vs kissing technique (nonparametric, Mann-Whitney *U* test).

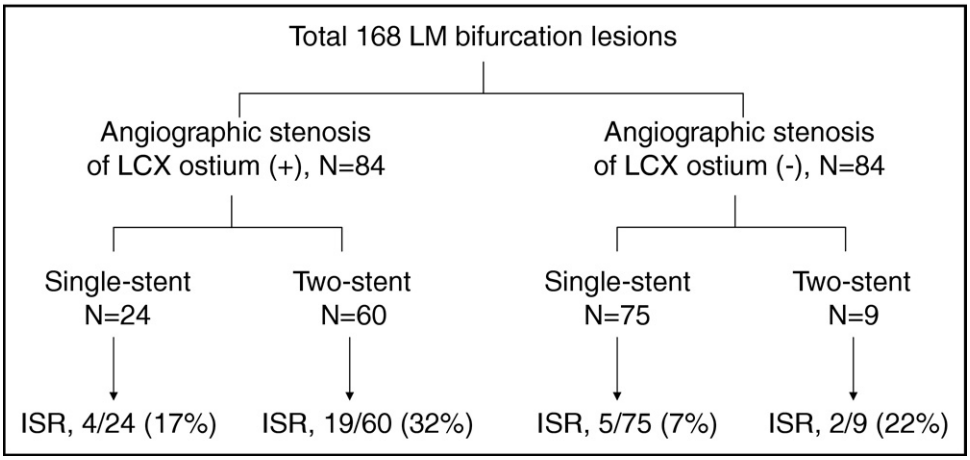

Figure 3. Rate of in-stent restenosis (ISR) according to presence of preprocedural angiographic stenosis of left circumflex artery (LCX) and applied stent techniques.

area within the distal portion of LM above the LAD carina (to include both the distal LM and the POC) was tabulated. In lesions treated with a kissing technique, the minimum stent area within the POC included both stents (Figure 2).

A post-stenting left circumflex artery pullback IVUS examination was performed in 66 lesions. The post-stenting MLA in the single-stent group and the post-stenting minimum stent area in the 2-stent group were measured <3 mm distal to the carina.

All statistical analyses were performed using Statistical Analysis Systems, release 9.1 (SAS Institute, Cary, North Carolina), or the Statistical Package for Social Sciences, version 10.0 (SPSS, Chicago, Illinois). All values are presented as the mean ± SD for continuous variables or counts and percentages for categorical variables. Continuous variables were compared using the unpaired *t* test or nonparametric Mann-Whitney *U* test. Categorical variables were compared using the chi-square statistics or Fisher's exact test.

Stepwise multiple linear regression analysis was performed to assess the independent predictors for the post-stenting minimum stent area of the distal LM and LAD ostium. Cox proportional hazard regression analyses were performed to find the predictors of long-term adverse outcomes. Variables with $p \leq 0.20$ on the univariate analyses were candidates for the multivariate Cox proportional hazard regression models. A backward elimination process was used to develop the final multivariate model, and the adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated. The proportional hazards assumption was confirmed by testing of partial (Schoenfeld) residuals, and no relevant violations were found. A p value <0.05 was considered statistically significant.

Results

The baseline clinical and procedural characteristics in 168 LM bifurcations are listed in Table 1. The most common types, using the Medina classification, were (1,1,1) in 71 (45%), (1,1,0) in 48 (30%), (0,1,0) in 16 (10%), and (1,0,0) in 10 (6%).

A comparison of the angiographic data and IVUS-defined stenoses is listed in Table 2. In both the distal LM and the LAD ostium, the sensitivity of an angiographically defined diameter stenosis >50% to predict for IVUS stenosis

Table 5
Univariate and multivariate predictors of major adverse cardiovascular events in 168 left main bifurcation lesions

	Univariate			Multivariate		
	Crude HR	95% CI	p Value	Adjusted HR	95% CI	p Value
Female gender	2.406	1.103–5.251	0.027	2.561	1.173–5.594	0.018
Old age	1.005	0.970–1.042	0.765			
Diabetes	0.542	0.251–1.172	0.119			
Two-stent technique	2.103	0.966–4.580	0.061			
Prestenting angiographic stenosis of left circumferential artery ostium	2.009	0.895–4.507	0.091			
Prestenting minimum lumen area within polygon of confluence	0.835	0.712–0.980	0.027	0.829	0.708–0.971	0.020
Post-stenting minimum stent area within distal left main*	0.791	0.641–0.976	0.029			

* Post-stenting minimum stent area within distal portion of LM above LAD carina (to include distal LM and POC.

was high (97% in the distal LM and 96% in the ostial LAD). In contrast, the specificity was low (33% in the distal LM and 41% in the ostial LAD).

The preintervention IVUS findings of the 168 LM bifurcations are listed in Table 3. The length of the POC was 3.3 ± 1.3 mm on the longitudinal IVUS image reconstruction and analysis. The MLA of the LM above the LAD carina was located within the POC in 68 lesions (41%) and within the distal LM in 100 (59%). The MLA within the POC correlated positively with the MLA within the distal LM ($r = 0.73$, $p < 0.001$), the plaque burden of the distal LM ($r = -0.63$, $p < 0.001$), the lumen area within the LAD carina ($r = 0.31$, $p < 0.001$), and the plaque burden of the LAD carina ($r = -0.28$, $p < 0.001$).

The 79 lesions with significant preprocedural angiographic stenosis of the left circumflex artery ostium had a smaller MLA within the POC than did the lesions without significant angiographic ostial left circumflex artery narrowing (5.4 ± 2.5 vs 7.5 ± 3.4 mm^2, $p < 0.001$). Similarly, the MLA within the distal LM was smaller (5.4 ± 2.8 vs 6.6 ± 3.2 mm^2, $p = 0.011$) and the plaque burden greater (70.5 ± 13.1% vs 64.7 ± 13.7%, $p = 0.007$) for lesions with compared to those without angiographic ostial left circumflex artery narrowing.

At the LAD ostium, significant plaque (>0.6 mm thickness) was mostly located opposite the flow divider (90° to 270°) in 155 lesions (92%). However, circumferential plaque (>0.6 mm thickness) was observed at the MLA site within the POC in 86 lesions (51%). Angiographic stenosis of the left circumflex artery ostium was seen in 51 (59%) of 86 lesions with circumferential POC plaque compared to 33 (40%) of 82 lesions without circumferential POC plaque ($p = 0.014$). Lesions with circumferential POC plaque showed a significantly smaller prepercutaneous coronary intervention MLA within the POC (5.4 ± 2.5 vs 7.4 ± 3.4 mm^2, $p < 0.001$) and the MLA within the distal LM (5.2 ± 2.5 vs 6.6 ± 3.3 mm^2, $p = 0.002$) compared to the lesions with noncircumferential POC plaque.

The post-stenting minimum stent area within the distal portion of LM above the LAD carina was located within the POC in 117 (70%) of 168 lesions. The postprocedural IVUS findings are summarized in Table 3, and Table 4 lists the pre- and post-stenting IVUS findings according to the different stenting techniques.

The post-stenting minimum stent area within the distal portion of the LM above the LAD carina was related to the preprocedural lumen area of the LAD carina ($r = 0.316$, $p < 0.001$), MLA within the POC ($r = 0.284$, $p < 0.001$), and MLA of the distal LM ($r = 0.342$, $p < 0.001$). Stepwise regression analysis included variables such as stent length, 2-stent technique, lumen area of the LAD carina, MLA within the POC, and angiographic involvement of the left circumflex artery ostium. The independent predictors for the post-stenting minimum stent area within the distal portion of the LM above the LAD carina (including both the distal LM and the POC) were the preprocedural lumen area of the LAD carina ($\beta = 0.253$, 95% CI 0.10 to 0.36, $p = 0.001$) and the preprocedural MLA within the POC ($\beta = 0.205$, 95% CI 0.04 to 0.23, $p = 0.008$).

The post-stenting minimum stent area within the LAD ostium correlated with the preprocedural MLA within the LAD ostium ($r = 0.423$, $p < 0.001$) and the MLA within the POC ($r = 0.281$, $p < 0.001$). The minimum stent area of the LAD ostium was greater in the single-stent group than in the 2-stent group (7.8 ± 1.9 vs 7.1 ± 1.7 mm^2, $p = 0.014$) and smaller in the lesions with angiographic stenosis of the left circumflex artery ostium (7.2 ± 1.7 vs 7.8 ± 1.9 mm^2, $p = 0.032$). Of these variables, the independent predictors for the post-stenting minimum stent area within the LAD ostium included the preprocedural MLA within the LAD ostium ($\beta = 0.376$, 95% CI 0.201 to 0.458, $p < 0.001$) and the MLA within the POC ($\beta = 0.159$, 95% CI 0.007 to 0.175, $p = 0.034$).

All 168 patients underwent follow-up angiography, and angiographic in-stent restenosis developed in 30 lesions (18%). The in-stent restenosis site was the ostium of the left circumflex artery in 16 (50%), the ostium of the LAD in 7 (22%), both ostia in 6 (19%), the distal LM in 1 (3%), and the LM shaft-to-ostium in 2 (6%). The frequency of in-stent restenosis was greater in the 2-stent group than in the single-stent group (21 [30%] of 69 vs 9 [9%] of 99, $p < 0.001$; Figure 3).

The 30 in-stent restenosis lesions had a significantly smaller preprocedural MLA within the POC (5.2 ± 1.6 vs 6.6 ± 3.3 mm^2, $p = 0.001$) and within the distal LM (4.8 ± 1.9 vs 6.1 ± 3.2 mm^2, $p = 0.005$), a smaller minimum stent area within the POC (7.1 ± 1.8 vs 8.0 ± 2.1 mm^2, $p = 0.020$), and a smaller post-stenting minimum stent area of

the LM above the LAD carina (7.0 ± 1.8 vs 7.8 ± 2.0 mm^2, p = 0.029) compared to lesions without in-stent restenosis.

During the 41.8 ± 18.0-month follow-up period, 26 patients experienced major adverse cardiovascular events. Of these 26 patients, 6 died (3 from cardiac causes), 2 experienced an acute myocardial infarction, 21 underwent target lesion revascularization.

The univariate predictors of the major adverse cardiovascular events are listed in Table 5. However, using the multivariate Cox model, only female gender (adjusted HR 2.56, 95% CI 1.173 to 5.594, p = 0.018) and the preprocedural MLA within the POC (adjusted HR 0.829, 95% CI 0.708 to 0.971, p = 0.020) were independent predictors for the occurrence of major adverse cardiovascular events during follow-up (Table 5). In addition, the independent predictors for target lesion revascularization were female gender (adjusted HR 3.02, 95% CI 1.253 to 7.287, p = 0.014), and the post-stenting minimum stent area of the LM above the LAD carina (adjusted HR 0.739, 95% CI 0.571 to 0.956, p = 0.021).

Discussion

The results of the present analysis have highlighted the importance of the POC in understanding distal LM disease and predicting the acute procedural results and long-term clinical events after drug-eluting stent implantation for unprotected distal LM bifurcation lesions. The POC is a confluent zone of the LAD and left circumflex artery just proximal to the carina and the distal LM above the carina. First, the preprocedural MLA and the post-stenting minimum stent area within the LM were mainly located within the POC, and the preprocedural MLA within the POC correlated with disease severity in the distal LM and in the ostia of the LAD and left circumflex artery. Second, the preprocedural MLA within the POC predicted stent underexpansion and major adverse cardiovascular events at 3 years of follow-up. Thus, the preprocedural MLA within the POC appeared to be a surrogate for the overall severity and complexity of LM bifurcation disease. In contrast, event-free survival after distal LM bifurcation lesion stenting was related to the overall distal LM bifurcation disease severity, as reflected in the preintervention MLA within the POC.

Considerable discrepancy was found between the angiographic and IVUS assessment of stenosis severity. An angiographic diameter stenosis of ≤50% in the distal LM or ostium of the LAD was uncommonly associated with significant IVUS stenosis (negative predictive value 85% to 90%). In addition, an angiographic diameter stenosis of >50% was often present, even in the absence of significant IVUS stenosis.

It has been proposed that transient impairment of the physiologic laminar flow at the bifurcation will increase to low-oscillatory shear stress and subsequent plaque progression at the region opposite the flow divider.[3,15] Consistently, the results of the present study have indicated that plaque was mainly distributed to the vessel wall opposite the flow divider (90° to 270°) at the ostial LAD.

The present results have clearly demonstrated that the preprocedural MLA within the POC is an independent determinant for the post-stenting minimum stent area within the distal portion of the LM, as well as the minimum stent area within the LAD ostium. Furthermore, the present analysis suggested that it was the severity and complexity of the underlying disease, as reflected in the MLA within the POC, that determined the final acute results, not the use of 1 or 2 stents. Nevertheless, the 2-stent group had a significantly smaller preprocedural MLA within the POC and a smaller post-stenting MLA of the left circumflex artery ostium, especially lesions treated with T-stenting and crush stenting, compared to the single-stent group. However, the present analysis does not suggest that a 2-stent strategy is inferior to a 1-stent strategy. More severe and complex IVUS lesion characteristics might have influenced an operator's preference for a 2-stent strategy; thus, the present findings might merely reflect the use of a 2-stent strategy for more complex disease.

It has been reported that stent underexpansion was responsible for most drug-eluting stent restenosis.[16] Also, we previously reported the postprocedural minimum stent area as an independent predictor of angiographic restenosis during follow-up.[17] Although few studies have assessed pre- and post-stenting IVUS predictors of clinical outcomes in patients with LM bifurcation disease, the present data suggest that the small preprocedural MLA of the POC contributes to stent underexpansion of the distal LM and subsequently leads to the development of in-stent restenosis and major adverse cardiovascular events during long-term follow-up.

Although the left circumflex artery ostium was the most frequent site of in-stent restenosis, the pre- and/or post-stenting left circumflex artery evaluation using direct left circumflex artery pullback could not be completed in many patients because of the technical difficulty in passing the guidewire into the side branch through tight turns, tight lesions, or stent struts. Although the evaluation of both side branch ostia is required to identify predictors for restenosis, left circumflex artery pullback images were available for only 39% after stenting, which might be realistic in clinical practice.

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