Title	Sirolimus-eluting stent implantation for ostial left anterior descending coronary artery lesions: three-year outcome from the j-Cypher Registry.
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Citation	Circulation. Cardiovascular interventions (2011), 4(4): 362-370
Issue Date	2011-08
URL	http://hdl.handle.net/2433/158747
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Type	Journal Article
Textversion	author

Sirolimus-eluting Stent Implantation for Ostial Left Anterior Descending Coronary Artery Lesions: Three-Year Outcome from the j-Cypher Registry

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Short title: Sirolimus-eluting stents for ostial LAD lesions

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Total word count: 5264 words

Journal Subject Code: [24] Catheter-based coronary interventions: stents

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Abstract

Background: Ostial left anterior descending coronary artery (LAD) lesion has been regarded as a lesion subset unsuitable for coronary stenting. Long-term outcomes of sirolimus-eluting stent (SES) implantation for ostial LAD lesions have not been yet adequately evaluated.

Methods and Results: Among 12824 patients enrolled in the j-Cypher registry, 3-year outcomes were compared between 481 patients with SES-treated ostial LAD lesions and 5369 patients with SES-treated non-ostial proximal LAD lesions. Patients with ostial LAD lesions, as compared with patients with non-ostial proximal LAD lesions, had similar incidences of target lesion revascularization (TLR) (9.4% vs. 9.7%, p=0.98; adjusted hazard ratio (HR) 0.99 (95% confidence interval (CI): 0.7-1.36), p=0.94) and death/myocardial infarction (MI) (10.7% vs. 11.4%, p=0.82; adjusted HR 1.05 (95%CI: 0.76-1.4), p=0.77), respectively. Among 481 patients with ostial LAD lesions, patients undergoing both main- and side-branch stenting (62 patients), as compared with main-branch stenting alone (419 patients), had higher risk for TLR (adjusted HR 4.65 (95%CI: 2.32-9.25), p < 0.0001) but had similar risk for death/MI (adjusted HR 1.15 (95%CI: 0.49-2.41), p=0.73). In patients with main-branch stenting alone, outcomes after crossover-stenting across circumflex (225 patients) were not different from those after ostial-stenting (194 patients) (adjusted HR 0.77 (95%CI: 0.33-1.82), p=0.55 for TLR, and adjusted HR 1.54 (95%CI: 0.78-3.2), p=0.22 for death/MI).

Conclusions: In terms of both safety and efficacy, 3-year outcomes of PCI using SES for ostial LAD lesions were comparable to those for non-ostial proximal LAD lesions. Crossover-stenting with

one-stent approach might be a reasonable option in treating ostial LAD lesions.

Key words: Coronary artery disease, Stent, Restenosis, Thrombosis

Text

The ostial left anterior descending coronary artery (LAD) lesion is an important target for coronary revascularization, since this lesion location subtends a large territory of myocardium. However, the ostial LAD lesion has been regarded as a lesion subset unsuitable for percutaneous coronary intervention (PCI) because of frequent atherosclerotic involvement of distal left main coronary artery (LMCA) and because of concerns for compromising the circumflex coronary artery (LCX). Furthermore, restenosis rate after implantation of bare-metal stents (BMS) for ostial LAD lesions remained high, ranging from 26% to 33% [1,2]. Although randomized controlled trials comparing drug-eluting stents (DES) with BMS demonstrated significant reduction in the rates of target-lesion revascularization (TLR) with use of DES, ostial LAD lesions have been excluded from most of these randomized controlled trials. Despite increasingly frequent use of DES for the treatment of ostial LAD lesions, its long-term outcome has not been yet adequately evaluated [3-5]. The current analysis was conducted to evaluate 3-year clinical outcomes of patients who underwent sirolimus-eluting stents (SES) implantation for ostial LAD lesions in a large cohort of patients enrolled in the j-Cypher registry.

Methods

Study Design and Patient Population

The study design for the j-Cypher registry was previously described [6]. In brief, the j-Cypher registry is a physician-directed, prospective, multicenter registry in Japan enrolling consecutive patients undergoing SES implantation without any exclusion criteria (Supplemental

Appendix A). While a center actively enrolled patients, technicians in the catheterization laboratory registered all the patients undergoing PCI in a screening log. When SES implantation was undertaken, the patient was invited to participate in the j-Cypher registry. Although data entry was basically left to the individual sites, the experienced clinical research coordinators (Supplemental Appendix B) in the data management center supported data entry when necessary. Logical inconsistencies were resolved by inquiries to the site investigators and/or by audits against the original data sources. Follow-up data were obtained from hospital charts or by contacting patients and/or referring physicians at 30 days, 6 months, one year and yearly thereafter. When death, myocardial infaction (MI), and stent thrombosis (ST) were reported, the events were adjudicated using the original source documents by a clinical events committee (Supplemental Appendix C). Adjudication of TLR events was left to the decision of the local investigators. The relevant review boards in all 37 participating centers approved the study protocol. Written informed consent was obtained from all patients enrolled.

The current pre-specified sub-analysis from the j-Cypher registry was intended to evaluate safety and efficacy of SES use in patients with ostial LAD lesions. Among 12824 patients enrolled in the j-Cypher registry from August 2004 to November 2006, 6230 patients underwent PCI for proximal LAD disease. Excluding 380 patients in whom proximal LAD lesions were treated by modalities other than SES, the current study population consisted of 5850 patients whose proximal LAD lesions were treated exclusively with SES. Baseline characteristics and clinical outcomes were compared between 481 patients with ostial LAD lesions, and 5369 patients with non-ostial proximal

LAD lesions. Subgroup analysis was also conducted in 481 patients whose ostial LAD lesions were treated exclusively by SES. Baseline characteristics and clinical outcomes were compared between main-branch stenting alone (one-stent approach; 419 patients) and both main- and side-branch stenting (two-stent approach; 62 patients). Furthermore, in patients with one-stent approach, baseline characteristics and clinical outcomes were compared between crossover stenting across LCX (crossover-stenting; 225 patients) and stenting just at the ostium of LAD (ostial-stenting; 194 patients) (Figure 1).

Definitions

A "lesion" was defined as the area covered by single or multiple overlapping stents. When two stents were placed without overlap, these two areas were regarded as two separate lesions. Ostial lesion was defined as a narrowing located within 3 mm of the vessel origin in the least foreshortened angiographic projection. Those ostial LAD lesions with concomitant significant LMCA distal bifurcation stenosis were regarded as LMCA lesions and were excluded from the current analysis. Proximal LAD was defined as the segment of LAD proximal to the first major septal branch. Techniques of stenting were pre-specified and recorded in the case report forms during the index stent implantation procedures. Crossover-stenting was defined as stent placement from distal LMCA to LAD across LCX, while ostial-stenting as the stenting strategy with an intention not to protrude the stent into LMCA. One-stent approach meant stenting of LAD only (including crossover-stenting and ostial-stenting) and two-stent approach denoted stenting of both ostial LAD and ostial LCX. Choice of the stenting strategies was left to the discretion of the operators.

The primary outcome measure for efficacy in the current analysis was defined as TLR for the index proximal LAD lesions. TLR was defined as either PCI or coronary artery bypass grafting (CABG) surgery due to restenosis or thrombosis of the target lesion that included the proximal and distal edge segments as well as the ostium of the side branches. The composite of death or MI was selected as the primary outcome measure for safety. Death was regarded as cardiac in origin unless obvious non-cardiac causes could be identified. Any death during the index hospitalization was regarded as cardiac death. Sudden death was defined as unexplained death in previously stable patients. MI was adjudicated according to the definition in the Arterial Revascularization Therapy Study [7]. ST was defined according to the Academic Research Consortium (ARC) definition [8].

Statistical Analysis

Categorical variables are presented as counts and percentages, and were compared with the chi-square test. Continuous variables were expressed as mean value ± SD unless otherwise indicated. Continuous variables were compared with the Student *t* test or Wilcoxon rank sum test on the basis of their distribution. Cumulative incidences of events were estimated by the Kaplan–Meier method, and curves were compared with the log-rank test. A multivariable Cox proportional hazard model was developed to adjust the differences in baseline characteristics. Proportional hazard assumptions for variables were assessed on the plots of log (time) versus log [-log (survival)] stratified by the variables, and were found justified. For the multivariable analysis, we first selected variables with p values < 0.1 in the univariate Cox models among 21 independent variables used in the previous report [6]. In the final multivariable model, we incorporated ostial LAD vs. non-ostial proximal LAD,

or one-stent approach vs. two-stents approach, and crossover-stenting vs. ostial-stenting together with those independent variables with multivariable p values < 0.05. Covariates used in the final model for adjustment were indicated in Supplemental Tables 1-3. The results of the multivariable analysis were expressed as adjusted hazard ratios (HR) and their 95% confidence intervals (CI).

Statistical analyses were conducted by two physicians (Kishi K and Kimura T) and a statistician (Morimoto T) with the use of JMP 8.0 (SAS Institute Inc, Cary, NC) software. P values < 0.05 were considered statistically significant.

Results

Baseline Characteristics: Ostial LAD vs. Non-ostial Proximal LAD

The baseline clinical characteristics were generally similar between the ostial LAD group and the non-ostial proximal LAD group, although patients >= 80 years of age, patients with prior MI and statin users were more prevalent in the ostial LAD group (Table 1-A). The baseline angiographic and procedural data were significantly different between the two groups (Table 1-B). The ostial LAD group had larger vessel size, resulting in use of stents and balloons with bigger sizes. Directional coronary atherectomy (DCA) before stenting, intravascular ultrasound (IVUS), and post dilatation were more frequently utilized in the ostial LAD group. Minimal lumen diameter (MLD) post procedure was significantly larger in the ostial LAD group.

Clinical Outcomes: Ostial LAD vs. Non-ostial proximal LAD

The follow-up interval in surviving patients was significantly longer in patients with ostial LAD lesions (median: 995 days; interquartile range (IQR): 732 to 1095 days) than in patients with

non-ostial proximal LAD lesions (median: 904 days; IQR: 730 to 1095 days) (P=0.02). Follow-up at 1 year was completed in 97% of patients.

Cumulative incidence of TLR in the ostial LAD group was not different from that in the non-ostial proximal LAD group (9.4% vs. 9.7%, p=0.98) (Table 2 and Figure 2-A). Adjusted hazard ratio of ostial LAD vs. non-ostial proximal LAD for TLR was 0.99 (95% CI: 0.7-1.36, p=0.94). Similarly, cumulative incidences of death or MI were not significantly different between the two groups (10.7% vs. 11.4%, p=0.82) (Figure 2-B). Adjusted hazard ratio of ostial LAD vs. non-ostial proximal LAD for death or MI was 1.05 (95% CI: 0.76-1.4, p=0.77).

Baseline Characteristics: One-stent vs. Two-stent approach

The baseline clinical characteristics were generally similar between the one-stent approach group and the two-stent approach group, although patients >= 80 years of age were more prevalent in the two-stent approach group (Supplemental Table 4-A). The baseline procedural and angiographic data were significantly different between the two groups. Crossover stenting approach and final kissing balloon technique were more frequently utilized in the two-stent approach group. The number and length of stents were greater in the two-stent approach group. Obviously, the prevalence of significant narrowing at the ostium of LCX was markedly higher in the two-stent approach group. Reference diameter (RD) and MLD of LCX before procedure were significantly smaller in the two-stent approach group than in the one-stent approach group. Despite these differences in procedural and angiographic characteristics, post-procedural MLD in the main branch did not differ between the two groups. Final MLD of LCX was significantly larger in the two-stent

approach group than in the one-stent approach group. (Supplemental Table 4-B)

Clinical Outcomes: One-stent vs. Two-stent Approach

Cumulative incidence of TLR in the two-stent group was significantly higher than that in the one-stent group (28.1% vs. 6.6%, p<0.0001) (Table 3 and Figure 3-A). The adjusted hazard ratio of the two-stent approach vs. one-stent approach for TLR was 4.65 (95% CI: 2.32-9.25, p<0.0001). Cumulative incidences of stroke, CABG, and any coronary revascularization were also significantly higher in the two-stent group than those in the one-stent group. However, cumulative incidences of death or MI were not significantly different between the two groups (16.8% vs. 9.8%, p=0.37) (Table 3 and Figure 3-B). Adjusted hazard ratio of two-stent approach vs. one-stent approach for death or MI was 1.15 (95% CI: 0.49-2.41, p=0.73).

Baseline Characteristics: Crossover-stenting vs. Ostial-stenting

Although the baseline clinical characteristics were generally similar between the ostial-stenting group and the crossover-stenting group, the latter included more male patients and patients with prior heart failure (Supplemental Table 5-A). The baseline procedural and angiographic data were significantly different between the two groups. Final kissing balloon technique was more frequently utilized in the crossover-stenting group, reflecting greater prevalence of significant narrowing at the ostium of LCX. Although the crossover-stenting group had larger stent size, larger maximum balloon size and longer stent length, post-procedural MLD in the main branch did not differ between the two groups. Final MLD of LCX was significantly smaller in the crossover-stenting group than in the ostial-stenting group. (Supplemental Table 5-B)

Clinical Outcomes: Crossover-stenting vs. Ostial-stenting

Cumulative incidences of TLR were not significantly different between the crossover-stenting group and the ostial-stenting group (5.4% vs. 7.9%, p=0.81) (Table 4 and Figure 4-A). Adjusted hazard ratio of crossover-stenting vs. ostial-stenting for TLR was 0.77 (95% CI: 0.33-1.82, p=0.55). Similarly, cumulative incidences of death or MI were not significantly different between the two groups (12.2% vs. 7.0%, p=0.07) (Table 4 and Figure 4-B). Adjusted hazard ratio of crossover-stenting vs. ostial-stenting for death or MI was 1.54 (95% CI: 0.78-3.2, p=0.22). Although the crude incidence of all-cause death was significantly higher in the crossover-stenting group (12.2% vs. 4.5%, p=0.01), the difference was no longer significant after adjusting confounders (adjusted HR 2.04 [95% CI: 0.94-4.93, p = 0.07]) (Table 4).

Discussion

The main findings of the current analysis in the largest ever reported series of patients undergoing SES implantation for ostial LAD lesions are as follows: (1) In terms of both safety and efficacy, 3-year outcomes of PCI using SES for ostial LAD lesions were comparable to those for non-ostial proximal LAD lesions; (2) The two-stent approach, as compared with the one-stent approach, was associated with significantly higher rate of TLR; and (3) Clinical outcomes after crossover-stenting with one-stent approach for ostial LAD lesions were similar to those after ostial-stenting.

Drawbacks of BMS Implantation for Ostial LAD Lesions

Ostial LAD lesion has historically been regarded as a lesion subset unsuitable for PCI using

218 coronary stents. One of the shortcomings of coronary stenting for ostial LAD lesions was the
219 potential for compromising LCX either by plaque shifting or by pinching the LCX ostium. When
220 the ostium of LCX had already been significantly narrowed before the procedure, stenting of both
221 LAD and LCX might be the only way to optimize the final angiographic result. However, in the era
222 of BMS, stenting both main- and side-branches was considered to be contraindicated in treating
223 bifurcation lesions due to unacceptably high restenosis rate [9]. Also, ostial LAD lesions are often
224 contiguous with the distal LMCA disease, even if the LMCA lesions are not angiographically
225 significant. Progression of the LMCA lesions subsequent to the injuries during stent implantation
226 procedure had been another potential concern related to coronary stenting for ostial LAD lesions.
227 Furthermore, it is technically demanding to place a stent just at the ostium of LAD without missing
228 the adequate coverage of the lesion and without excessive protrusion into the distal LMCA
229 bifurcation. Therefore, surgical revascularization could still be considered in patients with ostial
230 LAD lesions even if they have single-vessel coronary artery disease.

231 **Outcomes of DES Implantation for Ostial LAD Lesions**

232 Despite increasingly frequent use of DES for the treatment of ostial LAD lesions, there are only
233 a few small previous studies evaluating the outcome of DES implantation for ostial LAD lesions.
234 Seung et al. compared the clinical outcome of 68 consecutive patients undergoing SES implantation
235 with that of 77 historic control patients undergoing BMS implantation [3]. The rate of TLR at 1 year
236 was reported to be less frequent in the SES group than in the BMS group (0% vs. 17%, $p < 0.001$).
237 Tsagalou et al. compared the clinical outcome of 43 consecutive patients undergoing DES

implantation with that of 43 historic control patients undergoing BMS implantation [4]. The rate of TLR at 9 months was reported to be less frequent in the DES group than in the BMS group (7% vs. 25.6%, $p < 0.001$). Our current analysis evaluating larger number of patients clearly demonstrated that the rate of TLR at 3 years after SES implantation in patients with ostial LAD lesions was comparable to that in patients with non-ostial proximal LAD lesions, in whom PCI using DES has been regarded as the standard of care. The incidences of death or MI were also similar between patients with ostial LAD lesions and patients with non-ostial proximal LAD lesions, suggesting safety of PCI using SES for the ostial LAD lesions.

Stent Implantation Techniques for Ostial LAD Lesions

Relatively high restenosis rate in ostial lesions might be related to incomplete lesion coverage due to the technical difficulties in stent positioning in this lesion location. Encouraged by the favorable outcomes after unprotected LMCA stenting with DES, crossover-stenting technique emerged as a new stenting strategy for the ostial LAD lesions [3, 5, 10, 11]. In the current analysis, crossover-stenting was adopted in 56% of patients undergoing SES implantation for ostial LAD lesions. Cumulative incidences of TLR and death or MI after crossover-stenting were not different from those after ostial-stenting, suggesting safety and efficacy of crossover-stenting in selected anatomic situations. The Crossover-stenting technique enabling easier stent positioning and full coverage of the lesion seemed to be particularly relevant in treating those ostial LAD lesions with concomitant distal LMCA disease.

In the current analysis, the rate of TLR in patients who underwent stenting of both main- and

side-branches was unacceptably high, as was reported for unprotected LMCA stenting [12]. Although we could not address the safety issues of the two-stent approach due to the small sample size, it would be too premature to promote PCI using DES in patients in whom the two-stent approach is likely to be required.

Study Limitations

There are several important limitations in this study. First, we do not have the control group of patients treated by CABG. However, single digit TLR rate at 3 years after PCI seems to be clinically acceptable even if we do not have the surgical control patients. Second, the choices regarding treatment strategies for the ostial LAD lesions were left to discretion of the operators and were not based on randomized assignment. Treatment strategies were chosen according to the various anatomic features of the ostial LAD lesions. Therefore, the comparison between the crossover-stenting and the ostial stenting may not be clinically relevant. Also, we could not address the issue of optimal two-stent technique due to small number of patients treated with two-stent approach. Third, angiograms were not analyzed by a core angiographic laboratory and therefore, the adjudication of ostial lesion was left to the judgment of the local investigators. Fourth, we could not address the issue of lesion progression of LMCA and ostial LCX, since we did not evaluate the follow-up angiograms. Fifth, because we could not fully monitor the study patients, there is potential for under-reporting adverse events with potential for bias. Finally, although this is the largest series of patients undergoing SES implantation for the ostial LAD lesions, the study is obviously underpowered to evaluate potential small differences in clinical outcomes. Furthermore,

small numbers of events severely limit our ability to make adequate statistical adjustment by multivariable analysis. Therefore, the multivariable findings are exploratory due to the small sample size.

Conclusions

In terms of both safety and efficacy, 3-year outcomes of PCI using SES for ostial LAD lesions were comparable to those for non-ostial proximal LAD lesions. Crossover-stenting across LCX with one-stent approach might be a reasonable option in treating ostial LAD lesions. The two-stent approach for bifurcation was associated with markedly higher rate of TLR than the one-stent approach.

Acknowledgments

We thank the members of the cardiac catheterization laboratories of the participating centers and the clinical research coordinators.

Funding Sources

Cordis Cardiology Japan, a Johnson & Johnson company, Tokyo, Japan.

Conflict of Interest Disclosures

Takeshi Kimura is an advisory board member, speaker, and recipient of research grants from Cordis Cardiology Japan, Johnson and Johnson. Takaaki Isshiki is an advisory board member

and recipient of honoraria from Cordis Cardiology Japan, Johnson and Johnson. The remaining authors reported no conflicts.

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Figure Legends

Figure 1. Study flow chart for the current analysis among patients enrolled in the j-Cypher registry.

LAD = left anterior descending coronary artery, and SES = sirolimus-eluting stent.

Figure 2. Cumulative incidences of target lesion revascularization and death or myocardial infarction: ostial LAD lesions vs. non-ostial proximal LAD lesions.

LAD = left anterior descending coronary artery, and SES = sirolimus-eluting stent.

Figure 3. Cumulative incidences of target lesion revascularization and death or myocardial infarction among patients treated for ostial left anterior descending coronary artery lesions: one-stent vs. two-stent approach.

SES = sirolimus-eluting stent.

Figure 4. Cumulative incidences of target lesion revascularization and death or myocardial infarction among patients treated for ostial left anterior descending coronary artery lesions with one-stent approach: crossover-stenting vs. ostial-stenting.

SES = sirolimus-eluting stent.

Tables

Table 1. Baseline Characteristics of Patients Treated for Ostial LAD Lesion as Compared With Non-ostial Proximal LAD Lesion

(A) Patient characteristics

	Ostial LAD	Non-ostial Proximal LAD	P value
Number of patients	481	5369	
Age (years)	68.9±10.8	68.1±10.4	0.14
Age >= 80 years	84 (17%)	700 (13%)	0.006
Male	365 (76%)	3933 (73%)	0.21
Body mass index	23.7±3.2	24.0±3.4	0.046
Body mass index < 25.0	331 (69%)	3461 (64%)	0.06
Hypertension	341 (71%)	4023 (75%)	0.051
Diabetes mellitus	193 (40%)	2150 (40%)	0.97
Diabetes mellitus on insulin therapy	37 (7.7%)	468 (8.7%)	0.44
Current smoking	91 (19%)	1121 (21%)	0.31
Statin use	231 (48%)	2278 (42%)	0.02
eGFR (mL/min/1.73m2)	59.1±21.8	59.7±22.7	0.56
eGFR < 30, without hemodialysis	23 (4.8%)	248 (4.6%)	0.87
Hemodialysis	18 (3.7%)	235 (4.4%)	0.51

Acute coronary syndrome	127 (26%)	1479 (28%)	0.59
STEMI	37 (7.7%)	619（12%）	0.01
NSTEMI	11 (2.3%)	124 (2.3%)	0.97
Prior myocardial infarction	142 (30%)	1252 (23%)	0.002
Prior Stroke	45 (9.4%)	498 (9.3%)	0.95
Peripheral vascular disease	56 (12%)	548 (10%)	0.32
Prior heart failure	62 (13%)	746 (14%)	0.54
Multi-vessel disease	240 (50%)	2806 (52%)	0.32
Ejection fraction <= 40%	52 (12%)	521 (11%)	0.49
(B) Lesion and procedural characteristics			
Number of lesions	481	5369	
De novo lesion	343 (71%)	4084 (76%)	0.02
In-stent restenosis	76 (16%)	691 (13%)	0.07
Chronic total occlusion	45 (9.4%)	403 (7.5%)	0.14
Severe calcification	53 (11%)	583 (11%)	0.91
Lesion length >= 30mm	92 (19%)	882 (17%)	0.15
Reference vessel diameter pre < 2.5mm	76 (16%)	1504 (28%)	<0.0001
Use of intravascular ultrasound	351 (73%)	2579 (48%)	<0.0001
Direct stenting	94 (20%)	1269 (24%)	0.04

Atherectomy before stenting			
Directional coronary atherectomy	41(8.5%)	14 (0.3%)	<0.0001
Rotational atherectomy	32 (6.7%)	313 (5.8%)	0.46
Post dilatation	296 (62%)	2513 (47%)	<0.0001
Maximum inflation pressure (atm)	18.4±2.8	18.0±3.2	0.008
Number of stents used	1.6±0.8	1.4±0.7	<0.0001
Length of stents used (mm)	33.2±19.9	30.4±16.0	0.0003
Maximum stent size (mm)	3.2±0.3	3.0±0.3	<0.0001
Maximum balloon size (mm)	3.4±0.4	3.0±0.4	<0.0001
Quantitative coronary angiographic data			
Lesion length (mm)	19.4±13.8	19.9±11.7	0.45
Reference vessel diameter pre (mm)	2.99±0.55	2.73±0.49	<0.0001
Minimal lumen diameter pre (mm)	0.68±0.50	0.63±0.44	0.009
Diameter stenosis pre (%)	77.4±16.2	76.9±15.9	0.56
Reference vessel diameter post (mm)	3.25±0.48	2.94±0.43	<0.0001
Minimal lumen diameter post (mm)	2.95±0.55	2.68±0.47	<0.0001
Diameter stenosis post (%)	9.5±9.7	8.8±9.8	0.13

372 Data was missing for body mass index in 2 patients, for body mass index<25.0 in 2 patients, for
373 statin use in 49 patients, for eGFR in 1 patient, for eGFR < 30, without hemodialysis in 1 patient,
374 for ejection fraction <= 40% in 723 patients, de novo lesion in 1 lesion, in-stent restenosis in 1

lesion, chronic total occlusion in 14 lesions, lesion length >= 30mm in 68 lesions, reference vessel diameter pre < 2.5mm in 63 lesions, use of intravascular ultrasound in 17 lesions, direct stenting in 7 lesions, post dilatation in 9 lesions, maximum inflation pressure in 43 lesions, lesion length in 68 lesions, reference vessel diameter pre in 63 lesions, minimal lumen diameter pre in 63 lesions, diameter stenosis pre in 22 lesions, reference vessel diameter post in 53 lesions, minimal lumen diameter post in 53 lesions, and diameter stenosis post in 23 lesions.

eGFR = estimated glomerular filtration rate, LAD = left anterior descending coronary artery, NSTEMI = non-ST-segment elevation myocardial infarction, and STEMI = ST-segment elevation myocardial infarction.

384 Table 2. Unadjusted and Adjusted Outcomes Through 3 Years in Patients Treated for Ostial LAD

385 Lesion as Compared With Non-ostial Proximal LAD Lesion

	Ostial LAD (N=481)	Non-ostial Proximal LAD (N=5369)		Multivariable	
	N of events (Incidence)	N of events (Incidence)	p value	HR (95%CI)	p value
All-cause death	40 (9.7%)	397 (9.2%)	0.51	1.13 (0.8-1.54)	0.48
Cardiac death	18 (4.5%)	205 (4.7%)	0.92	1.05 (0.62-1.66)	0.84
Sudden death	4 (1.2%)	70 (1.6%)	0.37	0.69 (0.21-1.67)	0.45
Myocardial infarction	11 (2.7%)	171 (4.0%)	0.26	0.73 (0.37-1.28)	0.29
Stroke	23 (5.9%)	178 (4.2%)	0.09	1.38 (0.86-2.09)	0.17
Definite/Probable ST	5 (1.2%)	68 (1.6%)	0.65	0.82 (0.29-1.84)	0.66
Definite ST	4 (1.0%)	60 (1.4%)	0.55	0.77 (0.23-1.86)	0.59
TLR	38 (9.4%)	426 (9.7%)	0.98	0.99 (0.7-1.36)	0.94
CABG	5 (1.2%)	66 (1.4%)	0.73	1.03 (0.36-2.35)	0.94
Any coronary revascularization	110 (27.0%)	1372 (29.5%)	0.21	0.91 (0.74-1.1)	0.33
Death/Myocardial infarction	45 (10.7%)	480 (11.4%)	0.82	1.05 (0.76-1.4)	0.77

386 Incidence was estimated by Kaplan-Meier method.

387 CABG=coronary artery bypass grafting, CI=confidence interval, HR=hazard ratio, LAD=left

388 anterior descending coronary artery, ST=stent thrombosis, and TLR=target-lesion revascularization

389 Table 3. Unadjusted and Adjusted Outcomes Through 3 Years in Patients with Ostial LAD Lesions

390 Treated by One-stent Approach as Compared With Those Treated by the Two-stent Approach.

	One-stent approach (N=419)	Two-stent approach (N=62)		Multivariable	
	N of events (Incidence)	N of events (Incidence)	p value	HR (95%CI)	p value
All-cause death	32 (8.6%)	8 (16.8%)	0.2	1.3 (0.54-2.83)	0.54
Cardiac death	14 (3.6%)	4 (10.5%)	0.24	0.92 (0.25-2.79)	0.89
Sudden death	3 (0.9%)	1 (4.0%)	0.47		
Myocardial infarction	10 (2.8%)	1 (2.1%)	0.69	0.66 (0.04-3.46)	0.68
Stroke	16 (4.7%)	7 (1.4%)	0.01	3.38 (1.3-7.93)	0.01
Definite/Probable ST	4 (1.1%)	1 (2.1%)	0.64		
Definite ST	3 (0.8%)	1 (2.1%)	0.48		
TLR	22 (6.6%)	16 (28.1%)	<0.0001	4.65 (2.32-9.25)	<0.0001
CABG	1 (0.3%)	4 (7.4%)	<0.0001		
Any coronary revascularization	85 (24.3%)	25 (44.7%)	<0.0001	2.11 (1.3-3.33)	0.003
Death/Myocardial infarction	37 (9.8%)	8 (16.8%)	0.37	1.15 (0.49-2.41)	0.73

391 Incidence was estimated by Kaplan-Meier method.

392 Abbreviations are same as in Table 2.

393

394 Table 4. Unadjusted and Adjusted Outcomes Through 3 Years in Patients with One-stent Approach

395 Treated by Ostial-stenting Technique as Compared With Those Treated by Crossover-stenting

396 Technique

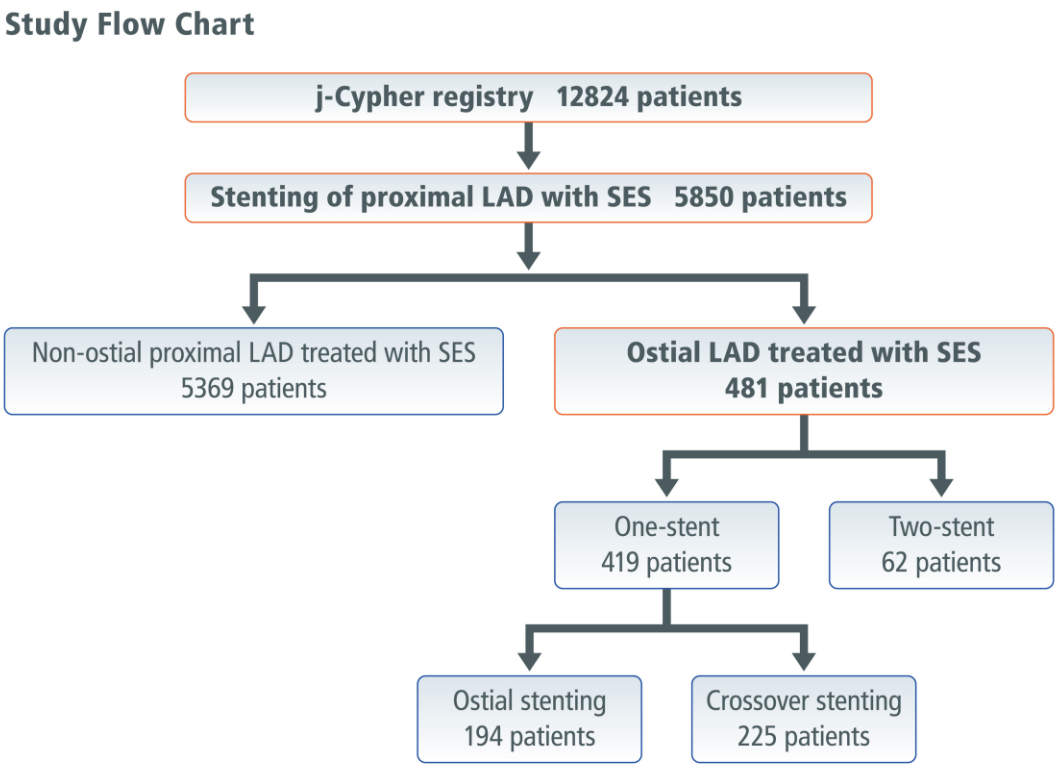
	Ostial-Stenting (N=194)	Crossover-Stenting (N=225)		Multivariable	
	N of events (Incidence)	N of events (Incidence)	p value	HR (95%CI)	p value
All-cause death	8 (4.5%)	24 (12.2%)	0.01	2.04 (0.94-4.93)	0.07
Cardiac death	3 (1.7%)	11 (5.2%)	0.06	1.7 (0.49-7.85)	0.42
Sudden death	0 (0%)	3 (1.6%)	0.1		
Myocardial infarction	6 (3.6%)	4 (2.0%)	0.41	0.59 (0.15-2.07)	0.41
Stroke	8 (4.8%)	8 (4.6%)	0.84	0.87 (0.32-2.38)	0.79
Definite/Probable ST	1 (0.5%)	3 (1.6%)	0.37		
Definite ST	1 (0.5%)	2 (1.1%)	0.62		
TLR	11 (7.9%)	11 (5.4%)	0.81	0.77 (0.33-1.82)	0.55
CABG	0 (0%)	1 (0.5%)	0.35		
Any coronary revascularization	41 (25.1%)	44 (23.5%)	0.8	0.93 (0.61-1.42)	0.73
Death/Myocardial infarction	12 (7.0%)	25 (12.2%)	0.07	1.54 (0.78-3.2)	0.22

397 Incidence was estimated by Kaplan-Meier method.

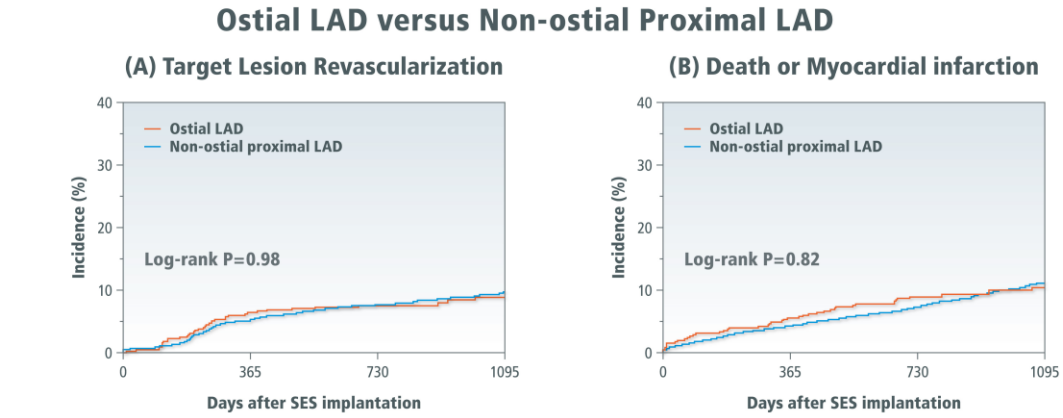
398 Abbreviations are same as in Table 2.

Figures

Figure 1.



403 Figure 2.



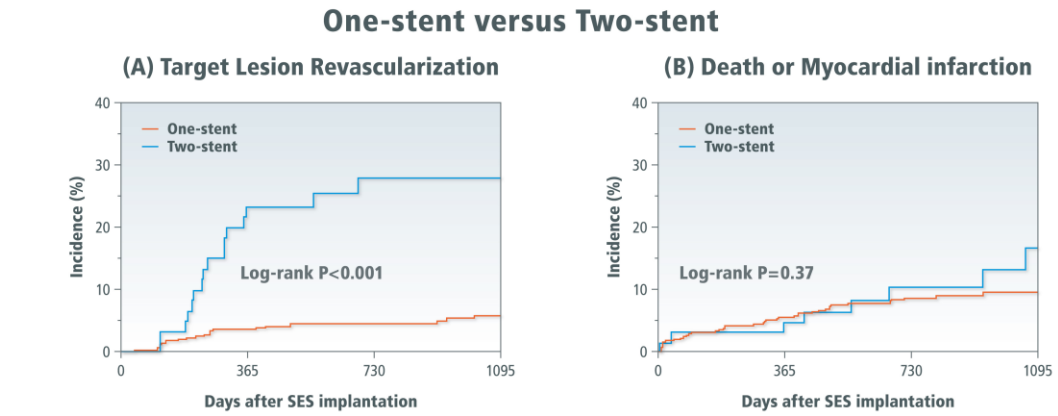
Days after SES implantation	0	365	730	1095
Ostial LAD				
Incidence		6.3%	7.6%	9.4%
No. of events		29	34	38
No. of patients at risk	481	417	316	170
Non-ostial proximal LAD				
Incidence		5.2%	7.7%	9.7%
No. of events		268	378	426
No. of patients at risk	5369	4727	3550	1562

Days after SES implantation	0	365	730	1095
Ostial LAD				
Incidence		5.7%	9.2%	10.7%
No. of events		27	41	45
No. of patients at risk	481	441	334	175
Non-ostial proximal LAD				
Incidence		4.5%	7.5%	11.4%
No. of events		237	374	480
No. of patients at risk	5369	4942	3797	1661

404

405

406 Figure 3.



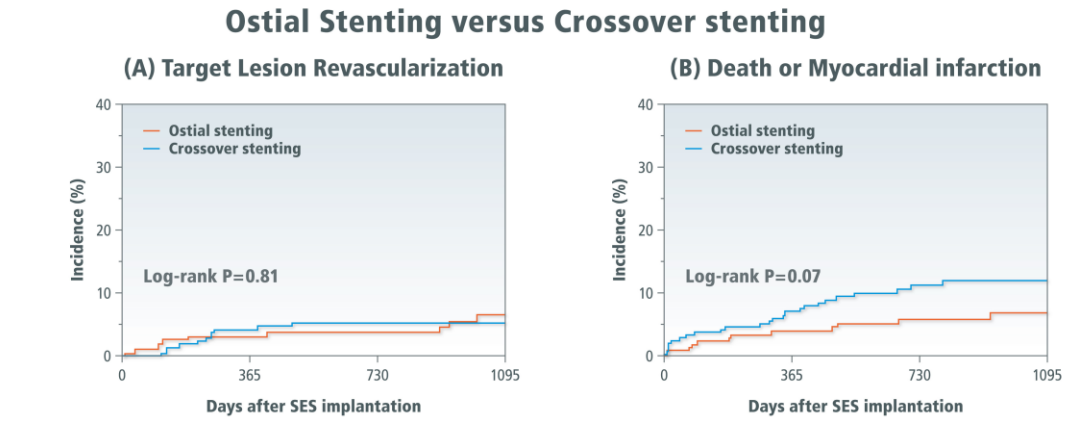
Days after SES implantation	0	365	730	1095
One-stent				
Incidence		3.8%	4.6%	6.6%
No. of events		15	18	22
No. of patients at risk	419	372	287	155
Two-stent				
Incidence		23.3%	28.1%	28.1%
No. of events		14	16	16
No. of patients at risk	62	47	30	15

Days after SES implantation	0	365	730	1095
One-stent				
Incidence		5.8%	9.0%	9.8%
No. of events		24	35	37
No. of patients at risk	419	382	291	154
Two-stent				
Incidence		4.8%	10.5%	16.8%
No. of events		3	6	8
No. of patients at risk	62	60	44	21

407

408

409 Figure 4.



Days after SES implantation	0	365	730	1095
Ostial stenting				
Incidence		3.2%	3.8%	7.9%
No. of events		6	7	11
No. of patients at risk	194	175	132	79
Crossover stenting				
Incidence		4.3%	5.4%	5.4%
No. of events		9	11	11
No. of patients at risk	225	197	147	76

Days after SES implantation	0	365	730	1095
Ostial stenting				
Incidence		4.2%	6.1%	7.0%
No. of events		8	11	12
No. of patients at risk	194	178	133	78
Crossover stenting				
Incidence		7.2%	11.5%	12.2%
No. of events		16	24	25
No. of patients at risk	225	204	150	76

410