Sirolimus-Eluting Stent Versus Balloon Angioplasty for Sirolimus-Eluting Stent Restenosis: Insights From the j-Cypher Registry

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Background—Optimal treatment strategies for restenosis of sirolimus-eluting stents (SES) have not been adequately addressed yet.

Methods and Results—During the 3-year follow-up of 12,824 patients enrolled in the j-Cypher registry, 1,456 lesions in 1,298 patients underwent target-lesion revascularization (TLR). Excluding 362 lesions undergoing TLR for stent thrombosis or TLR using treatment modalities other than SES or balloon angioplasty (BA), 1,094 lesions with SES-associated restenosis in 990 patients treated with either SES (537 lesions) or BA (557 lesions) constituted the study population for the analysis of recurrent TLR and stent thrombosis after the first TLR. Excluding 24 patients with both SES- and BA-treated lesions, 966 patients constituted the analysis set for the mortality outcome. Cumulative incidence of recurrent TLR in the SES-treated restenosis lesions was significantly lower than that in the BA-treated restenosis lesions (23.8% versus 37.7% at 2 years after the first TLR; P<0.0001). Among 33 baseline variables evaluated, only hemodialysis was identified to be the independent risk factor for recurrent TLR by a multivariable logistic regression analysis. After adjusting for confounders, repeated SES implantation was associated with a strong treatment effect in preventing recurrent TLR over BA (odds ratio, 0.44; 95% confidence interval, 0.32 to 0.61; P<0.0001). The 2-year mortality and stent thrombosis rates between the SES- and the BA-treated groups were 10.4% versus 10.8% (P=0.4) and 0.6% versus 0.6%, respectively.

Conclusions—Repeated implantation of SES for SES-associated restenosis is more effective in preventing recurrent TLR than treatment with BA, without evidence of safety concerns. (Circulation. 2010;122:42-51.)

Key Words: restenosis ■ angioplasty ■ stents ■ balloon

Although sirolimus-eluting stents (SES) significantly reduce the rates of angiographic restenosis and target-lesion revascularization (TLR),1 the widespread use of SES in complex lesions was reported to be associated with higher TLR rates in real-world clinical practice.2,3

In patients with bare-metal stent restenosis, several prospective multicenter randomized trials demonstrated that the implantation of SES was superior to balloon angioplasty (BA),4,5 implantation of bare-metal stent,6 or vascular brachytherapy.7 Although a few previous small observational studies compared the use of SES for restenosis of SES with the use of BA in preventing recurrent TLR,8–10 there is no report from either randomized trials or large-scale observational...
studies investigating the efficacy of SES for restenosis associated with SES use.

Although there are potential concerns for increased risk of death or stent thrombosis (ST) associated with repeated SES implantation for the treatment of SES restenosis, safety issues of this treatment strategy have not been adequately addressed yet.

In this report, we compared the incidences of recurrent TLR, ST, and mortality between the 2 groups of lesions with SES-associated restenosis treated with either SES or BA by analyzing the 3-year follow-up data from the large-scale cohort of the j-Cypher registry.3

Methods

Study Population

The j-Cypher registry is a physician-initiated prospective multicenter observational study in Japan enrolling consecutive patients undergoing SES implantation, and the study protocol and main results were reported previously.1 The relevant review boards in all 37 participating centers (see online-only Data Supplement) approved the study protocol. Written informed consent was obtained from all patients.

Follow-up data were obtained until October 2008 from hospital charts or by contacting patients and/or referring physicians at 30 days, 6 months, 1 year, and yearly thereafter. Data on TLR and the treatment modalities for TLR were prospectively collected. Clinical follow-up was continued after the TLR events.

Among 12 824 patients with 19 675 lesions enrolled in the registry, 17 050 lesions in 12 365 patients were treated exclusively with SES. During the 3-year follow-up (median, 829 days; interquartile range (IQR), 498 to 1108 days), 1456 lesions (8.5%) in 1298 patients underwent TLR. Multiple lesions within the same patient were considered to be independent observations for lesion-specific analyses. Cumulative incidences of TLR based on lesion estimated by the Kaplan-Meier method were 5.7% at 1 year, 8.1% at 2 years, and 10.0% at 3 years. Excluding 103 lesions with TLR for ST, 1353 lesions underwent TLR for SES-associated restenosis. Excluding 259 lesions with TLR using treatment modalities other than SES or BA, 1094 lesions with SES-associated restenosis in 990 patients (1 lesion in 899 patients, 2 lesions in 79 patients, 3 lesions in 11 patients, and 4 lesions in 1 patient) treated either with SES (537 lesions) or BA (557 lesions) constituted the study population for the

Figure 1. Patient and lesion flowchart for the current analysis. BMS indicates bare-metal stent; CABG, coronary artery bypass grafting; and DES, drug-eluting stent.
The primary outcome for the current analysis is recurrent TLR after the first TLR for SES-associated restenosis. TLR was defined as the primary outcome for the current analysis (Figure 1). The duration of follow-up after the first TLR was not statistically different between SES-treated (median, 627 days; IQR, 343 to 877 days) and BA-treated lesions (median, 580 days; IQR, 292 to 844 days; P=0.1). Incidences of recurrent TLR and ST on lesion basis after the first TLR were compared between the SES-treated lesions and the BA-treated lesions. Excluding 24 patients with both SES- and BA-treated lesions, 966 patients constituted the analysis set for the mortality outcome after first TLR.

Choice of the treatment strategy at the time of TLR was left to the discretion of the individual operators. Among 557 lesions treated with BA, “plain old” balloon angioplasty was performed in 471 lesions, and cutting balloon was used in 86 lesions. Recommended antiplatelet regimen after SES implantation was aspirin (≥81 mg daily) indefinitely and ticlopidine or 75 mg of clopidogrel daily for at least 3 months. Antiplatelet regimen after BA for SES-associated restenosis and duration of antiplatelet therapy were left to the discretion of each attending physician.

### Outcomes and Definitions

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and angiographic patterns of restenosis were determined by the site investigators according to the American Heart Association/American College of Cardiology lesion type classification and the scheme of Mehran et al., respectively. Angiographic data at first TLR were collected in 1045 lesions (96%) of 1094 lesions with first TLR. Outcome according to angiographic patterns of restenosis was evaluated in 1022 lesions treated either with SES (508 lesions) or BA (514 lesions), excluding 23 lesions with retreatment for restenosis in the side branch of a bifurcation lesion.

Statistical Analysis

Continuous variables are presented with mean±SD or median and IQR, and categorical variables are expressed as number and percentages. Categorical variables were compared with the χ² test. Continuous variables were compared with the t test or Wilcoxon rank-sum test based on the distribution. Incidences of the primary and secondary outcomes were estimated by the Kaplan-Meier method, and differences were assessed with the log-rank test.

In an attempt to adjust for the differences in baseline clinical, angiographic, and procedural characteristics between the SES- and BA-treated lesions, a multivariable logistic regression model was constructed using recurrent TLR within 1 year after the first TLR as dependent variable and 33 baseline factors as well as the treatment strategy of SES-associated restenosis (SES or BA treatment) as independent variables. Baseline factors used for analysis were those present at the time of initial entry into the j-Cypher registry, but not those present at the time of the first TLR. A multivariable logistic regression model instead of Cox proportional hazard model was used, because restenosis has been well known to be a time-related phenomenon, and also the timing of TLR could be highly influenced by physicians’ and patients’ decision. Actually, proportional hazard assumption for the variables was not verified. By using a logistic regression model, we could minimize the influence of the timing of TLR on the analysis of risk factors for recurrent TLR. Eligible lesions for logistic regression analysis included those lesions with recurrent TLR events within the first year after the first TLR relative to those lesions with complete follow-up and without recurrent TLR events at 1 year after the first TLR. Continuous variables were dichotomized by clinically meaningful reference values as shown in Table 1 and 2. We selected variables with P<0.05 in the univariate analyses together with the treatment strategy of SES-associated restenosis (SES or BA) and included them simultaneously in a multivariable model. Independent risk factors for recurrent TLR were expressed as odds ratios (ORs) and their 95% confidence intervals.

All analyses were conducted by physicians (M.A. and T.K.) and a statistician (T.M.) using JMP 8 (SAS Institute Inc, Cary, NC), and reported P values were 2-sided. The study sponsor was not involved in the study design; in the collection, analysis, and interpretation of data; writing of the report; or decision to submit the manuscript for publication.

Results

Baseline Characteristics

Baseline patient, lesion, and procedural characteristics were significantly different between SES- and BA-treated lesions. Patients treated with BA were more likely to have diabetes mellitus, especially diabetes on insulin therapy (Table 1). Lesions treated with SES were more frequently saphenous vein graft lesions, de novo lesions, and those treated with use of intravascular ultrasound and direct stenting. Lesions treated with BA were more likely to be left circumflex coronary artery lesions, in-stent restenosis, side branch stenting, and long lesion length (≥30 mm), and they were treated with a greater number and longer stents (Table 2).

Incidence and Risk Factors of Recurrent TLR

Cumulative incidence of recurrent TLR in SES-treated lesions was significantly lower than that in BA-treated lesions (17.0% and 23.8% versus 32.4% and 37.7% at 1 year and 2 years after the first TLR, respectively; P<0.0001) (Figure 2). Late catch-up phenomenon was observed in both groups comparing year 1 and 2 at follow-up, and there does not appear to be a significant difference between both treatment strategies.

Risk factors of recurrent TLR were evaluated by univariate (Table 3) and multivariate analysis (Table 4). Lesions included in the analysis for risk factors of recurrent TLR were 231 lesions...
After Treatment of SES-Associated Restenosis

### Table 3. Univariate Correlates of Recurrent TLR Within 1 Year After Treatment of SES-Associated Restenosis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Yes (n=231)</th>
<th>No (n=593)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>SES implantation</td>
<td>77 (33)</td>
<td>325 (55)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age ≥80 y</td>
<td>25 (11)</td>
<td>47 (8)</td>
<td>0.2</td>
</tr>
<tr>
<td>Male sex</td>
<td>179 (77)</td>
<td>455 (77)</td>
<td>0.8</td>
</tr>
<tr>
<td>Body mass index ≥25.0</td>
<td>68 (29)</td>
<td>214 (36)</td>
<td>0.07</td>
</tr>
<tr>
<td>Hypertension</td>
<td>175 (76)</td>
<td>449 (76)</td>
<td>1.0</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>132 (57)</td>
<td>323 (54)</td>
<td>0.5</td>
</tr>
<tr>
<td>Insulin therapy</td>
<td>48 (21)</td>
<td>105 (18)</td>
<td>0.3</td>
</tr>
<tr>
<td>Current smoking</td>
<td>35 (15)</td>
<td>111 (19)</td>
<td>0.2</td>
</tr>
<tr>
<td>Treatment for hypercholesterolemia</td>
<td>115 (50)</td>
<td>272 (46)</td>
<td>0.3</td>
</tr>
</tbody>
</table>

### Table 4. Univariate and Multivariable Analysis for the Risk Factors for Recurrent TLR Within 1 Year After Treatment of SES-Associated Restenosis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate (95% CI)</th>
<th>Multivariate (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>SES implantation (vs BA)</td>
<td>0.41 (0.30–0.56)</td>
<td>0.44 (0.32–0.61)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>1.95 (1.29–2.94)</td>
<td>1.61 (1.02–2.53)</td>
<td>0.04</td>
</tr>
<tr>
<td>Prior heart failure</td>
<td>1.62 (1.05–2.48)</td>
<td>1.44 (0.91–2.26)</td>
<td>0.1</td>
</tr>
<tr>
<td>De novo lesion</td>
<td>0.70 (0.51–0.96)</td>
<td>0.90 (0.55–1.51)</td>
<td>0.7</td>
</tr>
<tr>
<td>In-stent restenosis</td>
<td>1.56 (1.09–2.22)</td>
<td>1.21 (0.69–2.16)</td>
<td>0.5</td>
</tr>
<tr>
<td>Severe calcification</td>
<td>1.74 (1.18–2.54)</td>
<td>1.53 (0.99–2.33)</td>
<td>0.054</td>
</tr>
<tr>
<td>Use of IVUS</td>
<td>0.69 (0.50–0.94)</td>
<td>0.78 (0.56–1.08)</td>
<td>0.1</td>
</tr>
<tr>
<td>Direct stenting</td>
<td>0.49 (0.27–0.82)</td>
<td>0.70 (0.39–1.22)</td>
<td>0.2</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; IVUS, intravascular ultrasound.

With recurrent TLR events within the first year after the first TLR and 593 lesions that completed 1-year follow-up without recurrent TLR after the first TLR, excluding 270 lesions followed up less than 1 year without TLR. Univariate correlates of recurrent TLR included hemodialysis, prior heart failure, de novo lesion, in-stent restenosis, severe calcification, use of intravascular ultrasound, and direct stenting (Table 3).

Among 33 baseline variables evaluated, only hemodialysis was identified to be the independent risk factor for recurrent TLR by a multivariable logistic regression analysis (Table 4). After adjustment for the differences in baseline characteristics, repeated SES implantation to treat SES-associated restenosis as compared with treatment with BA was significantly associated with less recurrent TLR (OR, 0.44; 95% confidence interval, 0.32 to 0.61; P<0.0001).

### Angiographic Results

Reference vessel diameter in SES-treated lesions was larger than that in BA-treated lesions. However, percent diameter stenosis and minimal luminal diameter were similar between the 2 groups (Table 5).

Relative to angiographic patterns of SES-associated restenosis, focal pattern was more prevalent than nonfocal pattern (Figure 3). Angiographic patterns of SES-associated restenosis were similarly distributed in the SES-treated lesions and

### Table 5. Angiographic Findings at the First TLR

<table>
<thead>
<tr>
<th></th>
<th>SES (n=508)</th>
<th>BA (n=514)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference diameter, mm</td>
<td>2.95±0.48</td>
<td>2.88±0.45</td>
<td>0.02</td>
</tr>
<tr>
<td>Minimal lumen diameter, mm</td>
<td>0.70±0.46</td>
<td>0.67±0.47</td>
<td>0.3</td>
</tr>
<tr>
<td>Percent diameter stenosis</td>
<td>76.4±14.7</td>
<td>76.8±15.6</td>
<td>0.6</td>
</tr>
<tr>
<td>Angiographic patterns of restenosis</td>
<td>0.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monofocal</td>
<td>376 (74)</td>
<td>384 (75)</td>
<td></td>
</tr>
<tr>
<td>Multifocal</td>
<td>32 (6)</td>
<td>38 (7)</td>
<td></td>
</tr>
<tr>
<td>Diffuse</td>
<td>46 (9)</td>
<td>54 (11)</td>
<td></td>
</tr>
<tr>
<td>Proliferative</td>
<td>20 (4)</td>
<td>10 (2)</td>
<td></td>
</tr>
<tr>
<td>Occlusive</td>
<td>34 (7)</td>
<td>28 (5)</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean±SD or n (%).
the BA-treated lesions. Cumulative incidence of recurrent TLR events for nonfocal restenosis was significantly higher than that for focal restenosis in the BA-treated lesions, but not in the SES-treated lesions (Figure 4). Cumulative incidence of recurrent TLR events for the SES-treated lesions was significantly lower than that for the BA-treated lesions in both focal and nonfocal restenosis (Figure 5).

**Mortality and Stent Thrombosis**

Incidence of death after first TLR were evaluated among 475 patients treated with only SES and 491 patients treated with only BA for SES-associated restenosis. The overall mortality rates were not significantly different between SES- and BA-treated patients (4.5% and 10.4% versus 6.6% and 10.8% at 1 year and 2 years after the first TLR, respectively; \( P = 0.4 \) (Figure 6).
Cumulative incidences of definite ST between SES- and BA-treated lesions were 0.2% and 0.6% versus 0.6% and 0.6% at 1 year and 2 years after the first TLR, respectively (Figure 7).

**Discussion**
The main findings of the present study are that use of repeated SES implantation to treat SES-associated restenosis as compared with treatment with BA had a very strong treatment effect in preventing recurrent TLR and that repeated SES implantation was not associated with higher mortality nor increased incidence of ST as compared with treatment with BA.

Optimal treatment strategy of SES-associated restenosis has not been adequately defined yet. Because of the profound antirestenotic efficacy of SES, the studies investigating the outcome of various treatment strategies for SES-associated restenosis are often hampered by the small number of the study patients. However, with expanding indication of SES to more complex lesions, management of restenosis of SES has emerged as a clinically relevant issue. The very large sample size and inclusion of many complex patients in the j-Cypher registry provides an opportunity to evaluate the clinical outcome of patients after the first TLR for SES-associated restenosis.

To date, there is no report from either randomized trials or large-scale observational studies investigating the efficacy of SES over BA treatment for restenosis of SES. The results from a few previous small observational studies were not consistent in terms of efficacy of repeated SES implantation to prevent recurrent TLR as compared with use of BA. Cosgrave et al\(^9\) identified 250 drug-eluting stent-associated restenosis in 203 patients and divided these lesions into 2 groups: focal and nonfocal. For focal restenotic lesions, the incidence of TLR after drug-eluting stent implantation and BA treatment was 8.6% and 11.4%, respectively, whereas for nonfocal restenotic lesions, incidence was 22.6% and 24%, respectively. Kitahara et al\(^9\) reported that in 101 patients with 102 lesions undergoing TLR for SES-associated restenosis, recurrent TLR tended to be lower with SES implantation than with treatment with BA, both in the focal type (12.5% versus 35.5%) and in the nonfocal type (35.3% versus 50.0%), respectively, during the mean follow-up of 13.0±8.9 months. Angiographic analysis in the present study demonstrated consistent reduction in the rate of recurrent TLR by use of repeated SES implantation in both the focal-type and the nonfocal type SES-associated restenosis.

Our current analysis revealed a very strong treatment effect of repeated SES implantation over BA in preventing recurrent TLR in a large number of patients with adjustment for differences in baseline characteristics. Until otherwise proven by adequately sized randomized trials, our current observation supports the choice of repeated SES implantation for SES-associated restenosis.
It is interesting to note that Kim et al.\textsuperscript{10} reported that the recurrent TLR rate at 1 year was 3.3% for the SES group and 8.3% for the BA group. The reported incidences of both groups were extremely low compared with other studies, including ours. The discrepancy in the rate of recurrent TLR might be related to some differences in lesion complexity and in the pattern of restenosis. Focal restenosis was associated with lower incidence of target lesion failure compared with nonfocal restenosis in the case of treatment with bare-metal stent\textsuperscript{13} and SES.\textsuperscript{8,9} Previous reports demonstrated that focal restenosis remained the most common pattern (71.3% to 79.0%) with SES in real-world clinical practice.\textsuperscript{14,15} Although we could not fully address the pattern of restenosis in the current analysis, it is possible that the prevalence of nonfocal restenosis might increase with increasing complexity of the original target lesions. Also, it is likely that the routine follow-up angiography often performed in Japanese clinical practice might increase the rate of angiographically driven TLR.

**Figure 6.** Cumulative incidences of death after the first TLR in patients treated with SES as compared with those treated with BA for SES-associated restenosis.

<table>
<thead>
<tr>
<th>Days after the First TLR</th>
<th>0</th>
<th>180</th>
<th>365</th>
<th>730</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BA</strong> Overall mortality</td>
<td>3.5%</td>
<td>6.6%</td>
<td>10.0%</td>
<td></td>
</tr>
<tr>
<td>Number of events</td>
<td>16</td>
<td>28</td>
<td>41</td>
<td></td>
</tr>
<tr>
<td>Number of patients at risk</td>
<td>491</td>
<td>414</td>
<td>354</td>
<td>174</td>
</tr>
<tr>
<td><strong>SES</strong> Overall mortality</td>
<td>2.5%</td>
<td>4.5%</td>
<td>10.4%</td>
<td></td>
</tr>
<tr>
<td>Number of events</td>
<td>11</td>
<td>19</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Number of patients at risk</td>
<td>475</td>
<td>414</td>
<td>350</td>
<td>186</td>
</tr>
</tbody>
</table>

**Figure 7.** Cumulative incidences of stent thrombosis after the first TLR in lesions treated with SES as compared with those treated with BA for SES-associated restenosis.
Predicting which patients would be likely to have refractory restenosis after SES implantation is clinically important when choosing between percutaneous coronary intervention and coronary artery bypass grafting surgery in patients with complex coronary lesions. Hemodialysis was identified as the only independent risk factor for recurrent TLR other than use of BA. Other risk factors identified by univariate analysis, such as severe calcification and in-stent restenosis, did not emerge as independent risk factors by multivariate analysis, probably due to the strong influence of the treatment modality (SES or BA) on the outcome. Future investigation on the risk factors for refractory restenosis should focus on those patients undergoing repeated SES implantation for SES-associated restenosis.

Although SES implantation was demonstrated to be associated with better outcome rates as compared with BA in the treatment of SES-associated restenosis, the incidence of recurrent TLR after repeated SES implantation (17.0% at 1 year) was far from satisfactory. Outcome of treatment of drug-eluting stent restenosis might be improved with different types of drug-eluting stent. However, a recent report from a relatively large randomized trial comparing paclitaxel-eluting versus sirolimus-eluting stents for the treatment of SES-associated restenosis demonstrated similar rates of recurrent TLR. Considering the unacceptably high recurrence rate of SES-associated restenosis, development of some innovative treatment strategies is obviously needed. Some randomized, double-blind, multicenter trials demonstrated that drug-eluting balloon reduced the need for TLR compared with uncoated-balloon and paclitaxel-eluting stent. Although there is little information about drug-eluting balloon versus SES for SES-associated restenosis, drug-eluting balloon might be a promising alternative.

As for safety concerns, repeated SES implantation inside the previously placed SES might lead to alterations in drug release, hypersensitivity to “double-dose” polymers, and an inadequate stent expansion at the area of stent overlap. One or more of these factors might cause unexpected adverse events such as ST or death. Because of the growing concerns for potentially higher risk of ST and/or death after SES implantation, we evaluated the incidences of these 2 events after SES implantation or BA treatment for SES-associated restenosis; however, we did not find any significant differences in the incidences of death or ST between the 2 groups. Although the statistical power is obviously insufficient, we did not find any safety signal with use of SES treatment for SES-associated restenosis.

Study Limitations
There are several important limitations in this study. First, selection of treatment strategies for SES-associated restenosis were not randomized but were left to the discretion of the individual operators. Baseline characteristics were significantly different between SES- and BA-treated lesions. Although adjusted comparison using a multivariable regression model was conducted, there still might be some unmeasured confounders. However, treatment effect of repeated SES implantation in preventing recurrent TLR was very strong, suggesting the robustness of our observation. Second, TLR procedures constituting the study population were follow-up events in the j-Cypher registry. Although we had extensive data on clinical, lesion, and procedural characteristics at the time of the index procedures, information other than treatment modalities for TLR and angiographic findings were not collected at the time of the TLR procedures. Therefore, analysis of the risk factors for recurrent TLR was conducted based on baseline characteristics at the time of index procedures. Third, we did not systematically evaluate the reason why TLR was undertaken. We could not discriminate between clinically and angiographically driven TLR. Decisions on whether or not to perform TLR were largely dependent on the preferences of the patients and the attending physicians. It is likely that the routine follow-up angiography performed in many Japanese centers might increase the rate of angiographically driven TLR. Finally, we evaluated many baseline characteristics as potential risk factors. The issue of multiple comparison is unavoidable. However, our primary target is SES versus BA for SES-associated restenosis, and other factors were used only for adjustment. Therefore, this issue does not have strong impact on our result.

Conclusions
Despite these study limitations, we would conclude that repeated implantation of SES for treatment of SES-associated restenosis is more effective in preventing recurrent TLR than treatment with BA, without evidence of safety concerns.

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Disclosures
Dr Kimura serves on the advisory board and is a member of the speakers’ bureau for Cordis Cardiology, and he has received honoraria from Cordis Cardiology. Dr Miyazaki serves on the advisory board for Cordis Cardiology. The remaining authors report no conflicts.

References

**CLINICAL PERSPECTIVE**

Optimal treatment strategies for restenosis of sirolimus-eluting stents (SES) have not been adequately addressed yet. A few previous small observational studies compared the use of SES for restenosis of SES with the use of balloon angioplasty (BA) in preventing recurrent target-lesion revascularization (TLR). However, there is no report from either randomized trials or large-scale observational studies investigating the efficacy of SES for restenosis associated with SES use. Our current analysis revealed that cumulative incidence of recurrent TLR in the SES-treated restenosis lesions was significantly lower than that in the BA-treated restenosis lesions (23.8% versus 37.7% at 2 years after the first TLR; P<0.0001). Among 33 baseline variables evaluated, only hemodialysis was identified to be the independent risk factor for recurrent TLR by a multivariable logistic regression analysis. After adjusting for confounders, repeated SES implantation was associated with a strong treatment effect in preventing recurrent TLR over BA (odds ratio, 0.44; 95% confidence interval, 0.32 to 0.61; P<0.0001). The 2-year mortality and stent thrombosis rates between the SES- and the BA-treated groups were 10.4% versus 10.8% (P=0.4) and 0.6% versus 0.6%, respectively. Although other modalities like drug-eluting balloon catheters might be promising alternatives, our results indicate that repeated implantation of SES for SES-associated restenosis is more effective in preventing recurrent TLR than treatment with BA, without signals suggesting safety concerns. Until otherwise proven by adequately sized randomized trials, our current observation supports the choice of repeated SES implantation for SES-associated restenosis.
Sirolimus-Eluting Stent Versus Balloon Angioplasty for Sirolimus-Eluting Stent Restenosis: Insights From the j-Cypher Registry

for the j-Cypher Registry Investigators

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Supplemental Material

Supplemental Appendix: List of participating centers and investigators for the j-Cypher registry.

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