Comparison of the Efficacy of Large (≥3.5 mm) Sirolimus-Eluting and Bare-Metal Stents for De novo Lesions without Using the Bifurcation 2-Stent Technique : A Retrospective, Lesion-Based Study

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ABSTRACT

Background and Aim: The rate of target lesion revascularization (TLR) after elective implantation for de novo lesions was retrospectively compared between large-diameter (\geq 3.5 mm) sirolimus-eluting stents (SESs, n=251) and bare-metal stents (BMSs, n=191) on the basis of total stent length (SL).

Methods : This study was retrospective, single-center, nonrandomized, and lesion-based. The endpoint was TLR with coronary angiographic follow-up.

Results: The TLR rate did not differ between SESs and BMSs for the shortest stents (SES: SL=13 mm, n=30, 6.7%; and BMS: SL \leq 14 mm, n=14, 7.1%) or the longest stents (SES: SL= multiple, n=49, 18.4%; BMS: SL \geq 35 mm, n=16, 25.0%) but was significantly lower for intermediate-length SESs (18 or 23 mm, 1.4%, n=139; and 28 or 33 mm, 0%, n=49) than for intermediate-length BMSs (15 to 24 mm, 8.7%, n=103, p<0.05; and SL=25 to 34 mm, 33.3%, n=42, p<0.01).

Conclusion : SESs 18 to 33 mm long were more efficacious than BMSs. However, prospective large-scale studies are needed to determine the efficacy of single large-diameter, short SESs (13 mm) and multiple stents. (Jikeikai Med J 2009; 56 : 1-10)

Key words: sirolimus-eluting stent, stent length, target lesion revascularization, restenosis

INTRODUCTION

Drug-eluting stents (DESs) have been widely used to treat various types of lesion. Studies indicate that the rate of target lesion revascularization (TLR) due to in-stent restenosis (ISR) is markedly lower with DESs than with bare metal stents (BMSs)¹⁻⁴. However, the benefit of DESs for reducing TLR and ISR is limited : long-term prognoses with DESs and BMSs have been similar¹⁻⁴. An alternative is the use of sirolimus–eluting stents (SESs; Cypher[®], Cordis Corporation, Warren, NJ, USA), which may have several potential concerns of their own^{5–12}. Therefore, it is important to compare the efficacy (the incidence of TLR) between SES implantation and BMS implantation.

The characteristics of implanted BMSs and DESs, namely, their diameter, length, number, and

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overlap, are consistent predictors of TLR¹³⁻¹⁶. The advantage of BMS lies in their large size (≥ 3.5 mm)^{17,18} and short length^{19,20}. On the other hand, the overlap of SESs is a predictor of ISR²¹⁻²³. Because the maximal cell diameter is 3.0 mm for the SES platform (BX Velocity[®], Cordis Corporation), treatments of bifurcate lesions with a 2-stent technique have been limited to full dilation²⁴. Therefore, in the present study, these factors were considered simultaneously. To compare the efficacy of BMSs and SESs, the effect of stent length on the rate of TLR after SES implantation was compared retrospectively with that after BMS implantation. Elective implantation was performed with large (\geq 3.5 mm) SESs for de novo lesions in native coronary arteries, without using a bifurcation 2-stent technique.

Methods

Population

Outcomes of percutaneous coronary interventions (PCIs) performed at our cardiovascular center in January 2003 were pooled. After SESs were approved in August 2004, they were routinely used for both elective and emergency procedures, as described in our previous reports²⁵⁻²⁸. Patients gave consent after they had been informed of their clinical diagnoses and the use of SES. However, BMSs were used for the following patients: those known to have malignancies before surgery, those with social conditions requiring a shorter duration of ticlopidine treatment, and those with lesions of extremely large vessels. For patients with lesions of extremely large vessels, BMSs were used because SESs are not recommended for dilations larger than 4.75 mm. Exclusion criteria included lesions treated with hybrid stenting with BMSs and SESs and bifurcate lesions requiring a 2-stent technique because ostial lesions of side branches are limited to full dilation²⁴. Therefore, for 231 de novo lesions not treated with a bifurcation 2stent technique, BMSs were implanted electively in large (\geq 3.5 mm) native coronary arteries from January 2003 through August 2004 (before the approval of SESs), and BMSs were implanted for 20 lesions from September 2004 (after the approval of SESs) through May 2007 (251 lesions in total). From August 2004 through May 2007, SESs were electively implanted for 350 lesions.

A successful procedure was defined as one in which stents were implanted without distinct underexpansion, as shown by angiography or intravascular assessment with intravascular ultrasonography (IVUS) or both, and in which there were, within a 30day period, no major adverse cardiovascular events composite of death; Q-wave myocardial infarction (Q-wave formation in more than 2 leads and a maximum level of serum creatine phosphokinase more than 400 IU); no emergent coronary artery bypass grafts (CABGs); and no early (≤ 30 days) definite stent thrombosis, as defined by the Academic Research Consortium⁶. There was a single case of in -hospital death with early definite stent thrombosis, and there were 2 cases of Q-wave myocardial infarction after BMS implantation. After SES implantation, there was a single case of in-hospital death, and there were 2 cases of Q-wave myocardial infarction. Accordingly, beyond 30 days after the procedure, 248 lesions in the BMS group and 347 lesions in the SES group were followed up. There were no major adverse cardiovascular events, except TLR, more than 30 days after the procedure in either group. Thus, the rate of TLR (the primary end points, defined below) was estimated beyond 30 days, until follow-up coronary angiography (f-CAG) was performed after approximately 6 months²⁹ in the BMS group and after approximately 12 months³⁰ in the SES group.

PCI procedure

The PCI procedure has been described in our previous reports^{25–28}. Briefly, the procedure was performed with a 6–, 7–, or 8–Fr guiding catheter, mainly via the radial artery or femoral artery or both. Heparin (5,000–8,000 IU) was administered intravenously during the procedure. The use of IVUS (Atlantis[®] SR pro, Boston Scientific Scimed, Inc. Maple Grove, MN, USA) was encouraged to allow intravascular assessment of the geometry and stent apposition.

Stents were deployed to fully cover the targeted lesion so as not to implant the edges on the plaquerich areas shown by angiographic or intravascular assessment. When more than 2 stents were needed, they were implanted without gaps, as verified by angiogram; however, the length of overlap was minimized. When further stent dilation was needed, high-pressure ballooning with a noncompliant balloon was usually performed. To avoid stent underexpansion³¹, the sites of the proximal edge and stent overlap were dilated with large balloons under higher pressure. The size of stents was defined as the maximal diameter of the balloon needed to dilate a stent.

The selection of BMSs, from among 11 types, was left to the surgeon's discretion without prospective randomization. The 283 BMSs used for the 248 lesions were of the following types: Multi-Link PENTA® (Guidant Corp., Indianapolis, IN, USA; n=82, 28.7%), Express® (Boston Scientific, Natick, MA; n=53, 18.5%), Duraflex® (Goodman Co., Ltd., Nagoya; n=41, 14.3%), NIR® (Boston Scientific; n=38, 13.3%), BX Velocity® (Cordis Corp.; n=25, 8.7%), Driver® (Medtronics, Inc., Minneapolis, MN; n=11, 3.9%), Multi-Link ZETA® (Guidant Corp.; n=9, 3.2%), Tsunami® (Terumo Corp., Tokyo, Japan; n=8, 2.8%), Radius® (Boston Scientific; n=6, 2.1%), and Be 2® (Medtronics, Inc.; n=2, 0.7%).

The use of a rotablator was not randomized and was left to the surgeon's discretion. At our center, a rotablator was used in cases in which the inflated balloon was indented (i.e., stents could not be implanted without pulverizing the calcification with the rotablator and in cases in which the balloon was not fully dilated). This strategy was consistently used in the period before the SES was approved, and the kind of stent selected (BMS or SES) was not affected.

Antiplatelet therapy

Antiplatelet therapy for stent implantation has been described in our previous studies^{25–28}. Briefly, in elective cases, ticlopidine (200 mg/day) was prescribed 10 to 14 days before the planned PCI, in addition to aspirin (81–100 mg). In emergency cases, aspirin (162–200 mg) and ticlopidine (200 mg) were administered orally at the emergency care unit. Ticlopidine was prescribed for at least 2 weeks after BMS implantation and for at least 12 weeks⁷ after SES implantation. Following the recommendation of the American Heart Association⁸, dual antiplatelet therapy was preferably continued for at least 1 year after the procedure, but the timing of the discontinuation of dual antiplatelet therapy and use of aspirin alone were left to the physician's discretion.

When an adverse effect due to ticlopidine occurred, ticlopidine was replaced with cilostazol (200–300 mg/day). When adverse effects due to cilostazol occurred, cilostazol was replaced with clopidogrel. At our cardiovascular center, clopidogrel became available in September 2004, and SES implantation was routinely performed with clopidogrel as a backup with the patient's informed consent.

Follow-up coronary angiography

Beyond 30 days after the procedure, f-CAG studies were planned at approximately 6 months²⁹ for the BMS group and at approximately 12 months³⁰ for the SES group. Patients presenting with chest pain and acute coronary syndrome due to ISR (defined below) underwent ad hoc emergency PCI or CABG. The duration of the index procedure for f-CAG was defined as the follow-up interval. By November 2007, f-CAG had been performed for 77.0% of lesions (191 of 248 lesions) in the BMS group and for 72.3% of lesion (251 of 347 lesions) in the SES group.

End point

The study's end point was determined by the rate of a TLR composite of repeat PCI and CABG. TLR was defined as any (elective and emergency) repeat PCI or CABG performed because of visual ISR, including ISR at the 5-mm proximal and distal stent margins. The need for TLR was decided mainly on the basis of the visual angiographic outcome, the patient's symptoms, and the outcomes as indicated with stress electrocardiograms, cardiac ultrasonography, radionuclide images, and pressure flow wire.

Stent-length-based grouping

Stent length was defined as the length of the stented segment calculated by adding the length of each stent regardless of overlap. The TLR rates after implantation of SESs or BMSs were examined in groups divided by stent length: Group $1=(BMS \le 14 \text{ mm}, \text{SES}=13 \text{ mm})$, Group $2=(15 \le BMS \le 24 \text{ mm}, \text{SES}=18 \text{ or } 23 \text{ mm})$, Group $3=(25 \le BMS \le 34 \text{ mm}, \text{SES}=28 \text{ or } 33 \text{ mm})$, and Group $4=(35 \le BMS, \text{SES}=$ multiple). In Group 1, there were 14 lesions in 13 patients receiving SESs and 30 lesions in 23 patients receiving BMSs. In Group 2, there were 139 lesions in 116 patients receiving SESs and 103 lesions in 81 patients receiving BMSs. In Group 3, there were 49 lesions in 42 patients receiving SESs and 42 lesions in 38 patients receiving BMSs. Finally, in Group 4, there were 49 lesions in 41 patients receiving SESs and 16 lesions in 10 patients receiving BMSs.

Statistical analysis

Values of variables are expressed only as mean values. The variables given above and the incidence of end points were statistically compared by means of unpaired t-tests for continuous variables or the χ^2 test for categorical variables. A difference was significant when the *p* value was less than 0.05. Statistical analysis was performed with SPSS for Windows, version 11.5 (SPSS, Inc., Chicago, IL, USA).

RESULTS

Comparison of variables and angiographic outcomes between the BMS and SES groups

The rates of diabetes (p < 0.01) and chronic total occlusion (CTO) (p < 0.01) were significantly higher in the BMS group than in the SES group; however, the rates of previous myocardial infarction (p < 0.01), bifurcation (p < 0.01), and aorto-ostial lesions (p < 0.01), the mean stent number (p < 0.05), and mean stent length (p < 0.01) were significantly greater in the SES group than in the BMS group (Table 1). The overall incidence of angiographic TLR in the SES group (4.8%) was significantly lower than that in the BMS group (15.7%, p < 0.01). The mean duration of follow-up in the SES group (380 days) was significantly longer than that in the BMS group (217 days) (p < 0.01).

Comparison of variables and outcomes between BMS and SES patients in stent-length based groups

In Group 1 (Table 2–1), the rates of diabetes (p < 0.05) and hyperlipidemia (p < 0.01) were significantly higher in the BMS group than in the SES group; however, the rate of aorto-ostial lesions (p < 0.05) and the mean stent length (p < 0.01) were significantly greater in the SES group than in the BMS group. The TLR rate did not differ significantly between the SES group (7.1%) and the BMS group (6.8%; Fig. 1).

In Group 2 (Table 2–1), the rates of previous myocardial infarction (p < 0.01) and bifurcation (p < 0.01) and the mean stent length (p < 0.01) were significantly greater in the BMS group than in the SES group. The rates of proximal tortuosity (p < 0.05) and CTO (p < 0.05) were significantly greater in the SES group than in the BMS group. The TLR rate was significantly less in the SES group (1.44%) than in the BMS group (8.74%, p < 0.05; Fig. 1).

In Group 3 (Table 2–2), the rate of diabetes (p < 0.05) and the number of stents (p < 0.01) were significantly greater in the SES group than in the BMS group. The TLR rate in the SES group (0%) was significantly less than that in the BMS group (33.3%, p < 0.001; Fig. 1).

Thus, the TLR rates after single SES implantation in Groups 1, 2, and 3 (1.49%) were significantly lower (an 89.6% reduction) than those in the BMS group (14.3%, p < 0.01).

In Group 4 (Table 2–2), the rates of hypertension (p < 0.05), stable angina pectoris (p < 0.01), and bifurcation (p < 0.05), and the mean stent length (p < 0.01) were significantly greater in the SES group than in the BMS group. The TLR rates did not differ significantly between the SES group (18.4%) and the BMS group (25.0%; Fig. 1). The TLR rate after a second PCI procedure did not differ significantly between the SES group (180%) and the BMS group (88.9%) and the BMS group (100%).

SES group details regarding the single case of angiographic TLR in Group 1 and the 9 cases in Group 4

In the single case of TLR in Group 1, the lesion was located in the midportion of the left circumflex artery (LCx) at a bending site.

Among the 9 cases of TLR in Group 4, 8 lesions

| | | BMS | SES |
|-----------------------------|----------------------------|----------|------------|
| | Number | 191 | 251 |
| Patient characteristics | Male sex (%) | 84.3 | 83.3 |
| | Age (yr) | 66.4 | 66.0 |
| | Diabetes (%) | 42.4 | 30.3** |
| | Hyperlipidemia (%) | 83.8 | 82.9 |
| | Hypertension (%) | 78.2 | 81.5 |
| | Smoking (%) | 22.3 | 24.7 |
| Clinical characteristics | Old MI (%) | 24.6 | 43.0** |
| | Previous CABG (%) | 9.42 | 11.6 |
| | Hemodialysis (%) | 4.19 | 3.19 |
| Clinical diagnosis | RMI (%) | 10.0 | 12.2 |
| | SMI (%) | 36.7 | 37.8 |
| | SAP (%) | 53.3 | 37.8 |
| Lesion characteristics | LAD (%) | 38.2 | 31.4 |
| | LCx (%) | 13.6 | 15.1 |
| | RCA (%) | 44.5 | 48.6 |
| | LMT (%) | 3.7 | 4.4 |
| | Single-VD (%) | 43.5 | 48.6 |
| ACC/AHA task classification | Diffuse (%) | 50.3 | 55.8 |
| | Bifurcation (%) | 25.7 | 41.4** |
| | Calcification (%) | 12.6 | 9.16 |
| | Bending (%) | 14.7 | 16.3 |
| | Proximal tortuosity (%) | 5.76 | 3.19 |
| | СТО (%) | 8.38 | 3.59* |
| | Ao-ostial (%) | 3.66 | 10.8** |
| PCI characteristics | Stent number (/lesion) | 1.15 | 1.24* |
| | Stent diameter (mm) | 3.76 | 3.72 |
| | Stent length (mm) | 22.1 | 28.8** |
| | IVUS-guide (%) | 96.9 | 97.6 |
| | Rotablator (%) | 8.90 | 5.58 |
| Angiographic outcome | Follow-up interval (days) | 217 | 380** |
| | Visual ISR (%) | 15.7 | 4.78** |
| | Focal ISR (%/ISR) | 33.3 | 100.0** |
| | Angiographic TLR $(n, \%)$ | 30, 15.7 | 12, 4.78** |
| | re-PCI (%/TLR) | 96.7 | 91.7 |

Table 1. Comparison of variables between the BMS and SES groups.

p < 0.05 and p < 0.01 vs BMS.

were located in the right coronary artery (RCA). The ISR was aorto-ostial (i.e., RCA-ostial) in 3 cases, at stent overlap sites in 4 cases, and at the primary targeted occluded site of CTO in 1 case. The single lesion located in the proximal left anterior descending artery (LAD) was a primary, heavily calcified site where an SES had been implanted after ablation with a rotablator. The patient had received hemodialysis for many years.

DISCUSSION

Higher rate of angiographic TLR after implantation of large multiple SESs in the RCA

The rate of TLR after implantation of multiple SESs was significantly higher than that after implantation of a single SES (Fig. 1). The rate after implantation of multiple SESs was also higher than previously reported rates (less than 10%) after SES

| Table 2. | Comparison of | variables be | etween the | BMS and | SES grou | os according to | stent length. |
|----------|---------------|--------------|------------|---------|----------|-----------------|---------------|
|----------|---------------|--------------|------------|---------|----------|-----------------|---------------|

| | | Group-1 | | Group-2 | |
|-----------------------------|---------------------------|------------|----------------|----------|----------------|
| | Stent length (mm) | < = 14 mm | SES=13 mm | 15~24 mm | SES=18 & 23 mm |
| | | BMS | SES | BMS | SES |
| | Number | 30 | 14 | 103 | 139 |
| Patient characteristics | Male sex (%) | 76.7 | 78.6 | 86.4 | 83.5 |
| | Age (yr) | 70.2 | 68.0 | 66.0 | 65.5 |
| | Diabetes (%) | 53.3 | 21.4* | 35.9 | 28.1 |
| | Hyperlipidemia (%) | 100 | 57.1** | 80.6 | 87.8 |
| | Hypertension (%) | 80.0 | 92.9 | 77.2 | 78.1 |
| | Smoking (%) | 23.3 | 14.3 | 23.8 | 23.7 |
| Clinical characteristics | Old MI (%) | 20.0 | 28.6 | 24.3 | 48.9** |
| | Previous CABG (%) | 10.0 | 0 | 7.77 | 15.1 |
| | Heamodialysis (%) | 6.67 | 0 | 2.91 | 2.16 |
| Clinical diagnosis | RMI (%) | 10.0 | 0.0 | 3.9 | 2.9 |
| | SMI (%) | 36.7 | 50.0 | 39.8 | 45.3 |
| | SAP (%) | 53.3 | 50.0 | 56.3 | 49.6 |
| Lesion characteristics | LAD (%) | 26.7 | 21.4 | 45.6 | 35.3 |
| | LCx (%) | 13.3 | 21.4 | 14.6 | 20.1 |
| | RCA (%) | 50.9 | 42.9 | 36.9 | 40.3 |
| | LMT (%) | 10.0 | 14.3 | 2.9 | 4.3 |
| | Single-VD (%) | 33.3 | 64.3 (p=0.054) | 48.5 | 48.9 |
| ACC/AHA task classification | Diffuse (%) | 0 | 0 | 47.6 | 43.2 |
| | Bifurcation (%) | 16.7 | 7.14 | 28.2 | 44.6** |
| | Calcification (%) | 13.3 | 0 | 10.7 | 6.47 |
| | Bending (%) | 16.7 | 21.4 | 13.6 | 7.91 |
| | Proximal tortuosity (%) | 16.7 | 14.3 | 4.85 | 0.72* |
| | СТО (%) | 0 | 0 | 8.73 | 2.16* |
| | Ao-ostial (%) | 6.67 | 28.6* | 2.91 | 7.19 |
| PCI characteristics | Stent number (/lesion) | 1.00 | 1.00 | 1.01 | 1.00 |
| | Stent diameter (mm) | 3.85 | 3.91 | 3.75 | 3.69 |
| | Stent length (mm) | 11.6 | 13** | 18.5 | 20.3** |
| | IVUS-guide (%) | 100 | 92.9 | 95.1 | 97.1 |
| | Rotablator (%) | 10.0 | 0 | 7.77 | 2.88 |
| Angiographic outcome | Follow-up interval (days) | 219 | 363** | 220 | 378** |
| | Visual ISR (%) | 6.67 | 7.14 | 8.74 | 0.72** |
| | Focal ISR (%/ISR) | 50.0 | 100.0 | 38.8 | 100** |

implantation^{1-4,15,16,26}. Possible reasons for the high rate of angiographic TLR after implantation of multiple SESs, despite the absolute efficacy of the implantation of a single SES (Fig. 1), are as follows. A review of the 9 cases that required TLR (described in the last paragraph of Results) showed that certain variables (i.e., stent overlap, aorto-ostial lesions, number of stents, lesion in the RCA) were factors in the

increased rate of TLR after implantation of multiple SESs. First, stent overlap due to the higher number of stents was a major reason for ISR. Stent overlap is a consistent cause of TLR and ISR in patients treated with SESs^{10,14,20–22}. The reason for higher ISR rate at stent overlap was because of incomplete stent expansion^{33,34} owing to the rigid edge of the SES's platform (BX Velocity[®]), or stent fractures³⁵

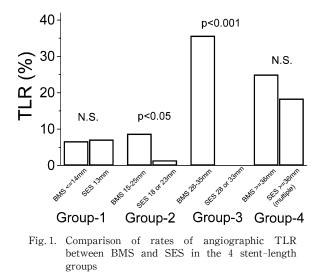
March, 2009

Table 2-2

| | | Group-3 | | Group-4 | |
|-----------------------------|---------------------------|----------|----------------|------------|------------|
| | Stent length (mm) | 25~34 mm | SES=28 & 33 mm | 35 mm < = | 35 mm < = |
| | | BMS | SES | BMS | SES |
| | Number | 42 | 49 | 17 | 49 |
| Patient characteristics | Male sex (%) | 86.4 | 87.8 | 76.5 | 79.6 |
| | Age (yr) | 64.8 | 67.3 | 66.1 | 65.8 |
| | Diabetes (%) | 47.7* | 28.6 | 52.9 | 40.8 |
| | Hyperlipidemia (%) | 81.8 | 79.6 | 76.5 | 79.6 |
| | Hypertension (%) | 83.3 | 77.6 | 70.6 | 91.8* |
| | Smoking (%) | 21.4 | 30.6 | 17.6 | 24.5 |
| Clinical characteristics | Old MI (%) | 31.8 | 36.7 | 23.5 | 36.8* |
| | Previous CABG (%) | 13.6 | 12.2 | 5.88 | 4.08 |
| | Heamodialysis (%) | 6.82 | 6.12 | 0 | 4.08 |
| Clinical diagnosis | RMI (%) | 2.3 | 4.1 | 0.0 | 10.2 |
| | SMI (%) | 29.5 | 38.8 | 5.9 | 38.8 |
| | SAP (%) | 56.8 | 59.2 | 94.1 | 51.2** |
| Lesion characteristics | LAD (%) | 34.1 | 49.0 | 29.4 | 8.2 |
| | LCx (%) | 15.9 | 12.2 | 0.0 | 2.0 |
| | RCA (%) | 45.2 | 34.7 | 64.7 | 87.8 |
| | LMT (%) | 2.3 | 4.1 | 5.9 | 2.0 |
| | Single-VD (%) | 38.6 | 42.9 | 41.1 | 49.0 |
| ACC/AHA task classification | Diffuse (%) | 77.3 | 75.5 | 88.2 | 87.8 |
| | Bifurcation (%) | 31.8 | 44.9 | 5.9 | 38.8* |
| | Calcification (%) | 13.6 | 18.4 | 23.5 | 10.2 |
| | Bending (%) | 13.6 | 10.2 | 17.6 | 44.9* |
| | Proximal tortuosity (%) | 2.27 | 0 | 0 | 10.2 |
| | СТО (%) | 11.4 | 2.04 (p=0.058) | 11.8 | 10.2 |
| | Ao-ostial (%) | 4.55 | 8.16 | 5.88 | 18.4 |
| PCI characteristics | Stent number (/lesion) | 1.18 | 1.00** | 2.24 | 2.24 |
| | Stent diameter (mm) | 3.70 | 3.65 | 3.72 | 3.81 |
| | Stent length (mm) | 29.6 | 30.7 | 44.2 | 55.5** |
| | IVUS-guide (%) | 97.7 | 100 | 100 | 98.0 |
| | Rotablator (%) | 11.4 | 10.2 | 5.88 | 10 |
| Angiographic outcome | Follow-up interval (days) | 195 | 388** | 252 | 382*** |
| | Visual ISR (%) | 34.1 | 0** | 23.5 | 18.4 |
| | Focal ISR (%/ISR) | 33.3 | 0.0 | 0 | 100.0** |

p < 0.05 and p < 0.01 vs BMS.

induced by excessive pressure or high-pressure expansion or by mechanical stress at the overlap site. Therefore, an antirestenotic effect was not exerted at the overlap site despite being a double-dosed site in large vessels. Second, an aorto-ostial lesion of the RCA was a consistent factor in the increased rate of TLR after SES or BMS implantation because of the histological and mechanical features of the RCA ostium^{27,36}. Thus, by involving the aorto-ostial lesion of the RCA in the implantation of multiple stents, the possibility of TLR is increased. Third, the effect of the rigid SES's platform on the RCA must be taken into account when the number of stents is increased. If a stent edge effect³⁸ is established along bending sites of the RCA, the rate of ISR is increased^{37–39}. Therefore, to avoid a stent edge effect, the number and length of implanted stents were increased. Thus, the rate of angiographic TLR was significantly in-



creased after implantation of multiple large SESs in the RCA. This increased rate of TLR was not dependent on an antirestenotic effect of sirolimus after implantation of a single SES but was dependent on the properties of the rigid SES platform and of the native RCA. Higher TLR ratio of SES after implantation to RCA was considered to be a limitation of the Cypher®stent, including its platform. Thus, to further evaluate the advantages and disadvantages of the implantation of multiple large SESs, future studies would be useful for comparing SESs and BMSs, for comparing SESs and SESs with flexible BMSs implanted at bending sites (hybrid stenting), or for comparing SESs and second-generation DESs with a revised platform.

Efficacy of a single large SES of intermediate length (18 to 33 mm)

The efficacy of a single large SES was indicated by the lower rate of angiographic TLR than with BMS (Table 1 and Fig. 1). Because the rate of late luminal loss was similar at any vessel size with both BMSs and DESs, the efficacy of large (\geq 3.5 mm) BMSs and DESs might be equivalent^{17,18}. However, a decreasing effect of stent length on TLR was observed in the BMS group (Groups 2 and 3), and the benefit of single SES implantation within the range of 18 to 33 mm was outstanding (Table 2, Fig. 1). Although the efficacy of large, intermediate–length BMSs (Group 2) was acceptable, SESs were far superior to BMSs (Fig. 1). In addition, SESs 28 to 33 mm long were more efficacious than BMSs (Group 3). The benefits of single SES might not be offset the low rates of late (30 days to 1 year) and very late (beyond 1 year) definite stent thrombosis⁵, because such thromboses are very rare in Japan²⁷. Thus, the antirestenotic effect of a single large SES was maximal when the stent was of intermediate length (18 to 33 mm) and electively implanted for de novo lesions.

Despite examining a very small population, this study suggests that spot stenting with a single short (13 mm) SES might be used instead of a short BMS^{19,20}, because the rates of angiographic TLR were similar (Table 2, Fig. 1). On the other hand, a longer (18 mm) SES was selected because a single case of TLR in Group 1 would reflect the technical miss at spot stenting in the LCx.

LIMITATIONS

This study has several limitations. The present study was a small, retrospective, nonrandomized, single-center study. Thus, larger prospective studies are needed to examine the efficacy of BMSs and SESs, in groups corresponding to this study's Group 1 and Group 4. The advantage of angiographic outcomes with a single large (18-33 mm) SES was consistent (Fig. 1). Although 442 lesions were examined, the rates of f-CAG were not extremely high. The parameters of quantitative coronary angiography were not examined. The effectiveness of BMSs might be overestimated because previous generations of BMS were examined. Because the optimal intervals between implantation and evaluation were different for BMSs²⁹ and SESs³⁰, observational durations were different.

CONCLUSION

SESs are most effective when they are electively implanted and of intermediate length (18 to 33 mm). However, large prospective studies are needed to determine whether short, large (\geq 3.5 mm) single SESs and multiple SESs electively implanted are as effective as BMSs for de novo lesions in native coronary arteries.

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