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Sirolimus- versus Everolimus- and Biolumus-eluting Stents after Long Stenting : A Propensity-Score-Matched Comparison of Angiographic Follow-up Outcomes

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ABSTRACT

We conducted a propensity-score-matched comparison of midterm angiographic outcomes in sirolimus-eluting stents (SESs) versus everolimus-eluting stents (EESs) and biolimus-eluting stents (BESs) after long stenting (total stent length ≥ 40 mm). This is because randomized trials have not shown the efficacy of newly developed EES and BES after long stenting when compared to SES. Our study was a nonrandomized, retrospective, lesion-based, multicenter study. We included 842 angiographically followed-up lesions within 550 days of successful SES (n = 546) or EES (n = 252) and BES (n = 44) (EES-BES group) placement for de novo native coronary stenosis performed from August 2004 through January 2014. The endpoint, as an angiographic surrogate of clinical efficacy, was the distribution of follow-up percent diameter stenosis (follow-up %DS), which consisted of the percentages of follow-up %DS > 50 (binary in-stent restenosis) and < 20 (cut-off as the stenotic lesion by intimal growth). Propensity-score-matched analyses were conducted to adjust the baselines. Using a crude baseline, the percentages of follow-up %DS > 50 (7.4%) and < 20 (65.5%) were significantly different in the EES-BES group compared to the SES group (13.6%, p = 0.008 ; and 38.3%, p<0.001 ; respectively). Baseline adjustment resulted in 266 lesions in each arm. The percentages of follow-up %DS > 50 (7.1%) and < 20 (67.3%) in the EES-BES group remained significant when compared to those of the SES group (14.7%, p = 0.008 ; 53.8%, p = 0.002 ; respectively). Thus, we firstly report the superiority of the midterm angiographic outcomes of EES and BES compared to SES after long stenting for de novo coronary stenosis. (Jikeikai Med J 2017 ; 64 : 1-9)

Key words : follow-up result, angioplasty, binary restenosis, target lesion revascularization, late luminal loss

INTRODUCTION

Stent length has been a consistent predictor of adverse clinical and angiographic outcomes in the use of drug-eluting stents (DESs)[1,2] of the first generation (sirolimus-eluting stents [SESs] and paclitaxel-eluting stents [PESs]) and

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second generation (everolimus-eluting stents [EESs] and biolimus-eluting stents [BESs]). Patients who have received long stents are at great risk for adverse clinical outcomes, and lesions treated with long stents have higher frequencies of in-stent restenosis (ISR) and target lesion revascularization (TLR)[1-7]. When first-generation DESs were used, antirestenotic effects exerted after the insertion of long stents were more potent with SESs than with bare-metal stents or PESs[3-5]. With second-generation DESs, vascular responses have been more favorable[8,9] and overall angiographic outcomes have been more promising[10] with EESs and BESs than with SESs. However, in terms of in-segment late luminal loss and TLR after the use of long stents, SESs lead to better angiographic outcomes than do BES[6]. Furthermore, SES and EES lead to equivalent angiographic outcomes in terms of in-stent late luminal loss and TLR, whereas SESs result in significantly smaller in-segment late luminal loss after long stenting[7].

Therefore, we have been interested in examining the effects of the advances in coronary stent technology from first-generation DESs (SESs) to second-generation DESs (EESs or BESs or both), particularly after the insertion of long stents. For this reason, we performed a retrospective comparison of midterm angiographic outcomes of SESs with those of EESs or BESs or both after elective insertion of long stents (total stent length ≥ 40 mm). We studied follow-up angiographic examinations of lesions within 550 days of the successful elective insertion of either an SES or an EES or BES. We used a unified database of 6 institutions which was used in our recent study[10]. As angiographic surrogate primary endpoints for clinical DES efficacy[11,12], we estimated the distribution of follow-up percent diameter stenosis (%DS) and the percentages of follow-up %DS > 50 (the frequency of binary in-stent restenosis) and < 20 (cut-off value as the stenotic lesion by intimal growth at quantitative coronary angiogram). Furthermore, a propensity-score-matching analysis was performed to adjust the baselines used for the above angiographic outcomes for use in retrospective, nonrandomized, and historical comparisons. We performed the analysis according to the design of a former report examining the efficacy of second-generation DES compared with that of first-generation DES[13].

METHODS

1. Study design, population, and follow-up secondary angiogram

We performed a retrospective, nonrandomized, lesion-based, multicenter study of stent-treated lesions in arteries listed in a database of divisions of cardiology at The Jikei University School of Medicine and 5 related institutions : The Jikei University Kashiwa Hospital, The Jikei University Daisan Hospital, Saitama Cardiovascular Respiratory Center, Fuji City General Hospital, and Nishi-Saitama Central Hospital. The study was approved by the ethics committee of the Division of Cardiology, Department of Internal Medicine, The Jikei University School of Medicine. The retrospective examination was performed from November 2014 through July 2015.

In the present study, the selection of stents (DES vs. bare-metal stents) ; the use of percutaneous coronary interventions (PCIs), such as intravascular ultrasonography (IVUS) and rotational atherectomy with a rotablator ; the duration of thienopyridine agent administration after placement of a stent ; and the conduction of follow-up coronary angiography (CAG) were not randomized in all institutions. The inclusion criteria were lesions with de novo stenosis in native coronary arteries that were successfully and exclusively treated with elective SESs or with elective EESs or BESs or both and had not been treated with coronary artery bypass graft surgery. Treatment was considered successful in the absence of periprocedural complications (i.e., death, Q-wave myocardial infarction, and emergency coronary artery bypass graft surgery). As in our previous study[14], lesions were excluded if patients had undergone PCI supported by intra-aortic balloon pumping, bailout stenting, or hybrid stenting or if the preprocedural reference diameter was > 5.0 mm. In the selected cohort the percentage of 1500-day patient-based severe cardiac events was less than 2%[14]. Thus, we did not examine patient characteristics, such as severe cardiac events, all causes of death, and medications. By avoiding such examinations we were able to focus on midterm follow-up angiographic examinations of the lesions after successful stent placement.

The total length of stents per lesion (length of stent) was calculated by summing the lengths of each stent regardless of overlap. The longest DES (SES or EES) was 38 mm. Thus, "long stenting" was defined as the implantation

in lesions of stents, including overlapping stents, with a total length of greater than 40 mm. Among the 842 lesions that had received long stents and follow-up CAGs within 550 days (8 to 18 months) of the index procedure, 546 lesions received an SES and 296 lesions had received either an EES (252 lesions) or a BES (44 lesions). For the present study, lesions treated with an EES or BES were defined as those treated with a second-generation DES. The NOBORI Biolimus-Eluting Versus XIENCE/PROMUS Everolimus-Eluting Stent Trial[15] has found the favorable and statistically equivalent ratios of TLR after EES and BES placement. Thus, the 546 lesions in the present study that had received a SES comprise 30.5% of all lesion viewed with follow-up angiographic examinations and treated with SES (n = 1793)[10], and the 298 lesions that had received an EES or a BES comprise 18.2% of all lesions treated with an EES (n = 1303) or a BES (n = 324)[10]. The SESs were made from a composite of Cypher Bx Velocity and Cypher Select+ stents (Cordis Corp., Miami, FL, USA). The EESs were made from a composite of Xience V/Promus, Xience Prime, and Xience Xpedition stents (Abbott Corp., Santa Clara, CA, USA), and Promus Element stents (Boston Scientific, Natick, MA, USA). The BESs were made from Nobori Drug-Eluting Stent System (Terumo Corp., Tokyo, Japan).

2. Procedures for stenting, and medications including antiplatelet therapy

All patients were informed of the necessity of PCI and stenting, and informed consent was obtained. The stents were implanted by visual angiographic estimation to cover the entire baseline lesion under the guidance of IVUS (Table 1). Periprocedural antiplatelet therapy was conducted as previously reported[10]. Aspirin (81-100 mg) and ticlopidine (200 mg), clopidogrel (75 mg), or prasugrel (3.75 mg) as the thienopyridine agent were orally administered on the basis of the physician's discretion before the index procedure. The administration of aspirin and the thienopyridine agent as continued for at least 12 months on the basis of the physician's discretion.

3. Quantitative coronary artery evaluation and target lesion revascularization

Quantitative coronary artery (QCA) data were measured with a test circulatory cardiovascular network systems (CAAS-2 or CAAS-5 system, Pie Medical Imaging, Maastricht, Netherlands ; QAngioXA 7.1. 40, Medis Medical Imaging Systems, Leiden, Netherlands) and a GOODNET multiframe Digital Imaging and Communication in Medicine picture archiving and communication system (GOODMAN, Nagoya, Japan). To minimize bias and variations in measurement, the chief physician of each catheter laboratory performed the QCA assessments.

Values were obtained at 3 time points : before PCI (preprocedural), immediately after successful PCI (postprocedural), and during the chronic phase (follow-up). The measurements included the minimal lumen diameter (MLD), %DS, and reference diameter. In cases with occlusions at the preprocedural and follow-up stages, the MLD was considered to be 0 and the %DS was 100. We also calculated the acute gain (postprocedural MLD minus preprocedural MLD), late luminal loss (postprocedural MLD minus MLD at the chronic phase), and late loss index (late luminal loss divided by acute gain). Binary in-stent restenosis (binary restenosis) was defined as a %DS > 50 at the follow-up CAG. ISR was classified as focal (lesion length at chronic phase ≤ 10 mm, type 1) or diffuse (> 10 mm, types 2, 3, and 4)[16].

The frequency of TLR after follow–up CAG, which comprised in-stent body restenosis, including definite stent thrombosis (TLR body), edge restenosis (TLR proximal edge and TLR distal edge), and side branch restenosis (TLR side branch), was compared between lesions receiving an SES and those receiving an EES or BES. The decision to perform TLR was based mainly on binary restenosis as assessed by QCA data. TLR was performed if there was : (1) a positive history of recurrent angina symptoms, presumably related to the target vessel, (2) objective signs of ischemia at rest (electrocardiogram changes) or during exercise test (or equivalent), presumably related to the target vessel, (3) abnormal results of any invasive functional diagnostic test (e.g., fractional flow reserve), or (4) a TLR with a diameter stenosis > = ≥ 65%, even in the absence of the above-mentioned ischemic signs or symptoms.

4. Estimated endpoints

The distributions of follow-up %DS > 50 (binary restenosis as defined above) and < 20, as measured by the percentages from each histogram, were examined and used as midterm angiographic outcomes for the clinical efficacy of DES. This is because follow-up %DS is a suitable surro-

gate angiographic marker for the clinical efficacy of DES[11,12]. A cut-off value of 20% was used as a measure of the potency of the antirestenotic effect of DES because lesion length was usually calculated for lesions with %DS more than 20[10]. The SES showed a bimodal pattern of distribution for follow-up %DS[11,12]. We thus calculated the shift in this pattern in the EES-BES group.

In addition, in-stent late luminal loss (LLL) and late loss index (defined above) were estimated, as they are used to evaluate the efficacy of DES[12].

5. Statistical analyses and variable definitions

Baseline characteristic variables are expressed as the means ± standard deviations (SDs). Variables and endpoints in the SES group were compared to those in the EES-BES group using unpaired t-tests for continuous values and χ^2 or Fisher's tests for categorical values. Our study was designed to compare the outcomes of SES vs. EES or BES after treatment over approximately a decade. Therefore, according to the previous report[10], a propensity-score matching analysis was performed to adjust the baseline values in the 2 groups. The following variables were adjusted using the STATA PSMATCH2 program (StataCorp LP, College Station, TX, USA) : age (age at the index procedure), male sex, diabetes (determined by blood tests for plasma glucose and hemoglobin A1c), hemodialysis (patients with chronic hemodialysis), left anterior descending, left circumflex coronary artery (LCX), right coronary artery (RCA), severe calcification (severe calcified lesions estimated using angiography and IVUS), RCA and LCX ostium (ostium lesions of the RCA and LCX), chronic total occlusion, IVUS (IVUS availability during PCI), rotablator (rotablator used during PCI), diameter of stent (maximum diameter of the balloon used to dilate the stent), length of stent (defined above), preprocedural MLD, preprocedural %DS, postprocedural MLD, postprocedural %DS, and postprocedural reference diameter (20 variables). Maximum pressure (pressure at the maximum inflation diameter of the balloon) and interval for follow-up CAG were not adjusted because these variables were different for the stents used and the institutions where the operations were performed, respectively. The number of stents (number of implanted stents per lesion) was excluded from the adjustment because of the linearity of the length of the stent. The left main coronary artery was excluded from the adjustment because the other three vessels were adjusted. After the adjustment, variables and endpoints in the SES group were compared to those in the EES-BES group using the Wilcoxon signed-rank test (STATA signrank program, StataCorp) for continuous values, and McNemar's chi-square test for categorical values (STATA mcc program, StataCorp). Distributions of follow-up %DS in the crude and adjusted cohorts were compared between the SES and EES-BES groups. A p-value of less than 0.05 was considered to be statistically significant. The Stata for Windows program (Version 13, StataCorp) was used for the statistical analyses by the physicians (M.T. and T.I.).

RESULTS

1. Crude baseline and angiographic follow-up outcomes in the SES and EES-BES groups

Table 1 summarizes the crude baseline and angiographic outcomes in the SES group (n = 546) and the EES-BES group (n = 296). The interval for follow-up CAG in the SES group was 327 ± 93 days, and that of EES-BES group was 329 ± 62 days (p = 0.785). The percentage of rotablator use (18.5%) in the SES group was significantly higher than that in the EES-BES group (4.4%, $p < 0.001$). The mean values of the number of stents (2.27 ± 0.55), diameter of stent (3.15 ± 0.42 mm), pressure (20.0 ± 3.0 atm), preprocedural MLD (0.76 ± 0.58 mm), preprocedural %DS (71.3 ± 20.7), postprocedural MLD (2.53 ± 0.47 mm), and postprocedural %DS (12.1 ± 10.0) in the SES group were significantly different from those in the EES-BES group (2.15 ± 0.44, $p < 0.001$; 3.33 ± 0.42 mm, $p < 0.001$; 17.1 ± 3.6 atm, $p < 0.001$; 0.62 ± 0.42 mm, $p < 0.001$; 74.3 ± 16.5, $p = 0.021$; 2.61 ± 0.54 mm, $p = 0.031$; and 8.33 ± 9.0, $p < 0.001$, respectively). The mean follow-up MLD (2.16 ± 0.72 mm), follow-up %DS (27.8 ± 19.6), and the magnitude of acute gain (1.78 ± 0.62 mm) in the SES group were significantly different from those in the EES-BES group (2.28 ± 0.73 mm, $p = 0.018$; 19.0 ± 18.8, $p < 0.001$; and 1.99 ± 0.67 mm, $p < 0.001$).

The incidences of follow-up %DS < 20 (38.3%), binary restenosis (13.6%), TLR (14.7%), TLR proximal edge (2.0%), and TLR body (12.3%) in the SES group were significantly different from those in the EES-BES group (65.5%, $p < 0.001$; 7.4%, $p = 0.008$; 5.1%, $p < 0.001$; 0.34, $p = 0.049$; and 4.7%, $p < 0.001$).

2. Adjusted baseline and endpoint outcomes in the SES and EES-BES groups

Table 2 shows the adjusted baseline and angiographic outcomes in the SES and EES-BES groups (n = 266 in each arm). The interval for follow-up CAG in the SES group was 333 ± 94 day, and that of EES-BES group was 331 ± 62 days (p = 0.577). The mean magnitude of follow-up %DS in the SES group (25.1 ± 21.1) was significantly higher than that in the EES-BES group (18.3 ± 18.3, $p < 0.001$).

The incidences of follow-up %DS < 20 (53.8%), binary restenosis (14.7%), TLR (14.7%), TLR proximal edge (3.0%), and TLR body (11.7%) in the SES group were significantly different from those in the EES-BES group (67.3%, p = 0.002 ; 7.1%, p = 0.008 ; 4.9%, $p < 0.001$; 0.37%, p = 0.039 ; and 4.5%, p = 0.004).

3. Distributions of follow-up %DS in the SES and EES-BES groups

The distributions of %DS in the crude (Fig. 1A) and adjusted (Fig. 1B) cohorts in the SES and EES-BES groups are shown. In the crude and adjusted cohorts, the percentages of follow-up %DS < 20 and > 50 in the SES group were significantly different from those in the EES-BES group (Tables 1 and 2). Therefore, the shifts in the pattern were better in the EES-BES group with a significant increase in the percentage of follow-up %DS < 20 and a decrease in binary restenosis (follow-up %DS > 50) in both graphs.

Discussion

We report the angiographic efficacy of second-generation "-limus" (i.e., EES and BES) over first-generation "-limus" (SES) for the treatment of lesions with total stented lengths of more than 40 mm. We assessed efficacy in terms of a shift toward a better pattern of distribution of follow-up %DS (Table 2 and Fig. 1), which is the most reliable angiographic surrogate for clinical efficacy[11]. Long-stented lesions lead to higher risks for ISR and TLR[1-7]. During the first-generation DES era, new innovative coronary stents have reduced these risks owing to better angiographic outcomes[1,3-5]. However, second-generation-limus eluting stents, such as EES[6] and BES[7], have statistically equivalent, partially inferior, angiographic outcomes after long stenting when compared to SES. Therefore, based on a former report (13), we designed and conducted a propensity-score matched analysis using for retrospective and historical comparisons by recruiting a cohort from a unified multicenter database. Although SES is no longer used, the present study highlights advances in stent technology by confirming the overall better angiographic outcomes of EES and BES in very long-stented lesions when compared to the formerly approved, widely used, and evidence-based SES in a daily practice environment.

The present cohort has a mean total stenting length of 56 to 57 mm. In addition, one-sixth of the lesions in this study are severely calcified (Table 2). Thus, our cohort includes higher-risk lesions compared to those of the LEADERS substudy (43 mm)[6] and the LONG-DES-III study (46 mm)[7]. In addition, the mean magnitude of late luminal loss (LLL) in the EES-BES group (0.31 mm) (Table 2) was far larger than that reported in the NEXT-OCT subtrial (approximately 0.09-0.16 mm), which recruited selected Japanese patients whose SYNTAX score was approximately 10[17]. The LLL in the EES-BES group was also larger than that of the postmarketing surveillance (PMS) study of cobalt-chromium EES in Japan (Xience Japan-PMS, 0.22 mm)[18]. Because LLL is monotonically related to the risk of ISR (12, the larger magnitude of LLL in the present EES-BES group indicates that the present crude and adjusted baselines include more complex lesions with higher propensities for ISR, which represent the real world clinical setting. In this setting, by estimating follow-up %DS as a surrogate for DES efficacy[11], we show more advantageous angiographic follow-up results for EES and BES vs. SES, unlike what has been found in prospective trials[6,7]. The percentages of binary restenosis and TLR in the EES-BES group were 7.1% and 4.9%, respectively. These values represent 52% and 67% reductions compared to those in the SES group (14.7% and 14.7%, respectively) (Table 2). The 1-2-year overall TLR rates in the Xience Japan-PMS (3.6-4.6%)[18] were slightly lower. On the other hand, the 1-year TLR rate in the PMS study on SES in Japan[19] was far lower (4.2%) than that found in the present study. This discrepancy indicates that EES and BES are effective in the present very high risk cohort in a daily practice environment. This is due to advances in stent technology, which are reflected in the favorable vascular responses to EES[8] and BES[9]. EES and BES advances over SES include revised stent platforms, anti-thrombogenic fluoropolymers, and the use of

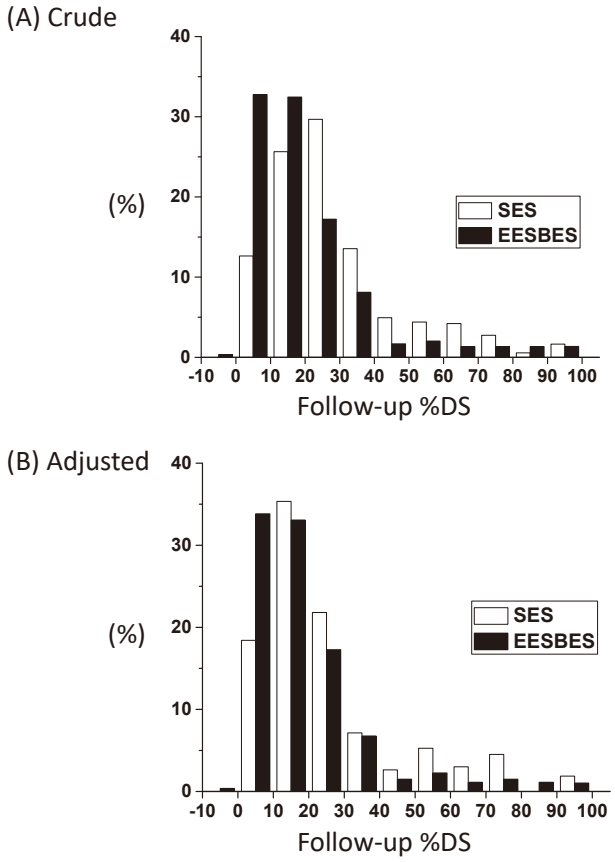

Fig. 1. Histogram showing the distributions of follow-up % diameter stenosis (DS) in the SES and EES-BES groups
The distributions of follow-up %DS in the SES (white bar) and EES-BES (black bar) groups in the (A) crude and (B) adjusted cohorts are shown. SES had a bimodal pattern of follow-up %DS distribution. The vertical axis represents the percentage of the angiographic follow-up lesions. The number of lesions was calculated in a follow-up %DS unit of 10.

biocompatible drugs. Advances in PCI techniques over the past decade might be a major confounding factor. The high percentage of PCI performed under the guidance of IVUS, high-pressure ballooning at stent placement, and the low incidence of TLR due to edge restenosis indicate that PCI was the most appropriate technique for the present cohort (Tables 1 and 2). However, as we have previously reported, the very low frequency of early definite stent thrombosis in the one-third of the patients with emergent PCI and the one-sixth of the patients with ST-elevation myocardial infarction in the SES era[20] and optimal stent placement under the guidance of IVUS with high pressure balloon inflation has been continued in our institutes (Tables 1 and 2). Therefore, by adjusting the baselines using a propensity-score-matched analysis, we confirmed the efficacy of second-generation limuses (EES and BES) compared to SES in very long-stented lesions.

The distribution of follow-up %DS more closely relates to TLR incidence compared to the magnitudes of LLL and late loss index (Table 2). The discrepancy in significance between the mean magnitudes of late luminal loss and late loss index and the incidence of TLR in the long-stented lesions was consistent with a previous report[11], which suggested that, compared to the mean magnitude of LLL, follow-up %DS has an advantage as a surrogate for clinical efficacy.

The following limitations must be taken into account in the present retrospective, nonrandomized, historical comparison. First, the details of all patients and the lesion characteristics in the integrated databases and those of the excluded lesions were not fully understood. Second, confounders may remain after baseline adjustment using the propensity-score–matched analyses. Third, the frequencies of stent fracture, which is the major causative factor of

Table 1. Crude baseline and angiographic follow-up outcomes in the sirolimus-eluting stent (SES) group and the everolimus-eluting stent (EES)-biolimus-eluting stent (BES) group

Variable	SES, $n = 546$	EES-BES, $n = 296$	p-value
Age (years)	66.9 ± 9.2	66.4 ± 10.4	0.469
Male sex (%)	80.2	82.4	0.435
Diabetes (%)	47.4	51.0	0.321
Hemodialysis (%)	2.9	4.7	0.179
Left anterior descending coronary artery (%)	50.0	51.7	0.640
left circumflex coronary artery (%)	17.9	16.2	0.526
Right coronary artery (%)	31.5	31.1	0.900
Severe calcification (%)	20.7	21.3	0.841
Right coronary artery ostium (%)	2.4	2.4	0.988
Left anterior descending coronary artery ostium (%)	2.4	1.0	0.165
Chronic total occlusion (%)	19.8	17.6	0.435
Intravascular ultrasonography (%)	97.3	98.6	0.193
Rotablator (%)	18.5	4.4	< 0.001
Number of stents	2.27 ± 0.55	2.15 ± 0.44	< 0.001
Diameter of stents (mm)	3.15 ± 0.42	3.33 ± 0.42	< 0.001
Length of stents (mm)	57.9 ± 16.7	56.9 ± 15.3	0.423
Pressure (atm)	20.0 ± 3.0	17.1 ± 3.6	< 0.001
Preprocedural MLD (mm)	0.76 ± 0.58	0.62 ± 0.42	< 0.001
Preprocedural %DS	71.3 ± 20.7	74.3 ± 16.5	0.021
Postprocedural MLD (mm)	2.53 ± 0.47	2.61 ± 0.54	0.031
Postprocedural %DS	12.1 ± 10.0	8.33 ± 9.0	< 0.001
Postprocedural reference diameter (mm)	2.91 ± 0.55	2.85 ± 0.51	0.132
Interval for follow-up coronary angiography (days)	327 ± 93.0	329 ± 62.4	0.785
Follow-up MLD (mm)	2.16 ± 0.72	2.28 ± 0.73	0.018
Follow-up %DS	27.8 ± 19.6	19.0 ± 18.8	< 0.001
Acute gain (mm)	1.78 ± 0.62	1.99 ± 0.67	< 0.001
Late luminal loss (mm)	0.38 ± 0.70	0.33 ± 0.61	0.342
Late loss index	0.21 ± 0.51	0.16 ± 0.33	0.128
Follow-up %DS < 20 (%)	38.3	65.5	< 0.001
Binary restenosis (%)	13.6	7.4	0.008
In-stent restenosis type 2-4 (%)	4.2	4.4	0.902
TLR (%)	14.7	5.1	< 0.001
TLR proximal edge (%)	2.0	0.34	0.049
TLR body (%)	12.3	4.7	< 0.001
TLR distal edge (%)	0.18	0	0.461
TLR side branch (%)	0.18	0	0.461

Abbreviations : %DS, percent diameter stenosis ; MLD, minimal lumen diameter ; TLR, target lesion revascularization

binary restenosis, TLR, and stent thrombosis of both of the first- and second-generation DESs, could not be fully estimated using only the follow-up CAG. Since the frequency of TLR body in the SES group was significantly higher than that in the EES-BES group (Table 2), the frequency of stent fracture in the SES group may be higher than that in the EES-BES groups. Thus, although the rates of stent fracture for these DESs at follow-up CAG could not be determined, the lower incidence of stent fracture with the use of second-generation DESs (EES and BES) may contribute to the overall better angiographic outcomes of EES and BES. Fourth, in-segment QCA data and at-edge QCA data were not estimated in the database. Fifth, the difference in the efficacy among EES and BES was not fully examined. However, since the frequencies of 1-year TLR ratios in EES and BES were very low with approximately 5% (15), those after long stenting were considered not to be statistically different. Finally, the impact of bifurcation 2-stent technique on

Table 2. Adjusted baseline and angiographic follow-up outcomes in the sirolimus-eluting stent (SES) group and the everolimus-eluting stent (EES)-biolimus-eluting stent (BES) group

Variable	SES, $n = 266$	EES-BES, $n = 266$	p-value
Age (years)	66.0 ± 8.91	66.5 ± 10.5	0.440
Male sex (%)	79.3	82.0	0.453
Diabetes (%)	48.5	49.2	0.856
Hemodialysis (%)	3.8	4.1	0.819
Left anterior descending coronary artery (%)	55.3	51.5	0.365
Left circumflex coronary artery (%)	12.8	17.3	0.188
Right coronary artery (%)	30.1	30.1	1.000
Severe calcification (%)	16.5	16.5	1.000
Right coronary artery ostium (%)	3.0	1.9	0.366
Left circumflex coronary artery ostium (%)	0	1.1	0.250
Chronic total occlusion (%)	14.3	17.3	0.374
Intravascular ultrasonography (%)	98.1	98.5	0.739
Rotablator (%)	6.0	4.9	0.513
Number of stents	2.19 ± 0.47	2.17 ± 0.43	0.836
Diameter of stents (mm)	3.30 ± 0.45	3.29 ± 0.40	0.966
Length of stents (mm)	56.6 ± 15.1	56.5 ± 15.5	0.730
Preprocedural MLD (mm)	0.65 ± 0.56	0.63 ± 0.42	0.775
Preprocedural %DS	74.0 ± 21.8	74.3 ± 16.3	0.931
Postprocedural MLD (mm)	2.63 ± 0.47	2.61 ± 0.54	0.800
Postprocedural %DS	7.09 ± 9.26	8.50 ± 9.06	0.124
Postprocedural reference diameter (mm)	2.83 ± 0.47	2.85 ± 0.51	0.583
Follow-up MLD (mm)	2.27 ± 0.77	2.30 ± 0.73	0.707
Follow-up %DS	25.1 ± 21.1	18.3 ± 18.3	< 0.001
Acute gain (mm)	1.98 ± 0.69	1.98 ± 0.65	0.922
Late luminal loss (mm)	0.36 ± 0.74	0.31 ± 0.59	0.299
Late loss index	0.18 ± 0.41	0.15 ± 0.32	0.368
Follow-up %DS < 20 (%)	53.8	67.3	0.002
Binary restenosis (%)	14.7	7.1	0.008
In-stent restenosis type 2-4 (%)	4.1	3.8	0.827
TLR (%)	14.7	4.9	< 0.001
TLR proximal edge (%)	3.0	0.37	0.039
TLR body (%)	11.7	4.5	0.004
TLR distal edge (%)	0	0	1.000
TLR side branch (%)	0	0	1.000

Abbreviations : %DS, percent diameter stenosis ; MLD, minimal lumen diameter ; TLR, target lesion revascularization

the angiographic outcomes in the present long-stenting cohort could not be estimated in the database. However, the ostium of LCX, the consistent predictor of ISR, was estimated as in the Tables.

CONCLUSION

Here we first show the superiority of midterm angiographic outcomes following EES and BES vs. SES for de novo coronary stenosis with long stenting in a clinical setting.

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