*Original Article*

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# The stenting strategy of drug-eluting stents for coronary artery disease in patients on dialysis

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**Abstract**

**Background:** Reports regarding the relationship between the length and diameter of implanted drug-eluting stents and clinical and angiographic outcomes in dialysis patients are limited.

**Aim:** We investigated the efficiency of drug-eluting stents for coronary artery disease in patients on dialysis from the viewpoint of stent sizing.

**Methods:** Sirolimus-eluting stents were implanted in 88 lesions and bare metal stents were implanted in 43 lesions. We compared stenting strategy, major adverse cardiac events, and angiographic results between sirolimus-eluting stent and bare metal stent groups.

**Results:** Stent diameter was smaller and stent length was longer in the sirolimus-eluting stent group than in the bare metal stent group in our routine practices. There was no significant between-group difference in late diameter loss. Rates of angiographic restenosis and target lesion revascularization were significantly higher in the sirolimus-eluting stent group than in the bare metal stent group. Although stent length was significantly longer and stent diameter was smaller in the sirolimus-eluting stent group, sirolimus-eluting stents did not improve the subsequent clinical and angiographic results compared with bare metal stents in dialysis patients.

**Conclusion:** In dialysis patients, a longer length and/or smaller diameter sirolimus-eluting stent implantation was associated with high rates of restenosis and target lesion revascularization compared with bare metal stents.

**Keywords**

Bare metal stent, dialysis, drug-eluting stent, major adverse cardiac events

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Cardiovascular disease is the major cause of mortality in dialysis patients.[1] However, the optimal method of revascularization in dialysis patients has not been fully determined. Coronary artery disease in dialysis patients frequently involves diffuse and severely calcified lesions. Therefore, the outcomes of percutaneous coronary intervention (PCI) are worse in this patient population than in nondialysis patients.[2,3] Since the introduction of drug-eluting stents (DES), several studies have demonstrated that DES implantation dramatically reduces the incidences of restenosis and revascularization in PCI compared with bare metal stents (BMS).[4–8] However, several reports indicated that the effectiveness of DES implantation in dialysis patients was limited and was not superior to BMS usage. In this retrospective observational study, we tried to clarify procedural points to be noted in the use of sirolimus-eluting stent (SES) in dialysis patients.[9,10]

## Methods

### *Study patients*

This retrospective study was performed at the Toyohashi Heart Center Hospital. The target population consisted of dialysis patients who had at least one lesion with significant stenosis in native coronary arteries and who underwent successful PCI with SES or BMS from March 2002 through

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February 2006. During this study period, all patients were treated with BMS from March 2002 through July 2004, and all patients were treated with SES from August 2004 through February 2006, following the approval of SES by the Ministry of Health, Labour and Welfare in Japan. Angiographic follow-up at 9 months and clinical follow-up at 12 months after stent implantation were performed. The internal review board of the Toyohashi Heart Center Hospital approved the study protocol. All patients gave written informed consent that they accepted to participate in this study at the same time when they consented to receive PCI procedure.

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### *Procedure and medication*

According to standard care, patients were orally pre-medicated with aspirin 100 mg once daily and ticlopidine 200 mg twice daily. An intravenous bolus of heparin was administered after sheath insertion, with a repeated bolus given as needed to maintain an activated clotting time in excess of 250 s during the procedure. After the intervention, antiplatelet therapy identical to the premedication continued for at least 12 months. Other medications (e.g. β-blockers, statins, and angiotensin-converting enzyme inhibitors) were administered as appropriate.

After a variety of procedures and devices, including plain old balloon angioplasty (POBA), cutting balloon™ (Boston Scientific, USA), Rotablator™ (Boston Scientific), and directional coronary atherectomy (DCA™; Boston Scientific), were used appropriately according to plaque characteristics, SES (Cypher™; Cordis, USA) or BMS was implanted at the lesion site. The SES was available in sizes from 2.5 to 3.5 mm in diameter and from 13 to 33 mm in length. BMS (Bx-Velocity™ (Cordis), Express™ (Boston Scientific), Multi-Link PENTA™ (Abbot Vascular, USA), or DRIVER™ (Medtronic, USA)) were available in sizes from 2.5 to 4.0 mm in diameter and from 8 to 32 mm in length. After stent implantation, angiographic optimization was performed with high-pressure dilatation to achieve an acceptable angiographic result of <25% residual stenosis by visual estimation.

### *Quantitative analysis*

Off-line quantitative coronary arteriography (QCA) was conducted using the view that revealed the greatest degree of stenosis. Severity of coronary stenosis was measured using the Cardiovascular Measurement System (CMS-MEDIS Medical Imaging System, Leiden, The Netherlands). Baseline, post-procedure, and follow-up angiography were evaluated in the same view. An isolated observer who was blinded to all patients' clinical data calculated the lesion length, reference diameter, minimal luminal diameter, and diameter stenosis. Analysis of angiographic frames was performed in end-diastole.

### *Patient follow-up*

The primary endpoint was major adverse cardiac events (MACEs) at 12 months (i.e. death, Q- and non-Q-wave myocardial infarction (MI), and target lesion revascularization (TLR)). Death was defined as all-cause death. Q- and non-Q-wave MI were defined as an increase in creatinine kinase >2 times normal and/or creatinine kinase-MB level >20 ng/mL with and/or without new pathologic Q-wave in >2 contiguous echocardiogram leads. TLR was characterized by repeated percutaneous or surgical intervention of the treated lesions. The secondary endpoint was the rate of restenosis and late lumen loss at 9 months. Binary angiographic restenosis was defined as diameter stenosis >50% in the in-stent lesion (including the stent area and 5-mm segments proximal and distal to the stent edges). Late lumen loss was calculated as the difference in minimal lumen diameters between post-procedure and follow-up.

### *Statistical analysis*

Statistical software (Statistical Package for the Social Sciences (SPSS) version 17.0; SPSS Inc., Chicago, IL) was used for statistical analysis. Continuous variables are shown as mean ± standard deviation (*SD*). Categorical variables were compared using the chi-square test, and continuous variables were compared using Student's unpaired *t*-test. We considered *p*-values <0.05 statistically significant.

## Results

From March 2002 through February 2006, PCI was performed for 132 dialysis patients with 174 de novo stenosis lesions. We studied 94 patients (131 lesions) from this population base who were implanted with SES or BMS. Patients who received PCI procedures without using stents were excluded from the study. A total of 58 patients with 88 lesions received SES from August 2004 through February 2006 (DES group), and 36 patients with 43 lesions received BMS (BMS group) from March 2002 through July 2004. The baseline patient characteristics of the two groups are presented in Table 1. The mean ages were approximately 65 and 63 years in the SES group and the BMS group, respectively. There were no significant between-group differences in baseline patient characteristics. Baseline lesion characteristics are shown in Table 2. The lesion characteristics were mostly similar between the groups, except for the American Heart Association/American College of Cardiology (AHA/ACC) classification of the lesion characteristics. The B1-type lesion was more common in the BMS group than in the SES group. Procedural data are summarized in Table 3. Pre-dilatation was performed in 93% of lesions in the SES group and in 98% of lesions in the BMS group. There was no significant difference in POBA, Rotablator, or DCA usage between the two groups. Post-procedure lesion characteristics are presented in Table 3. The number of implanted

**Table 1.** Patient characteristics.

| | BMS | DES | *p* |
|---|---|---|---|
| Number of patients | 36 | 58 | |
| Age, mean ± *SD*, years | 63.12 ± 9.42 | 65.17 ± 9.65 | 0.54 |
| Male, *n* (%) | 25 (69) | 43 (74) | 0.64 |
| Diabetes, *n* (%) | 17 (47) | 35 (60) | 0.29 |
| Hypertension, *n* (%) | 20 (56) | 43 (74) | 0.07 |
| Hyperlipidemia, *n* (%) | 5 (14) | 12 (21) | 0.58 |
| Current smoking, *n* (%) | 4 (11) | 12 (21) | 0.27 |
| Family history, *n* (%) | 4 (11) | 5 (8) | 0.73 |
| Prior CABG, *n* (%) | 18 (50) | 36 (62) | 0.29 |
| Prior MI, *n* (%) | 3 (8) | 2 (3) | 0.37 |
| 1VD/2VD/3VD | 6/12/18 | 4/22/32 | 0.54 |

BMS: bare metal stent; DES: drug-eluting stent; *SD*: standard deviation; CABG: coronary artery bypass grafting; MI: myocardial infarction; VD: vessel disease.

**Table 2.** Lesion characteristics.

| | BMS | DES | *p* |
|---|---|---|---|
| Number of lesions | 43 | 88 | |
| Treated vessel | | | |
| LMT | 5 | 5 | 0.3 |
| LAD | 12 | 27 | 0.84 |
| LCX | 8 | 16 | 0.95 |
| RCA | 18 | 40 | 0.71 |
| AHA/ACC lesion type | | | |
| A | 0 | 0 | NA |
| B1 | 5 (12) | 1 (1) | 0.007 |
| B2 | 21 (49) | 57 (65) | 0.09 |
| C | 17 (40) | 30 (34) | 0.57 |
| Angiographic calcification | 36 (84) | 77 (86) | 0.59 |
| Bending | 10 (23) | 29 (33) | 0.31 |
| Significant side branch | 6 (14) | 24 (27) | 0.12 |

BMS: bare metal stent; DES: drug-eluting stent; LMT: left mine trunk; LAD: left anterior descending; LCX: left circumflex; RCA: right coronary artery; AHA/ACC: American Heart Association/American College of Cardiology.
Data are presented as number (%) of patients.

**Table 3.** Procedure data.

| | BMS | DES | *p* |
|---|---|---|---|
| Number of lesions | 43 | 88 | |
| Procedure before stenting | | | |
| POBA, % | 84 | 88 | 0.56 |
| Rotablator, % | 42 | 47 | 0.61 |
| DCA, % | 2 | 0 | 0.15 |
| Direct stent, % | 2 | 8 | 0.21 |
| Mean number of stents | 1.14 | 1.41 | 0.014 |
| Mean stent diameter, mm | 3.45 ± 0.45 | 3.10 ± 0.37 | <0.0001 |
| Mean stent length, mm | 19.79 ± 9.97 | 33.12 ± 18.58 | <0.0001 |
| Post-dilatation balloon, mm | 3.48 ± 0.52 | 3.22 ± 0.39 | 0.0023 |
| Post-dilatation pressure, atm | 17.64 ± 4.13 | 19.67 ± 3.22 | 0.0033 |

BMS: bare metal stent; DES: drug-eluting stent; POBA: plain old balloon angioplasty; DCA: directional coronary atherectomy.
Data are presented as mean ± standard deviation (*SD*), or number (%) of patients.

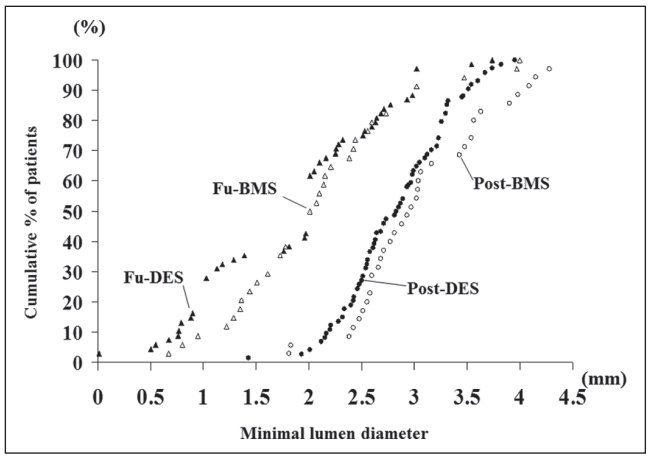


**Figure 1.** Cumulative distribution of post-procedure and 9-month follow-up minimal lumen diameter (mm) in the two groups. The post-procedure acute gain in the BMS group was well maintained throughout the follow-up period.
BMS: bare metal stent. DMS: drug eluting stent.

stents was higher in the SES group than in the BMS group. The mean stent length was significantly longer and the mean diameter was significantly smaller in the SES group than in the BMS group. Quantitative data are shown in Table 3, and the cumulative distribution of the minimum lumen diameter (MLD) is shown in Figure 1. The MLD after stent implantation differed significantly between the groups. Angiographic follow-up data at 9 months are shown in Table 4. Follow-up angiography was performed in 80% of patients in the SES group and in 88% patients in the BMS group. At 9 months, the MLD was significantly smaller in the SES group than in the BMS group, although there was no significant between-group difference in late lumen loss. The rate of binary restenosis was significantly higher in the SES group than in the BMS group. Clinical follow-up at 12 months was obtained in 91% of patients in the SES group and in 92% of patients in the BMS group (Table 5). The incidences of MACEs did not differ between the groups when excluding TLR.

## Discussion

The main finding of this study was that in dialysis patients who received PCI, higher incidences of binary restenosis and TLR were observed in patients that received SES than in patients that received BMS, although DES are known to be more likely to prevent restenosis than BMS. However, there was no significant difference in late lumen loss between the SES and BMS groups. Thus, a significantly smaller minimum lesion diameter in the SES group than in the BMS

**Table 4.** Quantitative angiographic follow-up data..

| | BMS | DES | *p* |
|---|---|---|---|
| Number of lesions | 43 | 88 | |
| Pre-procedure | | | |
| Lesion length, mm | 18.32 ± 9.84 | 20.93 ± 11.11 | 0.47 |
| Reference diameter, mm | 3.39 ± 1.03 | 3.09 ± 0.56 | 0.06 |
| Minimal lumen diameter, mm | 1.05 ± 0.55 | 1.00 ± 0.50 | 0.62 |
| % diameter stenosis | 68.08 ± 17.70 | 67.63 ± 15.03 | 0.89 |
| Post-procedure | | | |
| Reference diameter, mm | 3.55 ± 0.90 | 3.35 ± 0.59 | 0.16 |
| Minimal lumen diameter, mm | 3.15 ± 0.81 | 2.84 ± 0.50 | 0.014 |
| % diameter stenosis | 10.77 ± 10.89 | 13.93 ± 10.35 | 0.47 |
| Follow-up at 9 months *n*, (%) | 38 (88) | 70 (80) | |
| Minimal lumen diameter, mm | 2.16 ± 0.86 | 1.84 ± 0.88 | 0.014 |
| % diameter stenosis | 34.29 ± 17.72 | 37.63 ± 27.90 | 0.52 |
| Late lumen loss, mm | 0.96 ± 0.57 | 1.00 ± 0.94 | 0.83 |
| Binary restenosis, *n* (%) | 7 (18) | 27 (39) | 0.031 |

BMS: bare metal stent; DES: drug-eluting stent.
Data are presented as mean ± standard deviation (*SD*) or number (%) of patients.

**Table 5.** Clinical follow-up data.

| | BMS | DES | *p* |
|---|---|---|---|
| Clinical follow-up | | | |
| Number of patients | 33 (92) | 53 (91) | |
| MACE overall | 7 (21) | 28 (53) | 0.0037 |
| All death | 1 (3) | 3 (6) | 0.56 |
| Cardiac death | 1 (3) | 1 (2) | 0.73 |
| Myocardial infarction (Q and non-Q-wave) | 0 (0) | 0 (0) | – |
| CHF | 0 (0) | 1 (1) | 0.43 |
| TLR | 6 (18) | 26 (49) | 0.004 |

BMS: bare metal stent; DES: drug-eluting stent; MACE: major adverse cardiac event; CHF: congestive heart disease; TLR: target lesion revascularization.
All data are presented as *n* (%).

group after the procedure may have brought about the unfavorable outcomes.

Dialysis patients are at high risk of developing cardiovascular disease. If patients have an established cardiovascular disease, they are likely to encounter worse outcomes and higher mortality than nondialysis patients. Cardiovascular events are the primary cause of death in dialysis patients.[1] Therefore, these patients often needed invasive management of coronary artery disease in order to try to reduce the frequency of angina attacks and to maintain left ventricular function and quality of life. Most dialysis patients have severely calcified, tortuous, and diffuse lesions in their coronary arteries. Gruberg et al.[3] reported that the rates of TLR and event-free survival at 1 year after procedure in dialysis patients who underwent PCI were 32.1% and 41%, respectively. Several studies reported that the long-term mortality associated with surgical revascularization was lower than that associated with revascularization by PCI in dialysis patients.[2] On the other hand, coronary bypass surgery is invasive in nature and carries higher risks of peri-procedural complications and in-hospital mortality.[11,12] Optimal methods for treating coronary artery disease in dialysis patients remain controversial. In randomized trials, the introduction of DES dramatically reduced the incidences of restenosis and revascularization in the management of coronary artery disease compared with the use of BMS.[4–8] The significant suppression of neointimal hyperplasia by DES reduced late lumen loss and the rate of repeat revascularization.[4–8,13] Thus, DES is basically considered to have much greater potential to prevent restenosis compared with BMS. This story may not be true in dialysis patients. It has been acknowledged that incomplete lesion coverage is associated with the edge restenosis of DES; therefore when DES are implanted, "healthy to healthy" stenting has been the main strategy, in comparison with the "bigger and shorter are better" theory selected in the BMS era.[6,7,14–16] However, in dialysis patients, the lesions are severely calcified and tortuous, so that it is sometimes necessary for the distal stent to be smaller than the proximal stent in order to match the diameter of the distal reference. Thus, post-procedure MLD was generally smaller in the DES group than in the BMS group. However, late lumen loss at the 9-month angiographic follow-up was similar between the two groups in this study, still indicating the anti-restenosis potential of SES. The rates of restenosis and TLR in the SES group were 39% and 49%, respectively, and were significantly higher than in the BMS group. We consider these findings to be related to the difference in post-procedural MLD between SES and BMS groups. The "healthy to healthy parts" stent implantation strategy for dialysis patients resulted in the use of longer length and smaller diameter stenting and provoked a smaller post-procedural MLD. Meliga et al.[9] recently reported in dialysis patients that the use of DES was not associated with a reduction in TLR

compared with the use of BMS in patients with similar clinical characteristics, treated vessel features, and stenting strategy. Using the extensive data from United States Renal Data System, Shroff et al.[10] have also reported in dialysis patients that the probability of repeat revascularization was comparable in DES patients and in patients receiving BMS. Clinical characteristics of both groups were matched in this study; however, the study includes no data about vessel descriptions or details of the stenting procedure. Previous studies indicated that in dialysis patients, revascularization was observed with similar rates between patients who received DES and BMS. Considering this information in combination with our current findings, DES was not able to overcome the problem observed in BMS usage for coronary revascularization (i.e. longer length and/or smaller diameter stents often caused restenosis). The so-called shorter length and larger diameter stenting strategy might work to reduce the likelihood of restenosis for appropriate lesions in dialysis patients, even in the DES era.[14–16]

## Study limitations

This study has several limitations. This study was conducted in a single center and is a retrospective study. This study evaluated only a small number of patients, and angiographic and clinical follow-up were not obtained in all patients. The PCI procedures were conducted by several interventionists, and the strategy of PCI (e.g. selection of stent size and the procedures performed before and after stenting) was at the discretion of each interventionist. All measurements were performed on angiograms recorded after the administration of intracoronary nitroglycerin.

## Conclusion

In dialysis patients, a longer length and/or smaller diameter SES implantation was associated with high rates of restenosis and TLR, as well as a high rate of MACEs, compared with BMS. For dialysis patients, interventionists may need to carefully consider the length and diameter of DES in order to reduce rates of angiographic restenosis and TLR.

### Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the research, authorship, and/or publication of this article.

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