Comparison of Angiographic and 1-Year Outcomes Between a Long Single Stent and Overlapping Double Stents in Patients With Newer-Generation Drug-Eluting Stents for Long Narrowings

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Although some clinical studies have revealed adverse clinical and angiographic outcomes of early-generation overlapping drug-eluting stents (DES), the safety and efficacy of overlapping newer-generation DES for long narrowings have not been well established. This study aimed to compare angiographic and 1-year clinical outcomes between a long single stent (LSS) and overlapping double stents (ODS) in patients treated with newer-generation DES for similarly long narrowings. We analyzed 8 to 10 months angiographic and 1-year clinical outcomes of 112 lesions of 105 patients with long (30 to 38 mm) narrowings treated with everolimus-eluting stent, a newer-generation DES, using LSS or ODS. We divided our patients into LSS group (46 patients with 49 lesions) and ODS group (59 patients with 63 lesions). As a result, the rates of freedom from major adverse cardiac events (92.9% vs 93.1%, p = 0.91) and target lesion revascularization (94.5% vs 95.1%, p = 0.79) during 1-year follow-up were similar between the 2 groups. There was no stent thrombosis observed between the 2 groups. In conclusion, everolimus-eluting stent provided similar angiographic and 1-year clinical outcomes regardless of overlap status in long narrowings. **(Am J Cardiol 2016;117:1724−1728)**

Although overlapping drug-eluting stents (DES) has become routine practice,[1−4] some clinical studies have revealed adverse responses to overlapping early-generation DES, such as instent restenosis, stent fracture, and stent thrombosis.[3,5−7] Thus, overlapping early-generation DES might be associated with impaired clinical and angiographic outcomes during long-term follow-up, compared with nonoverlapping DES.[8] However, recent clinical reports have shown the safety and efficacy of overlapping newer-generation DES, compared with overlapping early-generation DES[9] and newer-generation nonoverlapping DES for short lesions.[10,11] Recently, longer DES (≥32 mm) have become available, and it is occasionally difficult to decide whether to use a long single stent (LSS) or overlapping double stents (ODS) for long narrowings. Thus, the aim of this study was to compare angiographic and 1-year clinical outcomes between LSS and ODS in patients treated with newer-generation DES for long narrowings.

Methods

From February 2010 to September 2013, 105 consecutive patients with long lesions (30 to 38 mm) and treated with everolimus-eluting stent (EES)−Xience V, Xience Prime (Abbott Vascular, Santa Clara, California), Promus or Promus Element (Boston Scientific, Natick, Massachusetts) were retrospectively enrolled in this study from our institution's registry. For LSS treatment, single 32-, 33-, or 38-mm stents were used, whereas patients with ODS received some combination of 2 shorter (15-, 18-, and/or 23-mm) stents. Stent overlap was defined as the presence of 2 stents within a single-treated lesion and an overlapping stent zone of ≥1 mm, as determined by angiography.[8] Percutaneous coronary intervention (PCI) was performed according to standard techniques and the choice of LSS or ODS was at the discretion of the operator (e.g., lesion calcification or tortuosity and vessel size discrepancy). In all patients, lesion length was measured by intravascular ultrasound (IVUS) before the stent implantation, and the stents were fully expanded and well apposed to the vessel wall based on IVUS. IVUS imaging was performed after intracoronary injection of 0.1 to 0.2 mg nitroglycerin using OptiCross 40 MHz (Boston Scientific) with motorized pullback (1.0 mm/s). All patients received 100 mg aspirin and 75 mg clopidogrel every day until the follow-up coronary angiography at 8 to 10 months after the stent implantation. All patients were scheduled to undergo follow-up coronary angiography at 8 to 10 months, and all patients underwent 1-year clinical follow-up by qualified personnel by telephone or office visit. Written informed consent was obtained from all patients before the cardiac catheterization. This study was in accordance with the Declaration of Helsinki and approved by the medical ethics committee of Osaka Rosai Hospital.

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Quantitative coronary angiography was performed at baseline, after PCI procedure, and at 8 to 10 months of follow-up with the use of an automated edge detection system (CAAS 5; Pie Medical Imaging, Maastricht, the Netherlands). All angiographic measurements of the target lesion were obtained in the "instent" and "in-segment" zone. The "in-segment" zone was defined as within the in-stent zone and 5 mm proximal and distal to each stent edge.[10] Quantitative measurements included the reference vessel diameter, the minimal lumen diameter, lesion length, and percentage of diameter stenosis. Binary restenosis was defined as stenosis ≥50% in the target lesion at angiographic follow-up.

The primary end point of the study was a composite of major adverse cardiac events (MACE) at 1 year, defined as the composite of cardiac death, myocardial infarction, or target vessel revascularization (TVR) up to a maximum follow-up of 1 year. The secondary end points included the single components of the primary end point, in addition to target lesion revascularization (TLR) and definite or probable stent thrombosis at 1 year according to Academic Research Consortium criteria.[12] We used previously published definitions of cardiac death, myocardial infarction, TVR, and TLR.[8,13]

All statistical analyses were performed using JMP 11 (SAS Institute, Inc., Cary, North Carolina). Results are reported as means ± SDs for continuous variables and as number (%) for nominal variables. Continuous variables with a normal distribution were compared using the Student *t* test for independent samples or the Mann−Whitney *U* test if a normal distribution could not be assumed. Categorical variables were compared using the chi-square test or Fisher's exact test. MACE-free survival rates and TLR-free rates were calculated using the Kaplan−Meier method. The log-rank test was used to compare the difference in curves among groups. To find independent factors correlating with the late loss, multiple regression analysis was performed. Values of $p < 0.05$ were considered to be statistically significant.

Results

A total of 105 patients were included in the study (LSS group, 46 patients with 49 lesions; ODS group, 59 patients with 63 lesions). The baseline clinical characteristics of the patients are listed in Table 1. There were significant differences between the 2 groups regarding the presence of insulin-dependent diabetes mellitus, impaired renal function, and hemodialysis. There were no significant differences in baseline lesion characteristics, including vessel tortuosity[14] and assessment of quantitative coronary angiograph and IVUS, between the 2 groups, although the selection of LSS or ODS was under the operator's choice (Table 2). Procedural and angiographic results are summarized in Table 3. Owing to stent overlap, total stent length was significantly longer in the ODS group than the LSS group ($p < 0.001$). There were no significant differences in medications at the time of discharge between the 2 groups (Table 4).

Angiographic follow-up at 8 to 10 months was obtained in 76% of the LSS group and 75% of the ODS group. The results are listed in Table 5. The angiographic restenosis rates were not significantly different between the LSS and ODS groups (5.7% vs 6.8%, $p = 0.84$). Kaplan−Meier 1-year event-free curves for MACE and TLR are shown in Figures 1 and 2, respectively. There were no significant differences between the 2 groups (MACE: $p = 0.91$, TLR: $p = 0.79$). There was no stent thrombosis observed between the 2 groups. Multiple regression analysis showed there were no significant factors correlating with the late loss including diabetes mellitus, impaired renal function and overlap status of stents in this study (Table 6).

Table 1
Baseline clinical characteristics

Variable	LSS group (n = 46)	ODS group (n = 59)	P Value
Age (yrs)	69.7 ± 9.73	71.3 ± 7.27	0.808
Men	36 (64.4%)	38 (78.3%)	0.123
Ever smoker	13 (28.3%)	21 (35.6%)	0.426
Current smoker	8 (17.4%)	12 (22.0%)	0.555
Diabetes mellitus	18 (39.1%)	33 (55.9%)	0.087
Insulin dependent	4 (8.7%)	16 (27.1%)	0.017
Hypertension	32 (69.6%)	37 (62.7%)	0.463
Dyslipidemia	24 (52.2%)	34 (57.6%)	0.577
Impaired renal function (Creatinine >1.5mg/dl)	1 (2.2%)	12 (20.3%)	0.005
Hemodialysis	0	5 (8.5%)	0.043
LVEF < 40%	2 (4.4%)	3 (5.1%)	0.860
Previous MI	5 (10.9%)	9 (15.3%)	0.512
Previous PCI	15 (32.6%)	20 (33.9%)	0.889
Previous coronary bypass	2 (4.4%)	2 (3.4%)	0.799
Reason for revascularization			
Stable angina pectoris	16 (34.8%)	28 (47.5%)	0.190
Acute coronary syndrome	12 (26.1%)	7 (11.7%)	0.060
Silent ischemia	16 (34.8%)	23 (39.0%)	0.658
Multi vessel coronary disease	14 (30.4%)	27 (45.8%)	0.110
Number of narrowed coronary arteries	1.4 ± 0.6	1.6 ± 0.7	0.106

Data are presented as mean ± SD or n (%).

Hypertension was defined as blood pressure ≥140/90 mm Hg or the use of antihypertensive drug. Dyslipidemia was defined as treatment with medication or serum low-density lipoprotein cholesterol level ≥140 mg/dl.

LSS = long single stent; LVEF = left ventricular ejection fraction; MI = myocardial infarction; ODS = overlapping double stents; PCI = percutaneous coronary intervention.

Discussion

The main findings of this study are that the implantation of a LSS or overlap double stents for long (30 to 38 mm) narrowings showed comparable clinical outcomes of freedom from MACE and TLR at 1-year follow up.

Several previous studies have suggested that the risk of MACE increased in patients with overlapping first-generation DES compared to those with nonoverlapping first-generation DES in terms of angiography,[8,15,16] angioscopy,[17] and pathology.[6] Recently, data have been published on the clinical outcomes of overlapping newer-generation DES compared with overlapping first-generation DES.[9−11] Kitabata et al[9] reported that compared with first-generation DES, overlapping EES may be associated with lower occurrence of MACE (6.5% for