Comparison of Clinical and Angiographic Outcomes After Bare Metal Stents and Drug-Eluting Stents Following Rotational Atherectomy

Hiroshi Tamura,[1] MD, Katsumi Miyauchi,[1] MD, Tomotaka Dohi,[1] MD, Shuta Tsuboi,[1] MD, Manabu Ogita,[1] MD, Takatoshi Kasai,[1] MD, Iwao Okai,[1] MD, Yoshiteru Katoh,[1] MD, Tadashi Miyazaki,[1] MD, Ryo Naito,[1] MD, Hirokazu Konishi,[1] MD, Ken Yokoyama,[1] MD, Shinya Okazaki,[1] MD, Kikuo Isoda,[1] MD, Takeshi Kurata,[1] MD, *and* Hiroyuki Daida,[1] MD

Summary

Few studies have investigated the clinical outcomes of rotational atherectomy (RA) prior to and during the drug-eluting stent (DES) era. The goal of this study was to assess the long-term outcome after RA followed by DES and bare metal stent (BMS) implantation in complex calcified coronary lesions and to compare the outcomes among various DESs.

This was a single center retrospective observational study. Consecutive 406 patients who underwent elective RA followed by BMS or DES implantation at our institution from 2001 to 2011 were included. This study compared the long-term outcomes after treatment with RA among BMS and 3 different DESs (sirolimus-eluting stent, paclitaxel-eluting stent, and everolimus-eluting stent) implantation.

The mean follow-up period was 4.6 years. Patients with DES were older and exhibited more vessel disease, longer lesion length, and smaller vessel size. Patients with BMS had a significantly higher rate of target lesion revascularization, restenosis, and larger late lumen loss than those with DES. Composite events including mortality, ACS, and target vessel revascularization were significantly higher in the BMS-RA group than in the DES-RA group. After adjustment, BMS remained an independent predictor of MACE and ACS plus death in patients treated with RA. However, there were no significant differences in late lumen loss, restenosis rate, and MACE among the 3 DES.

The combination of DES-RA has a favorable effect in both the angiographic and clinical outcomes compared with BMS-RA. However, no significant differences in late loss and events rates were observed among the 3 DES groups. (Int Heart J 2016; 57: 150-157)

Key words: Rotablator, Percutaneous coronary intervention, Clinical outcome

Previous studies have shown that drug-eluting stents (DES) have reduced revascularization in a wide range of patient and lesion subsets compared to bare-metal stents (BMS).[1-3] However, higher event rates are observed when treating complex lesions compared with simple lesions even with DES.[4-6] Therefore, the treatment of complex lesions still remains among the few technically challenging fields. One typical example of a complex lesion is diffuse severe calcified lesions. Rotational atherectomy (RA) can facilitate percutaneous coronary intervention (PCI) in calcified lesions through plaque remodeling and increasing its distensibility.[7,8] However, few studies have investigated the clinical outcomes of RA prior to and during the DES era. Multiple types of DES including sirolimus-eluting stents (SES), paclitaxel-eluting stents (PES), and everolimus-eluting stents (EES) were available. The goals of this study were to assess the long-term outcome of DES after RA compared with BMS after RA in complex calcified coronary lesions and to compare the long-term outcomes of SES, PES, and EES after RA.

Methods

Study design and subjects: This was a single-center retrospective study that aimed to compare the long-term outcome between patients treated by RA-DES and RA-BMS for calcified coronary lesions. Furthermore, a comparison of long-term clinical events among three DESs (SES, PES, and EES) was performed. In the period between January 2001 and July 2011, a consecutive series of patients with heavily calcified de novo lesions treated with RA was retrospectively identified from our institutional database. According to Mintz, *et al*, heavily calci-

From the [1] Department of Cardiovascular Medicine, Juntendo University Graduate School of Medicine, Tokyo, Japan.

This study was supported by a Grant-in-Aid for Scientific Research (23591063) from the Japan Society for the Promotion of Science.

Address for correspondence: Katsumi Miyauchi, MD, Department of Cardiology, Juntendo University Hospital, 3-1-3 Hongo, Bunkyo-ku, Tokyo, Japan. E-mail: ktmmy@juntendo.ac.jp

Received for publication August 28, 2014. Revised and accepted September 3, 2015.
Released in advance online on J-STAGE March 11, 2016.

fied lesions are defined visually as the presence of calcium within the arterial wall at the site of the stenosis compromising both sides of the arterial lumen.[9] The baseline characteristics and follow-up clinical information were obtained from medical records.

Written informed consent was obtained from all patients for analysis of their anonymized data. Data collection was approved by the institutional review board. All coronary angiograms were reviewed by board-certified interventional cardiologists. RA was performed using a Rotablator (Boston Scientific Scimed, Maple Grove, MN, USA). The burr size was selected to reach a burr/vessel ratio of 0.5 (maximum: 0.7 if needed). Rotablation speed ranged between 140,000 and 240,000 rotations per minute. The burr was platformed immediately proximal to the lesion to avoid injury to the other intact vessel segment. Nicorandil, verapamil, and nitroglycerin were administered during RA as an intracoronary infusion, and a temporary pacemaker wire was inserted during RA of the right coronary artery and the left circumflex artery in patients with a dominant left system. Procedural success was defined as achievement of < 30% angiographic residual stenosis by quantitative coronary angiography (QCA).

Baseline data including age, gender, body mass index (BMI), smoking status (current smoker or not), family history of coronary artery disease (CAD), diabetes mellitus, hypertension, dyslipidemia, chronic kidney disease (CKD), currently undergoing dialysis, history of myocardial infarction (MI), blood pressure, lipid profile, medications, left ventricular ejection fraction (LVEF), number of diseased vessels, target vessel, lesion characteristics, and device size and length were prospectively recorded in the database of our institution. Data regarding coronary risk factors were evaluated in each patient using the following criteria: Hypertension was defined as systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or currently taking antihypertensive medications; diabetes mellitus was defined as HbA1c ≥ 6.5% (NGSP; National Glycohemoglobin Standardization Program) or currently taking antidiabetic medication (oral hypoglycemic drugs or insulin injections). A current smoker was defined as a person who smoked cigarettes at the time of procedure or who had quit smoking within one year before the procedure.

Follow-up and endpoint definition: The primary endpoint was the incidence of major adverse cardiac events (MACE), which is a composite of all cause death, nonfatal-acute coronary syndrome (ACS), and target vessel revascularization (TVR). Secondary endpoints included restenosis, target lesion revascularization (TLR), and angiographic late lumen loss at 10 months after PCI and ACS plus all cause death. TVR was defined as a repeated procedure, either PCI or coronary artery bypass grafting (CABG), on the target vessel.

At 8-10 months, a repeat coronary angiography was performed unless symptoms or documentation of myocardial ischemia needed earlier coronary angiography. Off-line quantitative and qualitative analyses of all angiographic parameters were performed by our Angiographic Core Laboratory. Acute gain and late lumen loss were defined as the difference between pre- and post-procedural minimum lumen diameter (MLD), and between post-procedural and restudy MLD, respectively. Restenosis was defined as a diameter stenosis ≥ 50% within the stented segment plus the 5 mm proximal and distal persistent area at follow-up angiography and TLR was defined as any re-intervention inside the stent implanted plus the 5 mm proximal and distal persistent area. Clinical events were collected until September 2012. The data for these clinical events including cardiovascular events were collected by serial contact with the patients or their families by telephone interview or letter with questionnaires sent out by our institution every 5 years. The medical records of patients who died or who were treated at our hospital were analyzed. When patients were admitted to or followed-up at other hospitals or clinics, the details of the revascularization (PCI or CABG), ACS, and cause of death were obtained from these institutions.

Angiographic success is defined as a minimum stenosis diameter of < 20% (as visually assessed by angiography). Procedural success should achieve angiographic success without associated in-hospital major clinical complications (death, MI, stroke, emergency CABG).[10] PCI-related MI was defined by criteria according to the modified third universal definition of Myocardial Infarction: elevations of CPK or CK-MB > 3× occurring within 48 hours of the procedure — plus either 1) evidence of prolonged ischemia (> 20 minutes) as demonstrated by prolonged chest pain, or 2) ischemic ST changes or new pathological Q waves, or 3) angiographic evidence of a flow limiting complication, such as of loss of patency of a side branch, persistent slow-flow or no-reflow, embolization, or 4) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.[11] Only patients with the same kind of DES in the target lesion were analyzed. In other words, patients with a different type of DES in the target lesion were excluded.

Statistical analysis: Continuous variables are expressed as the mean ± SD and were compared using Student's *t*-test or the Mann-Whitney *U*-test. Categorical data were tabulated as frequencies and percentages and compared using the chi-square test or Fisher's exact test. Kaplan–Meier plots of cumulative incidence of MACE and ACS plus death with a log-rank test were constructed from the index procedure to the latest available follow-up. Cox proportional hazards modeling was used to assess independent predictors of MACE and ACS plus death. The hazard ratio (HR) and 95% confidence interval (CI) were computed using separate models. Variables included in the analysis for MACE were age, use of DES, BMI, family history of CAD, triglycerides, hemodialysis, LVEF impairment < 40%, and statin use. In the analysis of ACS plus death, the following variables were also considered: age, DES use, BMI, diastolic BP, hemodialysis, multivessel disease or left main trunk disease, beta-blocker use, and statin use. Multivariate models were constructed by including all univariate predictors with a *P*-value < 0.2. Non-significant covariates were removed from the model in a backward stepwise fashion. Statistical analysis was performed with JMP for Windows version (SAS inc., Cary, NC, USA).

Results

Patient characteristics: The total PCI volume during the period was 5339 cases, 496 (3.9%) of which were RA cases. A total of 406 patients met our study criteria and were analyzed in this study. A total of 84 cases were excluded because coronary stents had not been used. The study cohort represented complex high-risk patients, who were older (mean age 67.6 versus

Table I. Baseline Characteristics

	RA+BMS (n = 116)	RA+DES (n = 290)	P
Age (years)	65.9 ± 9.0	68.3 ± 8.9	0.01
Gender (male, %)	82.8	83.5	0.87
BMI	23.7 ± 2.9	23.3 ± 3.1	0.18
Current smoker (%)	28.5	18.3	0.08
Family history (%)	18.1	30.3	0.01
Diabetes (%)	50.9	55.5	0.40
Hypertension (%)	75.9	80.0	0.36
Dyslipidemia (%)	63.8	75.2	0.02
CKD (%)	42.2	41.0	0.82
Hemodialysis (%)	16.4	16.2	0.97
Previous MI (%)	19.8	17.6	0.60
SBP (mmHg)	130.5 ± 21.6	134.3 ± 21.5	0.20
DBP (mmHg)	68.3 ± 12.3	70.0 ± 12.0	0.20
Lipid profile			
LDL-C (mg/dL)	118.0 ± 29.2	104.7 ± 31.3	0.0001
Triglycerides (mg/dL)	120.9 ± 47.9	128.5 ± 58.8	0.22
HDL-C (mg/dL)	45.1 ± 13.0	46.0 ± 13.1	0.53
HbA1c (%)	6.02 ± 1.46	6.00 ± 0.94	0.84
Medication			
Dual antiplatelet	100	100	1.0
ACEI/ARB (%)	36.2	57.3	0.0001
Statin (%)	46.5	68.3	0.0001
Beta-blocker (%)	45.1	51.0	0.35
LVEF (%)	63.1 ± 12.4	61.6 ± 11.3	0.25
LVEF < 40	4.6	3.8	0.75
VD	1.8 ± 0.8	2.2 ± 0.8	< 0.0001
3VD/LMT (%)	21.6	39.7	0.0004
Location			0.01
LMT (%)	2.6	9.0	
LAD (%)	59.5	68.6	
LCX (%)	12.9	9.31	
RCA (%)	25.0	13.1	
B2/C complex (%)	94.8	99.3	0.006
Lesion length (mm)	16.8 ± 9.2	21.7 ± 9.1	< 0.0001
Reference vessel diameter (mm)	2.91 ± 0.43	2.78 ± 0.36	0.02
MLD pre (mm)	0.43 ± 0.29	0.48 ± 0.28	0.07
MLD post (mm)	2.71 ± 0.46	2.71 ± 0.35	0.97
% Diameter stenosis post (%)	6.47 ± 14.1	2.20 ± 7.90	0.0002
Acute gain (mm)	2.18 ± 0.72	2.21 ± 0.48	0.74
RA starting burr size (mm)	1.65 ± 0.20	1.69 ± 0.19	0.06
RA maximum burr size (mm)	1.90 ± 0.27	1.78 ± 0.21	< 0.0001
RA maximum burr/Stent diameter	0.62 ± 0.09	0.61 ± 0.08	0.06
Post balloon size (mm)	3.10 ± 0.33	3.02 ± 0.51	0.35
Stent total length (mm)	21.4 ± 9.6	35.0 ± 17.6	< 0.0001
Stent size (mm)	3.07 ± 0.30	2.95 ± 0.35	< 0.001
Stent size < 3 mm (%)	14.7	34.8	< 0.0001

BMI indicates body mass index; CKD, chronic kidney disease; MI, myocardial infarction; SBP, systolic blood pressure; DBP, diastolic blood pressure; ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; LVEF, left ventricular ejection fraction; VD, vessel disease; LMT, left main trunk; LAD, left ascending artery; LCX, left circumflex artery; RCA, right coronary artery; MLD, minimum luminal diameter; and RA, rotational coronary atherectomy.

65.4 years) and had a higher incidence of patients with diabetes mellitus (54.2% versus 44.1%) and chronic renal failure receiving hemodialysis (16.2% versus 5.7%) compared to the non-RA PCI group. The detailed baseline demographics and clinical risk factors in the BMS patients and DES patients are shown in Table I. All patients received dual antiplatelet therapy at the PCI procedure. The patients in the DES group were older and had a higher prevalence of dyslipidemia, whereas LDL-C was higher in the BMS group. ACEI/ARB use and statin use were higher in the DES group.

In a comparison of DES, only patients with the same kind of DES in the target lesion were analyzed. The patients with a different type of DES in the target lesion were excluded. The DES deployed was an SES in 61.1%, PES in 17.9%, and EES in 21.0% of the cases. Baseline characteristics stratified according to DES type are shown in Table II. EES patients had a lower incidence of MI and higher blood pressure than SES and PES patients.

Angiographic and procedure characteristics: The target lesions were primarily located in the left anterior descending artery (66%) and the vast majority were complex, type B2/C lesions (98%). The mean size of the maximum RA burrs was 1.81 ± 0.23 mm. The angiographic and procedural characteristics of the BMS patients and DES patients are shown in Table I.

Table II. Baseline Characteristics of DES Group

	RA+SES (n = 167)	RA+PES (n = 49)	RA+EES (n = 57)	P
Age (years)	67.7 ± 8.9	67.7 ± 10.1	70.8 ± 7.8	0.07
Gender (male)	83.8	85.7	82.5	0.9
BMI	23.3 ± 3.0	23.9 ± 3.2	22.8 ± 3.4	0.20
Current smoker (%)	19.2	18.4	15.8	0.13
Family history (%)	32.3	32.6	28.1	0.82
Diabetes (%)	53.3	51.0	64.9	0.25
Hypertension (%)	77.8	85.7	86.0	0.25
Dyslipidemia (%)	74.3	75.5	79.0	0.77
CKD (%)	41.9	32.7	49.1	0.23
Hemodialysis (%)	14.4	14.3	26.3	0.12
Previous MI (%)	22.2	10.2	7.0	0.008
SBP	128.9 ± 19.1	134.1 ± 21.0	150.0 ± 21.0	< 0.0001
DBP	67.3 ± 10.2	71.1 ± 13.8	76.2 ± 12.5	< 0.0001
Lipid profile				
LDL-C (mg/dL)	114.6 ± 31.2	97.2 ± 24.1	83.5 ± 24.0	< 0.0001
Triglycerides (mg/dL)	130.4 ± 63.3	135.9 ± 49.9	121.9 ± 57.1	0.47
HDL-C (mg/dL)	45.6 ± 12.0	45.0 ± 14.3	47.7 ± 14.9	0.51
HbA1c (%)	6.00 ± 0.74	5.88 ± 0.97	6.02 ± 0.89	0.30
Medication				
ACEI/ARB	57.5	53.0	66.7	0.33
Statin	67.7	73.4	68.5	0.70
Beta-blocker	52.7	46.9	50.9	0.77
LVEF (%)	60.4	62.7	62.7	0.31
VD	2.15 ± 0.74	2.12 ± 0.81	2.32 ± 0.74	0.30
EF < 40 (%)	4.6	4.7	2.0	0.72
Location				0.03
LMT	5.4	10.2	17.5	
LAD	74.3	65.3	56.1	
LCX	9.6	10.2	8.8	
RCA	10.8	14.3	17.5	
3VD or LMT (%)	35.9	38.7	43.4	0.31
B2/C complex	98.8	100	100	0.37
Lesion length	22.0 ± 9.4	19.0 ± 7.0	21.8 ± 9.2	0.12
Reference vessel diameter	2.74 ± 0.36	2.87 ± 0.33	2.84 ± 0.38	0.04
MLD diameter stenosis	0.45 ± 0.28	0.54 ± 0.27	0.51 ± 0.27	0.14
Acute gain	2.23 ± 0.49	2.21 ± 0.40	2.15 ± 0.53	0.55
Rota starting burr size	1.67 ± 0.18	1.73 ± 0.20	1.73 ± 0.19	0.04
Rota maximum burr size	1.77 ± 0.22	1.79 ± 0.20	1.76 ± 0.19	0.73
Rota max/Stent diameter	0.61 ± 0.08	0.62 ± 0.07	0.59 ± 0.07	0.051
Post balloon size	2.90 ± 0.52	3.09 ± 0.49	3.12 ± 0.47	0.03
Stent total length	34.2 ± 16.0	31.7 ± 16.3	36.5 ± 21.9	0.36
Stent size (mm)	2.92 ± 0.35	2.90 ± 0.30	3.04 ± 0.39	0.07
Stent size < 3 mm	30.5	53.1	33.5	0.017

DES indicates drug-eluting stent; BMI, body mass index; CKD, chronic kidney disease; MI, myocardial infarction; SBP, systolic blood pressure; DBP, diastolic blood pressure; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; LVEF, left ventricular ejection fraction; VD, vessel disease; LMT, left main trunk; LAD, left ascending artery; LCX, left circumflex artery; RCA, right coronary artery; MLD, minimum luminal diameter; and RA, rotational coronary atherectomy.

The lesion characteristics were more favorable in the BMS group. The DES group had more vessel disease and more complex lesions than the BMS group. Vessel size and stent size were smaller in the DES group than in the BMS group. Lesion length and stent total length were significantly longer in the DES group than in the BMS group. The mean size of maximum RA burrs was significantly smaller in the DES group, but the rate of RA maximum burr to stent size was similar in both groups.

Reference vessel diameter in the SES group was smaller than that in the PES and EES groups. There were no significant differences among the 3 DES in terms of stent size, length, and RA maximum burr size (Table II).

Clinical events for in-hospital and long-term outcomes: The angiographic success was 100% and there were only a few cases of perforation (1.0%) and MI (1.5%). In-hospital mortality was low (0.2%), and the incidence of in-hospital major clinical complications was 3.0%. Consequently, the procedural success rate was 97.0% (Table III).

The percentage of follow-up CAG was 81.0% (94 of 116) in RA-BMS cases and 84.8% (246 of 290) in RA-DES. The mean period until follow-up CAG after initial PCI was 173 days (Rota BMS) versus 237 days (Rota DES). Patients with BMS had significantly higher rates of restenosis (41.1% versus 10.5%, $P < 0.0001$) and TLR (28.9% versus 7.8%, $P < 0.0001$), and larger late lumen loss (1.32+/-0.86 mm versus 0.41+/-0.73 mm, $P < 0.0001$) than those with DES (Table IV). In addition, EES patients had no lower risk of restenosis and

Table III. Angiographic Success and In-Hospital Events

	RA+BMS (n = 116)	RA+DES (n = 290)	P
Angiographic success (%)	100%	100%	1
Procedural complications (%)	3 (2.6%)	7 (2.4%)	0.91
MI	2 (1.7%)	4 (1.4%)	0.79
Perforation	1 (0.9%)	3 (1.0%)	0.87
In-hospital death	0 (0%)	1 (0.34%)	0.52
CABG surgery	1 (0.9%)	0	
Procedural success (%)	96.6%	97.2%	0.91

MI indicates myocardial infarction; and CABG, coronary artery bypass graft.

Table IV. Follow-up Angiographic Data Between BMS and DES, and Among SES, PES, and EES

	BMS and DES			SES, PES, and EES			
	RA+BMS (n = 116)	RA+DES (n = 290)	P	RA+SES (n = 167)	RA+PES (n = 49)	RA+EES (n = 57)	P
Restenosis rate (%)	41.1	10.5	< 0.0001	8.3	11.9	13.3	0.56
TLR (%)	28.9	7.8	< 0.0001	6.3	7.1	11.1	0.57
Late lumen loss (mm)	1.32 ± 0.86	0.41 ± 0.73	< 0.0001	0.30 ± 0.70	0.61 ± 0.50	0.45 ± 0.90	0.046

BMS indicates bare metal stent; DES, drug-eluting stent; RA, rotational atherectomy; TLR, target lesion revascularization; SES, sirolimus-eluting stent; PES, paclitaxel-eluting stent; and EES; everolimus-eluting stent.

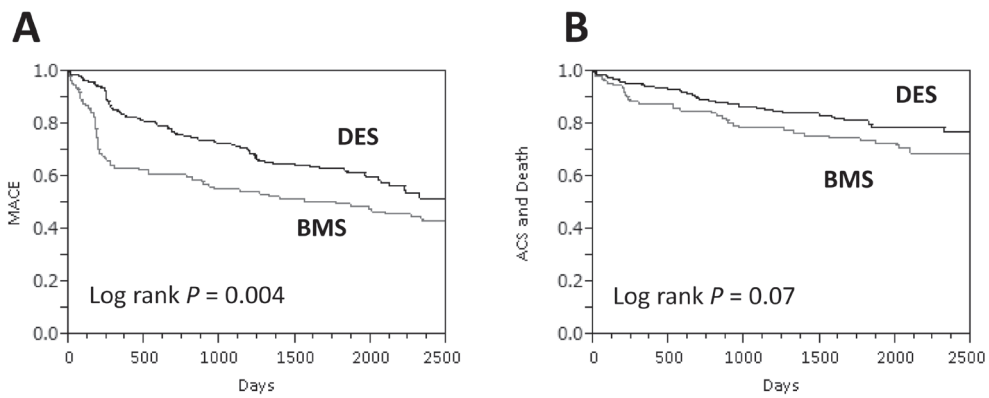

Figure. Kaplan-Meier curve for MACE and death plus ACS. Rate of MACE was significantly higher in RA-BMS than in RA-DES (**A:** Log-rank test: P = 0.004). The rate of all cause death and ACS in RA-DES was slightly lower than that in RA-BMS, but was not statistically significant (**B:** Log-rank P = 0.07).

TLR compared to patients treated with SES and PES. However, late lumen loss was lower in SES than in EES and PES (Table IV).

All patients were followed-up clinically and the mean clinical follow-up period was 4.6 years. The Kaplan–Meier curves showed that MACE and all cause death plus ACS rates continuously increased during the whole observation period (Figure). The incidence of MACE was 10.7 per 100 person-years in DES and 12.7 per 100 person-years in BMS. The incidence of ACS plus death was 2.0 per 100 person-years in DES and 2.4 per 100 person-years in BMS. The incidence of MACE was significantly lower in the RA-DES group (Figure A; Log-rank P = 0.004) than in the RA-BMS based on the Kaplan-Meier survival curves. The rate of all cause death and ACS in RA-DES was slightly lower than that in RA-BMS, but the difference was not statistically significant (Figure B; Log-rank P = 0.07)

Multivariate Cox regression analysis indicated that RA-DES was associated with lower MACE and all cause death plus ACS (HR 0.62, 95% CI 0.44-0.88, P = 0.0081, HR 0.59, 95% CI 0.37-0.95, P = 0.031, respectively). Age and hemodialysis were also independent predictors of MACE and all cause death plus ACS (Tables V and VI). There were no statistically significant differences in MACE and all cause death plus ACS among the 3 DES by multivariate Cox regression analysis (Table VII).

Discussion

The principal finding of the present study was that RA followed by DES implantation is feasible and effective for calcified complex coronary lesions, with lower incidences of MACE and ACS plus death during the long-term follow-up period compared to that of RA followed by BMS implantation. Furthermore, long-term clinical outcomes and angiographic

Table V. Cox Proportional Hazard Model for MACE

	Unadjusted			Adjusted		
	HR	95% CI	*P*	HR	95% CI	*P*
Age	2.92	1.28-6.75	0.011	2.91	1.64-7.33	0.022
Male	1.01	0.67-1.56	0.97			
DES	0.62	0.45-0.86	0.0047	0.62	0.44-0.88	0.0081
BMI	0.94	0.89-0.99	0.02	0.48	0.12-1.97	0.31
Current smoker	1.23	0.87-1.74	0.24		-	
Family history	0.79	0.50-1.05	0.09	0.73	0.50-1.09	0.14
SBP	1.47	0.65-3.27	0.35			
DBP	0.58	0.23-1.40	0.23			
LDL-C	0.90	0.37-2.14	0.82		-	
Triglycerides	0.43	0.15-1.17	0.10	0.61	0.18-1.88	0.40
HDL-C	1.21	0.43-3.26	0.72		-	
HbA1c	0.96	0.83-1.10	0.59		-	
Hemodialysis	1.80	1.22-2.59	0.0036	1.69	1.06-2.60	0.027
LVEF < 40%	1.65	0.78-3.04	0.18	1.57	0.73-3.00	0.23
3VD or LMT	1.19	0.85-1.62	0.31			
ACE/ARB	0.89	0.65-1.22	0.49		-	
β-Blockers	0.94	0.69-1.28	0.72			
Statins	0.72	0.53-0.99	0.04	0.79	0.57-1.11	0.17
Lesion length	0.56	0.18-1.93	0.37			
Reference lumen diameter	1.23	0.27-5.33	0.79		-	
Stent diameter < 3.0 mm	1.16	0.82-1.63	0.40			
Maximum burr size	0.87	0.31-2.10	0.68			

MACE indicates major adverse cardiac events (All cause death, ACS, and TVR); DES, drug-eluting stent; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LVEF, left ventricular ejection fraction; VD, vessel disease; ACEI, angiotensin-converting enzyme inhibitor; and ARB, angiotensin receptor blocker. In multivariable analysis, only variables which showed borderline significance (ie, $P < 0.20$) were included.

Table VI. Cox Proportional Hazard Model for All-Cause Death and ACS

	Unadjusted			Adjusted		
	HR	95% CI	*P*	HR	95% CI	*P*
Age	5.16	1.58-17.2	0.0062	5.65	1.62-20.2	0.0064
Male	0.84	0.49-1.53	0.55			
DES	0.66	0.42-1.04	0.076	0.59	0.37-0.95	0.031
BMI	0.88	0.0082-0.35	0.0021	0.20	0.03-1.32	0.096
Current smoker	0.91	0.50-1.60	0.76			
Family history	0.98	0.59-1.58	0.96			
SBP	1.87	0.59-5.74	0.28			
DBP	0.37	0.09-1.32	0.13	0.64	0.16-2.50	0.53
LDL-C	1.18	0.32-4.05	0.79			
Triglycerides	0.58	0.13-2.23	0.44			
HDL-C	0.53	0.10-2.35	0.41			
HbA1c	0.67	0.17-2.33	0.54			
Hemodialysis	2.92	1.78-4.66	< 0.0001	3.21	1.88-5.31	< 0.0001
LVEF < 40%	2.64	1.10-5.37	0.031			
3VD or LMT	1.35	0.85-2.10	0.19	1.36	0.83-2.17	0.21
ACE/ARB	0.83	0.53-1.27	0.39			
β-Blockers	0.70	0.45-1.09	0.12	0.77	0.49-1.19	0.24
Statins	0.68	0.44-1.05	0.08	0.98	0.63-1.57	0.99
Maximum burr size	0.68	0.28-1.63	0.39			

DES indicates drug-eluting stent; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LVEF, left ventricular ejection fraction; VD, vessel disease; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker. In multivariable analysis, only variables which showed borderline significance (ie, $P < 0.20$) were included.

outcomes were not significantly different among the 3 DESs (SES, PES, and EES) following RA.

To the best of our knowledge, the current study is the first to present long-term (more than 4 years) outcomes in patients receiving DESs and BMS following RA, including a second generation DES (EES). Previous studies reported that the clinical and angiographic outcomes in DES-RA were compared to those in BMS-RA and DES alone, but the follow-up period was a maximum of 3 years.[12-19] Furthermore, there is little data regarding comparisons between 1st generation DES and 2nd

Table VII. Cox Proportional Hazard Model for MACE and All Cause Death/ACS

	Unadjusted			Adjusted		
	HR	95% CI	*P*	HR	95% CI	*P*
MACE						
PES versus SES	0.88	0.53-1.40	0.62	0.99	0.59-1.59	0.98
EES versus SES	1.03	0.53-1.81	0.93	0.70	0.31-1.37	0.32
ACS and Death						
PES versus SES	0.44	0.15-0.99	0.046	0.50	0.17-1.14	0.10
EES versus SES	1.44	0.54-3.25	0.95	0.95	0.27-2.57	0.93

MACE indicates major adverse cardiac events (all cause death, ACS, and TVR); ACS, acute coronary syndrome; TVR, target vessel revascularization; SES, Sirolimus-eluting stent; PES, paclitaxel-eluting stent; EES, everolimus-eluting stent; HR, hazard ratio; and CI, confidence interval. In multivariable analysis, only variables which showed borderline significance (ie, $P < 0.20$) were included. HR for MACE was adjusted for age, BMI (body mass index), family history, triglycerides, hemodialysis, LVEF < 30%, and statin. HR for ACS and death was adjusted for age, BMI, diastolic blood pressure, 3 vessel disease or LMT lesion, beta-blocker, and statin.

DES after RA. It was not surprising that the angiographic results in DES were superior to those in BMS in the current analysis because several studies demonstrated a favorable angiographic outcome for RA followed by DES compared with RA-BMS [12-19] in the treatment of calcified complex lesions. An angiographic favorable effect of DES over BMS is consistent from simple lesions to complex lesions. However, a significant decrease of ACS plus death in the DES group compared with the BMS group was observed in the current study. These data suggest that in the subset of patients with calcified coronary lesions treated with RA, the benefit of DES is not limited to lowering restenosis rates, but also is associated with better long-term outcomes. The definitive mechanisms accounting for the mortality plus ACS reduction of DES-RA have not been elucidated. As suggested in the clinical setting, a plausible mechanistic explanation includes full coverage of the DES in the target lesions until the landing zone. In fact, DES length is much greater than that of BMS. Another possible explanation is that in-stent restenosis was significantly associated with long-term adverse clinical outcomes in our previous report.[20] The risk of future cardiovascular events due to in-stent restenosis must be carefully considered.[21,22]

RA-EES implantation was not superior to PES or SES in reducing the MACE and in-stent LLL at 9 months, indicating that EES does not increase the efficacy of DES in this complex group of patients compared with SES or PES. Previous studies compared the clinical and angiographic outcomes between PES and SES,[23] in which SES is superior in terms of reduction of revascularization, but is equal to PES in the incidence of ACS plus death. Our study found no differences among the 3 DES regarding long-term outcomes and angiographic results. It should be noted that EES superiority in long-term outcomes compared to SES and PES was not proven. A lot of published data has demonstrated that EES is associated with a better outcome than SES or PES, but this finding is not congruous to RA cases.

Clinical implication: PCI for severe complex calcified lesions is a challenging problem and a risk for DES implantation because of the potential failure of stent delivery or expansion failure, or low success rates. RA has been most useful for heavily calcified lesions which cannot be easily approached by balloon angioplasty or stenting alone. In this situation, RA followed by DES implantation, when applied to high-risk angiographic and clinical settings, has been demonstrated to be a safe and effective strategy, able not only to preserve the durability of vessel patency, but also to reduce the risk of death and ACS. It has been shown that the clinical benefit of DES increases in patients with a high risk profile, further supporting their use in those requiring RA.

Study limitations: The present study has a number of limitations. First, this result was achieved in a small sample size. This study was also a retrospective and single institution study. There was no randomization and the ROTA procedure and stenting strategy were performed at the operator's discretion. Furthermore, DES was available during these 10 years whereas BMS was mainly used 10 years previously. Some bias existed though any adjustment. However, this method using histological control could not be avoided because it is impossible to perform randomized trials that select BMS or DES in the current DES era. As a result, the use of DES can minimize MACE associated with RA in selected patients where RA is necessary to optimize stenting. A large, randomized, multicenter clinical study is necessary to be able to reach reliable conclusions.

Conclusion: A strategy of RA and DES implantation is a safe and effective treatment option in complex patients with complex calcified lesions. Furthermore, long-term clinical outcomes and angiographic outcomes were not significantly different among the 3 DESs (SES, PES, and EES) following RA.

Acknowledgments

The authors would like to thank Ms. Yumi Nozawa and Ms. Ayako Onodera for their assistance with the clinical research aspects of this study.

Disclosure

Dr Daida has received speakers' Bureau/Honorarium from MSD K.K., AstraZeneca K.K., Kowa Pharmaceutical Company Ltd., Sanofi-Aventis K.K., GlaxoSmithKline K.K., Shionogi & Co., Ltd., Daiichi-Sankyo Company, Limited, Takeda Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Corp., Pfizer Co., Ltd., Astellas Pharma Inc. and research funds from Takeda Pharmaceutical Co., Ltd., Bristol-Myers Squibb Company, Nippon Boehringer Ingelheim Co., Ltd.,

Astellas Pharma Inc., Novartis Pharma K.K., MSD K.K., Sanofi-Aventis K.K., Otsuka Pharmaceutical Co., Ltd., Dainippon Sumitomo Pharma Co., Ltd., Pfizer Co., Ltd., Kowa Pharmaceutical Company LTD., Shionogi & Co., Ltd., AstraZeneca K.K., Teijin Limited, and Morinaga Milk Industry Co., Ltd. Dr Miyauchi has received speakers' Bureau/Honorarium from MSD K.K., AstraZeneca K.K., Kowa Pharmaceutical Company Ltd., Sanofi-Aventis K.K., Shionogi & Co., Ltd., Daiichi-Sankyo Company, Limited, Takeda Pharmaceutical Co., Ltd., Pfizer Co., Ltd., Astellas Pharma Inc., and Novartis Pharma K.K.

Dr Okazaki received speakers' Bureau/Honorarium from Terumo and Daiichi-Sankyo Company.

The other authors report no conflicts.

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