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Comparison of neoatherosclerosis and clinical outcomes between bioabsorbable versus durable polymer drug-eluting stent: Verification by optical coherence tomography analysis

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Abstract

Background: *Neoatherosclerosis after drug-eluting stent (DES) implantation is known to be related with increased risk of late restenosis and stent thrombosis. Neoatherosclerosis and relevant clinical outcomes between bioabsorbable polymer DES (BP-DES) and second-generation durable polymer DES (DP-DES) were evaluated by optical coherence tomography (OCT) analysis.*

Methods: *A total of 311 patients (319 lesions) undergoing OCT analysis after DES implantation were enrolled and divided into two groups according to stent type (BP-DES [150 patients, 153 lesions] and DP--DES [161 patients, 166 lesions]). Follow-up OCT analysis was performed at least 9 months after index stent implantation. Neoatherosclerosis was defined as presence of thin-cap fibroatheroma, calcified plaque, and lipid plaque. Primary endpoint was the incidence of neoatherosclerosis, and the secondary endpoints were the occurrence of major adverse cardiac events (MACE), defined as a composite of death, myocardial infarction, target lesion revascularization, or stent thrombosis and to find independent predictors of neoatherosclerosis.*

Results: *The incidence of neoatherosclerosis was lower in the BP-DES group than the DP-DES group (5.2% vs. 14.5%, p = 0.008), which was driven by lipid plaque. However, the incidence of MACE did not show statistical difference between the two groups in median 4-year follow-up (3.3% vs. 7.8%, hazard ratio 1.964, 95% confidence interval 0.688–5.611, p = 0.207). Less use of angiotensin converting enzyme inhibitors/angiotensin II receptor blockade and higher degree of neointimal hyperplasia remained independent predictors of neoatherosclerosis on Cox regression analysis.*

Conclusions: *Patients undergoing BP-DES implantation had lower incidence of neoatherosclerosis than DP-DES, which did not reach statistically better clinical outcomes.* (Cardiol J 2023; 30, 6: 911–920)

Key words: neointima, coronary restenosis, drug-eluting stents, tomography, optical coherence

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Introduction

Introduction of drug-eluting stent (DES) have markedly reduced in-stent restenosis and repeat revascularizations. Yet, stent failure related to stent thrombosis or restenosis was a remnant of major concern, which in turn may be related to fatal clinical events [1, 2]. Development of neoatherosclerosis within neointimal tissues is one of the main mechanisms of stent failure, and the incidence of neoatherosclerosis in first-generation DES is reported from 36% to 67% [3–5] of cases. Second-generation durable polymer DES (DP-DES) have maintained the low restenosis rates of first--generation DES with reduced rates of stent failure. Recently, however, very late stent thrombosis and neoatherosclerosis, resulting in adverse clinical outcomes, have been observed with second-generation DP-DES [1, 6]. One mechanism of late stent failure has been attributed to the delayed endothelial healing secondary to a hypersensitivity reaction to the durable polymer [7, 8]. Development of bioabsorbable polymer DES (BP-DES) was one of the attempts to overcome this problem. Although most of the polymer degradation process is complete within 6–9 months, several studies have shown that polymers requiring active bioresorption are associated with higher rates of inflammation than durable polymer [9, 10]. There is no clear evidence and it remains controversial concerning the benefit of BP-DES on neoatherosclerosis development and clinical events after overcoming the inflammatory process during bioresorption [11–16]. The aim of the present study was to compare the incidence of neoatherosclerosis, relevant clinical outcomes after stent implantation between BP-DES and second-generation DP-DES by using optical coherence tomography (OCT).

Methods

Study patients

The Korea University Anam Hospital OCT Registry is a single-center registry of patients undergoing OCT imaging of the coronary arteries (ClinicalTrials.gov identifier NCT02966262). From OCT registry database, 656 lesions in 630 patients were retrospectively screened from March 2011 through April 2015. The inclusion criteria of the present study were as follows: 1) Patients who underwent percutaneous coronary intervention (PCI) with BP-DES or second-generation DP-DES; 2) Patients who underwent OCT follow-up, showing the mean neointimal thickness was $> 100\ \mu$m. The reasons for follow-up angiography and OCT were evidence of myocardial ischemia or symptoms of coronary artery disease or planned follow-up angiography for other stented lesions. Patients were excluded if first-generation DES or bare-metal stent was implanted; clinical event occurred before OCT analysis; time interval of OCT after PCI was less than 9 months or more than 36 months. The reason that cases of time interval of OCT after PCI less than 9 months were excluded was to examine the effect of polymer-free stent state, which needs a 6–9 month absorption period of bioabsorbable polymer coating [7]. Patients were then allocated into the BP-DES group or DP-DES group regarding stent polymer type. Stents used in the current study were biolimus-eluting stents (Nobori®, Terumo Corporation, Japan; Biomatrix®, Biosensors International, Singapore) in BP-DES and everolimus-eluting stents (Xience®, Abbott Vascular, USA) in DP-DES.

Demographic data, prescribed drugs, laboratory data, and clinical presentation, were collected based on the electronic chart review and were compared between the two groups. Primary endpoint was the incidence of neoatherosclerosis based on OCT analysis, and the secondary endpoints were the occurrence of major adverse cardiac events (MACE; a composite of death, myocardial infarction, target lesion revascularization, or stent thrombosis) and to find independent predictors of neoatherosclerosis. Stent thrombosis was defined according to the recommendations of the Academic Research Consortium [17]. Information on clinical outcome was collected by a retrospective review of the chart. This study was approved by the Korea University Hospital Institute Review Board (IRB No. 2016AN0095), and informed consent was waived due to the retrospective study design. This study also complied with the Declaration of Helsinki.

Angiographic analysis

Coronary angiograms were analyzed using a computer-based telecardiology system, version 2.02 (Medcon Inc., Tel Aviv, Israel) by three radiologic technicians who were blinded to the purpose of the study. The reference diameter, minimal luminal diameter, percentage of stenosis, and lesion length were evaluated from diastolic frames using guided catheter magnification calibration in a single, matched view with a computerized quantitative analyzer using a caliper. The average diameter of normal segments proximal and distal to the treated lesion was used as the reference diameter.

OCT acquisition

Optical coherence tomography examination and analysis were performed immediately after stent implantation (LightLab Imaging Inc., Ilumien Offline review workstation, Ver E.4.1, MA, USA). Using a 0.014" guide wire, an OCT imaging catheter (C7 Dragonfly™, LightLab Imaging Inc., MA, USA) was advanced into the distal end of the DES implantation site. The entire length of the stent was imaged with an automatic pullback device moving at 15 mm/s. The whole stent could be clearly visualized on each OCT image; in-segment cross-sectional views were also obtained.

OCT analysis

All baseline OCT images were reviewed by an independent observer who was blinded to the clinical presentation, lesion, and procedural characteristics. The analysis encompassed the intra-stent segment, defined by the first and the last cross-sections with a visible strut, and the adjacent vessel segments 5 mm proximal and distal to the stent, defined as edge segments. The stent and lumen areas were traced, and minimum, maximum, and mean neointimal thickness were semiautomatically determined. Plaque characteristics and restenotic tissue patterns were analyzed if the mean neointimal thickness was $> 100\ \mu m$ on ≥ 3 consecutive cross-sectional frames at a 1 mm interval.

Lipid plaque was defined as a diffusely bordered signal-poor region with rapid signal attenuation. In lipid plaque, lipid arc was measured at every 1-mm interval throughout the entire length of each lesion and the values were averaged. Lipid length was also measured on longitudinal view. Lipid index was defined as the averaged lipid arc multiplied by lipid length [18]. Calcified plaque was defined as a clearly delineated signal-poor region with low backscatter. Thin-cap fibroatheroma was defined as neointima with a fibrous cap thickness at the thinnest part $\leq 65\ \mu m$ and an angle of lipid-laden neointima $\geq 180°$ [4, 19]. The stent was considered to have neoatherosclerosis when lipid plaque, calcified plaque or thin-cap fibroatheroma were present [20, 21]. Microvessels were defined as well-delineated low backscattering structures $< 200\ \mu m$ in diameter showing a trajectory within the vessel [22]. Evagination was identified as outward bulges in the luminal contour between struts, with the depth of the bulge exceeding the actual strut thickness [23, 24]. For restenotic tissue pattern analysis, parameters were defined as follows: 1) homogeneous neointima, a uniform signal-rich band without focal variation or attenuation; 2) heterogeneous neointima, focally changing optical properties and various backscattering patterns; 3) layered neointima, layers with different optical properties, namely an adluminal high scattering layer and abluminal low scattering layer [22]. Representative OCT images of the neoatherosclerosis and in-stent restenosis pattern are visualized in Figure 1.

Statistical analysis

Data are expressed as mean ± standard deviation for continuous variables, whereas data for categorical variables are expressed as number and percentage of patients. The χ^2 test was used to compare categorical variables. Continuous variables were compared using a t test or the Mann-Whitney test.

Selected variables were tested for univariate logistic regression associated with neoatherosclerosis; if the p-value < 0.2, they were simultaneously entered into a multivariate logistic regression model to identify independent predictors of outcome and to calculate their adjusted odds ratios with an associated 95% confidence interval (CI). The logistic regression model included the following variables, which were considered to be related with neoatherosclerosis: age, male sex, hypertension, diabetes mellitus, chronic kidney disease, smoking status, low density lipid cholesterol, high sensitive C-reactive protein, statin use, renin–angiotensin system (RAS) blocker use, stent length and stent polymer type.

Clinical event rates were estimated using the Kaplan-Meier survival analysis at 4 years, and hazard ratios (HRs) were generated using the Cox regression analysis. Because patients may have experienced more than 1 MACE, each patient was assessed until the occurrence of his or her first event and only once during analysis.

The Cox multivariate analysis to compare MACE incidence between the two study groups was performed using same covariates mentioned above as well as clinical diagnosis, incidence of neoatherosclerosis, restenotic tissue pattern, lipid index and evagination. SPSS version 24.0 (IBM SPSS Statistics, IBM Corporation, Armonk, New York) was used for all analyses. A p-value < 0.05 was considered statistically significant.

Results

The study protocol is diagrammed in Figure 2. Overall, 150 patients (153 lesions) in BP-DES group and 161 patients (166 lesions) in DP-DES group were analyzed. The baseline characteristics of the

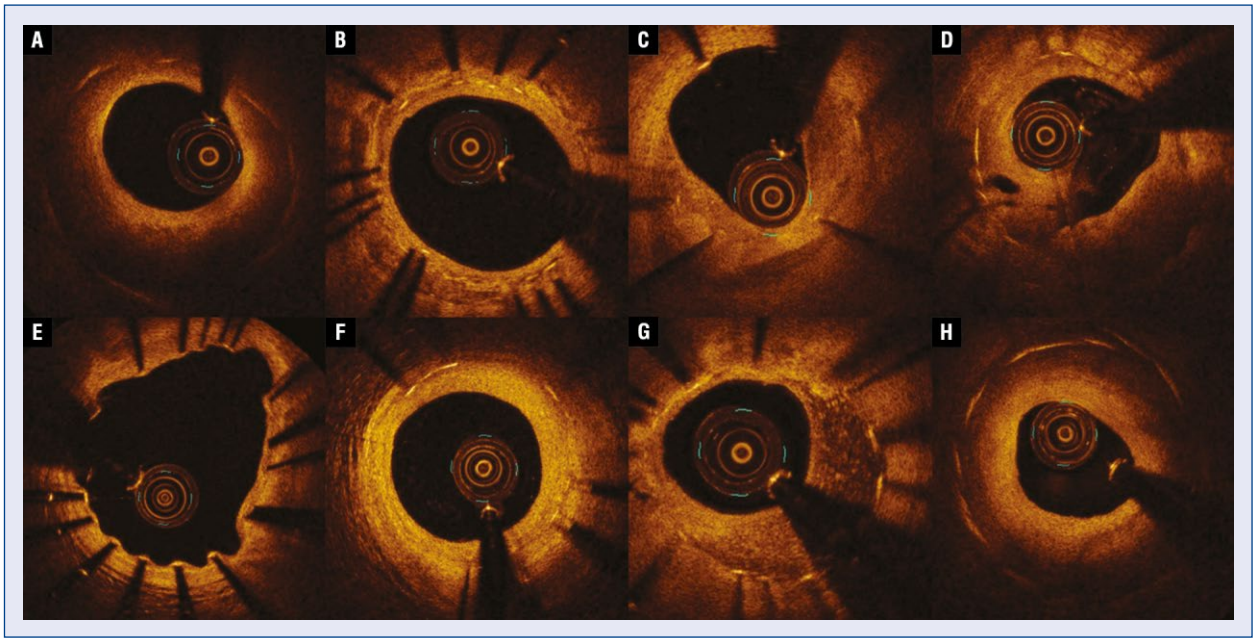

Figure 1. Representative optical coherence tomography (OCT) findings; **A.** Lipid plaque; **B.** Calcified plaque; **C.** Thin cap fibroatheroma; **D.** Microvessel; **E.** Evagination; **F.** Homogeneous pattern; **G.** Heterogeneous pattern; **H.** Layered pattern.

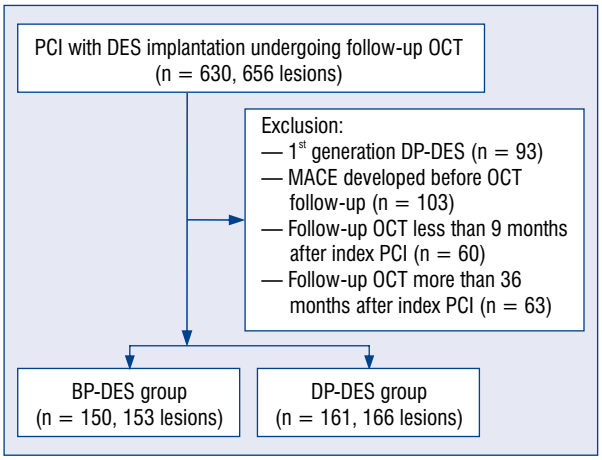

Figure 2. Study flow chart; PCI — percutaneous coronary intervention; DES — drug-eluting stent; BP-DES — bioabsorbable polymer drug-eluting stent; DP-DES — durable polymer drug-eluting stent; MACE — major adverse cardiac events; OCT — optical coherence tomography.

patients included in this study are presented in Table 1. Baseline characteristics of the BP-DES group were not statistically significantly different from those of the DP-DES group except when using antiplatelet agents and an onset diagnosis. The onset diagnosis of stable angina was more frequent in the BP-DES group than in the DP-DES group (61.4% vs. 47.6%, p = 0.044). Table 2 shows the quantitative coronary angiography results. Shorter stent length was used (20.3 ± ± 5.6 mm vs. 22.2 ± 7.6 mm, p = 0.011) in the BP-DES group. Otherwise, other angiographic data were well matched in the study.

OCT findings

Optical coherence tomography findings at follow-up are shown in Table 3. Although time from stent implantation to follow-up OCT was similar (12.1 ± 2.3 months vs. 12.6 ± 2.4 months, p = 0.062), the prevalence of neoatherosclerosis was lower in the BP-DES group compared with the DP-DES group (5.2% vs. 14.5%, p = 0.008), which was driven by lipid plaque (5.2% vs. 13.9%, p = 0.013). However, lipid index was numerically higher in the BP-DES group but showed no statistical difference between the two groups (1385.5 ± ± 2324.5 vs. 636.8 ± 984.6, p = 0.403). In quantitative analysis, mean neointimal area as well as mean neointimal thickness were similar among each group. In other hand, incidence (62.5% vs. 30.3%, p < 0.001), frame count (24.0 ± 16.8 vs. 12.2 ± 8.3, p < 0.001) and frame rate from total frame (28.1 ± 19.0% vs. 13.3 ± 8.8%, p < 0.001) of stent evagination had all presented significantly higher in the BP-DES group. The intra-observer

Table 1. Baseline patient characteristics.

Variable	BP-DES (n = 150)	DP-DES (n = 161)	P
Age [year]	60.2 ± 10	60.5 ± 9.6	0.726
Male sex	108 (72.0%)	113 (70.2%)	0.711
Body mass index [kg/m^2]	25.3 ± 2.7	24.8 ± 3.0	0.206
Smoking:			0.187
Previous	11 (7.3%)	19 (11.8%)	
Current	33 (22.0%)	44 (27.3%)	
Comorbidity:			
Hypertension	86 (57.3%)	92 (57.1%)	1.000
Diabetes mellitus	31 (20.7%)	47 (29.3%)	0.122
Chronic kidney disease	6 (4.0%)	12 (7.5%)	0.232
Laboratory data:			
White blood cell count [×10^3/μL]	7.3 ± 2.3	8.2 ± 3.1	0.008
Creatinine [mg/dL]	0.96 ± 0.19	0.98 ± 0.43	0.578
Total cholesterol [mg/dL]	171.2 ± 37.6	169.7 ± 40.6	0.772
Triglyceride [mg/dL]	144 ± 77.8	124.4 ± 65.3	0.038
HDL-C [mg/dL]	44.6 ± 10.5	45 ± 11.4	0.753
LDL-C [mg/dL]	99.9 ± 34.6	93.4 ± 26.5	0.115
Peak CK-MB [ng/mL]	27.8 ± 79.5	40.4 ± 84.4	0.305
hs-CRP [mg/dL]	5.558 ± 21.433	10.398 ± 33.544	0.248
ESR [mm/h]	9.8 ± 7.8	11 ± 10.3	0.387
HbA1c [%]	6.8 ± 1.2	6.5 ± 1.0	0.248
Drug:			
Acetylsalicylic acid	136 (90.7%)	158 (97.5%)	0.013
P2Y12 inhibitor	148 (98.7%)	151 (93.2%)	0.021
Cilostazol	8 (5.3%)	8 (4.9%)	1.000
Statin	144 (96.0%)	153 (94.4%)	0.603
RAS blocker	71 (47.3%)	89 (54.9%)	0.212
Beta-blocker	90 (60.0%)	107 (66.0%)	0.292
Calcium channel blocker	66 (44.0%)	64 (39.5%)	0.424
Clinical presentation:			0.044
Stable angina	92 (61.3%)	77 (47.8%)	
Unstable angina	35 (23.3%)	50 (31.1%)	
NSTEMI	13 (8.7%)	25 (15.5%)	
STEMI	10 (6.7%)	9 (5.6%)	

BP-DES — bioabsorbable polymer drug-eluting stent; DP-DES — durable polymer drug-eluting stent; HDL-C — high-density lipoprotein cholesterol; LDL-C — low-density lipoprotein cholesterol; hs-CRP — high sensitive C-reactive protein; ESR — erythrocyte sedimentation rate; HbA1c — glycated hemoglobin; RAS — renin–angiotensin system; NSTEMI — non–ST-segment elevation myocardial infarction; STEMI — ST-segment elevation myocardial infarction

κ coefficient for OCT findings was 0.91, and the interobserver κ coefficient was 0.90.

Predictors of neoatherosclerosis

Bioabsorbable polymer DES failed to predict neoatherosclerosis in the univariate model; only mean neointimal thickness showed statistical association. The multivariate model identified less use of RAS blocker and higher degree of neointimal hyperplasia as independent predictors of neoatherosclerosis (Table 4).

Clinical outcomes

Although the follow-up period was shorter in the BP-DES group (months after index PCI: 44.1 ± ± 13.2 vs. 51.2 ± 17.9, p < 0.001; months after

Table 2. Angiographic and procedural data.

Variable	BP-DES (153 lesions)	DP-DES (166 lesions)	P
Vessel:			0.940
LAD	96 (62.7%)	108 (65.1%)	
LCX	23 (15.0%)	25 (15.1%)	
RCA	30 (19.6%)	30 (18.1%)	
Left main	4 (2.6%)	3 (1.8%)	
Mean stent diameter [mm]	3.00 ± 0.44	3.03 ± 0.44	0.563
Mean stent length [mm]	20.3 ± 5.6	22.2 ± 7.6	0.011
Quantitative coronary analysis:			
Baseline:			
Proximal RD [mm]	3.0 ± 0.3	2.9 ± 0.5	0.907
Distal RD [mm]	2.3 ± 1.16	2.4 ± 1.1	0.554
MLD [mm]	0.8 ± 0.6	0.9 ± 0.6	0.791
Diameter stenosis [%]	68.6 ± 27.3	69.0 ± 21.8	0.941
Post-procedure:			
Proximal RD [mm]	3.1 ± 0.4	3.2 ± 0.5	0.433
Distal RD [mm]	2.9 ± 0.4	3.1 ± 0.5	0.227
MLD [mm]	2.8 ± 0.4	2.9 ± 0.5	0.377
Diameter stenosis [%]	5.7 ± 3.7	5.8 ± 4.8	0.867

BP-DES — bioabsorbable polymer drug-eluting stent; DP-DES — durable polymer drug-eluting stent; LAD — left anterior descending artery; LCX — left circumflex artery; RCA — right coronary artery; RD — reference diameter; MLD — minimal lumen diameter

Table 3. Comparison of OCT findings.

Variable	BP-DES (153 lesions)	DP-DES (166 lesions)	P
Index PCI to OCT duration [month]	12.1 ± 2.3	12.6 ± 2.4	0.062
OCT analysis:			
Mean stent area [mm^2]	6.39 ± 2.64	6.88 ± 2.59	0.227
Minimal luminal area [mm^2]	4.59 ± 2.03	4.99 ± 2.29	0.249
Mean neointimal area [mm^2]	1.80 ± 0.96	1.89 ± 1.05	0.554
Mean neointimal thickness [mm]	0.22 ± 0.09	0.24 ± 0.13	0.374
Neoatherosclerosis:	8 (5.2%)	24 (14.5%)	0.008
Microvessel	2 (1.7%)	3 (2.3%)	0.377
Thin cap fibroatheroma	0 (0%)	2 (1.2%)	0.499
Calcified plaque	1 (0.7%)	0 (0%)	0.478
Lipid plaque	8 (5.2%)	23 (13.9%)	0.013
Macrophage	5 (4.2%)	10 (7.4%)	0.300
Lipid plaque:			
Lipid plaque length [mm]	8.03 ± 9.97	4.54 ± 4.22	0.366
Lipid plaque arc [°]	109.6 ± 63.3	108.8 ± 67.7	0.978
Lipid index	1385.5 ± 2324.5	636.8 ± 984.6	0.403
ISR pattern:			< 0.001
Homogeneous	35 (22.9%)	79 (47.6%)	
Heterogeneous	16 (10.5%)	27 (16.3%)	
Layered	11 (7.2%)	14 (8.4%)	
Evagination:	95 (62.5%)	50 (30.3%)	< 0.001
Evagination frame	24.0 ± 16.8	12.2 ± 8.3	< 0.001
Evagination rate [%]	28.1 ± 19.0	13.3 ± 8.8	< 0.001

OCT — optical coherence tomography; BP-DES — bioabsorbable polymer drug-eluting stent; DP-DES — durable polymer drug-eluting stent; PCI — percutaneous coronary intervention; ISR — in-stent restenosis

Table 4. Predictors of neoatherosclerosis.

Variable	Univariate analysis				Multivariate analysis			
	OR	95% CI		P	OR	95% CI		P
Male sex	0.574	0.217	1.517	0.263				
Age	0.991	0.956	1.027	0.614				
Diabetes mellitus	1.186	0.461	3.055	0.724				
Hypertension	1.203	0.512	2.826	0.671				
CKD	1.020	0.239	4.344	0.979				
Smoking:								
Current	2.849	1.092	7.433	0.032				
Previous	1.171	0.453	3.031	0.745				
UA	1.241	0.345	4.471	0.741				
MI	1.949	0.429	8.862	0.388				
hs-CRP	1.003	0.983	1.024	0.762				
Triglyceride	1.001	0.995	1.007	0.654				
LDL-C	1.004	0.990	1.018	0.604				
Statin	1.552	0.210	11.459	0.666				
RAS blocker	0.511	0.234	1.118	0.093	0.388	0.175	0.859	0.020
BP-DES	2.177	0.917	5.170	0.078				
Stent diameter	1.019	0.437	2.376	0.966				
Stent length	1.031	0.977	1.088	0.271				
Mean neointimal thickness	9.178	1.349	62.454	0.023				
Mean neointimal area	1.377	1.049	1.809	0.021	1.318	1.012	1.717	0.040

OR — odds ratio; CI — confidence interval; CKD — chronic kidney disease; UA — unstable angina, MI — myocardial infarction; hs-CRP — high sensitive C-reactive protein; LDL-C — low-density lipoprotein cholesterol; RAS — renin-angiotensin system; BP-DES — bioabsorbable polymer drug-eluting stent

follow-up OCT: 31.4 ± 13.2 vs. 38.1 ± 17.6, $p < 0.001$), the incidence of MACE was very low and there was no significant difference between the two groups (3.3% vs. 7.8%, HR 1.964, 95% CI 0.688–5.611, $p = 0.207$) (Fig. 3, Table 5). Also, the incidence of each MACE component did not differ significantly between the two groups.

Discussion

This study showed that incidence of neoatherosclerosis was lower in the BP-DES group compared to the DP-DES group, which was driven by lipid plaque. However, the difference of neoatherosclerosis incidence among stent polymer type did not transform into incidence difference of clinical events over the follow-up (median 49 months). Independent predictors of neoatherosclerosis were less use of RAS blocker and higher degree of neointimal hyperplasia.

Development of atherosclerosis in neointima, so-called neoatherosclerosis is a significant risk for

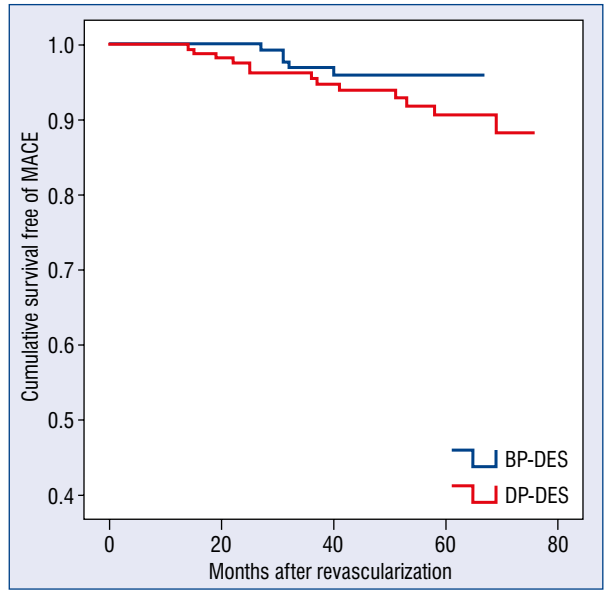

Figure 3. Kaplan-Meier curve regarding cumulative survival free of major adverse cardiac events (MACE); BP-DES — bioabsorbable polymer drug-eluting stent; DP-DES — durable polymer drug-eluting stent.

Table 5. Clinical outcomes.

Variable	BP-DES (n = 150)	DP-DES (n = 161)	P
MACE	5 (3.3%)	13 (7.8%)	0.207
Non-fatal MI	0 (0%)	2 (1.2%)	0.531
All cause death	0 (0%)	4 (2.4%)	0.124
TLR	4 (2.6%)	8 (4.8%)	0.432
TVR	5 (3.3%)	9 (5.4%)	0.477
Non-TLR, TVR	12 (7.8%)	14 (8.4%)	0.284
Stent thrombosis	0 (0%)	3 (1.8%)	0.435
MACE after index PCI [month]	44.1 ± 13.1	51.2 ± 17.9	< 0.001
MACE after OCT [month]	31.4 ± 13.2	38.1 ± 17.6	< 0.001

BP-DES — bioabsorbable polymer drug-eluting stent; DP-DES — durable polymer drug-eluting stent; MACE — major adverse cardiovascular events; MI — myocardial infarction; TLR — target lesion revascularization; TVR — target vessel revascularization, PCI — percutaneous coronary intervention; OCT — optical coherence tomography

late stent failure such as very late stent thrombosis or stent restenosis [4]. Pathological studies of first-generation DES have reported that the stent polymer might be the key of neoatherosclerosis acceleration by inducing inflammation in the vessel wall [25]. In advance, BP-DES was developed to overcome the risk of vessel wall damage by the durable polymer. However, benefit of BP-DES is still controversial. BP-DES showed superiority of neoatherosclerosis incidence compared to first--generation DES [14]. Meta-analysis has shown BP-DES were superior to second-generation DES in late lumen loss and late stent thrombosis [11]. However, other reports presented the incidence of neither neoatherosclerosis or clinical events were improved or were even worse with BP-DES compared to second-generation DES [12, 13, 15, 16]. The present study revealed lower incidence of neoatherosclerosis, mainly lipid plaque, in BP--DES. However, quantitative measurement of lipid plaque by lipid index was similar between the two groups. Lipid index is known to be related with plaque vulnerability [18, 26]. Since clinical event by neoatherosclerosis is mostly related with stent thrombosis, it can suggest the severity of neoatherosclerosis in terms of plaque vulnerability and that the existence of neoatherosclerosis only plays more of a role in future events by plaque rupture.

An animal-based pathological study compared BP-DES with platinum-chromium scaffold (Synergy®, Boston Scientific, USA), BP-DES with stainless scaffold (Nobori®) and second-generation DP-DES (Resolute Integrity, Medtronic, USA) concerning about neoatherosclerosis [27]. Inflammation score and neoatherosclerosis was lowest for BP-DES with platinum-chromium scaffold, followed by BP-DES with stainless scaffold and was the highest for second-generation DP-DES. Although both BP-DES were superior compared to second-generation DP-DES, there was also significant difference among two different BP--DES. Since BP-DES with platinum-chromium scaffold has strength with more biocompatible stent scaffold and a shorter degradation period than BP-DESs which were used in the current study, current findings about BP-DES may have a weak point in terms of biocompatibility. Another issue is about bioabsorbable polymer itself. Several animal-based pathologic studies have shown that bioabsorbable polymer are associated with higher rates of inflammation than durable polymer [9, 10, 28]. In the present study, evagination was less frequently observed in second-generation DP-DES than BP-DES. Evagination is known to be associated with late-acquired positive vessel remodeling and increased risk of late stent thrombosis [23, 24, 29, 30]. The polymer absorbing process may cause hypersensitivity and vessel wall inflammation leading to evagination. This finding could possibly explain the attenuated benefit of BP-DES.

Although predictors of neoatherosclerosis differed in previous reports, less use of RAS blocker and higher degree of neointimal thickness were independently correlated with neoatherosclerosis in several reports including the present study [21, 31, 32]. It is well known that activation of renin–––angiotensin–aldosterone system promotes vascular inflammation and remodeling and therefore RAS blocker inhibits atherosclerosis as reduced plaque burden in atherosclerotic vessels [33]. In addition to the anti-inflammatory effect, RAS blocker has

a protective effect of neointimal growth based on the findings of angiotensin II and angiotensin converting enzyme facilitates neointimal formation [5, 34]. Moreover, homogeneous and layered pattern of neointima which is linked with neointimal stabilization were more likely to be present in the use of RAS blocker in a single center OCT study [35]. With these synergistic effects, such mechanisms can possibly explain protective effect of RAS blocker on neoatherosclerosis.

Limitations of the study

This study had several limitations. This was a non-randomized retrospective study based on a relatively limited sample size and modest follow-up period, raising the possibility of selection bias and was therefore underpowered to clarify the incidence as well as clinical outcome of neoatherosclerosis. A few baseline demographics were mismatched between the BP-DES and DP-DES group, which may introduce a confounder in the statistical analysis and lead to a biased result. Also, as mentioned above, more biocompatible BP-DES was introduced yet available during study enrollment. Therefore, results of the present study should not be simplified to express no benefit of BP-DES as a class effect. The reasons for follow-up coronary angiography were mainly evidence of inducible myocardial ischemia or symptoms of coronary artery disease. Therefore, the incidence of neoatherosclerosis was derived from a biased population and caution is needed in extrapolating these results. Finally, all measurements were performed manually, meaning that a certain degree of manual error was present. Automatic plaque analysis on OCT imaging by artificial intelligence may be useful in reducing subjectivity in image interpretation and facilitate OCT quantification of neoatherosclerosis [36]. Larger studies with a longer follow-up duration with more biocompatible BP-DES are needed to confirm the relationships between neoatherosclerosis and stent polymer.

Conclusions

At 1 year after stent implantation, neoatherosclerosis was less frequently observed in BP-DES compared with DP-DES. However, this difference did not reach significant clinical outcome difference after up to 4-year follow-up. Future studies with a larger number of participants are warranted to confirm the relationship between stent polymer type and clinical outcomes.

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