



Two-year clinical outcomes of zotarolimus- and everolimus-eluting durable-polymer-coated stents versus biolimus-eluting biodegradable-polymer-coated stent in patients with acute myocardial infarction with dyslipidemia after percutaneous coronary intervention: data from the KAMIR

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Received: 20 June 2018 / Accepted: 24 August 2018 / Published online: 30 August 2018
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Abstract

There are limited data comparing the clinical outcomes among new-generation drug-eluting stents (DES) in acute myocardial infarction (AMI) patients with dyslipidemia after percutaneous coronary intervention (PCI). We thought to investigate 2-year clinical outcomes among durable-polymer (DP)-coated stents [zotarolimus eluting (ZES) and everolimus eluting (EES)] and biodegradable-polymer (BP)-coated biolimus-eluting stent (BES) in dyslipidemic AMI patients after PCI. Finally, a total 2403 enrolled patients were divided into ZES ($n = 953$), EES ($n = 1145$) or BES ($n = 305$) group. The primary endpoint was major adverse cardiac events (MACE) defined as total death (TD), cardiac death (CD), myocardial infarction (MI), target lesion revascularization (TLR), target vessel revascularization (TVR) and non-TVR. The secondary endpoint was the incidence of definite or probable stent thrombosis (ST). The 2-year adjusted hazard ratio (HR) of MACE for ZES vs. EES [HR, 1.066; 95% confidence interval (CI) 0.752–1.511; $p = 0.720$], ZES vs. BES (HR 0.933; 95% CI 0.565–1.541; $p = 0.786$), EES vs. BES (HR 1.876; 95% CI 0.535–1.436; $p = 0.600$) and ZES/EES vs. BES (HR 0.929; 95% CI 0.591–1.462; $p = 0.751$) was similar. The cumulative incidences of ST were comparable (ZES vs. EES vs. BES = 1.1% vs. 0.9% vs. 1.1%, $p = 0.675$) and adjusted HR was not different. In addition, the 2-year adjusted HR of TD, CD, MI, TLR, TVR, and non-TVR was similar. The AMI patients with dyslipidemia receiving ZES, EES, or BES after PCI showed comparable safety and efficacy during 2-year follow-up periods. Therefore, DP-DES or BP-DES is equally acceptable in dyslipidemic AMI patients during PCI.

Keywords Myocardial infarction · Dyslipidemia · Drug-eluting stents

Abbreviations

AMI	Acute myocardial infarction
BES	Biolimus-eluting stents
BP	Biodegradable polymer
DES	Drug-eluting stents
DP	Durable polymer
EEE	Everolimus-eluting stent
MACE	Major adverse cardiac events
PCI	Percutaneous coronary intervention
PES	Paclitaxel-eluting stent
SES	Sirolimus-eluting stent
ST	Stent thrombosis
TLR	Target lesion revascularization
TVR	Target vessel revascularization
ZES	Zotarolimus-eluting stent

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Introduction

The INTERHEART study demonstrated abnormal lipids were one of modifiable risk factors of myocardial infarction worldwide in both sexes and at all ages in all regions [1]. The Physician's Health Study also showed hypertension, hypercholesterolemia, diabetes mellitus (DM), smoking, and physical inactivity were associated with higher risk of coronary heart disease and stroke [2]. Naito et al. suggested dyslipidemia might be strongly associated with coronary artery events than cerebrovascular events [3]. However, previous comparative studies [4–6] related with new-generation drug-eluting stents (DES) were not focused on dyslipidemia especially, the milieu of acute myocardial infarction (AMI). Although AMI milieu tends to higher thrombotic condition compared to stable coronary artery disease, DES implantation during primary percutaneous coronary intervention (PCI) or staged PCI is commonly done from the beginning of DES era up to now. Compared to bare-metal stents (BMS), DES have reduced target lesion revascularization (TLR) by inhibition of neointimal hyperplasia but increased risk of fatal stent thrombosis (ST) is one of major concerns [7, 8]. Therefore, much longer duration of dual antiplatelet therapy (DAPT) was required for first-generation DES compared to BMS [9, 10]. Moreover, to overcome these limitations, stent platforms and polymers have rapidly evolved during a short period. Newer anti-proliferative drugs and more biocompatible polymers have been adapted in reducing the rate of late ST [11]. More recent meta-analyses showed a lowered incidence of ST in case of second-generation biodegradable-polymer-coated stent [12]. The aim of this study was to compare long-term safety and efficacy among zotarolimus-eluting (ZES) or everolimus-eluting durable-polymer-coated stents (EES) or biolimus-eluting biodegradable-polymer-coated stents (BES) in patients with AMI with dyslipidemia after PCI.

Methods

Study population

Data from the Korea AMI Registry (KAMIR) are used in this study. KAMIR is a nationwide, prospective, observational on-line registry in South Korea since November 2005 to evaluate current epidemiology, and short-term and long-term clinical outcomes of patients with AMI. Fifty-three high-volume university or community hospitals with facilities for primary PCI and onsite cardiac surgery participated in this study. These data are collected by

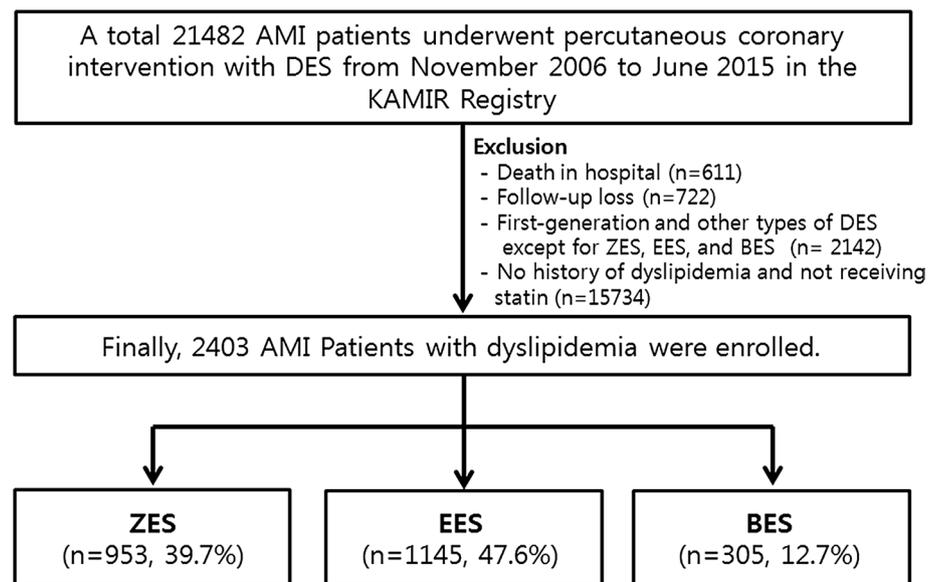
well-trained coordinators using a standardized web-based case report formed at each site. Details of the registry can be found at the KAMIR website (<http://www.kamir.or.kr>).

This study was a non-randomized, multicenter, observational, retrospective study. A total 21482 AMI patients who underwent PCI with DES were enrolled between November 2006 and June 2015 in the KAMIR Registry. Among them, the patients who have these conditions were excluded: (1) death in hospital, $n = 611$ (2.8%), (2) loss of follow-up, $n = 722$ (3.4%), (3) received the first-generation DES [sirolimus-eluting stents (SES) and paclitaxel-eluting stents (PES)] and other stents except for ZES, EES, and BES ($n = 2142$, 10.0%), (4) no history of dyslipidemia and not receiving statin treatment ($n = 15734$, 73.2%). Finally, a total of 2403 eligible AMI patients having dyslipidemia were enrolled. Among these patients, ZES (Resolute Integrity stent; Medtronic, Inc., Minneapolis, MN, USA) were deployed in 953 (39.7%) patients and EES (Xience Prime stent, Abbott Vascular, Santa Clara, CA, USA; or Promus Element stent, Boston Scientific, Natick, MA, USA) were deployed in 1145 (47.6%) patients, and BES (BioMatrix Flex stent, Biosensors International, Morges, Switzerland; or Nobori stent, Terumo Corporation, Tokyo, Japan) were deployed in the remaining 305 (12.7%) patients (Fig. 1). This study protocol was approved by the ethics committee at each participating center and was conducted according to the ethical guidelines of the 1975 Declaration of Helsinki. Informed consent was obtained from all individual participants included in the study prior to enrollment. In this study, all 2403 patients completed a 2-year clinical follow-up by face-to-face interviews, phone calls, or chart review.

Percutaneous coronary intervention and medical treatment

A diagnostic coronary angiography and PCI were done through either the femoral or the radial artery after an administration of unfractionated heparin (50–100 IU/kg). Patient's activated clotting time (ACT) was maintained > 250 s during the procedure. All patients were given loading doses of 200–300 mg aspirin and 300–600 mg clopidogrel before PCI. Revascularization was considered clinically indicated when the patient had typical angina and/or signs of ischemia, and $\geq 50\%$ diameter restenosis or $\geq 70\%$ diameter restenosis in a coronary artery by visual estimation. A successful PCI was defined as the achievement of an angiographic residual stenosis less than 30% and final thrombolysis in myocardial infarction (TIMI) blood flow grade as three. During in-hospital stay and after discharge, all patients' medical treatment included beta-blockers (BB) or calcium channel blockers (CCB), angiotensin-converting enzyme inhibitors (ACEI) or angiotensin II receptor blockers (ARB) and lipid

Fig. 1 Flow chart. *AMI* acute myocardial infarction, *DES* drug-eluting stents, *KAMIR* Korea Acute Myocardial Infarction Registry, *ZES* Zotarolimus-eluting stents, *EES* Everolimus-eluting stents, *BES* Biolimus-eluting stents



lowering agents. After discharge, the patients were recommended to stay on the same medications they received during hospitalization. Especially, the patients were maintained on 100–200 mg aspirin indefinitely and clopidogrel 75 mg for a minimum of 6 months after index PCI. In addition, the combination of aspirin (100 mg/day) and clopidogrel (75 mg/day) was recommended for at least 6 months to patients who had undergone PCI. Triple antiplatelet therapy (TAPT) [100 mg cilostazol (Pletaal[®], Otsuka Pharmaceutical Co., Tokyo, Japan) twice a day added on to DAPT] was left to the discretion of the individual operators.

Study definitions and endpoints

Dyslipidemia was defined as the patients whose serum low-density lipoprotein (LDL) cholesterol concentrations are of at least 140 mg/dL, high-density lipoprotein (HDL) cholesterol concentrations were <40 mg/dL, triglyceride (TG) concentrations were ≥ 150 mg/dL, or patients who were taking lipid-lowering medication [13]. ST-segment elevation myocardial infarction (STEMI) was defined as chest pain with ST-segment elevation ≥ 2 mm in ≥ 2 contiguous precordial leads, or ≥ 1 mm in ≥ 2 limb leads, or new left bundle branch block on the admission electrocardiogram, and elevation of cardiac enzymes at least 3 times the upper limit of normal range [14].

The primary endpoint was the occurrence of major adverse cardiac events (MACE) defined as total death (TD), cardiac death (CD), non-fatal re-myocardial infarction (re-MI), revascularization (TLR, target vessel revascularization [TVR], non-TVR) during the 2-year follow-up period. The secondary endpoint was the incidence of definite or probable

ST during the 2-year follow-up. Total deaths are classified as cardiac or non-cardiac death. Re-MI was defined as the presence of clinical symptoms, electrocardiographic changes, or abnormal imaging findings of MI, combined with an increase in the creatine kinase myocardial band fraction above the upper normal limits or an increase in troponin-T/troponin-I to greater than the 99th percentile of the upper normal limit [15, 16]. TLR was defined as a revascularization of the target lesion due to restenosis or re-occlusion within the stent or 5 mm in and adjacent to the distal or proximal segment. TVR was defined as a revascularization of the target vessel or any segment of the coronary artery containing the target lesion. Non-TVR is defined as a revascularization of any segment of the non-target coronary artery. ST is defined as acute (0–24 h), subacute (24 h–30 days), late (30 days–1 year) and very late (> 1 year) according to the onset time of stent thrombosis [17]. Moreover, Modified American College of Cardiology/American Heart Association criteria were used to classify coronary lesion morphology [14]. Thrombolysis in Myocardial Infarction score was used to determine the degree of coronary flow before and after the procedure [15].

Statistical analysis

All statistical analyses were performed using SPSS software, version 20 (SPSS Inc., Chicago, IL, USA). For continuous variables, differences among the three groups were evaluated by analysis of variance or the Jonckheere–Terpstra test, and post hoc analysis between the two groups was done using the Hochberg test or Dunnett-*T*3 test; data are expressed as means \pm standard deviations. For discrete variables, the

differences between the two groups among the three groups were analyzed with the χ^2 test or Fisher's exact test, as appropriate; data are expressed as counts and percentages. Multivariable Cox-proportional hazards regression, which includes baseline confounding factors, was used to assess independent predictors. We tested all available variables of potential relevance: age, gender (men), STEMI, non-ST-segment elevation myocardial infarction (NSTEMI), left ventricular ejection fraction (LVEF), Body Mass Index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), hypertension, diabetes mellitus (DM), serum creatine kinase myocardial band (CK-MB), serum troponin-I, serum glucose, hemoglobin A_{1c}, N-terminal pro-brain natriuretic peptide (NT-ProBNP), high-sensitivity CRP, serum creatinine, total cholesterol, triglyceride, low-density lipoprotein (LDL)-cholesterol, discharge medications (aspirin, BB, CCB, ACEI, ARB, lipid lowering agents), target vessel [left anterior descending artery (LAD)], American College of Cardiology/American Heart Association (ACC/AHA) type B2 and C lesion, extent of coronary artery disease [1-vessel disease, \geq 3-vessel disease, pre-PCI Thrombolysis In Myocardial Infarction (TIMI) grade 0, post-PCI TIMI grade 3, and the number of stent]. Various clinical outcomes were estimated with Kaplan–Meier curve analysis, and differences between groups were compared with the log-rank test. A two-tailed p value of <0.05 was considered statistically significant.

Results

Baseline clinical, angiographic and procedural characteristics

Baseline and laboratory characteristics of this study population are summarized in Table 1. Mean ages of participants were similar (61.4 ± 11.8 years, $p=0.360$). The gender (men) distribution was similar among these groups (74.9%, $p=0.612$). The numbers of STEMI (54.5%) and current smoker (43.1%) were higher in the ZES group and NSTEMI (54.1%) was higher in the BES group. The mean serum level of CK-MB was higher in the EES group. In the aspect of discharge medications, the prescription rates of clopidogrel (90.5%) and cilostazole (Pletaal[®], Otsuka Pharmaceutical Co., Tokyo, Japan, 20.8%) were higher in the ZES group and ACEI (57.8%), BB (85.5%) were higher in the EES group, and aspirin (100%) and ARB (37.0%) and lipid-lowering agents (90.5%) were higher in the BES group. Among the lipid-lowering agents, atorvastatin (39.1% vs. 43.6% vs. 41.6%) was the most frequently used agent. Angiographic characteristics among these three groups are summarized in Table 2. The diameter of deployed stent was larger in

the ZES group (3.16 ± 0.46 mm) and the length of deployed stent was longer in the EES group (27.8 ± 11.2 mm). The incidences of ACC/AHA type B2 lesion, one-vessel disease, and post-PCI TIMI grade 3 were higher in the BES group.

Clinical outcomes

The cumulative incidences of major clinical outcomes at 2 years are listed in Tables 3 and 4 and Figs. 2 and 3. Before adjustment, the cumulative incidence of MACE was not different among these patients (ZES vs. EES = 7.8% vs. 7.1%, Log-rank $p=0.448$; ZES vs. BES = 7.8% vs. 8.4%, Log-rank $p=0.737$; EES vs. BES = 7.1% vs. 8.4%, Log-rank $p=0.360$; ZES/EES vs. BES = 7.4% vs. 7.1%, Log-rank $p=0.503$, Fig. 2a). In addition, the incidences of total death, cardiac death, TLR, TVR, and non-TVR were not significantly different among these patients, except for the incidence of TVR between ZES and EES [3.1% vs. 1.6%, $p=0.019$, hazard ratio (HR) 1.883, 95% confidence interval (CI) 1.050–3.378, $p=0.034$] (Tables 3, 4). After adjustment, the incidence of MACE showed similar results among these patients (ZES vs. EES = adjusted HR, 1.066; 95% CI, 0.752–1.511; $p=0.720$; ZES vs. BES = adjusted HR, 0.933; 95% CI, 0.565–1.541; $p=0.786$; EES vs. BES = adjusted HR, 0.876; 95% CI, 0.535–1.436; $p=0.600$; ZES/EES vs. BES = adjusted HR, 0.929; 95% CI, 0.591–1.462; $p=0.751$, Table 4). Other cumulative incidences of TD, MI, TLR, and non-TVR were similar among these groups before and after adjustment (Table 4, Fig. 3).

The incidence of ST was not significantly different (ZES vs. EES = 1.1% vs. 0.9%, Log-rank $p=0.478$; ZES vs. BES = 1.1% vs. 1.1%, Log-rank $p=0.990$; EES vs. BES = 0.9% vs. 1.1%, Log-rank $p=0.551$; ZES/EES vs. BES = 1.0% vs. 1.1%, Log-rank $p=0.738$, Fig. 2b) before adjustment. After adjustment, the incidence of ST was ZES vs. EES = adjusted HR, 1.531; 95% CI, 0.554–4.231; $p=0.412$; ZES vs. BES = adjusted HR, 1.477; 95% CI, 0.354–6.165; $p=0.593$; EES vs. BES = adjusted HR, 0.442; 95% CI, 0.098–1.988; $p=0.287$; ZES/EES vs. BES = adjusted HR, 0.896; 95% CI, 0.251–3.197; $p=0.865$ (Table 4). Table 5 shows the independent predictors for MACE and ST at 2 years. LVEF $<40\%$, diabetes mellitus, ACEI, BB, ACC/AHA type B2 lesion, and one-vessel disease were significant independent predictors for MACE. By contrast, STEMI was significant independent predictor for ST in this study.

Discussion

KAMIR registry was a large-scale, nationwide, multicenter and prospective registry for AMI. In this study, we compared the major clinical outcomes among durable-polymer-coated

Table 1 Baseline and laboratory characteristics

Variables	ZES (<i>n</i> = 953)	EES (<i>n</i> = 1145)	ZES and EES (<i>n</i> = 2098)	BES (<i>n</i> = 305)	<i>p</i> value				
					ZES vs. EES	ZES vs. BES	EES vs. BES	ZES/ EES vs. BES	ZES vs. EES vs. BES
Age (years)	61.2 ± 12.0	61.2 ± 11.6	61.2 ± 11.8	62.3 ± 11.7	0.970	0.211	0.200	0.153	0.360
Men, <i>n</i> (%)	713 (74.8)	865 (75.5)	1578 (75.2)	222 (72.8)	0.722	0.452	0.333	0.359	0.612
LVEF (%)	53.0 ± 11.3	53.0 ± 10.8	53.0 ± 11.0	54.4 ± 9.9	0.921	0.052	0.047	0.048	0.141
BMI (kg/m ²)	24.8 ± 3.1	24.8 ± 3.1	24.8 ± 3.1	24.9 ± 3.2	0.733	0.573	0.416	0.444	0.705
SBP (mmHg)	132.4 ± 27.6	133.2 ± 27.4	132.8 ± 27.5	133.1 ± 29.7	0.528	0.648	0.967	0.867	0.811
DBP (mmHg)	80.0 ± 16.4	80.5 ± 16.0	80.3 ± 16.2	78.9 ± 16.3	0.483	0.328	0.132	0.167	0.300
STEMI, <i>n</i> (%)	519 (54.5)	584 (51.0)	1103 (52.6)	140 (45.9)	0.124	0.012	0.138	0.032	0.027
NSTEMI, <i>n</i> (%)	434 (45.5)	561 (49.0)	995 (47.4)	165 (54.1)	0.124	0.012	0.138	0.032	0.027
Hypertension, <i>n</i> (%)	583 (61.2)	695 (60.7)	1278 (60.9)	205 (67.2)	0.824	0.066	0.046	0.037	0.104
Diabetes mel- litus, <i>n</i> (%)	319 (33.5)	407 (35.5)	726 (34.6)	117 (38.4)	0.333	0.147	0.421	0.200	0.268
Previous MI, <i>n</i> (%)	58 (6.1)	91 (7.9)	149 (7.1)	19 (6.2)	0.105	0.891	0.393	0.632	0.214
Previous PCI, <i>n</i> (%)	120 (12.6)	152 (13.3)	272 (13.0)	33 (10.8)	0.648	0.481	0.288	0.313	0.516
Previous CABG, <i>n</i> (%)	7 (0.7)	8 (0.7)	15 (0.7)	6 (2.0)	0.923	0.095	0.089	0.041	0.089
Previous CVA, <i>n</i> (%)	70 (7.3)	86 (7.5)	156 (7.4)	23 (7.5)	0.933	0.905	0.903	0.907	0.988
Previous HF, <i>n</i> (%)	18 (1.9)	19 (1.7)	37 (1.8)	6 (2.0)	0.740	0.923	0.628	0.816	0.896
Current smokers, <i>n</i> (%)	411 (43.1)	471 (41.1)	882 (42.0)	111 (36.4)	0.374	0.033	0.115	0.062	0.113
CK-MB (mg/ dL)	125.1 ± 184.0	111.9 ± 173.5	117.9 ± 178.4	92.0 ± 139.4	0.094	0.005	0.073	0.016	0.013
Troponin-I (ng/mL)	35.8 ± 69.7	47.1 ± 174.0	41.9 ± 136.0	41.7 ± 70.7	0.090	0.230	0.638	0.989	0.204
Serum glucose (mg/dL)	168.3 ± 77.5	168.8 ± 79.2	168.6 ± 78.4	162.8 ± 62.5	0.888	0.255	0.218	0.225	0.475
Hemoglobin A1c (ng/dL)	6.7 ± 1.6	6.8 ± 1.5	6.7 ± 1.5	6.6 ± 1.3	0.140	0.584	0.097	0.222	0.151
NT-ProBNP (pg/mL)	1447.6 ± 4085.2	1479.8 ± 4264.0	1466.5 ± 4189.2	2067.2 ± 6595.2	0.894	0.178	0.181	0.111	0.280
hs-CRP (mg/ dL)	6.7 ± 45.3	7.7 ± 42.6	7.2 ± 43.9	8.1 ± 42.5	0.649	0.718	0.942	0.771	0.863
Serum creati- nine (mg/L)	1.1 ± 0.9	1.2 ± 2.9	1.2 ± 2.2	1.1 ± 2.1	0.221	0.868	0.437	0.558	0.365
Total chole- sterol (mg/ dL)	187.0 ± 51.3	183.9 ± 52.9	185.3 ± 52.2	184.7 ± 51.7	0.184	0.054	0.313	0.130	0.129
Triglyceride (mg/L)	154.6 ± 114.8	152.7 ± 115.3	153.6 ± 115.0	147.2 ± 132.9	0.705	0.362	0.493	0.392	0.647
HDL chole- sterol (mg/L)	42.9 ± 13.4	43.4 ± 15.7	43.2 ± 14.6	43.2 ± 12.6	0.480	0.725	0.880	0.987	0.772
LDL chole- sterol (mg/L)	116.6 ± 42.3	113.7 ± 42.8	115.0 ± 42.6	114.3 ± 43.2	0.139	0.430	0.845	0.816	0.326
Discharge medications									

Table 1 (continued)

Variables	ZES (<i>n</i> =953)	EES (<i>n</i> =1145)	ZES and EES (<i>n</i> =2098)	BES (<i>n</i> =305)	<i>p</i> value				
					ZES vs. EES	ZES vs. BES	EES vs. BES	ZES/ EES vs. BES	ZES vs. EES vs. BES
Aspirin, <i>n</i> (%)	946 (99.3)	1138 (99.4)	2084 (99.3)	305 (100)	0.792	0.206	0.356	0.239	0.336
Clopidogrel, <i>n</i> (%)	862 (90.5)	948 (82.8)	1810 (86.3)	239 (78.4)	<0.001	<0.001	0.078	0.001	<0.001
Cilostazole, <i>n</i> (%)	198 (20.8)	208 (18.2)	406 (19.4)	30 (9.8)	0.134	<0.001	<0.001	<0.001	<0.001
ACEI, <i>n</i> (%)	533 (55.9)	662 (57.8)	1195 (57.0)	130 (42.6)	0.400	<0.001	<0.001	<0.001	<0.001
ARB, <i>n</i> (%)	223 (23.4)	278 (24.3)	501 (23.9)	113 (37.0)	0.644	<0.001	<0.001	<0.001	<0.001
Beta-blocker, <i>n</i> (%)	774 (81.2)	979 (85.5)	1753 (83.6)	256 (83.9)	0.009	0.347	0.469	0.934	0.030
CCB, <i>n</i> (%)	89 (9.3)	92 (8.0)	181 (8.6)	30 (9.8)	0.310	0.956	0.417	0.515	0.452
Lipid lowering agents	722 (75.8)	1023 (89.3)	1745 (83.2)	276 (90.5)	<0.001	<0.001	0.526	0.001	<0.001
Atorvastatin, <i>n</i> (%)	373 (39.1)	499 (43.6)	872 (41.6)	127 (41.6)	0.041	0.420	0.603	0.980	0.121
Pravastatin, <i>n</i> (%)	7 (0.7)	14 (1.2)	21 (1.0)	8 (2.6)	0.281	0.014	0.107	0.024	0.031
Rosuvastatin, <i>n</i> (%)	215 (22.6)	359 (31.4)	574 (27.4)	105 (34.4)	<0.001	<0.001	0.300	0.012	<0.001
Pitavastatin, <i>n</i> (%)	58 (6.1)	67 (5.9)	125 (6.0)	23 (7.5)	0.853	0.350	0.285	0.307	0.548
Lovastatin, <i>n</i> (%)	1 (0.0)	0 (0.0)	1 (0.0)	0 (0.0)	0.454	0.572	–	0.703	0.467
Simvastatin, <i>n</i> (%)	47 (4.9)	46 (4.0)	93 (4.4)	12 (3.9)	0.338	0.424	0.958	0.881	0.549
Fluvastatin, <i>n</i> (%)	2 (0.2)	3 (0.3)	5 (0.2)	0 (0.0)	0.807	0.537	0.372	0.393	0.671
Fibrate, <i>n</i> (%)	10 (1.0)	12 (1.0)	22 (1.0)	6 (2.0)	0.998	0.239	0.239	0.156	0.377
Ezetimibe, <i>n</i> (%)	29 (3.0)	61 (5.3)	90 (4.3)	9 (3.0)	0.012	0.944	0.098	0.354	0.018

Values are mean ± SD or numbers and percentages. The *p* value for categorical data from Chi square or Fisher's exact test

LVEF left ventricular ejection fraction, *BMI* Body Mass Index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *STEMI* ST-segment elevation myocardial infarction, *NSTEMI* non-ST-segment elevation myocardial infarction, *MI* myocardial infarction, *PCI* percutaneous coronary intervention, *CABG* coronary artery bypass graft, *CVA* cerebrovascular events, *HF* heart failure, *CK-MB* creatine kinase myocardial band, *NT-ProBNP* N-terminal pro-brain natriuretic peptide, *hs-CRP* high-sensitivity C-reactive protein, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *ACEI* angiotensin-converting enzyme inhibitors, *ARB* angiotensin receptor blockers, *CCB* calcium channel blockers

stents (ZES and EES) versus biodegradable-polymer-coated stent (BES) for AMI with dyslipidemia milieu. The main findings of this study are as follows: (1) the MACE and ST rates were similar among the AMI patients with dyslipidemia receiving ZES, EES, or BES after PCI during 2-year follow-up periods, and (2) the comparison between durable-polymer-coated stents (ZES or EES) and biodegradable-polymer-coated stent (BES) also showed similar rates of MACE and ST in this study.

In COMPARE II [4], a randomized controlled study (RCT), there were similar incidences of major clinical outcomes (composite of CD, MI, and TVR) between BES and EES during 1-year follow-up period (5.2% vs. 4.8%, *p*=0.69). Another RCT [5] also showed that the BES was non-inferior to EES in the aspect of death and MI during 2-year follow-up (7.8% vs. 7.9% *p*=0.90). The Endeavor sprint® (Medtronic, Inc., Minneapolis, MN) and the everolimus-eluting stent (Xience stent V®; Abbott Vascular, Santa

Table 2 Angiographic characteristics

Variables	ZES (<i>n</i> =953)	EES (<i>n</i> =1145)	ZES and EES (<i>n</i> =2098)	BES (<i>n</i> =305)	<i>p</i> value				
					ZES vs. EES	ZES vs. BES	EES vs. BES	ZES/EES vs. BES	ZES vs. EES vs. BES
Targeted vessel									
Left anterior descending, <i>n</i> (%)	520 (54.6)	665 (58.1)	1185 (56.5)	154 (50.5)	0.111	0.210	0.016	0.056	0.039
Left circumflex, <i>n</i> (%)	272 (28.5)	316 (27.6)	588 (28.0)	92 (30.2)	0.660	0.562	0.352	0.454	0.661
Right coronary artery, <i>n</i> (%)	403 (42.3)	456 (39.8)	859 (40.9)	140 (45.9)	0.265	0.259	0.050	0.106	0.136
Left main, <i>n</i> (%)	30 (3.1)	40 (3.5)	70 (3.3)	6 (2.0)	0.715	0.330	0.202	0.291	0.400
ACC/AHA lesion type									
Type B1, <i>n</i> (%)	130 (13.6)	151 (13.2)	281 (13.4)	51 (16.7)	0.797	0.189	0.113	0.131	0.277
Type B2, <i>n</i> (%)	277 (29.1)	326 (28.5)	603 (28.7)	112 (36.7)	0.771	0.013	0.006	0.006	0.017
Type C, <i>n</i> (%)	428 (44.9)	555 (48.5)	983 (46.9)	127 (41.6)	0.104	0.289	0.033	0.097	0.062
Extent of coronary artery disease									
One vessel, <i>n</i> (%)	436 (45.8)	521 (45.5)	957 (46.6)	167 (54.8)	0.930	0.006	0.004	0.003	0.011
Two vessel, <i>n</i> (%)	297 (31.2)	359 (31.4)	656 (31.3)	80 (26.2)	0.962	0.114	0.093	0.084	0.203
≥ Three-vessel, <i>n</i> (%)	209 (21.9)	260 (22.7)	469 (22.4)	58 (19.0)	0.674	0.259	0.139	0.208	0.384
Pre-PCI TIMI 0, <i>n</i> (%)	420 (44.1)	493 (43.1)	913 (43.5)	115 (37.7)	0.658	0.062	0.117	0.063	0.143
Post-PCI TIMI 2, <i>n</i> (%)	32 (3.4)	26 (2.3)	58 (2.8)	7 (2.3)	0.142	0.449	0.972	0.850	0.278
Post-PCI TIMI 3, <i>n</i> (%)	817 (85.7)	1408 (91.5)	1865 (88.9)	288 (94.4)	<0.001	<0.001	0.118	0.002	<0.001
Stent diameter (mm)	3.16±0.46	3.10±0.42	3.13±0.43	3.15±0.41	0.001	0.640	0.075	0.424	0.004
Stent length (mm)	26.3±10.3	27.8±11.2	26.9±10.8	25.5±10.9	0.001	0.242	0.001	0.014	<0.001
Number of stent	1.56±0.89	1.50±0.80	1.53±0.84	1.52±0.81	0.154	0.509	0.772	0.828	0.351

Values are mean ± SD or numbers and percentages. The *p* value for categorical data from Chi square or Fisher's exact test

ACC/AHA American College of Cardiology/American Heart Association, PCI percutaneous coronary intervention, TIMI Thrombolysis In Myocardial Infarction, DES drug-eluting stents

Table 3 Cumulative clinical events at 2 years

Variables	ZES (<i>n</i> = 953)	EES (<i>n</i> = 1145)	ZES + EES (<i>n</i> = 2098)	BES (<i>n</i> = 305)	<i>p</i> value			
					ZES vs. EES	ZES vs. BES	EES vs. BES	ZES/EES vs. BES
Primary outcome								
Total death, <i>n</i> (%)	20 (2.1)	21 (1.8)	41 (2.0)	11 (3.6)	0.752	0.140	0.076	0.087
Cardiac death	15 (1.6)	14 (1.2)	29 (1.4)	7 (2.3)	0.574	0.450	0.176	0.209
Myocardial infarction, <i>n</i> (%)	14 (1.5)	22 (1.9)	36 (1.7)	5 (1.6)	0.501	0.790	0.753	0.923
Revascularization	42 (4.4)	36 (3.1)	78 (3.7)	11 (3.6)	0.133	0.626	0.715	0.923
TLR	14 (1.5)	7 (0.6)	21 (1.0)	3 (1.0)	0.076	0.776	0.446	0.977
TVR	30 (3.1)	18 (1.6)	48 (2.3)	8 (2.6)	0.019	0.847	0.225	0.685
Non-TVTR	12 (1.3)	18 (1.6)	30 (1.4)	4 (1.3)	0.585	0.937	0.747	0.870
MACE	72 (7.6)	72 (6.3)	144 (6.9)	23 (7.5)	0.261	0.991	0.434	0.631
Secondary outcome								
Stent thrombosis (prob- able or definite)	10 (1.0)	8 (0.7)	18 (0.9)	3 (1.0)	0.478	0.927	0.606	0.743
Acute	2 (0.2)	0 (0.0)	2 (0.1)	0 (0.0)	0.121	0.424	–	0.590
Subacute	3 (0.3)	0 (0.0)	3 (0.1)	1 (0.3)	0.057	0.969	0.052	0.419
Late	3 (0.3)	4 (0.3)	7 (0.3)	2 (0.7)	0.891	0.600	0.611	0.320
Very late	2 (0.2)	4 (0.3)	6 (0.3)	0 (0.0)	0.551	0.424	0.302	0.350

Values are mean ± SD or numbers and percentages. The *p* value for categorical data from Chi square or Fisher's exact test

TLR target lesion revascularization, TVR target vessel revascularization, Non-TVTR non-target vessel revascularization, MACE major adverse cardiac events

Clara, CA, USA) showed similar good results in the treatment of coronary artery disease [18, 19]. More recently, DUTCH PEERS trial [20] demonstrated that cobalt–chromium-based ZES (Resolute Integrity[®], Medtronic, Santa Rosa, CA, USA) and platinum–chromium-based EES (Promus Element, Boston Scientific, Natick, MA, USA) were similarly efficacious and safe in 1811 patients with AMI during 1-year follow-up period. In this study, the cumulative incidence of MACE for ZES vs. EES (7.8% vs. 7.1%, Log-rank *p* = 0.448, adjusted HR, 1.066; 95% CI, 0.752–1.511; *p* = 0.720), ZES vs. BES (7.8% vs. 8.4%, Log-rank *p* = 0.737, adjusted HR, 0.933; 95% CI, 0.565–1.541; *p* = 0.786), EES vs. BES (7.1% vs. 8.4%, Log-rank *p* = 0.360, adjusted HR, 0.876; 95% CI, 0.535–1.436; *p* = 0.600), and ZES/EES vs. BES (7.4% vs. 8.4%, Log-rank *p* = 0.503, adjusted HR, 0.929; 95% CI, 0.591–1.462; *p* = 0.751) was similar (Fig. 3a) and comparable with previous studies.

Even though, most second-generation DES showed non-inferior clinical outcomes compared with first-generation DES [21, 22], these durable-polymer-based stents have been associated with persistent local inflammatory and toxic reactions, delayed healing, hypersensitivity reactions, endothelial dysfunction, and neo-atherosclerosis [9,

23]. As a result, the polymer-free DES has become interesting recently. One randomized trial [24] showed that polymer-free DES was superior to a BMS in patients with high risk for bleeding after PCI. Another study [25] also demonstrated that polymer-free BES had significantly low rate of in-stent late lumen loss compared with paclitaxel-eluting stents (PES) (0.08 mm vs. 0.37 mm, *p* < 0.0001) during early 4 months after index PCI. The polymer of biodegradable-polymer BES consists of polylactic acid that is fully degraded into carbon dioxide and water within 6 months [26]. In spite of this peculiar advantage of biodegradable polymer, the long-term clinical outcome is debatable compared with durable polymer [27, 28]. In addition, the biodegradable-polymer DES did not further decrease the incidence of very late ST, MI, and CD over 1 year [29]. As similar as previous studies, even though the new-generation DES in our study (ZES, EES, and BES) have different stent platform, polymer and anti-proliferative drugs, the primary and secondary endpoints were not different among these groups in this study. Until now, the relationship between stent strut thickness and platform design, and long-term safety and efficacy of DES was not well defined. Kolandaivelu et al. [30] showed polymer coatings

Table 4 Hazard ratio for 2-year major clinical outcomes according to the type of stent by Cox-proportional hazard ratio analysis

	HR (95% confidence interval), <i>p</i> value			
	ZES vs. EES	ZES vs. BES	EES vs. BES	ZES + EES vs. BES
<i>Primary endpoint</i>				
MACE				
Unadjusted	1.152 (0.620–2.142), 0.654	1.152 (0.620–2.142), 0.654	1.152 (0.620–2.142), 0.654	1.152 (0.620–2.142), 0.654
^a Adjusted	1.066 (0.752–1.511), 0.720	0.933 (0.565–1.541), 0.786	0.876 (0.535–1.436), 0.600	0.929 (0.591–1.462), 0.751
Total death				
Unadjusted	1.152 (0.620–2.142), 0.654	0.498 (0.243–1.020), 0.057	0.435 (0.212–0.889), 0.023	0.464 (0.243–0.885), 0.020
^a Adjusted	0.719 (0.359–1.440), 0.351	0.474 (0.220–1.020), 0.056	0.757 (0.339–1.691), 0.498	0.581 (0.297–1.137), 0.113
Cardiac death				
Unadjusted	1.331 (0.633–2.799), 0.450	0.566 (0.240–1.336), 0.194	0.424 (0.176–1.023), 0.056	0.489 (0.223–1.073), 0.074
^a Adjusted	0.782 (0.345–1.776), 0.557	0.502 (0.197–1.281), 0.149	0.666 (0.251–1.767), 0.414	0.560 (0.247–1.272), 0.166
Myocardial infarction				
Unadjusted	0.717 (0.367–1.401), 0.330	0.836 (0.301–2.323), 0.731	1.137 (0.431–3.004), 0.795	0.989 (0.388–2.522), 0.982
Adjusted	0.734 (0.368–1.465), 0.381	1.124 (0.385–3.287), 0.831	1.138 (0.416–3.114), 0.801	1.134 (0.437–2.947), 0.796
Revascularization				
Unadjusted	1.311 (0.840–2.046), 0.233	1.114 (0.573–2.163), 0.751	0.834 (0.424–1.638), 0.598	0.962 (0.512–1.808), 0.904
^a Adjusted	1.147 (0.884–2.273), 0.148	1.296 (0.623–2.697), 0.488	0.925 (0.447–1.916), 0.834	1.119 (0.570–2.197), 0.744
TLR				
Unadjusted	2.256 (0.911–5.591), 0.079	1.376 (0.395–4.790), 0.616	0.600 (0.155–2.319), 0.458	0.961 (0.287–3.223), 0.949
^a Adjusted	2.374 (0.981–6.137), 0.074	1.366 (0.363–5.142), 0.645	0.723 (0.177–2.950), 0.651	1.090 (0.315–3.771), 0.892
TVR				
Unadjusted	1.883 (1.050–3.378), 0.034	1.099 (0.504–2.399), 0.812	0.575 (0.250–1.321), 0.192	0.818 (0.387–1.728), 0.598
^a Adjusted	1.926 (0.957–3.875), 0.066	1.286 (0.539–3.067), 0.571	0.641 (0.259–1.590), 0.338	0.998 (0.441–2.259), 0.997
Non-TVTR				
Unadjusted	0.734 (0.354–1.525), 0.407	0.856 (0.276–2.657), 0.789	1.148 (0.389–3.394), 0.802	1.006 (0.354–2.856), 0.991
^a Adjusted	0.802 (0.371–1.735), 0.575	0.788 (0.218–2.848), 0.716	1.111 (0.359–3.442), 0.855	0.946 (0.324–2.763), 0.919
<i>Secondary endpoint</i>				
Stent thrombosis				
Unadjusted	1.399 (0.552–3.546), 0.479	0.994 (0.273–3.616), 0.993	0.670 (0.178–2.525), 0.554	0.809 (0.238–2.749), 0.735
^a Adjusted	1.531 (0.554–4.234), 0.412	1.477 (0.354–6.165), 0.593	0.442 (0.098–1.988), 0.287	0.896 (0.251–3.197), 0.865
Acute				
Unadjusted	–	–	–	–
^a Adjusted	–	–	–	–
Subacute				
Unadjusted	–	0.962 (0.100–9.244), 0.973	–	0.436 (0.045–4.190), 0.472
^a Adjusted	–	3.167 (0.139–71.91), 0.469	–	1.343 (0.074–24.52), 0.842
Late				
Unadjusted	0.848 (0.190–3.789), 0.829	0.441 (0.074–2.640), 0.370	0.517 (0.095–2.823), 0.446	0.482 (0.100–2.322), 0.363
^a Adjusted	0.557 (0.089–3.495), 0.533	0.336 (0.027–4.136), 0.395	0.278 (0.034–2.298), 0.235	0.359 (0.063–2.054), 0.249
Very late				
Unadjusted	0.520 (0.095–2.839), 0.450	–	–	–
^a Adjusted	0.750 (0.128–4.379), 0.749	–	–	–

STEMI ST-segment elevation myocardial infarction, *NSTEMI* non-ST-segment elevation myocardial infarction, *LVEF* left ventricular ejection fraction, *BMI* Body Mass Index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *CK-MB* creatine kinase myocardial band, *ACEI* angiotensin-converting enzyme inhibitor, *ARB* angiotensin receptor blocker, *BB* beta-blocker, *LAD* left anterior descending, *ACC/AHA* American College of Cardiology/American Heart Association, *PCI* percutaneous coronary intervention, *TIMI* thrombolysis in myocardial infarction

^aAdjusted model was included age, gender (men), *STEMI*, *NSTEMI*, *LVEF*, *BMI*, *SBP*, *DBP*, hypertension, diabetes, *CK-MB*, clopidogrel, cilostazole, *ACEI*, *ARB*, *BB*, lipid-lowering agent, pravastatin, rosuvastatin, ezetimibe, *LAD*, *ACC/AHA* type B2 and C lesion, 1-vessel disease, post-*PCI* *TIMI* 3, stent diameter, stent length

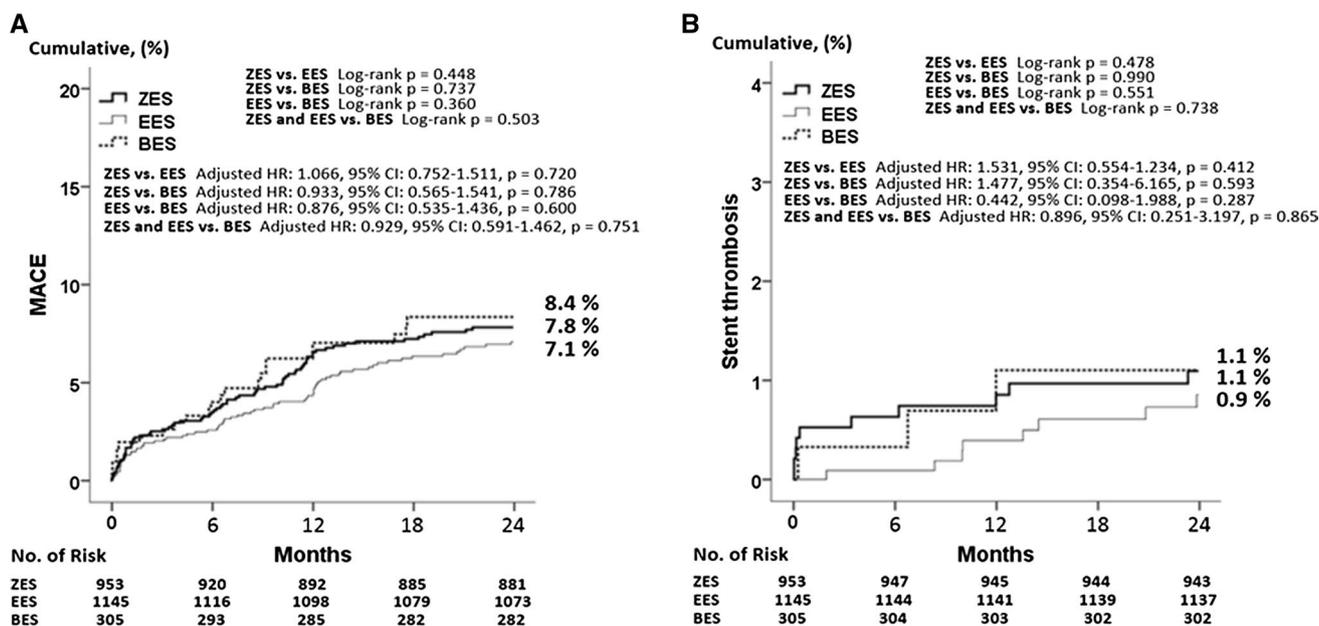


Fig. 2 Kaplan–Meier curved analysis for MACE (a) and stent thrombosis (b) at 2 years. MACE major adverse cardiac event, ZES zotarolimus-eluting stent, EES everolimus-eluting stent, BES biolimus-eluting stent, HR hazard ratio, CI confidence interval

and drugs do not increase the risk of acute ST, but rather serve as corrosive barriers and decrease the risk in ex vivo model. Nakazawa et al. [31] demonstrated similar inflammatory histomorphometric reaction between durable and biodegradable polymer-based DES in a porcine model. Another studies [29, 32] suggested that the concept that durable polymers are key in very late ST may be challengeable and may not have clinical significance. In our study, the total incidence of probable or definite ST was similar among ZES vs. EES (1.1% vs. 0.9%, Log-rank $p = 0.478$, adjusted HR, 1.531; 95% CI, 0.554–1.234; $p = 0.412$), ZES vs. BES (1.1% vs. 1.1%, Log-rank $p = 0.990$, adjusted HR, 1.477; 95% CI, 0.354–6.165; $p = 0.593$), EES vs. BES (0.9% vs. 1.1%, Log-rank $p = 0.551$, adjusted HR, 0.442; 95% CI, 0.098–1.988; $p = 0.287$), and ZES/EES vs. BES (1.0% vs. 1.1%, Log-rank $p = 0.738$, adjusted HR, 0.896; 95% CI, 0.251–3.197; $p = 0.865$) (Fig. 3b). Even though the cumulative incidence of acute ST was higher in ZES (2/10, 20%) than EES (0%) and BES (0%), the adjusted HR was not statistically significant (Table 4). Furthermore, the cumulative incidence of very late ST was much higher in EES group (4/8, 50%) compared with ZES (2/10, 20%) and BES group (0%). However, the adjusted HR was not statistically significant. These findings are comparable with previous studies [33–35].

The cumulative incidence of TD in BES was higher than the EES group (3.6% vs. 1.8%, $p = 0.076$, unadjusted HR,

0.435; 95% CI, 0.212–0.889; $p = 0.023$). After adjustment, the adjusted HR was not statistically different between BES and EES groups (Table 4). Before adjustment, the cumulative incidence of TVR was higher in ZES than EES group (3.1% vs. 1.6%, $p = 0.019$) (Table 3). However, the adjusted HR was not significantly different (adjusted HR, 1.926; 95% CI, 0.957–3.875; $p = 0.066$). Other cumulative incidences of TD, MI, TLR, and non-TVR were similar among these groups before and after adjustment (Table 4, Fig. 3).

The study population of these previous studies was different compared with this study. Characteristically, the overall enrolled patients of this study were solely dyslipidemic AMI patients. Because dyslipidemia is one of important risk factors of coronary artery disease, we tried to investigate the important role of dyslipidemia in AMI after PCI with new-generation DES. The characteristic effects of new-generation DES on long-term major clinical outcomes were not influenced by the presence of dyslipidemia in AMI patients after PCI in our study. Therefore, durable polymer DES or biodegradable-polymer DES are acceptable DES in dyslipidemia AMI patients during PCI. We think that the results of this study could be given some important message to interventional cardiologist during and before PCI especially, in case of dyslipidemic AMI patient.

In our study, there were several limitations. First, the present study was non-randomized study, similar to every

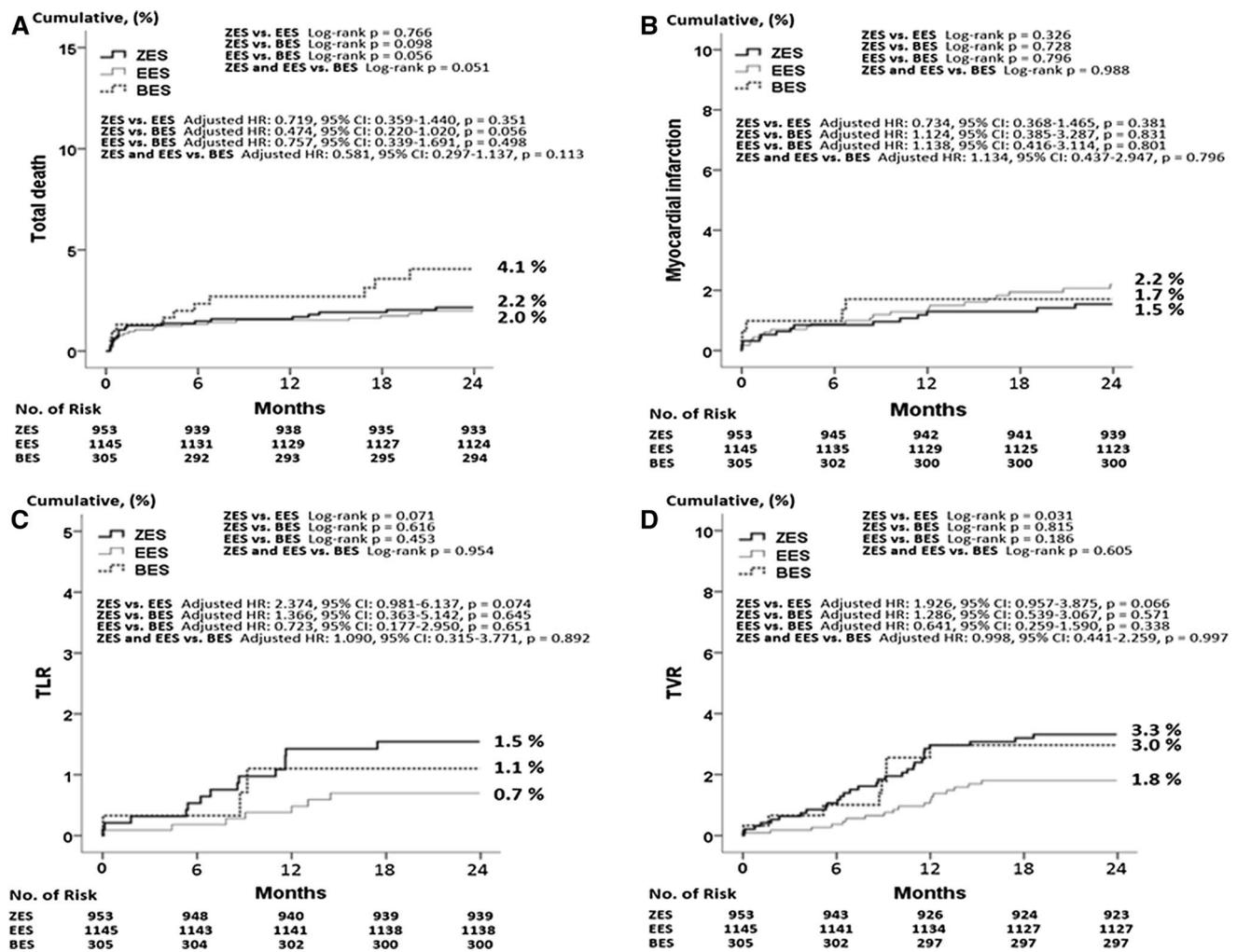


Fig. 3 Kaplan–Meier curved analysis for total death (a), myocardial infarction (b), TLR (c), and TVR (d) at 2 years

“real-world” registry; there may be some under-reporting and/or missed data. Second, there may be sample selection bias, because the total number of dyslipidemic patients in this study (2403/21482, 11.2%) was relatively lower than previous landmark trial (41–42%) [36]; this factor may act as an important bias in this study. Third, we defined the definition of dyslipidemia according to Asian guideline such as Japan Atherosclerosis Society guidelines, whereas this criteria may be some different according to race and region. Fourth, because the use of ZES, EES, or BES was at the discretion of the physician, this may play a bias role in this study. Fifth, this study enrolled only Korean patients; the present results may not be generalizable to all other ethnicities in different parts of the world. Sixth, we have done multivariate analysis to strengthen our results; variables

not included in this registry may have affected the study outcomes. Seventh, we did not consider individual specific effects of the different types of statins. Eighth, the 2-year follow-up period of this study was relatively short to determine the long-term major clinical outcomes and this could be another limitation of this study.

In conclusion, the AMI patients with dyslipidemia receiving ZES, EES, or BES after PCI showed comparable safety and efficacy during 2-year follow-up periods. Therefore, durable polymer DES or biodegradable-polymer DES are acceptable DES in dyslipidemic AMI patients during PCI. However, this result may be more precisely defined by any other large and long-term follow-up randomized and controlled trials in the future.

Table 5 Independent predictors for MACE and stent thrombosis at 2 years

Variables	MACE				Stent thrombosis			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
	HR (95% CI)	<i>p</i> value						
Age ≥ 65 years	1.047 (1.004–1.092)	0.032	1.050 (0.990–1.114)	0.105	1.054 (0.958–1.160)	0.281	1.077 (0.954–1.216)	0.231
Gender (men)	0.632 (0.459–0.870)	0.005	0.758 (0.511–1.122)	0.166	0.658 (0.266–1.630)	0.366	0.897 (0.300–2.686)	0.864
STEMI	0.875 (0.646–1.185)	0.387	1.046 (0.722–1.518)	0.811	1.865 (0.753–4.620)	0.178	3.869 (1.306–11.46)	0.015
LVEF < 40%	2.604 (1.765–3.840)	<0.001	1.870 (1.224–2.856)	0.004	1.008 (0.967–1.051)	0.710	1.029 (0.984–1.077)	0.203
BMI	0.975 (0.928–1.025)	0.317	1.007 (0.956–1.061)	0.788	0.931 (0.809–1.070)	0.313	0.943 (0.807–1.102)	0.459
Systolic blood pressure	0.994 (0.989–1.000)	0.043	0.994 (0.984–1.005)	0.279	1.009 (0.994–1.024)	0.264	1.013 (0.988–1.039)	0.300
Diastolic blood pressure	0.990 (0.981–1.000)	0.045	1.006 (0.989–1.024)	0.487	1.004 (0.977–1.031)	0.787	0.993 (0.948–1.039)	0.750
Hypertension	1.381 (0.996–1.917)	0.053	1.289 (0.880–1.888)	0.193	1.245 (0.503–3.086)	0.635	0.933 (0.346–2.516)	0.891
Diabetes mellitus	1.626 (1.200–2.204)	0.002	1.425 (1.000–2.031)	0.050	2.514 (1.059–5.965)	0.037	2.138 (0.804–5.688)	0.128
CK-MB	1.000 (0.999–1.001)	0.864	1.000 (0.999–1.001)	0.897	1.001 (0.999–1.002)	0.304	1.001 (1.000–1.003)	0.150
Clopidogrel	0.905 (0.577–1.419)	0.663	0.863 (0.513–1.454)	0.581	0.968 (0.228–2.665)	0.692	0.547 (0.144–2.072)	0.374
Cilostazole	1.194 (0.828–1.720)	0.342	1.201 (0.785–1.837)	0.399	0.780 (0.326–2.878)	0.953	1.442 (0.430–4.830)	0.553
ACEI	0.614 (0.452–0.833)	0.002	0.594 (0.387–0.913)	0.018	0.474 (0.197–1.144)	0.097	0.380 (0.117–1.231)	0.107
ARB	1.142 (0.813–1.603)	0.444	0.758 (0.477–1.203)	0.239	1.211 (0.470–3.121)	0.692	0.578 (0.168–1.993)	0.385
Beta-blocker	0.572 (0.404–0.812)	0.002	0.757 (0.487–1.178)	0.217	0.821 (0.276–2.440)	0.723	0.975 (0.260–3.653)	0.970
Lipid-lowering agent	0.622 (0.436–0.888)	0.009	0.679 (0.436–1.057)	0.087	0.496 (0.192–1.278)	0.146	0.327 (0.101–1.063)	0.063
Pravastatin	1.440 (0.460–4.510)	0.532	1.586 (0.482–5.217)	0.447	3.390 (0.527–29.29)	0.182	3.601 (0.381–34.10)	0.264
Rosuvastatin	0.856 (0.600–1.222)	0.392	1.005 (0.670–1.505)	0.982	0.651 (0.219–1.936)	0.440	1.054 (0.292–3.802)	0.936
Ezetimibe	1.019 (0.478–2.171)	0.962	0.915 (0.600–1.394)	0.679	1.156 (0.155–8.613)	0.888	1.569 (0.185–13.29)	0.679
Left anterior descending artery	1.065 (0.784–1.447)	0.685	0.950 (0.670–1.346)	0.771	1.070 (0.451–2.539)	0.879	0.917 (0.356–2.364)	0.858
ACC/AHA type B2 lesion	1.486 (1.087–2.032)	0.013	1.467 (1.028–2.095)	0.035	0.974 (0.378–2.511)	0.957	1.016 (0.367–2.816)	0.975
One-vessel disease	0.559 (0.404–0.773)	<0.001	0.678 (0.469–0.981)	0.039	0.476 (0.185–1.227)	0.124	0.259 (0.192–1.460)	0.219
Post-PCI TIMI 3	1.627 (0.904–2.927)	<0.001	1.946 (0.978–3.869)	0.058	2.545 (0.341–18.97)	0.362	2.354 (0.302–18.31)	0.414
Stent diameter	0.573 (0.394–0.832)	0.003	0.661 (0.433–1.008)	0.055	0.450 (0.154–1.321)	0.146	0.467 (0.152–1.436)	0.184
Stent length	1.006 (0.992–1.020)	0.415	1.002 (0.986–1.017)	0.829	0.966 (0.913–1.022)	0.225	0.965 (0.910–1.023)	0.229

MACE major adverse cardiac events, HR hazard ratio, STEMI ST-segment elevation myocardial infarction myocardial infarction, NSTEMI non-ST-segment elevation myocardial infarction, LVEF left ventricular ejection fraction, BMI Body Mass Index, CK-MB creatine kinase myocardial band, ACEI angiotensin-converting enzyme inhibitor, ARB angiotensin receptor blocker, ACC/AHA American College of Cardiology/American Heart Association, PCI percutaneous coronary intervention, TIMI thrombolysis in myocardial infarction

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest relevant to this article to disclose.

References

1. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanan F, McQueen M, Budaj A, Pais P, Varigos J, Lisheng L, INTERHEART Study Investigators (2004) Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 364:937–952
2. Glynn RJ, Rosner B (2005) Comparison of risk factors for the competing risks of coronary heart disease, stroke, and venous thromboembolism. *Am J Epidemiol* 162:975–982
3. Naito R, Miyauchi K, Nojiri S, Suzuki N, Daida H, PACIFIC Investigators, EVEREST Investigators (2018) Differences in clinical features in patients with acute coronary syndrome and stroke: Japanese multicenter registry results. *Intern Med.* <https://doi.org/10.2169/internalmedicine.1020-18>
4. Smits PC, Hofma S, Togni M, Vázquez N, Valdés M, Voudris V, Slagboom T, Goy JJ, Vuillomenet A, Serra A, Nouche RT, den Heijer P, van der Ent M (2013) Abluminal biodegradable polymer biolimus-eluting stent versus durable polymer everolimus-eluting stent (COMPARE II): a randomised, controlled, non-inferiority trial. *Lancet* 381:651–660
5. Natsuaki M, Kozuma K, Morimoto T, Shiomi H, Kimura T (2014) Two-year outcome of a randomized trial comparing second-generation drug-eluting stents using biodegradable or durable polymer. *JAMA* 311:2125–2127
6. Natsuaki M, Kozuma K, Morimoto T, Kadota K, Muramatsu T, Nakagawa Y, Akasaka T, Igarashi K, Tanabe K, Morino Y, Ishikawa T, Nishikawa H, Awata M, Abe M, Okada H, Takatsu Y, Ogata N, Kimura K, Urasawa K, Tarutani Y, Shiode N, Kimura

- T, NEXT Investigators (2013) Biodegradable polymer biolimus-eluting stent versus durable polymer everolimus-eluting stent: a randomized, controlled, noninferiority trial. *J Am Coll Cardiol* 62:181–190
7. Kastrati A, Mehilli J, Pache J, Kaiser C, Valgimigli M, Kelbaek H, Menichelli M, Sabaté M, Suttorp MJ, Baumgart D, Seyfarth M, Pfisterer ME, Schömig A (2007) Analysis of 14 trials comparing sirolimus-eluting stents with bare-metal stents. *N Engl J Med* 356:1030–1039
 8. Camenzind E, Steg PG, Wijns W (2007) Stent thrombosis late after implantation of first-generation drug-eluting stents: a cause for concern. *Circulation* 115:1440–1455
 9. Joner M, Finn AV, Farb A, Mont EK, Kolodgie FD, Ladich E, Kutys R, Skorija K, Gold HK, Virmani R (2006) Pathology of drug-eluting stents in humans: delayed healing and late thrombotic risk. *J Am Coll Cardiol* 48:193–202
 10. Nakazawa G, Otsuka F, Nakano M, Vorpahl M, Yazdani SK, Ladich E, Kolodgie FD, Finn AV, Virmani R (2011) The pathology of neoatherosclerosis in human coronary implants bare-metal and drug-eluting stents. *J Am Coll Cardiol* 57:1314–1322
 11. Stone GW, Rizvi A, Newman W, Mastali K, Wang JC, Caputo R, Doostzadeh J, Cao S, Simonton CA, Sudhir K, Lansky AJ, Cutlip DE, Kereiakes DJ, SPIRITIV Investigators (2010) Everolimus-eluting versus paclitaxel-eluting stents in coronary artery disease. *N Engl J Med* 362:1663–1674
 12. Kang SH, Park KW, Kang DY, Lim WH, Park KT, Han JK, Kang HJ, Koo BK, Oh BH, Park YB, Kandzari DE, Cohen DJ, Hwang SS, Kim HS (2014) Biodegradable-polymer drug-eluting stents vs. bare metal stents vs. durable-polymer drug-eluting stents: a systematic review and Bayesian approach network meta-analysis. *Eur Heart J* 35:1147–1158
 13. Teramoto T, Sasaki J, Ishibashi S, Birou S, Daida H, Dohi S, Egusa G, Hiro T, Hirobe K, Iida M, Kihara S, Kinoshita M, Maruyama C, Ohta T, Okamura T, Yamashita S, Yokode M, Yokote K, Japan Atherosclerosis Society (2013) Executive summary of the Japan Atherosclerosis Society (JAS) guidelines for the diagnosis and prevention of atherosclerotic cardiovascular diseases in Japan—2012 version. *J Atheroscler Thromb* 20:517–523
 14. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction, Katus HA, Lindahl B, Morrow DA, Clemmensen PM, Johanson P, Hod H, Underwood R, Bax JJ, Bonow RO, Pinto F, Gibbons RJ, Fox KA, Atar D, Newby LK, Galvani M, Hamm CW, Uretsky BF, Steg PG, Wijns W, Bassand JP, Menasché P, Ravkilde J, Ohman EM, Antman EM, Wallentin LC, Armstrong PW, Simoons ML, Januzzi JL, Nieminen MS, Gheorghiade M, Filippatos G, Luepker RV, Fortmann SP, Rosamond WD, Levy D, Wood D, Smith SC, Hu D, Lopez-Sendon JL, Robertson RM, Weaver D, Tendera M, Bove AA, Parkhomenko AN, Vasilieva EJ, Mendis S (2012) Third universal definition of myocardial infarction. *Circulation* 126:2020–2035
 15. O’Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, Granger CB, Krumholz HM, Linderbaum JA, Morrow DA, Newby LK, Ornato JP, Ou N, Radford MJ, Tamis-Holland JE, Tommaso CL, Tracy CM, Woo YJ, Zhao DX, Anderson JL, Jacobs AK, Halperin JL, Albert NM, Brindis RG, Creager MA, DeMets D, Guyton RA, Hochman JS, Kovacs RJ, Kushner FG, Ohman EM, Stevenson WG, Yancy CW (2013) American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 127:e362–e425
 16. Amsterdam EA, Wenger NK, Brindis RG, Casey DE Jr, Ganiats TG, Holmes DR Jr, Jaffe AS, Jneid H, Kelly RF, Kontos MC, Levine GN, Liebson PR, Mukherjee D, Peterson ED, Sabatine MS, Smalling RW, Zieman SJ (2014) 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol* 64:e139–e228
 17. Bundhun PK, Wu ZJ, Chen MH (2016) Is there any significant difference in stent thrombosis between sirolimus and paclitaxel eluting stents? A systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltimore)* 95:e2651
 18. Fajadet J, Wijns W, Laarman GJ, Kuck KH, Ormiston J, Münzel T, Popma JJ, Fitzgerald PJ, Bonan R, Kuntz RE, Investigators ENDEAVORII (2006) Randomized, double-blind, multicenter study of the Endeavor zotarolimus-eluting phosphorylcholine-encapsulated stent for treatment of native coronary artery lesions: clinical and angiographic results of the ENDEAVOR II trial. *Circulation* 114:798–806
 19. Gershlick A, Kandzari DE, Leon MB, Wijns W, Meredith IT, Fajadet J, Popma JJ, Fitzgerald PJ, Kuntz RE, ENDEAVOR Investigators (2007) Zotarolimus-eluting stents in patients with native coronary artery disease: clinical and angiographic outcomes in 1,317 patients. *Am J Cardiol* 100:45m–55m
 20. von Birgelen C, Sen H, Lam MK, Danse PW, Jessurun GA, Hautvast RW, van Houwelingen GK, Schramm AR, Gin RM, Louwerenburg JW, de Man FH, Stoel MG, Löwik MM, Linssen GC, Saïd SA, Nienhuis MB, Verhorst PM, Basalus MW, Doggen CJ, Tandjung K (2014) Third-generation zotarolimus-eluting and everolimus-eluting stents in all-comer patients requiring a percutaneous coronary intervention (DUTCH PEERS): a randomised, single-blind, multicentre, non-inferiority trial. *Lancet* 383:413–423
 21. Kedhi E, Joesoef KS, McFadden E, Wassing J, van Mieghem C, Goedhart D, Smits PC (2010) Second-generation everolimus-eluting and paclitaxel-eluting stents in real-life practice (COMPARE): a randomised trial. *Lancet* 375:201–209
 22. Serruys PW, Silber S, Garg S, van Geuns RJ, Richardt G, Buszman PE, Kelbaek H, van Boven AJ, Hofma SH, Linke A, Klaus V, Wijns W, Macaya C, Garot P, DiMario C, Manoharan G, Kornowski R, Ischinger T, Bartorelli A, Ronden J, Bressers M, Gobbens P, Negoita M, van Leeuwen F, Windecker S (2010) Comparison of zotarolimus-eluting and everolimus-eluting coronary stents. *N Engl J Med* 363:136–146
 23. Hassan AK, Berghean SC, Stijnen T, van der Hoeven BL, Snoep JD, Plevier JW, Schalij MJ, Wouter Jukema J (2010) Late stent malapposition risk is higher after drug-eluting stent compared with bare-metal stent implantation and associates with late stent thrombosis. *Eur Heart J* 31:1172–1180
 24. Urban P, Meredith IT, Abizaid A, Pocock SJ, Carrié D, Naber C, Lipiecki J, Richardt G, Iñiguez A, Brunel P, Valdes-Chavarri M, Garot P, Talwar S, Berland J, Abdellaoui M, Eberli F, Oldroyd K, Zambahari R, Gregson J, Greene S, Stoll HP, Morice MC, LEADERSFREE Investigators (2015) Polymer-free drug-coated coronary stents in patients at high bleeding risk. *N Engl J Med* 373:2038–2047
 25. Costa RA, Abizaid A, Mehran R, Schofer J, Schuler GC, Hauptmann KE, Magalhães MA, Parise H, Grube E, BioFreedom FIM Clinical Trial Investigators (2016) Polymer-free biolimus A9-coated stents in the Treatment of de novo coronary lesions: 4- and 12-month angiographic follow-up and final 5-year clinical outcomes of the prospective, multicenter BioFreedom FIM clinical trial. *JACC Cardiovasc Interv* 9:51–64
 26. Raungaard B, Jensen LO, Tilsted HH, Christiansen EH, Maeng M, Terkelsen CJ, Krusell LR, Kaltoft A, Kristensen SD, Bøtker HE, Thuesen L, Aarøe J, Jensen SE, Villadsen AB, Thayssen P, Veien KT, Hansen KN, Junker A, Madsen M, Ravkilde J, Lassen

- JF, Scandinavian Organization for Randomized Trials with Clinical Outcome (SORT OUT) (2015) Zotarolimus-eluting durable-polymer-coated stent versus a biolimus-eluting biodegradable-polymer-coated stent in unselected patients undergoing percutaneous coronary intervention (SORT OUT VI): a randomised non-inferiority trial. *Lancet* 385:1527–1535
27. Stefanini GG, Byrne RA, Serruys PW, de Waha A, Meier B, Massberg S, Jüni P, Schömig A, Windecker S, Kastrati A (2012) Biodegradable polymer drug-eluting stents reduce the risk of stent thrombosis at 4 years in patients undergoing percutaneous coronary intervention: a pooled analysis of individual patient data from the ISAR-TEST 3, ISAR-TEST 4, and LEADERS randomized trials. *Eur Heart J* 33:1214–1222
 28. Windecker S, Serruys PW, Wandel S, Buszman P, Trznadel S, Linke A, Lenk K, Ischinger T, Klauss V, Eberli F, Corti R, Wijns W, Morice MC, di Mario C, Davies S, van Geuns RJ, Eerdmans P, van Es GA, Meier B, Jüni P (2008) Biolimus-eluting stent with biodegradable polymer versus sirolimus-eluting stent with durable polymer for coronary revascularisation (LEADERS): a randomised non-inferiority trial. *Lancet* 372:1163–1173
 29. Kaiser C, Galatius S, Jeger R, Gilgen N, Skov Jensen J, Naber C, Alber H, Wanitschek M, Eberli F, Kurz DJ, Pedrazzini G, Moccetti T, Rickli H, Weilenmann D, Vuillomenet A, Steiner M, Von Felten S, Vogt DR, Wadt Hansen K, Rickenbacher P, Conen D, Müller C, Buser P, Hoffmann A, Pfisterer M, BASKET-PROVE II Study Group (2015) Long-term efficacy and safety of biodegradable-polymer biolimus-eluting stents: main results of the Basel Stent Kosten-Effektivitäts Trial—PROspective Validation Examination II (BASKET-PROVE II), a randomized, controlled noninferiority 2-year outcome trial. *Circulation* 131:74–81
 30. Kolandaivelu K, Swaminathan R, Gibson WJ, Kolachalama VB, Nguyen-Ehrenreich KL, Giddings VL, Coleman L, Wong GK, Edelman ER (2011) Stent thrombogenicity early in high-risk interventional settings is driven by stent design and deployment and protected by polymer–drug coatings. *Circulation* 123:1400–1409
 31. Nakazawa G, Shinke T, Ijichi T, Matsumoto D, Otake H, Torii S, Hiranuma N, Ohsue T, Otsuka F, Shite J, Hirata K, Ikari Y (2014) Comparison of vascular response between durable and biodegradable polymer-based drug-eluting stents in a porcine coronary artery model. *EuroIntervention* 10:717–723
 32. Kubo T, Akasaka T, Kozuma K, Kimura K, Fusazaki T, Okura H, Shinke T, Ino Y, Hasegawa T, Takashima H, Takamisawa I, Yamaguchi H, Igarashi K, Kadota K, Tanabe K, Nakagawa Y, Muramatsu T, Morino Y, Kimura T, NEXT Investigators (2014) Vascular response to drug-eluting stent with biodegradable vs. durable polymer. Optical coherence tomography substudy of the NEXT. *Circ J* 78:2408–2414
 33. Bangalore S, Toklu B, Amoroso N, Fusaro M, Kumar S, Hannan EL, Faxon DP, Feit F (2013) Bare metal stents, durable polymer drug eluting stents, and biodegradable polymer drug eluting stents for coronary artery disease: mixed treatment comparison meta-analysis. *BMJ* 347:f6625
 34. Navarese EP, Tandjung K, Claessen B, Andreotti F, Kowalewski M, Kandzari DE, Kereiakes DJ, Waksman R, Mauri L, Meredith IT, Finn AV, Kim HS, Kubica J, Suryaapranata H, Aprami TM, Di Pasquale G, von Birgelen C, Kedhi E (2013) Safety and efficacy outcomes of first and second generation durable polymer drug eluting stents and biodegradable polymer biolimus eluting stents in clinical practice: comprehensive network meta-analysis. *BMJ* 347:f6530
 35. Palmerini T, Biondi-Zoccai G, Della Riva D, Mariani A, Sabaté M, Smits PC, Kaiser C, D’Ascenzo F, Frati G, Mancone M, Genereux P, Stone GW (2014) Clinical outcomes with bioabsorbable polymer- versus durable polymer-based drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. *J Am Coll Cardiol* 63:299–307
 36. Stone GW, Lansky AJ, Pocock SJ, Gersh BJ, Dangas G, Wong SC, Witzenbichler B, Guagliumi G, Peruga JZ, Brodie BR, Dudek D, Möckel M, Ochala A, Kellock A, Parise H, Mehran R, HORIZONS-AMI Trial Investigators (2009) Paclitaxel-eluting stents versus bare-metal stents in acute myocardial infarction. *N Engl J Med* 360:1946–1959