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Comparison of Drug-Eluting Stents in Acute Myocardial Infarction Patients with Chronic Kidney Disease

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Background/Aims: To determine which drug-eluting stents are more effective in acute myocardial infarction (MI) patients with chronic kidney disease (CKD).
Methods: This study included a total of 3,566 acute MI survivors with CKD from the Korea Acute Myocardial Infarction Registry who were treated with stenting and followed up for 12 months: 1,845 patients who received sirolimus-eluting stents (SES), 1,356 who received paclitaxel-eluting stents (PES), and 365 who received zotarolimus-eluting stents (ZES). CKD was defined as an estimated glomerular filtration rate < 60 mL/min/1.73 m^2 calculated by the modification of diet in renal disease method.
Results: At the 12-month follow-up, patients receiving ZES demonstrated a higher incidence (14.8%) of major adverse cardiac events (MACEs) compared to those receiving SES (10.1%) and PES (12%, $p = 0.019$). The ZES patients also had a higher incidence (3.9%) of target lesion revascularization (TLR) compared to those receiving SES (1.5%) and PES (2.4%, $p = 0.011$). After adjusting for confounding factors, ZES was associated with a higher incidence of MACE and TLR than SES (adjusted hazard ratio [HR], 0.623; 95% confidence interval [CI], 0.442 to 0.879; $p = 0.007$; adjusted HR, 0.350; 95% CI, 0.165 to 0.743; $p = 0.006$, respectively), and with a higher rate of TLR than PES (adjusted HR, 0.471; 95% CI, 0.223 to 0.997; $p = 0.049$).
Conclusions: Our findings suggest that ZES is less effective than SES and PES in terms of 12-month TLR, and has a higher incidence of MACE due to a higher TLR rate compared with SES, in acute MI patients with CKD.

Keywords: Myocardial infarction; Renal insufficiency; Chronic; Stents

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INTRODUCTION

Primary percutaneous coronary intervention (PCI) with stent implantation is considered the standard treatment strategy in patients with acute myocardial infarction (MI) [1]. Compared with bare-metal stents (BMS), drug-eluting stents (DES) decrease late luminal loss and angiographic restenosis by reducing neointimal hyperplasia. Although recent studies have demonstrated that use of DES in acute MI is safe and effective [2-4], vessel healing at the primary pathological site in patients treated with DES for acute MI is delayed compared with in patients receiving DES for stable angina [5]. However, second-generation DES, such as zotarolimus-eluting stent (ZES), may improve vessel healing and endothelial function as well as biologic compatibility [6-8].

Chronic kidney disease (CKD) patients are known to be at high risk of developing coronary artery disease, and CKD is significantly associated with increased mortality, MI, and restenosis [9,10]. In these patients, DES has also been shown to be superior to BMS in terms of reduction of clinical and angiographic restenosis [11,12]. There have been many comparative studies of DES [13-15], but little data are available on the relative effectiveness of particular DES in acute MI patients with CKD. This issue has important implications for the selection of the most effective treatment strategy in these high-risk patients. Hence, the objective of this study was to determine which DES are more effective in acute MI patients with CKD.

METHODS

Korea Acute Myocardial Infarction Registry (KAMIR)

The KAMIR is a prospective multicenter online registry designed to describe the characteristics and clinical outcomes of Korean patients with acute MI and reflect current patient management practice. The registry included 52 community and university hospitals capable of primary PCI, and data on 13,133 patients with a 12-month clinical follow-up at the time of this study [16]. Data were collected at each site by an experienced study coordinator based on a standardized protocol. The study protocol was approved by the ethics committee of each participating institution.

Study population

A total of 3,566 acute MI survivors with CKD from the KAMIR who were treated with DES between November 2005 and January 2008 were included: 1,845 patients with sirolimus-eluting stents (SES; Cypher Stent, Cordis Co./Johnson and Johnson, Warren, NJ, USA), 1,356 with paclitaxel-eluting stents (PES; Taxus Express II Stent, Boston Scientific Co., Natick, MA, USA), and 365 with ZES (Endeavor Sprint Stent, Medtronic CardioVascular, Minneapolis, MN, USA). Data were collected for analysis during a 12-month period. CKD was defined as estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 calculated using the modification of diet in renal disease (MDRD) method [17].

Definitions and clinical endpoints

Renal function was assessed by eGFR, calculated using the MDRD method [17], based on the serum creatinine level upon admission. Acute MI was defined by clinical signs or symptoms, including increased cardiac biomarkers (creatine kinase-MB, troponin-I, or troponin-T), and 12-lead electrocardiographic findings. ST-segment elevation MI (STEMI) was defined by the presence of new ST-segment elevation of at least 1 mm (0.1 mV) in two or more contiguous leads or new left bundle-branch block on the index electrocardiogram. Left ventricular ejection fraction was checked by two-dimensional echocardiography. Left main (LM) complex lesion was defined as significant stenosis of the LM trunk artery with the presence of other epicardial coronary artery stenosis. The morphology of lesion in coronary angiography was classified using criteria established by the American College of Cardiology/American Heart Association [18]. The degree of coronary flow was classified according to Thrombolysis in MI (TIMI) flow grade [19].

Clinical follow-up was performed at 12 months after the commencement of the study. Major adverse cardiac events (MACE) included all-cause death, MI, and target lesion revascularization (TLR). TLR was defined as a repeat stent implantation at the initial site or within 5 mm proximal or distal to the stent [3].

Table 1. Baseline clinical characteristics

Characteristic	SES (n = 1,845)	PES (n = 1,356)	ZES (n = 365)	*p* value
Age, yr	65.1 ± 11.32	66.3 ± 11.03	65.1 ± 11.77	0.006
Male	1,240 (67.2)	938 (69.2)	238 (65.6)	0.309
BMI, kg/m^2	24.13 ± 3.248	23.83 ± 3.101	24.08 ± 3.168	0.035
Hypertension	1,019 (52.4)	737 (54.7)	189 (51.8)	0.450
Diabetes mellitus	582 (31.6)	396 (29.3)	114 (31.4)	0.363
Hyperlipidemia	175 (9.5)	111 (8.2)	42 (11.6)	0.120
Prior history of CAD	282 (15.3)	205 (15.2)	46 (12.6)	0.399
Prior history of stroke	143 (7.8)	90 (6.6)	22 (6.0)	0.327
Prior history of HF	34 (1.8)	18 (1.3)	7 (1.9)	0.485
Smoker	1,003 (54.8)	766 (57.0)	202 (55.8)	0.463
Family history of CAD	125 (6.8)	72 (5.3)	23 (6.3)	0.232
Killip class	237 (12.8)	162 (11.9)	46 (12.6)	0.747
Left ventricular EF, %	51.4 ± 12.15	51.4 ± 12.17	52.3 ± 11.88	0.393
eGFR, mL/min/1.73 m^2	45.8 ± 11.77	45.5 ± 12.13	46.2 ± 11.05	0.553
eGFR < 30	168 (9.2)	147 (11.0)	29 (8.0)	0.115
GP IIa/IIIb inhibitor	216 (11.8)	216 (16.0)	64 (17.7)	< 0.001
Aspirin[a]	1,827 (99.5)	1,342 (99.3)	359 (99.4)	0.902
Clopidogrel[a]	1,818 (99.0)	1,338 (99.0)	357 (98.9)	0.963
Cilostazol[a]	532 (29.0)	642 (47.5)	71 (19.7)	< 0.001
ACE-I or ARB[a]	1,462 (79.6)	1,104 (81.7)	280 (77.6)	0.137
Beta blocker[a]	1,369 (74.5)	986 (73.0)	258 (71.5)	0.384
Statin[a]	1,361 (74.1)	1,006 (74.5)	260 (72.0)	0.640

Values are presented as mean ± SD or number (%).

SES, sirolimus-eluting stent; PES, paclitaxel-eluting stent; ZES, zotarolimus-eluting stent; BMI, body mass index; CAD, coronary artery disease; HF, heart failure; EF, ejection fraction; eGFR, estimated glomerular filtration rate; GP, glycoprotein; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker.

[a]Medication at discharge.

Statistical analysis

All analyses were performed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). Continuous variables are presented as means ± standard deviation and were analyzed by one-way analysis of variance. Categorical variables are expressed as percentages and were compared using chi-square contingency table tests or Fisher's 2 × 2 exact tests. All statistical tests were two-tailed, with statistical significance defined as a $p < 0.05$. The crude survival curves were constructed using Kaplan-Meier analysis to assess the incidence of outcomes, and log-rank tests were applied to evaluate differences among the treatment groups. Adjusted survival curves were calculated using Cox regression models. To adjust for confounding factors in Cox regression models, we included variables as covariates with a $p < 0.1$ in univariate regression analysis, as well as other variables that have predicted prognosis of patients with acute MI. Included variables were age ≥ 65 years, male gender, body mass index (BMI), history of hypertension, history of diabetes mellitus, history of hyperlipidemia, history of coronary artery disease, smoking, eGFR < 30 mL/min/1.73 m^2, use of cilostazol and glycoprotein (GP) IIb/IIIa inhibitor, LM complex lesion, multivessel disease, type B2/C lesion, achievement of post-TIMI flow [3], stent length ≥ 25 mm, stent diameter ≤ 2.75 mm, total stent number, and STEMI patients. The results are presented as adjusted hazard ratios (HRs) with 95% confidence intervals (CIs).

Table 2. Coronary angiographic and procedural characteristics

Characteristic	SES (n = 1,845)	PES (n = 1,356)	ZES (n = 365)	*p* value
Left main complex	31 (1.7)	43 (3.2)	6 (1.6)	0.014
Multivessel	1,122 (61.3)	830 (61.6)	192 (52.7)	0.006
Type B2/C lesion[a]	1,296 (70.2)	1,043 (76.9)	286 (78.4)	< 0.001
Pre-procedural TIMI flow grade 0[b]	776 (44.1)	585 (44.4)	173 (50.3)	0.102
Post-procedural TIMI flow grade 3[b]	1,645 (93.7)	1,244 (95.3)	339 (97.7)	0.004
Stent length, mm	26.3 ± 5.81	25.2 ± 5.69	23.4 ± 5.36	< 0.001
Stent diameter, mm	3.10 ± 0.349	3.17 ± 0.400	3.22 ± 0.468	< 0.001
Total number of stent	1.49 ± 0.747	1.67 ± 0.989	1.45 ± 0.751	< 0.001
STEMI	1,169 (63.4)	870 (64.2)	248 (67.9)	0.248

Values are presented as number (%) or mean ± SD.

SES, sirolimus-eluting stent; PES, paclitaxel-eluting stent; ZES, zotarolimus-eluting stent; TIMI, Thrombolysis in Myocardial Infarction; STEMI, ST-segment elevation myocardial infarction.

[a]Type B2/C, the morphology of lesion in coronary angiography was classified according to the criteria of The American College of Cardiology/American Heart Association.

[b]Classified according to the TIMI flow grade.

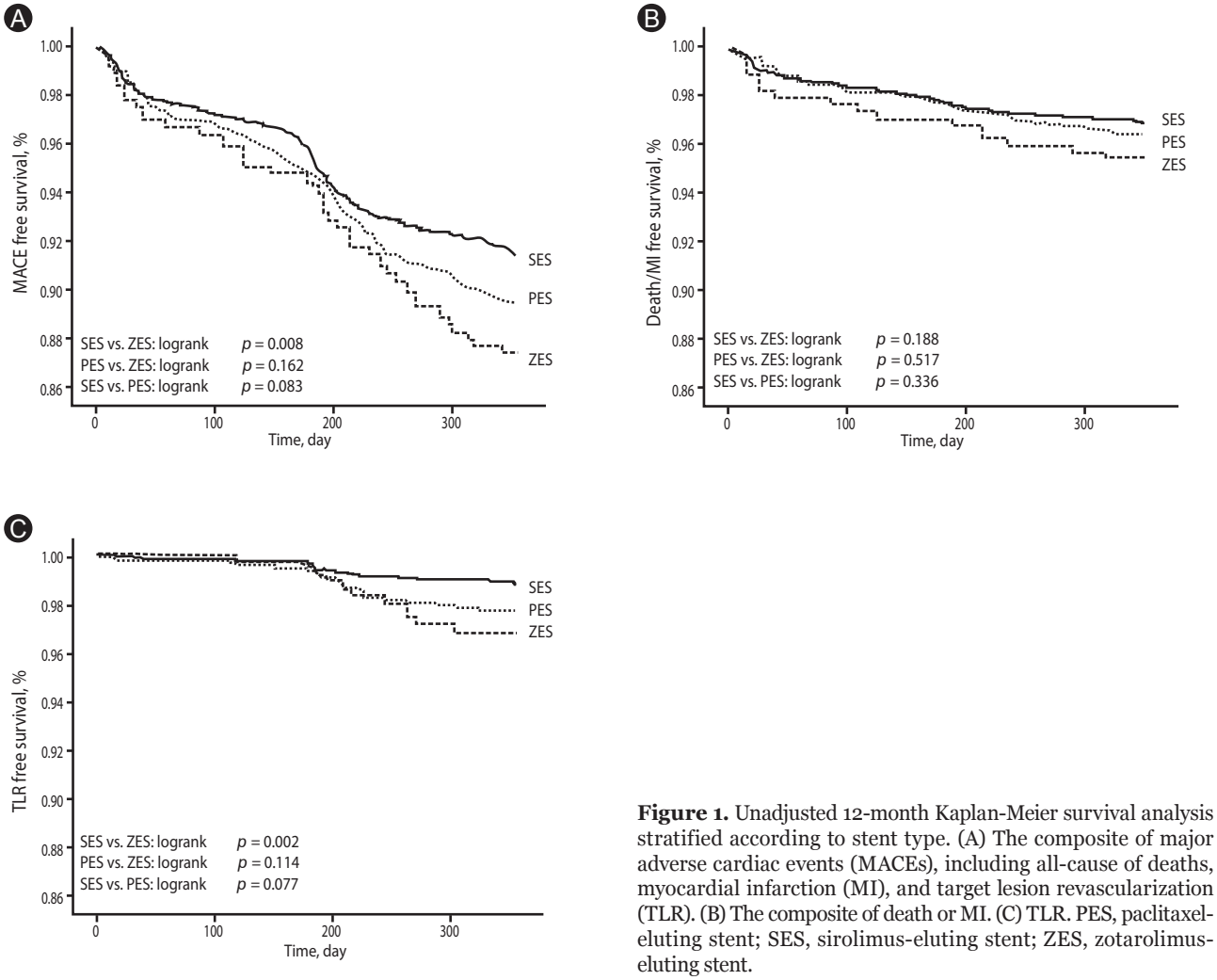

Figure 1. Unadjusted 12-month Kaplan-Meier survival analysis stratified according to stent type. (A) The composite of major adverse cardiac events (MACEs), including all-cause of deaths, myocardial infarction (MI), and target lesion revascularization (TLR). (B) The composite of death or MI. (C) TLR. PES, paclitaxel-eluting stent; SES, sirolimus-eluting stent; ZES, zotarolimus-eluting stent.

Table 3. Univariate and multivariate analyses of variables associated with major adverse cardiac events

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value
Age ≥ 65 yr	1.268 (1.023–1.571)	0.030	1.079 (0.841–1.385)	0.551
Male	0.847 (0.691–1.038)	0.110	1.173 (0.886–1.554)	0.265
BMI ≥ 25 kg/m^2	0.840 (0.684–1.031)	0.096	0.965 (0.932–1.000)	0.051
Hypertension	1.279 (1.048–1.562)	0.016	1.044 (0.828–1.316)	0.715
Diabetes mellitus	1.468 (1.201–1.794)	< 0.001	1.302 (1.032–1.643)	0.026
Hyperlipidemia	1.051 (0.755–1.463)	0.767	0.922 (0.625–1.362)	0.684
Prior history of CAD	1.177 (0.907–1.528)	0.220	1.005 (0.741–1.364)	0.973
Smoker	0.794 (0.652–0.966)	0.021	0.831 (0.640–1.079)	0.164
eGFR < 30 mL/min/1.73 m^2	1.851 (1.417–2.419)	< 0.001	1.491 (1.082–2.054)	0.015
Cilostazol	0.962 (0.780–1.188)	0.722	0.909 (0.718–1.152)	0.432
GP IIa/IIIb inhibitor	0.881 (0.658–1.179)	0.393	0.909 (0.656–1.258)	0.563
Left main complex	2.656 (1.726–4.088)	< 0.001	2.521 (1.558–4.079)	< 0.001
Multivessel	2.051 (1.637–2.570)	< 0.001	1.906 (1.464–2.483)	< 0.001
Type B2/C lesion[a]	1.237 (0.978–1.565)	0.076	1.165 (0.886–1.530)	0.274
Post-procedural TIMI flow grade 3[b]	1.234 (0.816–1.867)	0.319	0.754 (0.481–1.184)	0.220
Stent length ≥ 25 mm	1.131 (0.926–1.379)	0.227	1.125 (0.899–1.408)	0.305
Stent diameter ≤ 2.75 mm	1.143 (0.913–1.432)	0.244	1.023 (0.792–1.320)	0.863
STEMI	1.039 (0.847–1.275)	0.714	1.343 (1.056–1.708)	0.016
SES	Reference		Reference	
PES	1.204 (0.975–1.485)	0.084	1.204 (0.947–1.531)	0.129
ZES	1.498 (1.100–2.028)	0.009	1.604 (1.137–2.262)	0.007

HR, hazard ratio; CI, confidence interval; BMI, body mass index; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; GP, glycoprotein; TIMI, Thrombolysis in Myocardial Infarction; STEMI, ST-segment elevation myocardial infarction; SES, sirolimus-eluting stent; PES, paclitaxel-eluting stent; ZES, zotarolimus-eluting stent.

[a]Type B2/C, the morphology of lesion in coronary angiography was classified according to the criteria of The American College of Cardiology/American Heart Association.

[b]Classified according to the TIMI flow grade.

RESULTS

Baseline clinical and procedural characteristics

A comparison of the clinical characteristics among the three DES groups suggested that age was greater in the PES group, BMI was higher and usage rate of GP IIb/IIIa inhibitor during the procedure lower in the SES group, and usage rate of cilostazol was lower in the ZES group (Table 1). A comparison of the procedural characteristics demonstrated that the incidence of LM complex lesion and multivessel disease were higher and the total number of stents was greater in the PES group. Stent length was longer, stent diameter was smaller, and achievement rate of post-procedural TIMI 3 flow was lower in the SES group. The incidence of complex lesions was also higher in the ZES group (Table 2).

Twelve-month clinical outcomes

The cumulative MACE rate after 12 months was significantly higher in the ZES group than in the SES group (SES, 10.1%; PES, 12.0%; ZES, 14.8%; p = 0.019). All causes of death and MI were similar among the three groups (SES, 3.7%; PES, 4.4%; ZES, 5.2%; p = 0.357). The TLR rate was significantly higher in the ZES group than in the SES group (SES, 1.5%; PES, 2.4%; ZES, 3.9%; p = 0.002). Kaplan-Meier analysis was used to construct crude survival curves during the 12-month follow-up period and the pair-wise long-rank test re-

Table 4. Univariate and multivariate analyses of variables associated with death and myocardial infarction

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value
Age ≥ 65 yr	3.381 (2.144–5.334)	< 0.001	2.761 (1.623–4.696)	< 0.001
Male	0.753 (0.541–1.049)	0.093	1.273 (0.790–2.053)	0.322
BMI ≥ 25, kg/m^2	0.528 (0.364–0.767)	0.001	0.905 (0.850–0.962)	0.002
Hypertension	1.601 (1.141–2.248)	0.006	1.116 (0.744–1.674)	0.595
Diabetes mellitus	1.694 (1.190–2.286)	0.003	1.213 (0.815–1.806)	0.341
Hyperlipidemia	1.644 (1.036–2.610)	0.035	1.456 (0.816–2.600)	0.204
Prior history of CAD	1.474 (0.987–2.202)	0.058	0.915 (0.548–1.527)	0.734
Smoker	0.845 (0.611–1.167)	0.307	1.140 (0.724–1.796)	0.571
eGFR < 30 mL/min/1.73 m^2	4.132 (2.903–5.881)	< 0.001	3.369 (2.177–5.213)	< 0.001
Cilostazol	1.120 (0.797–1.574)	0.514	1.164 (0.786–1.723)	0.449
GP IIa/IIIb inhibitor	0.881 (0.544–1.428)	0.607	1.089 (0.625–1.897)	0.763
Left main complex	4.329 (2.444–7.668)	< 0.001	3.234 (1.609–6.499)	0.001
Multivessel	1.930 (1.334–2.792)	< 0.001	1.410 (0.908–2.189)	0.126
Type B2/C lesion[a]	1.672 (1.094–2.555)	0.018	1.606 (0.969–2.660)	0.066
Post-procedural TIMI flow grade3[b]	0.817 (0.480–1.389)	0.732	0.912 (0.396–2.101)	0.829
Stent length ≥ 25 mm	1.124 (0.808–1.563)	0.489	1.041 (0.709–1.527)	0.839
Stent diameter ≤ 2.75 mm	1.531 (1.080–2.172)	0.017	1.283 (0.852–1.931)	0.233
STEMI	0.815 (0.587–1.132)	0.222	1.185 (0.791–1.774)	0.411
SES	Reference		Reference	
PES	1.185 (0.838–1.675)	0.337	0.966 (0.640–1.460)	0.871
ZES	1.404 (0.845–2.334)	0.190	1.581 (0.892–2.802)	0.117

HR, hazard ratio; CI, confidence interval; BMI, body mass index; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; GP, glycoprotein; TIMI, Thrombolysis in Myocardial Infarction; STEMI, ST-segment elevation myocardial infarction; SES, sirolimus-eluting stent; PES, paclitaxel-eluting stent; ZES, zotarolimus-eluting stent.

[a]Type B2/C, the morphology of lesion in coronary angiography was classified according to the criteria of The American College of Cardiology/American Heart Association.

[b]Classified according to the TIMI flow grade.

sults for all comparisons are shown in Fig. 1.

Multivariate analysis

In the multivariate analysis, diabetes mellitus, LM complex lesion, multivessel disease, eGFR < 30 mL/min/1.73 m^2, and STEMI and use of ZES were identified as independent predictors of 12-month MACE (Table 3). In contrast, independent predictors of death after 12 months or MI were age ≥ 65 years, BMI, LM complex lesion, and eGFR < 30 mL/min/1.73 m^2 (Table 4). The independent predictors of 12-month TLR included use of ZES (Table 5). Adjusted survival curves are shown in Fig. 2. The ZES group was associated with a higher incidence of MACE (adjusted HR, 0.623; 95% CI, 0.442 to 0.879; p = 0.007) and TLR than the SES group (adjusted HR, 0.350; 95% CI, 0.165 to 0.743; p = 0.006). In addition, being in the ZES group was associated with a higher incidence of TLR than in the PES group (adjusted HR for TLR, 0.471; 95% CI, 0.223 to 0.997; p = 0.049).

DISCUSSION

This study was designed to compare the 12-month clinical outcomes among ZES, SES, and PES in acute MI patients with CKD. Multivariate analyses and Cox regression models showed that ZES was associated with a higher incidence of MACE than SES, and a higher rate of TLR than SES and PES.

In patients with acute MI, primary PCI with stent

Table 5. Univariate and multivariate analyses of variables associated with target lesion revascularization

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value
Age ≥ 65 yr	0.823 (0.632–1.070)	0.146	0.809 (0.452–1.447)	0.475
Male	0.951 (0.728–1.243)	0.713	1.095 (0.533–2.249)	0.806
BMI ≥ 25, kg/m^2	1.100 (0.853–1.420)	0.462	0.941 (0.859–1.030)	0.185
Hypertension	1.186 (0.918–1.531)	0.191	1.088 (0.621–1.906)	0.768
Diabetes mellitus	1.376 (1.060–1.785)	0.017	1.578 (0.905–2.751)	0.108
Hyperlipidemia	0.800 (0.495–1.294)	0.363	0.992 (0.387–2.539)	0.986
Prior history of CAD	1.045 (0.736–1.483)	0.807	0.826 (0.366–1.864)	0.645
Smoker	0.798 (0.619–1.027)	0.080	1.076 (0.562–2.058)	0.826
eGFR < 30 mL/min/1.73 m^2	0.859 (0.538–1.373)	0.526	0.489 (0.147–1.619)	0.241
Cilostazol	0.896 (0.681–1.178)	0.430	0.968 (0.549–1.705)	0.910
GP IIa/IIIb inhibitor	0.915 (0.630–1.328)	0.640	1.441 (0.756–2.746)	0.267
Left main complex	1.647 (0.813–3.337)	0.166	2.044 (0.613–6.815)	0.244
Multivessel	2.060 (1.538–2.759)	< 0.001	1.058 (0.564–1.984)	0.860
Type B2/C lesion[a]	1.024 (0.767–1.368)	0.871	0.630 (0.354–1.121)	0.116
Post-procedural TIMI flow grade 3[b]	0.801 (0.474–1.353)	0.407	0.578 (0.204–1.637)	0.302
Stent length ≥ 25 mm	1.145 (0.886–1.478)	0.300	1.244 (0.717–2.159)	0.437
Stent diameter ≤ 2.75 mm	0.971 (0.717–1.314)	0.850	0.936 (0.586–1.802)	0.843
STEMI	1.164 (0.889–1.524)	0.270	0.929 (0.529–1.630)	0.797
SES	Reference		Reference	
PES	1.280 (0.978–1.675)	0.073	1.346 (0.730–2.480)	0.341
ZES	1.472 (0.988–2.192)	0.057	2.875 (1.346–6.065)	0.006

HR, hazard ratio; CI, confidence interval; BMI, body mass index; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; GP, glycoprotein; TIMI, Thrombolysis in Myocardial Infarction; STEMI, ST-segment elevation myocardial infarction; SES, sirolimus-eluting stent; PES, paclitaxel-eluting stent; ZES, zotarolimus-eluting stent.

[a]Type B2/C, the morphology of lesion in coronary angiography was classified according to the criteria of The American College of Cardiology/American Heart Association.

[b]Classified according to the TIMI flow grade.

implantation is considered to be the gold standard in treatment for acute MI [1]. Although PCI with stent implantation is performed in increasing numbers of patients, in-stent restenosis is an important complication. Studies of patients with acute MI treated with BMS have reported the incidence of repeated revascularization to be about 10% [2,3]. Most suggested that DES was associated with a lower restenosis and TLR rate compared with BMS [2-4]. The data reported here support the use of DES in acute MI since the TLR rate for all types of DES was 2.1%.

CKD patients are known to be a high-risk population for coronary artery disease. Cardiovascular events, especially related to coronary artery disease, remain the main cause of mortality among patients with CKD [9,10]. Furthermore, the presence of CKD increases the risk of mortality after PCI even before end-stage renal disease and dialysis dependency have developed [20]. In support of this, an eGFR < 30 mL/min/1.73 m^2 in the current study was a significant independent predictor of MACE, MI, or death after 12 months.

A concern following DES implantation in acute MI patients is that vessel healing at the primary pathological site is delayed compared with in stable angina patients, which results in an increased risk of thrombotic complications [5]. ZES, which is second-generation DES and is based on a different type of polymer, is closer to BMS than first-generation DES. ZES implantation is associated with less inflammation and greater endothelialization [8], and preserved endothelial vasomotor response

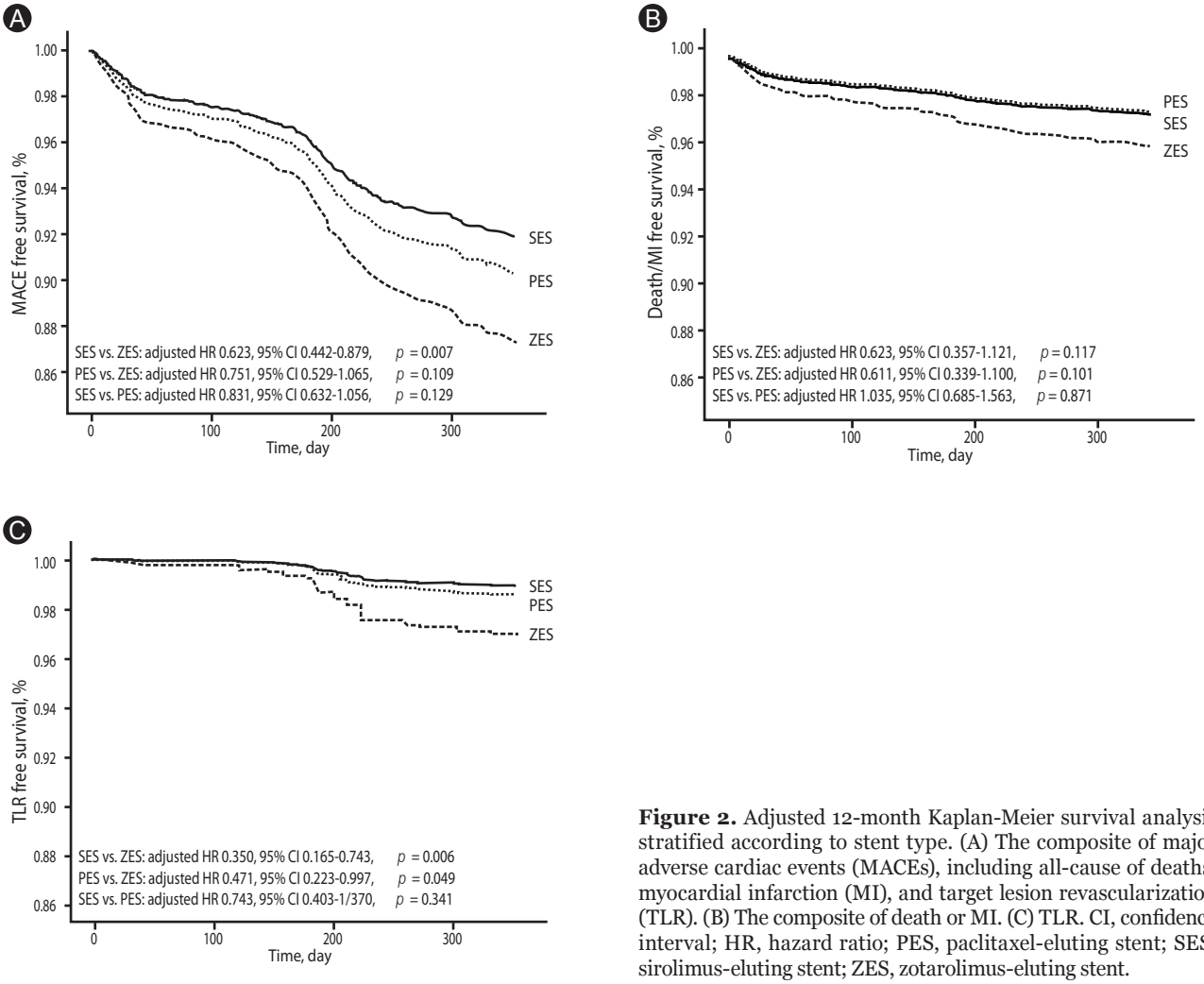

Figure 2. Adjusted 12-month Kaplan-Meier survival analysis stratified according to stent type. (A) The composite of major adverse cardiac events (MACEs), including all-cause of deaths, myocardial infarction (MI), and target lesion revascularization (TLR). (B) The composite of death or MI. (C) TLR. CI, confidence interval; HR, hazard ratio; PES, paclitaxel-eluting stent; SES, sirolimus-eluting stent; ZES, zotarolimus-eluting stent.

compared with first-generation DES [7]. The clinical outcomes of ZES treatment in acute MI patients are not significantly different than those of first-generation DES [21-23], and the use of ZES results in a lower risk of stent thrombosis [21]. In patients with CKD, DES significantly reduces clinical, angiographic restenosis compared with BMS [11,12], but there is no data comparing the different types of DES. In this study, we have determined that ZES promotes vessel healing and endothelial function compared to first-generation DES in acute MI. However, excessive neointimal proliferation might increase the TLR rate of ZES patients compared with first-generation DES. When taken together, particularly in acute MI patients who have CKD as comorbid disease, the disadvantages of ZES may outweigh the advantages. In fact, the present data demonstrate that the higher incidence of MACE in the ZES group, as compared with the SES and PES groups, is due mainly to a higher incidence of TLR and not to death or MI. However, TLR rates were around 2% and much lower than before, even though ZES was statistically inferior to the other stents in terms of TLR. Thus, the biological applicability of this result remains to be established.

Limitations

This is the first study based on observational registry data. We used Cox regression analysis to correct for confounding factors, but the results may be influenced by the nonrandomized assignment. Additionally, this registry does not record information concerning hemodialysis, so it was not possible to separate hemodialysis from non-hemodialysis patients. Recent studies have also shown that DES may be associated with increased rates of stent thrombosis, as compared with BMS

[24,25]. Unfortunately, in this registry, data concerning the rates of stent thrombosis were not available. As a consequence, it was not possible to assess one of the most important safety markers. Finally, we compared both first- and second-generation DES. However, the ZES in this study was not the Endeavor Resolute Stent (Medtronic Vascular) but the Endeavor Sprint Stent (Medtronic Vascular). Since some studies have already demonstrated that new-generation DES might be safer and more effective than earlier-generation types, further evaluations of new-generation DES are urgently needed.

In conclusion, our data suggest that ZES is inferior to SES and PES in terms of 12-month TLR, and has a higher incidence of MACE. The latter is due mainly to the higher TLR rate compared with SES in acute MI patients with CKD.

Conflict of interest

No potential conflict of interest relevant to this article is reported.

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