JACC: CARDIOVASCULAR INTERVENTIONS VOL. 5, NO. 9, 2012

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC. http://dx.doi.org/10.1016/j.jcin.2012.05.009

Unrestricted Use of 2 New-Generation Drug-Eluting Stents in Patients With Acute Myocardial Infarction

A Propensity Score-Matched Analysis

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Objectives This study sought to compare everolimus-eluting stents (EES) with zotarolimus-eluting stents (ZES) in patients with acute myocardial infarction (AMI).

Background There is a paucity of data to exclusively evaluate the safety and efficacy of second-generation drug-eluting stents (DES) in the setting of AMI.

Methods The present study enrolled 3,309 AMI patients treated with ZES (n = 1,608) or EES (n = 1,701) in a large-scale, prospective, multicenter registry—KAMIR (Korea Acute Myocardial Infarction Registry). Propensity score matching was applied to adjust for differences in baseline clinical and angiographic characteristics, producing a total of 2,646 patients (1,343 receiving ZES, and 1,343 receiving EES). Target lesion failure (TLF) was defined as the composite of cardiac death, recurrent nonfatal myocardial infarction, or target lesion revascularization. Major clinical outcomes at 1 year were compared between the 2 propensity score-matched groups.

Results After propensity score matching, baseline clinical and angiographic characteristics were similar between the 2 groups. Clinical outcomes of the propensity score-matched patients showed that, despite similar incidences of recurrent nonfatal myocardial infarction and in-hospital and 1-year mortality, patients in the EES group had significantly lower rates of TLF (6.5% vs. 8.7%, p = 0.029) and probable or definite stent thrombosis (0.3% vs. 1.6%, p < 0.001), compared with those in the ZES group. Furthermore, there was a numerically lower rate of target lesion revascularization (1.2% vs. 2.2%, p = 0.051) in the EES group than in the ZES group.

Conclusions In this propensity-matched comparison, EES seems to be superior to ZES in reducing TLF and stent thrombosis in patients with AMI. (J Am Coll Cardiol Intv 2012;5:936–45) © 2012 by the American College of Cardiology Foundation

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Manuscript received April 17, 2012; accepted May 14, 2012.

First-generation drug-eluting stents (DES), including sirolimus-eluting stents and paclitaxel-eluting stents, have been demonstrated to be superior to bare-metal stents (BMS) in reducing the need for repeat revascularization for the treatment of obstructive coronary artery disease (1). However, concerns have been raised with regard to the safety of DES, especially in the acute myocardial infarction (AMI) setting. Some studies showed that DES had a higher rate of stent thrombosis compared with BMS even long after the index procedure (2). Other studies revealed that the polymers of the first-generation DES were associated with local allergic reactions, inflammation, and delayed endothelialization, leading to early and late stent thrombosis (3). Therefore, second-generation DES with new stent platforms, polymers, and drugs have been developed with the goal to further improve upon the safety profile of first-generation DES while maintaining efficacy.

The second-generation DES use modified metal alloys that enable stent struts to be thinner and have different stent designs intended to provide better deliverability and conformability of the stent to the vessel wall. To date, the safety and efficacy of second-generation DES—such as zotarolimus-eluting stent (ZES) (Endeavor Sprint, Medtronic CardioVascular, Santa Rosa, California) and everolimus-eluting stent (EES) (Xience V, Abbott Vascular, Santa Clara, California)—has been well-established through comparisons with first-generation DES (4–8). However, the role of the second-generation DES in AMI has not been fully elucidated. Furthermore, no previous study has compared EES with ZES exclusively in patients with AMI. Therefore, the aim of the present study was to evaluate the safety and efficacy of EES versus ZES in the setting of AMI in a large-scale, prospective, multicenter registry—the KAMIR registry (Korea Acute Myocardial Infarction Registry).

Methods

KAMIR. The design of the KAMIR study has been introduced before (9). In brief, it is a Korean prospective multicenter online registry designed to reflect the "real-world" practice in a series of Asian patients presenting with AMI in the DES era since November 2005. Online registry of AMI has been performed at 57 university or community hospitals, which are high-volume centers with facilities for primary percutaneous coronary intervention (PCI) and on-site cardiac surgery. Data were collected at each site by a trained study coordinator with a standardized case report form. Standardized definitions of all patient-related variables and clinical diagnoses were used. The study protocol was approved by the ethics committee at each participating institution. Patients with AMI, including both ST-segment elevation myocardial infarction (STEMI) and non–ST-segment elevation myocardial infarction (NSTEMI) were enrolled.

Study population. From January 2008 to October 2010, a total of 13,726 patients were diagnosed with AMI. In the present study, we retrospectively enrolled patients with AMI who received EES (Xience V, Abbott Vascular), or ZES (Endeavor Sprint, Medtronic CardioVascular) implantation and completed 1-year clinical follow-up. The criteria to exclude the patients were other DES or BMS implantation, balloon angioplasty alone, conservative treatment without PCI, contraindication to antithrombotic agents, known bleeding disorders, infarction related to the grafted vessel, and estimated life expectancy of <12 months.

Therefore, a total of 3,309 eligible AMI patients were finally enrolled into the present analysis. According to the DES types, patients were divided into 2 groups as follows: ZES group (n = 1,608) and EES group (n = 1,701). The use percentages of EES among the centers ranged from 7.1% to 58.6% with a median 21.8% (interquartile range: 13.3% to 33.6%). Loading doses of aspirin and clopidogrel were administered immediately after patient arrival at the hospital. The loading/maintenance doses were 200 to 300 mg/100 mg q.d. for aspirin, 300 to 600 mg/75 mg q.d. for clopidogrel. All patients were encouraged to continue dual antiplatelet therapy with aspirin and clopidogrel for at least 12 months.

PCI procedure and medical treatment. Diagnostic angiography and PCI were performed through either femoral or radial artery after administration of unfractionated heparin (70 to 100 U/kg). Patients received unfractionated heparin to maintain the activated clotting time of >250 s during the procedure. Stents were deployed after prior balloon angioplasty, and the use of cilostazol or platelet glycoprotein (GP) IIb/IIIa receptor blockers was left to the discretion of the individual operator. The successful PCI was defined as the achievement of an angiographic residual stenosis <30% in the presence of Thrombolysis In Myocardial Infarction blood flow grade 3.

During the in-hospital period, the patients received medical treatment, including beta-blockers, angiotensin-

Abbreviations and Acronyms

AMI = acute myocardial infarction
BMS = bare-metal stent(s)
DES = drug-eluting stent(s)
EES = everolimus-eluting stent(s)
GP = glycoprotein
IVUS = intravascular ultrasound
LAD = left anterior descending artery
LCX = left circumflex
MACE = major adverse cardiac event(s)
MI = myocardial infarction
PCI = percutaneous coronary intervention
RCA = right coronary artery
Re-MI = recurrent myocardial infarction
STEMI = ST-segment elevation myocardial infarction
TLF = target lesion failure
TLR = target lesion revascularization
TVR = target vessel revascularization
ZES = zotarolimus-eluting stent(s)
ZES-R = zotarolimus-eluting stent-Resolute

Table 1. Baseline Characteristics and In-Hospital Medical Treatment

Variables	ZES (n = 1,608)	EES (n = 1,701)	p Value
Clinical characteristics			
Age, yrs	63.85 ± 12.63	62.64 ± 12.22	0.006
Male	1,164 (72.4)	1,243 (73.1)	0.685
History			
Hypertension	804 (50.0)	828 (48.7)	0.447
Dyslipidemia	244 (15.2)	255 (15.0)	0.883
Current smoking	720 (45.7)	768 (45.1)	0.829
Diabetes mellitus	461 (28.7)	556 (32.7)	0.012
Family history of CAD	148 (9.2)	151 (8.9)	0.743
Impaired renal function	27 (1.7)	25 (1.5)	0.628
Peptic ulcer	36 (2.2)	38 (2.2)	0.993
Cerebrovascular disease	114 (7.1)	104 (6.1)	0.258
Prior myocardial infarction	81 (5.0)	66 (3.9)	0.106
Prior heart failure (NYHA III/IV)	15 (0.9)	35 (2.1)	0.008
Diagnosis			
ST-segment elevation MI	985 (61.3)	1,022 (60.1)	0.490
Primary PCI	903 (91.7)	945 (92.5)	0.512
Non–ST-segment elevation MI	623 (38.7)	679 (39.9)	0.490
Early invasive treatment	492 (79.0)	519 (76.4)	0.272
Killip class			0.579
I	1,139 (70.8)	1,230 (72.3)	
II	244 (15.2)	256 (15.0)	
III	127 (7.9)	129 (7.6)	
IV	98 (6.1)	86 (5.1)	
Angiographic and procedural characteristics			
Target lesion			0.787
LAD	785 (48.8)	821 (48.3)	
RCA	528 (32.8)	546 (32.1)	
LCX	260 (16.2)	291 (17.1)	
Left main	35 (2.2)	43 (2.5)	
Diseased vessels			0.799
Single	679 (42.2)	704 (41.4)	
Double	504 (31.3)	521 (30.6)	
Triple	376 (23.4)	421 (24.8)	
Left main disease	49 (3.0)	55 (3.2)	
Pre-procedure TIMI flow grade			0.144
0	786 (48.9)	803 (47.2)	
I	172 (10.6)	207 (12.2)	
II	262 (16.3)	245 (14.4)	
III	388 (24.1)	446 (26.2)	
Stent diameter, mm	3.15 ± 0.43	3.18 ± 0.43	0.039
Stent length, mm	24.10 ± 6.08	22.88 ± 4.97	<0.001
Total stents/patient, n	1.52 ± 0.80	1.49 ± 0.80	0.418
Post-procedure TIMI flow grade			0.974
0	7 (0.4)	8 (0.5)	
I	6 (0.4)	8 (0.5)	
II	10 (0.6)	10 (0.6)	
III	1,585 (98.6)	1,675 (98.5)	
Use of intravascular ultrasound	363 (22.6)	453 (26.6)	0.007
Use of glycoprotein IIb/IIIa receptor blockers	312 (19.4)	288 (16.9)	0.065
In-hospital medical treatment			
Aspirin	1,595 (99.2)	1,687 (99.2)	0.963
Clopidogrel	1,589 (98.8)	1,683 (98.9)	0.736
Glycoprotein IIb/IIIa receptor blockers	223 (13.9)	224 (13.2)	0.556
Cilostazol	466 (29.0)	495 (29.1)	0.939
Low molecular weight heparin	339 (21.1)	346 (20.3)	0.599
Unfractionated heparin	1,095 (68.1)	1,130 (66.4)	0.308
Beta-blockers	1,389 (86.4)	1,487 (87.4)	0.376
Angiotensin-converting enzyme inhibitors	1,076 (66.9)	1,159 (68.1)	0.453
Angiotensin II receptor blockers	321 (20.0)	376 (22.1)	0.131
Calcium-channel blockers	94 (5.8)	111 (6.5)	0.418
Statins	1,306 (81.2)	1,389 (81.7)	0.745

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Values are mean ± SD or n (%).

CAD = coronary artery disease; EES = everolimus-eluting stent(s); LAD = left anterior descending artery; LCX = left circumflex; MI = myocardial infarction; NYHA = New York Heart Association functional class; PCI = percutaneous coronary intervention; RCA = right coronary artery; TIMI = Thrombolysis In Myocardial Infarction; ZES = zotarolimus-eluting stent(s).

converting enzyme inhibitors or angiotensin II receptor blockers, calcium channel blockers, and statins. After discharge, the patients were encouraged to continue the same medications they received in the hospital, except some intravenous or temporary medications.

Study definitions and clinical follow-up. The cardiovascular risk factors and past history records (age, sex, hypertension, dyslipidemia, smoking, diabetes mellitus, family history of coronary heart disease, prior myocardial infarction [MI], chronic heart failure and prior cerebrovascular disease, peripheral arterial disease) were mainly dependent on patient self-report, but the final records were left to physician discretion after he or she had comprehensively considered the patient self-report and in-hospital examination results. All deaths were considered cardiac in origin unless a noncardiac origin was definitely documented. Recurrent myocardial infarction (Re-MI) was defined as recurrent symptoms with new ST-segment elevation or re-elevation of cardiac markers to at least twice the upper limit of normal. Target lesion revascularization (TLR) was defined as ischemia-induced PCI of the target lesion due to restenosis or re-occlusion within the stent or in an adjacent 5 mm of the distal or proximal segment. Target vessel revascularization (TVR) was defined as clinically driven PCI of the target lesion or any segment of the coronary artery containing the target lesion. Target lesion failure (TLF) was defined as the composite of cardiac death, nonfatal Re-MI, or TLR. Total major adverse cardiac events (MACE) included total death, nonfatal Re-MI, or TVR. Stent thrombosis was defined according to the Academic Research Consortium definitions and categorized according to the timing of the event as acute (occurrence within the first

Table 2. Baseline Characteristics and In-Hospital Medical Treatment of Propensity Score-Matched Patients

Variables	ZES (n = 1,343)	EES (n = 1,343)	p Value
Clinical characteristics			
Age, yrs	63.44 ± 12.59	63.64 ± 11.98	0.680
Male	967 (72.0)	976 (72.6)	0.698
History			
Hypertension	678 (50.5)	666 (49.6)	0.643
Dyslipidemia	171 (12.9)	188 (14.2)	0.312
Current smoking	607 (46.1)	594 (45.5)	0.703
Diabetes mellitus	384 (28.6)	363 (27.0)	0.366
Family history of CAD	129 (9.6)	116 (8.6)	0.384
Impaired renal function	23 (1.7)	20 (1.5)	0.645
Peptic ulcer	27 (2.0)	26 (1.9)	0.890
Cerebrovascular disease	87 (6.5)	93 (6.9)	0.643
Prior myocardial infarction	45 (3.4)	60 (4.5)	0.135
Prior heart failure (NYHA III/IV)	13 (1.0)	12 (0.9)	0.841
Diagnosis			
ST-segment elevation MI	825 (61.4)	833 (62.0)	0.751
Primary PCI	759 (92.0)	780 (93.6)	0.197
Non–ST-segment elevation MI	518 (38.6)	510 (38.0)	0.751
Early invasive treatment	414 (79.9)	395 (77.5)	0.333
Killip class			0.899
I	972 (72.4)	964 (71.8)	
II	206 (15.3)	201 (15.0)	
III	95 (7.1)	103 (7.7)	
IV	70 (5.2)	75 (5.6)	
Angiographic and procedural characteristics			
Target lesion			0.949
LAD	647 (48.2)	654 (48.7)	
RCA	448 (33.4)	439 (32.7)	
LCX	220 (16.4)	225 (16.8)	
Left main	28 (2.1)	25 (1.9)	
Diseased vessels			0.516
Single	576 (42.9)	557 (41.5)	
Double	424 (31.6)	413 (30.8)	
Triple	303 (22.6)	336 (25.0)	
Left main disease	40 (3.0)	37 (2.8)	
Pre-procedure TIMI flow grade			0.280
0	646 (48.1)	641 (47.7)	
I	140 (10.4)	157 (11.7)	
II	223 (16.6)	192 (14.3)	
III	334 (24.9)	353 (26.3)	
Stent diameter, mm	3.14 ± 0.43	3.13 ± 0.40	0.393
Stent length, mm	23.68 ± 5.46	24.05 ± 4.56	0.056
Total stents/patient, n	1.50 ± 0.80	1.49 ± 0.79	0.698
Post-procedure TIMI flow grade			0.695
0	6 (0.4)	5 (0.4)	
I	5 (0.4)	2 (0.1)	
II	9 (0.7)	8 (0.6)	
III	1,323 (98.5)	1,328 (98.9)	
Use of intravascular ultrasound	298 (22.2)	266 (19.8)	0.130
Use of glycoprotein IIb/IIIa receptor blockers	250 (18.6)	270 (20.1)	0.329
In-hospital medical treatment			
Aspirin	1,335 (99.4)	1,331 (99.1)	0.369
Clopidogrel	1,327 (98.8)	1,328 (98.9)	0.857
Glycoprotein IIb/IIIa receptor blockers	190 (14.1)	210 (15.6)	0.278
Cilostazol	378 (28.1)	416 (31.0)	0.108
Low molecular weight heparin	286 (21.3)	279 (20.8)	0.740
Unfractionated heparin	894 (66.6)	916 (68.2)	0.365
Beta-blockers	1,179 (87.8)	1,184 (88.2)	0.767
Angiotensin-converting enzyme inhibitors	865 (64.4)	886 (66.0)	0.395
Angiotensin II receptor blockers	301 (22.4)	298 (22.2)	0.889
Calcium channel blockers	86 (6.4)	89 (6.6)	0.815
Statins	1,147 (85.4)	1,133 (84.4)	0.451

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Table 2. Continued

Values are mean ± SD or n (%).
Abbreviations as in Table 1.

24 h after the index procedure), subacute (from 24 h to 30 days), and late (from 30 days to 1 year) (10).

Patients were required to visit the outpatient department of cardiology at the end of the first month and then every 6 months after the PCI procedure as well as whenever angina-like symptoms occurred. The cumulative incidences of various MACE during hospital stay and at 1 year were compared between the 2 groups.

Statistical analysis. Continuous variables were presented as mean ± SD and compared with the Student *t* test. Categorical variables were expressed as percentages and compared with the chi-square test or the Fischer exact test, where indicated. To account for the selection bias of different stents, we calculated propensity score predicting probability for receiving different DES in each patient. The covariates that were adjusted for exposure to DES included age, sex, Killip class on admission, cardiovascular risk factors (hypertension, dyslipidemia, smoking, diabetes mellitus, family history of coronary artery disease), prior MI, chronic heart failure and prior cerebrovascular disease, moderate to severe renal dysfunction, diagnosis (STEMI vs. NSTEMI), target vessel, number of diseased vessels, pre-procedure Thrombolysis In Myocardial Infarction blood flow grade, stent diameter, stent length, total stent number/patient, use of intravascular ultrasound (IVUS), and use of GP IIb/IIIa receptor blockers in procedure. The C-statistic for the logistic regression model that was used to calculate the propensity score matching for the 2 groups was 0.684.

Patients receiving EES were then 1-to-1 matched to the patients receiving ZES on the propensity scores with the nearest available pair matching method. Subjects were matched with a caliper width equal to 0.05. The procedure yielded 1,343 well-matched pairs. After propensity score matching, the

Table 3. Clinical Outcomes of ZES Versus EES Groups Before and After Propensity Score Matching

Variables	Entire Patients			Propensity Score-Matched Patients		
	ZES (n = 1,608)	EES (n = 1,701)	p Value	ZES (n = 1,343)	EES (n = 1,343)	p Value
In-hospital outcomes						
Cardiac death	87 (5.4)	67 (3.9)	0.045	62 (4.6)	56 (4.2)	0.572
Total death	96 (6.0)	70 (4.1)	0.015	67 (5.0)	59 (4.4)	0.465
Outcomes at 1 yr						
Cardiac death	99 (6.2)	71 (4.2)	0.010	71 (5.3)	60 (4.5)	0.324
Total death	144 (9.0)	101 (5.9)	0.001	106 (7.9)	82 (6.1)	0.070
Recurrent MI	28 (1.7)	23 (1.4)	0.364	25 (1.9)	20 (1.5)	0.452
TLR	34 (2.1)	20 (1.2)	0.033	29 (2.2)	16 (1.2)	0.051
TVR	46 (2.9)	28 (1.6)	0.018	39 (2.9)	24 (1.8)	0.056
TLF	152 (9.5)	103 (6.1)	<0.001	117 (8.7)	87 (6.5)	0.029
Total MACE	208 (12.9)	139 (8.2)	<0.001	161 (12.0)	115 (8.6)	0.003
Probable or definite stent thrombosis	22 (1.4)	6 (0.4)	0.001	22 (1.6)	4 (0.3)	<0.001
Acute	2 (0.1)	1 (0.1)	0.615	2 (0.1)	0 (0)	0.500
Subacute	12 (0.7)	2 (0.1)	0.005	12 (0.9)	1 (0.1)	0.002
Late	8 (0.5)	3 (0.2)	0.109	8 (0.6)	3 (0.2)	0.131
1–6 months	1 (0.1)	1 (0.1)	1.000	1 (0.1)	1 (0.1)	1.000
6–12 months	7 (0.4)	2 (0.1)	0.100	7 (0.5)	2 (0.1)	0.179

Values are n (%). Target lesion failure (TLF) was defined as the composite of cardiac death, recurrent MI and target lesion revascularization (TLR). MACE = major adverse cardiac events; TVR = target vessel revascularization; other abbreviations as in Table 1.

baseline covariates were compared between the 2 stent groups. Continuous variables were compared with the paired *t* test, and categorical variables were compared with chi-square test or Fisher exact test, as appropriate. Various clinical outcomes at 1 year were estimated with the Kaplan-Meier method, and differences between groups were compared with the log-rank test in the propensity score-matched patients.

The proportional hazard models were used to assess the adjusted hazard ratio comparing the 2 stent types in both entire patients and propensity score-matched patients. The outcomes of both groups were censored at a fixed point of 1 year (365 days) to avoid any bias caused by different follow-up duration.

For all analyses, a 2-sided $p < 0.05$ was considered statistically significant. All data were processed with SPSS (version 13.0, SPSS-PC, Inc. Chicago, Illinois).

Results

There was considerable imbalance in baseline clinical and angiographic characteristics between the patients in the ZES group versus the EES group, including age, stent diameter, stent length, the rates of diabetes, prior heart failure, use of platelet GP IIb/IIIa receptor blockers, and use of IVUS during procedure (Table 1). However, the in-hospital medical treatments were similar between the 2 groups (Table 1).

After propensity score matching, the baseline clinical and angiographic characteristics of the 2 propensity-matched groups (1,343 pairs, n = 2,686 total) were balanced in most measured characteristics, except that patients in the EES group tended to receive longer stents compared with those in the ZES group (24.05 ± 4.56 mm vs. 23.68 ± 5.46 mm, p = 0.056) (Table 2).

Clinical outcomes are summarized in Table 3. In the entire patient cohort before propensity score matching, patients in the EES group had significantly lower incidences of in-hospital cardiac death, total death, and 1-year cardiac death than patients in the ZES group. Furthermore, the incidences of TLR, TVR, TLF, total MACE, probable or definite stent thrombosis, and subacute stent thrombosis were also significantly lower in the EES group than in the ZES group.

In the propensity score-matched cohort, the differences of in-hospital and 1-year mortality were no longer statistically significant. But patients in the EES group still showed significantly lower rates of TLF, total MACE, probable or definite stent thrombosis, and subacute stent thrombosis compared with those in the ZES group. Furthermore, there were numerically lower rates of TLR (p = 0.051) and TVR (p = 0.056) in the EES group than in the ZES group (Table 3).

Figure 1 shows Kaplan-Meier curves for various clinical outcomes up to 1 year in the propensity-matched cohort. Figure 2 presents adjusted hazard ratios for various 1-year clinical outcomes associated with EES compared with ZES

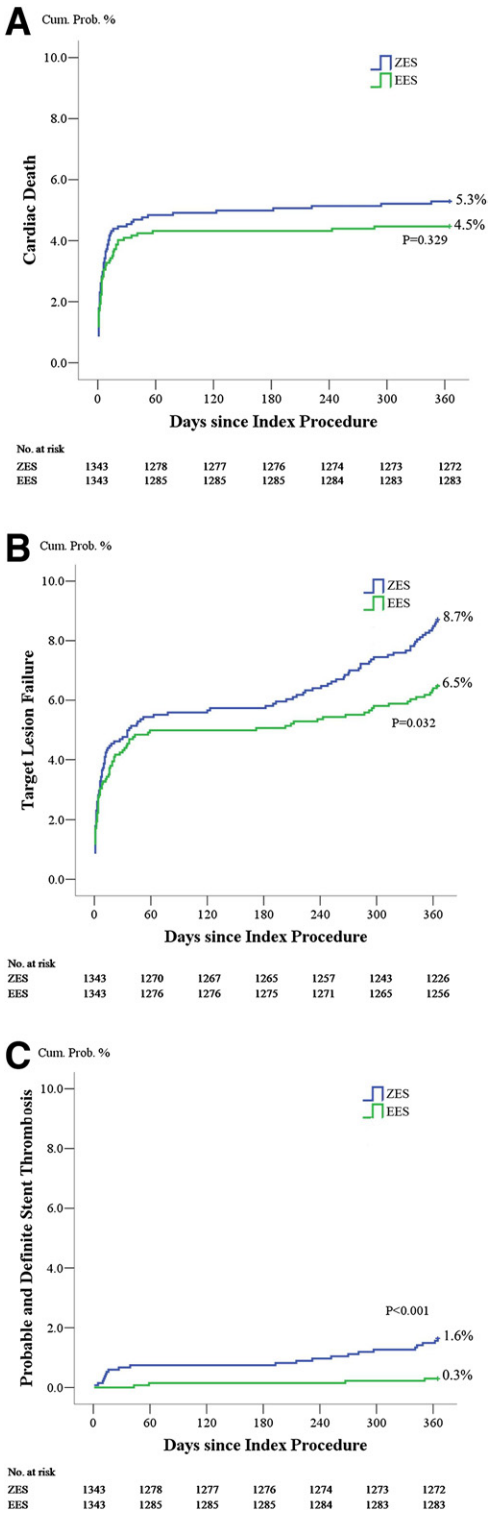

Figure 1. Kaplan-Meier Survival Curves Describing Cumulative Incidences of Various 1-Year Clinical Outcomes in Propensity Score-Matched Patients

EES = everolimus-eluting stent(s); ZES = zotarolimus-eluting stent(s).

in the entire patient (Fig. 2A) and propensity score-matched cohort (Fig. 2B). The use of EES was a statistically significant predictor of 1-year total death, TLR, TVR, TLF, total MACE, and probable or definite stent thrombosis in the entire patient cohort (Fig. 2A). In the propensity score-matched cohort, the use of EES was an independent protective predictor of TLR, TLF, total MACE, and probable or definite stent thrombosis (Fig. 2B). Figure 3 lists the independent predictors of TLF (Fig. 3A) and probable or definite stent thrombosis (Fig. 3B).

Discussion

The main finding of this "real-world" propensity score-matched analysis was that the use of EES was associated with a reduction in 1-year TLF and probable or definite stent thrombosis compared with ZES in the setting of AMI.

Although both ZES (Endeavor Sprint) and EES (Xience V) are considered second-generation DES, the performances of these 2 stents have been shown to be different. Some previous studies suggested that late lumen loss in EES was low (approximately 0.15 mm) (11,12), whereas it was much greater in ZES (approximately 0.6 mm) (4,13). However, there are limited data that directly compare these 2 stents.

Recently, 2 small-scale nonrandomized studies compared EES with ZES in patients with bifurcation lesions and reported that the use of EES resulted in superior 1-year clinical outcomes (14,15). Another registry study evaluated the relationship between the stent design and periprocedural MI and showed that the use of EES was associated with less periprocedural myocardial injury compared with ZES (16).

Although there is a paucity of data directly comparing EES with ZES (Endeavor Sprint), 1 large-scale randomized study was performed to compare the safety and efficacy of the next-generation ZES Resolute (ZES-R) with EES (17,18). The RESOLUTE All Comers trial enrolled 2,292 patients undergoing PCI, and it showed that next-generation ZES-R was noninferior to EES with comparable outcomes both at 1 year and 2 years (17,18). Recently, an observational study comprising 1,402 patients undergoing PCI was done to evaluate the clinical effectiveness of ZES-R compared with ZES (Endeavor Sprint), and it showed that the 1-year adverse event rate (cardiac death, MI, and clinically driven TLR) for patients who received ZES-R was 3.7% compared with 6.5% for those who received ZES (19).

Consistent with the aforementioned studies (14–19), our study also showed that the unrestricted use of EES compared with ZES was associated with a lower rate of TLF, which was mainly driven by a reduction in TLR. We suppose the inferior efficacy profiles of ZES might be partially attributed to its shorter duration of eluting drug release compared with EES and ZES-R. Both ZES and

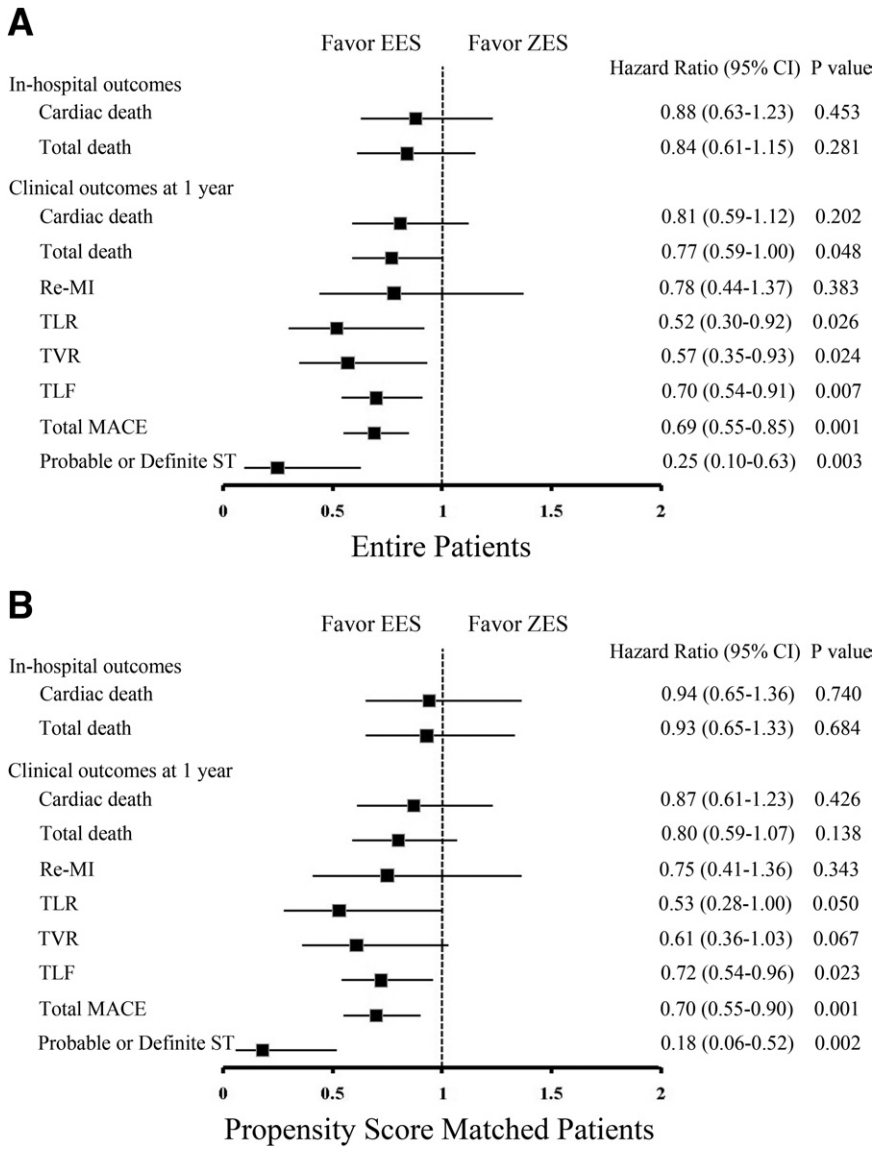

Figure 2. Adjusted Hazard Ratios for Various Clinical Outcomes Associated With EES Compared With ZES

Adjusted hazard ratios for various clinical outcomes associated with EES compared with ZES in the entire **(A)** and propensity score-matched patient cohort **(B)**. Variables in the multivariable Cox proportional hazard models: stent types (EES vs. ZES), age, sex, Killip class on admission, cardiovascular risk factors (hypertension, dyslipidemia, smoking, diabetes mellitus, family history of coronary artery disease), prior myocardial infarction, chronic heart failure and prior cerebrovascular disease, moderate-to-severe renal dysfunction, diagnosis (ST-segment elevation myocardial infarction vs. non-ST-segment elevation myocardial infarction), target vessel, number of diseased vessels, pre- and post-procedure Thrombolysis In Myocardial Infarction blood flow grade, stent diameter, stent length, total stent number/patient, use of intravascular ultrasound, and use of glycoprotein IIb/IIIa receptor blockers in procedure. CI = confidence interval; MACE = major adverse cardiac events; Re-MI = recurrent myocardial infarction; ST = stent thrombosis; TLF = target lesion failure; TLR = target lesion revascularization; TVR = target vessel revascularization.

ZES-R release zotarolimus and have the same cobalt chromium platform, but the biocompatible polymer of ZES-R allows for an extended drug release of approximately 6 months compared with the 14-day release with ZES (Endeavor Sprint) (19).

It should be noted that the present study showed lower event rates compared with some other studies (5,20,21). We speculate that the difference between our study and some previous studies might be due to the different study populations and follow-up regimens. First, approximately 92% of STEMI patients received primary PCI, and nearly 80% of NSTEMI patients received early invasive treatment in the present study. In addition, optimal medical therapy with high use rates of cardiovascular beneficial medications might have

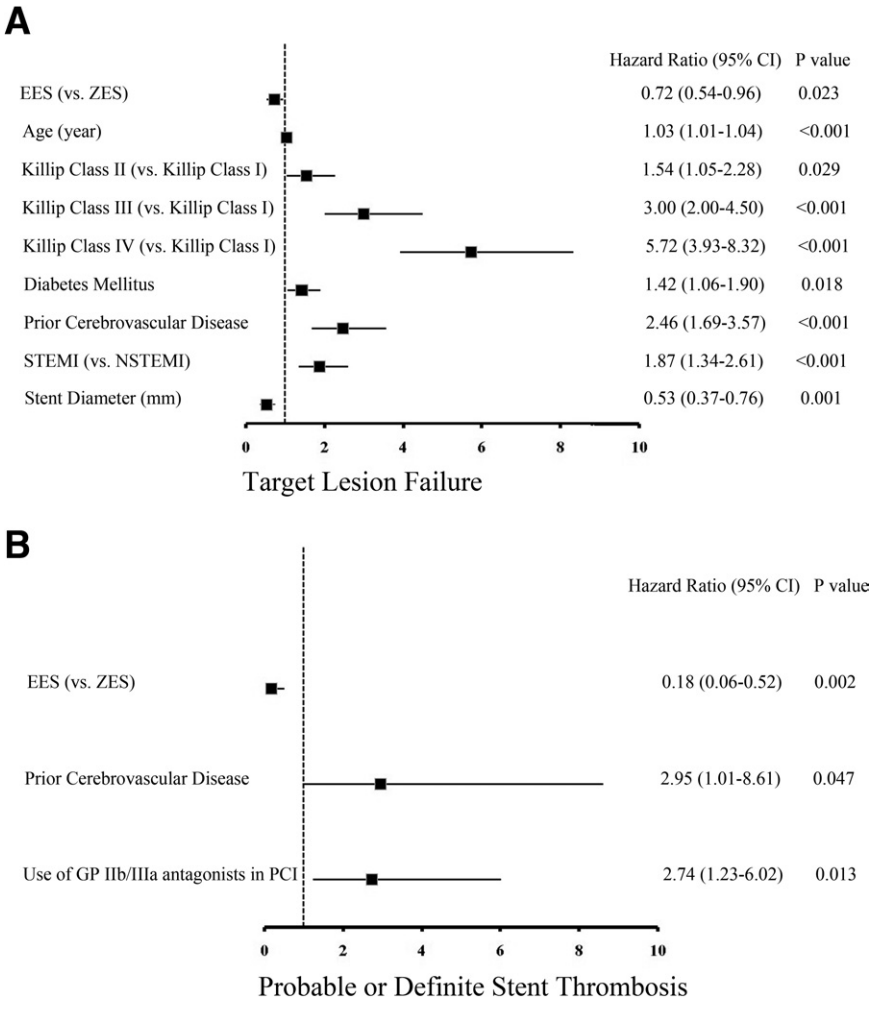

Figure 3. Independent Predictors of TLF and Probable or Definite ST

Independent predictors of TLF **(A)** and probable or definite ST **(B)**. GP = glycoprotein; NSTEMI = non–ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction; other abbreviations as in Figure 2.

improved the clinical outcomes of our patients (Tables 1 and 2). Second, we routinely performed clinical follow-up, but the angiographic follow-up was not routinely performed in the present study. Some patients with angiographic in-stent restenosis might be asymptomatic and could not be found in the clinical follow-up. And this might be an important reason for the lower incidence of clinically driven TLR in the present study.

Although the second-generation DES have been proved to be safer than the first-generation DES in reducing stent thrombosis, there is still a paucity of data with regard to the real-world incidence of late stent thrombosis after implantation of the second-generation DES (8,21). De la Torre Hernandez et al. (20) evaluated second-generation DES thrombosis in clinical practice. A total of 4,768 patients were included (2,549 treated with ZES, and 2,219 with EES). The 1-year cumulative incidence of probable or definite stent thrombosis was 1.3% in the ZES group and 1.4% in the EES group ($p = 0.800$). In the present study, the incidence of stent thrombosis in the patients treated with ZES was similar to the results of the previous studies (20). However, the rate of probable or definite stent thrombosis in the patients treated with EES was relatively lower compared with some previous studies, which showed 1-year stent thrombosis ranging from 0.7% to 0.8% (7,22). But the SPIRIT (Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System) IV study showed that the rate of probable or definite stent thrombosis was 0.29% at 1 year in 2,459 EES-treated patients (23). Furthermore, a meta-analysis from Baber et al. (24) also suggested that EES was associated with highly significant reductions in stent thrombosis (relative risk: 0.55, 95%

confidence interval: 0.38 to 0.78, $p < 0.001$) compared with other DES. We suppose that the high use rates of IVUS (24.7%) and GP IIb/IIIa receptor blockers (18.1%) during the procedure might have effectively reduced stent underexpansion, intimal dissection, and stent malapposition, which have been proved to be major risk factors for early and late stent thrombosis (2,25). Furthermore, the use rate of additional cilostazol was high (29.0%) in the present study, which might also have a favorable outcome toward reduction of stent thrombosis (26). The mechanism behind the lower rate of probable or definite stent thrombosis in the EES group compared with that in the ZES group remains unclear. But it was seen that—going by recent comparative animal study where PCI was performed in rabbit iliac arteries—more rapid re-endothelialization was observed with EES compared with ZES as assessed by both a higher degree of morphometric (electron microscopy) and functional (CD-31 expression) extent of endothelialization (27).

Study limitations. First, stents were assigned by the individual operator, so possibility of operator bias might be considered. Although we used propensity score matching in the present study to adjust potential bias of stent selection, some important variables might have been ignored. However, this prospective multicenter registry might help complete the picture gained from randomized trials, which usually have highly selected patients treated in a nonroutine setting. Second, although all the patients were encouraged to receive dual antiplatelet therapy with aspirin and clopidogrel for at least 1 year, antiplatelet treatment compliance was not recorded in the KAMIR database. The early discontinuation of dual antiplatelet therapy would probably be a major determinant of stent thrombosis. Therefore, the results of the stent thrombosis in the present study should be considered cautiously. Also, although all the patients had baseline quantitative coronary angiography data and were encouraged to receive 6-month follow-up angiography, 6-month angiographic follow-up was available for only 21.2% of patients. Therefore, we didn't list quantitative coronary angiography results in this study.

Conclusions

In the present propensity-matched comparison, EES seems to be superior to ZES in reducing 1-year TLF and stent thrombosis in patients with AMI. These findings may be considered hypothesis-generating, and further randomized studies are warranted to get definite conclusions.

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Key Words: acute myocardial infarction ■ everolimus-eluting stents ■ percutaneous coronary intervention ■ zotarolimus-eluting stents.