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Two-year Clinical Outcomes Following Everolimus-eluting Stent Use for Off-label Versus On-label Indications: From the Korean Multicenter Drug-eluting Stent Registry

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• The authors report no conflict of interest in this work.

Background: Everolimus-eluting stent (EES) implantations have a relatively low rate of major adverse cardiac event (MACE) and target lesion revascularization (TLR) in patients with off-label use. However, the clinical outcome in the Korean population regarding EES in patients with off-label use is not well known. **Objects**: The aim of the current analysis was to compare the clinical outcomes of on-label and off-label EES use over a 2-year follow-up period. **Methods**: Using patient-level data from a stent-specific, prospective, all-comer registry, we evaluated 987 patients (1,342 lesions) who received an EES (XIENCE V®, Abbott Vascular, Santa Clara, CA, USA) implantation between February 2009 and April 2011. The primary outcome was assessed: 2-year MACE (a composite endpoint of death from any cause, spontaneous myocardial infarction (MI), and any repeat revascularization). The clinical outcomes in the on- and off-label groups were compared at 2 years. **Results**: The majority of patients (79.0%) were treated for ≥1 off-label indication. The median duration of the clinical follow-up in the overall population was 2.0 years (interquartile range 1.9-2.1). At 2-years after the EES implantation in the enrolled patients, MACE occurred in 71 (7.9%) patients, cardiac death in 12 (1.3%), MI in 4 (0.5%), target vessel revascularization (TVR) in 33 (3.8%), TLR in 22 (2.5%), and definite or probable stent thrombosis (ST) in 1 (0.1%). Off-label EES implantations tend to increase the risk of 2-year MACE (4.7% vs. 8.8%, p = 0.063) without statistical significance. However, the rates of TLR

were higher in the off-label EES implantations (0.0% vs. 3.2%, p = 0.013). In the multivariable analysis, renal failure, previous bypass surgery, previous cerebrovascular accident, and left main lesions were associated with 2-year MACE in patients with EES implantations. **Conclusions:** The incidence of 2-year MACE was 7.9%, which that might be acceptable in all-comer patients treated with EES implantations. Although the off-label use of EES was not statistically associated with an increased risk of MACE, the TLR rate was higher in the off-label group, suggesting that physicians need to pay attention to high risk patients with the use of EES implantations.

Keywords: Coronary artery disease, Drug-eluting stents, Off-label use

Introduction

Since the Food and Drug Administration approval of the use of the first drug-eluting stent (DES) in April 2003, DES has been widely used as the gold standard for the treatment of coronary artery disease. DES implantations markedly reduced the rate of in-stent restenosis [1] (ISR), and consequently, DES has been increasingly used in patients who are characterized by a higher clinical event risk and more complex lesions. However, over the past few years, cases of late stent thrombosis (ST) began to be reported and the long-term risk of DES remained debatable [2-4].

With technical developments, second-generation DES has adopted biocompatible polymers for the improvement in the clinical outcomes and has shown favorable clinical outcomes [5,6]. In practice, each manufacturer recommends appropriate patients for the use of second-generation DES as an on-label use for the patients' safety. In the real-world, however, more complex patients and lesion subsets have been treated with second-generation DES, namely an off-label use. A study reported that the XIENCE V® everolimus-eluting stent (EES) (Abbott Vascular, Santa Clara, CA, USA) had a relatively low rate of major adverse cardiac events (MACE) and target lesion revascularization (TLR) in patients with an off-label use [7]. Under these circumstances, clinical follow-up data in the Korean population regarding EES in patients with off-label use are lacking. Thus, we sought to compare the clinical outcomes of EES implanted for on-label and off-label indications over a period of 2 years.

Methods

Study design and population

Korean Registry of Xience V EVERolimus Eluting coronary STent system (K-EVEREST) study is a prospective, multicenter, all-comer, observational study of 1012 consecutive patients who underwent implantations of EES from February 2009 to April 2011 at 21 large-volume percutaneous coronary intervention (PCI) centers in Korea.

Off-label indications for EES use were defined as: 1) renal insufficiency (serum creatinine level >2.0 mg/dL); 2) ejection fraction <30%; 3) occurrence of an acute myocardial infarction (MI) within the previous 72 hours; 4) more than two vessels treated; 5) more than one lesion/vessel; 6) bypass graft treated; 7) ISR; 8) unprotected left main lesion; 9) lesion length >27 mm; 10) lesion with a thrombus; and 11) lesion with a total occlusion.

This registry was supported by the Keimyung University Dongsan Medical Center, Deagu, Korea, and there was no industry involvement in the design, conduct, or analysis of the study. The study protocol was approved by the ethics committee at each participating center, and all patients provided written, informed consent for participation in this prospective registry.

PCI procedures and clinical follow-up

In the K-EVEREST registry, PCI procedures were performed according to standard techniques at the discretion of the treating physician. Periprocedural anticoagulant was administered according to standard regimens. Glycoprotein IIb/IIIa inhibitors were administered at the discretion of the operator. All patients undergoing PCI received a loading dose of aspirin and $P2Y_{12}$ receptor inhibitor (clopidogrel, prasugrel, or ticagrelor) before or during the PCI. The duration of the dual antiplatelet agent administration was determined according to the physician's discretion based on the recommendations of the American College of Cardiology/American Heart Association [7]. Drugs for secondary prevention were prescribed according to the current guidelines.

Clinical follow-up was conducted during hospitalization and at 1 month, 12 months, and 24 months. At each visit, information pertaining to the patients' clinical status, all interventions, and outcome events were recorded. Baseline characteristics and outcome data were collected using a dedicated, electronic case report form by specialized personnel at each participating center. The internet-based system provided each center with immediate and continuous feedback on the processes and quality-of-care measures. Monitoring and verification of the registry data were periodically performed in the participating hospitals by members of the academic coordinating center (Clinical Research Center, Keimyung University Dongsan Medical Center, Daegu, Korea).

Study outcomes and definitions

The primary endpoints of this study were a composite of the 2-year MACE, which was defined as a death from any cause, spontaneous MI, or any repeat revascularization. The secondary endpoints included death (cardiac or non-cardiac), MI (Q-wave or non Q-wave), repeat revascularization (target-vessel or target-lesion), and ST.

All deaths were considered from cardiac causes unless non-cardiac causes were otherwise documented. The definition of a MI was based on the universal definition of a MI [8]. Repeat revascularization included any type of percutaneous or surgical revascularization procedures and was categorized as a revascularization of any lesion, target lesion, or target vessel. Definite ST was assessed according to the Academic Research Consortium definition [9]. All outcomes of interest were confirmed by source documentation collected at each hospital and were centrally adjudicated by an independent clinical events committee.

Statistical analysis

All statistical analyses were performed using SPSS Statistics version 22.0 for Windows software (SPSS Inc., Chicago, Illinois, USA) and the R programming language. Continuous variables are presented as the mean ± standard deviation (SD) or median, and categorical variables are expressed as frequencies. Comparisons between groups were tested with a chi-square or Fisher's exact test for categorical variables and an independent sample t-test or the Wilcoxon rank-sum test for continuous variables. A value of $p < 0.05$ was considered statistically significant. The observed event rates at 2-years and survival curves were generated using the Kaplan-Meier method and compared with the log-rank test. Univariate and multivariate analyses of hazard ratios, including 95% confidence intervals, were calculated using the Cox proportional hazard method. Variables with a p value less than 0.1 in the univariate analysis were all included in a backward stepwise multiple logistic regression model to identify the independent predictors of MACE in the off-label group.

Results

Patient characteristics

Of the 1,012 study subjects, 987 patients from the stent-specific, prospective K-EVERST registry were included for the current analysis; 13 patients were excluded due to follow-up loss, and 12 that the procedural data were insufficient (Fig. 1). EES was implanted for an off-label indication in 1,134 (84.5%) lesions, in 780 (79.0%) patients. The baseline demographics and clinical characteristics of the on- and off-label groups are shown in Table 1. The mean age of the overall patients was 64.1 years and approximately 66.6% of the patients were men. The groups were similar in terms of the age, sex, hypertension, diabetes mellitus, hyperlipidemia, smoking, and previous medical history. However, the patients in the off-label group had a slightly higher prevalence of renal failure (on-label; 0.0% vs. off-label; 2.9%; p = 0.025), lower ejection fraction value (55.7% vs. 61.8%; $p < 0.001$), and MI at presentation (0.0% vs. 47.6%; $p < 0.001$). More patients in the off-label group were taking cilostazol (21.3% vs. 31.7%; p = 0.005), and β-blocker (67.1% vs. 77.4%; p = 0.003). The rate of use of calcium channel blocker (CCB) was higher with on-label EES use (23.2% vs. 16.2%; p = 0.024). There was no difference in the discharge medications between the two groups except for cilostazol, β-blocker, and CCB.

Table 2 shows the lesion and procedural characteristics of the study population according to the on- and off-label groups. In the patients in the off-label group, there were more B2/C lesion types (54.8% vs. 80.2%; $p < 0.001$), more ISR (0.0% vs. 2.9%; p = 0.025), more severe calcified lesions (4.3% vs. 10.7%; p = 0.007), more thrombi (0.0% vs. 12.6%; $p < 0.001$), more chronic total occlusion (CTO) lesions (0.0% vs. 5.3%; p = 0.001), a longer mean lesion length (16.9 mm vs. 24.9 mm; $p < 0.001$), smaller proximal and distal reference vessel diameter (RVD) (3.2 mm vs. 3.1 mm; p = 0.026, 2.9 mm vs. 2.8

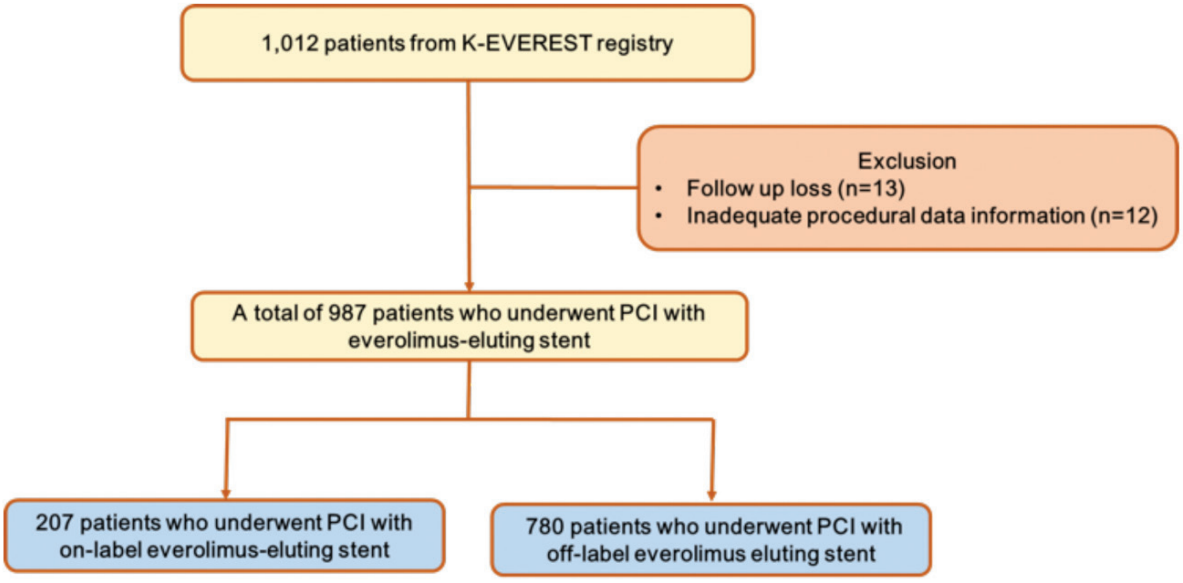

Fig. 1. Study flow.

mm; $p = 0.001$), longer stent length (20.0 mm vs. 29.9 mm; $p < 0.001$), and smaller stent diameter (3.2 mm vs. 3.1 mm; $p = 0.016$). The number of stents were greater in the off-label group (1.0 vs. 1.2; $p < 0.001$).

Clinical outcomes

The median duration of the clinical follow-up in the overall population was 2.0 years (interquartile

Table 1. Baseline demographic and clinical characteristics of the patients

Variable	All patients (n = 987)	On-label (n = 207)	Off-label (n = 780)	*P* Value
Age (years)	64.1 ± 10.5	64.3 ± 9.7	64.0 ± 10.7	0.691
Men	657 (66.6%)	135 (65.2%)	522 (66.9%)	0.704
Body-mass index (kg/m^2)	24.3 ± 3.2	24.4 ± 3.1	24.3 ± 3.2	0.688
Diabetes mellitus	311 (31.5%)	63 (30.4%)	248 (31.8%)	0.772
Hypertension	525 (53.2%)	106 (51.2%)	419 (53.7%)	0.572
Hyperlipidemia	188 (19.0%)	33 (15.9%)	155 (19.9%)	0.238
Current smoker	356 (36.1%)	68 (32.9%)	288 (36.9%)	0.316
Atrial fibrillation	24 (2.4%)	5 (2.4%)	19 (2.4%)	0.99
Previous MI	16 (1.6%)	3 (1.4%)	13 (1.7%)	0.99
Previous PCI	93 (9.4%)	26 (12.6%)	67 (8.6%)	0.109
Previous CABG	13 (1.3%)	3 (1.4%)	10 (1.3%)	0.99
Renal failure*	23 (2.3%)	0 (0.0%)	23 (2.9%)	0.025
Previous CVA	63 (6.4%)	8 (3.9%)	55 (7.1%)	0.132
Ejection fraction (%)	56.9 ± 10.8	61.8 ± 8.2	55.7 ± 11.0	<0.001
Clinical presentation				<0.001
Stable angina	301 (30.5%)	104 (50.2%)	197 (25.3%)	
Unstable angina	314 (31.8%)	103 (49.8%)	211 (27.1%)	
NSTEMI	179 (18.1%)	0 (0.0%)	179 (22.9%)	
STEMI	193 (19.6%)	0 (0.0%)	193 (24.7%)	
Discharge medications				
Aspirin	967 (98.0%)	206 (99.5%)	761 (97.6%)	0.135
ADP receptor antagonist	964 (97.7%)	205 (99.0%)	759 (97.3%)	0.228
Cilostazol	291 (29.5%)	44 (21.3%)	247 (31.7%)	0.005
β-blocker	743 (75.3%)	139 (67.1%)	604 (77.4%)	0.003
Calcium channel blocker	174 (17.6%)	48 (23.2%)	126 (16.2%)	0.024
ACE inhibitor or ARB	668 (67.7%)	128 (61.8%)	540 (69.2%)	0.053
Statin	737 (74.7%)	149 (72.0%)	588 (75.4%)	0.362

Data are shown as the mean (standard deviation) for continuous variables and absolute numbers (percentage) for dichotomous variables.

* Renal failure was defined by a serum creatinine level of >2.0 mg/dL.

MI: myocardial infarction, PCI: percutaneous coronary intervention, CABG: coronary-artery bypass grafting, NSTEMI: non-ST-elevation myocardial infarction, STEMI: ST-elevation MI, ADP: adenosine diphosphate, ACE: angiotensin-converting enzyme, ARB: angiotensin II receptor blocker.

Table 2. Lesion and procedural characteristics

Variable	All lesions (n = 1342)	On-label (n = 208)	Off-label (n = 1134)	*P* Value
Treated lesion				
LM	51 (3.8%)	0 (0%)	51 (4.5%)	0.003
LAD	653 (48.7%)	117 (56.2%)	536 (47.3%)	0.021
LCX	270 (20.1%)	44 (21.2%)	226 (19.9%)	0.756
RCA	387 (28.8%)	47 (22.6%)	340 (30.0%)	0.038
ACC–AHA lesion type				<0.001
A/B1	318 (23.7%)	94 (45.2%)	224 (19.8%)	
B2/C	1024 (76.3%)	114 (54.8%)	910 (80.2%)	
Restenotic lesions	33 (2.5%)	0 (0.0%)	33 (2.9%)	0.025
Moderate to severe CAC	130 (9.7%)	9 (4.3%)	121 (10.7%)	0.007
Bifurcation lesions	237 (17.7%)	38 (18.3%)	199 (17.5%)	0.879
Ostial lesion	118 (8.8%)	18 (8.7%)	100 (8.8%)	0.99
Thrombus present	143 (10.7%)	0 (0.0%)	143 (12.6%)	<0.001
Chronic total occlusion	60 (4.5%)	0 (0.0%)	60 (5.3%)	0.001
Lesion length (mm)	23.6 ± 11.9	16.9 ± 5.5	24.9 ± 12.4	0
Proximal RVD (mm)	3.1 ± 0.5	3.2 ± 0.5	3.1 ± 0.5	0.026
Distal RVD (mm)	2.8 ± 0.5	2.9 ± 0.5	2.8 ± 0.5	0.001
Diameter stenosis (%)	83.3 ± 10.5	82.4 ± 8.3	83.5 ± 10.9	0.139
Pre-balloon dilatation	1201 (89.5%)	188 (90.4%)	1013 (89.3%)	0.739
Post-high pressure NC balloon	572 (42.6%)	89 (42.8%)	483 (42.6%)	0.99
No. of stents per lesion	1.2 ± 0.5	1.0 ± 0.1	1.2 ± 0.5	<0.001
Stent diameter (mm)	3.1 ± 0.4	3.2 ± 0.4	3.1 ± 0.4	0.016
Total stent length (mm)	28.4 ± 13.6	20.0 ± 3.3	29.9 ± 14.2	<0.001
Procedure-related MI*	6 (0.6%)	0 (0.0%)	6 (0.8%)	0.446

Data are shown as the mean (standard deviation) for continuous variables and absolute numbers (percentage) for dichotomous variables.
* Procedure-related MI was all calculated as per patient.
LM: left main, LAD: left anterior descending artery, LCX: left circumflex artery, RCA: right coronary artery, CAC: coronary artery calcification, RVD: reference vessel diameter, NC: non-compliant, MI: myocardial infarction.

range 1.9-2.1). A total of 987 patients were followed up for 2 years. The clinical follow-up outcome data are shown in Table 3. At 2 years after the EES implantation in the enrolled patients, MACE occurred in 71 (7.9%) patients, cardiac death in 12 (1.3%), MI in 4 (0.5%), target vessel revascularization (TVR) in 33 (3.8%), TLR in 22 (2.5%), and a definite or probable stent thromboses (ST) in 1 (0.1%). Off-label EES implantations tended to slightly increase the risk of a 2-year MACE (on-label; 4.7% vs. off-label; 8.8%, p = 0.063) without statistical significance. However, the rates of TLR were higher for the off-label EES implantations (0.0% vs. 3.2%, p = 0.013). The Kaplan-Meier estimates of the primary and secondary outcomes at 2-years according to whether in the on- or off-label groups are shown in Table 3 and Figure 2. Table 4 shows the univariate and multivariate analysis of the MACE in the patients with EES implantations. A history of coronary artery bypass grafting (CABG) (hazard ratio [HR], 4.75; 95%

Table 3. Clinical outcomes after two years

Variable	All patients (n = 987)	On-label (n = 207)	Off-label (n = 780)	*P* Value
MACE	71 (7.9%)	9 (4.7%)	62 (8.8%)	0.063
Death from any cause	20 (2.2%)	0 (0.0%)	20 (2.8%)	0.020
Cardiac death	12 (1.3%)	0 (0.0%)	12 (1.7%)	0.069
Non-cardiac death	8 (0.9%)	0 (0.0%)	8 (1.1%)	0.10
Myocardial infarction	4 (0.5%)	0 (0.0%)	4 (0.6%)	0.29
Q wave MI	-	-	-	
Non-Q wave MI	4 (0.5%)	0 (0.0%)	4 (0.6%)	0.29
Repeat revascularization	53 (6.0%)	9 (4.7%)	44 (6.4%)	0.40
Target vessel	33 (3.8%)	4 (2.0%)	29 (4.2%)	0.18
Target lesion	22 (2.5%)	0 (0.0%)	22 (3.2%)	0.013
Definite or probable stent thrombosis	1 (0.1%)	0 (0.0%)	1 (0.2%)	0.60

*Event rates are shown as Kaplan-Meier estimates (percentage and number of events).
MACE: major adverse cardiac event, MI: myocardial infarction.

confidence interval [CI], 1.48 to 15.23; p = 0.009), cerebrovascular accidents (CVA) (HR, 2.39; 95% CI, 1.21 to 4.72; p = 0.012), renal failure (HR, 3.75; 95% CI, 1.59 to 8.82; p = 0.003), left main lesions (HR, 2.24; 95% CI, 1.02 to 4.92; p = 0.044), and taking aspirin (HR, 0.27; 95% CI, 0.10 to 0.75; p = 0.012) had a high correlation to the clinical outcome in the multivariate analysis.

Discussion

The main findings of this well-managed registry were: (1) off-label EES use tended to slightly increase the risk of 2-year MACE as compared to on-label use; in addition, (2) the event rate of TLR was significantly higher for the off-label EES implantations; (3) although the patients in the off-label group had a higher risk, the overall 2-year clinical outcomes of the overall enrolled patients were acceptable; and (4) in the multivariate analysis, a history of a CABG and CVA, renal failure, and left main lesions were associated with MACE in the patients with an EES implantation.

The US Food and Drug Administration approved DES when a reasonable assurance existed that DES could be used safely and effectively in a specific patient population. Those patient populations were defined by the well-defined criteria, termed 'on-label'. However, in real-world clinical practice, the application of DES has been extended beyond the on-label indications, based on the assumptions that benefits extend to more complex patients and lesion subsets.

Previous studies of Drug-Eluting Stent

Previous studies showed that the off-label use of DES was associated with a higher risk of death, MI, and/or repeat revascularization procedures [10-12]. The D.E.S. cover Registry [10] is a prospective, multicenter, observation study of patients treated with

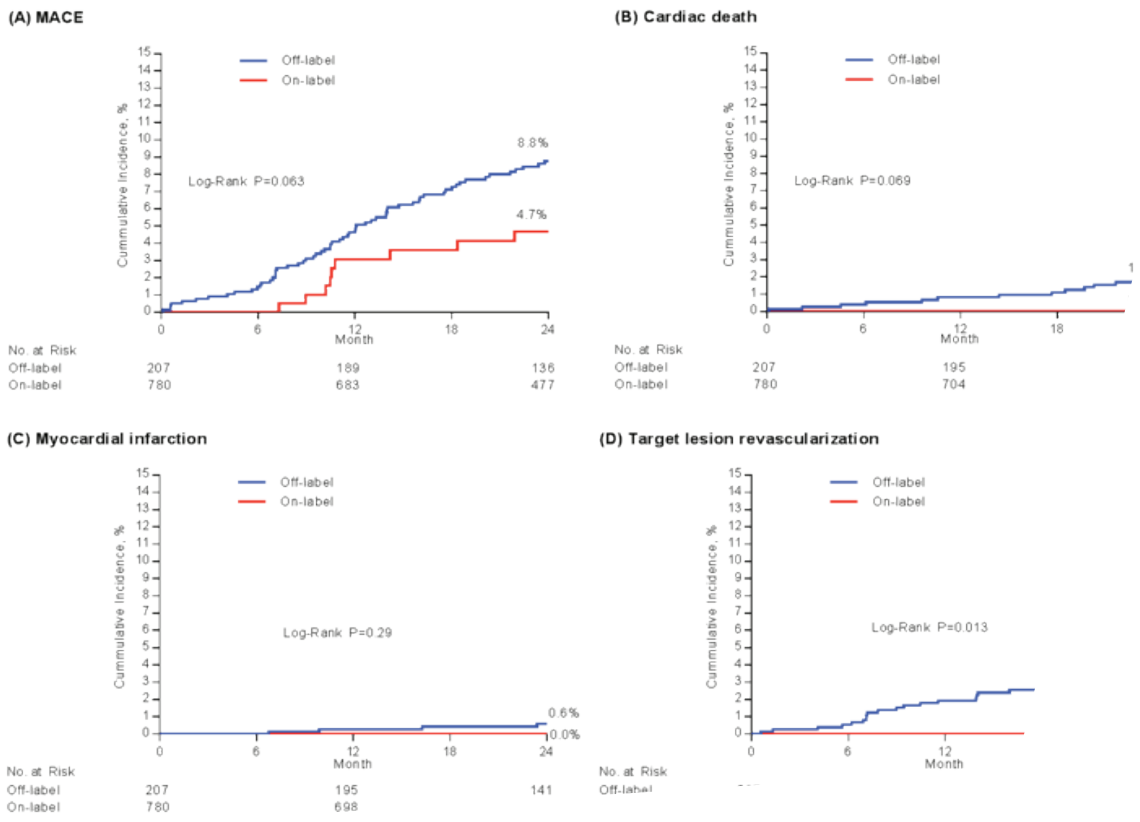

Fig. 2. Kaplan-Meier curves for adverse events according to on- and off-label everolimus-eluting stent use. In each figure, the cumulative-incidence curves are shown for the major adverse cardiac events (MACE) stratified by on- and off-label use (Panel A), cardiac death (Panel B), myocardial infarction (Panel C), and target lesion revascularization (Panel D). MACE was defined as a composite of deaths from any cause, myocardial infraction, or repeat revascularization.

sirolimus- (SES) and paclitaxel-eluting stents (PES). This study reported that significantly higher rates of TVR were associated with off-label use (adjusted HR, 1.49; 95% CI, 1.13 to 1.98; p = 0.005). Another registry of SES and PES reported that the off-label use of DES is associated with a higher rate of adverse outcomes compared with on-label use (17.5% vs. 8.9%, $p < 0.001$) [11]. In one prospective registry of patients treated with SES [12], the incidence of TLR and MACE at 1 year was substantially greater among the off-label use compared with the on-label use (9.2% vs. 3.0%, p = 0.001 and 17.7% vs. 6.6%, $p <$ 0.001, respectively).

From the view point of second generation DES, in the large-scale SPIRIT III (Clinical Evaluation of the Xience V Everolimus Eluting Coronary Stent System in the Treatment of Patients With De Novo Native Coronary Artery Lesions III) trial [5], a second-generation EES compared with a PES resulted in a reduced angiographic late loss (0.14 mm vs. 0.28 mm, $p \leq 0.004$), non-inferior rates of target vessel failure (7.2% vs. 9.0%, $p < 0.001$), and fewer MACE (6.0% vs. 10.3%, p = 0.02) during 1 year of follow-up. Likewise, in the COMPARE (Second-Generation

Table 4. Univariate and multivariate Cox proportional hazard analysis for major adverse cardiac events in the enrolled patients

Variable	Univariate		Multivariate	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Renal failure	4.38 (1.90-10.10)	0.001	3.75 (1.59-8.82)	0.003
Previous CABG	4.13 (1.30-13.14)	0.016	4.75 (1.48-15.23)	0.009
Previous CVA	2.72 (1.39-5.30)	0.003	2.39 (1.21-4.72)	0.012
Left main lesion	2.00 (0.92-4.37)	0.081	2.24 (1.02-4.92)	0.044
Diabetes mellitus	1.77 (1.10-2.82)	0.018	*	
Aspirin	0.29 (0.11-0.80)	0.017	0.27 (0.10-0.75)	0.012
ADP receptor antagonist	0.32 (0.12-0.87)	0.026	*	
Statin	0.65 (0.40-1.06)	0.085	*	

*Not retained as an independent predictor in the multivariate analysis.
HR: hazard ratio, CABG: coronary-artery bypass grafting, CVA: cerebrovascular accident, ADP: adenosine diphosphate.

Everolimus-Eluting and Paclitaxel-Eluting Stents in Real-Life Practice) trial [13], EES was superior to PES in unselected patients in terms of MACE (5% vs. 8%, $p = 0.005$). These trials demonstrated that EES was safer and more efficacious than PES. Considering that the current study was a 2-year clinical outcome that included an off-label use as an EES-specific all-comer registry, we found that the clinical outcome of our cohort was similar compared to the previous studies.

On-label vs. Off-label use in Second-generation DESs

Analyses of the clinical outcomes following off-label use of second-generation DES have been performed in a few studies [14-16]. In one registry of patients treated with the second-generation Endeavor Resolute® DES, implantation of a DES for off-label indications showed an excellent safety and efficacy [15]. Another study proved zotarolimus-eluting stent and EES were safe and effective, regardless of the complexity, with similar clinical and angiographic outcomes for both stent types through 1 year [16]. Latib et al. reported that in unrestricted daily practice, EES was implanted predominantly for off-label indications and associated with a relatively low rate of MACE and TLR [14].

In the present study, we sought the clinical follow-up data in a Korean population regarding EES in patients with on- and off-label uses and compared the clinical outcomes over a period of 2-years. In our analysis, the rates of 2-year MACE for the off-label EES implantations tended to slightly be higher than that for on-label EES implantations without any statistical significance. Further, the 2-year TLR rate was significantly higher in the patients with an off-label EES use. The higher rate of TLR can be explained by the fact that these patients had a greater number of lesions treated and most of those were complex, justifying a higher rate of re-intervention. As in the other studies mentioned above, off-label EES implantations were also performed in a large

number of patients in the current study, which represented real practice. Although the patients in the off-label group had a higher risk, the overall 2-year clinical outcomes of the overall enrolled patients were acceptable.

Predictors of MACE

A previous study reported that the patient factors such as diabetes mellitus (DM), a low ejection fraction, and chronic kidney disease, were important factors in the second-generation DES era [17]. In a report from the EVENT (Evaluation of Drug Eluting Stents and Ischemic Events) registry, renal function was an independent and powerful predictor of bleeding and ischemic complications in the era of DES [18]. Left main coronary disease is a well-known predictor of the outcome in patients undergoing PCI [19]. The present analysis was consistent with the other clinical results. In our study, a previous CABG and CVA, renal failure, and left main lesions significantly increased the risk of 2-year MACE in the enrolled patients.

Study Limitations

Several limitations of our study should be considered. First, because of the observational nature of this analysis, the overall results should be considered as hypothesis-generating only. Second, the analysis of the clinical outcome was limited to 2-years after the index PCI, because of the study protocol. Our study was not able to make any conclusions regarding the very long-term prognosis of over 2-years. Third, because the data were from an observational registry, the clinical events may not have been captured with scrutiny, and the patient follow-up may not have been as strict as it would be in a randomized trial. This may have been the reason for the low event rates, especially the rate of target MI, which was much lower in our study than in the previous randomized controlled trial and pooled analysis. Although we used the Korean national database using a citizen registration number that is unique to each individual, we cannot exclude the possibility of under-reporting of clinical outcomes in the patients who were lost to follow-up but are still alive. Despite these shortcomings, our data showed a high follow-up rate compared with the other Korean registry, which was a meaningful value.

Conclusions

In all-comer patients, 2-year MACE after EES implantation was approximately 8%, which might be acceptable. Off-label use of EES was frequently performed in real world practice. Although the off-label use of EES was not statistically associated with the increased risk of MACE, the TLR rate was higher in the off-label group, suggesting that physicians need to pay attention to high risk patients with the use of EES.

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