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Clinical Investigations

Three-Year Clinical Outcomes With the Cilotax Dual Drug-Eluting Stent vs Everolimus-Eluting Stents in Patients With Acute Myocardial Infarction

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Abstract

Background: This study compared the safety and effectiveness of paclitaxel/cilostazol–eluting Cilotax stents with those of everolimus-eluting stents in patients with acute myocardial infarction. Real-world data from the Korea Acute Myocardial Infarction Registry were examined.

Methods: A total of 5,472 patients with acute myocardial infarction underwent percutaneous coronary intervention with Cilotax stents (n = 212) or everolimus-eluting stents (n = 5,260). The primary end point was the 3-year rate of target lesion failure. The other end points were major adverse cardiovascular events (a composite of cardiac death, target vessel myocardial infarction, and ischemia-driven target lesion revascularization), target vessel revascularization, and stent thrombosis. A propensity score matching analysis was performed to adjust for potential confounders by using a logistic regression model; propensity score matching generated 2 well-balanced groups (Cilotax group, n = 180; everolimus-eluting stents group, n = 170; N = 350). After propensity score matching, baseline clinical characteristics were similar between the groups.

Results: After percutaneous coronary intervention, compared with the everolimus-eluting stents group, the Cilotax group more often had major adverse cardiovascular events (24.1% vs 18.5%; $P = .042$), myocardial infarction (8.0% vs 3.2%; $P < .001$), target lesion revascularization (8.0% vs 2.6%; $P < .001$), target vessel revascularization (11.3% vs 4.5%; $P < .001$), and stent thrombosis (4.7% vs 0.5%; $P < .001$) before matching. Even after matching, the Cilotax group had more frequent target lesion revascularization (9.4% vs 2.9%; $P = .22$) and stent thrombosis (5.6% vs 1.2%; $P = .34$).

Conclusion: In patients with acute myocardial infarction who underwent percutaneous coronary intervention, use of the Cilotax stent was associated with higher rates of target lesion revascularization, target vessel revascularization, and stent thrombosis than were everolimus-eluting stents. Use of the Cilotax dual drug-eluting stent should be avoided in the treatment of myocardial infarction.

Keywords: Myocardial infarction; drug-eluting stents; percutaneous coronary intervention

Introduction

For patients undergoing percutaneous coronary intervention (PCI), the use of drug-eluting stents (DESs) has improved clinical and angiographic outcomes beyond those obtained with bare-metal stents.[1-3] Although DESs have

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greater clinical efficacy than bare-metal stents, some studies have associated first-generation DESs (ie, sirolimus-eluting stents and paclitaxel-eluting stents [PESs]) with higher rates of late stent thrombosis. Studies have also associated first-generation DESs with a high rate of late restenosis in the treatment of patients with acute coronary syndrome and stable coronary artery disease (CAD), even during long-term follow-up after the index procedure.[4,5] In contrast, second-generation DESs, which use more advanced stent technology, have shown promise in improving clinical outcomes not only for patients with stable CAD but also for patients with acute myocardial infarction (AMI).[6-8]

In an attempt to improve DESs beyond the first-generation and second-generation models, a stent that elutes 2 drugs (Cilotax; Osstem Cardiotec Co, Ltd) has been developed and has shown acceptable results.[9] This stent, called the Cilotax stent, was designed to increase the antiproliferative effect of paclitaxel and reduce thrombogenicity by incorporating the antiplatelet agent cilostazol (Fig. 1). This study investigated the effectiveness and safety of the Cilotax stent by comparing its 3-year clinical outcomes with those of everolimus-eluting stents (EESs) in patients with AMI who underwent PCI. This study used real-world data from the Korea Acute Myocardial Infarction Registry.

Key Points

- This study is a multicenter registry study that examined Korean patients with MI. The results represent real-world evidence.
- In the treatment of patients with MI, the Cilotax stent, a dual DES, produced inferior clinical outcomes to those of an EES. Cilotax recipients had higher cumulative incidence rates of TLR, TVR, and stent thrombosis for up to 3 years after stent placement, before and after PSM analysis.
- The 3-year cumulative incidence rates of major adverse cardiac events and other individual hard end points did not differ between groups before or after PSM analysis.

Abbreviations and Acronyms

AMI	acute myocardial infarction
CAD	coronary artery disease
DES	drug-eluting stent
EES	everolimus-eluting stent
PCI	percutaneous coronary intervention
PES	paclitaxel-eluting stent
PSM	propensity score matching
STEMI	ST-elevation myocardial infarction
TLF	target lesion failure
TLR	target lesion revascularization
TVR	target vessel revascularization

Patients and Methods

Study Population

In this a nonrandomized, multicenter, observational, retrospective cohort study, data were obtained from 5,472 patients with AMI enrolled in the Korea Acute Myocardial Infarction Registry, the largest multicenter nationwide registry of Korean patients with AMI. These patients underwent PCI at 15 institutions from November 2011 to June 2015.[10] Eligible patients were at least 18 years old at the time of hospital presentation and had to be admitted for an AMI, defined in accordance with current guidelines.[11,12]

The study team obtained written informed consent from each individual and provided a verbal explanation of study procedures; data collection began after patient enrollment. Patients were allocated to 1 of 2 groups based on stent type: patients who received the Cilotax stent (n = 212) and patients who received 1 of 2 EESs (XIENCE Prime [Abbott Vascular] or PROMUS Element [Boston Scientific]; n = 5,260). Three-year clinical follow-up was completed through face-to-face interviews, chart reviews, and phone calls. This study was conducted in accordance with the principles of the Declaration of Helsinki. Approval was obtained from the institutional review board of the corresponding author's institution.

Intervention and Medical Treatment

Stent implantation was performed according to the current guidelines and with standard interventional techniques. Patients were administered loading doses of either aspirin (200-300 mg), clopidogrel (300-600 mg), ticagrelor (180 mg), or prasugrel (60 mg) before the procedure. After sheath insertion at the arterial access site, weight-adjusted, unfractionated heparin was administered at a bolus dose of 100 U/kg, with an additional bolus given to maintain an activated clotting time of 250 to 300 seconds. Use of platelet glycoprotein IIb/IIIa receptor blockers in addition to heparin was left to the operator's discretion. Patients who underwent PCI received either aspirin (100 mg daily) with clopidogrel (75 mg daily), ticagrelor 180 mg, or prasugrel 60 mg because a dual-antiplatelet maintenance regimen longer than 12 months was recommended by their physicians. In-hospital and postdischarge medications included

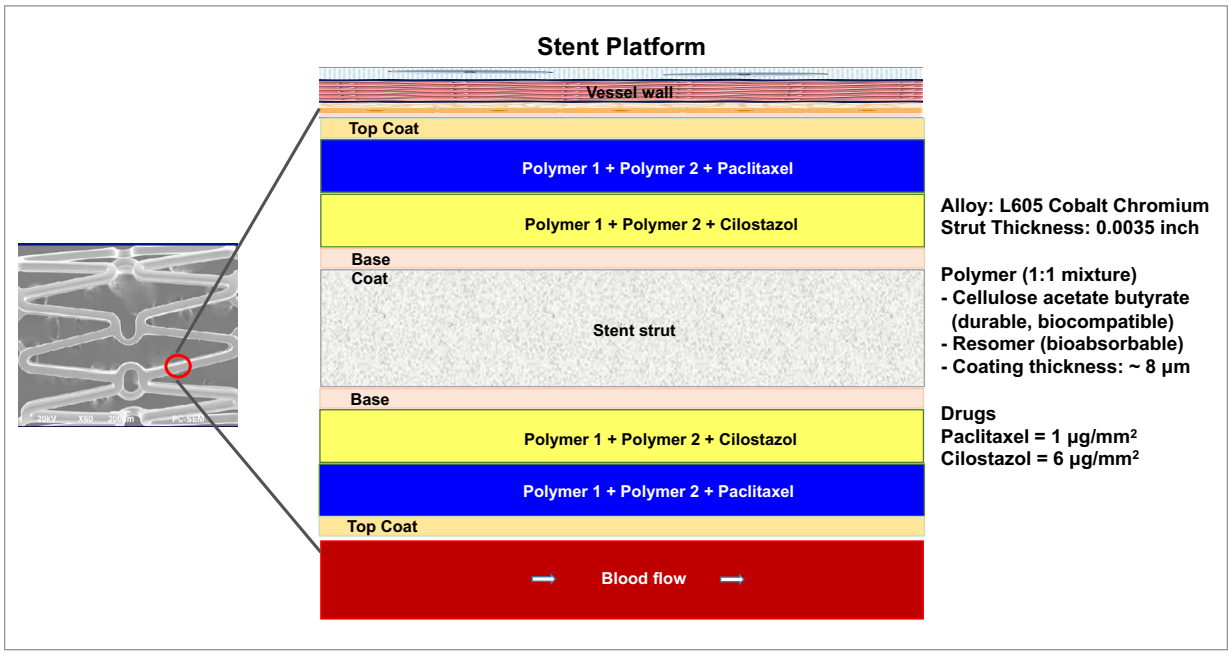

Fig. 1 A pictogram identifies the layers of the Cilotax stent platform.

aspirin, clopidogrel, ticagrelor, prasugrel, β-blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and lipid-lowering agents such as statins; use of these medications was recorded in a dedicated, computerized database along with other clinical information.

Study Definition and End Points

The main study end points were the 3-year rates of death from any cause, cardiac death, recurrent MI, coronary revascularization, stent thrombosis, target lesion failure (TLF), and major adverse cardiovascular events. Major adverse cardiovascular events were defined as the composite of all-cause death, MI, and stroke. Myocardial infarctions included ST-segment elevation MIs (STEMIs) and non-STEMIs, which were defined in accordance with current guidelines.[11,12] Coronary revascularization included target lesion revascularization (TLR), target vessel revascularization (TVR), and non-TVR during the 3-year clinical follow-up period. Target lesion failure was a composite of cardiac death, recurrent MI, and TLR. Target lesion revascularization was defined as a repeat intervention on the target lesion to control luminal stenosis within the same vessel segment treated during the index procedure. Target vessel revascularization was defined as any reintervention on the target vessel, on any segment of the target vessel, or on any segment of the target coronary artery. Non-TVR was defined as any reintervention in vessels other than the target vessel. The current consensus defines the incidence of stent thrombosis as acute (0-24 hours), subacute (24 hours to 30 days), late (1-12 months), and very late (>1 year).[13] The primary study end point was the 3-year incidence of TLF, and the secondary study end points were the other individual and composite clinical end points.

Statistical Analysis

For continuous variables, differences between the groups were evaluated by an unpaired *t* test; if the data did not have a normal distribution, a Mann-Whitney rank sum test was performed. Continuous data were summarized using mean (SD) values. Categorical data were summarized as numerical counts and percentages and were analyzed with χ^2 tests; if more than 20% of table cells had an expected frequency of less than 5, the Fisher exact test was performed between the groups as appropriate. Statistical significance was set at $P<.05$.

Propensity score matching (PSM) analysis was performed to adjust for potential confounders by using a logistic regression model. All available variables that could have been relevant were tested: age, male sex, differences in allocated hospitals, and cardiovascular risk factors (hypertension, diabetes, dyslipidemia, current smoking, and current alcohol consumption).

The propensity score was estimated with C statistics in the logistic regression model. The C statistic value was 0.710. Matching was performed by a 1:1 matching protocol without replacement (nearest-neighbor matching algorithm), with a caliper width equal to 0.02 of the SD of the logit of the propensity score.

A logistic regression model analysis was performed to estimate the risk of adverse events. After PSM, variables with $P<.20$ were adjusted to calculate the hazard ratio for minimizing biases. Various clinical outcomes were also estimated by the Kaplan-Meier method, and differences between the groups were compared using the log-rank test. For all analyses, 2-sided $P<.05$ were considered statistically significant. All statistical analyses were performed with SPSS Statistics 20 (IBM Corp).

Results

Between November 2011 and June 2015, a total of 5,472 patients with AMI underwent PCI with the Cilotax stent (n = 212) or an EES (n = 5,260) (Fig. 2). Propensity score matching analysis generated propensity-matched groups of Cilotax recipients (n = 180) and EES recipients (n = 170) (Table I).

Baseline Characteristics

The baseline clinical, laboratory, and angiographic characteristics of the patients are listed in Table I. Age, heart rate, cholesterol level, and the frequencies of male sex, non-STEMI, and hypertension were higher in the EES group than in the Cilotax group. The presence of current smokers, STEMI expression, and triglyceride levels were higher in the Cilotax group than in the EES group. Ticagrelor and angiotensin receptor blockers were more frequently used in the EES group than in the Cilotax group. In contrast, angiotensin-converting enzyme inhibitors and clopidogrel were more frequently used in the Cilotax group than in the EES group. In the angiographic and procedural results, the EES group more commonly had disease of the left main and left anterior descending arteries. Both stent length and the total number of stents placed were greater in the EES group than in the Cilotax group.

In the PSM analysis, the baseline clinical, laboratory, and angiographic characteristics of the 2 PSM groups were similar for all measured criteria ($P>.05$ for all). Some baseline clinical characteristics could not be perfectly matched with a standardized mean difference less than 0.1 even after PSM analysis, but the differences were not considered to have enough clinical significance to affect the results.

Three-Year Clinical Outcomes

The 3-year clinical outcomes are presented in Table II. Before PSM analysis, the incidence of TLF, the primary study end point, was similar between the groups. The incidence rates of major adverse cardiovascular events, MI (both STEMI and non-STEMI), revascularization (TLR, TVR, and non-TVR), and stent thrombosis, however, were higher in the Cilotax group than in the EES group. The all-cause death rate was higher in the EES group than in the Cilotax group, but the cardiac death rate did not differ significantly between groups.

After PSM analysis was performed to control for confounding variables, the incidence rates of hard clinical end points such as all-cause death and cardiac death were not different between the groups; however, the 3-year incidence rates of revascularization, TLR, TVR, and stent thrombosis remained higher in the Cilotax group than in the EES group even after PSM. The TLF rate did not differ between the groups before or after PSM analysis. During the follow-up period, the cumulative incidence of TLR, TVR, and stent thrombosis was higher in the Cilotax group than in the EES group even though the incidence rates of cardiac death and STEMI were not significantly different between the groups (Table II and Fig. 3).

Discussion

This study of patients with AMI undergoing PCI with DESs had 2 main findings. First, the cumulative 3-year incidence rates of TLR, TVR, and stent thrombosis were higher in the Cilotax group than in the EES group before and after PSM analysis. Second, and in contrast, the cumulative 3-year incidence rates of TLF, major adverse cardiovascular events, and other individual end points such as cardiac death were not different between the groups before or after PSM analysis.

It has been established that newer-generation DESs are superior to first-generation DESs in treating CAD.[14] A comparative study on the efficacy and safety of PESs and EESs in patients with MI reported that EESs were superior.[15] Many studies have proven that second-generation DESs are safer and more efficacious than first-generation DESs in treating patients with CAD, even patients who present with AMI.[16,17] The accumulated data from randomized controlled studies to date

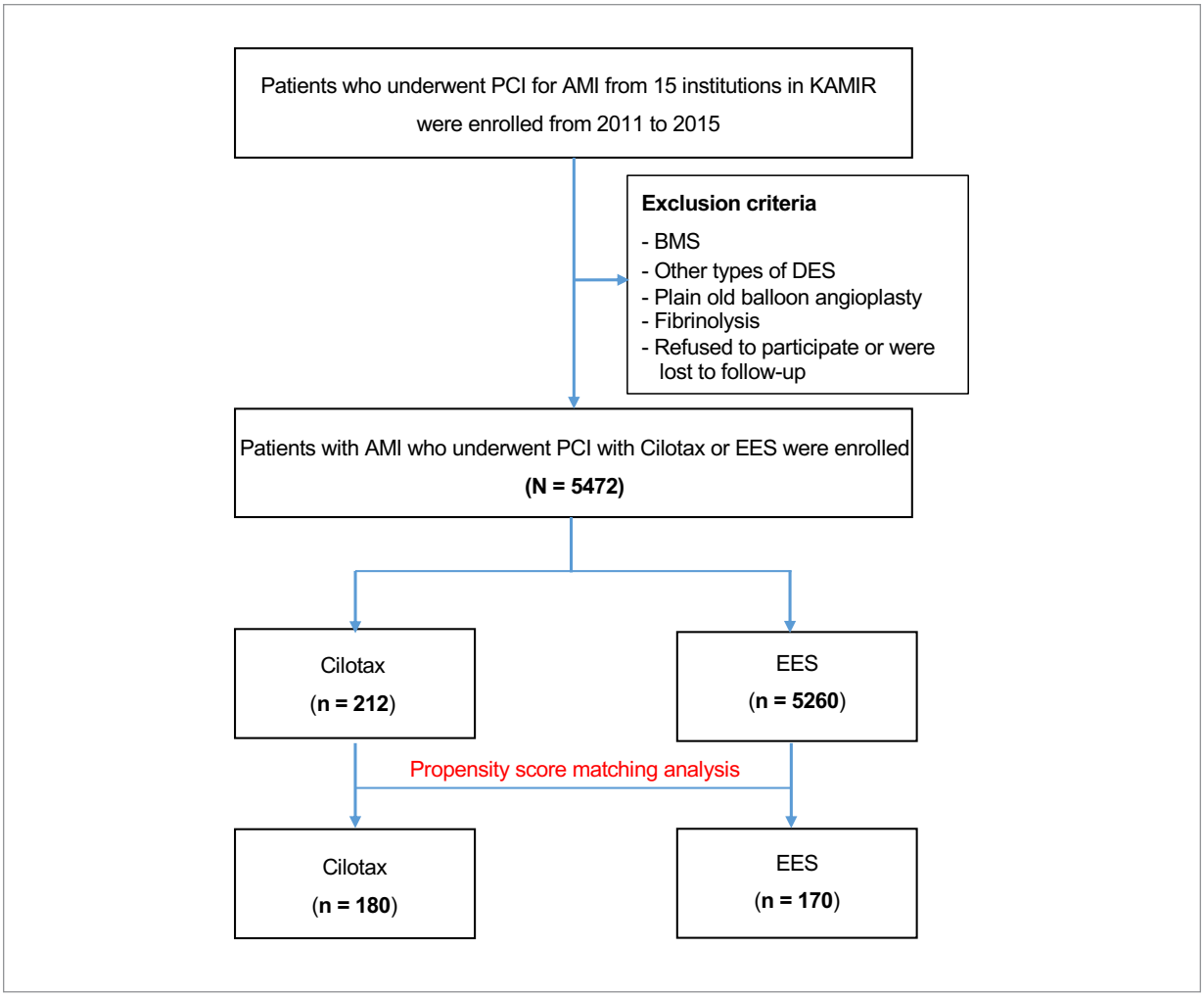

Fig. 2 A study flow chart demonstrates the individual steps of enrollment and analysis in this study.

AMI, acute myocardial infarction; BMS, bare-metal stent; Cilotax, Cilotax stent; DES, drug-eluting stent; EES, everolimus-eluting stent; KAMIR, the Korea Acute Myocardial Infarction Registry; PCI, percutaneous coronary intervention.

also show that second-generation DESs are better than first-generation DESs for the treatment of MI and stable CAD.[18] Despite remarkable clinical outcomes with the development of newer-generation DES technologies, the problem of stent thrombosis related to delayed endothelialization must be solved to improve the clinical outcomes of revascularization.[19]

To improve the clinical outcomes of PCI by preventing posttreatment restenosis and stent thrombosis, the Cilotax stent was developed by a South Korean company to increase the antiproliferative activity and antiplatelet effect of PESs by adding cilostazol.[9,20] The stent platform consists of a thin-strut tube stent (77 μm) manufactured from L605 cobalt chromium, and the drug-carrying polymers comprise a mixture of hydrophilic, biocompatible cellulose acetate butyrate and bioabsorbable RESOMER polymers (Evonik Industries AG) (Fig. 1). Most of the incorporated paclitaxel (1 μm/mm^2) is released within 1 month of stent placement, and most of the incorporated cilostazol (6 μm/mm^2) is released within 6 months of stent placement (Fig. 1).

There have been only 2 previous clinical studies of the Cilotax stent, so it is difficult to completely guarantee the safety and efficacy of the Cilotax stent in treating CAD, including in patients with AMI, despite the promising results of these studies.[9,21] The first trial showed better clinical outcomes with the Cilotax stent than with a PES stent when it came to lowering the risk of late lumen loss

TABLE I. Baseline Clinical, Angiographic, and Procedural Characteristics of Patients With Acute Myocardial Infarction, by Stent Type

	All patients				Propensity-matched patients			
Characteristic	Cilotax stent n=212	EES n=5,260	*P* value	Standardized mean difference	Cilotax stent n=180	EES n=170	*P* value	Standardized mean difference
Male sex, No. (%)	174 (82.1)	3,968 (75.4)	.027	−0.75	145 (80.6)	132 (77.6)	.50	−0.33
Age, mean (SD), y	60.1 (12.8)	64.2 (12.3)	<.001	−0.33	60.7 (12.9)	60.8 (12.7)	.95	−0.01
Blood pressure, mean (SD), mm Hg								
Systolic	133 (28)	130 (27)	.22	0.09	132 (28)	133 (30)	.78	−0.03
Diastolic	79 (17)	79 (16)	.88	−0.01	79 (17)	80 (19)	.50	−0.07
Heart rate, mean (SD), beats/min	76 (18)	79 (19)	.036	−0.15	76 (19)	78 (19)	.45	−0.08
Body mass index, mean (SD)	24.3 (3.4)	24.0 (3.3)	.24	0.08	24.3 (3.2)	24.2 (3.0)	.60	0.06
Left ventricular ejection fraction, mean (SD), %	51.3 (11.6)	51.4 (10.7)	.82	−0.02	51.6 (11.6)	50.2 (11.2)	.27	0.12
Final diagnosis, No. (%)								
STEMI	171 (80.7)	2,746 (52.2)	<.001	−3.50	139 (77.2)	130 (76.5)	.86	−0.09
Non-STEMI	41 (19.3)	2,514 (47.8)	<.001	4.92	41 (22.8)	40 (23.5)	.86	0.16
Hypertension, No. (%)	91 (42.9)	2,652 (50.4)	.032	1.10	81 (45.0)	81 (47.6)	.62	0.39
Type 2 diabetes, No. (%)	48 (22.6)	1,487 (28.3)	.07	1.12	42 (23.3)	40 (23.5)	.96	0.04
Dyslipidemia, No. (%)	24 (11.3)	589 (11.2)	.95	−0.04	21 (11.7)	19 (11.2)	.88	−0.15
Stroke, No. (%)	11 (5.2)	300 (5.7)	.75	0.22	10 (5.6)	12 (7.1)	.56	0.60
Smoking history, any, No. (%)	126 (59.4)	3,100 (58.9)	.88	−0.07	109 (60.6)	103 (60.6)	.99	0.00
Current smoker	110 (51.9)	2,084 (39.6)	<.001	−1.82	94 (52.2)	86 (50.6)	.76	−0.23
Ex-smoker	16 (7.5)	1,016 (19.3)	<.001	3.21	15 (8.3)	17 (10.0)	.58	0.55
Multivessel disease, No. (%)	124 (58.5)	2,840 (54.0)	.19	−0.60	101 (56.1)	88 (51.8)	.41	−0.59
Diseased vessels, mean (SD), No. (%)	1.8 (0.8)	1.8 (0.8)	.18	0.09	1.8 (0.8)	1.8 (0.8)	.77	0.03
Left main artery	1 (0.5)	204 (3.9)	.01	2.31	1 (0.6)	0 (0.0)	.33	−1.05
Left anterior descending coronary artery	114 (53.8)	3,196 (60.8)	.041	0.93	97 (53.9)	95 (55.9)	.70	0.27
Left circumflex coronary artery	47 (22.2)	1,451 (27.6)	.08	1.09	42 (23.3)	41 (24.1)	.86	0.16

Continued

TABLE I. Baseline Clinical, Angiographic, and Procedural Characteristics of Patients With Acute Myocardial Infarction, by Stent Type, continued

	All patients				Propensity-matched patients			
Characteristic	Cilotax stent n=212	EES n=5,260	*P* value	Standardized mean difference	Cilotax stent n=180	EES n=170	*P* value	Standardized mean difference
Right coronary artery	88 (41.5)	2,155 (41.0)	.87	−0.08	74 (41.1)	64 (37.6)	.50	−0.55
Stents used, mean (SD), No. (%)	1.1 (0.3)	1.2 (0.4)	<.001	−0.26	1.1 (0.3)	1.1 (0.3)	.99	0.00
Maximum stent diameter, mean (SD), mm	3.1 (0.3)	3.2 (0.4)	.50	−0.04	3.1 (0.3)	3.1 (0.4)	.99	0.00
Total stent length, mean (SD), mm	24.8 (8.7)	31.2 (14.0)	<.001	−0.55	25.5 (9.1)	25.0 (10.4)	.64	0.05
Laboratory findings, mean (SD)								
Total cholesterol, mg/dL	188 (51)	180 (45)	.015	0.16	185 (42)	184 (39)	.85	0.02
Triglycerides, mg/dL	151 (124)	135 (111)	.045	0.14	146 (125)	146 (110)	.99	0.00
High-density lipoprotein cholesterol, mg/dL	42 (18)	43 (12)	.64	−0.03	42 (19)	43 (11)	.54	−0.07
Low-density lipoprotein cholesterol, mg/dL	111 (36)	114 (40)	.31	−0.09	114 (36)	108 (36)	.19	0.16
Hemoglobin A_{1c}, %	6.4 (1.4)	6.5 (1.5)	.42	−0.08	6.4 (1.2)	6.5 (1.6)	.48	−0.10
Discharge medications, No. (%)								
Aspirin	209 (98.6)	5,151 (97.9)	.50	−0.07	178 (98.9)	167 (98.2)	.60	−0.07
Clopidogrel	166 (78.3)	3,514 (66.8)	<.001	−1.35	138 (76.7)	125 (73.5)	.49	−0.36
Cilostazol	14 (6.6)	500 (9.5)	.15	1.02	13 (7.2)	11 (6.5)	.78	−0.29
Prasugrel	16 (7.5)	517 (9.8)	.27	0.77	14 (7.8)	12 (7.1)	.79	−0.26
Ticagrelor	26 (12.3)	1,112 (21.1)	.002	2.17	25 (13.9)	29 (17.1)	.41	0.81
Calcium channel blockers	3 (1.4)	308 (5.9)	.006	2.33	3 (1.7)	2 (1.2)	.69	−0.41
β-blockers	193 (91.0)	4,453 (84.7)	.011	−0.68	161 (89.4)	144 (84.7)	.18	−0.51
Renin-angiotensin system inhibitors	171 (80.7)	4,226 (80.3)	.90	−0.04	150 (83.3)	128 (75.3)	.06	−0.91
Angiotensin receptor blockers	23 (10.8)	1,634 (31.1)	<.001	4.42	23 (12.8)	21 (12.4)	.90	−0.12
Angiotensin-converting enzyme inhibitors	151 (71.2)	2,626 (49.9)	<.001	−2.75	130 (72.2)	108 (63.5)	.08	−1.06
Statins	199 (93.9)	4,873 (92.6)	.50	−0.13	168 (93.3)	157 (92.4)	.72	−0.10

EES, everolimus-eluting stent; STEMI, ST-elevation myocardial infarction.

P < .05 was considered statistically significant.
To convert mm Hg to kPa, multiply by 0.133.
To convert cholesterol values from mg/dL to mmol/L, multiply by 0.0259.
To convert triglyceride values from mg/dL to mmol/L, multiply by 0.0113.
To convert glycated hemoglobin from a percentage to a proportion of total hemoglobin, multiply by 0.01.

TABLE II. Clinical Outcomes of Patients With Acute Myocardial Infarction, by Stent Type

	All patients				Propensity-matched patients			
Variable	Cilotax stent, No. (%) n = 212	EES, No. (%) n = 5,260	Hazard ratio (95% CI)	*P* value	Cilotax stent, No. (%) n = 180	EES, No. (%) n = 170	Hazard ratio (95% CI)	*P* value
In-hospital death	3 (1.4)	169 (3.2)	0.43 (0.13-1.36)	.14	2 (1.1)	3 (1.8)	0.81 (0.11-5.68)	.83
Cardiac death	3 (1.4)	140 (2.7)	0.52 (0.16-1.66)	.26	2 (1.1)	3 (1.8)	0.81 (0.11-5.68)	.83
Noncardiac death	0 (0.0)	29 (0.6)[a]	0.96 (0.95-0.96)	.27	0 (0.0)	0 (0.0)	–	–
3-year follow-up								
Major adverse cardiovascular event	51 (24.1)	973 (18.5)	1.39 (1.01-1.92)	.042	44 (24.4)	35 (20.6)	1.33 (0.79-2.22)	.27
TLF	25 (11.8)	488 (9.3)	1.30 (0.85-2.00)	.21	24 (13.3)	15 (8.8)	1.74 (0.85-3.53)	.12
All-cause death	10 (4.7)	515 (9.8)	0.45 (0.24-0.86)	.014	9 (5.0)	15 (8.8)	0.64 (0.26-1.56)	.33
Cardiac death	8 (3.8)	351 (6.7)	0.54 (0.26-1.12)	.09	7 (3.9)	9 (5.3)	0.92 (0.31-2.70)	.88
Noncardiac death	2 (0.9)	164 (3.1)	0.29 (0.07-1.20)	.07	2 (1.1)	6 (3.5)	0.32 (0.06-1.66)	.17
MI	17 (8.0)	167 (3.2)	2.65 (1.58-4.46)	<.001	15 (8.3)	7 (4.1)	1.94 (0.76-4.92)	.16
STEMI	13 (6.1)	45 (0.9)	7.57 (4.01-14.25)	<.001	12 (6.7)	4 (2.4)	2.95 (0.92-9.48)	.06
Non-STEMI	4 (1.9)	122 (2.3)	0.80 (0.29-2.21)	.68	3 (1.7)	3 (1.8)	0.76 (0.14-3.97)	.75
Coronary revascularization	40 (18.9)	449 (8.5)	2.49 (1.74-3.56)	<.001	36 (20.0)	18 (10.6)	2.09 (1.13-3.86)	.018
Coronary artery bypass grafting	1 (0.5)	18 (0.3)	1.38 (0.18-10.38)	.75	1 (0.6)	1 (0.6)	0.80 (0.04-13.2)	.88
PCI	39 (18.4)	434 (8.3)	2.50 (1.74-3.59)	<.001	35 (19.4)	17 (10.0)	2.17 (1.16-4.06)	.015
TLR	17 (8.0)	136 (2.6)	3.28 (1.94-5.54)	<.001	17 (9.4)	5 (2.9)	3.33 (1.19-9.32)	.022
TVR	24 (11.3)	239 (4.5)	2.68 (1.71-4.18)	<.001	22 (12.2)	8 (4.7)	2.76 (1.19-6.44)	.018
Non-TVR	16 (7.5)	219 (4.2)	1.87 (1.10-3.18)	.017	14 (7.8)	10 (5.9)	1.19 (0.50-2.81)	.68
Stroke	3 (1.4)	104 (2.0)	0.71 (0.22-2.26)	.56	3 (1.7)	2 (1.2)	1.37 (0.22-8.47)	.73
Stent thrombosis	10 (4.7)	27 (0.5)	9.59 (4.58-20.09)	<.001	10 (5.6)	2 (1.2)	5.34 (1.13-25.2)	.034

EES, everolimus-eluting stent; MI, myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; TLF, target lesion failure (the composite of cardiac death, recurrent MI, and TLR); TLR, target lesion revascularization; TVR, target vessel revascularization.

[a] 0.6 is rounded from 0.55 to display the percentage to 1 decimal place.

P < .05 was considered statistically significant.

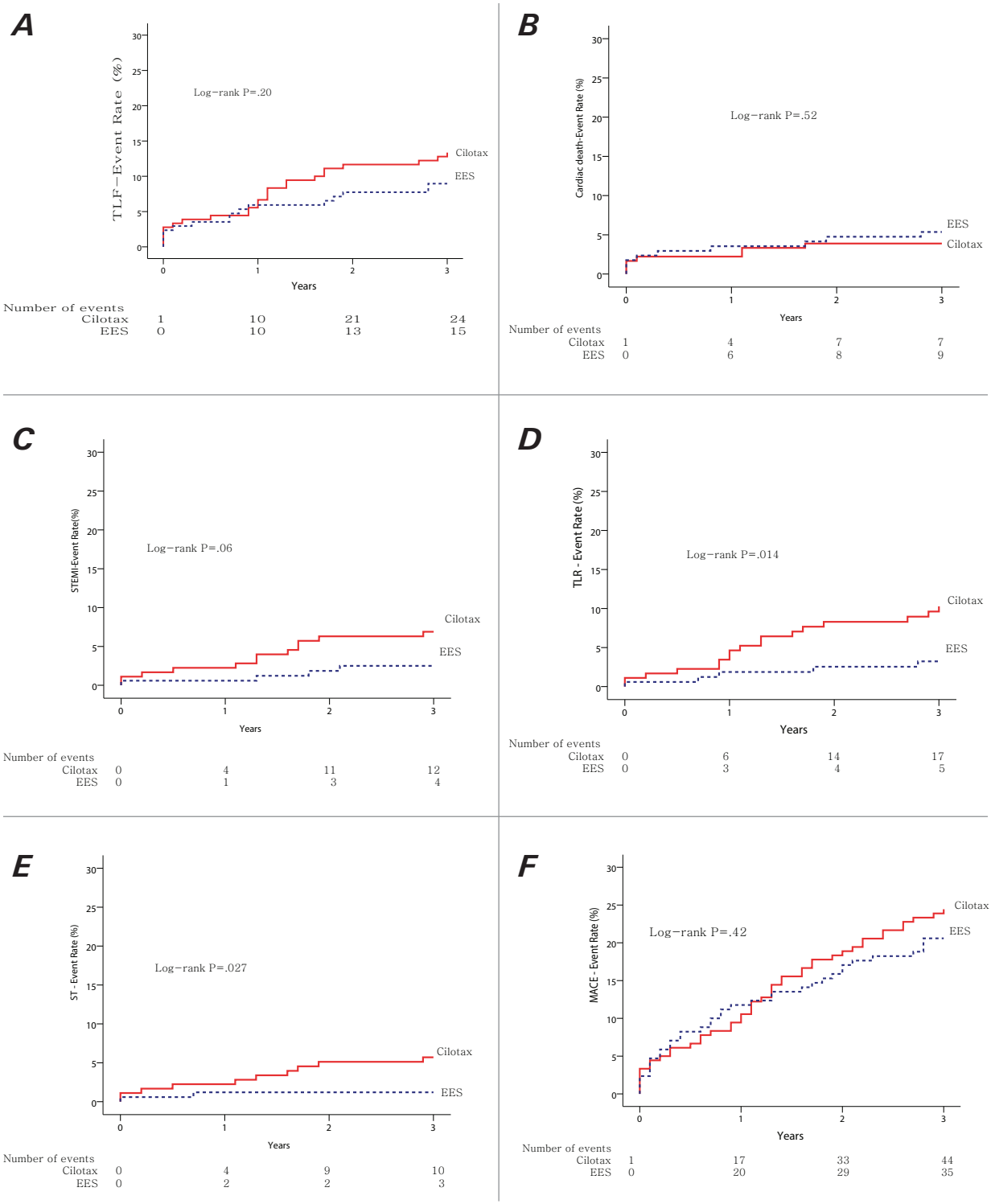

Fig. 3 Kaplan-Meier curves of 3-year clinical outcomes by stent type in propensity-matched patients estimate (**A**) the incidence of TLF, (**B**) the incidence of cardiac death, (**C**) the incidence of STEMI, (**D**) the incidence of TLR, (**E**) the incidence of stent thrombosis; and (**F**) the incidence of major adverse cardiac events.

Statistical significance was set at $P < .05$.

Cilotax, Cilotax stent; EES, everolimus-eluting stent; STEMI, ST-elevation myocardial infarction; TLF, target lesion failure (the composite of cardiac death, recurrent MI, and TLR); TLR, target lesion revascularization.

associated with late intimal proliferation.[9] That study, however, was limited by its small number of patients and by the use of the PES, a first-generation DES, for comparison. The other study, also a prospective observational study with a small number of patients, compared the next-generation model, the Cilotax DSR, which has a thinner strut than the existing Cilotax stent, with the previous-generation Cilotax stent.[21] This study was not randomized and had a small number of patients, making it difficult to interpret the results in terms of the efficacy and safety of the Cilotax stent in real-world practice, especially in high-risk subpopulations such as patients with AMI.

Stenting with DESs has been widely adopted as the most effective antirestenotic strategy to inhibit neointimal hyperplasia and re-endothelialization in coronary intervention areas, including in patients with AMI and acute coronary syndrome.[22] Despite the development of newer-generation stent technology, various mechanisms of restenosis and late thrombogenesis remain problematic.[23] The Cilotax stent used in this study was developed in Korea as a dual DES made by modifying the PES to elute cilostazol as well as paclitaxel. The intent was to use the antithrombotic and antiproliferative effects of cilostazol to enhance the safety and efficacy of the stent.[9,20,24] In the present study, the Cilotax stent was associated with a significantly higher rate of revascularization, including TLR and TVR, than the EES; however, the stent thrombosis rate was also significantly higher in the Cilotax group. This result was consistent even after PSM analysis.

In this study, the stent thrombosis rate in the Cilotax group was 5.6%. Considering that stent thrombosis rates reported in previous studies of second-generation DESs have been approximately 1%,[25] the stent thrombosis rate in Cilotax stents in this study can be considered extremely high. The increase in molecular weight to elute 2 drugs and the resulting thickening of the stent strut may have led to a higher stent thrombosis incidence rate than the rate associated with the EES. This outcome occurred despite the addition of cilostazol, which has antithrombotic properties.[26,27] There is little doubt that the delivery of 2 different drugs from a thin strut is key to the successful treatment of restenosis and stent thrombosis. More advances in stent technology and ideal drug-release kinetics also need to be made for dual DESs to be clinically useful. Despite the high rates of stent thrombosis and revascularization in the Cilotax group, there were no significant differences in cardiac death between the groups in this study (3.9% in the Cilotax group vs 5.3% in the EES group; $P = .88$). These results may have various complex causes, such as the underlying propensity of high-risk patients in the EES group, the gap between the groups in the number of enrolled patients, and the selection bias of the clinicians.

This study had some limitations. First, this study examined data from a multicenter observational registry, comparing the outcomes of the Cilotax stent and the EES in patients undergoing PCI for AMI. This resulted in several inconsistencies that could have affected the results: (1) different follow-up durations for each group, (2) differences among the institutions involved in this research, (3) an absence of uniform or routine follow-up with coronary angiography, and (4) more missing data than a randomized study would have had. Although PSM analysis was used in an effort to rigorously adjust for allocation bias and uneven distribution of risk factors, unmeasured variables were not controlled for, possibly resulting in differences in baseline clinical characteristics between groups. Second, the choice of stent was left to each operator's discretion, which could have affected clinical outcomes. For instance, the absolute number and relative number of patients and the number of high-risk patients in the EES group were high, which could have been the result of selection bias. Finally, the 3-year follow-up period was relatively short for determining long-term major clinical outcomes, especially hard end points such as cardiac death. A well-designed study with a longer follow-up period is therefore required.

Conclusion

This 3-year follow-up study showed that the Cilotax stent, which is designed as a dual DES, was associated with higher rates of TLR, TVR, and stent thrombosis than EESs in patients with AMI, even after adjustment for differences in baseline clinical characteristics with PSM analysis. Randomized studies with larger study cohorts, long-term follow-up, and routine follow-up imaging will be necessary to draw firm conclusions.

Article Information

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