Comparison of Dual Versus Triple Antiplatelet Therapy After Drug-Eluting Stent According to Stent Length (from the Pooled Analysis of DECLARE Trials)

Seung-Whan Lee, MD[a], Jong-Young Lee, MD[a], Jung-Min Ahn, MD[a], Duk-Woo Park, MD[a], Seungbong Han, MD[b], Yong Kyu Park, MD[a], Woo Seok Lee, MD[a], Jeong Yoon Jang, MD[a], Chang Hee Kwon, MD[a], Gyung-Min Park, MD[a], Young-Rak Cho, MD[c], Won-Jang Kim, MD[a], Soo-Jin Kang, MD[a], Young-Hak Kim, MD[a], Cheol Whan Lee, MD[a], Jae-Joong Kim, MD[a], Seong-Wook Park, MD[a], and Seung-Jung Park, MD, PhD[a,*]

There are no practical criteria for the use of triple antiplatelet therapy after drug-eluting stent (DES) implantation. In our present report, pooled analysis of 3 randomized studies in patients with diabetes mellitus (Drug-Eluting Stenting Followed by Cilostazol treatment reduces LAte Restenosis in patients with diabetes mellitus trial) and long coronary narrowings (Drug-Eluting Stenting Followed by Cilostazol Treatment Reduces Late Restenosis in Patients with Long Coronary Lesions trials I and II) compared triple (aspirin, clopidogrel, and cilostazol; triple group, n = 700) and dual antiplatelet therapies (aspirin and clopidogrel; dual group, n = 699) after DES implantation. Among pooled population (n = 1,399 patients), 1,173 patients with follow-up angiography were divided into 3 stent length categories (≤20, 20 to 40, and >40 mm). There was no statistical significance of in-stent restenosis (ISR) in ≤20- and 20- to 40-mm categories between 2 groups. However, ISR rate was significantly reduced in triple versus dual group in >40-mm stent length category (12.4% vs 22.1%, p = 0.008). In diabetic patients, triple group also showed significant reduction in the ISR rate in >40-mm stent length category (15.4% vs 32.3%, p = 0.003). According to postprocedural minimal lumen diameter, triple group showed a trend toward a lower ISR than that of the dual group in all categories (p = 0.033 for ≤2.5 mm, p = 0.087 for 2.5 to 3.0 mm, and p = 0.119 for >3.0 mm). In conclusion, the triple group had a significantly reduced ISR in patients with >40-mm stent length after DES implantation compared with the dual group. Therefore, this suggestion for use of triple antiplatelet therapy could be easily applied after DES implantation in routine clinical practice. **(Am J Cardiol 2013;112:1738−1744)**

Cilostazol, a phosphodiesterase III inhibitor, has antiproliferative effects, as shown by its ability to reduce angiographic restenosis rate after bare-metal and drug-eluting stent (DES) implantations.[1−5] We previously performed a randomized, multicenter, prospective study in which we reported that triple antiplatelet therapy (aspirin, clopidogrel, and cilostazol) reduced restenosis and subsequent repeat revascularization after first generation (sirolimus- [SES] and paclitaxel-eluting stents) or newer generation DES (Endeavor zotarolimus-eluting stent, Medtronic Vascular, Santa Rosa, California) implantation in diabetics (Drug-Eluting Stenting Followed by Cilostazol treatment reduces LAte Restenosis in patients with diabetes mellitus [DECLARE-DIABETES] trial) or patients with long lesion (Drug-Eluting Stenting Followed by Cilostazol Treatment Reduces Late Restenosis in Patients with Long Coronary Lesions [DECLARE-LONG] I and II trials).[1−3] Accordingly, we suggested that triple antiplatelet therapy is a valuable strategy in patients at high risk of restenosis after DES implantation. However, there remains doubt regarding which patients benefit most from triple antiplatelet therapy in terms of restenosis. Interventional cardiologists still hesitate to use cilostazol in daily clinical practice because there are no practical criteria for its use. From a practical point of view, implanted stent length is an easily applicable criteria for cilostazol use immediately after stenting. Therefore, to find appropriate use criteria of triple antiplatelet therapy based on the association between the length of the stented segment and the risk of angiographic restenosis after DES implantation, we analyzed follow-up angiographic outcomes of patients included in the DECLARE-DIABETES, -LONG I, and -LONG II trials.

Divisions of [a]Cardiology and [b]Biostatistics, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; and [c]Division of Cardiology, Department of Internal Medicine, Dong-A University College of Medicine, Busan, Korea. Manuscript received April 12, 2013; revised manuscript received and accepted August 14, 2013.

Drs. S.-W. Lee and J.-Y. Lee contributed equally to this study.

This study was supported by a grant A120711 from the Korea Healthcare Technology Research and Development Project, Ministry of Health and Welfare and the CardioVascular Research Foundation, Seoul, Republic of Korea.

See page 1744 for disclosure information.

*Corresponding author: Tel: (+82) 2-3010-4812; fax: (+82) 2-475-6898.

E-mail address: sjpark@amc.seoul.kr (S.-J. Park).

0002-9149/13/$ - see front matter
http://dx.doi.org/10.1016/j.amjcard.2013.08.008

Table 1
Baseline clinical characteristics

Variable	Restenosis		p
	Yes, n = 145 (%)	No, n = 1,028 (%)	
Triple antiplatelet therapy	53 (36.6)	533 (51.8)	0.001
Age (yrs)	61 ± 8	60 ± 9	0.271
Men	99 (68.3)	679 (66.1)	0.596
Hypertension	86 (59.3)	599 (58.3)	0.812
DM	83 (57.2)	534 (51.9)	0.232
Total cholesterol level of ≥200 mg/dl	46 (31.7)	355 (34.5)	0.504
Current smoker	49 (33.8)	330 (32.1)	0.683
Previous percutaneous coronary intervention	17 (11.7)	95 (9.2)	0.341
Previous coronary artery bypass surgery	0 (0)	11 (1.1)	0.378
Clinical diagnosis			0.484
Stable angina pectoris	65 (44.8)	473 (46.0)	
Unstable angina pectoris	61 (42.1)	388 (37.7)	
Acute myocardial infarction	19 (13.1)	167 (16.2)	
Left ventricular ejection fraction (%)	60 ± 9	60 ± 9	0.947
Multivessel coronary disease	70 (48.3)	560 (54.5)	0.161

Table 2
Angiographic characteristics and procedural results

Variable	Restenosis		p
	Yes, n = 145 (%)	No, n = 1,028 (%)	
DESs			<0.001
SES	14 (9.7)	372 (36.2)	
Paclitaxel-eluting stent	62 (42.8)	297 (28.9)	
Zotarolimus-eluting stent	69 (47.6)	359 (34.9)	
Target coronary artery			0.270
Left anterior descending	94 (64.8)	642 (62.5)	
Left circumflex	12 (8.3)	133 (12.9)	
Right coronary	39 (26.9)	253 (24.6)	
Maximal inflation pressure (atm)	15.4 ± 3.8	15.7 ± 3.6	0.372
Use of intravascular ultrasound	77 (53.1)	554 (53.9)	0.859
Use of glycoprotein IIb/IIIa inhibitor	2 (1.4)	20 (1.9)	0.781
Total stent length at the target lesion (mm)	44.1 ± 16.1	37.1 ± 13.5	<0.001
Multivessel coronary stenting	53 (36.6)	392 (38.1)	0.713
Number of used stents at the target lesion	1.69 ± 0.68	1.43 ± 0.58	<0.001
Procedure-related non–Q-myocardial infarction	9 (6.2)	98 (9.5)	0.220

Methods

The design, exclusion and inclusion criteria, and data collection of the DECLARE-DIABETES, -LONG I, and -LONG II trials have been previously described.[1–3] In brief, the 3 randomized studies included 1,399 patients (400 patients of the DECLARE-DIABETES trial, 500 of the DECLARE-LONG I trial, and 499 of the DECLARE-LONG II trial) aged ≥18 years with angina pectoris and/or

Table 3
Quantitative angiographic measurements

Variable	Restenosis		p
	Yes (n = 145)	No (n = 1,028)	
Reference diameter (mm)	2.82 ± 0.49	2.92 ± 0.43	0.038
Lesion length (mm)	38.6 ± 15.9	31.7 ± 12.9	<0.001
MLD (mm)			
In-segment			
Before procedure	0.76 ± 0.49	0.81 ± 0.48	0.200
After procedure	2.16 ± 0.53	2.26 ± 0.48	0.018
At follow-up	1.05 ± 0.49	2.15 ± 0.44	<0.001
In-stent			
After procedure	2.48 ± 0.44	2.59 ± 0.42	0.002
At follow-up	1.11 ± 0.57	2.31 ± 0.48	<0.001
Diameter stenosis (%)			
In-segment			
Before procedure	70.4 ± 14.6	70.4 ± 15.8	0.958
After procedure	19.2 ± 11.7	16.9 ± 11.1	0.033
At follow-up	62.8 ± 16.8	23.1 ± 12.1	<0.001
In-stent			
After procedure	9.4 ± 12.8	7.3 ± 12.8	0.089
At follow-up	59.8 ± 20.5	18.4 ± 15.4	<0.001
Acute gain (mm)			
In-segment	1.39 ± 0.63	1.45 ± 0.64	0.368
In-stent	1.72 ± 0.59	1.78 ± 0.59	0.225
Late loss (mm)			
In-segment	1.09 ± 0.58	0.12 ± 0.39	<0.001
In-stent	1.35 ± 0.59	0.28 ± 0.41	<0.001

Table 4
Predictors of angiographic restenosis on multivariate analysis

Variable	Odds Ratio	95% CI	p
Cilostazol	0.49	0.35–0.67	<0.001
SES	0.12	0.09–0.14	<0.001
DM	1.99	1.37–2.89	<0.001
Bifurcation lesion	1.33	1.17–1.52	<0.001
Stent length	1.03	1.02–1.04	<0.001
Postprocedural MLD	0.38	0.17–0.87	0.021

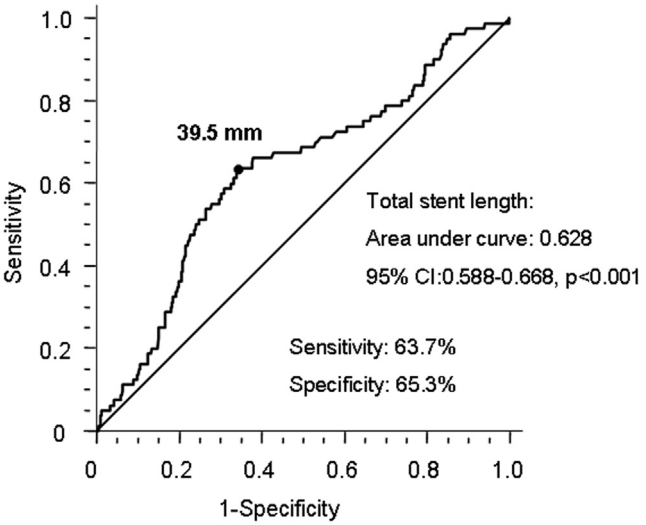

Figure 1. A receiver operating characteristic curve to identify stent length for predicting ISR.

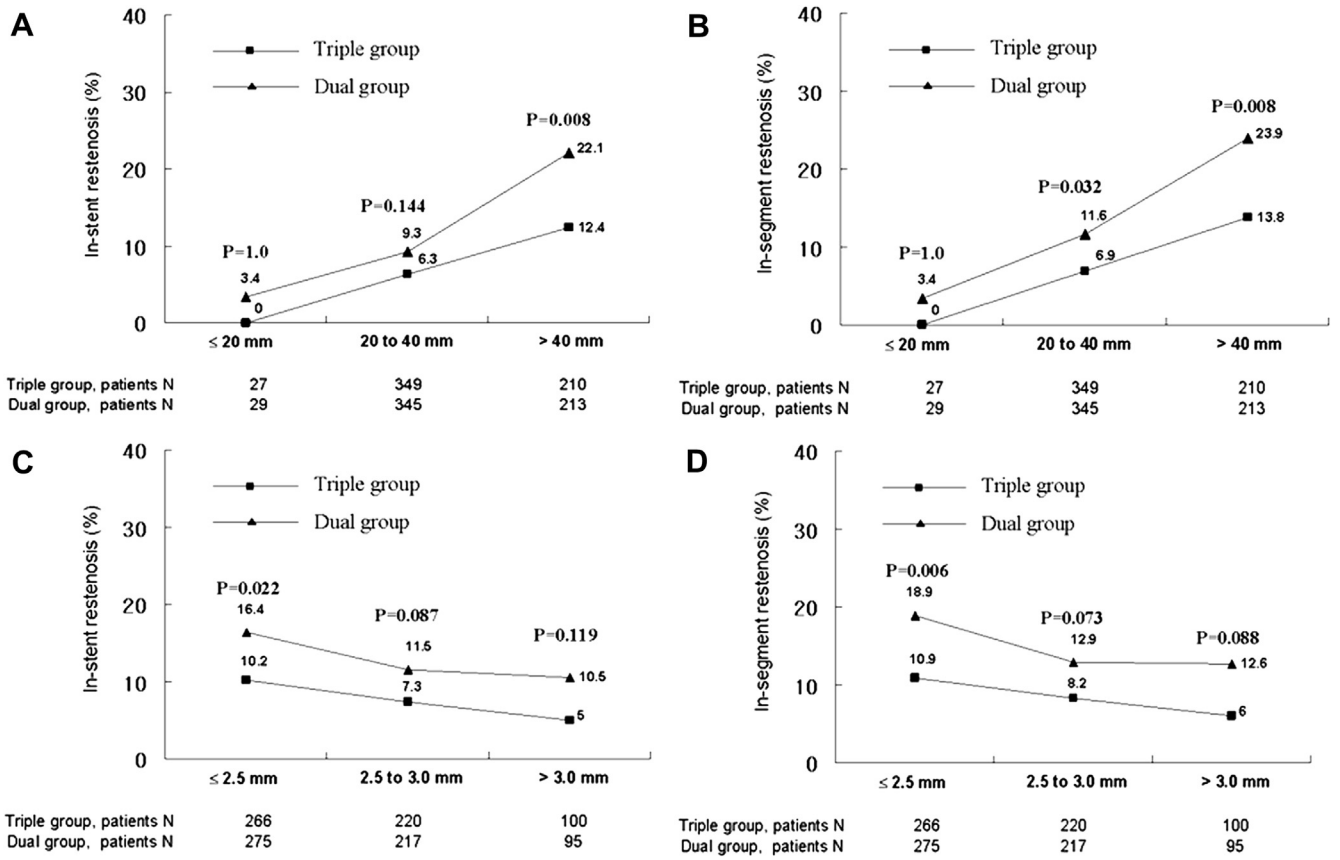

Figure 2. ISR *(A)* and in-segment restenosis *(B)* according to stent length between triple and dual antiplatelet therapy groups. ISR *(C)* and in-segment restenosis *(D)* according to postprocedural MLD between triple and dual antiplatelet therapy groups.

a positive result of a stress test and a native coronary lesion. The DECLARE-DIABETES and -LONG I studies involved 5 cardiac centers in Korea from August 2004 to March 2006. The DECLARE-LONG II study involved 10 cardiac centers in Korea from December 2007 to December 2008. Patients were considered eligible if they had diabetes mellitus (DM) or a long lesion (lesion length of $\geq$25 mm), presented with angina pectoris and/or had a positive result of a stress test, and had clinically significant angiographic stenosis in a native coronary vessel with a diameter stenosis of $\geq$50% and visual reference diameter of $\geq$2.5 mm. Patients were excluded if aspirin, clopidogrel, or cilostazol use was contraindicated or if they had left main disease (diameter stenosis of $\geq$50% by visual estimate), graft vessel disease, a left ventricular ejection fraction of $<$30%, a recent history of hematologic disease or leukocyte count of $<$3,000/mm^3 and/or platelet count of $<$100,000/mm^3, hepatic dysfunction with aspartate or alanine aminotransferase of $\geq$3$\times$ the upper normal reference limit, a history of renal dysfunction or serum creatinine level of $\geq$2.0 mg/dl, a serious noncardiac co-morbid disease with a life expectancy of $<$1 year, planned bifurcation stenting in the side branch, primary angioplasty for acute myocardial infarction within 24 hours, or an inability to follow the protocol. The same type of allocated stent was used for all lesions in patients with multiple lesions. The institutional review board at each participating center approved the protocol. All patients provided written informed consent.

Once the guidewire had crossed the target lesion, patients were randomly assigned in a 1:1 ratio to SES or paclitaxel-eluting stent implantation. After DES randomization, patients were randomly allocated in a 1:1 ratio to the triple (200 patients of the DECLARE-DIABETES trial and 250 of the DECLARE-LONG I trial; aspirin, clopidogrel, and cilostazol; triple group, n = 450) or the dual antiplatelet therapy group (200 patients of the DECLARE-DIABETES trial and 250 of the DECLARE-LONG trial; aspirin and clopidogrel; dual group, n = 450) on the basis of a 2 $\times$ 2 factorial design with a computer-generated randomization sequence. In the DECLARE-LONG II trial, after successful Endeavor zotarolimus-eluting stent implantation, patients were randomly allocated in a 1:1 ratio to the triple (aspirin, clopidogrel, and cilostazol; triple group, n = 250) or the dual antiplatelet therapy group (aspirin, clopidogrel, and placebo; dual group, n = 249) with an interactive web response system. From at least 24 hours before the procedure and thereafter, all patients received aspirin (200 mg/day) and clopidogrel (loading dose of 300 mg, followed by 75 mg/day for at least 6 months in the DECLARE-DIABETES and -LONG I trials or 8 months in the DECLARE-LONG II trial). Patients in the triple group received a loading dose of 200 mg cilostazol immediately after the procedure and 100 mg twice a day for 6 or 8 months. Coronary stenting was performed with the standard technique. The decision of predilation or direct stenting was made by the operator. The use of intravenous glycoprotein IIb/IIIa inhibitors was at the operators'

Table 5
Unadjusted and adjusted odds ratios for restenosis after triple antiplatelet therapy compared with dual antiplatelet therapy according to the stent length and postprocedural minimal lumen diameter (MLD)

Variable	Unadjusted			Adjusted*		
	OR	95% CI	p	OR	95% CI	p
In-segment restenosis						
All patients (n = 1,173)	0.54	0.37−0.77	0.001	0.51	0.35−0.74	<0.001
Stent length						
≤20 mm (n = 56)	NA	NA	NA	NA	NA	NA
20−40 mm (n = 694)	0.56	0.33−0.96	0.034	0.53	0.31−0.91	0.022
>40 mm (n = 423)	0.51	0.31−0.84	0.008	0.50	0.29−0.86	0.012
Postprocedural MLD						
≤2.5 mm (n = 541)	0.53	0.32−0.86	0.01	0.52	0.31−0.86	0.011
2.5−3.0 mm (n = 437)	0.60	0.32−0.12	0.11	0.54	0.28−1.05	0.069
>3.0 mm (n = 195)	0.44	0.16−1.13	0.12	0.46	0.15−1.36	0.16
ISR						
All patients (n = 1,173)	0.57	0.39−0.83	0.003	0.53	0.36−0.79	0.002
Stent length						
≤20 mm (n = 56)	NA	NA	NA	NA	NA	NA
20−40 mm (n = 694)	0.66	0.37−1.16	0.15	0.62	0.35−1.11	0.11
>40 mm (n = 423)	0.50	0.30−0.84	0.009	0.48	0.27−0.84	0.01
Postprocedural MLD						
≤2.5 mm (n = 541)	0.58	0.35−0.96	0.035	0.56	0.33−0.95	0.030
2.5−3.0 mm (n = 437)	0.60	0.31−1.16	0.13	0.53	0.26−1.09	0.083
>3.0 mm (n = 195)	0.45	0.15−1.36	0.16	0.49	0.15−1.60	0.24

OR = odds ratio.
* These models were adjusted for type of DES, DM, bifurcation lesion, stent length, and postprocedural MLD, listed in Table 4.

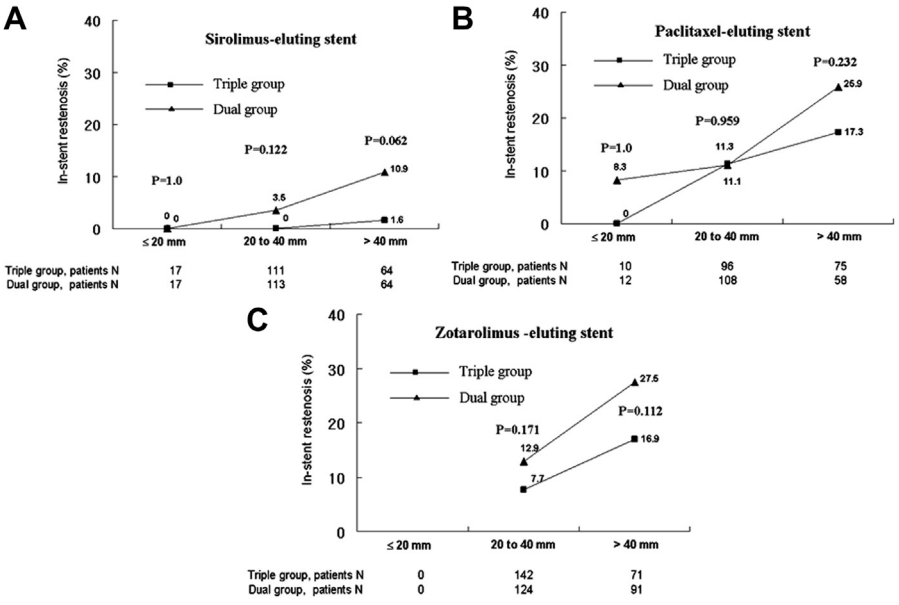

Figure 3. ISR according to stent length between triple and dual antiplatelet therapy groups in 3 different stent types: *(A)* SES, *(B)* paclitaxel-eluting stent, and *(C)* zotarolimus-eluting stent.

discretion. A 12-lead electrocardiogram was obtained after the procedure and before discharge. Serum levels of creatine kinase and its MB isoenzyme were assessed 8, 12, and 24 hours after the procedure and thereafter if considered necessary.

Primary end point was to find the relation between implanted stent length and angiographic in-stent restenosis (ISR) to find an optimal indicator of cilostazol addition after DES implantation. The relation between the postprocedural minimal lumen diameter (MLD) and angiographic ISR was also assessed.

Angiographic restenosis was defined as a diameter stenosis of >50% on follow-up angiography. Repeat coronary angiography was mandatory at 6 months in the DECLARE-DIABETES and -LONG I trials, or 8 months in the DECLARE-LONG II trial after stenting, or earlier if

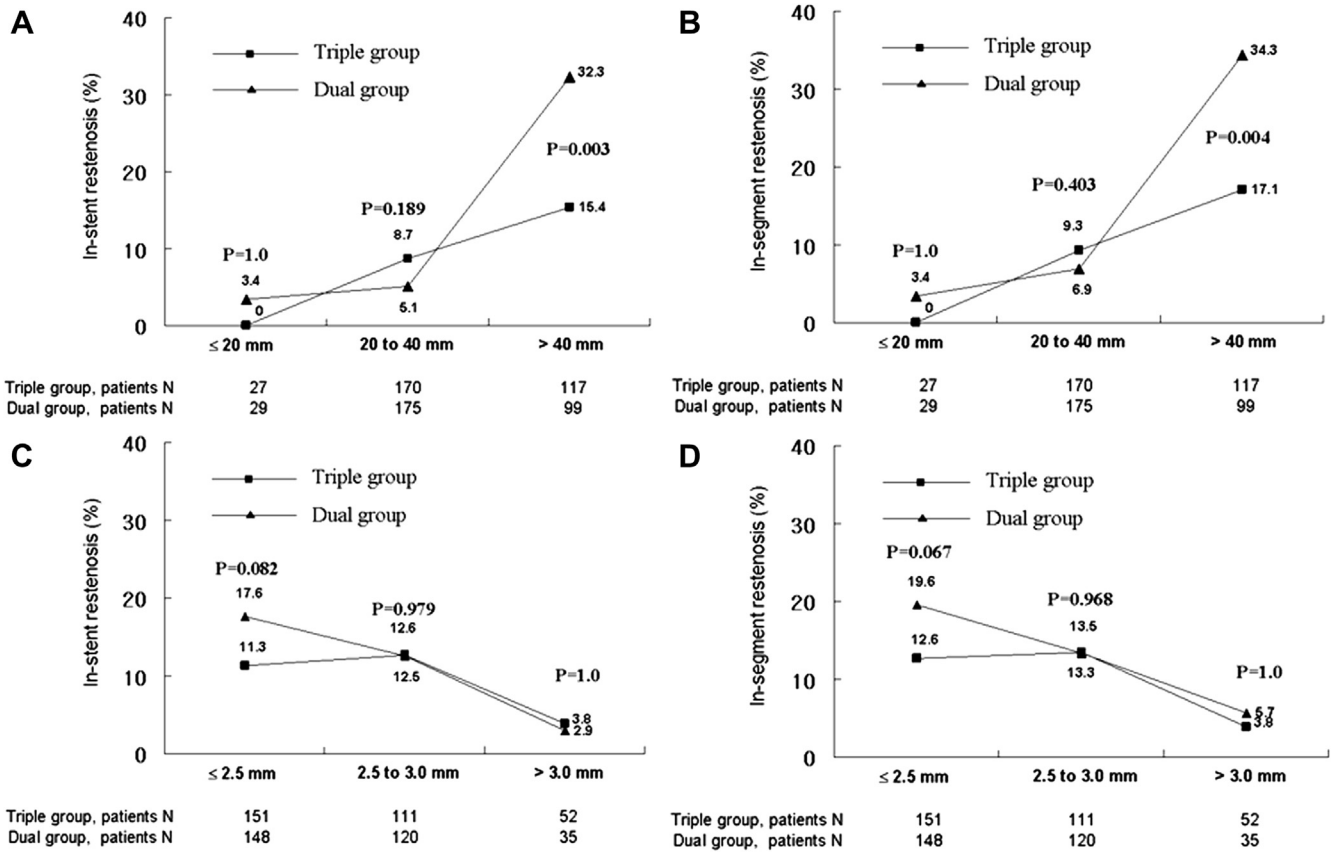

Figure 4. ISR *(A)* and in-segment restenosis *(B)* according to stent length between triple and dual antiplatelet therapy in diabetic patients. ISR *(C)* and in-segment restenosis *(D)* according to postprocedural MLD between triple and dual antiplatelet therapy in diabetic patients.

indicated by clinical symptoms or evidence of myocardial ischemia. Coronary angiograms were obtained after intracoronary nitroglycerin administration. Preprocedure (baseline), postprocedure, and follow-up angiograms were submitted to the angiographic core analysis center (Asan Medical Center, Seoul, Korea) for analysis by independent angiographers. Digital angiograms were analyzed using an automated edge detection system (CASS II; Pie Medical, Maastricht, The Netherlands). Angiographic variables included lesion length, stent length, reference vessel diameter, MLD, percent diameter stenosis, restenosis rate, acute gain, and late loss. Quantitative coronary angiographic measurements of target lesions were obtained for both the stented segment only (in-stent) and the region that included the stented segment and the margins 5 mm proximal and distal to the stent (in-segment).

Continuous variables are presented as mean ± SD and were compared using Student unpaired *t* or Mann-Whitney *U* test according to the restenosis. Categorical variables are presented as numbers or percentages and were compared using chi-square or Fisher's exact test. Because we combined the 3 trials, we performed a test of heterogeneity (Q statistics and I^2 index) across the trials. Based on the heterogeneity test, the 3 trials could be combined (Q statistics and I^2 index; $p = 0.787$ and 0% [0% to 56.5%] for ISR and $p = 0.903$ and 0% [0% to 0%] for in-segment restenosis, respectively). Multivariate analyses involved a backward elimination technique, and variables with a p value of <0.20 were used to find risk factors associated with the restenosis. The relative risk for the restenosis and its 95% confidence interval (CI) were computed and receiver operating characteristic curve analysis was conducted to find a stent length cutoff for predicting ISR in the dual group. Then, we computed the restenosis rates according to the stent length and the postprocedural MLD between the triple and dual groups. A p value of <0.05 was considered to indicate a significant difference. In the subgroup analysis, we conducted several testing together for 2 outcome variables, respectively. Therefore, we used the Bonferroni-corrected significance level α to adjust for the multiplicity (e.g., $0.05/3 = 0.017$). Multivariate logistic regression analysis was used to obtain the adjusted odds ratio. This model was adjusted for type of DES, DM, bifurcation lesion, stent length, and postprocedural MLD, which were identified as independent predictors of restenosis.

All p values were 2-sided and a probability value of $p < 0.05$ was considered significant. Statistical analysis was performed using SAS software, version 9.1 (SAS Institute, Cary, North Carolina).

Results

In the pooled population (n = 1,399), there were no significant differences between the 2 groups in baseline clinical characteristics and risk factors except left ventricular ejection fraction between triple and dual groups (not shown). Among them, follow-up angiography was performed in 1,173

patients (83.8%). In follow-up angiographic analysis, triple group significantly reduced ISR (8.2% vs 13.6%; relative risk 0.60; 95% CI 0.53 to 0.84; p = 0.003) and in-segment restenosis (9.0% vs 15.7%; relative risk 0.58, 95% CI 0.53 to 0.65; p = 0.001) compared with dual group. Tables 1 and 2 list the angiographic characteristics and procedural results with or without restenosis. The restenosis group had a longer stent length and more number of stents at target lesion. Baseline and postprocedural quantitative coronary angiographic outcomes for the 2 groups are listed in Table 3. The restenosis group had a longer lesion length, smaller reference vessel diameter, smaller postprocedural and follow-up MLDs, and smaller postprocedural and follow-up diameter stenoses than no restenosis group. Restenosis group had a higher late loss than no restenosis group.

On multivariate analysis, all clinical and angiographic variables with p <0.2 in univariate analysis were tested. Independent predictors of angiographic restenosis were use of cilostazol, SES, DM, stent length, bifurcation lesion, and postprocedural MLD (Table 4).

The threshold of stent length for predicting ISR in dual group was 39.5 mm (area under the receiver operating characteristic curve, 0.628; 95% CI 0.588 to 0.668, p <0.001), which had a sensitivity and specificity of 63.7% and 65.3%, respectively (Figure 1). Therefore, the patients with follow-up angiography (n = 1,173) were divided into 3 stent length categories (≤20, 20 to 40, and >40 mm). The ISR (12.4% vs 22.1%, p = 0.008) and in-segment restenosis rates (13.8% vs 23.9%, p = 0.008) were significantly different between the triple and dual groups in the >40-mm stent length group (Figure 2). If patients were divided into 3 categories (≤2.5, 2.5 to 3.0, and >3.0 mm) according to postprocedural MLD, triple group showed lower ISR (p = 0.022 for ≤2.5 mm, p = 0.087 for 2.5 to 3.0 mm, and p = 0.119 for >3.0 mm) and in-segment restenosis (p = 0.006 for ≤2.5 mm, p = 0.073 for 2.5 to 3.0 mm, and p = 0.088 for >3.0 mm) compared with dual group in all categories (Figure 2). After adjustment, triple group showed consistent findings in >40-mm group (Table 5). In patients with >40-mm stent length, triple group showed similar trend toward a lower ISR (14.5% vs 22.2% for ≤2.5 mm, 10.2% vs 23.9% for 2.5 to 3.0 mm, and 8.8% vs 16% for >3.0 mm) according to postprocedural MLD compared with dual group in all categories. In addition, each stent type also showed similar trend according to stent length between triple and dual groups (Figure 3).

In diabetic population, ISR and in-segment restenosis rates were not significantly different in ≤20- and 20- to 40-mm stent length categories between triple and dual groups. However, ISR (15.4% vs 32.3%, p = 0.003) and in-segment restenosis rates (17.1% vs 34.3%, p = 0.004) significantly diverged in >40-mm group between triple and dual groups (Figure 4). According to postprocedural MLD, triple group showed a trend toward a lower ISR and in-segment restenosis compared with dual group in ≤2.5-mm categories (Figure 4).

Discussion

The major findings of this study are (1) the triple group after DES has a significantly reduced ISR rate in the >40-mm stent length group compared with the dual group, (2) triple therapy had a trend toward a lower ISR rate regardless of postprocedural MLD, and (3) triple therapy had a prominent effect in diabetic patients in the >40-mm stent length and smaller postprocedural MLD categories. Therefore, these practical criteria for the use of triple antiplatelet therapy based on stent length could be easily applied after DES implantation in routine clinical practice and could improve DES performance in complex coronary lesions.

The DECLARE-DIABETES, -LONG I, and -LONG II trials consistently showed a reduction in late loss, restenosis, and subsequent repeat revascularization rates in the triple therapy group. Our pooled analysis of the DECLARE trials showed that stent length is one of the predictors of angiographic restenosis after DES implantation. In addition, we found a stent length threshold of 39.5 mm, above which there is a greater likelihood in the dual group of ISR with a sensitivity and specificity of 63.7% and 65.3%, respectively. From a practical point of view, stent length is the most easily adoptable guideline in routine practice for cilostazol use after DES implantation. In the present study, patients implanted with a stent of >40 mm in length had a lower restenosis rate in the triple group compared with the dual group. Furthermore, detailed analysis showed that the triple group had a strong tendency to have a lower restenosis rate regardless of postprocedural MLD. In the diabetic population, the triple group showed a more prominent effect in patients with stent lengths of >40 mm, which indicates that triple therapy may be a more useful strategy in those at a higher risk of angiographic restenosis.

Although DES implantation has reduced angiographic restenosis and improved long-term clinical outcomes compared with bare-metal stent implantation in patients with DM or complex lesions,[6–9] patients with DM or those with complex lesions still have greater adverse cardiac outcomes, including restenosis or revascularization, after DES implantation.[9,10] Meanwhile, in the current practice, the newer generation DES has largely replaced the first generation DES because of the reduced very late stent thrombosis and late target lesion revascularization rates of the newer generation of stents.[11–13] However, the newer generation DES has been reported to have a similar rate of angiographic restenosis, in particular compared with SES. Furthermore, anatomic complexity has been reported to increase the restenosis rate, even after newer generation DES implantation.[14,15] Therefore, in the newer generation DES era, a long stent length remains a concern for restenosis and stent thrombosis.

Previously we reported that triple antiplatelet therapy reduced stent thrombosis and myocardial infarction after DES implantation.[16] Therefore, given our present analysis, use of triple antiplatelet therapy for long stent length after DES implantation is a valuable option in routine clinical practice. Furthermore, a longer stent length usually has a smaller postprocedural MLD. In the present study, the triple group showed an improved effect even for a smaller postprocedural MLD. Therefore, regardless of postprocedural MLD, patients with >40-mm stent length are potentially good candidates for cilostazol addition immediately after coronary stenting.

The present study has several limitations. First, our use of routine 6- or 8-month angiography may have resulted in an underestimation of the rates of restenosis in comparison

with a study with a longer angiographic follow-up period. Second, follow-up angiograms were obtained in a different period in the DECLARE-LONG II trial (8 months) compared with the DECLARE-DIABETES and -LONG I trials (6 months). Third, our analyses cannot be extrapolated to the current newer generation DES because our results were drawn from a patient population who received SES, paclitaxel-eluting stent, and Endeavor zotarolimus-eluting stent. Fourth, we only used a clopidogrel loading dose of 300 mg. Several years have lapsed since the end of the study timeframe and higher loading doses are now more common. Furthermore, our results cannot be extrapolated to combination therapy conducted with newer agents such as ticagrelor and prasugrel. Finally, based on multivariate predictors of angiographic restenosis, we analyzed the angiographic outcomes according to stent length and postprocedural MLD. Although diabetic patients were also analyzed with the same methods, bifurcation lesions were not analyzed because of the small sample size.

Disclosures

The authors have no conflicts of interest to disclose.

1. Lee SW, Park SW, Kim YH, Yun SC, Park DW, Lee CW, Kang SJ, Park SJ, Lee JH, Choi SW, Seong IW, Lee NH, Cho YH, Shin WY, Lee SJ, Lee SW, Hyon MS, Bang DW, Choi YJ, Kim HS, Lee BK, Lee K, Park HK, Park CB, Lee SG, Kim MK, Park KH, Park WJ. A randomized, double-blind, multicenter comparison study of triple antiplatelet therapy with dual antiplatelet therapy to reduce restenosis after drug-eluting stent implantation in long coronary lesions: results from the DECLARE-LONG II trial. *J Am Coll Cardiol* 2011;57:1264−1270.
2. Lee SW, Park SW, Kim YH, Yun SC, Park DW, Lee CW, Hong MK, Kim HS, Ko JK, Park JH, Lee JH, Choi SW, Seong IW, Cho YH, Lee NH, Kim JH, Chun KJ, Park SJ. Drug-eluting stenting followed by cilostazol treatment reduces late restenosis in patients with diabetes mellitus the DECLARE-DIABETES Trial (A Randomized Comparison of Triple Antiplatelet Therapy with Dual Antiplatelet Therapy After Drug-Eluting Stent Implantation in Diabetic Patients). *J Am Coll Cardiol* 2008;51:1181−1187.
3. Lee SW, Park SW, Kim YH, Yun SC, Park DW, Lee CW, Hong MK, Kim HS, Ko JK, Park JH, Lee JH, Choi SW, Seong IW, Cho YH, Lee NH, Kim JH, Chun KJ, Park SJ. Comparison of triple versus dual antiplatelet therapy after drug-eluting stent implantation (from the DECLARE-Long trial). *Am J Cardiol* 2007;100:1103−1108.
4. Douglas JS Jr, Holmes DR Jr, Kereiakes DJ, Grines CL, Block E, Ghazzal ZM, Morris DC, Liberman H, Parker K, Jurkovitz C, Murrah N, Foster J, Hyde P, Mancini GB, Weintraub WS, Cilostazol for Restenosis Trial (CREST) Investigators. Coronary stent restenosis in patients treated with cilostazol. *Circulation* 2005;112:2826−2832.
5. Park SW, Lee CW, Kim HS, Lee NH, Nah DY, Hong MK, Kim JJ, Park SJ. Effects of cilostazol on angiographic restenosis after coronary stent placement. *Am J Cardiol* 2000;86:499−503.
6. Boyden TF, Nallamothu BK, Moscucci M, Chan PS, Grossman PM, Tsai TT, Chetcuti SJ, Bates ER, Gurm HS. Meta-analysis of randomized trials of drug-eluting stents versus bare metal stents in patients with diabetes mellitus. *Am J Cardiol* 2007;99:1399−1402.
7. Sabaté M, Jiménez-Quevedo P, Angiolillo DJ, Gómez-Hospital JA, Alfonso F, Hernández-Antolín R, Goicolea J, Bañuelos C, Escaned J, Moreno R, Fernández C, Fernández-Avilés F, Macaya C. Randomized comparison of sirolimus-eluting stent versus standard stent for percutaneous coronary revascularization in diabetic patients: the diabetes and sirolimus-eluting stent (DIABETES) trial. *Circulation* 2005;112:2175−2183.
8. Kim YH, Park SW, Lee CW, Hong MK, Gwon HC, Jang Y, Lee MM, Koo BK, Oh DJ, Seung KB, Tahk SJ, Yoon J, Park SJ. Comparison of sirolimus-eluting stent, paclitaxel-eluting stent, and bare metal stent in the treatment of long coronary lesions. *Catheter Cardiovasc Interv* 2006;67:181−187.
9. Ortolani P, Balducelli M, Marzaroli P, Piovaccari G, Menozzi A, Guiducci V, Sangiorgio P, Tarantino F, Geraci G, Castriota F, Tondi S, Saia F, Cooke RM, Guastaroba P, Grilli R, Marzocchi A, Maresta A. Two-year clinical outcomes with drug-eluting stents for diabetic patients with de novo coronary lesions: results from a real-world multicenter registry. *Circulation* 2008;117:923−930.
10. Tsagalou E, Chieffo A, Iakovou I, Ge L, Sangiorgi GM, Corvaja N, Airoldi F, Montorfano M, Michev I, Colombo A. Multiple overlapping drug-eluting stents to treat diffuse disease of the left anterior descending coronary artery. *J Am Coll Cardiol* 2005;45:1570−1573.
11. Baber U, Mehran R, Sharma SK, Brar S, Yu J, Suh JW, Kim HS, Park SJ, Kastrati A, de Waha A, Krishnan P, Moreno P, Sweeny J, Kim MC, Suleman J, Pyo R, Wiley J, Kovacic J, Kini AS, Dangas GD. Impact of everolimus-eluting stent on stent thrombosis: a meta-analysis of 13 randomized trials. *J Am Coll Cardiol* 2011;58:1569−1577.
12. Räber L, Magro M, Stefanini GG, Kalesan B, van Domburg RT, Onuma Y, Wenaweser P, Daemen J, Meier B, Jüni P, Serruys PW, Windecker S. Very late stent thrombosis of a newer generation everolimus-eluting stent compared with early generation drug-eluting stents: a prospective cohort study. *Circulation* 2012;125:1110−1121.
13. Applegate RJ, Yaqub M, Hermiller JB, Sood P, Yu S, Doostzadeh J, Williams JE, Farhat N, Caputo R, Lansky AJ, Cutlip DE, Sudhir K, Stone GW. Long-term (three-year) safety and efficacy of everolimus-eluting stents compared to paclitaxel-eluting stents (from the SPIRIT III Trial). *Am J Cardiol* 2011;107:833−840.
14. Park DW, Kim YH, Song HG, Ahn JM, Kim WJ, Lee JY, Kang SJ, Lee SW, Lee CW, Park SW, Yun SC, Seung KB, Yang TH, Lee SG, Lee JH, Seong IW, Cheong SS, Lee BK, Lee NH, Lee SW, Lee SW, Lee K, Kim HS, Jeon DS, Kim MK, Nah DY, Tahk SJ, Park SJ. Comparison of everolimus- and sirolimus-eluting stents in patients with long coronary artery lesions: a randomized LONG-DES-III (Percutaneous Treatment of LONG Native Coronary Lesions With Drug-Eluting Stent-III) Trial. *JACC Cardiovasc Interv* 2011;4:1096−1103.
15. Stefanini GG, Serruys PW, Silber S, Khattab AA, van Geuns RJ, Richardt G, Buszman PE, Kelbæk H, van Boven AJ, Hofma SH, Linke A, Klauss V, Wijns W, Macaya C, Garot P, Di Mario C, Manoharan G, Kornowski R, Ischinger T, Bartorelli AL, Gobbens P, Windecker S. The impact of patient and lesion complexity on clinical and angiographic outcomes after revascularization with zotarolimus- and everolimus-eluting stents: a substudy of the RESOLUTE All Comers Trial (a randomized comparison of a zotarolimus-eluting stent with an everolimus-eluting stent for percutaneous coronary intervention). *J Am Coll Cardiol* 2011;57:2221−2232.
16. Lee SW, Park SW, Yun SC, Kim YH, Park DW, Kim WJ, Lee JY, Lee CW, Hong MK, Kim JJ, Park SJ. Triple antiplatelet therapy reduces ischemic events after drug-eluting stent implantation: Drug-Eluting stenting followed by Cilostazol treatment REduces Adverse Serious cardiac Events (DECREASE registry). *Am Heart J* 2010;159:284−291.