Clinical Investigation

Biodegradable-Polymer Biolimus-Eluting Stents versus Durable-Polymer Everolimus-Eluting Stents at One-Year Follow-Up:

A Registry-Based Cohort Study

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We compared outcomes of percutaneous coronary intervention patients who received biodegradable-polymer biolimus-eluting stents with those who received durable-polymer everolimus-eluting stents.

At Tehran Heart Center, we performed a retrospective analysis of the data from January 2007 through December 2011 on 3,270 consecutive patients with coronary artery disease who underwent percutaneous coronary intervention with the biodegradable-polymer biolimus-eluting stent or the durable-polymer everolimus-eluting stent. We excluded patients with histories of coronary artery bypass grafting or percutaneous coronary intervention, acute ST-segment-elevation myocardial infarction, or the implantation of 2 different stent types. Patients were monitored for 12 months. The primary endpoint was a major adverse cardiac event, defined as a composite of death, nonfatal myocardial infarction, and target-vessel and target-lesion revascularization.

Durable-polymer everolimus-eluting stents were implanted in 2,648 (81%) and biodegradable-polymer biolimus-eluting stents in 622 (19%) of the study population. There was no significant difference between the 2 groups (2.7% vs 2.7%; P*=0.984) in the incidence of major adverse cardiac events. The cumulative adjusted probability of major adverse cardiac events in the biodegradable-polymer biolimus-eluting stent group did not differ from that of such events in the durable-polymer everolimus-eluting stent group (hazard ratio=0.768; 95% confidence interval, 0.421–1.44;* P*=0.388).*

We conclude that in our patients the biodegradable-polymer biolimus-eluting stent was as effective and safe, during the 12-month follow-up period, as was the durable-polymer everolimus-eluting stent. ***(Tex Heart Inst J 2016;43(2):126-30)***

Coronary artery stenting is widely accepted as the treatment of choice for most cases of coronary artery disease (CAD). Implantation of the drug-eluting stents (DESs), in comparison with the bare-metal stents (BMS), has conferred better outcomes for coronary artery stenting.[1-4] Although the administration of the first-generation DES showed a higher rate of success than that of the BMS, doubts were raised over its safety because of the reported cases of late stent thrombosis and very late restenosis.[5] The link between late stent thrombosis and incomplete endothelial coverage of the stent struts caused changes in the design and materials of the platforms and polymers of the stents.[6] Randomized controlled trials and studies have revealed promising results after the implantation of the zotarolimus- and the everolimus-eluting stents, in comparison with the first-generation DES and the BMS.[7-9] On the other hand, concerns about late stent failure caused by untoward reactions to the stent polymer led to the introduction of a new-generation DES in which polymers degrade after the termination of drug release.[10] In these stents, drug release lasts about 28 days and an abluminal biodegradable polymer is absorbed after 6 to 9 months, thus turning the DES into a BMS and, theoretically, averting late stent failure as a result of reaction to polymers. Trials have shown the noninferiority of the biodegradable-polymer biolimus-eluting stent (BP-BES) to the previous generations of DESs; however, only a few investigators have compared the biodegradable-polymer with the durable-polymer DES in real-world registries.[11,12] Further analysis of large and

comprehensive data registries seemed to be necessary to compare the efficacy and safety of those stents.

During a 12-month follow-up period, we compared the incidence of major adverse cardiac events (MACE) in patients who underwent percutaneous coronary intervention (PCI) with the biodegradable-polymer biolimus-eluting stent (BP-BES) versus the incidence of MACE in patients who underwent PCI with the durable-polymer everolimus-eluting stent (DP-EES).

Patients and Methods

We conducted a retrospective registry analysis of all patients presenting with CAD who had undergone PCI with the BP-BES or DP-EES in Tehran Heart Center from January 2007 through December 2011. Biomatrix® (Biosensors International; Morges, Switzerland) and Nobori® (Terumo; Tokyo, Japan) stents were used in the BP-BES group, and the XIENCE® V or PRIME® (Abbott Vascular; Santa Clara, Calif) and PROMUS® (Boston Scientific Corporation; Natick, Mass) stents were used in the DP-EES group. Stent selection in the individual case depended solely on each operator's routine judgments, but mainly on the proper size for each patient. All the demographic, laboratory, angiographic, procedural, and follow-up data were recorded in the Tehran Heart Center PCI Registry. The exclusion criteria were primary PCI in the presence of acute ST-segment-elevation myocardial infarction (MI) or the presence of cardiogenic shock; a history of coronary artery bypass grafting (CABG) or PCI; and implantation of the 2 different stent types in single or separate sessions of the index procedure. The study complied with the Declaration of Helsinki, and the Medical Ethics Committee of Tehran University of Medical Sciences approved the study protocol.

Before the procedure, all patients were given 70 to 100 U/kg of unfractionated heparin intravenously, 300 to 600 mg of clopidogrel, and 325 mg of aspirin orally; and they were advised to take 80 mg of aspirin and 75 mg of clopidogrel daily for 12 months after discharge from the hospital. Follow-up was performed during the 12th month after the procedure. The primary endpoint was MACE, defined as a composite of death, nonfatal MI, target-vessel revascularization (either via PCI or CABG), and target-lesion revascularization.

Statistical Analysis

Data were analyzed with use of SPSS version 20 (IBM Corporation; Armonk, NY). The quantitative variables are presented as mean ± SD and the categorical variables as frequencies and percentages. Continuous variables were compared between the DP-EES and BP-BES groups with use of the Student *t* or Mann-Whitney test. The χ^2 method or the Fisher exact test was used to compare the categorical variables, and the Kaplan-Meier and log-rank methods were used to compare survival rates between the 2 groups. Variables in the univariate analysis with a *P* value ≤0.15 were considered to be probable confounding factors and were selected to enter the multivariable model. The hazard ratio (HR) was presented with its 95% confidence interval (CI). A *P* value <0.05 was considered statistically significant.

Results

The study population comprised 3,270 patients (mean age, 58.53 ± 10.52 yr), of whom 2,648 (81%) received the DP-EES and 622 (19%) the BP-BES. The baseline characteristics of both groups are summarized in Table I. Hypertension (60.3% vs 54.3%; *P*=0.006) and chronic lung disease (5.9% vs 3.4%; *P*=0.004) occurred more often among the BP-BES group. There was no significant difference in the prevalence of diabetes mellitus, dyslipidemia, renal failure, and congestive heart failure between the 2 groups of patients.

The baseline and procedural characteristics of the study patients are presented in Table II. In total, 163 Nobori, 551 Biomatrix, 1,160 PROMUS, and 2,007 XIENCE stents were implanted in the 3,270 patients. Coronary angiography revealed that triple-vessel disease was more prevalent in the BP-BES group and that the DP-EES group had more single-vessel disease (*P*=0.025).

After PCI, 98% of the patients (97.6% of the DP-EES and 99.7% of the BP-BES group) completed their 12 months of follow-up. Sixty-three (1.9%) patients did not complete 12 months of follow-up. There was no significant difference between the follow-up subgroups. Table III shows the incidence rate of MACE in the DP-EES versus the rate in the BP-BES group. There was no significant difference in MACE between the 2 groups at 12 months of follow-up (2.7% vs 2.7%; *P*=0.984). The potential confounding factors were age, positive family history, renal failure, dyspnea upon exertion (New York Heart Association functional class III/IV), left ventricular ejection fraction, lesions at bifurcation site, and stent length. After adjustment, the cumulative probability of MACE in the BP-BES group did not differ from that of the DP-EES group (HR=0.768; 95% CI, 0.421–1.44; *P*=0.388) (Fig. 1).

Discussion

Results of the present study revealed that, in CAD patients during a 12-month follow-up period, implantation of the biodegradable-polymer DES was similar in efficacy and safety to those characteristics of the durable-polymer DES.

Use of biodegradable polymers in the latest generations of DES is assumed to attenuate the concerns over late stent failure occurring with permanent polymers

TABLE I. Baseline Characteristics of the Study Groups

Variable	DP-EES Group (n=2,648)	BP-BES Group (n=622)	*P* Value
Male sex	1,752 (66.2)	406 (65.3)	0.673
Age (yr)	58.29 ± 10.36	59.52 ± 11.1	0.012
Body mass index (kg/m^2)	27.71 ± 4.36	27.89 ± 4.34	0.376
Positive family history of CAD	479 (18.1)	98 (15.8)	0.162
Current smoker	633 (23.9)	157 (25.2)	0.476
Opium addict	247 (9.3)	66 (10.6)	0.341
Diabetes mellitus	924 (34.9)	223 (35.9)	0.661
Hypertension	1,437 (54.3)	375 (60.3)	0.006
Dyslipidemia	1,780 (67.2)	421 (67.7)	0.82
Renal failure (Cr >2 mg/dL)	35 (1.3)	13 (2.1)	0.153
Congestive heart failure	27 (1)	11 (1.8)	0.233
Chronic lung disease	79 (3)	37 (5.9)	0.004
Dyspnea (NYHA III/IV)	355 (13.4)	102 (16.4)	0.065
Clinical status within recent 2 mo			
Unstable angina	996 (37.6)	243 (39.1)	0.501
NSTEMI	363 (13.7)	88 (14.1)	0.846
STEMI	650 (24.5)	161 (25.9)	0.487
Left ventricular ejection fraction	0.50 ± 0.95	0.50 ± 0.10	0.14
Serum creatinine level (mg/dL)	1 ± 0.28	0.95 ± 0.3	0.005
Hemoglobin (g/dL)	14.07 ± 1.67	14.01 ± 1.71	0.639

BP-BES = biodegradable-polymer biolimus-eluting stent; CAD = coronary artery disease; Cr = serum creatinine; DP-EES = durable-polymer everolimus-eluting stent; NSTEMI = non-ST-segment-elevation myocardial infarction; NYHA = New York Heart Association functional class; STEMI = ST-segment-elevation myocardial infarction

Data are presented as mean ± SD or as number and percentage. *P* <0.05 was considered statistically significant.

TABLE II. Baseline Lesions and Procedural Characteristics of the Study Groups

Variable	DP-EES Group (n=2,648)	BP-BES Group (n=622)	*P* Value
Angiographic disease findings	—	—	0.025
Single-vessel	1,223 (46.2)	256 (41.1)	—
Double-vessel	934 (35.3)	225 (36.2)	—
Triple-vessel	491 (18.5)	141 (22.7)	—
Target-lesion territory			
LAD	1,947 (73.5)	418 (67.2)	0.002
RCA	530 (20)	145 (23.3)	0.068
LCx	498 (18.8)	122 (19.6)	0.644
AHA grade B2 or C	2,181 (82.4)	478 (76.8)	0.001
Bifurcation lesion	443 (16.7)	88 (14.1)	0.116
Ostial lesion	304 (11.5)	74 (11.9)	0.778
Occlusion	277 (10.5)	66 (10.6)	0.912
Reference-vessel diameter (mm)	3.08 ± 0.39	3.06 ± 0.42	0.299
No. treated lesions per patient	1.27 ± 0.53	1.25 ± 0.49	0.456
Stent length (mm)	29.81 ± 14.4	25.91 ± 11.62	<0.001
Multivessel PCI	325 (12.3)	62 (10)	0.102

AHA = American Heart Association; BP-BES = biodegradable-polymer biolimus-eluting stent; DP-EES = durable-polymer everolimus-eluting stent; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; PCI = percutaneous coronary intervention; RCA = right coronary artery

Data are presented as mean ± SD or as number and percentage. *P* <0.05 was considered statistically significant.

used in the first-generation DES, because the polymer is completely absorbed after the termination of drug release.[13-17] Trials have revealed the lower rates of MACE in short- and long-term follow-up after the DP-EES implantation in comparison to the earlier generation and have introduced the DP-EES as the standard of DES, versus other design improvements.[18] Investigators have also confirmed the superiority of the BP-BES over the first-generation DES.[19,20] In the Limus Eluted from A Durable vs ERodable Stent Coating (LEADERS) trial,[19]

TABLE III. Incidence Rate of MACE in the DP-EES Group versus the BP-BES Group

Variable	DP-EES Group (n=2,648)	BP-BES Group (n=622)	*P* Value
MACE	72 (2.7)	17 (2.7)	0.984
Nonfatal myocardial infarction	15 (0.6)	1 (0.2)	0.401
All-cause death	31 (1.2)	13 (2.1)	0.073
Target-vessel revascularization	26 (1)	3 (0.5)	0.34
Target-lesion revascularization	14 (0.5)	0	0.091
CABG	4 (0.2)	1 (0.2)	0.999

BP-BES = biodegradable-polymer biolimus-eluting stent; CABG = coronary artery bypass grafting; DP-EES = durable-polymer everolimus-eluting stent; MACE = major adverse cardiac events

Data are presented as number and percentage. $P < 0.05$ was considered statistically significant.

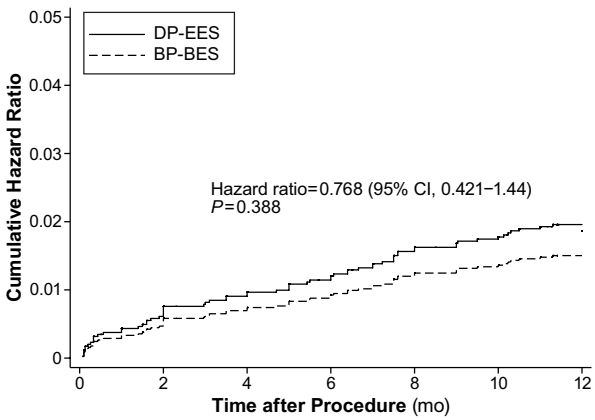

Fig. 1 *Graph shows adjusted cumulative probability of major adverse cardiac events.*

BP-BES = biodegradable-polymer biolimus-eluting stent; CI = confidence interval; DP-EES = durable-polymer everolimus-eluting stent

the incidence of MACE was not higher in the BP-BES group than that in the sirolimus-eluting stent group. In that trial, survival curves showed increasing divergence at 1, 2, and 3 years, in favor of the BP-BES. After the establishment of BP-BES's noninferiority to DP-EES in randomized trials,[16,21,22] some recent studies have focused on evaluating the advantages of BP-BES over DP-EES.[11,12] Puricel and colleagues[12] compared clinical outcomes in 200 propensity-score-matched pairs of patients (one treated by EES and the other treated by BES) and reported that, at 24 months after PCI, MACE had occurred in 10.5% of the BP-BES group and in 11.5% of the DP-EES group, with no significant difference. At the one-year follow-up, an analysis of a single-center registry of unrestricted use of EES and Biomatrix BES in 406 propensity-score-matched pairs showed a similar rate of target-lesion failure, stent thrombosis, and patient-oriented composite outcome.[11] In accordance with these findings, our present study (with a larger sample size) showed no significant differences in MACE during the first year after BP-BES implantation, a year in which 98% of the patients were successfully monitored.

The incidence of MACE in our study population was 2.7% in both groups, which is relatively lower than incidences in earlier studies. This is almost certainly explained by two factors. First, we excluded patients with acute MI, cardiogenic shock, and histories of CABG and PCI, which probably reduces the incidence of MACE. Second, the mean age of our patients was lower than the mean ages of patients in the other studies. The mean age was 58 years in our study, as opposed to 65 years in the studies by Lee and co-authors[11] and Tada and associates,[22] and 62 and 63 years in the studies by Smits and colleagues[21] and Kaiser and associates,[16] respectively.

Study Limitations

This study has some potential limitations. One of the chief limitations is the nature of the study—a retrospective analysis of a registry in which the results might possibly be confounded; however, our study does reflect the facts from a real-world routine practice in a large tertiary referral center. In addition, a 12-month follow-up period might not be long enough for comparison of BP-BES efficacy and safety with DP-EES efficacy and safety. Consequently, further studies of real-world registries, with longer follow-up periods, are necessary.

Conclusion

Our analysis of a single-center registry yielded similar one-year efficacy and safety between the BP-BES and DP-EES at 12 months of follow-up.

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