Journal of the American College of Cardiology
© 2009 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 54, No. 9, 2009
ISSN 0735-1097/09/$36.00
doi:10.1016/j.jacc.2009.04.071

INTERVENTIONAL CARDIOLOGY

Long-Term Clinical Outcomes of Sirolimus- Versus Paclitaxel-Eluting Stents for Patients With Unprotected Left Main Coronary Artery Disease

Analysis of the MAIN-COMPARE (Revascularization for Unprotected Left Main Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty Versus Surgical Revascularization) Registry

Jong-Young Lee, MD,* Duk-Woo Park, MD, PHD,* Sung-Cheol Yun, PHD,†
Seung-Whan Lee, MD, PHD,* Young-Hak Kim, MD, PHD,* Cheol Whan Lee, MD, PHD,*
Myeong-Ki Hong, MD, PHD,* Seong-Wook Park, MD, PHD,* Seung-Jung Park, MD, PHD*

Seoul, Korea

Objectives The aim of this study was to evaluate long-term clinical outcomes after implantation of sirolimus-eluting stents (SES) or paclitaxel-eluting stents (PES) among patients with unprotected left main coronary artery (LMCA) disease.

Background There have been few comparisons of long-term outcomes among currently available drug-eluting stents (DES) for the treatment of LMCA disease.

Methods A total of 858 consecutive patients with unprotected LMCA stenosis were treated with SES (n = 669) or PES (n = 189) between May 2003 and June 2006. Primary outcome was the composite of death, myocardial infarction (MI), or target vessel revascularization (TVR).

Results Baseline clinical and angiographic characteristics were similar in the 2 groups. During 3 years of follow-up, the adjusted risk of primary composite outcome was similar among the groups (SES vs. PES: 25.8% vs. 25.7%, hazard ratio [HR]: 0.95, 95% confidence interval [CI]: 0.64 to 1.41, p = 0.79). The 2 groups also showed a comparable adjusted rate of each component of outcome: death (9.1% vs. 11.0%, HR: 0.92, 95% CI: 0.47 to 1.80, p = 0.82), MI (8.1% vs. 8.0%, HR: 0.80, 95% CI: 0.43 to 1.48, p = 0.47), and TVR (12.1% vs. 10.6%, HR: 1.10, 95% CI: 0.53 to 2.29, p = 0.81). The 3-year rates of definite or probable stent thrombosis were 0.6% in the SES group and 1.6% in the PES group (adjusted p = 0.18).

Conclusions In consecutive patients with unprotected LMCA disease undergoing DES implantation, SES and PES showed similar long-term clinical outcomes in terms of death, MI, repeat revascularization, and stent thrombosis.
(J Am Coll Cardiol 2009;54:853–9) © 2009 by the American College of Cardiology Foundation

Bypass surgery has been recommended—on the basis of clinical studies comparing coronary artery bypass grafting (CABG) with medical therapy—as the treatment of choice for patients with unprotected left main coronary artery (LMCA) disease, and recent appropriateness criteria for coronary revascularization regard CABG as the most appropriate treatment for LMCA disease (1–3). However, recent improvements in interventional techniques and adjunctive pharmacology have led to a reevaluation of the role of percutaneous coronary intervention (PCI) as a viable treatment option for LMCA disease (4–8). In addition, interest in left main stenting has intensified with the availability of drug-eluting stents (DES), which have been found to significantly reduce the rates of restenosis and repeat revascularization (9–16), as compared with bare-metal stents. However, few data are available on the long-term clinical outcomes of currently available DES for treatment of unprotected LMCA disease. Therefore, we compared the 3-year

From the *Department of Cardiology, Asan Medical Center, and the †Division of Biostatistics, Center for Medical Research and Information, University of Ulsan College of Medicine, Seoul, Korea. This study was partly supported by the Cardiovascular Research Foundation, Seoul, Korea, and a Grant of the Korea Health 21 R&D Project, Ministry of Health & Welfare, Korea (0412-CR02-0704-0001). Drs. Jong-Young Lee and Duk-Woo Park contributed equally to this work.

Manuscript received January 19, 2009; revised manuscript received April 6, 2009, accepted April 6, 2009.

Abbreviations and Acronyms

CABG = coronary artery bypass grafting
DES = drug-eluting stent(s)
LMCA = left main coronary artery
MI = myocardial infarction
PCI = percutaneous coronary intervention
PES = paclitaxel-eluting stent(s)
SES = sirolimus-eluting stent(s)
TVR = target vessel revascularization

clinical outcomes after implantation of sirolimus-eluting stents (SES) and paclitaxel-eluting stents (PES) in patients with unprotected LMCA disease.

Methods

Study population and procedures. As previously described (8), the MAIN-COMPARE (Revascularization for Unprotected Left Main Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty versus Surgical Revascularization) registry holds data on consecutive patients from 12 major academic cardiac centers in Korea that performed PCI or CABG for unprotected LMCA disease (defined as stenosis >50%) between January 2000 and June 2006. The registry is initiated and sponsored by the Korean Society of Interventional Cardiology, and there was no industry involvement in the design, conduct, or analysis of this study. Current study population comprised 858 consecutive patients with unprotected LMCA disease who underwent DES implantation between May 2003 and June 2006.

Stent implantation methods for left main disease have been described previously (4,10,17). The choice of SES (Cypher and Cypher Select, Cordis, Johnson & Johnson, New Brunswick, New Jersey) or PES (Taxus Express and Liberté, Boston Scientific, Natick, Massachusetts) was at the discretion of the physician. Interventions for any other clinically important types of coronary artery disease were performed according to current practice guidelines (2). All patients undergoing PCI were prescribed aspirin plus clopidogrel (loading dose, 300 or 600 mg) before or during the coronary intervention. After the procedure, aspirin was continued indefinitely, and clopidogrel was continued for at least 6 months. Extended use of clopidogrel beyond 6 months was at the discretion of the physician.

This study was approved by the ethics committee at each hospital, which allowed the use of clinical data for this study.

Study end points and definitions. The primary outcome was the composite of death, myocardial infarction (MI), and target vessel revascularization (TVR) during follow-up. Secondary outcomes were each clinical outcome (death, MI, or TVR) and stent thrombosis.

All-cause mortality was considered. An MI was defined as a pathologic new Q wave on an electrocardiogram or an increase in creatine kinase-myocardial band level to >3 times the upper limit of the normal range. In our study, TVR was defined as repeat revascularization of the treated vessel, including any segments of the left anterior descending and/or left circumflex artery (15). Stent thrombosis was assessed by Academic Research Consortium definitions, with the pre-specified key end point being definite or probable (18). By the timing of presentation, stent thrombosis was classified as acute, subacute, late, and very late if it occurred within 24 h, 30 days, 30 days to <1 year, or >1 year, respectively, after the procedure. Procedural success was defined as a residual diameter stenosis of ≤30% by quantitative coronary angiography, without in-hospital major adverse events (death, Q-wave MI, stent thrombosis, or emergent revascularization).

All outcomes of interest were confirmed by documentation at each hospital and were centrally adjudicated by an independent group of clinicians who were blinded to stent type.

Data collection and follow-up. Clinical, angiographic, procedural or operative, and outcome data were collected with the use of a dedicated Internet-based reporting system. For validation of complete follow-up data, information about vital status was obtained through July 15, 2007, from the National Population Registry of the Korea National Statistical Office with a unique personal identification number. Follow-up MI, stent thrombosis, and TVR were based on clinical diagnoses assigned by the patient's physician and were centrally adjudicated by the local events committee at the University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea.

Statistical analysis. Continuous variables were compared with the Student *t* test or the Wilcoxon rank sum test, and categorical variables were compared with the chi-square test or Fisher exact test as appropriate. Unadjusted cumulative event rates were estimated by the Kaplan-Meier method and compared with the log-rank test.

Crude and adjusted risk for adverse outcomes were compared by univariate and multivariable Cox proportional hazards regression analysis (19). Variables reported in Tables 1 and 2 with a p value ≤0.2 in univariate analyses were candidates for multivariable Cox proportional hazards models. The final models were determined by backward elimination procedure. The proportional hazards assumption was confirmed by examination of log (−log [survival]) curves and by testing of partial (Schoenfeld) residuals (20), and no relevant violations were found.

A propensity score analysis was also performed to control selection biases among the DES groups (21). The propensity scores were estimated without regard to outcome variables, with multiple logistic regression analysis that included all covariates listed in Tables 1 and 2. Model discrimination was assessed with *c*-statistics (0.79), and model calibration was assessed with Hosmer-Lemeshow statistics ($p = 0.38$). The individual propensity score as well as type of stent were incorporated into Cox proportional hazard regression models as a covariate to calculate the propensity adjusted hazard ratio.

All p values were 2-sided, and a probability value of $p < 0.05$ was considered significant. All statistical analyses were

Table 1 Baseline Clinical Characteristics of Patients According to Stent Group

Variable	SES (n = 669)	PES (n = 189)	p Value
Demographic characteristics			
Age (yrs)	62.1 ± 11.2	64.9 ± 10.8	0.002
Male sex	483 (72.2)	133 (70.4)	0.62
Coexisting conditions or other risk factors			
Diabetes			
Any type	211 (31.5)	65 (34.4)	0.46
Insulin-treated	52 (7.8)	18 (9.5)	0.44
Hypertension	346 (51.7)	101 (53.4)	0.68
Hyperlipidemia	197 (29.4)	52 (27.5)	0.61
Current smoker	174 (26.0)	49 (25.9)	0.98
Family history of CAD	44 (6.6)	12 (6.3)	0.91
Previous myocardial infarction	52 (7.8)	18 (9.5)	0.44
Previous coronary angioplasty	132 (19.7)	34 (18.0)	0.59
Previous congestive heart failure	21 (3.1)	4 (2.1)	0.46
Cerebrovascular disease	59 (8.8)	12 (6.3)	0.28
Peripheral vascular disease	13 (1.9)	4 (2.1)	0.88
Chronic lung disease	25 (3.7)	3 (1.6)	0.14
Renal failure	27 (4.0)	9 (4.8)	0.66
Atrial fibrillation	17 (2.5)	3 (1.6)	0.44
Clinical indications for index procedure			0.07
Silent ischemia	22 (3.3)	4 (2.1)	
Stable angina	221 (33.0)	45 (23.8)	
Unstable angina	308 (46.0)	101 (53.4)	
Acute myocardial infarction	118 (17.6)	39 (20.6)	
Ejection fraction (%)			0.51
Median	61	60	
Interquartile range	55–67	54–67	
EuroScore			
Mean EuroScore	4.1 ± 2.8	4.6 ± 2.5	0.02
EuroScore ≥6 (high-risk score)	177 (26.5)	60 (31.7)	0.15

Data are mean ± SD or n (%).
CAD = coronary artery disease; PES = paclitaxel-eluting stent(s); SES = sirolimus-eluting stent(s).

performed with SPSS version 12.0 for Windows (SPSS Inc., Chicago, Illinois).

Results

Baseline characteristics and procedure. Of the 858 patients with unprotected LMCA disease who underwent DES implantation, 669 patients (78%) were treated with SES and 189 patients (22%) were treated with PES. The baseline clinical, angiographic, and procedural characteristics of these 2 groups are listed in Tables 1 and 2. There were no significant between-group differences in clinical characteristics, except that patients treated with PES were older and had higher mean EuroScore than those treated with SES. The 2 groups also had comparable angiographic and procedural characteristics, except that a higher percentage of patients with SES underwent the procedure with intravascular ultrasound guidance and direct stenting.

In-hospital and long-term clinical outcomes. During the index hospital stay, there were 21 (2.4%) in-hospital deaths (2.4% in the SES, and 2.6% in the PES group), 4 (0.5%) Q-wave MIs (0.4% in the SES, and 0.5% in the PES group), and 4 (0.5%) urgent revascularizations (0.3% in the SES, and 1.1% in the PES group). The rate of procedural success was similar in the SES (97.4%) and PES (98.1%) groups (p = 0.37).

The median follow-up was 852 days (interquartile range 605 to 1,118 days) in the overall population, 875 days (interquartile range 635 to 1,143 days) in the SES group, and 876 days (interquartile range 627 to 1,143 days) in the PES group. Complete follow-up data for major clinical events were obtained in 98.9% of the overall cohort. During the entire follow-up period, 65 patients (8.6%) died, 42 (64.6%) from a cardiovascular cause; 66 (7.7%) had an MI (5 Q-wave, >61 non–Q-wave), and 92 (10.7%) had TVR. Table 3 summarizes the cumulative incidences and long-term relative risks of clinical outcomes during the 3-year follow-up among the 2 groups. A crude analysis showed that the risks of death, MI, TVR, and the primary composite outcome were similar in the SES and PES groups (Fig. 1, Table 3).

Table 2 Angiographic and Procedural Characteristics of Patients According to Stent Group

Variable	SES (n = 669)	PES (n = 189)	p Value
Lesion location			0.08
Ostium and shaft	277 (41.4)	92 (48.7)	
Bifurcation	392 (58.6)	97 (51.3)	
Extent of diseased vessel			0.19
Left main only	125 (18.7)	29 (15.3)	
Left main plus single-vessel disease	164 (24.5)	36 (19.0)	
Left main plus 2-vessel disease	178 (26.6)	58 (30.7)	
Left main plus 3-vessel disease	202 (30.2)	66 (34.9)	
Right coronary artery disease	280 (41.9)	89 (47.1)	0.20
Restenotic lesion	19 (2.8)	8 (4.2)	0.33
Use of glycoprotein IIb/IIIa inhibitors	51 (7.6)	8 (4.2)	0.10
Guidance of intravascular ultrasound	495 (76.4)	123 (65.8)	0.004
Direct stenting	154 (23.0)	25 (13.2)	0.003
Lesion preparation			
Cutting balloon	25 (3.7)	4 (2.1)	0.28
Directional atherectomy	18 (2.7)	3 (1.6)	0.39
Rotational atherectomy	2 (0.3)	0	0.45
Maximal inflation pressure (mm Hg)	15.8 ± 3.9	15.8 ± 4.4	0.99
Number of stents implanted in LMCA lesion	1.2 ± 0.5	1.2 ± 0.5	0.70
Total stent length (mm) in LMCA lesion	33.4 ± 22.1	31.5 ± 20.6	0.28
Average stent diameter (mm)	3.3 ± 0.2	3.4 ± 0.2	0.04
Number of stents implanted/patients (including LMCA and other vessels)	2.1 ± 1.2	2.1 ± 1.2	0.96
Total stent length/patients (including LMCA and other vessels)	58.5 ± 23.2	55.1 ± 21.3	0.26
Bifurcation treatment			0.94
Single stenting (cross over)	244 (62.2)	60 (61.9)	
Complex stenting (≥2 stents)	148 (37.8)	37 (38.1)	0.90
Kissing stenting	48 (32.4)	10 (27.0)	
T stenting	26 (17.6)	8 (21.6)	
Crush stenting	71 (48.0)	18 (48.6)	
Others	3 (2.0)	1 (2.7)	

Data are mean ± SD or n (%).
LMCA = left main coronary artery; other abbreviations as in Table 1.

These results were also consistent after multivariable and propensity-adjusted Cox regression analyses.

During the follow-up period, 7 patients (0.8%) had definite or probable stent thrombosis: 4 (0.6%) in the SES, and 3 (1.6%) in the PES group (adjusted p = 0.18). Of the patients treated with SES, 1 had acute stent thrombosis and 3 had subacute stent thrombosis (2, 5, and 11 days after the procedure). Of those treated with PES, 2 patients had subacute stent thrombosis (3 and 22 days after the procedure) and 1 had late stent thrombosis (201 days after the procedure). Two patients died of stent thrombosis (case-fatality rate, 28.6%).

Table 3 Crude and Adjusted Hazard Ratios of Clinical Outcomes According to Stent Group

Outcome	Outcome Rates (%) at 3 Yrs* SES	PES	Crude Hazard Ratio (95% CI)	p Value	Multivariable Adjusted Hazard Ratio† (95% CI)	p Value	Adjusted for Propensity Hazard Ratio (95% CI)	p Value
Primary composite outcomes								
Death, MI, or TVR	25.8	25.7	1.02 (0.71–1.49)	0.90	0.95 (0.64–1.41)	0.79	0.99 (0.67–1.46)	0.95
Secondary outcome								
Death	9.1	11.0	0.88 (0.49–1.56)	0.66	0.92 (0.47–1.80)	0.82	0.93 (0.50–1.71)	0.81
MI	8.1	8.0	0.95 (0.54–1.70)	0.87	0.80 (0.43–1.48)	0.47	0.87 (0.48–1.59)	0.66
TVR	12.1	10.6	1.04 (0.63–1.73)	0.87	1.10 (0.53–2.29)	0.81	1.11 (0.55–2.26)	0.77

*Outcome rates were derived from Kaplan-Meier curves. †Hazard ratio for SES with reference of PES.
CI = confidence interval; MI = myocardial infarction; TVR = target vessel revascularization; other abbreviations as in Table 1.

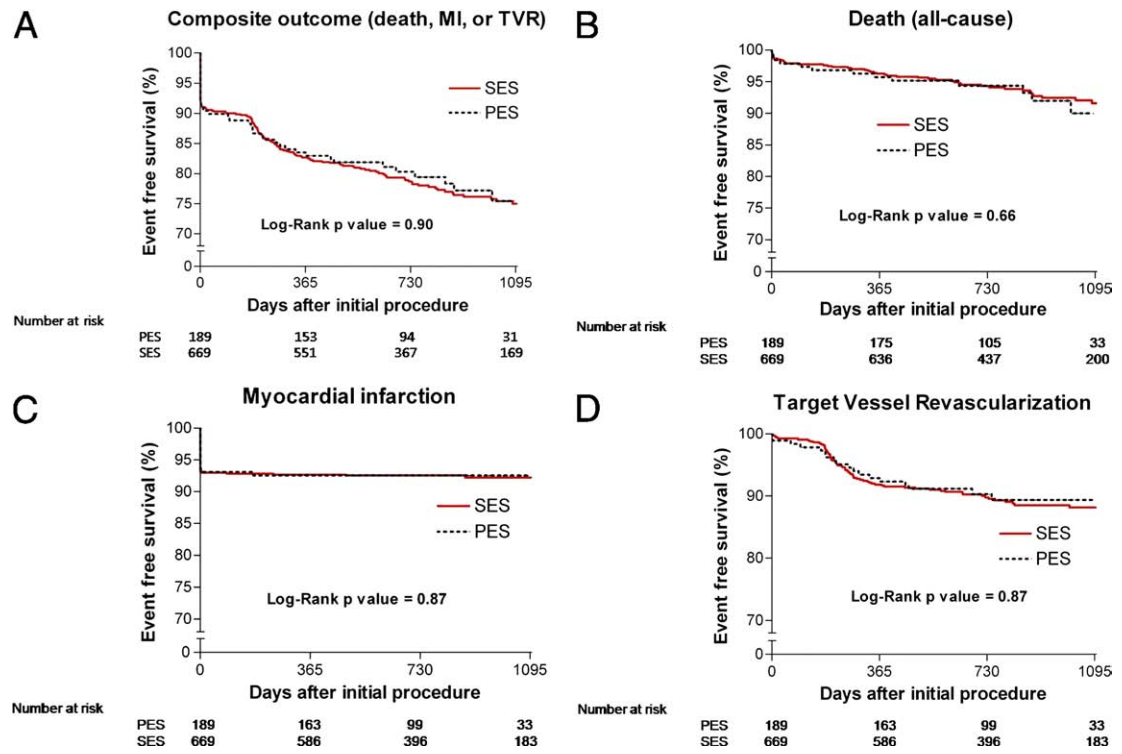

Figure 1 Kaplan-Meier Curves of the Primary Composite End Point (Death, MI, TVR) and Each Component Between SES abd PES

MI = myocardial infarction; PES = paclitaxel-eluting stent(s); SES = sirolimus-eluting stent(s); TVR = target vessel revascularization.

Discussion

Major findings in the current study were that: 1) PCI with DES implantation was effective and safe in patients with unprotected LMCA disease; 2) no significant differences in long-term cardiovascular events were observed between SES and PES; and 3) the documented stent thrombosis rate after LMCA stenting with both stent types was low.

Current guidelines have recommended CABG as the treatment of choice for patients with unprotected LMCA disease (1,2), on the basis of clinical trials demonstrating survival benefit of CABG over medical treatment (22–25). However, because of technical feasibility and marked advancements in PCI devices and adjunctive pharmacology, many clinicians have performed PCI as an alternative revascularization option for these patients. Several registry trials (9–11,13,14,26) have also reported encouraging results—that elective DES implantation in patients with LMCA disease shows acceptable mid-term outcomes, with mortality rates of 0% to approximately 5% and need for TLR rates of 5% to approximately 14% during 1 year. These studies had several limitations, however, including relatively low patient numbers, limited duration of follow-up, and use of a single-center registry.

Several small observational studies have compared outcomes of the 2 first-generation types of DES (SES vs. PES) for LMCA stenting (12,27,28). In a single-center, nonrandomized study comparing SES and PES in 110 patients with LMCA disease, angiographic results (late loss in the main branch [0.32 vs. 0.46 mm] and side branch [0.36 vs. 0.52 mm]) and long-term clinical outcomes (death/MI [16% vs. 18%] and TVR [9% vs. 11%]) were comparable (28). A recent large randomized trial (ISAR-LEFT MAIN [Intracoronary Stenting and Angiographic Results: Drug-Eluting Stents for Unprotected Coronary Left Main Lesions]) found that SES and PES were equally effective and safe in patients undergoing unprotected LMCA stenting (29). After 12 months, the incidences of death (6.6% vs. 5.0%), MI (4.6% vs. 5.0%), stroke (1.0% vs. 1.7%), and major adverse cardiac event (death, MI, or revascularization; 15.8% vs. 13.6%) were similar in the SES and PES groups, as were angiographic restenosis rates at 6 to 9 months (19.4% vs. 16.0%) and 2-year revascularization rates (7.8% vs. 6.5%). Our results validate the findings from the recent RCT (ISAR-LEFT MAIN). In addition, our study provides the longer-term follow-up results up to median 3 years in a routine clinical practice.

Most clinical studies comparing SES and PES for non-LMCA coronary lesions have reported better angiographic results with SES than with PES due to higher suppression of neointimal growth by the former. This

angiographic trend, however, was not directly reflected in significant differences in clinical outcomes (30,31). In patients with LMCA stenting, the impact of late lumen loss on clinical outcomes such as TVR might be less pronounced, due to the relatively short length of the lesions and the larger artery diameter, as compared with other coronary lesions.

Concerns have been raised recently regarding the long-term safety of DES, with particular regard to late stent thrombosis and late mortality (32–34). Increasing concern over stent thrombosis, which might have more catastrophic consequences in patients undergoing unprotected LMCA stenting, and a lack of long-term clinical data have hampered the widespread use of PCI with DES as an alternative to CABG. A recent multicenter registry of 731 patients undergoing LMCA stenting with DES found that the rate of definite or probable thrombosis after 30 months was 0.95% (35). Similar results were observed in another large registry (DELFT study [Sirolimus Versus Paclitaxel Drug-Eluting Stent for Left Main Registry]), with 3-year rates of definite, probable, and possible stent thrombosis of 0.6%, 1.1%, and 4.4%, respectively (27,36), and in a clinical study (ISAR-LEFT MAIN) with a 2-year rate of definite or probable stent thrombosis of 1.3%. We observed a similar incidence of definite or probable stent thrombosis (0.8%), providing further evidence that DES implantation in patients with unprotected LMCA disease results in lower or, at worst, similar rates of stent thrombosis and long-term mortality than are observed in patients with other coronary lesions (37).

Study limitations. First, our study was a nonrandomized observational study. Second, because the choice of specific DES type was mainly determined according to the physician's or patients' preference, there might be selection bias. Despite multivariable adjustment with propensity score, hidden biases might exist because of the influence of unmeasured hidden confounders. In addition, because we did not perform a detailed angiographic analysis, we could not exclude the possibility of concealed angiographic superiority for a specific type of DES. Due to the exploratory nature of the current study, a priori sample size calculation was not pre-specified. Therefore, our results could be underpowered to detect significant differences. Finally, because we did not study whether newer-generation stents are as effective or more effective for LMCA lesions, the current findings apply only to the first-generation DES platform, such as PES and SES.

Conclusions

In a large cohort of patients with unprotected LMCA disease who underwent DES implantation, SES and PES showed similar long-term clinical outcomes.

Randomized trials with long-term follow-up are required to clarify the long-term efficacy and safety of DES implantation compared with CABG for treatment of unprotected LMCA disease.

Reprint requests and correspondence: Dr. Seung-Jung Park, Department of Cardiology, University of Ulsan College of Medicine, Cardiac Center, Asan Medical Center, 388-1 Poongnap-dong, Songpa-gu, Seoul 138-736, Korea. E-mail: sjpark@amc.seoul.kr.

REFERENCES

1. Eagle KA, Guyton RA, Davidoff R, et al. ACC/AHA 2004 guideline update for coronary artery bypass graft surgery: summary article. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for Coronary Artery Bypass Graft Surgery). J Am Coll Cardiol 2004;44:e213–310.
2. Smith SC Jr., Feldman TE, Hirshfeld JW Jr., et al. ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update 2001 Guidelines for Percutaneous Coronary Intervention). J Am Coll Cardiol 2006;3:47:e1–121.
3. Patel M, Dehmer G, Hirshfeld J, Smith P, Spertus J. ACCF/SCAI/STS/AATS/AHA/ASNC 2009 appropriateness criteria for coronary revascularization: a report by the American College of Cardiology Foundation Appropriateness Criteria Task Force, Society for Cardiovascular Angiography and Interventions, Society of Thoracic Surgeons, American Association for Thoracic Surgery, American Heart Association, and the American Society of Nuclear Cardiology Endorsed by the American Society of Echocardiography, the Heart Failure Society of America, and the Society of Cardiovascular Computed Tomography. J Am Coll Cardiol 2009;53:530–53.
4. Park SJ, Park SW, Hong MK, et al. Stenting of unprotected left main coronary artery stenoses: immediate and late outcomes. J Am Coll Cardiol 1998;31:37–42.
5. Park SJ, Hong MK, Lee CW, et al. Elective stenting of unprotected left main coronary artery stenosis: effect of debulking before stenting and intravascular ultrasound guidance. J Am Coll Cardiol 2001;38:1054–60.
6. Silvestri M, Barragan P, Sainsous J, et al. Unprotected left main coronary artery stenting: immediate and medium-term outcomes of 140 elective procedures. J Am Coll Cardiol 2000;35:1543–50.
7. Black A, Cortina R, Bossi I, Choussat R, Fajadet J, Marco J. Unprotected left main coronary artery stenting: correlates of midterm survival and impact of patient selection. J Am Coll Cardiol 2001;37:832–8.
8. Park SJ, Seung KB, Park DW, et al. Stents versus coronary-artery bypass grafting for left main coronary artery disease. N Engl J Med 2008;358:1781–92.
9. Chieffo A, Stankovic G, Bonizzoni E, et al. Early and mid-term results of drug-eluting stent implantation in unprotected left main. Circulation 2005;111:791–5.
10. Park SJ, Kim YH, Lee BK, et al. Sirolimus-eluting stent implantation for unprotected left main coronary artery stenosis: comparison with bare metal stent implantation. J Am Coll Cardiol 2005;45:351–6.
11. Valgimigli M, van Mieghem CA, Ong AT, et al. Short- and long-term clinical outcome after drug-eluting stent implantation for the percutaneous treatment of left main coronary artery disease: insights from the Rapamycin-Eluting and Taxus Stent Evaluated At Rotterdam Cardiology Hospital registries (RESEARCH and T-SEARCH). Circulation 2005;111:1383–9.
12. Ge L, Cosgrave J, Iakovou I, et al. Long-term outcomes following drug-eluting stent implantation in unprotected left main bifurcation lesions. Chin Med J (Engl) 2007;120:545–51.
13. Sheiban I, Meliga E, Moretti C, et al. Long-term clinical and angiographic outcomes of treatment of unprotected left main coronary artery stenosis with sirolimus-eluting stents. Am J Cardiol 2007;100:431–5.

14. Kim YH, Dangas GD, Solinas E, et al. Effectiveness of drug-eluting stent implantation for patients with unprotected left main coronary artery stenosis. Am J Cardiol 2008;101:801–6.
15. Chieffo A, Morici N, Maisano F, et al. Percutaneous treatment with drug-eluting stent implantation versus bypass surgery for unprotected left main stenosis: a single-center experience. Circulation 2006;113: 2542–7.
16. Biondi-Zoccai GG, Lotrionte M, Moretti C, et al. A collaborative systematic review and meta-analysis on 1278 patients undergoing percutaneous drug-eluting stenting for unprotected left main coronary artery disease. Am Heart J 2008;155:274–83.
17. Park S-J, Lee CW, Kim Y-H, et al. Technical feasibility, safety, and clinical outcome of stenting of unprotected left main coronary artery bifurcation narrowing. Am J Cardiol 2002;90:374–8.
18. Cutlip DE, Windecker S, Mehran R, et al. Clinical end points in coronary stent trials: a case for standardized definitions. Circulation 2007;115:2344–51.
19. Cox D. Regression models and life tables. J R Stat Soc B 1972;34: 187–220.
20. Cain KC, Lange NT. Approximate case influence for the proportional hazards regression model with censored data. Biometrics 1984;40: 493–9.
21. D'Agostino RB Jr. Propensity score methods for bias reduction in the comparison of a treatment to a non-randomized control group. Stat Med 1998;17:2265–81.
22. Yusuf S, Zucker D, Peduzzi P, et al. Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. Lancet 1994;344:563–70.
23. Chaitman BR, Fisher LD, Bourassa MG, et al. Effect of coronary bypass surgery on survival patterns in subsets of patients with left main coronary artery disease. Report of the Collaborative Study in Coronary Artery Surgery (CASS). Am J Cardiol 1981;48:765–77.
24. Takaro T, Peduzzi P, Detre KM, et al. Survival in subgroups of patients with left main coronary artery disease. Veterans Administration Cooperative Study of Surgery for Coronary Arterial Occlusive Disease. Circulation 1982;66:14–22.
25. Caracciolo EA, Davis KB, Sopko G, et al. Comparison of surgical and medical group survival in patients with left main equivalent coronary artery disease. Long-term CASS experience. Circulation 1995;91: 2335–44.
26. Chieffo A, Park SJ, Valgimigli M, et al. Favorable long-term outcome after drug-eluting stent implantation in nonbifurcation lesions that involve unprotected left main coronary artery: a multicenter registry. Circulation 2007;116:158–62.
27. Meliga E, Garcia-Garcia HM, Valgimigli M, et al. Impact of drug-eluting stent selection on long-term clinical outcomes in patients treated for unprotected left main coronary artery disease: the sirolimus vs paclitaxel drug-eluting stent for left main registry (SP-DELFT). Int J Cardiol 2008 Aug 6 [E-pub ahead of print].
28. Valgimigli M, Malagutti P, Aoki J, et al. Sirolimus-eluting versus paclitaxel-eluting stent implantation for the percutaneous treatment of left main coronary artery disease: a combined RESEARCH and T-SEARCH long-term analysis. J Am Coll Cardiol 2006;47:507–14.
29. Mehilli J Kastrati A, Byrne RA, et al., LEFT-MAIN Intracoronary Stenting and Angiographic Results: Drug-Eluting Stents for Unprotected Coronary Left Main Lesions Study Investigators. Paclitaxel-versus sirolimus-eluting stents for unprotected left main coronary artery disease: ISAR-LEFT MAIN trial. J Am Coll Cardiol 2009;53: 1760–8.
30. Morice MC, Colombo A, Meier B, et al. Sirolimus- vs paclitaxel-eluting stents in de novo coronary artery lesions: the REALITY trial: a randomized controlled trial. JAMA 2006;295:895–904.
31. Kastrati A, Dibra A, Eberle S, et al. Sirolimus-eluting stents vs paclitaxel-eluting stents in patients with coronary artery disease: meta-analysis of randomized trials. JAMA 2005;294:819–25.
32. Lagerqvist B, James SK, Stenestrand U, Lindback J, Nilsson T, Wallentin L. Long-term outcomes with drug-eluting stents versus bare-metal stents in Sweden. N Engl J Med 2007;356:1009–19.
33. Stone GW, Moses JW, Ellis SG, et al. Safety and efficacy of sirolimus- and paclitaxel-eluting coronary stents. N Engl J Med 2007;356:998–1008.
34. Mauri L, Hsieh WH, Massaro JM, Ho KK, D'Agostino R, Cutlip DE. Stent thrombosis in randomized clinical trials of drug-eluting stents. N Engl J Med 2007;356:1020–9.
35. Chieffo A, Park SJ, Meliga E, et al. Late and very late stent thrombosis following drug-eluting stent implantation in unprotected left main coronary artery: a multicentre registry. Eur Heart J 2008;29:2108–15.
36. Meliga E, Garcia-Garcia HM, Valgimigli M, et al. Longest available clinical outcomes after drug-eluting stent implantation for unprotected left main coronary artery disease: the DELFT (Drug Eluting stent for LeFT main) Registry. J Am Coll Cardiol 2008;51:2212–9.
37. Daemen J, Wenaweser P, Tsuchida K, et al. Early and late coronary stent thrombosis of sirolimus-eluting and paclitaxel-eluting stents in routine clinical practice: data from a large two-institutional cohort study. Lancet 2007;369:667–78.

Key Words: drug-eluting stent ■ left main coronary artery disease ■ PCI.