

Complexity of Atherosclerotic Coronary Artery Disease and Long-Term Outcomes in Patients With Unprotected Left Main Disease Treated With Drug-Eluting Stents or Coronary Artery Bypass Grafting

Duk-Woo Park, MD,* Young-Hak Kim, MD,* Sung-Cheol Yun, PhD,† Hae Geun Song, MD,* Jung-Min Ahn, MD,* Jun-Hyok Oh, MD,* Won-Jang Kim, MD,* Jong-Young Lee, MD,* Soo-Jin Kang, MD,* Seung-Whan Lee, MD,* Cheol Whan Lee, MD,* Seong-Wook Park, MD,* Seung-Jung Park, MD*

Seoul, Korea

- Objectives** The aim of this study was to compare treatment effects of drug-eluting stents (DES) or coronary artery bypass grafting (CABG) for left main coronary artery (LMCA) disease according to the complexity of atherosclerotic disease burden.
- Background** Limited information is available on the relationships between the extent of coronary atherosclerosis and very long-term outcomes of surgical or percutaneous LMCA revascularization.
- Methods** A total of 1,146 patients with unprotected LMCA disease who received DES (n = 645) or underwent CABG (n = 501) were evaluated. The extent of atherosclerotic disease burden was measured using the SYNTAX (Synergy Between PCI With Taxus and Cardiac Surgery) score; a low-risk score was defined as ≤ 22 , an intermediate-risk score as 23 to 32, and a high-risk score as ≥ 33 .
- Results** After multivariate adjustment with the inverse-probability-of-treatment weighting method, the 5-year risks for death (6.1% for DES vs. 16.2% for CABG; hazard ratio [HR]: 0.52; 95% confidence interval [CI]: 0.21 to 1.28; $p = 0.15$) and the composite of death, Q-wave myocardial infarction, or stroke (6.4% vs. 16.2%; HR: 0.54; 95% CI: 0.22 to 1.34; $p = 0.18$) favored DES in patients with low-risk SYNTAX scores; in contrast, the 5-year risks for death (26.9% vs. 17.8%; HR: 1.46; 95% CI: 0.92 to 2.30; $p = 0.11$) and the composite outcome (27.6% vs. 19.5%; HR: 1.36; 95% CI: 0.87 to 2.12; $p = 0.18$) favored CABG in patients with high-risk SYNTAX scores (interaction $p = 0.047$ for death, interaction $p = 0.08$ for composite outcome). Patients undergoing CABG consistently had lower rates of target vessel revascularization.
- Conclusions** According to the complexity of concomitant coronary disease, there were differential treatment effects on long-term mortality in patients with unprotected LMCA disease who received DES or underwent CABG. (J Am Coll Cardiol 2011;57:2152-9) © 2011 by the American College of Cardiology Foundation

Over the past few years, revascularization of patients with significant coronary artery disease (CAD) has markedly improved because of advances in both coronary artery bypass grafting (CABG) and percutaneous coronary intervention

(PCI), contributing to reductions in mortality and morbidity (1,2). In particular, PCI involving drug-eluting stents (DES) is increasingly used to treat complex CAD, such as unprotected left main coronary artery (LMCA) disease, for which CABG has been regarded historically as the treatment of choice (3).

The choice of PCI or CABG for treatment of LMCA disease or multivessel CAD depends on several clinical and anatomical features, making optimal patient selection crucial in determining the appropriate treatment and in achieving favorable long-term outcomes (4). Among these factors, observational comparisons of CABG and PCI suggest a strong relation between the extent of atherosclerotic CAD

From the *Division of Cardiology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea; 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 by grant 0412-CR02-0704-0001 from the Korea Health 21 R&D Project, Ministry of Health and Welfare (Seoul, Korea). All authors have reported that they have no relationships to disclose.

Manuscript received October 20, 2010; revised manuscript received December 13, 2010, accepted January 11, 2011.

and the relative effectiveness of these procedures on clinical outcomes (5–11). However, in these studies, only a crude proxy of atherosclerotic disease burden (i.e., the number of disease vessels or involvement of specific disease location) has been used, and therefore significant interaction between the extent of atherosclerosis and treatment effect was underestimated.

We previously reported that PCI with stenting showed similar rates of safety outcomes, but inferior rates of efficacy outcomes, compared with CABG in patients with unprotected LMCA disease (12). However, the lack of information to measure the extent of atherosclerosis would act as important unmeasured confounders, and it could penalize the apparent long-term benefits of surgery over PCI. Recently, a detailed angiographic scoring system (SYNTAX [Synergy Between PCI With Taxus and Cardiac Surgery] score) to reflect complexity of CAD has been developed and validated in several cohorts of patients with atherosclerotic coronary disease (13–17).

In this study, to determine whether atherosclerotic disease burden may influence the treatment choice and, importantly, may also be linked to long-term outcomes, we compared the relative treatment effects of PCI or CABG for unprotected LMCA disease according to a more detailed measure of extent of disease, such as the SYNTAX score.

Methods

Study group and design. The MAIN-COMPARE (Revascularization for Unprotected Left Main Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty Versus Surgical Revascularization) study enrolled patients with unprotected LMCA stenosis who underwent CABG or PCI as the index procedure at 12 major cardiac centers in Korea between January 2000 and June 2006 (18). From January 2000 through May 2003, coronary stenting was performed exclusively with bare-metal stents, whereas from May 2003 through June 2006, DES were used exclusively. Because the SYNTAX score was developed in the DES era, as an integral part of the SYNTAX trial design, and methods of stent implantation have evolved from the bare-metal stent era to the DES era with an attempt to fully cover the diseased segments, we included only the post-DES cohort (wave 2 of the registry; DES vs. concurrent CABG between May 2003 and June 2006) among the overall cohort for these analyses. The details of the overall cohort and a separate cohort from bare-metal stents to DES have been described previously (12). Patients who had prior CABG, those who underwent concomitant valvular or aortic surgery, and those who had ST-segment elevation myocardial infarction (MI) or presented with cardiogenic shock were excluded. The local ethics committee at each hospital approved the use of clinical data for this study, and all patients provided written informed consent.

Patients underwent PCI, instead of CABG, because of either patient or physician preference or the high risk associated with CABG. Methods of stent implantation for patients with LMCA disease have been described previously (19,20). All procedures were performed using standard interventional techniques. Antiplatelet therapy and periprocedural anticoagulation followed standard regimens. After the procedure, patients were prescribed aspirin indefinitely and clopidogrel for at least 6 months, regardless of DES type. Surgical revascularization was performed using standard bypass techniques (21). Complete revascularization was performed when possible using arterial conduits or saphenous vein grafts. Clinical follow-up after PCI and after CABG was recommended at 1 month, 6 months, and 1 year and then annually thereafter. For this analysis, the follow-up period extended through October 30, 2009, to ensure that all patients had an opportunity for at least 3 years and approximately up to 7 years of follow-up information.

The primary safety outcomes were death and the composite of death, Q-wave MI, or stroke. The primary efficacy outcome was target vessel revascularization (TVR). Death was defined as death from any cause. Q-wave MI was defined as documentation of a new abnormal Q-wave after the index revascularization. Stroke, as indicated by neurological deficits, was confirmed by a neurologist on the basis of imaging studies. TVR was defined as any repeat revascularization in any left anterior descending coronary artery or left circumflex coronary artery, as well as in the target segment. All outcomes of interest were confirmed by source documentation collected at each hospital and were centrally adjudicated by an independent group of clinicians.

The SYNTAX score reflects a comprehensive anatomical assessment, with higher scores indicating more complex CAD. As previously defined (13,14), we categorized study patients according to the SYNTAX score; a low score was defined as ≤ 22 , an intermediate score as 23 to 32, and a high score as ≥ 33 . SYNTAX scores were calculated by the independent angiographers blinded to patient information and treatment types. The details of angiographic measurements and the SYNTAX scoring algorithm at the core laboratory have been described elsewhere (22).

Statistical analysis. For each category of the SYNTAX score, patient characteristics pertaining to the index revascularization, including demographic characteristics, the presence or absence of a variety of clinical and coexisting conditions, cardiac presentation, left ventricular function, and lesion characteristics were compared between DES and CABG with the use of the Student *t* tests or Wilcoxon

Abbreviations and Acronyms

| | |
|-------------|--------------------------------------|
| CABG | = coronary artery bypass grafting |
| CAD | = coronary artery disease |
| DES | = drug-eluting stent(s) |
| LMCA | = left main coronary artery |
| MI | = myocardial infarction |
| PCI | = percutaneous coronary intervention |
| TVR | = target vessel revascularization |

nonparametric tests for continuous variables and the chi-square or Fisher exact test for categorical variables. Five-year cumulative incidence rates of clinical outcomes were estimated using the Kaplan-Meier method and compared using the log-rank test.

To reduce the impact of treatment selection bias and potential confounding in an observational study, we performed rigorous adjustment for differences in baseline characteristics of patients by use of weighted Cox proportional-hazards regression models using inverse-probability-of-treatment weighting (23). With that technique, weights for patients receiving CABG were the inverse of (1 - propensity score), and weights for patients receiving DES were the inverse of the propensity score. Propensity scores were estimated without regard to outcomes, using multiple logistic regression analysis. A full nonparsimonious model was developed that included all variables shown in Table 1. Model discrimination was assessed using c-statistics, and model calibration was assessed using Hosmer-Lemeshow statistics. For each SYNTAX category (low, intermediate, and high risk), a separate propensity score for DES versus CABG was derived. Interactions between the levels of SYNTAX score and treatment strategy were tested by the incorporation of formal interaction terms in the multivariate

Cox model. Weighted Cox proportional-hazards regression models and adjusted survival curves were constructed using inverse probability weights (24). All statistical analyses were performed using SAS version 9.1 (SAS Institute, Inc., Cary, North Carolina), and a 2-sided p value of ≤0.05 was considered to indicate statistical significance.

Results

Population. Between May 2003 and June 2006, 1,474 patients with unprotected LMCA disease were treated with DES implantation (n = 784) or CABG (n = 690). During the study enrollment period, the SYNTAX score algorithm was not available for the physicians. A retrospective retrieval of a baseline angiogram for a detailed measurement of the SYNTAX score was available in 1,146 patients (78%) of the overall cohort (645 patients [82%] in the DES group and 501 patients [73%] in the CABG group). The mean SYNTAX score was significantly lower in the DES group than in the CABG group (24.8 ± 10.9 vs. 38.7 ± 13.3, p < 0.001).

Comparisons of the baseline characteristics between 2 treatment groups in each of the SYNTAX categories are shown in Table 1. In each category of the SYNTAX score,

Table 1 Baseline Characteristics of Patients According to SYNTAX Score

| Variable | Low Risk (≤22) (n = 363) | | | Intermediate Risk (23–32) (n = 292) | | | High Risk (≥33) (n = 491) | | |
|--|--------------------------|---------------|---------|-------------------------------------|----------------|---------|---------------------------|----------------|---------|
| | DES (n = 302) | CABG (n = 61) | p Value | DES (n = 188) | CABG (n = 104) | p Value | DES (n = 155) | CABG (n = 336) | p Value |
| Clinical characteristics | | | | | | | | | |
| Age (yrs) | 58.5 ± 11.2 | 62.0 ± 9.8 | 0.02 | 64.9 ± 10.1 | 62.8 ± 9.4 | 0.08 | 66.1 ± 10.2 | 64.5 ± 8.8 | 0.09 |
| Men | 202 (66.9%) | 47 (77.0%) | 0.12 | 139 (73.9%) | 75 (72.1%) | 0.74 | 112 (72.3%) | 237 (70.5%) | 0.70 |
| Diabetes mellitus | 76 (25.2%) | 18 (29.5%) | 0.48 | 64 (34.0%) | 34 (32.7%) | 0.82 | 69 (44.5%) | 137 (40.8%) | 0.44 |
| Hypertension | 132 (43.7%) | 25 (41.0%) | 0.70 | 119 (63.3%) | 51 (49.0%) | 0.02 | 95 (61.3%) | 179 (53.3%) | 0.10 |
| Hyperlipidemia | 93 (30.8%) | 17 (27.9%) | 0.65 | 58 (30.9%) | 31 (29.8%) | 0.85 | 64 (41.3%) | 152 (45.2%) | 0.41 |
| Current smoker | 76 (25.2%) | 21 (34.4%) | 0.14 | 53 (28.2%) | 30 (28.8%) | 0.91 | 24 (15.5%) | 75 (22.3%) | 0.08 |
| Previous coronary angioplasty | 59 (19.5%) | 11 (18.0%) | 0.79 | 45 (23.9%) | 11 (10.6%) | 0.005 | 36 (23.2%) | 35 (10.4%) | <0.001 |
| Previous MI | 18 (6.0%) | 7 (11.5%) | 0.12 | 22 (11.7%) | 11 (10.6%) | 0.77 | 18 (11.6%) | 37 (11.0%) | 0.84 |
| Previous congestive heart failure | 2 (0.7%) | 0 (0%) | >0.99 | 4 (2.1%) | 3 (2.9%) | 0.70 | 5 (3.2%) | 12 (3.6%) | 0.85 |
| Chronic obstructive pulmonary disease | 8 (2.6%) | 2 (3.3%) | 0.68 | 5 (2.7%) | 1 (1.0%) | 0.43 | 3 (1.9%) | 11 (3.3%) | 0.56 |
| Cerebrovascular disease | 15 (5.0%) | 2 (3.3%) | 0.75 | 22 (11.7%) | 4 (3.8%) | 0.02 | 17 (11.0%) | 29 (8.6%) | 0.41 |
| Peripheral vascular disease | 3 (1.0%) | 2 (3.3%) | 0.20 | 4 (2.1%) | 2 (1.9%) | >0.99 | 4 (2.6%) | 21 (6.3%) | 0.09 |
| Renal failure | 5 (1.7%) | 2 (3.3%) | 0.33 | 6 (3.2%) | 3 (2.9%) | >0.99 | 9 (5.8%) | 15 (4.5%) | 0.52 |
| Left ventricular ejection fraction (%) | 61.9 ± 9.1 | 59.3 ± 10.6 | 0.08 | 59.1 ± 11.8 | 59.1 ± 11.3 | 0.98 | 58.3 ± 10.7 | 55.1 ± 11.6 | 0.008 |
| Acute coronary syndromes | 186 (61.6%) | 38 (62.3%) | 0.92 | 113 (60.1%) | 71 (68.3%) | 0.17 | 93 (60.0%) | 268 (79.8%) | <0.001 |
| EuroSCORE | 3.3 ± 2.1 | 4.0 ± 2.7 | 0.06 | 4.1 ± 2.4 | 4.1 ± 2.1 | 0.84 | 4.3 ± 2.6 | 4.8 ± 2.3 | 0.04 |
| Angiographic characteristics | | | | | | | | | |
| Distal LMCA bifurcation disease | 151 (50.0%) | 39 (63.9%) | 0.047 | 123 (65.4%) | 62 (59.6%) | 0.32 | 100 (64.5%) | 171 (50.9%) | 0.005 |
| Extent of diseased vessels | | | 0.56* | | | 0.16* | | | <0.001* |
| LMCA only | 113 (37.4%) | 15 (24.6%) | | 8 (4.3%) | 2 (1.9%) | | 6 (3.9%) | 0 (0%) | |
| LMCA plus single-vessel disease | 87 (28.8%) | 13 (21.3%) | | 39 (20.7%) | 15 (14.4%) | | 16 (10.3%) | 10 (3.0%) | |
| LMCA plus double-vessel disease | 57 (18.9%) | 19 (31.1%) | | 72 (38.3%) | 36 (34.6%) | | 50 (32.3%) | 64 (19.0%) | |
| LMCA plus triple-vessel disease | 45 (14.9%) | 14 (23.0%) | | 69 (36.7%) | 51 (49.0%) | | 83 (53.5%) | 262 (78.0%) | |
| Right coronary artery disease | 70 (23.2%) | 21 (34.4%) | 0.06 | 99 (52.7%) | 73 (70.2%) | 0.004 | 100 (64.5%) | 296 (88.1%) | <0.001 |

Data are expressed as mean ± SD or n (%). *p value for trend.

CABG = coronary artery bypass grafting; DES = drug-eluting stents; EuroSCORE = European System for Cardiac Operative Risk Evaluation; LMCA = left main coronary artery; SYNTAX = Synergy Between PCI With Taxus and Cardiac Surgery.

there were some imbalances of baseline clinical and angiographic features between the 2 treatment groups with statistical significance. Overall, with increasing SYNTAX score, patients had higher risk clinical and angiographic profiles.

Procedural characteristics of the study patients were as follows: 1) among DES patients, 78% received sirolimus-eluting stents and 22% received paclitaxel-eluting stents; 2) the mean number of stents implanted in a patient's LMCA lesions was 1.2 ± 0.5 , the mean total length of the stents was 32.8 ± 22.0 mm, and the mean stent diameter was 3.4 ± 0.2 mm; 3) among CABG patients, 46% underwent off-pump surgery; and 4) 96% underwent revascularization of the left anterior descending coronary artery with an internal thoracic artery. Complete revascularization was achieved in 64% of DES patients and 80% of CABG patients.

Outcomes. The median follow-up duration was 55.1 months (interquartile range: 45.8 to 65.5 months) in the overall patient group. Complete follow-up for major clinical events was obtained in 98.3% of the overall cohort (98.4% for the DES group and 98.0% for the CABG group; $p = 0.57$).

During 5 years of follow-up, the observed long-term rates of death and the composite of death, Q-wave MI, or stroke were significantly lower in the DES group than in the CABG group in patients with low SYNTAX scores (Table 2, Fig. 1). These safety outcomes were similar between the 2 treatment groups among patients with intermediate scores, but there was evidence of a nonsignificant increase in the rate of safety outcomes associated with DES compared with CABG in patients with high scores. The advantage of CABG was quite consistent for TVR.

After adjustment of baseline covariates using inverse-probability-of-treatment weighting in each of the SYNTAX

score categories, the adjusted hazard ratios for death and serious composite outcomes favored DES treatment in patients with low SYNTAX scores; in contrast, the adjusted hazard ratios for these safety outcomes favored CABG in patients with high scores (Table 2, Fig. 2). When we assessed the effect on outcomes of treatment strategy and its interaction with SYNTAX score category, treatment effects for death and composite outcomes, but not TVR, were modified by the level of SYNTAX score (interaction $p = 0.047$ for death, interaction $p = 0.08$ for composite outcome, and interaction $p = 0.45$ for TVR).

In the DES group, the rates of death and the composite of death, Q-wave MI, or stroke were significantly increased in patients with high SYNTAX scores compared with those with low or intermediate scores. In the CABG group, however, there was no uniform increase of safety outcomes according to SYNTAX score.

In the overall population, the unadjusted risks for death and the composite of death, Q-wave MI, or stroke were significantly lower in the DES group than in the CABG group, whereas the rate of TVR was significantly higher in the DES group (Table 3). After adjustment of the SYNTAX score, however, the 5-year risks for death and the composite of death, Q-wave MI, or stroke were similar in the 2 groups, but the adjusted risk for TVR was consistently higher with DES. Similar results were observed even after adjustments of the SYNTAX score and all potentially explanatory factors for clinical outcomes.

Discussion

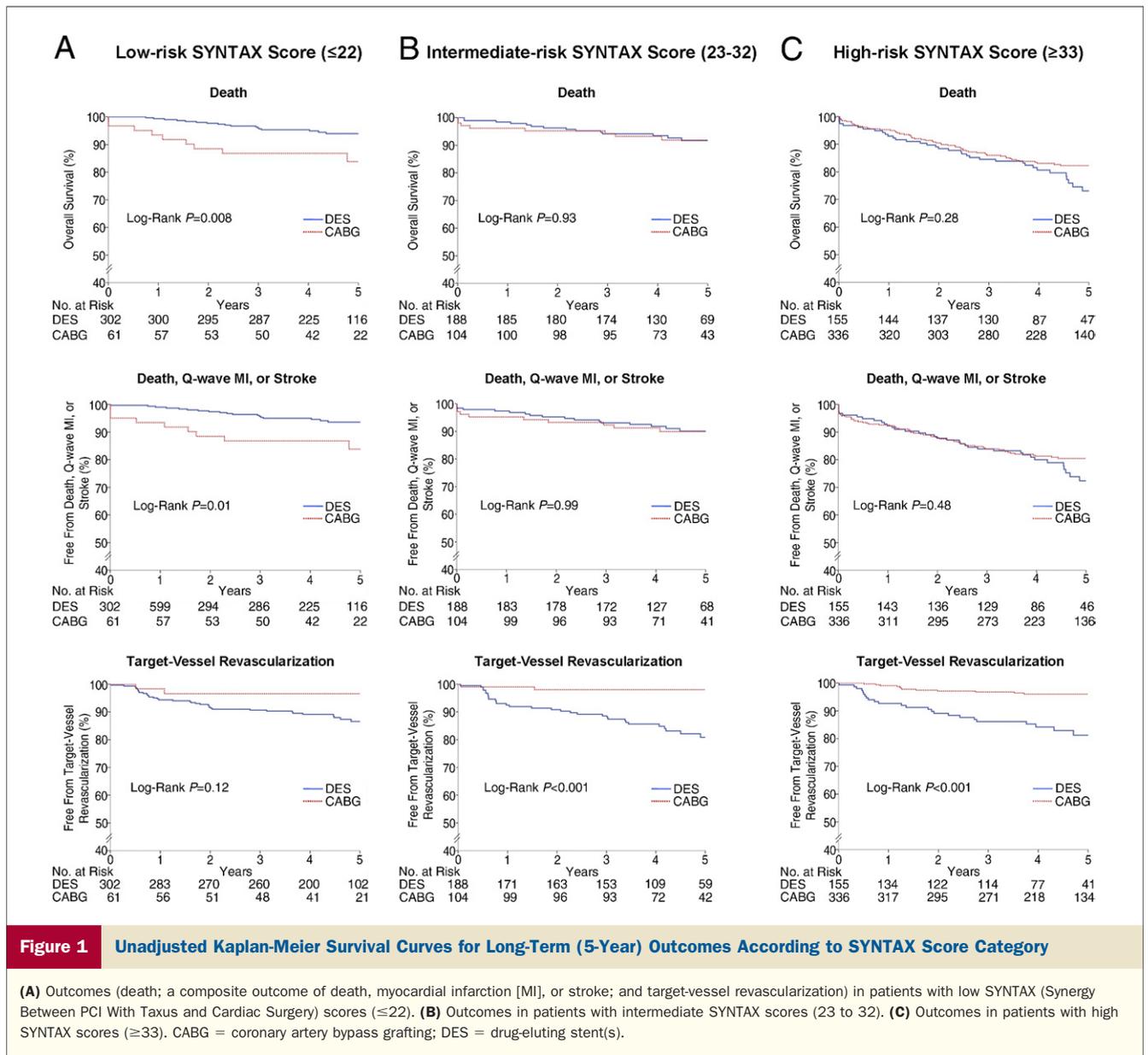
In this large-scale, multicenter study, which included 1,146 patients with unprotected LMCA disease, we found that the adjusted long-term (5-year) risks for death and a composite of serious outcomes (death, Q-wave MI, or stroke) favored DES implantation over CABG in patients

Table 2 HRs for Clinical Outcomes After DES Implantation Compared With CABG, According to SYNTAX Score Category*

| Outcome | n/Total Number of Events | | Cumulative Event Rate at 5 Yrs (%) | | Unadjusted | | Adjusted by Inverse-Probability-of-Treatment Weights† | |
|--|--------------------------|------|------------------------------------|------|-------------------|---------|---|---------|
| | DES | CABG | DES | CABG | HR (95% CI) | p Value | HR (95% CI) | p Value |
| Low risk (SYNTAX score ≤ 22) | | | | | | | | |
| Death | 302 | 61 | 6.1 | 16.2 | 0.35 (0.16-0.79) | 0.01 | 0.52 (0.21-1.28) | 0.15 |
| Composite outcome‡ | 18 | 9 | 6.4 | 16.2 | 0.38 (0.17-0.84) | 0.02 | 0.54 (0.22-1.34) | 0.18 |
| TVR | 37 | 3 | 13.4 | 3.5 | 2.46 (0.76-7.98) | 0.13 | 2.45 (0.75-8.08) | 0.14 |
| Intermediate risk (SYNTAX score 23-32) | | | | | | | | |
| Death | 188 | 104 | 8.3 | 8.1 | 1.04 (0.44-2.45) | 0.93 | 1.00 (0.38-2.62) | 0.99 |
| Composite outcome‡ | 18 | 10 | 9.9 | 10.1 | 0.99 (0.46-2.15) | 0.99 | 1.01 (0.42-2.45) | 0.97 |
| TVR | 31 | 2 | 19.2 | 2.0 | 9.06 (2.17-37.84) | 0.003 | 10.99 (2.56-47.33) | 0.001 |
| High risk (SYNTAX score ≥ 33) | | | | | | | | |
| Death | 155 | 336 | 26.9 | 17.8 | 1.26 (0.83-1.90) | 0.28 | 1.46 (0.92-2.30) | 0.11 |
| Composite outcome‡ | 36 | 70 | 27.6 | 19.5 | 1.15 (0.77-1.73) | 0.49 | 1.36 (0.87-2.12) | 0.18 |
| TVR | 25 | 12 | 18.8 | 4.0 | 4.95 (2.49-9.86) | <0.001 | 5.24 (2.28-12.06) | <0.001 |

*HRs are for the DES group relative to the CABG group. †p value for the treatment by covariate (SYNTAX score category) interaction: interaction $p = 0.047$ for death, interaction $p = 0.08$ for composite outcome, interaction $p = 0.45$ for TVR. ‡Death, Q-wave MI, or stroke.

CI = confidence interval; HR = hazard ratio; TVR = target vessel revascularization; other abbreviations as in Table 1.



with low risk for lesion complexity, as measured by the SYNTAX score. Otherwise, the long-term risks for death and the composite of serious outcomes favored CABG over PCI in patients with high risk for lesion complexity. The rates of TVR were consistently higher with DES than CABG, regardless of SYNTAX score.

Compared with clinical trials, observational studies such as ours may more accurately reflect “real-world” experience in treating patients with LMCA disease. As with all observational research, however, patient selection bias may have a profound impact on outcomes, and there are many considerations when one is choosing a treatment intervention (4). Many patients with LMCA disease have concomitant multivessel disease. It is likely that patients with less complex anatomy of atherosclerotic CAD tend to be more often referred for PCI, whereas those with more severe

disease tend to be preferentially considered for bypass surgery. Sometimes, patients with very complex angiographic features have contraindications or are deemed ineligible for PCI. As such, because treatment type is considerably correlated with the extent of atherosclerotic disease burden, it is difficult to design a convincing observational study that compares PCI with CABG for outcomes that are related to disease burden. These factors therefore may cause potential bias due to confounding by indication in comparative clinical strategies studies (25).

Although several observational studies have attempted to correct for atherosclerotic disease burden with covariates such as the extent of diseased vessels (i.e., a count of diseased vessels), this is a relatively generic concept that lacks specificity to measure the extent of atherosclerotic burden of disease. Therefore, adjustment for high-quality

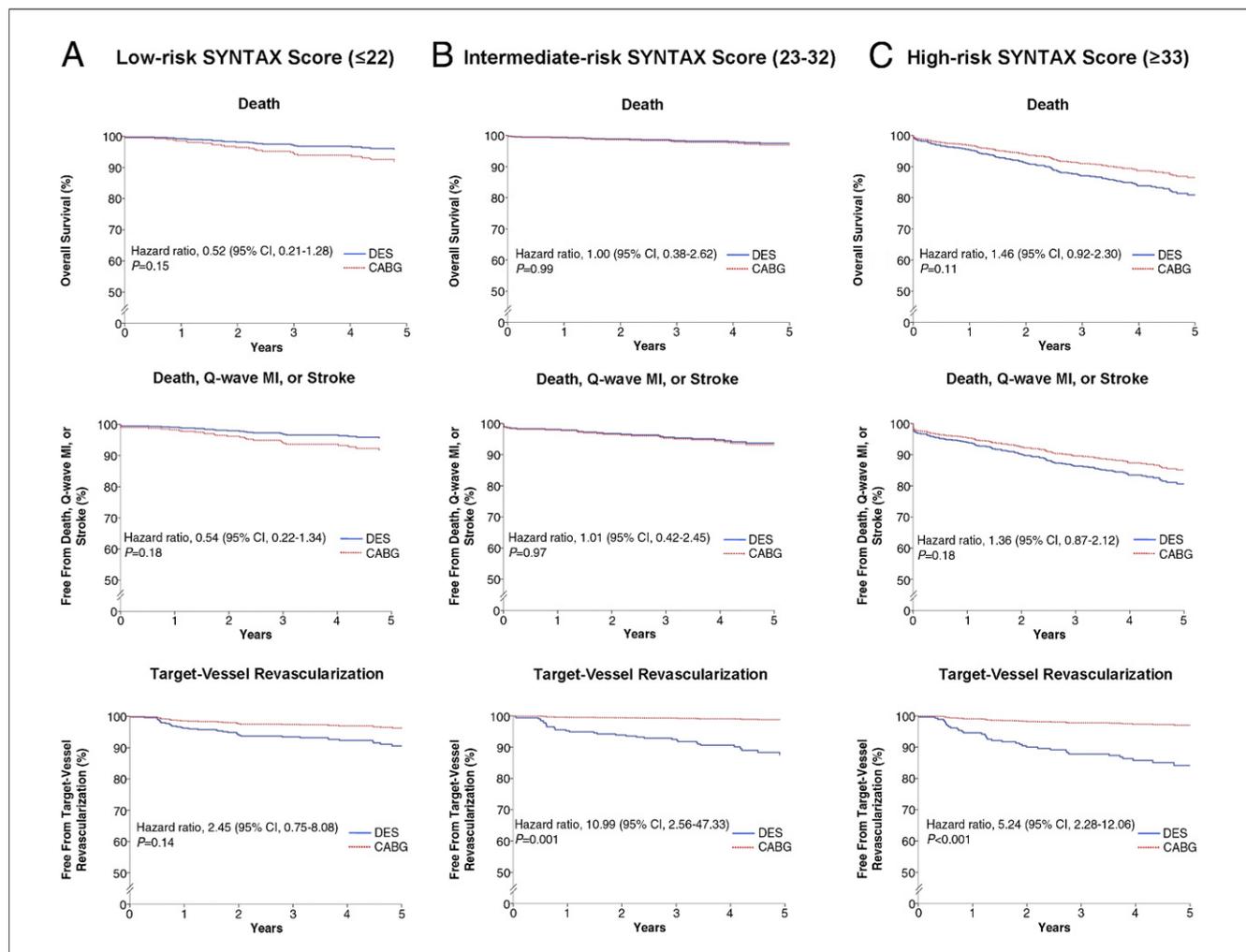


Figure 2 Adjusted Survival Curves for Long-Term (5-Year) Outcomes According to SYNTAX Score Category

(A) Outcomes (death; a composite outcome of death, MI, or stroke; and target-vessel revascularization) in patients with low SYNTAX scores (≤ 22). (B) Outcomes in patients with intermediate SYNTAX scores (23 to 32). (C) Outcomes in patients with high SYNTAX scores (≥ 33). Abbreviations as in Figure 1.

anatomical data representing atherosclerotic burden might minimize confounding by indication. The SYNTAX score is a detailed anatomical scoring system that reflects atherosclerotic disease burden. In our large cohort of patients with unprotected LMCA disease, even after comprehensive anatomical adjustment using the SYNTAX score, PCI with DES implantation showed similar long-term safety outcomes, but inferior effectiveness outcomes, compared with CABG.

The recent SYNTAX trial reported that patients with the least extensive CAD had better outcomes after DES treatment, whereas patients with the most extensive disease had better outcomes after CABG among those with 3-vessel or LMCA disease (13,14). However, the follow-up in this study was limited in duration, which may have resulted in a disadvantage for CABG, because the apparent benefits of surgery over PCI are usually not fully evident until 1 to 5 years after the procedure (26). Furthermore, the long-term

Table 3 Cox Proportional-Hazards Analyses of Time to Clinical Events Among Overall Patient Group*

| Outcome | Unadjusted | | Adjusted for SYNTAX Score | | Adjusted for SYNTAX Score and All Covariates† | |
|--------------------|------------------|---------|---------------------------|---------|---|---------|
| | HR (95% CI) | p Value | HR† (95% CI) | p Value | HR† (95% CI) | p Value |
| Death | 0.63 (0.46-0.87) | 0.006 | 1.08 (0.74-1.56) | 0.70 | 0.92 (0.63-1.35) | 0.66 |
| Composite outcome‡ | 0.61 (0.45-0.83) | 0.002 | 1.03 (0.72-1.48) | 0.85 | 0.91 (0.63-1.31) | 0.62 |
| TVR | 4.40 (2.62-7.38) | <0.001 | 5.35 (3.04-9.44) | <0.001 | 5.84 (3.26-10.48) | <0.001 |

*HRs are for the DES group relative to the CABG group. †For a list of covariates, see Table 1. ‡Death, Q-wave MI, or stroke. Abbreviations as in Tables 1 and 2.

safety of DES has been questioned by recent reports suggesting increased risks for late stent thrombosis, mortality, and MI (27,28). Therefore, very long-term assessment of safety and efficacy of DES treatment, compared with standard CABG, in a large cohort of patients with unprotected LMCA disease is clinically essential. Consistent with previous data and our hypothesis, we found an important relationship between a more detailed measure of the complexity of atherosclerotic CAD and long-term (5-year) treatment effects. These results suggested that the extent of atherosclerotic burden of CAD be considered an important clinical factor affecting the choice between CABG and DES and as a determinant for predicting long-term outcomes after LMCA revascularization, suggesting an important role of the SYNTAX score as an aid in decision making for patient selection and risk stratification in clinical practice.

Study limitations. First, the inherent limitations of a nonrandomized, registry study should be acknowledged. The choice of revascularization was at the discretion of the treating physician and/or patient. Despite rigorous adjustment for selection bias and confounding with the inverse-probability-of-treatment weighting method, hidden biases or residual confounding may have affected the results. Therefore, our findings should be confirmed or refuted through large, randomized clinical trials with long-term follow-up. Second, our analysis was underpowered to detect significant differences in mortality and serious composite outcomes. Nonsignificant trends for these outcomes might have been significant with a larger cohort of patients. Third, in the present analysis, SYNTAX scoring was performed retrospectively and only in 78% of cases, introducing at least the potential of an unmeasured bias. Finally, because this study evaluated the first generation of DES, the direct application of these findings to second-generation or next-generation DES may be limited.

Conclusions

In patients with unprotected LMCA disease, according to the anatomical complexity of concomitant CAD measured by the SYNTAX score, PCI with DES compares favorably with CABG for patients with a low burden of disease with regard to serious safety outcomes (death or the composite of death, Q-wave MI, or stroke). Conversely, CABG compares favorably with PCI for patients with a high atherosclerotic burden of disease.

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

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Key Words: coronary disease ■ revascularization ■ stents ■ surgery.