ORIGINAL ARTICLE

Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease

G.W. Stone, J.F. Sabik, P.W. Serruys, C.A. Simonton, P. Généreux, J. Puskas, D.E. Kandzari, M.-C. Morice, N. Lembo, W.M. Brown III, D.P. Taggart, A. Banning, B. Merkely, F. Horkay, P.W. Boonstra, A.J. van Boven, I. Ungi, G. Bogáts, S. Mansour, N. Noiseux, M. Sabaté, J. Pomar, M. Hickey, A. Gershlick, P. Buszman, A. Bochenek, E. Schampaert, P. Pagé, O. Dressler, I. Kosmidou, R. Mehran, S.J. Pocock, and A.P. Kappetein, for the EXCEL Trial Investigators*

ABSTRACT

BACKGROUND

Patients with obstructive left main coronary artery disease are usually treated with coronary-artery bypass grafting (CABG). Randomized trials have suggested that drug-eluting stents may be an acceptable alternative to CABG in selected patients with left main coronary disease.

METHODS

We randomly assigned 1905 eligible patients with left main coronary artery disease of low or intermediate anatomical complexity to undergo either percutaneous coronary intervention (PCI) with fluoropolymer-based cobalt–chromium everolimus-eluting stents (PCI group, 948 patients) or CABG (CABG group, 957 patients). Anatomic complexity was assessed at the sites and defined by a Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score of 32 or lower (the SYNTAX score reflects a comprehensive angiographic assessment of the coronary vasculature, with 0 as the lowest score and higher scores [no upper limit] indicating more complex coronary anatomy). The primary end point was the rate of a composite of death from any cause, stroke, or myocardial infarction at 3 years, and the trial was powered for noninferiority testing of the primary end point (noninferiority margin, 4.2 percentage points). Major secondary end points included the rate of a composite of death from any cause, stroke, or myocardial infarction at 30 days and the rate of a composite of death, stroke, myocardial infarction, or ischemia-driven revascularization at 3 years. Event rates were based on Kaplan–Meier estimates in time-to-first-event analyses.

RESULTS

At 3 years, a primary end-point event had occurred in 15.4% of the patients in the PCI group and in 14.7% of the patients in the CABG group (difference, 0.7 percentage points; upper 97.5% confidence limit, 4.0 percentage points; P=0.02 for noninferiority; hazard ratio, 1.00; 95% confidence interval, 0.79 to 1.26; P=0.98 for superiority). The secondary end-point event of death, stroke, or myocardial infarction at 30 days occurred in 4.9% of the patients in the PCI group and in 7.9% in the CABG group (P<0.001 for noninferiority, P=0.008 for superiority). The secondary end-point event of death, stroke, myocardial infarction, or ischemia-driven revascularization at 3 years occurred in 23.1% of the patients in the PCI group and in 19.1% in the CABG group (P=0.01 for noninferiority, P=0.10 for superiority).

CONCLUSIONS

In patients with left main coronary artery disease and low or intermediate SYNTAX scores by site assessment, PCI with everolimus-eluting stents was noninferior to CABG with respect to the rate of the composite end point of death, stroke, or myocardial infarction at 3 years. (Funded by Abbott Vascular; EXCEL ClinicalTrials.gov number, NCT01205776.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Stone at Columbia University Medical Center, Cardiovascular Research Foundation, 1700 Broadway, 8th Fl., New York, NY 10019, or at gs2184@columbia.edu.

*A complete list of investigators, institutions, and research organizations participating in the Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trial is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on October 31, 2016, at NEJM.org.

DOI: 10.1056/NEJMoa1610227

Left main coronary artery disease is associated with high morbidity and mortality owing to the large amount of myocardium at risk. European and U.S. guidelines recommend that most patients with left main coronary artery disease undergo coronary-artery bypass grafting (CABG).[1,2] Randomized trials have suggested that percutaneous coronary intervention (PCI) with drug-eluting stents might be an acceptable alternative for selected patients with left main coronary disease.[3-5] Specifically, in the subgroup of patients with left main coronary disease in the Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) trial, the rate of a composite of death, stroke, myocardial infarction, or unplanned revascularization at 5 years was similar among patients treated with paclitaxel-eluting stents and those treated with CABG.[4] However, the outcomes of PCI were acceptable only in the patients with coronary artery disease of low or intermediate anatomical complexity.[4] Because these results represented a subgroup of a subgroup, they were hypothesis generating. Moreover, contemporary metallic drug-eluting stents have a better safety and efficacy profile than do the first-generation stents used in earlier trials.[6,7] Surgical techniques and outcomes have also continued to improve, and an evaluation of alternative methods of revascularization for patients with left main coronary artery disease is warranted in a contemporary trial.

Methods

Trial Design

The design of the Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trial has been reported previously.[8] In brief, EXCEL was an international, open-label, multicenter randomized trial that compared everolimus-eluting stents with CABG in patients with left main coronary artery disease. Details of the organization of the study are provided in the Supplementary Appendix, which is available with the full text of this article at NEJM.org. The protocol, also available at NEJM.org, was designed by the principal investigators and trial committees, in which interventional cardiologists and cardiac surgeons were represented equally. The trial was approved by the investigational review board or ethics committee at each participating center. The trial was sponsored by Abbott Vascular, which participated in the design of the protocol and in the selection and management of the sites but was not involved in the writing of the drafts of the manuscript or in the management or analysis of the data, although it had the right to a nonbinding review. The principal investigators (the first three authors and the last author) had unrestricted access to the data, were involved in the analysis and interpretation of the data, wrote the first and subsequent drafts of the manuscript, and made the decision to submit the manuscript for publication. The principal investigators vouch for the completeness and accuracy of the data and analyses and for the fidelity of the trial to the protocol. The equipment and drugs used in the study were purchased by the participating hospitals.

Enrollment, Randomization, and Follow-up

Patients were assessed for eligibility at each participating site by a heart team that consisted of an interventional cardiologist and a cardiac surgeon. Inclusion criteria were stenosis of the left main coronary artery of 70% or more, as estimated visually, or stenosis of 50% to less than 70% if determined by means of noninvasive or invasive testing to be hemodynamically significant,[8] and a consensus among the members of the heart team regarding eligibility for revascularization with either PCI or CABG. In addition, participants were required to have low-to-intermediate anatomical complexity of coronary artery disease, as defined by a site-determined SYNTAX score of 32 or lower[9] (the SYNTAX score reflects a comprehensive angiographic assessment of the coronary vasculature, with 0 as the lowest score and higher scores [no upper limit] indicating more complex coronary anatomy). Complete details of the inclusion and exclusion criteria are provided in Table S1 in the Supplementary Appendix. A cohort of 1000 consecutive patients with stenosis of the left main coronary artery of 50% or more, as estimated visually, who did not otherwise meet criteria for randomization, were enrolled in a screening registry during the initial recruitment phase of the trial and were followed through their initial treatment to determine the applicability of the study results. The treatment these patients received was based on the assessments of all caregivers and on the personal preferences of the patients. Written informed consent was obtained from all the patients.

Randomization was performed with the use of an interactive voice-based or Web-based sys-

tem in block sizes of 16, 24, or 32, with stratification according to diabetes (present vs. absent), SYNTAX score (≤22 vs. ≥23), and study center. Twelve-lead electrocardiography was performed at baseline, within 24 hours after the procedure, at discharge, and at 1 year. Levels of the MB fraction of creatine kinase were measured at baseline and at 12 and 24 hours after the procedure. Additional electrocardiograms and biomarker measurements were obtained to assess for recurrent ischemia or to evaluate adverse cardiac events. Clinical follow-up was performed at 1 month, 6 months, and 1 year and then annually through 5 years. The primary composite end point was assessed at a median follow-up of 3 years, with a minimum follow-up of 2 years for all patients. When the last randomly assigned patient reached the 2-year time point, an additional follow-up visit was performed to minimize bias and facilitate a more reliable ascertainment of the primary end point.[10] Guideline-directed medical therapy was recommended for all the patients, and risk factors were managed as described previously.[8] Routine angiographic follow-up was not permitted.

REVASCULARIZATION STRATEGIES AND MEDICATIONS

The goal of PCI was complete revascularization of all ischemic territories with the use of fluoropolymer-based cobalt–chromium everolimus-eluting stents (XIENCE, Abbott Vascular). The recommended technical approach to performing PCI has been described in detail elsewhere.[8] Intravascular ultrasonographic guidance was strongly recommended. The use of heparin or bivalirudin was allowed for procedural anticoagulation, and the use of glycoprotein IIb/IIIa inhibitors was discouraged. Dual antiplatelet therapy was initiated before PCI and was continued for a minimum of 1 year thereafter.

CABG was performed with or without cardiopulmonary bypass according to the discretion of the operator, as described previously.[8] The goal of CABG was complete anatomical revascularization of all vessels 1.5 mm or larger in diameter in which the angiographic diameter stenosis was 50% or more; the use of arterial grafts was strongly recommended. Epiaortic ultrasonography and transesophageal ultrasonography were recommended to assess the ascending aorta and ventricular and valvular function. Aspirin was administered during the perioperative period, and the use of clopidogrel during follow-up was allowed, but not mandatory, according to the local standard of care.

OBJECTIVES AND END POINTS

The trial was designed to determine whether PCI was noninferior to CABG with respect to the primary composite end point of death from any cause, stroke, or myocardial infarction at 3 years. Secondary objectives were to determine whether PCI was noninferior to CABG with respect to the rate of a composite of death from any cause, stroke, or myocardial infarction at 30 days and the rate of a composite of death, stroke, myocardial infarction, or ischemia-driven revascularization at 3 years. Additional secondary end points included the components of the primary end point, as well as revascularization, stent thrombosis, symptomatic graft stenosis or occlusion, bleeding complications, and a prespecified composite of periprocedural major adverse events. Definitions of the end points are provided in Table S2 in the Supplementary Appendix. Study monitors collected source documents of all primary and secondary end-point events for adjudication by an independent events committee. The extent of disease and SYNTAX score were assessed at an angiographic core laboratory.

STATISTICAL ANALYSIS

We estimated that the random assignment of 1900 patients would provide 80% power (at a one-sided alpha level of 0.025) to show the noninferiority of PCI to CABG with respect to the 3-year primary end point, with a noninferiority margin of 4.2 percentage points for the upper 97.5% confidence limit for the between-group difference in event rates, assuming an 11% event rate in each study group[11] (with a minimum follow-up of 2 years and a median follow-up of 3 years) and an 8% rate of loss to follow-up or withdrawal from the trial. The noninferiority margin of 4.2 percentage points was agreed on by the study leadership of cardiac surgeons and interventional cardiologists as consistent with an interpretation of equipoise between the two treatments,[12] given the lower periprocedural morbidity associated with PCI. Our original intention was to randomly assign 2600 patients, which would have provided 90% power. Because enrollment was slower than anticipated, the sample size was reduced to 1900 patients for 80% power. The sponsor and study leadership were unaware of the study results at the time of this decision.

With respect to the 30-day secondary composite end point of death, stroke, or myocardial infarction, we estimated that the random assignment of 1900 patients would provide 80% power (at a one-sided alpha level of 0.05) to show the noninferiority of PCI to CABG with a noninferiority margin of 2.0 percentage points, assuming a 3.0% event rate in each study group.[11] With respect to the 3-year secondary composite end point of death, stroke, myocardial infarction, or ischemia-driven revascularization, we estimated that the random assignment of 1900 patients would provide 99% power (at a one-sided alpha level of 0.05) to show the noninferiority of PCI to CABG with a noninferiority margin of 8.4 percentage points, assuming a 22.0% event rate in each group.[11] Hierarchical family-wise testing for the primary and first two secondary end points was prespecified to control the type I error (Fig. S1 in the Supplementary Appendix).[8]

All principal analyses were performed with data from the time of randomization in the intention-to-treat population, which included all patients according to the group to which they were randomly assigned, regardless of the treatment received. Sensitivity analyses were performed in the per-protocol and as-treated populations.[8] Event rates were based on Kaplan–Meier estimates in time-to-first-event analyses. Noninferiority was calculated with the use of the Com–Nougue approach to estimating the z statistic for the Kaplan–Meier failure rates, with standard errors estimated by means of Greenwood's formula.[13] In time-to-first-event analyses, hazard ratios with 95% confidence intervals were determined, and event rates were compared with the use of the log-rank test. Categorical variables were compared with the use of the chi-square test or Fisher's exact test. Continuous variables were compared with the use of Student's t-test or the Wilcoxon rank-sum test for non-normally distributed data. For superiority, a two-sided P value of 0.05 or less was considered to indicate statistical significance. All statistical analyses were performed with the use of SAS software, version 9.4 (SAS Institute).

RESULTS

PATIENT ENROLLMENT

From September 29, 2010, to March 6, 2014, a total of 2905 patients with left main coronary artery disease were recruited at 126 sites in 17 countries, including 1905 patients who were randomly assigned to a treatment group and 1000 patients who were enrolled in the registry (registry patients). The CONSORT diagram is provided in Figure S2 in the Supplementary Appendix. During the initial recruitment period (the period during which the 1000 registry patients were enrolled), 747 of 1747 consecutive enrolled patients (42.8%) underwent randomization. The registry patients were at higher risk at baseline than were the patients who underwent randomization. Among the 1000 registry patients, 648 underwent CABG, 331 underwent PCI, and 21 did not undergo revascularization. Thus, of the 1747 patients enrolled during the initial recruitment period, 1078 (61.7%) were eligible for PCI and 1395 (79.9%) were eligible for CABG. After enrollment in the registry was concluded, an additional 1158 patients underwent randomization. Further details of the reasons for exclusion from randomization and patient characteristics are provided in Tables S3 and S4 in the Supplementary Appendix.

BASELINE FEATURES AND PROCEDURES

Among the 1905 patients who underwent randomization, 948 were assigned to the PCI group and 957 to the CABG group. Baseline clinical and angiographic characteristics were well balanced between the groups (Table 1). The SYNTAX score according to assessment at local sites was low (≤22) in 60.5% of the patients and intermediate (23 to 32) in 39.5% of the patients. The SYNTAX score according to the angiographic core laboratory analysis (Table S5 in the Supplementary Appendix) was low in 35.8% of the patients, intermediate in 40.0%, and high (≥33) in 24.2% and was slightly higher among the patients in the PCI group than among those in the CABG group. Distal left main bifurcation or trifurcation disease was present in 80.5% of the patients, and two-vessel or three-vessel coronary artery disease was present in 51.3% of the patients.

Among the 948 patients assigned to the PCI group, 942 underwent revascularization; PCI was the first procedure in 935 patients. A mean of 2.4 stents with a mean total stent length of 49.1 mm were implanted per patient; 99.2% of the stents implanted were everolimus-eluting stents. Among the 957 patients assigned to the CABG group, 940 underwent revascularization; CABG was the first procedure in 923 patients. A

Table 1. Baseline Clinical and Angiographic Characteristics.*

Characteristic	PCI (N=948)	CABG (N=957)
Age — yr	66.0±9.6	65.9±9.5
Male sex — no. (%)	722 (76.2)	742 (77.5)
White race — no./total no. (%)†	844/922 (91.5)	853/927 (92.0)
Continent of enrollment — no. (%)		
Europe	534 (56.3)	541 (56.5)
North America	381 (40.2)	371 (38.8)
Other	33 (3.5)	45 (4.7)
Diabetes — no. (%)	286 (30.2)	268 (28.0)
Insulin-treated diabetes — no. (%)	73 (7.7)	74 (7.7)
Hypertension, medically treated — no./total no. (%)	703/943 (74.5)	701/949 (73.9)
Hyperlipidemia, medically treated — no./total no. (%)	668/934 (71.5)	652/941 (69.3)
Current smoker — no./total no. (%)	222/923 (24.1)	193/927 (20.8)
Prior myocardial infarction — no./total no. (%)	169/935 (18.1)	161/953 (16.9)
Prior PCI — no./total no. (%)	174/946 (18.4)	152/956 (15.9)
Prior CABG — no.	0	0
Congestive heart failure — no./total no. (%)	67/946 (7.1)	59/952 (6.2)
Prior stroke or transient ischemic attack — no./total no. (%)	52/947 (5.5)	67/956 (7.0)
Peripheral vascular disease — no./total no. (%)	97/945 (10.3)	84/951 (8.8)
Chronic obstructive pulmonary disease — no./total no. (%)	65/945 (6.9)	81/951 (8.5)
Clinical presentation — no./total no. (%)		
Recent myocardial infarction within 7 days before randomization	141/942 (15.0)	141/950 (14.8)
STEMI‡	13/938 (1.4)	14/945 (1.5)
Non-STEMI‡	124/938 (13.2)	122/945 (12.9)
Unstable angina, biomarker negative	228/942 (24.2)	234/950 (24.6)
Stable angina	500/942 (53.1)	505/950 (53.2)
Silent ischemia or other	73/942 (7.7)	70/950 (7.4)
Body-mass index§	28.6±5.0	28.8±4.9 (956)
Renal insufficiency — no./total no. (%)¶	164/934 (17.6)	144/935 (15.4)
Anemia — no./total no. (%)‖	253/939 (26.9)	214/947 (22.6)
Thrombocytopenia — no./total no. (%)**	37/528 (7.0)	37/532 (7.0)
Left ventricular ejection fraction — %††	57.0±9.6	57.3±9.0
SYNTAX score by site assessment‡‡	20.6±6.2	20.5±6.1
Low — no./total no. (%)	560/946 (59.2)	590/955 (61.8)
Intermediate — no./total no. (%)	386/946 (40.8)	365/955 (38.2)

* Plus–minus values are means ±SD. There were no significant between-group differences in baseline characteristics. CABG denotes coronary-artery bypass grafting, PCI percutaneous coronary intervention, and STEMI ST-segment elevation myocardial infarction.
† Race was reported by the investigator.
‡ Information on the type of myocardial infarction was not available for 4 patients in the PCI group and 5 patients in the CABG group.
§ Body-mass index is the weight in kilograms divided by the square of the height in meters.
¶ Baseline creatinine clearance was calculated by means of the Cockcroft–Gault equation; a creatinine clearance of less than 60 ml per minute indicated renal insufficiency.
‖ Anemia was defined according to the World Health Organization criteria (hematocrit value at initial presentation, <39% for men and <36% for women).
** Thrombocytopenia was defined as less than 150,000 cells per cubic millimeter at baseline.
†† Information on left ventricular ejection fraction was not available for 55 patients in the PCI group and 46 patients in the CABG group.
‡‡ The Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score reflects a comprehensive angiographic assessment of the coronary vasculature, with a score of 22 or less indicating low anatomical complexity and scores of 23 to 32 indicating intermediate anatomical complexity (0 is the lowest score and there is no upper limit). The SYNTAX score was not available for 2 patients in the PCI group and 2 patients in the CABG group.

mean of 2.6 grafts per patient were placed; an internal thoracic artery graft was used in 98.8% of the patients. Medication use differed between the groups. Additional procedural data and information on medication use are provided in Tables S6 and S7, respectively, in the Supplementary Appendix.

PRIMARY AND HIERARCHICAL SECONDARY END POINTS

The median duration of follow-up was 3.0 years (interquartile range, 2.4 to 3.0) in both groups. The results of the analyses of the primary and hierarchical secondary end points are provided in Table 2. The primary composite end-point event of death, stroke, or myocardial infarction at 3 years occurred in 15.4% of the patients in the PCI group and in 14.7% of the patients in the CABG group (difference, 0.7 percentage points; upper 97.5% confidence limit, 4.0 percentage points; P=0.02 for noninferiority; hazard ratio, 1.00; 95% confidence interval [CI], 0.79 to 1.26; P=0.98 for superiority) (Fig. 1). The relative treatment effect for the primary end point was consistent across prespecified subgroups, including the subgroup defined according to the presence versus absence of diabetes (Fig. 2).

At 30 days, the composite end-point event of death, stroke, or myocardial infarction had occurred in 4.9% of the patients in the PCI group and in 7.9% of the patients in the CABG group (difference, –3.1 percentage points; upper 95.0% confidence limit, –1.2 percentage points; P<0.001 for noninferiority). At 3 years, the composite end-point event of death, stroke, myocardial infarction, or ischemia-driven revascularization had occurred in 23.1% of the patients in the PCI group and in 19.1% of the patients in the CABG group (difference, 4.0 percentage points; upper 95% confidence limit, 7.2 percentage points; P=0.01 for noninferiority). The results of the analyses of the primary and major secondary end points were similar in the per-protocol and as-treated populations (Table S8 in the Supplementary Appendix).

OTHER SECONDARY END POINTS

The results of the analyses of additional secondary end points are provided in Table 3 and Figure 1 and have not been adjusted for multiple testing. There were no significant between-group differences in the 3-year rates of the components of the primary end point (death, stroke, and myocardial infarction). At 30 days, the rate of the composite end point of death, stroke, or myocardial infarction was lower among patients in the PCI group than among those in the CABG group (hazard ratio, 0.61; 95% CI, 0.42 to 0.88; P=0.008 for superiority), which was driven by fewer myocardial infarctions among the patients in the PCI group. In a post hoc landmark analysis of the period between 30 days and 3 years after randomization to PCI or CABG, more primary end-point events occurred in the PCI group than in the CABG group (Table S9 in the Supplementary Appendix). Ischemia-driven revascularization during follow-up was more frequent after PCI than after CABG (in 12.6% vs. 7.5% of the patients, P<0.001), although symptomatic graft occlusion after CABG occurred more frequently than definite stent thrombosis after PCI (5.4% vs. 0.7%, P<0.001). Major and minor bleeding events were also less common after PCI than after CABG.

Major periprocedural adverse events within 30 days after randomization to PCI or CABG occurred in 77 patients (8.1%) in the PCI group and in 220 patients (23.0%) in the CABG group (P<0.001); the lower rate of major periprocedural adverse events in the PCI group was due principally to fewer major arrhythmias, fewer infections that required antibiotics, and fewer blood transfusions among the patients in this group. Eighteen more deaths occurred after PCI than after CABG; these deaths were mostly from noncardiovascular causes (infections and malignant conditions), whereas cardiovascular mortality was similar in the PCI group and the CABG group. Additional details of major periprocedural adverse events and adjudicated causes of death within 3 years after PCI or CABG are provided in Tables S10 and S11, respectively, in the Supplementary Appendix.

DISCUSSION

In this large-scale randomized trial involving patients with left main coronary artery disease and low or intermediate SYNTAX scores, PCI with everolimus-eluting stents was noninferior to CABG with respect to the primary composite end point of death, stroke, or myocardial infarction at 3 years. The rate of the composite end point of death, stroke, or myocardial infarction within 30 days after PCI or CABG was lower in

the PCI group than in the CABG group, whereas fewer primary end-point events occurred in the CABG group than in the PCI group between 30 days and 3 years after the procedure. The 3-year rate of revascularization was 5 percentage points higher with PCI with everolimus-eluting stents than with CABG, whereas the rates of early myocardial infarction and major adverse events — including bleeding, infection, major arrhythmia, and renal failure — were 15 percentage points lower with PCI than with CABG.

The results of the EXCEL trial suggest that PCI with everolimus-eluting stents is an acceptable or perhaps preferred alternative to CABG in selected patients with left main coronary artery disease who are candidates for either procedure. An analysis of the screening registry suggests that approximately 62% of patients with left main coronary artery disease might be eligible for PCI, and approximately 80% might be eligible for CABG. Decisions with respect to revascularization should be made after discussion among the members of the heart team and take into account each patient's individual circumstances and preferences.[16]

In the SYNTAX trial, among 417 patients with left main coronary artery disease and SYNTAX scores of 32 or lower, the rate of the composite end point of death, stroke, or myocardial infarction at 5 years was similar among those who underwent CABG and those who underwent PCI with first-generation paclitaxel-eluting stents,[4,17] a hypothesis-generating subgroup observation that motivated the current trial. Since the time that the SYNTAX trial was conducted, changes in practice have occurred that would be expected to improve outcomes with PCI. In the EXCEL trial, we used everolimus-eluting stents almost exclusively; these stents are associated with a low rate of stent thrombosis.[6,7] Definite stent thrombosis occurred in only 0.7% of patients within 3 years after the procedure and was less common than symptomatic graft occlusion. Conversely, in the SYNTAX trial, rates of stent thrombosis with paclitaxel-eluting stents were substantially higher and were similar to the rates of graft occlusion.[18] In addition, intravascular ultrasonographic imaging guidance was used in nearly 80% of the patients in the PCI group in our trial, a practice that has been associated with higher event-free survival after left main coronary-artery stenting.[19,20] However, improvements in

Table 2. Primary and Hierarchical Secondary Clinical End Points.

End Point	PCI (N=948)		CABG (N=957)		Difference in Event Rates	P Value for Noninferiority	Hazard Ratio (95% CI)	P Value for Superiority
	Events	Event Rate*	Events	Event Rate*				
	no.	%	*no.*	%	*percentage points (upper confidence limit)*			
Primary end point								
Death, stroke, or myocardial infarction at 3 yr	137	15.4	135	14.7	0.7 (4.0†)	0.02	—	—
Secondary end points								
Death, stroke, or myocardial infarction at 30 days	46	4.9	75	7.9	−3.1 (−1.2‡)	<0.001	—	—
Death, stroke, myocardial infarction, or ischemia-driven revascularization at 3 yr	208	23.1	174	19.1	4.0 (7.2‡)	0.01	—	—
Death, stroke, or myocardial infarction at 3 yr§	137	15.4	135	14.7	—	—	1.00 (0.79–1.26)	0.98

* Event rates were based on Kaplan–Meier estimates in time-to-first-event analyses.
† The value represents the upper 97.5% confidence limit.
‡ The value represents the upper 95.0% confidence limit.
§ The test for superiority with respect to death, stroke, or myocardial infarction at 3 years was a secondary end point.

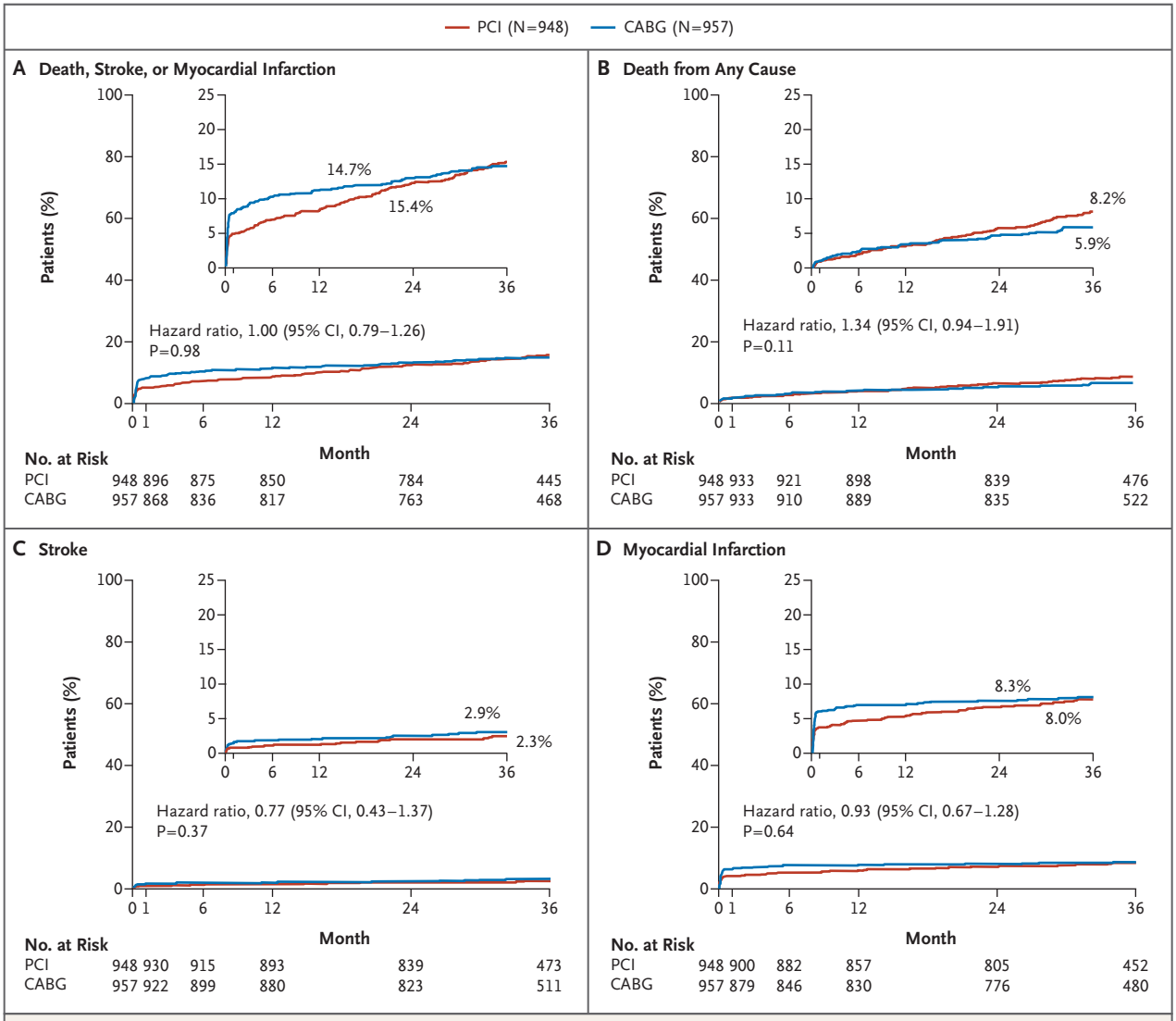

Figure 1. Time-to-Event Curves for the Primary Composite End Point and its Components.

Panel A shows the results of the analysis of the primary composite end point of death, stroke, or myocardial infarction at 3 years. Results of analyses of the components of the primary end point are shown in Panel B (death from any cause), Panel C (stroke), and Panel D (myocardial infarction). Event rates were based on Kaplan–Meier estimates in time-to-first-event analyses. Hazard ratios are for the patients who underwent percutaneous coronary intervention (PCI) with everolimus-eluting stents. The rates of stroke and myocardial infarction are nonhierarchical (i.e., fatal and nonfatal events were included). In each panel, the inset shows the same data on an enlarged y axis. CABG denotes coronary-artery bypass grafting.

Figure 2 (facing page). Subgroup Analyses of the Primary Composite End Point.

Data are shown as the number of primary end-point events per total number of patients in that subgroup and the event rate. Event rates were based on Kaplan–Meier estimates in time-to-first-event analyses. Hazard ratios are for the primary composite end point of death, stroke, or myocardial infarction at 3 years. The P value for interaction represents the likelihood of interaction between the variable and the treatment. The estimated glomerular filtration rate (eGFR) was calculated by means of the Cockcroft–Gault equation. The Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score reflects a comprehensive angiographic assessment of the coronary vasculature, with higher scores indicating more complex coronary anatomy.

Subgroup	PCI (N=948)		CABG (N=957)		Hazard Ratio (95% CI)	P Value for Interaction
	Events/total patients	Event rate	Events/total patients	Event rate		
	no.	%	*no.*	%		
All patients	137/948	15.4	135/957	14.7	1.00 (0.79–1.26)	
Age (median cutoff)						0.07
<67 yr	55/482	12.2	68/485	14.4	0.78 (0.55–1.11)	
≥67 yr	82/466	18.7	67/472	15.0	1.22 (0.89–1.69)	
Sex						0.06
Male	94/722	14.0	107/742	14.9	0.87 (0.66–1.14)	
Female	43/226	19.7	28/215	14.1	1.48 (0.93–2.41)	
Diabetes mellitus, medically treated						0.77
Yes	51/256	21.2	47/249	19.4	1.04 (0.70–1.55)	
No	86/692	13.3	88/707	13.1	0.97 (0.72–1.30)	
Chronic kidney disease						0.36
eGFR ≤60 ml/min	37/163	24.5	26/143	19.3	1.24 (0.75–2.07)	
eGFR >60 ml/min	98/767	13.5	104/789	13.6	0.95 (0.72–1.25)	
Left ventricular ejection fraction						0.99
<50%	20/111	20.4	20/115	18.2	0.98 (0.52–1.83)	
≥50%	109/782	14.7	111/796	14.4	0.98 (0.75–1.27)	
Geographic location						0.14
North America	55/381	15.5	44/371	12.4	1.22 (0.82–1.82)	
Europe	79/534	15.5	81/541	15.6	0.95 (0.69–1.29)	
Other	3/33	9.5	10/45	22.2	0.37 (0.08–1.20)	
Non–left main diseased coronary arteries (core laboratory assessment)						0.78
0	22/163	14.6	22/167	14.4	0.99 (0.54–1.79)	
1	34/292	12.3	45/292	16.0	0.72 (0.46–1.12)	
2	57/325	18.8	36/295	12.7	1.44 (0.96–2.21)	
3	24/162	15.2	30/182	16.8	0.87 (0.50–1.48)	
Left main bifurcation or trifurcation stenosis ≥50% (core laboratory assessment)						0.82
Yes	114/771	15.6	109/741	15.3	0.98 (0.75–1.27)	
No	23/171	14.8	24/195	12.9	1.05 (0.59–1.87)	
SYNTAX score (site reported)						0.70
≤22	75/560	14.3	81/590	14.4	0.95 (0.70–1.31)	
23–32	62/386	17.0	54/365	15.4	1.05 (0.73–1.51)	
SYNTAX score (core laboratory assessment)						0.49
≤22	28/294	10.3	46/364	13.3	0.71 (0.44–1.13)	
23–32	65/391	17.6	55/345	16.5	1.02 (0.71–1.47)	
≥33	37/22	16.9	30/217	14.3	1.15 (0.71–1.87)	

Table 3. Additional Secondary Clinical End Points.*

Variable	PCI (N=948)		CABG (N=957)		Hazard Ratio (95% CI)	P Value
	Events	Event Rate†	Events	Event Rate†		
	no.	%	*no.*	%		
Clinical end points at 30 days						
Death, stroke, or myocardial infarction	46	4.9	75	7.9	0.61 (0.42–0.88)	0.008
Death	9	1.0	10	1.1	0.90 (0.37–2.22)	0.82
Stroke	6	0.6	12	1.3	0.50 (0.19–1.33)	0.15
Myocardial infarction	37	3.9	59	6.2	0.63 (0.42–0.95)	0.02
Periprocedural	34	3.6	56	5.9	0.61 (0.40–0.93)	0.02
Spontaneous	3	0.3	3	0.3	1.00 (0.20–4.95)	1.00
STEMI	7	0.7	22	2.3	0.32 (0.14–0.74)	0.005
Non-STEMI	30	3.2	37	3.9	0.82 (0.50–1.32)	0.41
Q-wave	7	0.7	14	1.5	0.50 (0.20–1.24)	0.13
Non–Q-wave	30	3.2	43	4.5	0.70 (0.44–1.12)	0.13
Death, stroke, myocardial infarction, or ischemia-driven revascularization	46	4.9	80	8.4	0.57 (0.40–0.82)	0.002
Revascularization						
Ischemia-driven revascularization	6	0.6	13	1.4	0.46 (0.18–1.21)	0.11
All revascularization	7	0.7	13	1.4	0.54 (0.21–1.35)	0.18
Stent thrombosis, definite or probable‡	6	0.6	0	0	—	0.01
Graft occlusion, symptomatic	0	0	11	1.2	—	<0.001
Definite stent thrombosis or symptomatic graft occlusion‡	3	0.3	11	1.2	0.27 (0.08–0.97)	0.03
Bleeding according to BARC criteria§[15]						
Any	69	7.3	123	13.0	0.55 (0.41–0.74)	<0.001
Type 2–5	51	5.4	111	11.7	0.45 (0.32–0.63)	<0.001
Type 3–5	23	2.4	82	8.7	0.27 (0.17–0.43)	<0.001
Bleeding according to TIMI criteria[15]						
Major or minor	35	3.7	85	9.0	0.41 (0.27–0.60)	<0.001
Major	11	1.2	37	3.9	0.29 (0.15–0.58)	<0.001
Minor	24	2.5	49	5.2	0.49 (0.30–0.79)	0.003
Blood transfusion	30	3.2	120	12.7	0.24 (0.16–0.36)	<0.001
Clinical end points at 3 yr						
Death, stroke, or myocardial infarction: primary end point	137	15.4	135	14.7	1.00 (0.79–1.26)	0.98
Death	71	8.2	53	5.9	1.34 (0.94–1.91)	0.11
Cardiovascular	39	4.4	33	3.7	1.18 (0.74–1.87)	0.48
Definite	33	3.7	30	3.4	1.10 (0.67–1.80)	0.71
Undetermined cause	6	0.8	3	0.3	2.00 (0.50–7.98)	0.32
Noncardiovascular	32	3.9	20	2.3	1.60 (0.91–2.80)	0.10
Stroke	20	2.3	26	2.9	0.77 (0.43–1.37)	0.37

Table 3. (Continued.)

Variable	PCI (N=948)		CABG (N=957)		Hazard Ratio (95% CI)	P Value
	Events	Event Rate†	Events	Event Rate†		
	no.	%	*no.*	%		
Myocardial infarction	72	8.0	77	8.3	0.93 (0.67–1.28)	0.64
Periprocedural	36	3.8	57	6.0	0.63 (0.42–0.96)	0.03
Spontaneous	37	4.3	23	2.7	1.60 (0.95–2.70)	0.07
STEMI	12	1.3	26	2.8	0.46 (0.23–0.91)	0.02
Non-STEMI	62	7.0	54	5.9	1.15 (0.80–1.65)	0.46
Q-wave	11	1.2	15	1.6	0.73 (0.34–1.59)	0.43
Non–Q-wave	61	6.8	60	6.5	1.01 (0.71–1.45)	0.95
Death, stroke, myocardial infarction, or ischemia-driven revascularization	208	23.1	174	19.1	1.18 (0.97–1.45)	0.10
Revascularization						
Ischemia-driven revascularization	112	12.6	66	7.5	1.72 (1.27–2.33)	<0.001
PCI	92	10.3	59	6.8	1.57 (1.13–2.18)	0.006
CABG	30	3.5	7	0.8	4.29 (1.88–9.77)	<0.001
Ischemia-driven target-vessel revascularization	97	10.9	63	7.2	1.55 (1.13–2.13)	0.006
Ischemia-driven target-lesion revascularization	84	9.5	60	6.9	1.40 (1.00–1.95)	0.05
Ischemia-driven non–target-lesion revascularization	28	3.2	5	0.6	5.64 (2.18–14.61)	<0.001
Ischemia-driven non–target-vessel revascularization	21	2.5	6	0.7	3.50 (1.41–8.67)	0.004
All revascularization	114	12.9	67	7.6	1.72 (1.27–2.33)	<0.001
Stent thrombosis, definite or probable‡	12	1.3	0	0	—	<0.001
Definite	6	0.7	0	0	—	0.01
Probable	6	0.7	0	0	—	0.01
Early, 0 to 30 days	7	0.7	0	0	—	0.008
Late, 30 days to 1 yr	1	0.1	0	0	—	0.32
Very late, 1 to 3 yr	4	0.5	0	0	—	0.05
Graft occlusion, symptomatic	0	0	48	5.4	—	<0.001
Definite stent thrombosis or symptomatic graft occlusion‡	6	0.7	48	5.4	0.12 (0.05–0.28)	<0.001

* Results have not been adjusted for multiple testing. Rates of stroke and myocardial infarction are nonhierarchical (i.e., fatal and nonfatal events were included). TIMI denotes Thrombolysis in Myocardial Infarction.
† Event rates were based on Kaplan–Meier estimates in time-to-first-event analyses.
‡ Definite stent thrombosis and probable stent thrombosis were defined according to the Academic Research Consortium criteria.[14]
§ Bleeding Academic Research Consortium (BARC) type 2–5 is bleeding that requires medical attention, and type 3–5 is severe or fatal bleeding.

CABG have also occurred. Off-pump surgery, arterial revascularization, and transesophageal ultrasonography were used more frequently in the current trial than in the SYNTAX trial,[21] which probably contributed to the low rates of surgery-related death and stroke that we observed.

The composite primary end point is sensitive to the protocol definition of myocardial infarc-

tion, which varied from the definition used in the SYNTAX trial and the Third Universal Definition of Myocardial Infarction.[22,23] The study leadership of surgeons and interventionalists thought it important to use an identical definition of myocardial infarction for both PCI and CABG to minimize ascertainment bias and to use a definition that is clinically relevant. The biomarker threshold chosen to indicate periprocedural myocardial infarction in the case of both revascularization procedures (a rise in the level of the MB fraction of creatine kinase to more than 10 times the upper reference limit of the assay or more than 5 times if additional angiographic, electrocardiographic, or imaging evidence of infarction was present) represents large infarctions, which have been shown to be prognostically important.[24]

Several limitations of the trial should be considered. First, blinding of the patients and investigators to the treatment assignments was not possible, and the possibility of some degree of event ascertainment bias cannot be excluded. Second, although the investigators recruited only patients with low and intermediate SYNTAX scores, 24% of the patients who underwent randomization had a high SYNTAX score according to the angiographic core laboratory analysis. Although the results of the primary end-point analysis were consistent in this subgroup, further studies are required to determine whether PCI is an acceptable alternative to CABG in patients with high anatomical complexity of left main coronary artery disease. Third, long-term medication use after PCI and CABG varied, which reflects differences in practice with respect to the two revascularization strategies. Further study is required to determine the extent to which these differences contributed to the observed results. Finally, longer-term follow-up is required to examine whether additional differences between PCI and CABG emerge over time; a 5-year follow-up is currently being undertaken.

In conclusion, for the treatment of patients with left main coronary artery disease and low or intermediate SYNTAX scores, PCI with everolimus-eluting stents was noninferior to CABG with respect to the composite of death, stroke, or myocardial infarction at 3 years.

Supported by Abbott Vascular.

Dr. Stone reports receiving consulting fees from Velomedix, Toray, Matrizyme, Miracor, TherOx, Reva, V-Wave, Vascular Dynamics, Ablative Solutions, Neovasc, and Medical Development Technologies, serving as a consultant on prasugrel patent litigation paid for by Lupin Pharmaceuticals, and holding equity, stock options, or both, in the MedFocus family of funds, Guided Delivery Systems, Micardia, Vascular Nanotransfer Technologies, Cagent, Qool Therapeutics, Caliber Therapeutics, Aria, and the Biostar family of funds, and he reports Columbia University receiving royalties from Abbott Vascular for the sale of the MitraClip; Dr. Sabik, receiving fees for serving on advisory boards from Medtronic and the Sorin Group, training fees from Medtronic, and research funding from Abbott and Edwards Lifesciences; Dr. Serruys, receiving consulting fees from Abbott, AstraZeneca, Biotronik, Cardialysis, GLG Research, Medtronic, Sinomedical Sciences Technology, Stentys France, Svelte Medical Systems, Volcano, and St. Jude Medical; Dr. Simonton, being an employee of Abbott Vascular; Dr. Généreux, receiving consulting fees from Abbott Vascular, lecture fees from Abbott Vascular and Boston Scientific, and grant support from Boston Scientific and Cardiovascular Systems; Dr. Puskas, receiving royalties from the sale of coronary surgery instruments by Scanlan; Dr. Kandzari, receiving consulting fees from Medtronic and Boston Scientific and grant support from Medtronic, Boston Scientific, Biotronik, and Medinol; Dr. Lembo, receiving fees for lectures and serving on advisory boards from Abbott Vascular, Boston Scientific, and Medtronic; Dr. Banning, receiving lecture fees from Abbott Vascular, Medtronic, and Boston Scientific, and grant support from Boston Scientific; Dr. Merkely, receiving lecture fees and grant support from Abbott; Dr. Mansour, receiving lecture fees and grant support from Abbott Vascular; Dr. Sabaté, receiving consulting fees from Abbott Vascular; Dr. Gershlick, receiving lecture fees and travel support from Abbott; Dr. Schampaert, receiving fees for serving on an advisory board from Abbott Vascular; Dr. Mehran, receiving fees for serving on a data safety and monitoring board from Watermark Research Partners, fees for serving on executive committees from Janssen Pharmaceuticals and Osprey Medical, and consulting fees from AstraZeneca, the Medicines Company, Medscape, Boston Scientific, Merck, Cardiovascular Systems, Sanofi, and Shanghai BraccoSine Pharmaceuticals, and she reports Mount Sinai Medical Center receiving grant support from Eli Lilly/Daiichi-Sankyo, Bristol-Myers Squibb, AstraZeneca, the Medicines Company, OrbusNeich, Bayer, CSL Behring, Abbott Laboratories, Watermark Research Partners, Novartis Pharmaceuticals, Medtronic, and AUM Cardiovascular; and Dr. Pocock, receiving consulting fees from Abbott Vascular. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

APPENDIX

The authors' full names and academic degrees are as follows: Gregg W. Stone, M.D., Joseph F. Sabik, M.D., Patrick W. Serruys, M.D., Ph.D., Charles A. Simonton, M.D., Philippe Généreux, M.D., John Puskas, M.D., David E. Kandzari, M.D., Marie-Claude Morice, M.D., Nicholas Lembo, M.D., W. Morris Brown III, M.D., David P. Taggart, M.D., Adrian Banning, M.D., Béla Merkely, M.D., Ferenc Horkay, M.D., Piet W. Boonstra, M.D., Ad J. van Boven, M.D., Imre Ungi, M.D., Gabor Bogáts, M.D., Samer Mansour, M.D., Nicolas Noiseux, M.D., Manel Sabaté, M.D., José Pomar, M.D., Mark Hickey, M.D., Anthony Gershlick, M.D., Pawel Buszman, M.D., Andrzej Bochenek, M.D., Erick Schampaert, M.D., Pierre Pagé, M.D., Ovidiu Dressler, M.D., Ioanna Kosmidou, M.D., Roxana Mehran, M.D., Stuart J. Pocock, Ph.D., and A. Pieter Kappetein, M.D., Ph.D.

The authors' affiliations are as follows: New York Presbyterian Hospital and Columbia University Medical Center (G.W.S.), the Cardiovascular Research Foundation (G.W.S., P.G., O.D., I.K., R.M.), and Mount Sinai Medical Center (J. Puskas, R.M.), New York; the Cleveland Clinic Foundation, Cleveland (J.F.S.); the International Centre for Circulatory Health, National Heart and Lung Institute, Imperial College London (P.W.S.), and London School of Hygiene and Tropical Medicine (S.J.P.), London, Oxford University Hospitals, Oxford (D.P.T., A. Banning), and University Hospitals of Leicester NHS Trust, Leicester (M.H., A.G.) — all in the United Kingdom; Abbott Vascular, Santa Clara, CA (C.A.S.); Hôpital du Sacré-Coeur de Montréal (P.G., E.S., P.P.) and Centre Hospitalier de l'Université de Montréal, Hôpital Hôtel-Dieu de Montréal (S.M., N.N.), Montreal; Piedmont Hospital, Atlanta (D.E.K., N.L., W.M.B.); Ramsay Générale de Santé, Hopital Privé Jacques Cartier, Massy, France (M.-C.M.); Semmelweis University, Budapest (B.M., F.H.) and University of Szeged, Szeged (I.U., G.B.) — both in Hungary; Medisch Centrum Leeuwarden, Leeuwarden (P.W.B., A.J.B.), and Erasmus Medical Center, Rotterdam (A.P.K.) — both in the Netherlands; Hospital Clinic, Barcelona (M.S., J. Pomar); and Medical University of Silesia, Katowice, and American Heart of Poland, Ustron — both in Poland (P.B., A. Bochenek).

REFERENCES

1. Fihn SD, Blankenship JC, Alexander KP, et al. 2014 ACC/AHA/AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol 2014;64:1929-49.
2. Windecker S, Kolh P, Alfonso F, et al. 2014 ESC/EACTS Guidelines on myocardial revascularization: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur Heart J 2014;35:2541-619.
3. Capodanno D, Stone GW, Morice MC, Bass TA, Tamburino C. Percutaneous coronary intervention versus coronary artery bypass graft surgery in left main coronary artery disease: a meta-analysis of randomized clinical data. J Am Coll Cardiol 2011;58:1426-32.
4. Morice MC, Serruys PW, Kappetein AP, et al. Five-year outcomes in patients with left main disease treated with either percutaneous coronary intervention or coronary artery bypass grafting in the Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery trial. Circulation 2014;129:2388-94.
5. Cavalcante R, Sotomi Y, Lee CW, et al. Outcomes after percutaneous coronary intervention or bypass surgery in patients with unprotected left main disease. J Am Coll Cardiol 2016;68:999-1009.
6. Palmerini T, Biondi-Zoccai G, Della Riva D, et al. Clinical outcomes with bioabsorbable polymer- versus durable polymer-based drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. J Am Coll Cardiol 2014;63:299-307.
7. Bangalore S, Kumar S, Fusaro M, et al. Short- and long-term outcomes with drug-eluting and bare-metal coronary stents: a mixed-treatment comparison analysis of 117 762 patient-years of follow-up from randomized trials. Circulation 2012;125:2873-91.
8. Kappetein AP, Serruys PW, Sabik JF, et al. Design and rationale for a randomised comparison of everolimus-eluting stents and coronary artery bypass graft surgery in selected patients with left main coronary artery disease: the EXCEL trial. EuroIntervention 2016;12:861-72.
9. SYNTAX score calculator (http://ir-nwr.ru/calculators/syntaxscore.htm).
10. Wittes J, Palensky J, Asner D, et al. Experience collecting interim data on mortality: an example from the RALES study. Curr Control Trials Cardiovasc Med 2001;2:59-62.
11. Ahn JM, Roh JH, Kim YH, et al. Randomized trial of stents versus bypass surgery for left main coronary artery disease: 5-year outcomes of the PRECOMBAT Study. J Am Coll Cardiol 2015;65:2198-206.
12. Ware JH, Antman EM. Equivalence trials. N Engl J Med 1997;337:1159-61.
13. Com-Nougue C, Rodary C, Patte C. How to establish equivalence when data are censored: a randomized trial of treatments for B non-Hodgkin lymphoma. Stat Med 1993;12:1353-64.
14. 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.
15. Mehran R, Rao SV, Bhatt DL, et al. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the Bleeding Academic Research Consortium. Circulation 2011;123:2736-47.
16. Walsh MN, Bove AA, Cross RR, et al. ACCF 2012 health policy statement on patient-centered care in cardiovascular medicine: a report of the American College of Cardiology Foundation Clinical Quality Committee. J Am Coll Cardiol 2012;59:2125-43.
17. Mohr FW, Morice MC, Kappetein AP, et al. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. Lancet 2013;381:629-38.
18. Farooq V, Serruys PW, Zhang Y, et al. Short-term and long-term clinical impact of stent thrombosis and graft occlusion in the SYNTAX trial at 5 years: Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery trial. J Am Coll Cardiol 2013;62:2360-9.
19. de la Torre Hernandez JM, Baz Alonso JA, Gómez Hospital JA, et al. Clinical impact of intravascular ultrasound guidance in drug-eluting stent implantation for unprotected left main coronary disease: pooled analysis at the patient-level of 4 registries. JACC Cardiovasc Interv 2014;7:244-54.
20. Park SJ, Kim YH, Park DW, et al. Impact of intravascular ultrasound guidance on long-term mortality in stenting for unprotected left main coronary artery stenosis. Circ Cardiovasc Interv 2009;2:167-77.
21. Serruys PW, Morice M-C, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med 2009;360:961-72.
22. Ong AT, Serruys PW, Mohr FW, et al. The SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery (SYNTAX) study: design, rationale, and run-in phase. Am Heart J 2006;151:1194-204.
23. Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. J Am Coll Cardiol 2012;60:1581-98.
24. Moussa ID, Klein LW, Shah B, et al. Consideration of a new definition of clinically relevant myocardial infarction after coronary revascularization: an expert consensus document from the Society for Cardiovascular Angiography and Interventions (SCAI). J Am Coll Cardiol 2013;62:1563-70.