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Everolimus Eluting Stents vs. Coronary Artery Bypass Graft Surgery for Patients with Diabetes and Multivessel Disease

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Abstract

Background—In patients with diabetes and multivessel disease, coronary artery bypass graft surgery (CABG) and percutaneous coronary intervention (PCI) are treatment options. However, there is paucity of data comparing CABG against newer generation stents.

Methods and Results—Patients included in the New York State registries who had diabetes and underwent isolated CABG or PCI with everolimus eluting stent (EES) for multivessel disease were included. Propensity score matching was used to assemble a cohort with similar baseline characteristics. The primary outcome was all-cause mortality. Secondary outcomes were myocardial infarction (MI), stroke and repeat revascularization. Short-term (within 30 days) and long-term outcomes were evaluated.

Among 16,089 patients with diabetes and multivessel disease, 8,096 patients with similar propensity scores were included. At short-term, EES was associated with a lower risk of death (HR=0.58; 95% CI 0.34–0.98; P=0.04) and stroke (HR=0.14; 95% CI 0.06–0.30; P<0.0001) but

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higher risk of myocardial infarction (HR=2.44; 95% CI 1.13–5.31; P=0.02). At long-term, EES was associated with a similar risk of death [425(10.50%) vs. 414(10.23%) events; HR=1.12; 95% CI 0.96–1.30; P=0.16], a lower risk of stroke [118(2.92%) vs. 157(3.88%) events; HR=0.76; 95% CI 0.58–0.99; P=0.04] but a higher risk of myocardial infarction [260(6.42%) vs. 166(4.10%) events; HR=1.64; 95% CI 1.32–2.04; P<0.0001] and repeat revascularization [889(21.96%) vs. 421(10.40%) events; HR=2.42; 95% CI 2.12–2.76; P<0.0001]. The higher risk of myocardial infarction was not seen in the subgroup of EES patients who underwent complete revascularization (HR=1.37; 95% CI 0.76–2.47; P=0.30).

Conclusion—In patients with diabetes and multivessel disease, EES was associated with lower upfront risk of death and stroke when compared with CABG. However at long-term, EES was associated with similar risk of death, a higher risk of MI (in those with incomplete revascularization) and repeat revascularization but a lower risk of stroke.

Keywords

coronary artery bypass graft surgery; multivessel disease; percutaneous coronary intervention

Subject codes:

[7] Chronic ischemic heart disease; [24] Catheter-based coronary interventions: stents; [36] CV surgery: coronary artery disease; [190] Type 2 diabetes

Introduction

In patients with diabetes and coronary artery disease (CAD), coronary artery bypass graft surgery (CABG) and percutaneous coronary intervention (PCI) are revascularization options. The 2014 American College of Cardiology/American Heart Association (ACC/AHA) guidelines updated its previous recommendation in favor of CABG over PCI for patients with diabetes and multivessel disease from a class IIa to a class I indication,[1, 2] driven largely by the results of the Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM) trial. Similarly, the 2014 European Society of Cardiology/European Association for Cardio-Thoracic Surgery guidelines on Myocardial Revascularization recommends CABG over PCI in patients with diabetes and stable multivessel disease (Class I, Level of evidence: A).[3]

In the only well-powered, well conducted trial in patients with diabetes and multivessel disease-FREEDOM trial, with 1900 patients, CABG significantly reduced primary composite outcome of death, myocardial infarction (MI) or stroke at 5 years compared with 1st generation drug eluting stents (DES) (sirolimus eluting stent 51%, paclitaxel eluting stent 43%) (18.7% vs 26.6%; P=0.005), driven by reduction in MI (6.0% vs 13.9%, P<0.0001) and all-cause mortality (10.9% vs 16.3%, P=0.049).[4] However, it is not known if the mortality benefit seen in FREEDOM extends to PCI with current generation stents such as the everolimus eluting stent (EES). We used data from the New York State registries to assess the comparative effectiveness of CABG when compared with PCI using EES on short and long-term cardiovascular outcomes.

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Methods

Study Population

Patients with diabetes who underwent either PCI with EES or isolated CABG surgery for multivessel disease between January 1, 2008 and December 31, 2011 in New York State were included. The inclusion criteria were the following: 1) Patients with diabetes; 2) Patients with multivessel disease defined as severe stenosis (≥70%) in at least 2 major epicardial coronary arteries; and 3) Patients undergoing PCI with implantation of EES or those undergoing CABG. The exclusion criteria were the following: 1) Revascularization within 1 year prior to the index procedure; 2) Prior cardiac surgery (CABG or valve surgery) as such patients are unlikely to undergo repeat surgery; 3) Severe left main coronary artery disease (degree of stenosis ≥50%) as these patients preferentially undergo CABG; 4) PCI with a stent other than EES or using a mixture of stents; 5) Myocardial infarction (MI) within 24 hours preceding the index procedure as these patients preferentially undergo PCI; and 6) Unstable hemodynamics or in cardiogenic shock. The institutional review board at New York University School of Medicine approved the study.

Registries

The patients were identified using the New York State Department of Health's (DOH) Percutaneous Coronary Intervention Reporting System (PCIRS) and the Cardiac Surgery Reporting System (CSRS) registries. These are mandatory reporting systems for all PCI and CABG procedures performed in non-federal hospitals in New York State. Data is entered by trained data coordinators at participating hospitals. Data quality is ensured by regular audits of a sample of medical records by DOH's utilization review agent with regular feedback to sites.

Follow-up information on the patients undergoing PCI or CABG was obtained by linking the above registries with a number of other registries. The PCIRS and CSRS provide data on in-hospital events and on subsequent revascularization procedures. In addition, the registries were linked with the New York State Vital Statistics Death registry and to the Statewide Planning and Research Cooperative System (SPARCS) registry to obtain follow-up information. For the SPARCS registry, data are edited monthly to identify errors, audit reports are generated and related data are verified with 2 data sources for consistency.

Outcomes

The primary outcome of the study was all-cause death. Secondary outcomes were MI, stroke and repeat revascularization tabulated separately. Short-term (within 30 days) and long-term (including first 30 days) outcomes were evaluated. The definitions of outcomes are below.

MI was defined as either complication during the index admission after the procedure (procedural MI-defined as new Q waves in both the PCIRS and the CSRS) or MI at readmission (defined as an emergency admission with a principal diagnosis of MI or principal diagnosis of cardiogenic shock with a secondary diagnosis of MI). Similarly stroke was identified either as a complication at the time of index procedure or at readmission (principal diagnosis of stroke). Repeat revascularization was identified as any unstaged

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revascularization after the index procedure. Staged revascularization was defined as a non-target vessel revascularization within 90 days of the index procedure.

Statistical Analysis

Propensity Score Matching—Given baseline differences in characteristics between participants in the 2 groups (Table 1, Table S1), propensity score matching was used to identify a cohort of patients with similar baseline characteristics. The propensity score is a conditional probability of having a particular exposure (EES vs. CABG) given a set of baseline measured covariates.[5, 6] A non-parsimonious multivariable logistic regression model[7] using EES use as the dependent variable and all the baseline characteristics outlined in Table 1 and Table S1 as covariates was used to estimate the propensity scores. Matching was performed using a 1:1 matching protocol without replacement (Greedy matching algorithm) using a caliper width equal to 0.2 of the standard deviation of the logit of the propensity score. Absolute standardized differences (ASD) were estimated for all the baseline covariates before and after matching to assess pre-match and post-match imbalance.[8] ASD<10% for a given covariate indicate a relatively small imbalance.[8]

The risks of primary and secondary outcomes were further assessed in the matched cohort using a Cox proportional hazards regression model after stratifying on the matched pair. Unless otherwise specified, the event rates reports are raw events rates.

Subgroup Analyses—The following subgroup analyses based on anatomy were performed: 1) 3-vessel disease vs. 2-vessel disease; 2) with or without proximal left anterior descending (LAD) territory involvement; and 3) based on completeness of revascularization in the PCI cohort. For the subgroup analysis, only the corresponding match pairs in a subgroup were chosen in order to maintain the baseline balance between EES and CABG groups.

A P value <0.05 was used to denote statistical significance except for the subgroup analyses where a Bonferroni adjustment was used and a threshold of 0.006 (0.05/8) was used to denote statistical significance. All analyses were performed with SAS version 9.3 (SAS Institute, Cary, NC).

Results

We identified 16,089 patients with diabetes and multivessel disease who satisfied the inclusion criteria and none of the exclusion criteria. Of the 16,089 patients, 7,326 (45%) underwent PCI with EES and 8,763 (55%) patients underwent CABG. The baseline characteristics are outlined in table 1. Prior to propensity score matching there were differences (as indicated by ASD ≥10%) between the 2 groups. Propensity score matching matched 4,048 EES patients with 4,048 CABG patients with similar propensity scores. Post matching the ASD was <10% for all variables (Table 1 and Table S1).

Short-term (within 30 days) Outcomes

In the matched cohort, at short-term, EES was associated with a lower risk of death [23(0.57%) vs. 45(1.11%) events; HR=0.58; 95% CI 0.34–0.98; P=0.04] and stroke

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[10(0.25%) vs. 57(1.41%) events; HR=0.14; 95% CI 0.06–0.30; P<0.0001] but higher risk of myocardial infarction [18(0.44%) vs. 11(0.27%) events; HR=2.44; 95% CI 1.13–5.31; P=0.02] when compared with CABG (Figure 1).

Long-term (includes first 30 days) Outcomes

Death—In the matched cohort, at long-term follow-up, EES was associated with a similar risk of death [425(10.50%) vs. 414(10.23%) events; HR=1.12; 95% CI 0.96–1.30; P=0.16] when compared with CABG (Figure 2). This was true across anatomic subgroups based on number of vessel disease or proximal LAD involvement ($P_{interaction}$ >0.05) (Table 2).

Myocardial Infarction—In the matched cohort, EES was associated with a higher risk of myocardial infarction [260(6.42%) vs. 166(4.10%) events; HR=1.64; 95% CI 1.32–2.04; P<0.0001] when compared with CABG (Figure 3). The test for interaction was significant ($P_{interaction}$ =0.02) for the number of vessel disease such that the increased risk of MI with EES was seen in those with 3-vessel disease but not in those with 2-vessel disease (HR=1.34; 95% CI 0.85–2.12; P=0.21) (Table 2). The higher risk of myocardial infarction was not seen in the subgroup of EES patients who underwent complete revascularization (HR=1.37; 95% CI 0.76–2.47; P=0.30) although the test for interaction was not significant (Table 3).

Stroke—In the matched cohort, EES was associated with a lower risk of stroke [118(2.92%) vs. 157(3.88%) events; HR=0.76; 95% CI 0.58–0.99; P=0.04] when compared with CABG (Figure 4).

Repeat Revascularization—In the matched cohort, EES was associated with a higher risk of repeat revascularization [889(21.96%) vs. 421(10.40%) events; HR=2.42; 95% CI 2.12–2.76; P<0.0001] when compared with CABG (Figure 5). The test for interaction was significant both for the number of vessel disease and completeness of revascularization for the magnitude of effect size rather than the direction such that the risk of repeat revascularization with EES (vs. CABG) was significantly higher in those with 3-vessel disease (vs. 2-vessel disease) and in those with incomplete revascularization (vs. complete revascularization) (Table 4).

Discussion

In a contemporary cohort of patients with diabetes (predominantly non-insulin dependent) and multivessel disease, with a sample size >4 times that enrolled in the FREEDOM trial, PCI with EES when compared with CABG was associated with lower short-term risk of death and stroke at the expense of a higher risk of MI. However, PCI with EES was associated with similar long-term risk of death, lower risk of stroke but higher risk of MI (in those with incomplete revascularization) and repeat revascularization when compared with CABG.

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Revascularization in Patients with Diabetes

Patients with diabetes often have a high burden of atherosclerosis with extensive CAD and multivessel involvement.[9] In addition, atherosclerosis tend to progress rapidly, leading to long and diffuse lesions in small caliber coronary arteries which renders revascularization challenging.[10] Moreover, following revascularization, patients with diabetes are more likely to have increased risk of adverse consequences. For example, patients with diabetes undergoing PCI are more likely to develop restenosis, stent thrombosis and have higher rates of death and MI when compared with patients without diabetes.[10, 11] Similarly, patients with diabetes undergoing CABG are more likely to have increased risk of perioperative complications such as deep sternal wound infections, renal failure and fatal and non-fatal cardiovascular events when compared with patients without diabetes.[12, 13]

In the Providing Regional Observations to Study Predictors of Events in the Coronary Tree (PROSPECT) study, roughly similar percentage of follow-up events were attributable to the culprit lesion (12.9%) and non-culprit lesion (11.6%), attesting to the importance of both.[14] Most non-culprit lesions that resulted in an event were angiographically mild, consistent with similar prior observations.[15] Patients with diabetes have greater plaque burden[16] with higher proportion of mixed plaques which have increased amount of necrotic core[16] and hence a greater propensity to rupture (vulnerable plaque). CABG therefore offers better protection against future MI by bypassing a larger extent of potentially vulnerable plaque than the ‘spot’ treatment afforded by PCI. Moreover, PCI in patients with diabetes is associated with poor outcomes when compared with patients without diabetes with increased risk of restenosis and stent thrombosis and consequently increased risk of death or MI (due to stent related events). Both the above factors widen the gap in the outcomes between PCI and CABG. However, it can be hypothesized that stents which reduce the later risk, i.e. the risk of restenosis and stent thrombosis, can potentially bridge this gap between CABG and PCI.

In the FREEDOM trial, CABG significantly reduced the primary composite outcome compared with PCI driven by reduction in MI and all-cause mortality.[4] Similarly, in the subgroup analysis of 452 patients with diabetes from the Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery (SYNTAX) trial, CABG was associated with numerically lower mortality (12.9% vs 19.5%; p=0.065), and MI (5.4% vs 9.0%; p=0.20) when compared with PCI at 5 years.[17, 18] Consequently in a meta-analysis of 8 trials, revascularization of patients with diabetes and multivessel disease by CABG decreased long-term mortality compared with PCI using either BMS or DES.[19] The DES used in the above studies were first generation DES. The newer generation DES (such as EES) have thinner struts (81 μm vs. 132–140 μm), thinner and more biocompatible polymer (7.8 μm vs. 13.7–17.8 μm) both of which reduce inflammation, thrombogenicity and promote rapid endothelialization when compared with the 1st generation DES.[20] Data from randomized controlled trials,[21] observational registries[22] and meta-analyses of randomized trials[21, 23] indicate reduction in morbidity and even mortality with newer generation stents when compared with older generation stents in the overall cohort of patients who underwent PCI. In the largest analysis so far in patients with diabetes, with data from 42 randomized trials and 22,844 patient years of follow-up we had shown that EES was the most efficacious

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(defined as lowest rate of restenosis) and safest (defined as lowest rate of stent thrombosis) when compared with all FDA approved stents including the bare metal stent.[24] Consequently, in an indirect comparison analysis of 68 randomized trials that enrolled 24 015 patients with diabetes with a total of 71 595 patient-years of follow-up, there was similar mortality between CABG and PCI using EES, with CABG associated with numerically excess stroke and PCI with EES with numerically increased repeat revascularization and concluded that this hypothesis needs to be tested in future trials.[25] The current study offers additional insights into the comparative effectiveness of CABG and PCI using newer generation DES. The current study reiterates the excess upfront risk of CABG with significant increase in death and stroke within 30 days when compared with PCI. However, PCI with EES was associated with similar risk of long term death as that of CABG. The results are largely concordant with the data from the BEST trial (overall cohort)[26] and our publication on the overall cohort[27] where PCI with EES was associated with increased risk of MI and repeat revascularization without any mortality difference when compared with CABG. However, data on individual endpoints for the subgroup of patients with diabetes was not presented. Our study with a sample size which is 22 folds larger than the 363 patients with diabetes included in the BEST trial, offers important additional insights on individual endpoints.

It therefore appears that the selection between PCI and CABG for patients with multivessel disease and diabetes should be based on weighing the risks of future myocardial infarction and repeat revascularization with PCI and the upfront risk of death and stroke with CABG. However, in patients with complete revascularization, the increased risk of MI with PCI was no longer present and the magnitude of increase in repeat revascularization diminished. It is therefore prudent to conclude that in contemporary clinical practice the decision between PCI and CABG in patients with diabetes should be based on the ability to achieve complete revascularization with PCI. If complete revascularization is not achievable for any reason with PCI, patients should be considered for CABG.

Study Limitations

This is a non-randomized study and therefore is limited by selection and ascertainment bias despite propensity score matching. It is conceivable that the highest risk patients are referred for CABG (resulting in worse outcomes in the CABG cohort). However, it is also conceivable that patients who are poor candidates for CABG (due to comorbidities) are referred for PCI (resulting in worse outcomes in the PCI cohort). The New York state registries do not make a distinction between the zotarolimus eluting Endeavor stent from the zotarolimus eluting Resolute stent and hence this was not included in the analysis even though the Resolute stent is a 2nd generation DES. Moreover, the registry does not distinguish between cobalt chromium and platinum chromium EES. Furthermore stent thrombosis is not captured in the database. However, most stent thrombosis present as death or MI-both of the outcomes were tracked in the current analysis. The long-term insulin use status was captured from the SPARCS registry using ICD-9 codes and is likely underestimated. The sample size of matched patients using insulin was too small to perform subgroup analysis based on insulin use status. However, the results are largely applicable to patients with non-insulin dependent diabetes. Although, there was no statistically significant

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difference in mortality between PCI and CABG differences may emerge with longer term follow-up or with larger sample size (Type 2 error). The Kaplan-Meier estimator for MI and repeat revascularization likely over-estimates the event rates for these outcomes as it does not account for the competing risk of death.

Conclusions

In a contemporary cohort of patients with diabetes and multivessel disease, CABG was associated with an upfront risk of death and stroke. However, PCI with EES was associated with similar risk of long-term death, higher risk of MI (in those with incomplete revascularization) and repeat revascularization but lower risk of stroke when compared with CABG. The decision between PCI and CABG in patients with diabetes should therefore be based on ability to achieve complete revascularization by PCI. Randomized controlled trials are needed to test these associations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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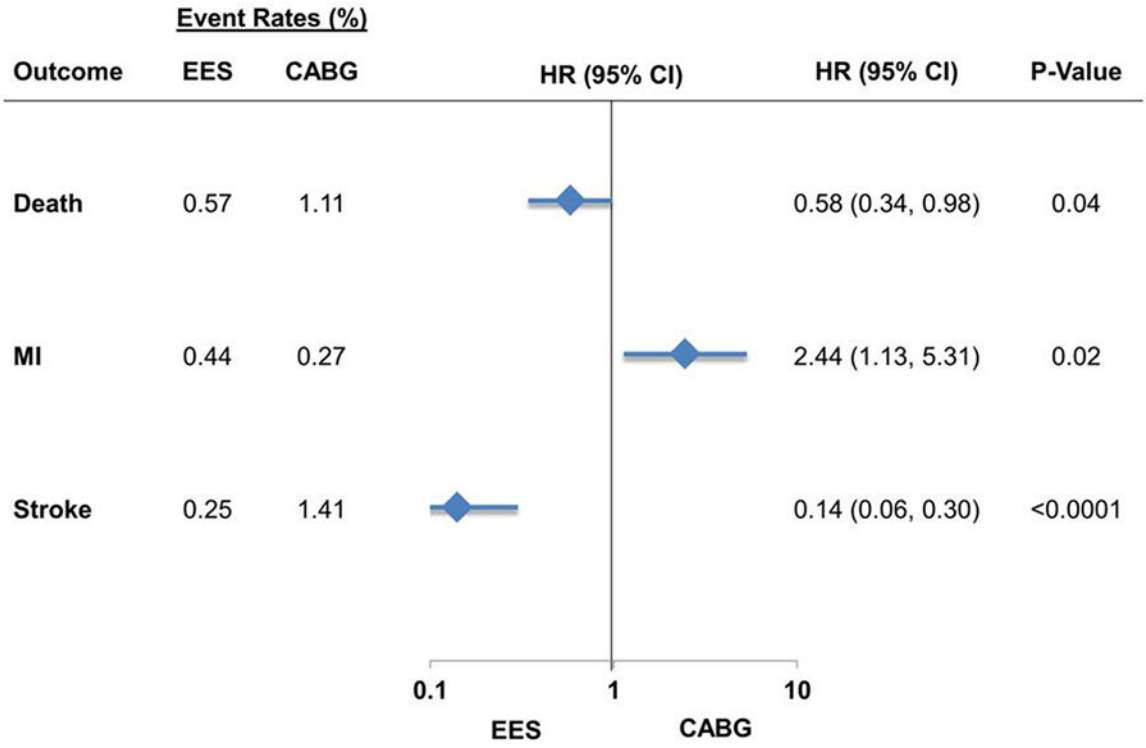

Figure 1.
EES vs. CABG: Short-term (within 30 days) outcomes

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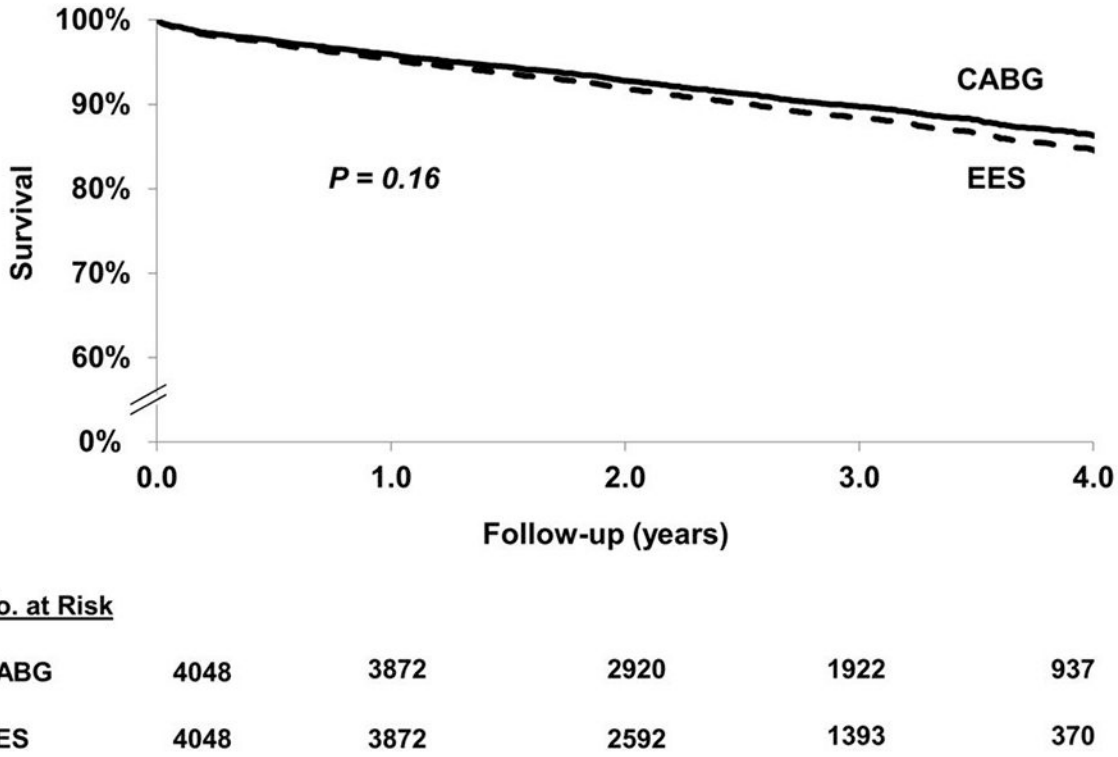

No. at Risk

CABG	4048	3872	2920	1922	937
EES	4048	3872	2592	1393	370

Figure 2.
EES vs. CABG: long-term (includes first 30 days) death

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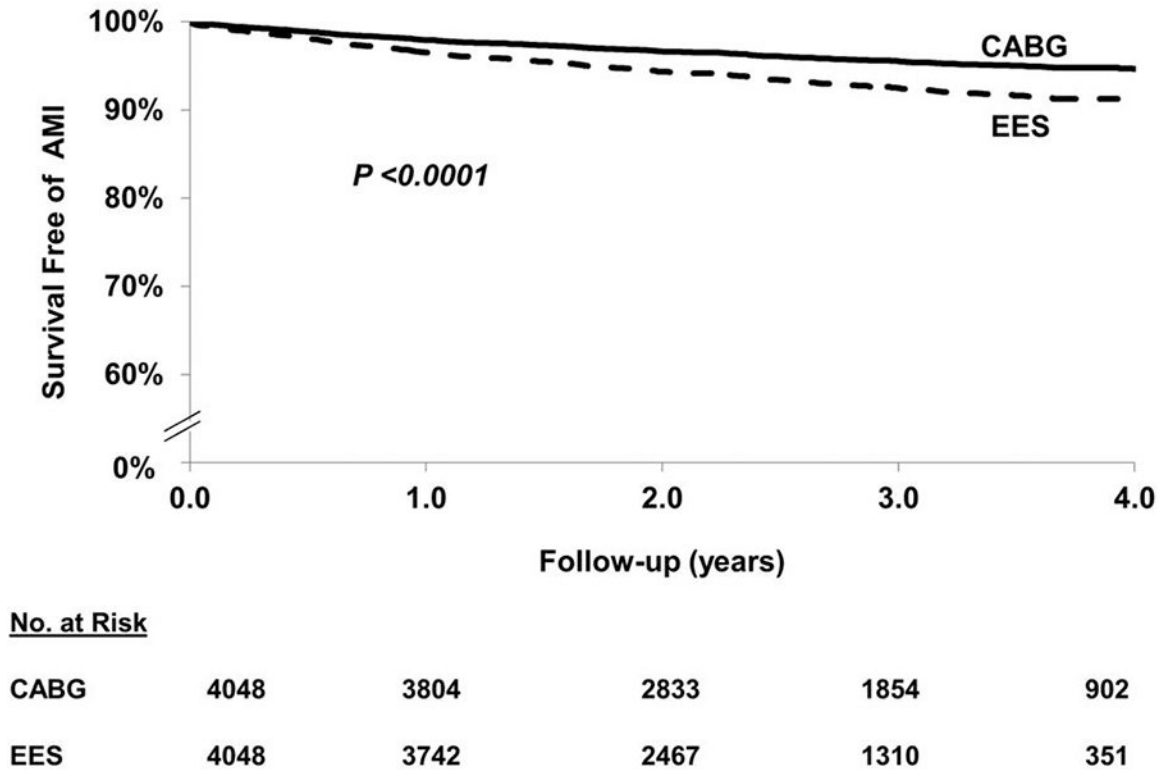

No. at Risk

CABG	4048	3804	2833	1854	902
EES	4048	3742	2467	1310	351

Figure 3.
EES vs. CABG: long-term (includes first 30 days) myocardial infarction

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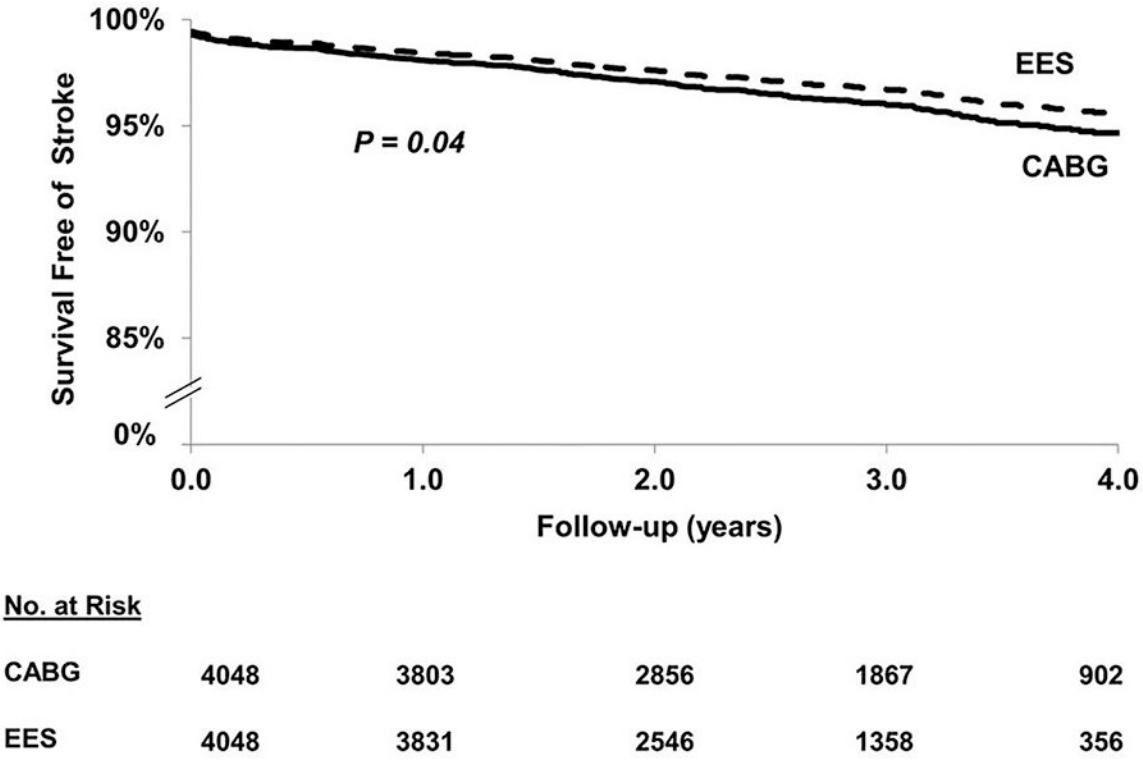

No. at Risk

CABG	4048	3803	2856	1867	902
EES	4048	3831	2546	1358	356

Figure 4.
EES vs. CABG: long-term (includes first 30 days) stroke

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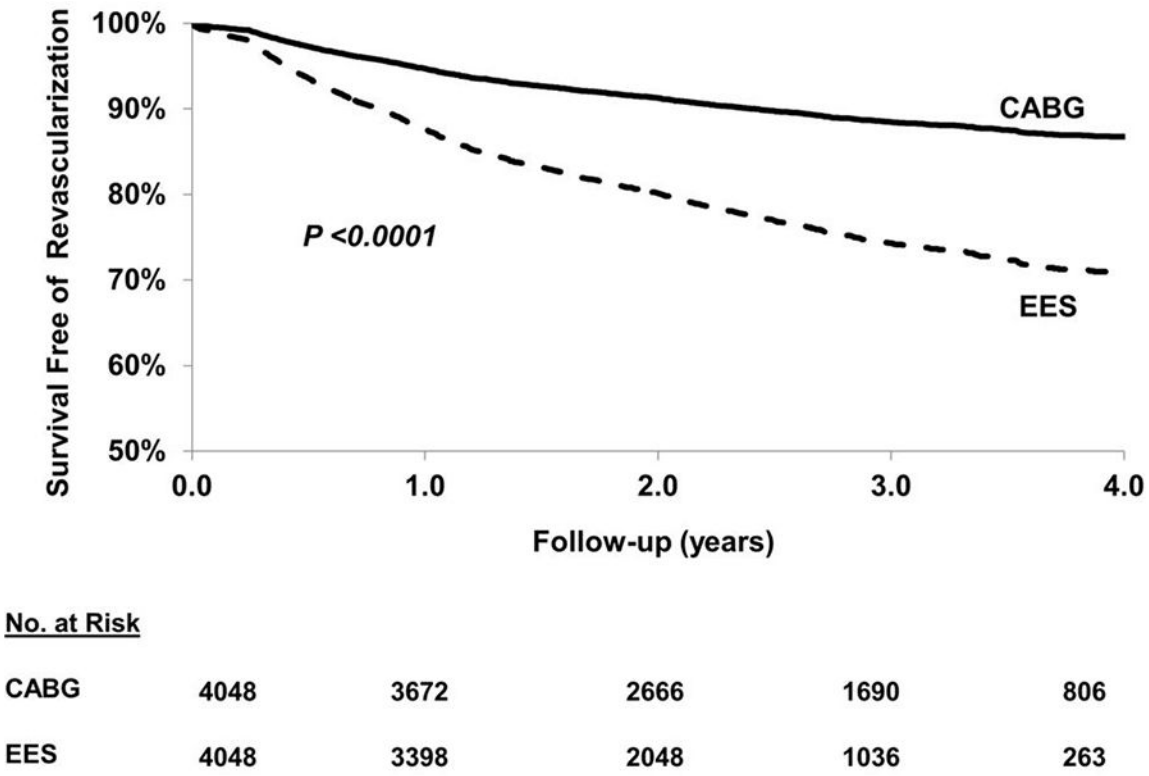

No. at Risk					
CABG	4048	3672	2666	1690	806
EES	4048	3398	2048	1036	263

Figure 5.
EES vs. CABG: long-term (includes first 30 days) repeat revascularization

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Table 1.

Baseline characteristics before and after propensity score matching

Variables	Pre-Matching EES (N=7,326)	Pre-Matching CABG (N=8,763)	Pre-Matching ASD	Post-Matching EES (N=4,048)	Post-Matching CABG (N=4,048)	Post-Matching ASD
Mean Age (yr)	64.8±10.5	64.6±10.2	1.7	64.9±10.5	64.7±10.3	2.3
Sex (%)						
Male	66	70	10.1	68	68	0.4
Female	34	30	10.1	32	32	0.4
Race (%)						
White	70	81	26.1	76	75	1.4
Black	15	10	15.4	12	12	0.5
Other	15	9	18.7	12	13	1.4
Ejection Fraction (%)						
<20%	1	2	11.8	1	1	0.0
20–29%	3	7	17.9	5	5	0.9
30–39%	5	13	25.6	8	8	0.4
40–49%	12	19	18.0	15	16	2.1
>=50%	73	59	30.5	70	70	1.5
missing	5	0	30.0	1	1	0.3
Previous myocardial infarction (%)						
Within 1–7days	14	17	10.2	16	16	0.1
Within 8–14 days	1	6	23.6	2	2	0.5
Within 15–20 days	0	1	10.0	0	1	1.3
>20 days	18	24	14.1	20	20	0.3
No previous MI	66	52	30.1	61	60	0.2
Peripheral arterial disease (%)	10	13	8.9	11	11	0.9
Congestive heart failure (%)						
None	92	81	30.5	88	89	0.4
At current admission	5	15	33.0	8	8	0.3
Before current admission	3	4	3.3	4	4	1.0

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Variables	Pre-Matching EES (N=7,326)	Pre-Matching CABG (N=8,763)	Pre-Matching ASD	Post-Matching EES (N=4,048)	Post-Matching CABG (N=4,048)	Post-Matching ASD
Prior PCI (%)	35	20	34.0	27	27	0.2
Renal Failure (%)						
dialysis	4	4	0.6	4	5	1.8
<1.3	73	68	9.3	71	70	1.6
1.3–1.5	13	14	3.1	14	14	0.6
1.6–2.0	7	8	5.5	7	7	0.8
>2.0	3	5	8.1	4	4	0.3
No. of diseased vessels (%)						
2, with proximal LAD artery	17	16	2.7	22	22	0.5
2, without proximal LAD artery	54	15	89.5	31	31	0.2
3, with proximal LAD artery	9	36	66.9	16	17	1.7
3, without proximal LAD artery	19	33	31.1	31	30	0.8

Plus-minus values are means±SD. ASD = absolute standardized differences; CABG = coronary artery bypass graft surgery; COPD = chronic obstructive pulmonary disease; EES = everolimus eluting stent; LAD = left anterior descending artery. ASD <10% for a given covariate indicate a relatively small imbalance.

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Table 2.

Risk of death in anatomic subgroups

Variables	No. of Patients	No. of Events	Event Rate (K-M estimate)	Hazard Ratio (95% CI)	P-value	P-value for interaction
3 Diseased Vessels						0.14*
With or without proximal LAD artery						
EES	773	80	14.8	1.24(0.85,1.80)	0.26	
CABG	773	69	11.9	Reference		
With proximal LAD artery						0.70†
EES	278	26	11.3	1.14(0.64,2.02)	0.66	
CABG	278	28	12.3	Reference		
Without proximal LAD artery						
EES	495	54	16.7	1.32(0.81,2.16)	0.27	
CABG	495	41	11.8	Reference		
2 Diseased Vessels						
With or without proximal LAD artery						
EES	1008	72	10.9	0.85(0.60,1.19)	0.34	
CABG	1008	89	11.3	Reference		
With proximal LAD artery						0.55†
EES	250	20	12.8	1,00(0.52,1.92)	0.99	
CABG	250	21	10.0	Reference		
Without proximal LAD artery						
EES	758	52	10.1	0.79(0.53,1.19)	0.26	
CABG	758	68	11.8	Reference		
Complete Revascularization						0.05‡
EES	748	64	11.7	0.80(0.56,1.15)	0.23	
CABG	748	81	13.3	Reference		
Incomplete Revascularization†						
EES	3300	361	16.8	1.20(1.01,1.42)	0.03	
CABG	3300	333	13.5	Reference		

*Test for interaction for the number of diseased vessels (3 diseased vessels vs. 2 diseased vessels);

†Test for interaction based on the proximal LAD disease status (with vs. without proximal LAD).

‡Test for interaction based on completeness of revascularization (complete vs. incomplete) in the PCI cohort.

†Based on incomplete revascularization in the PCI group. CABG = coronary artery bypass graft surgery; EES = everolimus eluting stent; LAD = left anterior descending artery.

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Table 3.

Risk of myocardial infarction in anatomic subgroups

Variables	No. of Patients	No. of Events	Event Rate (K-M estimate)	Hazard Ratio (95% CI)	P-value	P-value for interaction
3 Diseased Vessels						0.02 *
With or without proximal LAD artery						
EES	773	57	10.2	3.33(1.87,5.94)	<0.0001	
CABG	773	23	4.7	Reference		
With proximal LAD artery						0.12 †
EES	278	42	6.7	14.0(1.84,106.4)	0.01	
CABG	278	18	3.8	Reference		
Without proximal LAD artery						
EES	495	15	12.1	2.57(1.39,4.77)	0.003	
CABG	495	5	5.2	Reference		
2 Diseased Vessels						
With or without proximal LAD artery						
EES	1008	52	6.0	1.34(0.85,2.12)	0.21	
CABG	1008	42	5.2	Reference		
With proximal LAD artery						0.99 †
EES	250	10	4.3	1.33(0.46,3.84)	0.59	
CABG	250	9	4.4	Reference		
Without proximal LAD artery						
EES	758	42	6.5	1.35(0.81,2.24)	0.25	
CABG	758	33	5.4	Reference		
Complete Revascularization						0.52 ‡
EES	748	33	5.6	1.37(0.76,2.47)	0.30	
CABG	748	25	3.9	Reference		
Incomplete Revascularization †						
EES	3300	227	9.5	1.69(1.33,2.14)	<0.0001	
CABG	3300	141	5.7	Reference		

* Test for interaction for the number of diseased vessels (3 diseased vessels vs. 2 diseased vessels);

† Test for interaction based on the proximal LAD disease status (with vs. without proximal LAD).

‡ Test for interaction based on completeness of revascularization (complete vs. incomplete) in the PCI cohort.

† Based on incomplete revascularization in the PCI group. CABG = coronary artery bypass graft surgery; EES = everolimus eluting stent; LAD = left anterior descending artery.

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Table 4.

Risk of repeat revascularization in anatomic subgroups

Variables	No. of Patients	No. of Events	Event Rate (K-M estimate)	Hazard Ratio (95% CI)	P-value	P-value for interaction
3 Diseased Vessels						0.01*
With or without proximal LAD artery						
EES	773	202	32.8	3.30(2.43,4.49)	<0.0001	
CABG	773	79	13.6	Reference		
With proximal LAD artery						0.31†
EES	278	65	30.2	2.67(1.62,4.40)	0.0001	
CABG	278	33	16.4	Reference		
Without proximal LAD artery						
EES	495	137	34.2	3.72(2.52,5.49)	<0.0001	
CABG	495	46	12.1	Reference		
2 Diseased Vessels						
With or without proximal LAD artery						
EES	1008	213	28.0	1.92(1.49,2.48)	<0.0001	
CABG	1008	115	14.8	Reference		
With proximal LAD artery				1.44(0.86,2.40)	0.16	0.21†
EES	250	50	29.7			
CABG	250	29	149	Reference		
Without proximal LAD artery						
EES	758	163	26.9	2.11(1.57,2.84)	<0.0001	
CABG	758	86	14.9	Reference		
Complete Revascularization						0.005‡
EES	748	120	23.3	1.56(1.12,2.16)	0.01	
CABG	748	76	13.0	Reference		
Incomplete Revascularization†						
EES	3300	769	29.8	2.62(2.26,3.03)	<0.0001	
CABG	3300	345	13.6	Reference		

*Test for interaction for the number of diseased vessels (3 diseased vessels vs. 2 diseased vessels);

†Test for interaction based on the proximal LAD disease status (with vs. without proximal LAD).

‡Test for interaction based on completeness of revascularization (complete vs. incomplete) in the PCI cohort.

†Based on incomplete revascularization in the PCI group. CABG = coronary artery bypass graft surgery; EES = everolimus eluting stent; LAD = left anterior descending artery.