Everolimus Eluting Stents Versus Coronary Artery Bypass Graft Surgery for Patients With Diabetes Mellitus and Multivessel Disease

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

Methods and Results—Patients included in the New York State registries who had diabetes mellitus and underwent isolated coronary artery bypass graft surgery or percutaneous coronary intervention 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 mellitus and multivessel disease, 8096 patients with similar propensity scores were included. At short-term, EES was associated with a lower risk of death (hazard ratio [HR] =0.58; 95% confidence interval [CI], 0.34–0.98; *P*=0.04) and stroke (HR=0.14; 95% CI, 0.06–0.30; *P*<0.0001) but higher risk of MI (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%] versus 414 [10.23%] events; HR=1.12; 95% CI, 0.96–1.30; *P*=0.16), a lower risk of stroke (118 [2.92%] versus 157 [3.88%] events; HR=0.76; 95% CI, 0.58–0.99; *P*=0.04) but a higher risk of MI (260 [6.42%] versus 166 [4.10%] events; HR=1.64; 95% CI, 1.32–2.04; *P*<0.0001) and repeat revascularization (889 [21.96%] versus 421 [10.40%] events; HR=2.42; 95% CI, 2.12–2.76; *P*<0.0001). The higher risk of MI 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).

Conclusions—In patients with diabetes mellitus and multivessel disease, EES was associated with lower upfront risk of death and stroke when compared with coronary artery bypass graft surgery. 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. **(*Circ Cardiovasc Interv*. 2015;8:e002626. DOI: 10.1161/CIRCINTERVENTIONS.115.002626.)**

Key Words: coronary artery bypass graft ■ diabetes mellitus ■ multivessel disease ■ percutaneous coronary intervention

In patients with diabetes mellitus and coronary artery disease, coronary artery bypass graft surgery (CABG) and percutaneous coronary intervention (PCI) are revascularization options. The 2014 American College of Cardiology/American Heart Association guidelines updated its previous recommendation in favor of CABG over PCI for patients with diabetes mellitus 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 mellitus and stable multivessel disease (Class I, Level of evidence: A).[3]

In the only well-powered, well-conducted trial in patients with diabetes mellitus 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 first generation drug eluting stents (DES; sirolimus eluting stent 51%, paclitaxel eluting stent 43%; 18.7% versus 26.6%; *P*=0.005), driven by

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WHAT IS KNOWN

- In patients with diabetes mellitus and multivessel disease, coronary artery bypass graft surgery and percutaneous coronary intervention are treatment options.
- Studies comparing coronary artery bypass graft surgery versus percutaneous coronary intervention with older generation stents show a mortality benefit of coronary artery bypass graft surgery in patients with diabetes mellitus.

WHAT THE STUDY ADDS

- In this propensity score-matched analysis from the New York State registries in patients with diabetes mellitus and multivessel disease, percutaneous coronary intervention using latest generation stents (everolimus eluting stent) was associated with lower early risk of death and stroke when compared with coronary artery bypass graft surgery.
- At long-term, everolimus eluting stent was associated with similar risk of death, a higher risk of myocardial infarction (in those with incomplete revascularization), and repeat revascularization but a lower risk of stroke.

reduction in MI (6.0% versus 13.9%, $P<0.0001$) and all-cause mortality (10.9% versus 16.3%, $P=0.049$).[4] However, it is not known whether 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.

Methods

Study Population

Patients with diabetes mellitus 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 mellitus; (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 before the index procedure; (2) prior cardiac surgery (CABG or valve surgery) because such patients are unlikely to undergo repeat surgery; (3) severe left main coronary artery disease (degree of stenosis ≥50%) because these patients preferentially undergo CABG; (4) PCI with a stent other than EES or using a mixture of stents; (5) MI within 24 hours preceding the index procedure because 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 nonfederal hospitals in New York State. Data are entered by trained 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 several 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 revascularization after the index procedure. Staged revascularization was defined as a nontarget 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 I in the Data Supplement), 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 versus CABG) given a set of baseline measured covariates.[5,6] A nonparsimonious multivariable logistic regression model[7] with EES use as the dependent variable and all the baseline characteristics outlined in Table 1 and Table I in the Data Supplement 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 were estimated for all the baseline covariates before and after matching to assess prematch and postmatch imbalance.[8] Absolute standardized differences <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 versus 2-vessel disease; (2) with or without proximal left anterior descending artery 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 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

Table 1. Baseline Characteristics Before and After Propensity Score Matching

	Prematching			Postmatching		
Variables	EES (N=7326)	CABG (N=8763)	ASD	EES (N=4048)	CABG (N=4048)	ASD
Mean age, y	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% to 29%	3	7	17.9	5	5	0.9
30% to 39%	5	13	25.6	8	8	0.4
40% to 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 1–7 days	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
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 <10% for a given covariate indicate a relatively small imbalance. ASD indicates absolute standardized differences; CABG, coronary artery bypass graft surgery; COPD, chronic obstructive pulmonary disease; EES, everolimus eluting stent; LAD, left anterior descending artery; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

significance. All analyses were performed with SAS version 9.3 (SAS Institute, Cary, NC).

Results

We identified 16089 patients with diabetes mellitus and multivessel disease who satisfied the inclusion criteria and none of the exclusion criteria. Of the 16089 patients, 7326 (45%) underwent PCI with EES and 8763 (55%) patients underwent CABG. The baseline characteristics are outlined in Table 1. Before propensity score matching, there were differences (as indicated by absolute standardized differences ≥10%) between the 2 groups. Propensity score matching matched 4048 EES patients with 4048 CABG patients with similar propensity scores. Post matching the absolute standardized differences was <10% for all variables (Table 1; Table I in the Data Supplement).

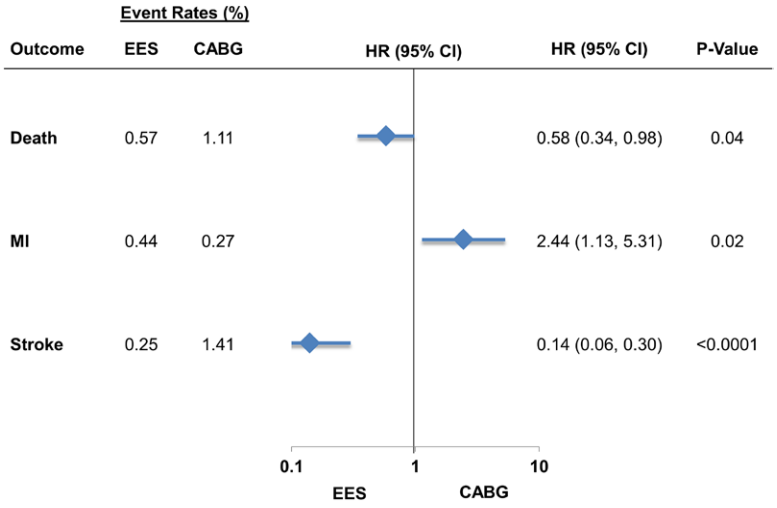


Figure 1. Everolimus eluting stent (EES) vs coronary artery bypass graft surgery (CABG): short-term (within 30 days) outcomes. CI indicates confidence interval; HR, hazard ratio; and MI, myocardial infarction.

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%] versus 45 [1.11%] events; HR=0.58; 95% CI, 0.34–0.98; *P*=0.04) and stroke (10 [0.25%] versus 57 [1.41%] events; HR=0.14; 95% CI, 0.06–0.30; *P*<0.0001) but higher risk of MI (18 [0.44%] versus 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%] versus 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 left anterior descending involvement ($P_{interaction}$ >0.05; Table 2).

Myocardial Infarction

In the matched cohort, EES was associated with a higher risk of MI (260 [6.42%] versus 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 MI 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%] versus 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%] versus 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 (versus CABG) was significantly higher in those with 3-vessel disease (versus 2-vessel disease) and in those with incomplete revascularization (versus complete revascularization; Table 4).

Discussion

In a contemporary cohort of patients with diabetes mellitus (predominantly noninsulin-dependent) and multivessel disease, with a sample size >4× 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.

Revascularization in Patients With Diabetes Mellitus

Patients with diabetes mellitus often have a high burden of atherosclerosis with extensive coronary artery disease

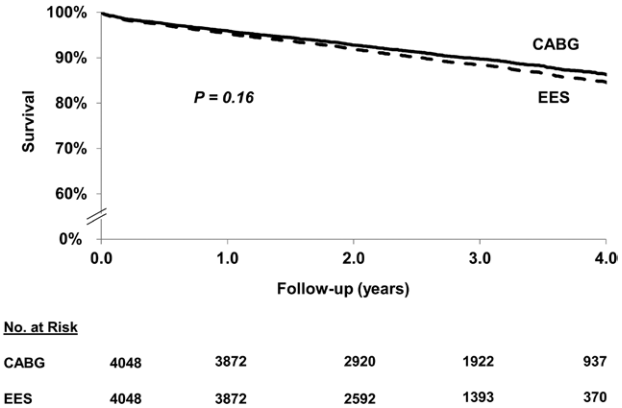


Figure 2. Everolimus eluting stent (EES) vs coronary artery bypass graft surgery (CABG): long-term (includes first 30 days) death.

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		

CABG indicates coronary artery bypass graft surgery; CI, confidence interval; EES, everolimus eluting stent; LAD, left anterior descending artery; and PCI, percutaneous coronary intervention.

*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.

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, after revascularization, patients with diabetes mellitus are more likely to have increased risk of adverse consequences. For example, patients with diabetes mellitus undergoing PCI are more likely to develop restenosis and stent thrombosis and have higher rates of death and MI when compared with patients without diabetes mellitus.[10,11] Similarly, patients with diabetes mellitus undergoing CABG are more likely to have increased risk of perioperative complications, such as deep sternal wound infections, renal failure, and fatal and nonfatal cardiovascular events when compared with patients without diabetes mellitus.[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 nonculprit lesion (11.6%), attesting to the importance of both.[14] Most nonculprit lesions that resulted in an event were angiographically mild, consistent with similar prior observations.[15] Patients with diabetes mellitus 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 mellitus is associated with poor outcomes when compared with patients without diabetes mellitus with increased risk of restenosis and stent thrombosis and consequently increased risk of death or MI (because of 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, that is, the risk of restenosis and stent thrombosis, can potentially bridge this gap between CABG and PCI.

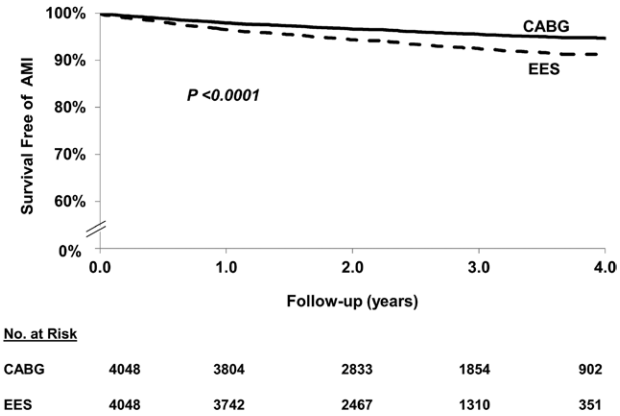


Figure 3. Everolimus eluting stent (EES) vs coronary artery bypass graft surgery (CABG): long-term (includes first 30 days) myocardial infarction.

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 mellitus from the Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery (SYNTAX) trial, CABG was associated with numerically lower mortality (12.9% versus 19.5%; *P*=0.065) and MI (5.4% versus 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 mellitus and multivessel disease by CABG decreased long-term mortality compared with PCI using either bare metal stent 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 versus 132–140 μm), thinner and more biocompatible polymer (7.8 μm versus 13.7–17.8 μm) both of which reduce inflammation and thrombogenicity and promote rapid endothelialization when compared with the first 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

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		

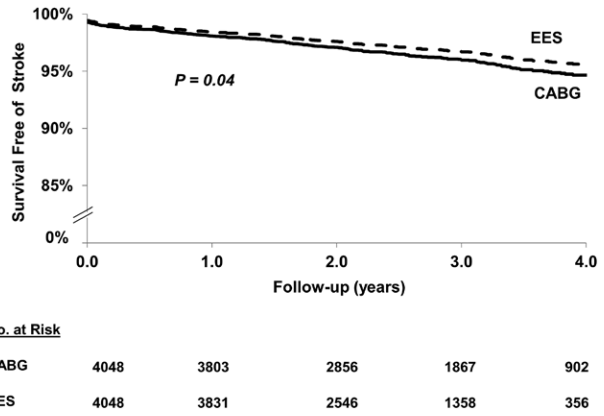
CABG indicates coronary artery bypass graft surgery; CI, confidence interval; EES, everolimus eluting stent; LAD, left anterior descending artery; and PCI, percutaneous coronary intervention.

*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.



No. at Risk

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

Figure 4. Everolimus eluting stent (EES) vs coronary artery bypass graft surgery (CABG): long-term (includes first 30 days) stroke.

the largest analysis to date in patients with diabetes mellitus, with data from 42 randomized trials and 22 844 patient years of follow-up, we had shown that EES was the most efficacious (defined as lowest rate of restenosis) and safest (defined as lowest rate of stent thrombosis) when compared with all Food and Drug Administration-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 mellitus 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 end points for the subgroup of patients with diabetes mellitus was not presented. Our study with a sample size which is 22-folds larger than the 363 patients with diabetes mellitus included in the BEST trial offers important additional insights on individual end points.

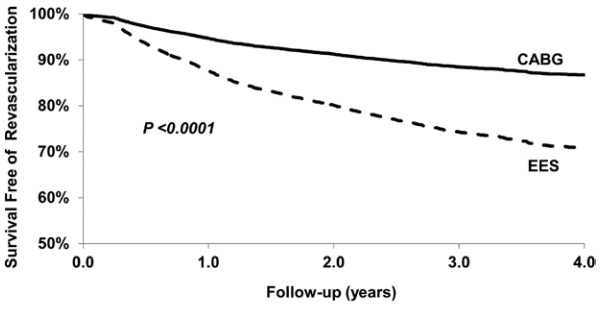
It therefore seems that the selection between PCI and CABG for patients with multivessel disease and diabetes mellitus should be based on weighing the risks of future MI and repeat revascularization with PCI and the upfront risk of death and stroke with CABG. However, in patients with complete revascularization, 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 mellitus 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 nonrandomized 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 (because of 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 second 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 noninsulin-dependent diabetes mellitus. Although, there was no statistically significant 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 overestimates the event rates for these outcomes because it does not account for the competing risk of death.

Conclusions

In a contemporary cohort of patients with diabetes mellitus 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 mellitus should therefore be based on ability to achieve complete revascularization by PCI. Randomized controlled trials are needed to test these associations.



No. at Risk

CABG	4048	3672	2666	1690	806
EES	4048	3398	2048	1036	263

Figure 5. Everolimus eluting stent (EES) vs coronary artery bypass graft surgery (CABG): long-term (includes first 30 days) repeat revascularization.

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		

CABG indicates coronary artery bypass graft surgery; CI, confidence interval; EES, everolimus eluting stent; LAD, left anterior descending artery; and PCI, percutaneous coronary intervention.

*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.

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Supplementary Appendix

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This appendix has been provided by the authors to give readers additional information about their work.

Contents

Table S1. Additional baseline characteristics before and after propensity score matching

Variables	Pre-Matching			Post-Matching		
	EES (N=7,326)	CABG (N=8,763)	ASD	EES (N=4,048)	CABG (N=4,048)	ASD
Age (%)						
<59	31	30	2.0	30	31	1.0
60-69	34	36	3.6	35	35	0.9
70-79	26	27	1.9	26	27	0.6
>=80	8	7	6.1	8	8	1.0
Body Surface Area	2.06±0.28	2.07±0.28	0.1	2.07±0.28	2.06±0.28	2.6
Hispanic ethnic background (%)	17	12	15.2	15	15	0.2
Cerebrovascular disease (%)	3	8	24.1	5	4	0.8
COPD (%)	5	12	25.9	7	7	0.4
Malignant ventricular arrhythmia (%)	0	1	5.0	0	0	1.2
DM Complications (%)	6	14	26.3	9	10	3.3
Long-term Insulin (%)	8	11	10.7	9	9	0.8

Plus-minus values are means±SD. COPD = chronic obstructive pulmonary disease.