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Long-term Outcomes in Patients With Severely Reduced Left Ventricular Ejection Fraction Undergoing Percutaneous Coronary Intervention vs Coronary Artery Bypass Grafting

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Invited Commentary

Supplemental content

IMPORTANCE Data are lacking on the outcomes of patients with severely reduced left ventricular ejection fraction (LVEF) who undergo revascularization by percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).

OBJECTIVE To compare the long-term outcomes in patients undergoing revascularization by PCI or CABG.

DESIGN, SETTING, AND PARTICIPANTS This retrospective cohort study performed in Ontario, Canada, from October 1, 2008, and December 31, 2016, included data from Ontario residents between 40 and 84 years of age with LVEFs less than 35% and left anterior descending (LAD), left main, or multivessel coronary artery disease (with or without LAD involvement) who underwent PCI or CABG. Exclusion criteria were concomitant procedures, previous CABG, metastatic cancer, dialysis, CABG and PCI on the same day, and emergency revascularization within 24 hours of a myocardial infarction (MI). Data analysis was performed from June 2, 2018, to December 28, 2018.

EXPOSURES Revascularization by PCI or CABG.

MAIN OUTCOMES AND MEASURES The primary outcome was all-cause mortality. Secondary outcomes were death from cardiovascular disease, major adverse cardiovascular events (MACE; defined as stroke, subsequent revascularization, and hospitalization for MI or heart failure), and each of the individual MACE.

RESULTS A total of 12 113 patients (mean [SD] age, 64.8 (11.0) years for the PCI group and 65.6 [9.7] years for the CABG group; 5084 (72.5%) male for the PCI group and 4229 (82.9%) male for the PCI group) were propensity score matched on 30 baseline characteristics: 2397 patients undergoing PCI and 2397 patients undergoing CABG. The median follow-up was 5.2 years (interquartile range, 5.0-5.3). Patients who received PCI had significantly higher rates of mortality (hazard ratio [HR], 1.6; 95% CI, 1.3-1.7), death from cardiovascular disease (HR 1.4, 95% CI, 1.1-1.6), MACE (HR, 2.0; 95% CI, 1.9-2.2), subsequent revascularization (HR, 3.7; 95% CI, 3.2-4.3), and hospitalization for MI (HR, 3.2; 95% CI, 2.6-3.8) and heart failure (HR, 1.5; 95% CI, 1.3-1.6) compared with matched patients who underwent CABG.

CONCLUSIONS AND RELEVANCE In this study, higher rates of mortality and MACE were seen in patients who received PCI compared with those who underwent CABG. The findings may provide insight to physicians who are involved in decision-making for these patients.

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Coronary artery disease (CAD) is the most frequent cause of death globally and the most common cause of heart failure (HF) in resource-abundant countries.[1-5] The incidence of systolic myocardial dysfunction is increasing among patients with CAD in part because of improved survival after acute myocardial infarction (MI).[5] However, the long-term prognosis for this condition remains poor.[6,7]

Professional society guidelines differ with regard to the recommended treatment for this population. The European guidelines recommend revascularization, with a preference for CABG over PCI, in patients with reduced left ventricular ejection fraction (LVEF) and multivessel CAD.[8] The US guidelines favor the use of CABG but do not provide recommendations about PCI,[9] stating that "the choice of revascularization ... is best based on clinical variables, ... magnitude of LV systolic dysfunction, patient preferences, clinical judgment, and consultation between the interventional cardiologist and the cardiac surgeon."[9] The vagueness of the guidelines reflects a lack of evidence from adequately powered randomized clinical trials or large observational studies,[9-12] resulting in wide variations across practitioners and institutions in the treatment of patients with CAD and reduced LVEF.[13,14] We conducted a population-based cohort study in Ontario, Canada, that compared the long-term outcomes in patients with CAD and reduced LVEF who underwent PCI or CABG as their index revascularization procedure.

Key Points

Question Is there a difference in outcomes for patients with coronary artery disease and severely reduced left ventricular ejection function who undergo revascularization by percutaneous coronary intervention vs coronary artery bypass grafting?

Findings In this cohort study of 12 113 patients with coronary artery disease, coronary artery bypass grafting was associated with greater long-term survival compared with percutaneous coronary intervention. This survival benefit was observed across different subgroups, including patients with left anterior descending–only disease.

Meaning The findings suggest that coronary artery bypass grafting should be considered for most patients with severely reduced left ventricular function who require revascularization.

Methods

Design and Study Population

We conducted a population-based retrospective cohort study in Ontario, Canada, of patients who underwent a first myocardial revascularization procedure between October 1, 2008, and December 31, 2016. Data analysis was performed from June 2, 2018, to December 28, 2018. The research ethics board at Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada approved this study and waived the need for individual patient consent because data were deidentified.

Patients included in the study were those who underwent first-time PCI or isolated CABG, were between 40 and 84 years of age, had an LVEF less than 35%, and presented with at least 1 of the following CAD features: 50% or greater stenosis in the left main artery, 70% or greater stenosis in the left anterior descending (LAD) artery, or 70% or greater stenosis in 2 or more major epicardial arteries.[15] Exclusion criteria were non-Ontario residency status, concomitant procedures, history of CABG, CABG and PCI on the same day, emergency revascularization within 24 hours of presentation for acute MI, dialysis dependency, and presence of metastatic malignant tumor.

Data Sources

We used the clinical registry data from CorHealth Ontario[16] and the population-level administrative health care databases from the Institute for Clinical Evaluative Sciences. Ontario is Canada's most populous province with a publicly funded universal health care system that reimburses all insured services and practitioners. CorHealth maintains a detailed prospective registry of all patients undergoing invasive cardiac procedures in Ontario. All 20 advanced cardiac care hospitals participate in this registry, for which demographic, comorbidity, and procedural data have been validated through multiple medical record audits.[13] In addition, the CorHealth registry captures and validates LVEF and angiographic data on a regular basis.[13]

We deterministically linked administrative databases by using encrypted unique confidential codes to preserve patient confidentiality. We linked the CorHealth registry (date and type of revascularization procedure, preoperative LVEF, comorbidities, and the location and severity of CAD) with the Canadian Institute for Health Information's Discharge Abstract Database (DAD; comorbidities and hospital admissions), Ontario Health Insurance Plan (OHIP) database (physician service claims), Registered Persons Database (RPDB; vital statistics), Office of the Registrar General Database (ORGD; cause-specific death), and the Canadian Census. These administrative databases have been validated for outcomes, exposures, and comorbidities, including HF, chronic obstructive pulmonary disease, asthma, hypertension, MI, and diabetes.[17-20]

Baseline Patient Characteristics

Patient characteristics were identified from the CorHealth registry and supplemented with data from the DAD and OHIP using codes from the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10)*[21] within 5 years before the index revascularization procedure, according to validated algorithms.[17,19,22-24] We estimated each patient's socioeconomic status by using the neighborhood median income from the Canadian Census[25] and determined residence status (rural vs urban) using Statistics Canada definitions.[26] Urgent procedural status (intervention within the same index admission) was ascertained using the CorHealth registry. Height, weight, and body mass index (calculated as weight in kilograms divided by height in meters squared) were identified from the CorHealth Ontario registry and used to determine morbid obesity (defined as weight >159 kg or body mass index ≥40).[7,27,28]

Outcomes

The primary outcome was all-cause mortality. Secondary outcomes consisted of death from cardiovascular disease; major adverse cardiovascular events (MACE), defined as stroke, subsequent revascularization, or hospitalization for MI or HF; and each of the individual MACE outcomes. All-cause mortality was ascertained by using the RPDB and death from cardiovascular disease by using the ORGD. Stroke was identified with a validated algorithm based on hospitalization records.[29] Subsequent revascularization procedures were identified from the CorHealth registry, OHIP physician billings, and the DAD. Subsequent hospitalizations that occurred after the index revascularization procedure, with MI or HF as the primary diagnosis, were identified using the DAD.

Statistical Analysis

Continuous variables were compared with a 2-sample *t* test or with a Wilcoxon rank sum test for nonnormally distributed data. Categorical variables were compared with a χ^2 test. All outcomes were first assessed from the date of the procedure until 30 days postoperatively. All-cause death and MACE were assessed from the date of the procedure through December 31, 2017. Death from cardiovascular disease was assessed through December 31, 2016, because the availability of cause of death data lagged behind that of all-cause death. Patients were censored at the end of the follow-up period or when they lost possession of a valid Ontario health insurance card.

In the time to first event analyses, mortality rates were calculated using the Kaplan-Meier method. Hazard ratios (HRs) and 95% CIs were determined and event rates were compared with a log-rank test. To account for death as a competing event, we estimated the cumulative incidence of each of the secondary outcomes by using cumulative incidence functions and compared event rates between groups using the Fine and Gray test of inequality.

Because the PCI and CABG groups differed in baseline characteristics (**Table 1**), we conducted a propensity score–matched analysis to compare the outcomes between groups while accounting for imbalances in baseline risk. We developed a nonparsimonious multivariable logistic regression model to estimate a propensity score for CABG using CABG as the dependent variable and the characteristics listed in Table 1. Between-group imbalances were considered to be small if the absolute standardized difference for a given covariate was less than 10%.[30] We used a greedy algorithm to match 1:1, without replacement, those who underwent PCI with those who underwent CABG by using a caliper width of 0.2 SD of the logit of the propensity score. The risk of mortality in the matched groups was assessed using a Cox proportional hazards regression model stratified on the matched pairs. The secondary outcomes were assessed by using Fine and Gray subdistribution hazards models fitted to the propensity score–matched sample, with death as a competing risk. We used a robust variance estimator to account for the matched nature of the sample.[31] Because case mix, procedural volumes, PCI to CABG ratio, and outcomes varied by site, we used generalized estimating equations to account for the clustering of patients at the institution level. We examined the modification of the number of diseased vessels, diabetes, completeness of revascularization, and type of stents (ie, bare metal [BMS] vs drug eluting [DES]) on the association between revascularization strategy and long-term outcomes in the propensity score–matched cohort using multiplicative interaction terms.

Analyses were performed using SAS statistical software, version 9.4 (SAS Institute Inc) and R software, version 3.5.3 (R Foundation for Statistical Computing). Statistical significance was defined as a 2-sided $P < .05$.

Sensitivity Analyses

We conducted several sensitivity analyses to test the robustness of our findings. First, we repeated our analyses using pneumonia and hip fracture as falsification end points. Second, we compared the rates of death from cardiovascular disease and death from other causes in the PCI and CABG groups at 30 days and in long-term follow-up. Third, we performed a landmark analysis of matched patients who were event free at 30 days to compare the outcomes of PCI vs CABG. Fourth, we excluded patients without LAD disease. Fifth, we matched patients based on their propensity to receiving PCI vs CABG within subgroups stratified by the number of diseased vessels, presence of diabetes, and completeness of revascularization.

Results

A total of 12 113 patients (mean [SD] age, 64.8 (11.0) years for the PCI group and 65.6 [9.7] years for the CABG group; 5084 (72.5%) male for the PCI group and 4229 (82.9%) male for the PCI group) with CAD and severely reduced LVEF who underwent first-time revascularization met our inclusion criteria. Of these patients, 7013 (57.9%) underwent PCI and 5100 (42.1%) underwent CABG. A cohort flow diagram is presented in eFigure 1 in the Supplement.

Table 1 outlines the patient characteristics in the PCI and CABG groups before and after propensity score matching. Differences were observed across most covariates before matching. After we matched 2397 patients who underwent PCI with 2397 who underwent CABG, baseline characteristics were balanced between the groups. In the PCI group, a mean (SD) of 1.9 (1.1) stents were implanted per patient. In the CABG group, a mean (SD) of 3.3 (1.0) grafts per patient were placed. The mean (SD) wait time was 4.1 (9.7) days from diagnostic coronary angiogram to PCI and 14.5 (25.3) days to CABG. During the study period, the mean (SD) PCI volume was 265.6 (119.5) cases per year among interventional cardiologists, and the mean (SD) CABG volume was 135.0 (54.0) cases per year among surgeons.

30-Day Outcomes

The 30-day outcomes of the matched groups are summarized in **Table 2**. Among the 4794 patients in the matched cohort, patients who underwent PCI compared with CABG had higher rates of all-cause 30-day mortality (4.8% vs 4.0%), death from cardiovascular disease (3.5% vs 2.8%), MACE (19.8% vs 8.3%), subsequent revascularization (10.9% vs 3.2%), and hospitalization for MI (7.8% vs 1.4%) or HF (5.6% vs 3.0%). The HRs among subgroups defined by the number of diseased vessels, the presence of diabetes, and the completeness of revas-

Table 1. Baseline Patient Characteristics Before and After Propensity Score Matching

Characteristic	Before matching No. (%) PCI (n = 7013)	CABG (n = 5100)	ASD	P value	After matching No. (%) PCI (n = 2397)	CABG (n = 2397)	ASD	P value
Age, mean (SD), y	64.8 (11.0)	65.6 (9.7)	0.08	<.001	66.5 (10.3)	66.0 (10.0)	0.05	.07
Age category, y								
40-64	3459 (49.3)	2267 (44.5)	0.10	<.001	1000 (41.7)	1047 (43.7)	0.04	.38
65-74	1922 (27.4)	1769 (34.7)	0.16		796 (33.2)	762 (31.8)	0.03	
75-84	1632 (23.3)	1064 (20.9)	0.06		601 (25.1)	588 (24.5)	0.01	
Female	1929 (27.5)	871 (17.1)	0.25	<.001	492 (20.5)	477 (19.9)	0.02	.59
Rurality	873 (12.4)	825 (16.2)	0.11	<.001	371 (15.5)	356 (14.9)	0.02	.51
Income quintile								
Missing	43 (0.6)	32 (0.6)	0	>.99	18 (0.8)	10 (0.4)	0.04	.58
1	1485 (21.2)	1103 (21.6)	0.01		556 (23.2)	545 (22.7)	0.01	
2	1463 (20.9)	1060 (20.8)	0		492 (20.5)	492 (20.5)	0	
3	1436 (20.5)	1039 (20.4)	0		479 (20.0)	505 (21.1)	0.03	
4	1349 (19.2)	977 (19.2)	0		447 (18.6)	426 (17.8)	0.02	
5	1237 (17.6)	889 (17.4)	0.01		405 (16.9)	419 (17.5)	0.02	
BMI, mean (SD)	28.03 (5.55)	28.45 (5.46)	0.08	<.001	28.53 (5.77)	28.18 (5.45)	0.06	.06
Morbid obesity	1894 (27.0)	1755 (34.4)	0.16	<.001	755 (31.5)	754 (31.5)	0	.98
Hypertension	5143 (73.3)	4463 (87.5)	0.36	<.001	2036 (84.9)	2019 (84.2)	0.02	.5
MI within 30 d of surgery	2321 (33.1)	2825 (55.4)	0.46	<.001	1242 (51.8)	1196 (49.9)	0.04	.18
Remote MI	1326 (18.9)	1250 (24.5)	0.14	<.001	619 (25.8)	618 (25.8)	0	.97
Previous PCI	1300 (18.5)	689 (13.5)	0.14	<.001	511 (21.3)	463 (19.3)	0.05	.09
LVEF, %								
20-34	6015 (85.8)	4288 (84.1)	0.05	.01	1967 (82.1)	1988 (82.9)	0.02	.43
<20	998 (14.2)	812 (15.9)	0.05		430 (17.9)	409 (17.1)	0.02	
Heart failure	2246 (32.0)	2770 (54.3)	0.46	<.001	1261 (52.6)	1229 (51.3)	0.03	.36
Atrial fibrillation	403 (5.7)	347 (6.8)	0.04	.02	185 (7.7)	162 (6.8)	0.04	.20
Cerebrovascular disease	455 (6.5)	557 (10.9)	0.16	<.001	227 (9.5)	246 (10.3)	0.03	.36
Peripheral arterial disease	505 (7.2)	783 (15.4)	0.26	<.001	313 (13.1)	313 (13.1)	0	>.99
COPD or asthma	2137 (30.5)	1646 (32.3)	0.04	.04	794 (33.1)	784 (32.7)	0.01	.76
Diabetes	2811 (40.1)	2799 (54.9)	0.30	<.001	1256 (52.4)	1244 (51.9)	0.01	.73
Hypothyroidism	88 (1.3)	81 (1.6)	0.03	.12	37 (1.5)	36 (1.5)	0	.91
Liver disease	55 (0.8)	43 (0.8)	0.01	.72	23 (1.0)	21 (0.9)	0.01	.76
Alcohol abuse	123 (1.8)	136 (2.7)	0.06	<.001	65 (2.7)	66 (2.8)	0	.93
Anemia	434 (6.2)	646 (12.7)	0.22	<.001	246 (10.3)	248 (10.3)	0	.92
Renal disease	154 (2.2)	189 (3.7)	0.09	<.001	96 (4.0)	79 (3.3)	0.04	.19
Paraplegia	31 (0.4)	15 (0.3)	0.02	.19	17 (0.7)	≤5	0.08	.004
Primary malignant tumor	293 (4.2)	245 (4.8)	0.03	.10	111 (4.6)	114 (4.8)	0.01	.84
Dementia	37 (0.5)	19 (0.4)	0.02	.21	18 (0.8)	8 (0.3)	0.06	.05
Depression	110 (1.6)	99 (1.9)	0.03	.12	48 (2.0)	46 (1.9)	0.01	.84
Psychosis	14 (0.2)	24 (0.5)	0.05	.008	7 (0.3)	11 (0.5)	0.03	.35
Charlson Comorbidity Index, mean (SD)	1.37 (1.72)	2.49 (1.72)	0.65	<.001	2.16 (1.88)	2.28 (1.71)	0.07	.02
Complete revascularization	3394 (48.4)	4223 (82.8)	0.78	<.001	507 (21.2)	1950 (81.4)	1.51	<.001
No. of diseased vessels								
LAD-only disease	2781 (39.7)	144 (2.8)	1.01	<.001	158 (6.6)	143 (6.0)	0.03	.10
LM or 2-vessel disease	2920 (41.6)	2628 (51.5)	0.20		1467 (61.2)	1414 (59.0)	0.05	
3-Vessel disease	1312 (18.7)	2328 (45.6)	0.60		772 (32.2)	840 (35.0)	0.06	
No. of stents implanted, mean (SD)	1.7 (1.0)	NA	NA	NA	1.9 (1.1)	NA	NA	NA
No. of grafted vessels, mean (SD)	NA	3.4 (1.0)	NA	NA	NA	3.3 (1.0)	NA	NA

Abbreviations: ASD, absolute standardized difference; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; LAD, left anterior descending; LM, left main coronary artery; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention.

Table 2. Thirty-Day and Long-term Outcomes in Patients Who Underwent PCI vs CABG in the Propensity Score–Matched Cohort

Outcome	PCI (n = 2397)			CABG (n = 2397)			HR (95% CI)	*P* value
	Events, No.	Event rate, %	Event rate (range)[a]	Events, No.	Event rate, %	Event rate (range)[a]		
30-d Outcomes								
Primary outcome: all-cause mortality	115	4.8	1.7 (1.4-2.0)	97	4.0	1.4 (1.1-1.7)	1.2 (0.9-1.6)	.21
Secondary outcomes								
Death from cardiovascular disease	83	3.5	1.2 (1.0-1.5)	67	2.8	1.0 (0.8-1.2)	1.3 (0.9-1.7)	.17
MACE	475	19.8	8.0 (7.3-8.7)	199	8.3	3.0 (2.6-3.4)	2.6 (2.2-3.0)	<.001
Stroke	16	0.7	0.2 (0.1-0.4)	32	1.3	0.5 (0.3-0.7)	0.5 (0.3-0.9)	.02
Revascularization	262	10.9	4.1 (3.6-4.6)	77	3.2	1.1 (0.9-1.4)	3.5 (2.7-4.5)	<.001
Myocardial infarction	188	7.8	2.9 (2.5-3.3)	33	1.4	0.5 (0.3-0.7)	5.9 (4.1-8.5)	<.001
Hospitalization for HF	134	5.6	2.0 (1.7-2.4)	71	3.0	1.0 (0.8-1.3)	1.9 (1.5-2.6)	<.001
Long-term outcomes								
Primary outcome: all-cause mortality	720	30.0	79.6 (73.9-85.6)	558	23.3	50.3 (46.2-54.6)	1.6 (1.4-1.7)	<.001
Secondary outcomes								
Death from cardiovascular disease	260	10.8	35.5 (31.3-40.1)	213	8.9	23.1 (20.1-26.4)	1.4 (1.1-1.6)	<.001
MACE	1221	50.9	215.7 (203.8-228.2)	770	32.1	87.0 (81.0-93.4)	2.0 (1.9-2.2)	<.001
Stroke	96	4.0	10.8 (8.8-13.2)	146	6.1	13.6 (11.5-16.0)	0.7 (0.5-0.9)	.006
Revascularization	657	27.4	95.3 (88.1-102.9)	207	6.4	20.1 (17.5-23.0)	3.7 (3.2-4.3)	<.001
Myocardial infarction	426	17.8	53.5 (48.5-58.8)	154	20.1	14.4 (12.2-16.8)	3.2 (2.6-3.8)	<.001
Hospitalization for HF	618	25.8	79.3 (73.2-85.8)	481	9861	48.8 (44.5-53.3)	1.5 (1.3-1.6)	<.001

Abbreviations: CABG, coronary artery bypass grafting; HF, heart failure; HR, hazard ratio; MACE, major adverse cardiovascular event; PCI, percutaneous coronary intervention.

[a] For 30-day outcomes, data are per 1000 person-days; for long-term outcomes, per 1000 person-years

cularization are presented in **Table 3**. Across all subgroups, the 30-day risk of MACE were consistently higher among patients who underwent PCI compared with those who underwent CABG. The subgroup analysis by BMS and DES compared with CABG is presented in eTable 1 in the Supplement.

Long-term Outcomes

The median follow-up duration was 5.2 years (interquartile range [IQR], 5.0-5.3 years; maximum, 9.2 years) in the overall cohort, 5.7 years (IQR, 5.5-5.9 years) in the CABG group, and 4.6 years (IQR, 4.4-4.8 years) in the PCI group. The 5-year mortality rates were 30.0% in the PCI group and 23.3% in the CABG group. The event rates and adjusted HRs are summarized in Table 2.

Primary Outcome (All-Cause Death)

During follow-up, 1278 of the 4794 patients (26.7%) in matched groups died, including 720 of 2397 patients (30.0%) who underwent PCI and 558 of 2397 patients (23.3%) who underwent CABG (**Figure 1**). Patients who underwent PCI had higher rates of long-term mortality (HR, 1.6; 95% CI, 1.4-1.7) than did those who underwent CABG (Table 2). The HRs were consistent across subgroups defined according to the number of diseased vessels, the presence of diabetes, and the completeness of revascularization (Table 3). When comparing DES and BMS with CABG (eTable 1 and eFigure 2 in the Supplement), mortality was higher among patients undergoing PCI regardless of stent type.

Death From Cardiovascular Disease

A total of 260 patients (10.8%) in the PCI group and 213 (8.9%) in the CABG group died of cardiovascular disease. Patients who underwent PCI had a higher risk of death from cardiovascular disease than did those who underwent CABG (HR, 1.4; 95% CI, 1.1-1.6) (**Figure 2**A). These results were consistent across subgroups of patients with 3-vessel disease and diabetes (Table 3). When comparing patients who received DES vs BMS, the risk of death from cardiovascular disease was higher than in patients who underwent CABG regardless of stent type (eTable 1 and eFigure 3 in the Supplement).

Major Adverse Cardiovascular Events

MACE occurred in a total of 1221 patients (50.9%) who underwent PCI and 770 (32.1%) who underwent CABG. In patients who underwent PCI, there was a higher risk of MACE compared with those who underwent CABG (HR, 2.0; 95% CI, 1.9-2.2) (Figure 2B). These results were consistent across subgroups of patients regardless of the number of diseased vessels, diabetes status, or whether complete revascularization was achieved (Table 3). When comparing DES and BMS

Table 3. Thirty-Day and Long-term Outcomes in Subgroups by Number of Diseased Vessels, Presence of Diabetes, and Completeness of Revascularization in the Propensity Score–Matched Cohort

	30-d Outcomes		Long-term outcomes	
Outcome	HR (95% CI)	*P* value for interaction	HR (95% CI)	*P* value for interaction
All-cause mortality				
LAD-only disease	6.4 (0.8-52.0)	<.001	1.7 (1.0-3.0)	<.001
LM-only or 2-vessel disease	0.8 (0.5-1.1)		1.3 (1.1-1.5)	
3-Vessel disease	2.0 (1.3-3.1)		2.2 (1.8-2.7)	
Diabetes				
Yes	1.3 (0.9-1.8)	.60	1.7 (1.5-2.0)	.02
No	1.1 (0.7-1.7)		1.3 (1.1-1.6)	
Revascularization				
Complete	1.1 (0.6-1.8)	.41	1.3 (1.0-1.6)	.15
Incomplete	0.8 (0.5-1.2)		1.0 (0.9-1.3)	
Death from cardiovascular disease				
LAD-only disease	5.5 (0.7-46.1)	<.001	1.6 (0.6-4.1)	<.001
LM-only or 2-vessel disease	0.7 (0.4-1.1)		1.0 (0.8-1.2)	
3-Vessel disease	2.4 (1.4-4.0)		2.3 (1.7-3.1)	
Diabetes				
Yes	1.3 (0.9-2.1)	.64	1.5 (1.2-1.9)	.31
No	1.1 (0.7-1.9)		1.2 (0.9-1.6)	
Revascularization				
Complete	1.3 (0.7-2.2)	.20	0.9 (0.6-1.3)	.54
Incomplete	0.8 (0.5-1.2)		1.0 (0.8-1.4)	
MACE				
LAD-only disease	2.2 (1.1-4.4)	.05	1.4 (1.0-2.1)	.001
LM-only or 2-vessel disease	2.2 (1.8-2.7)		1.9 (1.7-2.1)	
3-Vessel disease	3.4 (2.6-4.5)		2.5 (2.2-3.0)	
Diabetes				
Yes	2.6 (2.1-3.2)	.88	1.9 (1.7-2.2)	.16
No	2.5 (2.0-3.2)		2.2 (1.9-2.5)	
Revascularization				
Complete	1.8 (1.3-2.4)	.68	1.5 (1.3-1.7)	.16
Incomplete	1.7 (1.3-2.2)		1.7 (1.5-2.0)	

Abbreviations: HR, hazard ratio; LAD, left anterior descending; LM, left main; MACE, major adverse cardiovascular event.

with CABG (eTable 1 and eFigure 4 in the Supplement), the risk of MACE was higher among patients who underwent both PCI modalities.

Stroke

Stroke occurred in 96 patients (4.0%) who underwent PCI and 146 (6.1%) who underwent CABG. The risk of stroke was lower in patients who underwent PCI compared with those who underwent CABG (HR, 0.7; 95% CI, 0.5-0.9) (Figure 2C).

Subsequent Revascularization

A total of 657 patients (27.4%) who underwent PCI and 207 who underwent CABG (8.6%) required subsequent revascularization. In patients who underwent PCI, there was a higher risk of subsequent revascularization compared with those who underwent CABG (HR, 3.7; 95% CI, 3.2-4.3) (Figure 2D).

Hospitalization for MI

Subsequent hospitalization for MI occurred in 426 patients (17.8%) who underwent PCI and 154 (6.4%) who underwent CABG. Among patients who underwent PCI, there was a higher risk of MI compared with those who underwent CABG (HR, 3.2; 95% CI, 2.6-3.8) (Figure 2E).

Hospitalization for HF

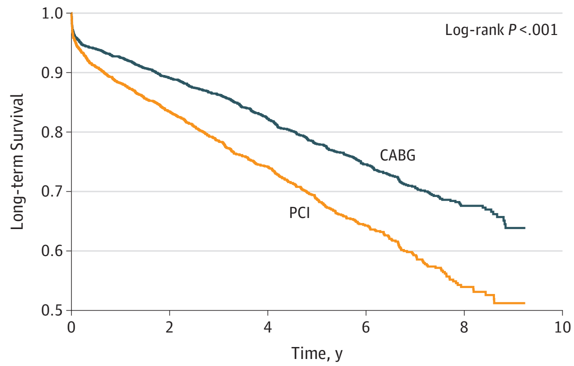
Subsequent hospitalization for HF after an index revascularization procedure occurred in 618 patients (25.8%) after PCI and 481 (20.1%) after CABG. There was a higher risk of hospitalization for HF among patients who underwent PCI compared with those who underwent CABG (HR, 1.5; 95% CI, 1.3-1.6) (Figure 2F). These results were consistent across subgroups with multivessel disease and subgroups based on presence of diabetes and completeness of revascularization (Table 3).

Sensitivity Analyses

Falsification End Points

We found no statistically significant differences in the incidence of pneumonia (HR, 1.1; 95% CI, 0.8-1.5) and hip fracture (HR, 1.1; 95% CI, 0.7-1.8) between the PCI and CABG groups (eFigure 5 and eFigure 6 in the Supplement).

Figure 1. Estimated Long-term Survival After Percutaneous Coronary Intervention (PCI) vs Coronary Artery Bypass Grafting (CABG)



No. at risk						
CABG	2397	1929	1375	818	304	0
PCI	2397	1717	1033	496	152	0

Death From Cardiovascular vs Noncardiovascular Causes

After propensity score matching, the rate of death from cardiovascular disease at 30 days was numerically higher in the PCI group, whereas the rate of deaths from other causes was numerically higher in the CABG group (eFigure 7 and eFigure 8 in the Supplement). In long-term follow-up, the rates of deaths from cardiovascular and noncardiovascular causes were statistically significantly higher in the PCI group compared with the CABG group after matching (eFigure 9 and eFigure 10 in the Supplement).

Landmark Analysis

Among patients who were event free at 30 days, those who were treated with PCI had higher rates of all-cause death, death from cardiovascular disease, and MACE compared with those who were treated with CABG (eFigures 11-13, eTable 2, and eTable 3 in the Supplement).

Patient Exclusion and Propensity Score Matching

Our findings remained robust after exclusion of 573 patients who did not have LAD disease (eFigures 14-16, eTable 4, and eTable 5 in the Supplement). Our findings also remained robust after propensity score matching within subgroups stratified by the number of diseased vessels, presence of diabetes, and completeness of revascularization (eTables 6-15 in the Supplement).

Discussion

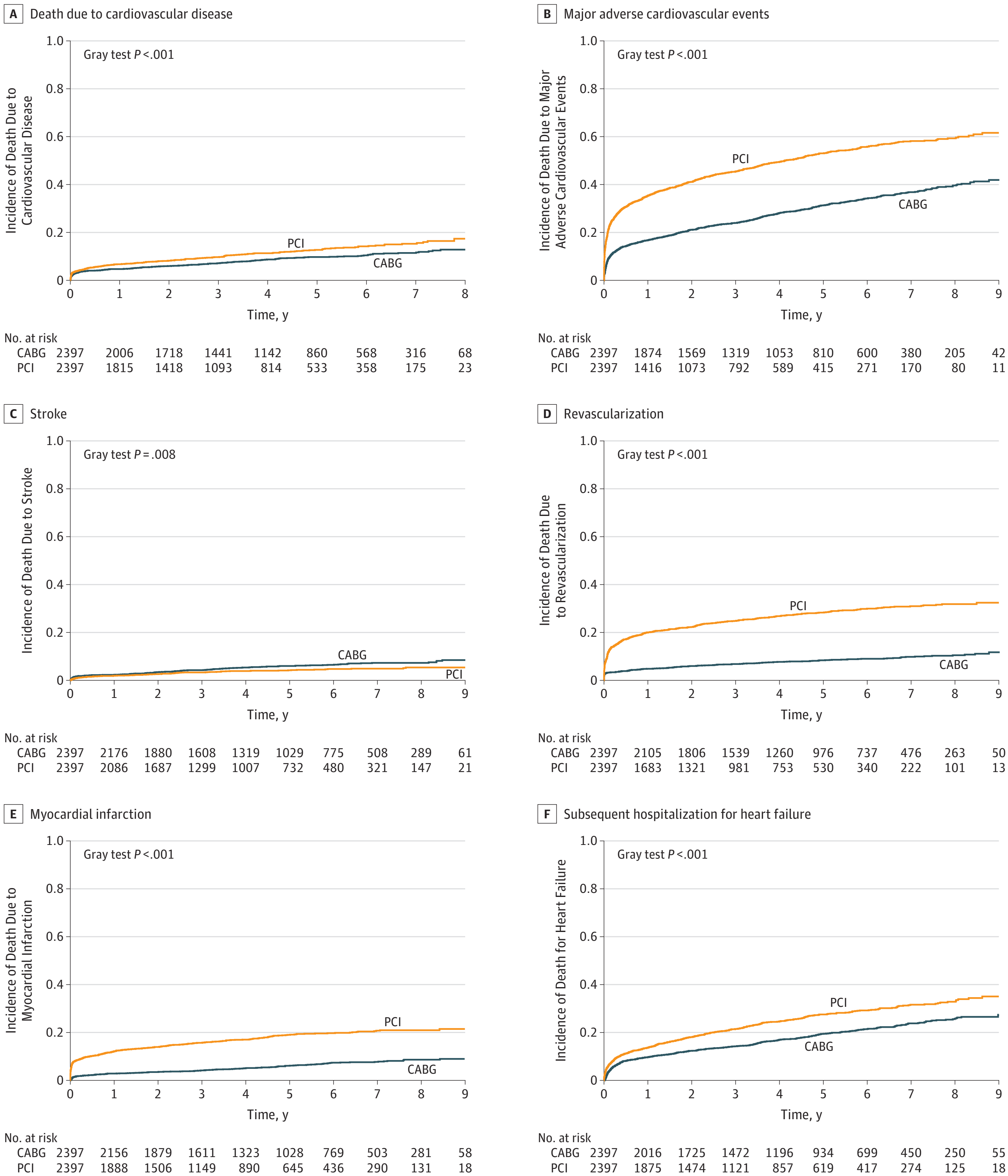
To our knowledge, this is the largest published study examining the long-term outcomes of PCI vs CABG in patients with CAD and severely reduced LVEF. We observed higher 30-day risks of MACE, subsequent revascularization, and hospitalization for MI or HF among patients who underwent PCI compared those who underwent CABG. During long-term follow-up, the risks of all-cause death from cardiovascular disease, MACE, subsequent revascularization, and hospitalization for MI or HF were higher among patients who underwent PCI, and these patterns were consistent across subgroups defined according to the number of diseased vessels, the completeness of revascularization, and the type of stent. The risk of death from cardiovascular disease after PCI vs CABG was significantly higher only in the subgroup with diabetes.

Decisions regarding the best therapeutic option for patients with CAD and severely reduced LVEF are particularly challenging partly because long-term outcomes for this condition are largely undefined in the contemporary era. Neither the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial nor the International Study of Comparative Health Effectiveness With Medical and Invasive Approaches (ISCHEMIA) trial evaluated patients with CAD and severely reduced LVEF. Major trials that compared PCI vs CABG also have routinely excluded this patient group.[32] For example, only 34 patients (approximately 2%) from the Synergy Between PCI With TAXUS and Cardiac Surgery (SYNTAX) trial[33] and 32 (2.5%) from in the Future Revascularization Evaluation in Patients With Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM) trial[34] had severely reduced LVEF, thus rendering the data from these trials insufficient to inform clinical decisions.

To date, there has been only 1 randomized clinical trial to guide treatment decisions in this group,[35] and PCI was not an integral part of the investigational therapeutic regimen. The Surgical Treatment for Ischemic Heart Failure Extension Study (STICHES) found that CABG compared with optimal medical therapy conveyed a 7% absolute mortality reduction at 10 years of follow-up and fewer cardiovascular-related hospitalizations.[36] However, STICHES was performed in an earlier surgical era (ie, 2002-2007), and the safety outcomes of CABG in the context of severely reduced LVEF have since improved.[6] In the present study, the 5-year mortality rates were 30.0% in the PCI group and 23.3% in the CABG group. In addition to temporal improvement in procedural techniques and perioperative care, these lower mortality rates possibly also reflect the relative homogeneity of perioperative practices in Ontario compared with those used in STICHES, which was an international study with recruitment from 99 centers.[37] The 5-year mortality rates in the present study are comparable to those reported by a population-based study (2008-2011) that propensity score matched 1063 patients who underwent PCI to an equal number who underwent CABG.[38]

PCI and CABG have differed historically in terms of risk, morbidity, completeness of revascularization, and the need for reintervention. A meta-analysis[39] comparing PCI with CABG in patients with severely reduced LVEF found CABG to be associated with improved survival (HR, 0.82; 95% CI, 0.75-0.90), a lower rate of MI (HR, 0.50; 95% CI, 0.36-0.68), and a lower rate of subsequent revascularization (HR, 0.34; 95% CI, 0.24-0.47). Nonetheless, a concurrently published cohort study by Bangalore et al[38] (not incorporated in the meta-analysis) found no difference in 3-year survival among patients treated with PCI and CABG. Congruent with the meta-analysis, Bangalore et al[38] found a greater association of PCI with MI and subsequent revascularization and a greater association of CABG with stroke. The present multicenter study had a considerable follow-up window (median, 5.2 years; maximum, 9.2

Figure 2. Postprocedure Incidences of Study End Points Among Patients Who Underwent Coronary Intervention (PCI) or Coronary Artery Bypass Grafting (CABG)



years) and supports a potential benefit of CABG in patients with CAD and severely reduced LVEF; those who underwent CABG had lower risks of all-cause death, death from cardiovascular disease, MACE, subsequent revascularization, and hospitalization for MI and HF.

The findings of the present study could be explained by a higher frequency of complete revascularization and longer revascularized epicardial coronary segments and thus fewer sudden cardiac deaths in the CABG group.[39] In addition, CABG protects against the development of new proximal and midvessel lesions, provides a newly perfused distal bed for collateralization,[40] and may slow native CAD progression through the use of multiple arterial grafts. Our finding of lower long-term stroke risk in association with PCI in patients with multivessel disease and incomplete revascularization are similar to the findings of other studies[38,39] and may reflect the risk associated with aortic cross-clamping, the embolic risk associated with cardiopulmonary bypass, and a greater likelihood of being exposed to intraoperative hypotension during CABG.[41]

Our inclusion of patients with LAD-only disease, analysis of outcomes by the number of diseased vessels, and examination of death from cardiovascular disease provide added insight into the long-term outcomes of PCI and CABG. Specifically, we found that CABG was associated with a lower risk of death from cardiovascular disease only among patients with 3-vessel disease. This observation may be explained by complete revascularization being more frequently achieved with CABG than with PCI[42] as well as a higher CAD burden and more complex coronary anatomy in patients with ischemic HF. More complex coronary anatomy may be associated with a higher risk of MI and subsequent revascularization in the PCI group because of stent placement being limited to specific stenotic segments rather than revascularization of longer epicardial segments as achieved with CABG.[39,43] This may also in part explain the improved long-term survival among patients with LAD-only disease who underwent CABG.

Limitations

This study has limitations. First, periprocedural MIs according to biochemical factors could not be captured because of the lack of these factors in the databases. However, rates of periprocedural MI after PCI and CABG vary substantially depending on the definitions used.[44] In addition, rates of subsequent hospitalization for MI were identified using a definition that is consistent with the Nordic-Baltic-British Left Main Revascularization Study (NOBLE).[45] Second, patients with previous PCIs were included in our analyses. However, this inclusion was used by previous landmark studies, such as that by Bangalore et al,[38] and therefore this cohort was comparable with those previously described. Third, the data sources used lacked some relevant detailed information, such as anatomical risk score (ie, SYNTAX), viability data, or the generation and type of DES used. The inability to measure and thereby adjust for differences in such characteristics could have in part explained the differences in event rates observed in this study. Fourth, because universal drug coverage is only offered to Ontarians aged 66 years and older, the adequacy of guideline-directed therapy could not be described and PCI and CABG could not be compared with optimal medical therapy. Fifth, the large between-group difference in the rate of early MI subsequent hospitalization could in part reflect detection bias from staged revascularization at 30 days. However, the landmark analysis of patients who did not require revascularization or subsequent hospitalization for MI or HF at 30 days demonstrated consistency in the direction of the findings. Sixth, cohort studies are subject to residual confounding and indication bias despite rigorous statistical techniques. Nonetheless, to our knowledge, this study was the largest to date to examine the association of common revascularization strategies with outcomes in this population. The inclusion of patients with LAD-only disease and BMS may have enhanced the generalizability of the findings and provided new information to assist with therapeutic decision-making for patients with CAD and severely reduced LVEF.

Conclusions

In the present study, CABG was associated with lower risk of long-term all-cause mortality and death from cardiovascular disease, MACE, subsequent revascularization, and hospitalization for MI and HF compared with PCI in patients with CAD and LVEF less than 35%. The mortality benefit associated with CABG was consistent in subgroups of patients regardless of the presence of diabetes and was especially evident in those with multivessel disease. Although these findings may suggest that CABG should be considered as a first-line treatment for these patients, they should be interpreted in light of the limitations that are inherent to observational studies.

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