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NEW RESEARCH PAPER

CORONARY

Real-World Examination of Revascularization Strategies for Left Main Coronary Disease in Ontario, Canada

Derrick Y. Tam, MD, PhD,[a,b] Jiming Fang, PhD,[c] Rodolfo V. Rocha, MD, PhD,[d] Sunil V. Rao, MD, PhD,[e] Vladimir Dzavik, MD, PhD,[f] Jennifer Lawton, MD,[g] Peter C. Austin, PhD,[b,c] Mario Gaudino, MD,[h] Stephen E. Fremes, MD, MSc,[a,b] Douglas S. Lee, MD, PhD[b,c,f]

ABSTRACT

BACKGROUND Randomized trials have compared percutaneous coronary intervention and coronary artery bypass grafting (CABG) in patients with left main coronary artery disease undergoing nonemergent revascularization. However, there is a paucity of real-world contemporary observational studies comparing percutaneous coronary intervention (PCI) and CABG.

OBJECTIVES The purpose of this study was to compare the long-term clinical outcomes of CABG versus PCI in patients with left main coronary disease.

METHODS Clinical and administrative databases for Ontario, Canada, were linked to obtain records of all patients with angiographic evidence of left main coronary artery disease (≥50% stenosis) treated with either isolated CABG or PCI from 2008 to 2020. Emergent, cardiogenic shock, and ST-segment elevation myocardial infarction patients were excluded. Baseline characteristics of patients were compared and 1:1 propensity score matching was performed. Late mortality and major adverse cardiac and cerebrovascular events were compared between the matched groups using a Cox proportional hazard model.

RESULTS After exclusions, 1,299 and 21,287 patients underwent PCI and CABG, respectively. Prior to matching, PCI patients were older (age 75.2 vs 68.0 years) and more likely to be women (34.6% vs 20.1%), although they had less CAD burden. Propensity score matching on 25 baseline covariates yielded 1,128 well-matched pairs. There was no difference in early mortality between PCI and CABG (5.5% vs 3.9%; $P = 0.075$). Over 7-year follow-up, all-cause mortality (53.6% vs 35.2%; HR: 1.63; 95% CI: 1.42-1.87; $P < 0.001$) and major adverse cardiac and cerebrovascular events (66.8% vs 48.6%; HR: 1.77; 95% CI: 1.57-2.00) were significantly higher with PCI than CABG.

CONCLUSIONS CABG was the most common revascularization strategy in this real-world registry. Patients undergoing PCI were much older and of higher risk at baseline. After matching, there was no difference in early mortality but improved late survival and freedom from major adverse cardiac and cerebrovascular events with CABG. (J Am Coll Cardiol Intv 2023;16:277–288) © 2023 Published by Elsevier on behalf of the American College of Cardiology Foundation.

From the [a]Division of Cardiac Surgery, Department of Surgery, Schulich Heart Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada; [b]Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Ontario, Canada; [c]ICES, Toronto, Ontario, Canada; [d]Division of Cardiac Surgery, Department of Surgery, Peter Munk Cardiac Centre, University Health Network, University of Toronto, Toronto, Ontario, Canada; [e]Division of Cardiology, Durham VA Health System, Duke University Health System, Durham, North Carolina, USA; [f]Division of Cardiology, Department of Medicine, Peter Munk Cardiac Centre, University Health Network, University of Toronto, Toronto, Ontario, Canada; [g]Division of Cardiac Surgery, Department of Surgery, Johns Hopkins University, Baltimore, Maryland, USA; and the [h]Department of Cardiothoracic Surgery, Weill Cornell Medical College, New York, New York, USA.

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ABBREVIATIONS AND ACRONYMS

CIHI-DAD = Canadian Institute for Health Information Discharge Abstract Database

CABG = coronary artery bypass grafting

LMD = left main coronary artery disease

MACCE = major adverse cardiac and cerebrovascular event(s)

MI = myocardial infarction

PCI = percutaneous coronary intervention

PS = propensity score

STEMI = ST-segment elevation myocardial infarction

Early work by Yusuf et al[1] confirmed that mortality for untreated significant left main coronary artery disease (LMD) was high, at 50% at 5 years, and that coronary artery bypass grafting (CABG) improved life expectancy compared with medical management. There have been no trials comparing percutaneous coronary intervention (PCI) with medical therapy and no recent trials comparing CABG and medical therapy. There have been, however, 5 high-quality randomized trials (and 1 prespecified subgroup analysis) comparing PCI with mostly drug-eluting stents with CABG to inform the choice of revascularization in LMD patients.[2-7] The 2018 European Revascularization Guidelines were developed following the 3-year results of EXCEL (Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization trial) and the NOBLE (Nordic-Baltic-British Left Main Revascularisation trial).[5,8] The 2021 American Guidelines were informed by the 5-year results of EXCEL, and updates of 2 other trials with 10 years follow-up, SYNTAXES (SYNTAX Extended Survival) and the extended follow-up PRECOMBAT (Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease).[7,9] Overall, left main PCI received a Class I recommendation for patients with LMD and low complexity coronary disease and Class IIa recommendation for patients with LMD and intermediate complexity in the European guidelines, which only differed from previous guidelines in the level of evidence, rather than in class of recommendation.[8] The American Guidelines instead provided a Class IIa recommendation for PCI when PCI can provide equivalent revascularization to that possible with CABG.[9] The results of 4 of the 6 studies using drug-eluting stents and with 5-year follow-up have since been aggregated in an individual-patient meta-analysis recently published in *The Lancet* by Sabatine et al.[10] However, the treatment of LMD remains very controversial.

While CABG remains the standard of care for patients with LMD, there may be a role for left main PCI in selected patients. Contemporary comparative outcomes of CABG and PCI outside of the clinical trial setting have not been well described. Importantly, there are limited contemporary, large observational studies that have compared PCI with CABG for LMD. Given our understanding of PCI and CABG efficacy from clinical trials, it is prudent to understand the real-world utilization and comparative effectiveness of PCI and CABG for left main coronary artery disease.

METHODS

STUDY DESIGN. We conducted a retrospective analysis of records for all patients in the province of Ontario, Canada, who had invasive coronary angiography demonstrating significant LMD between October 1, 2008, and October 31, 2020, and subsequently underwent revascularization with CABG or left main PCI within 90 days of the index angiography. Clinical registries of all patients undergoing angiography, PCI and CABG, were linked to multiple population-based health databases using patient-level encrypted health card numbers at ICES. As a prescribed entity under Ontario's Personal Health Information Protection Act, ICES is able to collect, construct, and store registries and link and analyze individual health data without the need to obtain individual patient consent. Therefore, we were able to study all patients undergoing these revascularization procedures without participation bias. The use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a Research Ethics Board. These datasets were linked using unique encoded identifiers and analyzed at ICES.

DATA SOURCES. Similar to previously published studies, coronary angiography records were obtained from the CorHealth Ontario Registry.[11,12] Baseline demographics were obtained from the CorHealth Registry, Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD), or previously validated algorithms where applicable.[13] Hospitalizations and the primary admission diagnoses were determined via the CIHI-DAD, using the International Classification of Diseases-10th Edition coding system, as previously described.[14] Deaths were determined using the Registered Persons Database, which contains vital status information

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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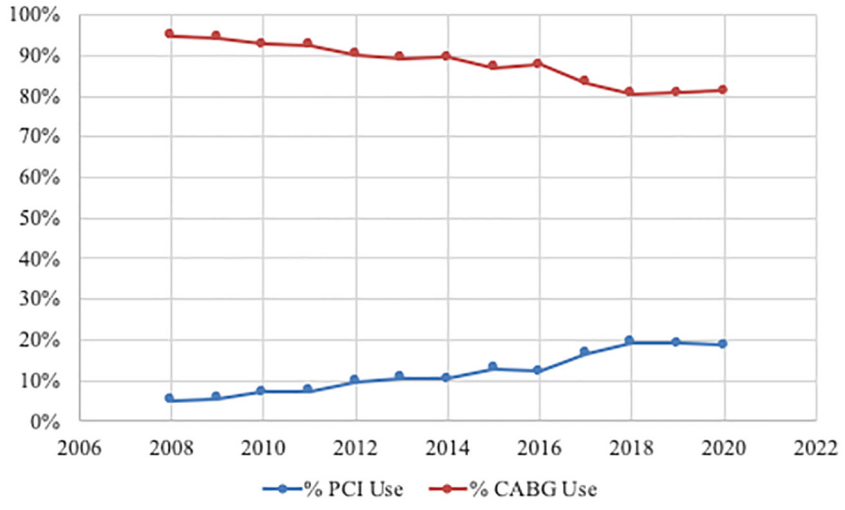
FIGURE 1 Time Trends in Percutaneous Coronary Intervention and Coronary Artery Bypass Grafting for Left Main Coronary Disease



Linear regression of percent left main percutaneous coronary intervention (PCI) and percent coronary artery bypass grafting (CABG) use in patients with left main disease undergoing revascularization by time (year).

for all Ontarians. The Ontario Diabetes Database was used to identify patients with diabetes, as employed previously.[14] We used Statistics Canada's census data to determine sociodemographic information based on median neighborhood income of individuals to serve as a proxy for socioeconomic status.

STUDY POPULATION AND DATA LINKAGES. Significant coronary artery narrowing in the CorHealth angiographic database was defined as ≥50% for the left main and ≥70% for all other coronary arteries.[11] In addition to isolated LMD, we further classified significant multivessel disease as left main with additional single vessel disease, double vessel disease, or triple vessel disease. We included patients with angiographic evidence of significant LMD and who underwent either left main PCI or CABG. Patients who underwent another concomitant cardiac operation (such as valve procedures and aortic surgery) were excluded to ensure that patients were comparable in terms of procedural risk. For all patients, we excluded those with a history of previous cardiac surgical procedures, and we excluded patients who underwent PCI procedure within the 6 months prior to the index coronary angiogram using the CIHI-DAD and the CorHealth PCI registry data. Finally, we excluded patients with ST-segment elevation myocardial infarction (STEMI), those with cardiogenic shock, those undergoing emergent or salvage procedures, and those with a diagnosis of dementia, as these patients are primarily treated by PCI and are at high risk for mortality. In our primary analysis, we also excluded patients who underwent ad hoc PCI (ie, same-sitting PCI), as we inferred that these patients may potentially be higher risk.

EARLY OUTCOMES. Our primary safety outcome was 30-day mortality, defined as death that occurred in hospital or within 30 days of the index revascularization procedure. In-hospital clinically diagnosed acute myocardial infarction (MI) and stroke were obtained from the CIHI-DAD.

LONG-TERM OUTCOMES. Long-term outcomes included all events from the index procedure (defined as the date of either PCI or CABG) to date of last follow-up on December 31, 2020. Our primary study outcome was long-term all-cause mortality. The secondary outcomes included: 1) long-term major adverse cardiac and cerebrovascular events (MACCE), a composite of all cause death, new hospital admission for MI, stroke, or repeat revascularization; and 2) the individual nonfatal components of MACCE. Because revascularization procedures may be staged, PCI of a new vessel (ie, not previously stented) within 90 days of the index procedure PCI was not counted as a repeat revascularization procedure. Repeat PCI was subcategorized based on the target of intervention (vessel with prior PCI, PCI after CABG, or PCI of a new vessel). If PCI was performed on the same vessel

TABLE 1 Baseline and Institutional Characteristics Before and After Propensity Score Matching

	Before Propensity Score Matching			After Propensity Score Matching		
	PCI (n = 1,299)	CABG (n = 21,287)	SMD	PCI (n = 1,128)	CABG (n = 1,128)	SMD
Age, y	75.2 ± 11.2	68.0 ± 9.5	0.695	73.6 ± 10.8	73.6 ± 10.6	0.003
Charlson index	3.0 ± 2.5	1.9 ± 1.9	0.497	2.9 ± 2.4	2.8 ± 2.3	0.034
Hospital Frailty Risk Score	5.8 ± 6.3	3.7 ± 4.4	0.385	5.5 ± 6.2	5.3 ± 6.0	0.03
Admission category (elective)	591 (45.5)	9,228 (43.4)	0.043	517 (45.8)	514 (45.6)	0.005
Female	450 (34.6)	4,285 (20.1)	0.33	369 (32.7)	386 (34.2)	0.032
Hypertension	1,147 (88.3)	18,179 (85.4)	0.086	989 (87.7)	992 (87.9)	0.008
Hyperlipidemia	844 (65.0)	13,692 (64.3)	0.014	726 (64.4)	738 (65.4)	0.022
Diabetes	586 (45.1)	9,425 (44.3)	0.017	516 (45.7)	497 (44.1)	0.034
History of smoking						
Current	203 (15.6)	4,503 (21.2)	0.143	188 (16.7)	199 (17.6)	0.026
Former	450 (34.6)	8,030 (37.7)	0.064	393 (34.8)	385 (34.1)	0.015
Never	570 (43.9)	8,386 (39.4)	0.091	489 (43.4)	485 (43.0)	0.007
Unknown	76 (5.9)	368 (1.7)	0.217	58 (5.1)	59 (5.2)	0.004
CCS class						
0	165 (12.7)	1,150 (5.4)	0.256	132 (11.7)	124 (11.0)	0.022
1	73 (5.6)	1,413 (6.6)	0.042	66 (5.9)	80 (7.1)	0.05
2	197 (15.2)	3,557 (16.7)	0.042	177 (15.7)	175 (15.5)	0.005
3	155 (11.9)	3,682 (17.3)	0.152	142 (12.6)	136 (12.1)	0.016
4	45 (3.5)	1,041 (4.9)	0.071	40 (3.5)	36 (3.2)	0.02
ACS high risk	124 (9.5)	1,435 (6.7)	0.103	102 (9.0)	96 (8.5)	0.019
ACS intermediate risk	304 (23.4)	4,336 (20.4)	0.073	269 (23.8)	282 (25.0)	0.027
ACS low risk	236 (18.2)	4,673 (22.0)	0.095	200 (17.7)	199 (17.6)	0.002
NYHA group						
No symptoms	867 (66.7)	15,222 (71.5)	0.103	766 (67.9)	776 (68.8)	0.019
Symptoms with any	60 (4.6)	320 (1.5)	0.182	49 (4.3)	46 (4.1)	0.013
Symptoms with less	141 (10.9)	1,057 (5.0)	0.22	115 (10.2)	113 (10.0)	0.006
Symptoms with ordinary	183 (14.1)	1,946 (9.1)	0.155	151 (13.4)	147 (13.0)	0.01
Unknown	48 (3.7)	2,742 (12.9)	0.338	47 (4.2)	46 (4.1)	0.004
Left ventricular function						
20%-34%	136 (10.5)	1,785 (8.4)	0.071	124 (11.0)	129 (11.4)	0.014
35%-49%	212 (16.3)	4,349 (20.4)	0.106	194 (17.2)	196 (17.4)	0.005
<20%	55 (4.2)	360 (1.7)	0.15	51 (4.5)	53 (4.7)	0.008
≥50%	565 (43.5)	14,069 (66.1)	0.466	530 (47.0)	522 (46.3)	0.014
Unknown	331 (25.5)	724 (3.4)	0.662	229 (20.3)	228 (20.2)	0.002
History of MI	420 (32.3)	4,043 (19.0)	0.309	354 (31.4)	375 (33.2)	0.04
Recent MI	508 (39.1)	6,788 (31.9)	0.151	424 (37.6)	394 (34.9)	0.055
Peripheral vascular disease	157 (12.1)	1,430 (6.7)	0.185	135 (12.0)	132 (11.7)	0.008
Cerebrovascular disease	165 (12.7)	1,415 (6.6)	0.206	130 (11.5)	116 (10.3)	0.04
COPD	292 (22.5)	2,251 (10.6)	0.325	232 (20.6)	247 (21.9)	0.033
Cancer history	233 (17.9)	2,235 (10.5)	0.214	191 (16.9)	198 (17.6)	0.016
Congestive heart failure history	577 (44.4)	4,282 (20.1)	0.538	461 (40.9)	465 (41.2)	0.007
Creatinine level						
0-120 mg/dL	914 (70.4)	17,772 (83.5)	0.315	810 (71.8)	825 (73.1)	0.03
121-180 mg/dL	166 (12.8)	1,845 (8.7)	0.133	139 (12.3)	136 (12.1)	0.008
181+ mg/dL	109 (8.4)	729 (3.4)	0.212	91 (8.1)	75 (6.6)	0.054
Missing	110 (8.5)	941 (4.4)	0.165	88 (7.8)	92 (8.2)	0.013
Dialysis	88 (6.8)	1,147 (5.4)	0.058	79 (7.0)	56 (5.0)	0.086

Continued on the next page

TABLE 1 Continued

	Before Propensity Score Matching			After Propensity Score Matching		
	PCI (n = 1,299)	CABG (n = 21,287)	SMD	PCI (n = 1,128)	CABG (n = 1,128)	SMD
Extent of CAD						
LM isolated	202 (15.6)	1,454 (6.8)	0.279	159 (14.1)	167 (14.8)	0.02
LM + SVD	285 (21.9)	3,523 (16.6)	0.137	238 (21.1)	267 (23.7)	0.076
LM + DVD	438 (33.7)	7,578 (35.6)	0.04	383 (34.0)	385 (34.1)	
LM + TVD	374 (28.8)	8,732 (41.0)	0.259	348 (30.9)	309 (27.4)	0.062
Income level						
1 (lowest)	326 (25.1)	4,239 (19.9)	0.124	288 (25.5)	287 (25.4)	0.002
2	258 (19.9)	4,444 (20.9)	0.025	232 (20.6)	220 (19.5)	0.027
3	268 (20.6)	4,379 (20.6)	0.001	226 (20.0)	229 (20.3)	0.007
4	231 (17.8)	4,099 (19.3)	0.038	198 (17.6)	200 (17.7)	0.005
5 (highest)	216 (16.6)	4,126 (19.4)	0.072	184 (16.3)	192 (17.0)	0.019
NSTEMI/unstable angina or ACS low, intermediate, or high risk	809 (62.3)	12,550 (59.0)	0.068	697 (61.8)	695 (61.6)	0.004
Cath hospital type						
Cath only	97 (7.5)	839 (3.9)	0.152	147 (6.5)	82 (7.3)	0.061
Cath/PCI	313 (24.1)	4,344 (20.4)	0.089	459 (20.3)	262 (23.2)	0.144
Cath/PCI/CABG	889 (68.4)	16,104 (75.7)	0.161	1,650 (73.1)	784 (69.5)	0.165
Interventional cardiologists						
Cath only	60 (4.6)	1,061 (5.0)	0.017	112 (5.0)	54 (4.8)	0.016
Cath + PCI	1,239 (95.4)	20,226 (95.0)	0.017	2,144 (95.0)	1,074 (95.2)	0.016
Length of stay, d	3 (1-8)	8 (6-12)	0.821	3 (1-8)	10 (7-15)	1.149

Values are mean ± SD, n (%), or median (IQR).

ACS = acute coronary syndrome; CABG = coronary artery bypass grafting; CAD = coronary artery disease; CCS = Canadian Cardiovascular Society; COPD = chronic obstructive pulmonary disease; DVD = double vessel disease; LM = left main coronary artery; MI = myocardial infarction; NSTEMI = non–ST-segment elevation myocardial infarction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; SMD = standardized mean difference; SVD = single vessel disease; TVD = triple vessel disease.

within 90 days or CABG was performed after index PCI, this was considered a repeat revascularization procedure.

STATISTICAL ANALYSES. Baseline characteristics were first compared in the overall sample between those undergoing PCI and CABG. Student's *t*-test was used for normally distributed continuous variables and the Wilcoxon rank sum test for non-normally distributed continuous variables, while the chi-square test was used for categorical variables. Propensity score (PS) matching was performed to account for baseline differences in patient characteristics between PCI and CABG in order to reduce the effects of confounding. The PS for each patient was estimated using a multivariable logistic regression model in which the intervention performed (PCI vs CABG) was regressed on 25 important baseline characteristics that may influence the choice of intervention or that were prognostically important for the outcome (see the full list in the Supplemental Appendix). Subjects were matched on the logit of the PS using 1:1 greedy nearest-neighbor matching with a caliper distance of 0.2 times the SD of the logit of the PS.[15] Success of matching was assessed by computing the standardized difference of each covariate with a cutoff of 0.1 to denote acceptable balance.[16] Early events were compared between the 2 cohorts using the McNemar test for binary outcomes and paired *t* test and the Wilcoxon signed rank test for normally and non-normally distributed continuous variables, respectively.

For long-term mortality and MACCE, a time to event analysis using Kaplan-Meier survival curves was conducted in the matched sample, using a stratified log-rank test (stratified on the matched pairs) to test the equality of the estimated survival curves.[17] In addition, HRs were estimated using a Cox proportional hazards model, which incorporated a robust sandwich-type variance estimator to account for the matched nature of the data.[18] For MI, stroke, and repeat revascularization, we estimated cumulative incidence functions to estimate the incidence of these events after accounting for death as a competing risk. In the matched sample, equality of cumulative incidence functions was assessed using a univariate Fine-Gray subdistribution hazard model in which the subdistribution hazard of the outcome was regressed on a single variable denoting treatment status, with

a robust variance estimator to account for the matched nature of the sample.[19]

For outcomes with <6 events per group, privacy legislation prevents the reporting of the actual number of events; as such, we instead report absolute risk differences between the PCI and CABG, which is compliant with Ontario privacy legislation. All curves were truncated to 7 years, given the small numbers at risk after that time point.

SECONDARY ANALYSIS. Our primary analysis excluded patients with ad hoc procedures, as these patients potentially represented a higher-risk cohort that required same day sitting left main PCI stenting. We performed a secondary analysis that compared outcomes in patients inclusive of those that underwent ad hoc PCI.

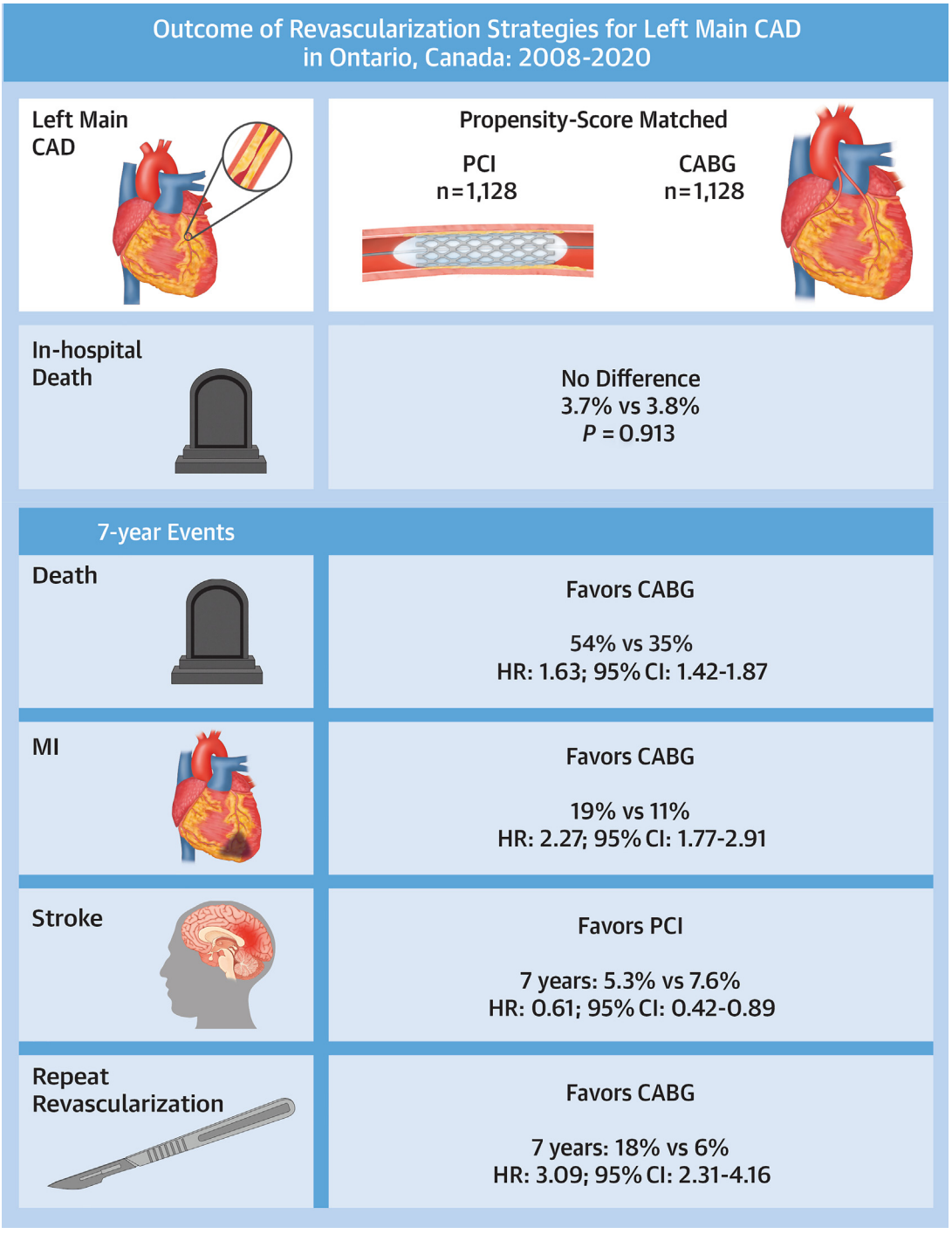
SENSITIVITY ANALYSES. In a series of sensitivity analyses, we excluded patients of higher periprocedural mortality risk for either PCI or CABG to ascertain the robustness of our primary outcome of long-term mortality after PS matching. Specifically, we excluded patients that underwent PCI after a cardiac surgery consult, as these patients might be considered possible surgical turndowns, those with an initial diagnosis of acute coronary syndrome (ie, non-STEMI or unstable angina), and those with severe renal disease requiring dialysis. Given procedural advancements in both PCI and CABG with time, we performed additional sensitivity analyses to account for the potential impact of year of procedure on our primary outcome by exact matching on the year of procedure in addition to matching on the PS. In addition, we tested for subgroup interactions between treatment assignment and era of procedure (early defined as 2008-2015 and late defined as 2016-2020) for the outcome of 30-day mortality. To determine the impact of index hospital type (hospitals with PCI and cath-only capabilities vs hospitals with CABG and PCI capabilities) where the patient underwent their angiogram, we tested for subgroup interaction between hospital type and treatment group. Finally, we performed a sensitivity analysis to determine the potential impact of unmeasured confounders on the association between the treatment and primary outcome as previously described by Lin et al.[20] In these sets of regression models, we adjusted the strength (ie, magnitude) of the unmeasured confounder and the prevalence of this unmeasured confounder in the 2 treatment groups, in addition to accounting for measured confounders to determine the "true exposure effect" of treatment allocation and its association with the primary outcome.[20,21] Robustness was inferred, when the lower limit of CI of the HR for the treatment group was >1, despite adjusting for all measured and potential unmeasured confounders.

Statistical significance was assumed for $P < 0.05$. The primary outcome was tested initially, while there was no adjustment for multiplicity for secondary or early outcomes. All analyses were conducted with SAS (version 9.4, SAS Institute).

RESULTS

PRIMARY MATCHED ANALYSIS. In total, there were 2,526 patients in the PCI group and 21,287 patients in the CABG group (Supplemental Figure 1, Supplemental Table 1), and after exclusion of patients with ad hoc PCI procedures, there were 1,299 PCI patients. Over the entire study, there was an annual increase in the proportion of patients with LMD undergoing left main PCI ($P < 0.05$) (**Figure 1**), with a concomitant decrease in the proportion of patients receiving CABG. The variation in the ratio of left main PCI relative to all revascularization (PCI+CABG for LMD) ranged from 2.2% to 17.4% across 20 institutions that were included in the registry (Supplemental Figure 2). Overall, there were significant differences in important baseline characteristics between the PCI and CABG subjects before propensity matching (**Table 1,** Supplemental Figure 3). Those who underwent PCI were older, more often were women, more likely presented with an ACS event, and had a higher burden of comorbidities but had fewer diseased coronary vessels. Patients who underwent ad hoc (same-sitting) PCI were younger and had fewer comorbidities than those who underwent non-ad hoc PCI (Supplemental Table 2)—however, early mortality in the ad hoc group was higher. Patients who underwent left main PCI were less likely to have had their index angiogram performed at a hospital that offered both PCI and CABG (ie, angiogram performed at cath ± PCI-only centers) compared with those who underwent CABG (68.4% vs 75.7%). PS matching on 25 baseline covariates (including year of procedure) yielded 1,128 pairs of patients (ie, 87% of PCI patients were matched to a CABG patient), who were well matched, with standardized mean differences <0.10 for all covariates (Supplemental Figure 3). Characteristics of patients in the CABG and PCI cohort who were unmatched are provided in Supplemental Table 3. CABG patients who were not included in the match were younger than those who were matched. Conversely, PCI patients who were not included in the match were older than those who were matched.

CENTRAL ILLUSTRATION **Summary of Key Study Findings**



Tam DY, et al. J Am Coll Cardiol Intv. 2023;16(3):277–288.

Summary of key study findings that showed no difference in in-hospital mortality between percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) in patients undergoing revascularization with left main disease. However, all-cause mortality was higher with PCI along with late acute myocardial infarction (MI) and late repeat revascularization. Late stroke was higher in the CABG group at 7 years. CAD = coronary artery disease.

TABLE 2 Early Outcomes Before and After Propensity Score Matching

	Before Propensity Score Matching			After Propensity Score Matching		
	PCI	CABG	*P* Value	PCI	CABG	*P* Value
Early death	70 (5.4)	484 (2.3)	<0.0001	62 (5.5)	44 (3.9)	0.075
In-hospital stroke	10 (0.8)	248 (1.2)	0.1932	8 (0.71)	14 (1.2)	0.201
In-hospital acute MI	31 (2.4)	195 (0.9)	<0.0001	31 (2.75)	13 (1.6)	0.007

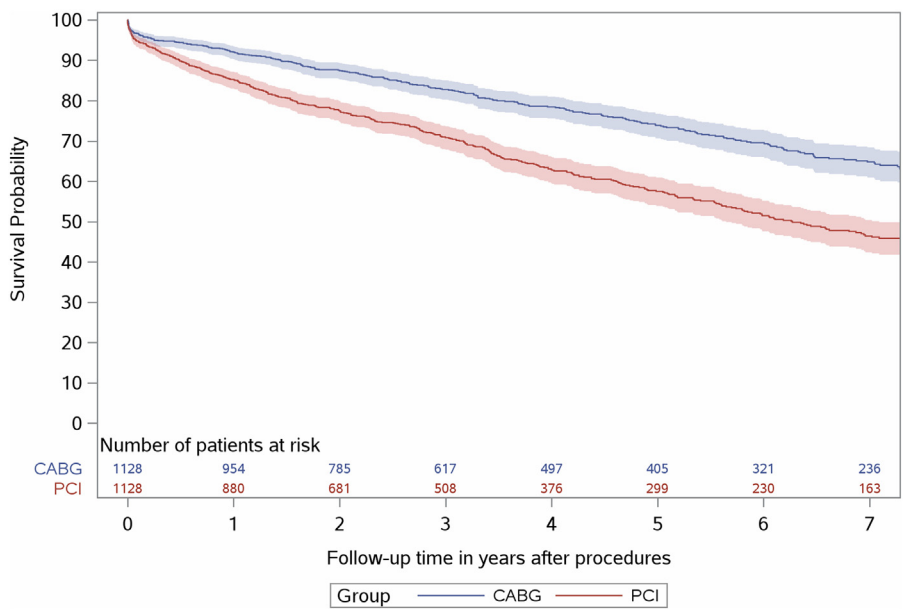
Values are n (%).
Abbreviations as in Table 1.

In the PS-matched patients, there was no difference in in-hospital death (3.7% vs 3.8%; $P = 0.913$) or early death (5.5% vs 3.9%; $P = 0.0750$) between the PCI and CABG groups (**Central Illustration**). There was a higher rate of new in-hospital MI in the PCI group compared with the CABG group (2.7% vs 1.2%; $P = 0.007$). The rate of new in-hospital stroke was similar between PCI and CABG (0.7% vs 1.2%; $P = 0.201$). Early outcomes before and after PS matching are provided in **Table 2**.

At 7-year follow-up (median of 5 [IQR: 2.4-8.2; maximum: 12.3] years), survival in the PS-matched cohorts was 46.4% for patients who underwent PCI and 64.8% for patients undergoing CABG surgery (HR: 1.63; 95% CI: 1.42-1.87; $P < 0.0001$) (**Figure 2**) over the entire follow-up period. Additionally, in long-term follow-up, freedom from MACCE was 33.2% in patients undergoing PCI and 51.3% in those undergoing CABG surgery 7 years (HR: 1.77; 95% CI: 1.57-2.00) (**Figure 3**) over the entire follow-up period ($P < 0.0001$). HR for outcomes before and after PS matching are provided in Supplemental Table 4.

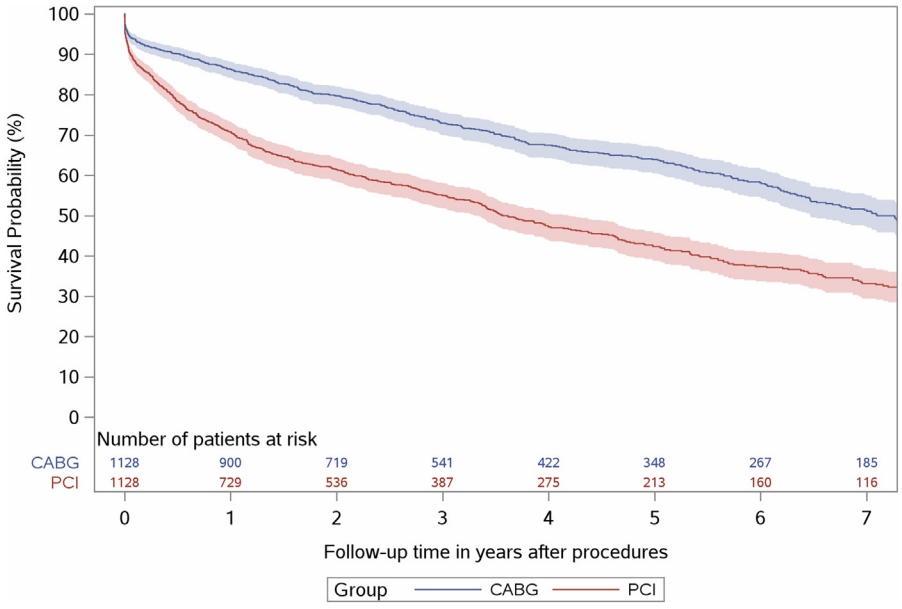
When the components of MACCE were analyzed separately, we found that the cumulative incidence of MI was 19.3% among those undergoing PCI compared with 10.6% after CABG (see Supplemental Figure 4). The subdistribution HR was 2.27 (95% CI: 1.77-2.91) indicating an increased risk of MI in the PCI group ($P < 0.0001$). Repeat revascularization occurred more frequently in the PCI group compared with CABG (18.4% vs 6.4%) (Supplemental Figure 5). The risk of repeat revascularization was higher in the PCI group (subdistribution HR: 3.09; 95% CI: 2.31-4.16; $P < 0.0001$). The details of the repeat revascularization procedures can be found in Supplemental Table 5. The cumulative incidence of stroke at 7 years was lower in PCI than CABG (5.3% vs 7.6%) (Supplemental Figure 6) with a subdistribution HR of 0.61 (95% CI: 0.42-0.89; $P < 0.001$) over the entire study period.

FIGURE 2 Freedom From All-Cause Mortality at 7 Years Between PCI and CABG



Survival was compared between PCI vs CABG after propensity score (PS) matching in patients with left main coronary disease (46.4% vs 64.8%; HR: 1.63; 95% CI: 1.42-1.87; $P < 0.001$). The **shaded region around the curve** represents the 95% CI. KM = Kaplan-Meier; other abbreviations as in Figure 1. CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention.

FIGURE 3 **Freedom From Major Adverse Cardiac and Cerebrovascular Events at 7 Years Between PCI and CABG**



Major adverse cardiac and cerebrovascular events was a composite of death, myocardial infarction, stroke, and repeat revascularization and compared between PCI vs CABG after PS matching in patients with left main coronary disease (33.2% vs 51.3%; HR: 1.77; 95% CI: 1.57-2.00; $P < 0.001$). The **shaded region around the curve** represents the 95% CI. Abbreviations as in Figures 1 and 2.

SENSITIVITY ANALYSIS. In the cohort of 2,526 patients with LMD undergoing PCI, only 518 (20.5%) patients were seen by a cardiac surgeon for consultation. These 518 patients were older and had more comorbidities compared with patients that underwent PCI without a cardiac surgical consult. After exclusion of patients who had pre-PCI cardiac surgical consultation and repeating the PS match, there were 1598 pairs of patients. Again, mortality was higher in the PCI group (HR: 1.59; 95% CI: 1.40-1.80) (Supplemental Figure 7). When patients with a diagnosis of acute coronary syndrome (ie, non-STEMI or unstable angina) were excluded, late mortality was higher in the PCI group (HR: 1.53; 95% CI: 1.25-1.89) (Supplemental Figure 8) in 727 pairs of well-matched patients. The interaction *P* value for acute coronary syndrome status and treatment group in a multivariable Cox regression model was not significant ($P = 0.14$) for late mortality; these findings supported the robustness of the primary analysis. Given that the use of PCI and CABG for LMD varied between institutions, we assessed the effects of variation in PCI/CABG use and found no difference in late mortality with increasing tertiles of proportion of CABG use and the treatment group in a multivariable Cox regression model (*P* for interaction = 0.362). Finally, in the analysis that included the entire cohort of same-sitting PCI and non-same-sitting PCI, late mortality was higher in the PCI group (HR: 1.66; 95% CI: 1.48-1.85) (Supplemental Figure 9) in 1,979 well-matched patient pairs. When accounting for the year of procedure, the findings of the primary outcome of late mortality continued to favor CABG (HR: 1.58; 95% CI: 1.37-1.82). In addition, there was no difference in 30-day mortality between the early era (HR: 1.34; 95% CI: 0.79-2.28) and late era (HR: 1.28; 95% CI: 0.69-2.38) when PCI was compared with CABG (*P* for interaction = 0.917). When we compared outcomes between hospitals without CABG (ie, PCI and cath-only hospitals) vs hospitals with CABG (PCI+CABG hospitals), we found that all-cause mortality remained higher with PCI in both groups (HR: 1.87 95% CI: 1.57-2.20; and HR: 1.49; 95% CI: 1.32-1.68, respectively). The interaction *P* value between hospital type and treatment was significant ($P = 0.022$), suggesting that all-cause mortality was higher in those that underwent PCI in non-CABG hospitals. Finally, in the sensitivity analysis to determine the impact of unmeasured confounders, in all scenarios (of differing prevalence and strength of an

unmeasured confounder), late mortality remained higher in PCI compared with CABG, although the magnitude of the true estimate varied (from an HR of 1.17 [95% CI: 1.02-1.34] to an HR of 1.60 [95% CI: 1.39-1.84]). Supplemental Table 6 contains all the true estimates based on varying prevalence and strength of this unmeasured confounder.

DISCUSSION

There were several important findings in this analysis. First, while CABG remained the preferred revascularization approach (CABG-to-PCI ratio of ~8:1), the utilization of left main PCI increased throughout the study period in Ontario. Second, left main PCI was used in patients who were older and who had more comorbidities. Although PS matching yielded 2 groups with similar baseline characteristics, the matched patients were considerably older and had more comorbidities compared with the unmatched CABG patients—suggesting that our comparison was performed in a higher-than-average-risk cohort (as compared with recent clinical trials). Our study found that CABG was associated with improved long-term survival and freedom from MACCE compared with PCI for LMD. These findings were consistent in secondary and sensitivity analyses that excluded patients with additional risk factors. While stroke occurred less frequently in the PCI arm compared with CABG over the entire study period, there was an increased incidence MI and repeated revascularization in the PCI group.

While the PCI vs CABG debate in LMD is well studied and has been the subject of 6 RCTs, management of LMD remains highly controversial. A particular area of debate includes the definition of periprocedural MI in RCTs. In EXCEL, a biochemical definition of MI was used rather than the Third Universal Definition of MI and repeated revascularization was removed as part of the composite outcome. Our analysis used a clinical definition for MI that relied on administrative codes obtained from discharge abstracts. Unlike the per-protocol definition for MI in EXCEL, we found that procedural MI was higher with PCI (2.8%) than CABG (1.6%). Consistent with our analysis, when the EXCEL investigators reanalyzed MI outcomes using the Third Universal Definition of MI, procedural MI was higher with PCI (3.3%) compared with CABG (1.4%).

More recently, a patient-level meta-analysis was published that included the 4 randomized controlled trials using drug-eluting stents and with at least 5 years of follow-up comparing PCI and CABG for LMD.[10] Compared with the Ontario patients, the pooled patients were generally of lower risk; they were younger (median age 66 years), had lower prevalence of diabetes (25.1%), and had lower incidence of reduced left ventricular ejection fraction (12.3%). All-cause mortality was similar between the 2 groups (HR: 1.10; 95% CI: 0.91-1.32) in the pooled frequentist analysis. However, using a Bayesian approach, the authors found that there was an 87.5% chance that a small increase in mortality may exist with PCI. However, the rate of spontaneous MI, procedural MI using the Universal definition, repeat revascularization, and composite outcomes that included the Universal definition were significantly higher in the PCI group than the CABG group, while stroke was reduced early after PCI, consistent with our results.

While several observational studies have examined CABG and PCI for unprotected LMD, most of these studies were small and noncontemporaneous.[22] Of the larger registry studies, Park et al[23] published 10-year outcomes from the MAIN-COMPARE (Revascularization for Unprotected Left Main Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty versus Surgical Revascularization) registry, a multicenter registry from Korea, and showed that PCI was associated with a higher risk for repeated revascularization at 10 years. A landmark analysis after 5 years showed an increased risk of all-cause mortality and major adverse cardiac events in 2,240 patients with LMD. Compared with our analysis, the population in the study by Park et al[23] were younger (mean age: 61.3-62.9 years), and as such, different long-term outcomes can be expected, with higher overall survival compared with our population of older patients. Previous work by Sibbald et al[24] examined outcomes from a large Ontario tertiary cardiac center and showed that PCI of unprotected LMD was traditionally reserved for very high-risk patients and initial in-hospital mortality was high (13.1%) from 2000 to 2011. Our study from 2008 to 2020 suggests that left main PCI utilization is increasing and being used in less high-risk patients with improvement in in-hospital mortality.

STUDY LIMITATIONS. We recognize that the despite the use of PS matching to account for known confounders, unmeasured or unknown confounders may still exist. Evidence of such unmeasured confounders is the higher early mortality that we observed in the PCI patients. To address these concerns, we conducted extensive sensitivity analyses to exclude

high-risk patient groups that may have preferentially undergone PCI (ie, surgical turndowns or acute coronary syndrome patients), and findings from our primary analysis were robust in these sensitivity analyses. Furthermore, a sensitivity analysis that adjusted for an unmeasured confounder over various prevalence and strength of this covariate showed that the findings from the primary analysis to be robust. The use of clinical and administrative datasets may lack data granularity, particularly around the details of coronary anatomy disease, which precludes knowledge around the exact lesion location, the SYNTAX score, and understanding the completeness of revascularization after the procedure. These details are pertinent, as PCI is only recommended in operable patients with low- to intermediate-risk SYNTAX scores, and completeness of revascularization may impact long-term clinical outcomes. Our analysis relied on administrative codes for the ascertainment of clinical outcomes and recognize that outcomes of stroke or MI may have different definitions under clinical trial settings. Also, our event rates were higher than those of recent trials in younger patients eligible for both modes of revascularization according to a Heart Team. While improvements in CABG (multiple arterial grafts, no-touch aortic techniques, and minimally invasive CABG) have been made, there have been substantial technical advancements in left main PCI (complex stenting techniques, use of adjunctive imaging such as intravascular ultrasound or optical coherence tomography) that will likely continue to improve outcomes for patients with LMD requiring revascularization. To address potential improvements with time, we adjusted for the year of procedure in our primary analysis and showed that findings were robust to support CABG for late mortality. In addition, there was no difference in 30-day mortality between an early and late era in our study.

CONCLUSIONS

CABG was associated with improved late outcomes compared with PCI for patients with LMD. Overlaid on existing published data, our findings suggest that CABG should be the preferred revascularization approach for LMD in those who are good surgical candidates.

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ADDRESS FOR CORRESPONDENCE: Dr Douglas S. Lee, Division of Cardiology, Peter Munk Cardiac Centre & University Health Network, ICES, G1 06, 2075 Bayview Avenue, Toronto, Ontario M4N 3M5, Canada. E-mail: dlee@ices.on.ca.

PERSPECTIVES

WHAT IS KNOWN? Clinical outcomes comparing PCI and CABG for LMD are conflicting in recent large clinical trials. Furthermore, effectiveness outside of the clinical trial setting has not been well described.

WHAT IS NEW? In this real-world observational propensity-matched cohort study of 1,128 pairs of patients undergoing PCI or CABG for LMD, CABG was associated with improved long-term survival and freedom from MACCE compared with PCI.

WHAT IS NEXT? Recent clinical trials provided outcomes to 5 years and as such longer-term follow-up studies are necessary to corroborate findings from observational studies with longer follow-up.

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KEY WORDS CABG, left main coronary disease, PCI, revascularization

APPENDIX For an expanded Methods section and supplemental tables and figures, please see the online version of this paper.