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ORIGINAL RESEARCH

CORONARY, PERIPHERAL, AND STRUCTURAL INTERVENTIONS

Mortality After Multivessel Revascularization in Patients With Diabetes and Acute Coronary Syndromes

Lucas C. Godoy, MD, PhD,[a,b,c,d] Michael E. Farkouh, MD, MSc,[a,e] Peter C. Austin, PhD,[b,c] Baiju R. Shah, MD, PhD,[b,c,f] Feng Qiu, MSc,[b] Maneesh Sud, MD,[b,c,f] Jose C. Nicolau, MD, PhD,[d] Stephen E. Fremes, MD, MSc,[c,f] Rodolfo V. Rocha, MD, PhD,[a] Derrick Y. Tam, MD, PhD,[c,e,f] Karin H. Humphries, DSc, MBA,[g] Patrick R. Lawler, MD, MPH,[h,i] Harindra C. Wijeysundera, MD, PhD,[b,c,f] Douglas S. Lee, MD, PhD,[a,b,c] Mario F.L. Gaudino, MD, PhD,[j] Dennis T. Ko, MD, MSc[b,c,f]

ABSTRACT

BACKGROUND The optimal revascularization strategy in patients with diabetes and multivessel disease in the setting of a non-ST-segment elevation myocardial infarction (NSTEMI) is unknown.

OBJECTIVES The purpose of this study was to compare all-cause mortality between coronary artery bypass grafting (CABG) and multivessel percutaneous coronary intervention (PCI) among patients with diabetes and NSTEMI.

METHODS All patients with diabetes and multivessel disease admitted for NSTEMI in Ontario, Canada, between April 2009 and March 2020 were included. Those with previous CABG, PCI in the previous 90 days, or shock were excluded. The primary outcome was all-cause mortality. Propensity score matching was used to account for confounding. Patients who had a cardiac surgeon consultation and then received PCI were classified as being potentially ineligible for CABG.

RESULTS The cohort included 4,649 CABG and 6,760 PCI patients (mean age: 67.8 ± 11.5 years; 70.4% males), resulting in 2,385 matched pairs. CABG was associated with reduced all-cause mortality compared to PCI over a median follow-up of 5.5 years (5-year estimates: 23.4% vs 26.5%; HR: 0.89; 95% CI: 0.80-0.98; $P = 0.021$). However, no significant differences in mortality were observed between CABG and PCI patients without a surgical consultation (2,130 pairs; HR: 0.97; 95% CI: 0.86-1.08), while CABG was associated with reduced mortality when compared against PCI patients who had received a surgical consultation (388 pairs; HR: 0.72; 95% CI: 0.58-0.88; $P = 0.002$).

CONCLUSIONS While CABG was associated with reduced all-cause mortality compared to multivessel PCI in patients with diabetes and NSTEMI, CABG benefit was seen only against PCI patients potentially ineligible for CABG after receiving a preprocedure surgical consultation. (JACC Adv. 2024;3:101203) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

From the [a]Peter Munk Cardiac Centre, University Health Network, Toronto, Ontario, Canada; [b]ICES, Toronto, Ontario, Canada; [c]Institute of Health Policy Management, and Evaluation, University of Toronto, Toronto, Ontario, Canada; [d]Instituto do Coracao (InCor), Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, Sao Paulo, Brazil; [e]Cedars-Sinai Health System, Los Angeles, California, USA; [f]Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada; [g]Faculty of Medicine, University of British Columbia, Vancouver, British Columbia, Canada; [h]McGill University Health Centre, McGill University, Montreal, Quebec, Canada; [i]Division of Cardiology and Interdepartmental Division of Critical Care Medicine, University of Toronto, Ontario, Canada; and the [j]Department of Cardiothoracic Surgery, Weill Cornell Medicine, New York, New York, USA.

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ABBREVIATIONS AND ACRONYMS

CABG = coronary artery bypass grafting

NSTEMI = non-ST-segment elevation myocardial infarction

PCI = percutaneous coronary intervention

Landmark clinical trials have demonstrated that coronary artery bypass grafting (CABG) reduces mortality and myocardial infarction compared to percutaneous coronary intervention (PCI) in patients with diabetes and chronic multivessel coronary artery disease.[1-4] In the setting of a non-ST-segment elevation myocardial infarction (NSTEMI), however, the optimal coronary revascularization modality remains uncertain.[5-8] Proponents of CABG suggest that data derived from the chronic coronary artery disease population could potentially be extended to the acute setting, as noted by clinical practice guidelines.[9,10] Indeed, the largest observational study to date included 2,947 patients with diabetes and acute coronary syndrome and found that CABG was associated with reductions of approximately 50% in the incidence of death and myocardial infarction compared with PCI in the short and long terms.[11]

Because decisions to proceed with surgical versus percutaneous revascularization for multivessel disease are often based on clinical information not captured in clinical registries, many PCI procedures might have been performed among patients deemed ineligible for CABG.[12] This concept is supported by an evaluation among 1,013 patients with surgical anatomy undergoing PCI in 2 academic centers in the United States, where 22% of the patients were deemed ineligible for CABG.[13] Frequent reasons for CABG ineligibility were advanced age, multimorbidity, and frailty, all factors associated with poor prognosis.[13-15] Observational studies comparing revascularization modalities are likely to place CABG ineligible patients in the PCI group, thereby artificially favoring CABG-associated outcomes.[16] In this study, we aimed to compare long-term all-cause mortality in patients with diabetes and multivessel coronary disease admitted for NSTEMI undergoing CABG or PCI according to suitability for CABG among PCI patients.

METHODS

DATA SOURCES. The Ontario Diabetes Database was used to identify patients with diabetes mellitus. This registry contains all individuals in Ontario with any type of non-gestational diabetes.[17-19] Information regarding the NSTEMI hospitalization, comorbidities, cardiovascular outcomes and procedures were collected from the Canadian Institute for Health Information-Discharge Abstract Database, the National Ambulatory Care Reporting System, and the Ontario Health Insurance Plan Physician Claims Database. These databases were linked to the CorHealth Ontario Cardiac Registry to identify patients who had coronary angiography and a revascularization procedure while hospitalized for a NSTEMI.[20,21] We utilized the ICES Physician Database to identify patients who were evaluated by a cardiac surgeon during the hospitalization. This database contains yearly information about all physicians in Ontario, including their main specialty.[22] All-cause mortality was captured from the Registered Persons Database, which provides basic demographics and date of death in Ontario.[23] Cardiovascular mortality was assessed from the Office of the Registrar General's Vital Statistics—Death, based on the underlying cause of death in the death certificate.[24] Additional databases are listed in the Supplemental Table 1. All data sets were linked using unique encoded identifiers and analyzed at ICES (formerly known as the Institute for Clinical Evaluative Sciences). The use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act and did not require review by a research ethics board.

STUDY POPULATION. The study cohort included all individuals over 18 years of age hospitalized with a NSTEMI in Ontario from April 1, 2009, to March 31, 2020. NSTEMI was identified by the International Classification of Diseases, Tenth Revision codes I21 or I22 (acute and subsequent myocardial infarction), excluding the code R94.30 (ST-segment elevation myocardial infarction).[25] Patients were included if they had a previous diagnosis of diabetes mellitus, a coronary angiography with multivessel coronary disease (defined as obstructions above 70% in the 3 main coronary arteries or in 2 coronary arteries including the left anterior descending artery), and underwent a coronary revascularization procedure while hospitalized for NSTEMI. Only the first admission was considered for those with multiple NSTEMI admissions during the study period. Patients with dementia, metastatic cancer, hemi/paraplegia, or residing in

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a long-term care facility were excluded to create a cohort similar to that of a clinical trial. Patients with previous CABG (at anytime), previous PCI, or an ST-segment elevation myocardial infarction in the previous 90 days were also excluded because they are less likely to be treated with CABG, as well as patients with hemodynamic instability or shock.

EXPOSURE ASSESSMENT. Patients were classified according to the revascularization procedure received while in hospital—PCI or CABG. In a prespecified analysis, we classified patients who had a cardiac surgeon consultation and then received PCI as being potentially ineligible or suboptimal for CABG.

OUTCOMES. The main outcome was all-cause mortality, assessed from the day of the revascularization procedure. Secondary outcomes included: 1) the composite of major adverse cardiovascular events (defined as the first occurrence of all-cause death, myocardial infarction, or stroke); 2) myocardial infarction; 3) stroke; 4) repeat revascularization (with either PCI or CABG); 5) cardiovascular death; and 6) noncardiovascular death. To identify staged procedures, PCIs performed within 90 days of an index PCI were not considered a repeat revascularization if they only treated lesions in different locations as of the index PCI. Patients were followed until March 31, 2021, except for the outcomes of cause-specific death, for which data were available until December 31, 2018.

STATISTICAL ANALYSIS. Demographics and clinical characteristics were compared between patients undergoing CABG and PCI using chi-squared and Student's *t*-tests, as appropriate.[26] A propensity score for the probability of undergoing CABG (vs PCI) was estimated using a logistic regression model that incorporated hospital-specific random effects to account for the clustering of patients in the hospital where the coronary angiography was performed.[27] The propensity score model was composed of 32 variables including demographics, comorbidities, cardiovascular, and laboratory test results (Supplemental Figure 1A). Patients were 1:1 matched on the logit of the propensity score using a greedy algorithm, without replacement, with a caliper width of 0.2 SDs of the logit of the propensity score.[28] Balance between CABG and PCI patients in the matched sample was assessed using standardized differences (values <0.1 taken as indicative of adequate balance).[29]

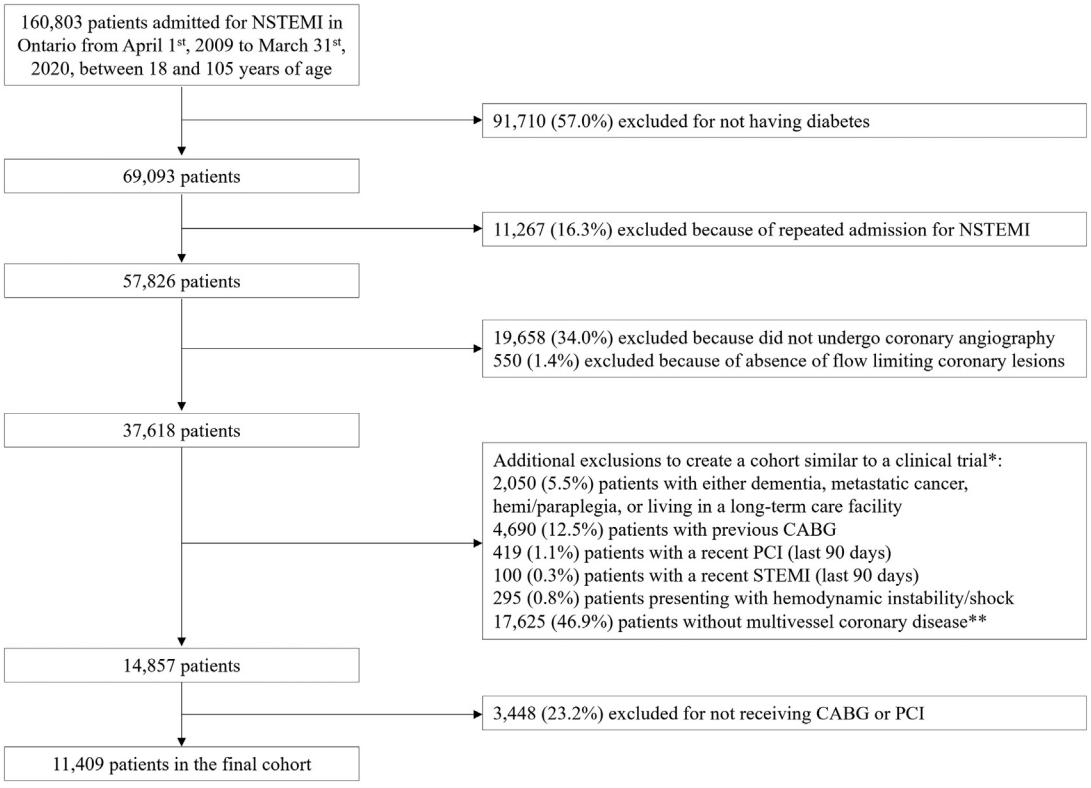
The association between coronary revascularization and the cardiovascular outcomes was assessed in the matched cohort using cause-specific HRs, estimated using univariate Cox proportional hazards models with a robust variance estimator.[30] Death was considered a competing risk for the nonfatal outcomes and cumulative incidence estimates were used to summarize all endpoints, with CIs of the absolute differences computed using 1,000 bootstrap resamples. Violations of the proportional hazards assumption were noted for some outcomes, including all-cause mortality (time-varying covariate effect, $P = 0.018$; Kolmogorov-Smirnov supremum test, $P = 0.013$; nonlinear pattern when using restricted cubic splines to model the HR as a function of time) (Supplemental Figure 2).[31,32] Accordingly, we reported cumulative incidence estimates at different time points.[33] Differences in the restricted mean survival times were also calculated for the primary and the composite outcomes over 8 years, with 95% CIs estimated using bootstrap resampling.[34] Differences in the restricted mean survival times can be interpreted as the difference in the number of event-free days experienced on average by patients from the CABG versus PCI groups from time zero until 8 years.[35] Treatment-interaction terms were used to perform subgroup analyses.

Two additional propensity score matched samples were created, using similar variables as in the previous model: 1) between CABG patients and PCI patients not evaluated by a cardiac surgeon before undergoing PCI; and 2) between CABG patients and PCI patients evaluated by a cardiac surgeon before undergoing PCI (Supplemental Figures 1B and 1C). As a sensitivity analysis, we evaluated the primary outcome of all-cause mortality between CABG and the subsets of PCI patients with and without a cardiac surgeon consultation in the same propensity score matched cohort used for the main analyses. A 2-sided P value of <0.05 was considered statistically significant in all comparisons. SAS EG version 7.15 (SAS Institute) was used to perform all statistical analyses.

RESULTS

STUDY COHORT. Between April 2009 and March 2020, 57,826 individuals between 18 and 105 years of age with diabetes were hospitalized for a NSTEMI in Ontario (**Figure 1**). Patients were then excluded due to previous CABG (12.5%), PCI, or ST-segment elevation myocardial infarction in the previous 90 days (1.1% and 0.3%, respectively), hemodynamic instability or shock (0.8%), absence of multivessel coronary disease (46.9%), or for not undergoing a coronary revascularization procedure (23.2% of the remaining patients). The final cohort comprised 11,409 patients.

FIGURE 1 Flow Diagram Illustrating the Cohort Formation



*Not mutually exclusive. **Defined as obstructions above 70% in the 3 main coronary arteries or in 2 coronary arteries including the left anterior descending artery. CABG = coronary artery bypass grafting; NSTEMI = non-ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

BASELINE CHARACTERISTICS BEFORE AND AFTER MATCHING ON THE PROPENSITY SCORE. Before matching, 4,649 (40.7%) patients underwent CABG and 6,760 (59.3%) underwent PCI. Compared to the PCI group, those who underwent CABG were more likely to be male (73.9% vs 67.9%) or have triple vessel disease (72.1% vs 41.6%). Propensity score-based matching resulted in 2,385 matched pairs (51.3% of the CABG patients were successfully matched), adequately balanced for all demographic characteristics, comorbidities, laboratory tests, and coronary lesions (**Table 1**).

ALL-CAUSE MORTALITY. The estimated HR comparing the rate of all-cause mortality between the CABG and PCI groups in the matched cohort was 0.89 (95% CI: 0.80-0.98; $P = 0.021$), over a median follow-up of 5.5 years (**Figure 2**). However, the proportional hazards assumption was not met. At 1 month, the cumulative incidence of all-cause mortality was 3.2% in the CABG group and 3.0% in the PCI group (absolute risk reduction favoring PCI: 0.2%; 95% CI: −0.7% to 1.3%). At 3 years, the mortality incidence was 14.2% in the CABG group and 17.6% in the PCI group (absolute risk reduction favoring CABG: −3.4%; 95% CI: −5.3% to −1.1%), while at 5 years it was 23.4% and 26.5%, respectively (absolute risk reduction favoring CABG: −3.1%; 95% CI: −5.0% to 0.5%) (Supplemental Table 2). In the restricted mean survival time analysis over 8 years, CABG was associated with a delay in death of 84.3 days (approximately 12 weeks; 95% CI: 18.3-128.1 days) compared with PCI. In the subgroup analyses, the association of CABG versus PCI in all-cause mortality was more pronounced in patients with left main disease or proximal left anterior descending artery disease, those diagnosed with diabetes more than 5 years ago, and patients with chronic heart failure or chronic kidney disease (Supplemental Figure 3A).

TABLE 1 Baseline Characteristics Before and After Propensity Score Matching, Comparing CABG Versus All PCI Patients

	Before Matching				After Matching		
	CABG (n = 4,649)	PCI (n = 6,760)	SD	*P* Value	CABG (n = 2,385)	PCI (n = 2,385)	SD
Demographics							
Age, y	66.76 ± 9.99	68.52 ± 12.34	0.156	<0.001	67.25 ± 10.69	67.21 ± 10.79	0.003
Male	3,436 (73.9%)	4,592 (67.9%)	0.132	<0.001	1,679 (70.4%)	1,692 (70.9%)	0.012
Rural dwelling	751 (16.2%)	923 (13.7%)	0.070	0.001	338 (14.2%)	341 (14.3%)	0.004
Income quintile				0.014			
1	1,098 (23.6%)	1,691 (25.0%)	0.033		587 (24.6%)	572 (24.0%)	0.015
5	721 (15.5%)	965 (14.3%)	0.035		357 (15.0%)	377 (15.8%)	0.023
Immigrant status				0.066			
Canadian born or long-term resident	3,962 (85.2%)	5,661 (83.7%)	0.041		1,991 (83.5%)	2,023 (84.8%)	0.037
Recent immigrant (≤5 y)	83 (1.8%)	117 (1.7%)	0.004		50 (2.1%)	43 (1.8%)	0.021
Non-recent immigrant	604 (13.0%)	982 (14.5%)	0.045		344 (14.4%)	319 (13.4%)	0.030
Ontario Marginalization Index	3.12 ± 0.77	3.20 ± 0.77	0.105	<0.001	3.16 ± 0.77	3.16 ± 0.77	0.001
Diabetes-related variables							
Recent diagnosis of diabetes (<5 y)	1,206 (25.9%)	2,012 (29.8%)	0.085	<0.001	649 (27.2%)	691 (29.0%)	0.039
Insulin use	1,362 (29.3%)	1,752 (25.9%)	0.076	<0.001	673 (28.2%)	637 (26.7%)	0.034
Other hypoglycemic drugs	2,632 (56.6%)	3,536 (52.3%)	0.087	<0.001	1,310 (54.9%)	1,301 (54.5%)	0.008
Cardiovascular comorbidities							
Hypertension	3,634 (78.2%)	5,396 (79.8%)	0.041	0.033	1,903 (79.8%)	1,895 (79.5%)	0.008
Dyslipidemia	1,911 (41.1%)	3,018 (44.6%)	0.072	<0.001	1,020 (42.8%)	1,014 (42.5%)	0.005
Smoking				0.037			
Never	2,024 (43.5%)	3,089 (45.7%)	0.043		1,077 (45.2%)	1,058 (44.4%)	0.016
Current	1,020 (21.9%)	1,433 (21.2%)	0.018		528 (22.1%)	546 (22.9%)	0.018
Former	1,389 (29.9%)	1,890 (28.0%)	0.042		667 (28.0%)	667 (28.0%)	0
Atrial fibrillation	270 (5.8%)	660 (9.8%)	0.148	<0.001	162 (6.8%)	173 (7.3%)	0.018
Heart failure	1,400 (30.1%)	2,156 (31.9%)	0.038	0.044	728 (30.5%)	730 (30.6%)	0.002
Peripheral artery disease	579 (12.5%)	883 (13.1%)	0.018	0.340	312 (13.1%)	314 (13.2%)	0.002
Cerebrovascular disease	123 (2.6%)	225 (3.3%)	0.040	0.037	74 (3.1%)	66 (2.8%)	0.020
Carotid endarterectomy or stent	38 (0.8%)	39 (0.6%)	0.029	0.123	20 (0.8%)	14 (0.6%)	0.030
Previous myocardial infarction	166 (3.6%)	320 (4.7%)	0.058	0.003	91 (3.8%)	96 (4.0%)	0.011
Previous PCI	545 (11.7%)	1,355 (20.0%)	0.229	<0.001	338 (14.2%)	341 (14.3%)	0.004
Clinical comorbidities							
Chronic kidney disease	690 (14.8%)	1,275 (18.9%)	0.108	<0.001	407 (17.1%)	415 (17.4%)	0.009
Chronic kidney disease on dialysis	165 (3.5%)	272 (4.0%)	0.025	0.194	100 (4.2%)	91 (3.8%)	0.019
COPD	922 (19.8%)	1,671 (24.7%)	0.118	<0.001	520 (21.8%)	530 (22.2%)	0.010
Liver disease	25 (0.5%)	64 (0.9%)	0.048	0.015	20 (0.8%)	17 (0.7%)	0.014
Cancer	163 (3.5%)	270 (4.0%)	0.026	0.180	92 (3.9%)	97 (4.1%)	0.011
Frailty score*	1.18 ± 2.85	1.83 ± 3.76	0.194	<0.001	1.43 ± 3.29	1.53 ± 3.42	0.031
NSTEMI presentation							
Ischemic changes on ECG				<0.001			
Absent	2,110 (45.4%)	3,349 (49.5%)	0.083		1,129 (47.3%)	1,131 (47.4%)	0.002
Persistent (fixed)	1,356 (29.2%)	1,883 (27.9%)	0.029		700 (29.4%)	678 (28.4%)	0.020
Transient without pain	96 (2.1%)	130 (1.9%)	0.061		45 (1.9%)	52 (2.2%)	0.025
Transient with pain	420 (9.0%)	498 (7.4%)	0.010		174 (7.3%)	190 (8.0%)	0.021
Left ventricular ejection fraction				<0.001			
<20%	85 (1.8%)	167 (2.5%)	0.044		49 (2.1%)	45 (1.9%)	0.012
20%-34%	562 (12.1%)	685 (10.1%)	0.062		267 (11.2%)	262 (11.0%)	0.007
35%-49%	1,223 (26.3%)	1,617 (23.9%)	0.055		611 (25.6%)	610 (25.6%)	0.001
≥50%	2,152 (46.3%)	2,857 (42.3%)	0.081		1,087 (45.6%)	1,088 (45.6%)	0.001
Left main disease	1,217 (26.2%)	479 (7.1%)	0.530	<0.001	399 (16.7%)	340 (14.3%)	0.068
Proximal left anterior descending	2,501 (53.8%)	2,811 (41.6%)	0.246	<0.001	1,191 (49.9%)	1,206 (50.6%)	0.013
Triple vessel disease	3,350 (72.1%)	2,813 (41.6%)	0.646	<0.001	1,415 (59.3%)	1,320 (55.3%)	0.081
Laboratory tests							
Glomerular filtration rate, mL/min/1.73 m^2	69.97 ± 25.82	66.91 ± 26.49	0.117	<0.001	68.26 ± 26.45	69.31 ± 25.88	0.040
HbA1c, %	7.64 ± 1.64	7.51 ± 1.59	0.085	0.001	7.60 ± 1.61	7.56 ± 1.56	0.022
HbA1c ≥ 7%	1,988 (42.8%)	2,732 (40.4%)	0.048	0.006	1,000 (41.9%)	981 (41.1%)	0.016
LDL-C, mg/dL	89.76 ± 41.11	88.93 ± 40.72	0.020	0.393	89.40 ± 41.38	88.74 ± 40.62	0.016

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TABLE 1 Continued

	Before Matching				After Matching		
	CABG (n = 4,649)	PCI (n = 6,760)	SD	*P* Value	CABG (n = 2,385)	PCI (n = 2,385)	SD
Procedure-related characteristics							
Completeness of revascularization	4,227 (90.9%)	3,065 (45.3%)	1.122	<0.001	1,989 (83.4%)	1,929 (80.9%)	0.066
Isolated CABG	4,360 (93.8%)	-			2,233 (93.6%)	-	
Off-pump surgery	811 (17.4%)	-			466 (19.5%)	-	
Number of grafts	3.39 ± 0.98	-			3.18 ± 1.01	-	
At least 1 arterial graft	4,439 (95.5%)	-			2,242 (94.0%)	-	
Cardiac surgeon evaluation before PCI	-	411 (6.1%)			-	298 (12.5%)	
Radial access	-	4,018 (59.4%)			-	1,361 (57.1%)	
Number of stents	-	2.05 ± 1.15			-	2.38 ± 1.31	
Mean total stent length	-	42.79 ± 26.83			-	49.92 ± 30.53	
Stent types							
Bare metal stent	-	1,268 (18.8%)			-	403 (16.9%)	
Everolimus	-	3,732 (55.2%)			-	1,455 (61.0%)	
Zotarolimus	-	1,299 (19.2%)			-	434 (18.2%)	
Sirolimus	-	145 (2.1%)			-	57 (2.4%)	
Paclitaxel	-	73 (1.1%)			-	29 (1.2%)	
Other drug-eluting stents	-	523 (7.7%)			-	210 (8.8%)	

Values are mean ± SD or n (%). *The Hospital Frailty Risk Score was calculated as per the UK National Health Service algorithm.[26] Percentage of missing observations: glomerular filtration rate: 18.1%; HbA1c: 27.2%; income quintile: 0.4%; ischemic changes on ECG: 13.7%; LDL-C: 36.8%; left ventricular ejection fraction: 18.1%; bypass grafts: 1.2%; rural dwelling: 0.2%; smoking: 4.9%; stent length: 3.8%; stent number and type: 3.7%.

CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease; HbA1c = glycated hemoglobin A1c; ECG = electrocardiogram; LDL-C = low-density lipoprotein cholesterol; NSTEMI = non-ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention.

CARDIOVASCULAR OUTCOMES. CABG was associated with a 19% reduction in the rate of the composite of major adverse cardiovascular events as compared to PCI (HR: 0.81; 95% CI: 0.74-0.88; $P < 0.001$) (Table 2). Over 8 years, on average, a major cardiovascular event could be delayed by 165.7 days (approximately 24 weeks; 95% CI: 90.9-222.3 days) among those who underwent CABG versus PCI. Compared to PCI, CABG was also associated with reduced rates of myocardial infarction (HR: 0.44; 95% CI: 0.37-0.52; $P < 0.001$) and repeat revascularization (HR: 0.31; 95% CI: 0.26-0.37; $P < 0.001$) and increased rates of stroke (HR: 1.54; 95% CI: 1.19-1.99; $P = 0.001$). The reduction in all-cause mortality associated with CABG was driven by reductions in cardiovascular mortality (HR: 0.74; 95% CI: 0.61-0.89; $P = 0.002$), while no differences were observed in noncardiovascular mortality between CABG and PCI patients (HR: 1.00; 95% CI: 0.84-1.20).

RECEIPT OF A CARDIAC SURGEON CONSULTATION. Before propensity score matching, there were 6,349 (93.9%) PCI patients who did not receive a cardiac surgeon consultation before undergoing PCI, resulting in 2,130 matched pairs with CABG patients (Supplemental Table 3). CABG-associated mortality rates were not significantly different from mortality rates of PCI patients without a cardiac surgeon consultation (5-year estimates: 23.2% versus 23.8%, respectively; HR over the entire follow-up: 0.97; 95% CI: 0.86-1.08), while a 16% decrease in major adverse cardiovascular events was observed favoring CABG (5-year estimates: 31.1% vs 36.5%; HR for the entire follow-up: 0.84; 95% CI: 0.76-0.93; $P = 0.001$), driven by reductions in myocardial infarction (Table 3).

Before propensity score matching, there were 411 (6.1%) PCI patients who received a cardiac surgeon consultation before undergoing PCI. Compared to CABG patients, PCI patients with a cardiac surgery consultation were older (mean age: 70.1 ± 10.8 years vs 66.8 ± 10.0 years), more likely to be females (36.7% vs 26.1%), have heart failure (51.6% vs 30.1%) or chronic kidney disease (27.3% vs 14.8%) (Supplemental Table 4). Propensity score-based matching resulted in 388 matched pairs between PCI patients with a cardiac surgeon consultation and CABG patients, adequately balanced for all baseline characteristics (except the lower level of income quintile). Compared to PCI patients with a cardiac surgeon consultation, CABG was associated with marked reductions both in all-cause mortality (5-year estimates: 37.8% vs 47.1%; HR for the entire follow-up: 0.72; 95% CI: 0.58-0.88; $P = 0.002$) and major adverse cardiovascular events (5-year estimates:

44.7% vs 56.8%; HR for the entire follow-up: 0.68; 95% CI: 0.56-0.82; $P < 0.001$) (**Table 3**). Subgroup analyses are presented in the Supplemental Figure 3B and 3C. Similar results were obtained in a sensitivity analysis of all-cause mortality conducted in the same matched population utilized in the primary analyses (Supplemental Figure 4).

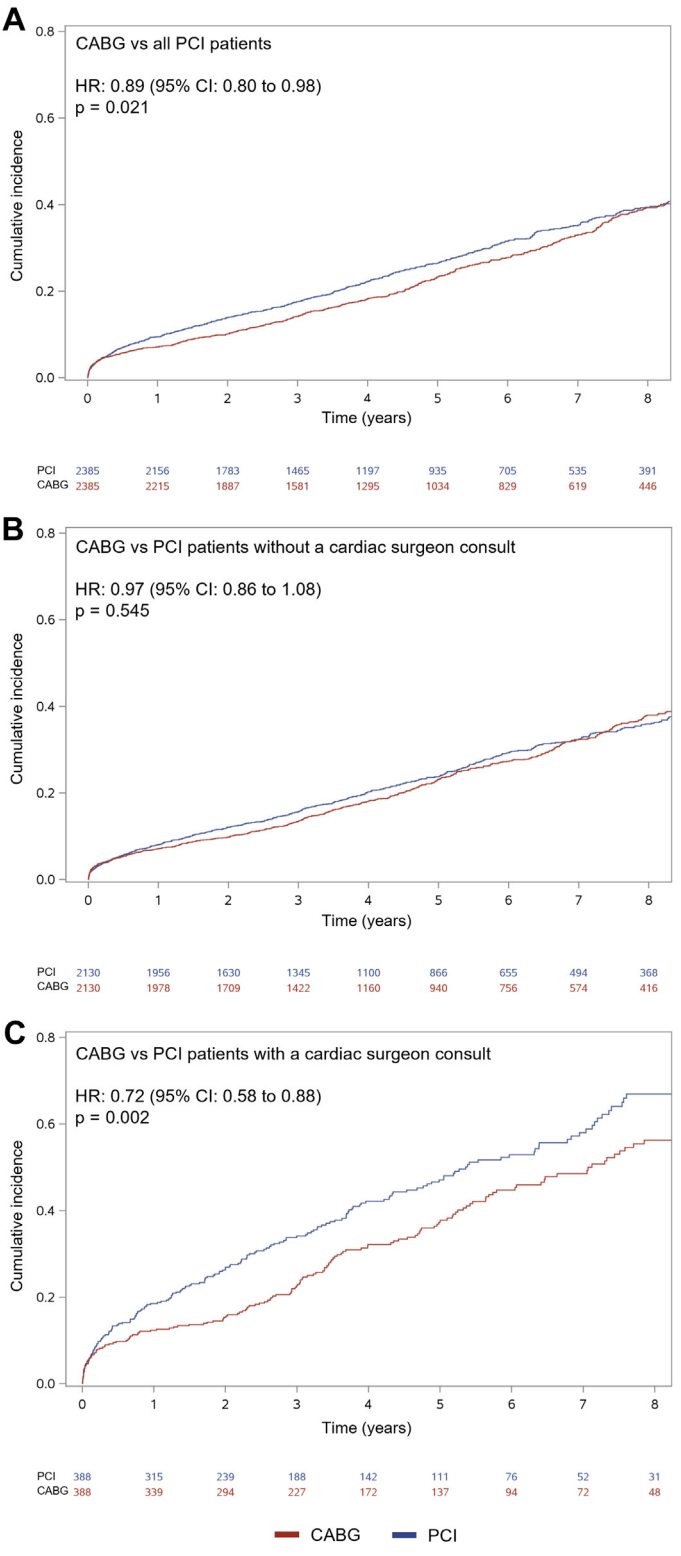
DISCUSSION

In this cohort study of NSTEMI patients with diabetes and multivessel disease, CABG was associated with an 11% relative reduction in the rate of all-cause mortality and 19% reduction in the rate of major adverse cardiovascular events compared to PCI over a median follow-up of 5.5 years. However, approximately 6% of the PCI patients received a cardiac surgeon consultation before undergoing PCI, which might be a marker of CABG ineligibility. When excluding these patients, the benefit of CABG versus PCI was attenuated, and all-cause mortality was no longer significantly different between the groups (**Central Illustration**).

In patients with diabetes and chronic multivessel coronary disease, the FREEDOM (Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease) trial demonstrated that CABG, compared to PCI, reduces long-term cardiovascular events, including all-cause mortality, myocardial infarction, and repeat revascularization.[1,2,36] Given the lack of dedicated trials in patients with diabetes and NSTEMI, both the American and European guidelines recommend an individualized approach for coronary revascularization in these patients, taking into account the evidence in the chronic coronary disease setting and the heart team recommendations.[9,10] The current study shows that CABG is associated with reductions in all-cause and cardiovascular mortality, myocardial infarction, and repeat revascularization in patients with diabetes and NSTEMI, potentially broadening the conclusions of the FREEDOM trial to this high-risk population. As in FREEDOM, we also reported that CABG was associated with increased rates of stroke compared to PCI.[1,37] This study indicates that CABG may delay the occurrence of death compared to PCI by 12 weeks on average over a follow-up of 8 years. Benefits and risks associated with CABG compared to PCI need to be put into context by patients and clinicians when making individual decisions on the optimal revascularization strategy.[38,39]

Our study extends findings of previous smaller observational analyses by evaluating the impact that patients who received a cardiac surgery consultation

FIGURE 2 All-Cause Mortality Between CABG and PCI



Plots were generated in 3 different propensity score-matched populations. (A) Event risks in patients undergoing CABG vs all PCI patients. (B) Event risks in patients undergoing CABG vs PCI patients without a cardiac surgeon consultation. (C) Event risks in patients undergoing CABG vs PCI patients with a cardiac surgeon consultation (potentially ineligible for CABG). Abbreviations as in **Figure 1**.

TABLE 2 Primary and Secondary Outcomes After Propensity Score Matching Between CABG and PCI Patients

	CABG, %[a] (n = 2,385)	PCI, %[a] (n = 2,385)	Absolute Risk Reduction at 5 Years, % (95% CI)[b]	HR (95% CI)[c]	*P* Value
Primary outcome					
All-cause death	23.4	26.5	−3.1 (−5.0 to 0.5)	0.89 (0.80-0.98)	0.021
Secondary outcomes					
MACE[d]	32.1	39.0	−6.9 (−9.2 to −3.2)	0.81 (0.74-0.88)	<0.001
Myocardial infarction	7.6	16.7	−9.1 (−11.0 to −6.9)	0.44 (0.37-0.52)	<0.001
Stroke	5.5	3.5	2.0 (0.8-3.7)	1.54 (1.19-1.99)	0.001
Repeat revascularization	7.3	20.9	−13.6 (−15.3 to −10.9)	0.31 (0.26-0.37)	<0.001
Cardiovascular death[e]	10.1	13.5	−3.4 (−5.5 to −0.6)	0.74 (0.61-0.89)	0.002
Non-cardiovascular death[e]	14.0	13.9	0.1 (−2.5 to 3.0)	1.00 (0.84-1.20)	0.968

[a]Cumulative incidence function estimates in the matched cohort at 5 y. [b]Absolute risk reductions were calculated from the cumulative incidence estimates, with 95% CI generated in 1,000 bootstrap resamples. Negative values favor CABG, while positive values favor PCI. [c]HRs were estimated from cause-specific proportional hazards models. The proportional hazards assumption was not met for the outcomes of all-cause death, myocardial infarction, stroke, and MACE. Accordingly, absolute event rates at different time points are reported in the Supplementary Appendix. [d]MACE was defined as the first occurrence of the composite of all-cause death, myocardial infarction, or stroke. [e]For patients enrolled up to December 31, 2018 (n = 4,038).

MACE = major adverse cardiovascular event; other abbreviations as in Table 1.

could have on the comparative effectiveness of CABG versus PCI.[11,40,41] We observed that all-cause mortality did not differ between CABG patients and PCI patients not evaluated by a cardiac surgeon before undergoing PCI, while there was a significant survival difference favoring CABG when compared against PCI patients evaluated by a cardiac surgeon. A previous study reported that, among patients with diabetes and predominantly stable multivessel coronary disease, CABG was associated with reductions in all-cause mortality even when compared against PCI patients not evaluated by surgeons.[42] Differences in patient's baseline risks and physician's referral patterns for surgical consultations between the acute

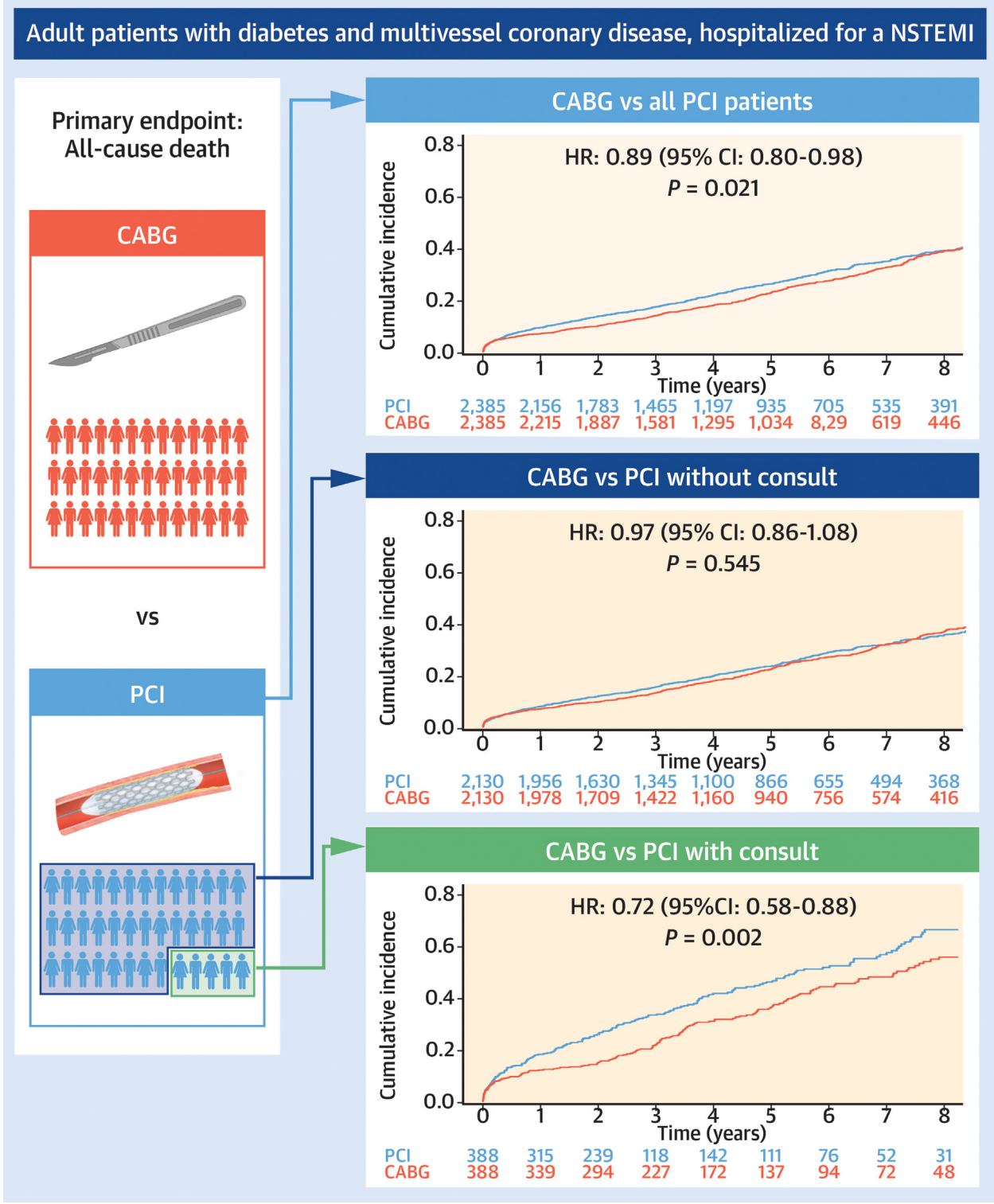
TABLE 3 Primary and Secondary Outcomes After Propensity Score Matching Between CABG and PCI Patients Without and With a Cardiac Surgeon Consultation

	CABG, %[a]	PCI, %[a]	Absolute Risk Reduction at 5 Years, % (95% CI)[b]	HR (95% CI)[c]	*P* Value
CABG vs PCI without a cardiac surgeon consultation (2,130 pairs)					
All-cause death	23.2	23.8	−0.6 (−2.8 to 2.8)	0.97 (0.86-1.08)	0.545
MACE[d]	31.1	36.5	−5.4 (−7.4 to −0.8)	0.84 (0.76-0.93)	0.001
Myocardial infarction	7.6	15.8	−8.2 (−10.5 to −6.3)	0.47 (0.39-0.57)	<0.001
Stroke	4.9	3.7	1.2 (0.6-3.5)	1.46 (1.11-1.92)	0.007
Repeat revascularization	8.0	20.2	−12.2 (−14.5 to −10.0)	0.37 (0.31-0.44)	<0.001
Cardiovascular death[e]	10.3	11.7	−1.4 (−3.9 to 1.1)	0.89 (0.73-1.09)	0.264
Noncardiovascular death[e]	12.8	13.7	−0.9 (−1.7 to 3.8)	0.95 (0.79-1.15)	0.595
CABG vs PCI with a cardiac surgeon consultation (388 pairs)					
All-cause death	37.8	47.1	−9.3 (−21.5 to −6.3)	0.72 (0.58-0.88)	0.002
MACE[d]	44.7	56.8	−12.1 (−23.1 to −6.9)	0.68 (0.56-0.82)	<0.001
Myocardial infarction	8.6	20.3	−11.7 (−16.9 to −6.6)	0.39 (0.27-0.56)	<0.001
Stroke	6.1	3.4	2.7 (0.0-7.2)	1.34 (0.68-2.63)	0.396
Repeat revascularization	8.4	28.2	−19.8 (−27.3 to −15.7)	0.24 (0.16-0.35)	<0.001
Cardiovascular death[f]	18.2	26.9	−8.7 (−17.9 to −3.1)	0.60 (0.42-0.85)	0.004
Noncardiovascular death[f]	21.2	23.2	−2.0 (−13.2 to 2.8)	0.86 (0.61-1.22)	0.407

[a]Cumulative incidence function estimates in the matched cohorts at 5 y. [b]Absolute risk reductions were calculated from the cumulative incidence estimates, with 95% CI generated in 1,000 bootstrap resamples. Negative values favor CABG, while positive values favor PCI. [c]HRs were estimated from cause-specific proportional hazards models (the proportional hazards assumption was satisfied for all outcomes). [d]MACE was defined as the first occurrence of the composite of all-cause death, myocardial infarction, or stroke. [e]For patients enrolled up to December 31, 2018 (n = 3,611). [f]For patients enrolled up to December 31, 2018 (n = 656).

Abbreviations as in Tables 1 and 2.

CENTRAL ILLUSTRATION Summary of the Main Study Results



Godoy LC, et al. JACC Adv. 2024;3(9):101203.

While CABG was associated with reduced long-term all-cause mortality compared to multivessel PCI in patients with diabetes and NSTEMI (upper plot), CABG benefit was seen only against PCI patients potentially ineligible for CABG After receiving a preprocedure surgical consultation (bottom plot). When comparing CABG vs PCI patients who did not receive a surgical consultation, no significant difference was found between these 2 strategies (central plot). Abbreviations as in **Figure 1**.

and chronic coronary disease settings might partially explain the reasons for the distinct conclusions in the 2 studies.[42] In our study, not all patients who had a cardiac surgeon consultation and then received PCI necessarily represent a surgical turndown. Likewise, consultations might be under-captured, since surgeons can also provide an informal patient evaluation or case discussion without billing. Patients who received a cardiac surgeon consultation represented only 6% of the PCI population and, nevertheless, excluding these patients was enough to essentially eliminate the mortality benefit of CABG following NSTEMI.

The current study highlights the fact that even when considering a large number of possible confounders, differences in patients treated with CABG and PCI in real-world observational studies remain, which may lead to confounding biases that cannot be fully addressed by adjustment methods.[12,43] Most landmark trials in coronary revascularization would only enroll patients after the heart team evaluation, which would likely exclude randomization of surgical turndowns.[1,44-46] In real-world studies, however, these patients are usually included as part of the PCI group and our results suggest that this practice can increase the event rates associated with PCI. Interestingly, in the AWESOME (Angina With Extremely Serious Operative Mortality Evaluation) trial, patients with unstable angina considered at high risk for CABG were randomized to either CABG or PCI and overall mortality at 3 years was numerically higher in the CABG group, including in patients with diabetes.[47]

This study has some potential limitations. As is the case of most nonrandomized studies, unmeasured confounders might influence the effect estimates reported herein, which is further highlighted by the analysis according to cardiac surgeon consultation. Still, we accounted for a large number of possible confounders when estimating the propensity score model and achieved adequate balance of all measured covariates. This study included patients starting from 2009, and changes in clinical practice patterns over the years might have impacted the results (for example, approximately 17% of the PCI patients were treated with bare metal stents). We believe that PCI patients who had cardiac surgeon consultations and received PCI were deemed ineligible for surgery or were suboptimal candidates, which was supported by their high burden of comorbid illness. Yet, we did not have exact information on why they received PCI. Finally, the results of the current study are not generalizable to all patients with diabetes and NSTEMI, but rather to those more likely to be suitable to both CABG and PCI (as suggested by a matching rate of only 51% of the CABG patients). Patients revascularized after hospital discharge or those managed medically were not included in this study, which needs to be taken into account at the time of clinical decision-making.

CONCLUSIONS

While we observed that CABG is associated with reduced long-term all-cause mortality compared to multivessel PCI in patients with diabetes and NSTEMI, CABG benefit was seen only against PCI patients potentially ineligible for CABG after referral for a preprocedure surgical consultation. Randomized clinical trials comparing revascularization strategies among patients with diabetes and multivessel coronary disease in the acute setting are warranted in patients deemed eligible for both CABG and PCI through a heart team approach.

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ADDRESS FOR CORRESPONDENCE: Dr Dennis T. Ko, ICES, 2075 Bayview Avenue, G106, Toronto, Ontario M4N 3M5, Canada. E-mail: dennis.ko@ices.on.ca.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: CABG is associated with reduced long-term all-cause mortality compared to multivessel PCI in patients with diabetes and NSTEMI. However, CABG benefit was seen only against PCI patients potentially ineligible for CABG after referral for a preprocedure surgical consultation.

TRANSLATIONAL OUTLOOK: Randomized clinical trials comparing revascularization strategies among patients with diabetes and multivessel coronary disease in the acute setting are warranted in patients deemed eligible for both CABG and PCI through a heart team approach.

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KEY WORDS acute coronary syndrome, coronary artery bypass grafting, coronary revascularization, diabetes, percutaneous coronary intervention

APPENDIX For supplemental tables and a figure, please see the online version of this paper.

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