Percutaneous coronary intervention versus coronary artery bypass grafting in patients with reduced ejection fraction

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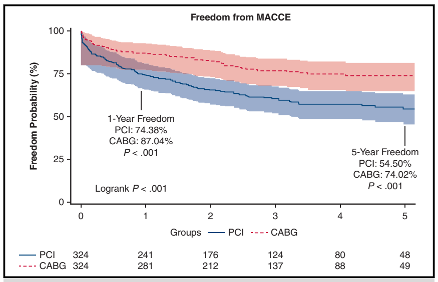
ABSTRACT

Objective: The aim of this study was to evaluate comparative outcomes for percutaneous coronary intervention (PCI) versus coronary artery bypass grafting (CABG) in patients with reduced ejection fraction.

Methods: All patients from the University of Pittsburgh Medical Center from 2011 to 2018 who had reduced preoperative ejection fraction (<50%) and underwent CABG or PCI for coronary revascularization were included in this study. Patients were risk-adjusted with propensity matching (1:1) and primary outcomes included long-term survival, readmission, and major adverse cardiac and cerebrovascular events (MACCE).

Results: A total of 2000 patients were included in the current study, consisting of CABG (n = 1553) and PCI (n = 447) cohorts with a mean ejection fraction of 35% ± 9.53%. Propensity matching yielded a 1:1 match with 324 patients in each cohort, controlling for all baseline characteristics. Thirty-day mortality was similar for PCI versus CABG (6.2% vs 4.9%; *P* = .49). Overall mortality over the study follow-up period (median, 3.23 years; range, 1.83-4.98 years) was significantly higher for the PCI cohort (37.4% vs 21.3%; *P* < .001). Total hospital readmissions (24.1% vs 12.9%; *P* = .001), cardiac readmissions (20.4% vs 11.1%; *P* = .001), myocardial infarction event (7.7% vs 1.8%; *P* = .001), MACCE (41.4% vs 23.8%; *P* < .001), and repeat revascularization (6.5% vs 2.6%; *P* = .02) occurred more frequently in the PCI cohort. Freedom from MACCE at 1 year (74.4% vs 87.0%; *P* < .001) and 5 years (54.5% vs 74.0%; *P* < .001) was significantly lower for the PCI cohort. On multivariable cox regression analysis, CABG (hazard ratio, 0.57; 95% confidence interval, 0.44-0.73; *P* < .001) was significantly associated with improved survival. Prior liver disease, dialysis, diabetes, and peripheral artery disease were the most significant predictors of mortality. The cumulative incidence of hospital readmission was lower for the CABG cohort (hazard ratio, 0.51; 95% confidence interval, 0.37-0.71; *P* < .001). Multivariable cox regression for MACCE (hazard ratio, 0.48; 95% confidence interval, 0.39-0.58; *P* < .001) showed significantly fewer events for the CABG cohort.

Conclusions: Patients with reduced ejection fraction who underwent CABG had significantly improved survival, lower MACCE, and fewer repeat revascularization procedures compared with patients who underwent PCI. (J Thorac Cardiovasc Surg 2021;161:1022-31)



CABG patients have greater freedom from long-term MACCE compared with PCI patients.

CENTRAL MESSAGE

Patients with coronary artery disease and reduced ejection fraction who undergo CABG have improved long-term outcomes compared with patients who undergo PCI.

PERSPECTIVE

There is a known increased risk for surgical revascularization of patients with coronary artery disease. Options for revascularization include PCI or CABG and controversy exists as to which treatment is more efficacious. The current study indicates that patients with reduced ejection fraction who undergo CABG may have better long-term survival, fewer readmissions, and less need for repeat revascularizations.

See Commentaries on pages 1032 and 1033.

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Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
CIF	= cumulative incidence function
EF	= ejection fraction
MACCE	= major adverse cardiac and cerebrovascular events
MI	= myocardial infarction
PCI	= percutaneous coronary intervention
SMD	= standardized mean difference

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Patients with coronary artery disease and reduced left ventricular ejection fraction (EF) pose a unique challenge to clinicians, with definitive treatment options limited to percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). Previous randomized controlled trials have established improved outcomes for surgical revascularization in patients with impaired left ventricular function[1,2] and contemporary guidelines recommend CABG as the preferred management of patients with coronary artery disease and reduced left ventricular EF.[3,4] Despite prevailing recommendations for surgical revascularization, controversy still exists over whether CABG or PCI is the appropriate treatment for patients with coronary artery disease with low EF. Relatively limited literature exists on the topic, with some recent reports favoring CABG as the preferred treatment for this patient population. Recent studies support that patients who undergo CABG have significantly better survival, reduced adverse postoperative events, and a lower number of repeat revascularizations.[5-10] However, other recent outcomes indicate that CABG and PCI have comparable postoperative survival for patients with low EF,[11,12] although postoperative myocardial infarction (MI) and repeat revascularization remain more prevalent in patients undergoing PCI.

Given that there is a known association between reduced left ventricular EF and CABG mortality,[13] the decision to undertake surgical revascularization in these patients is not taken lightly and primarily based in the benefits of CABG outweighing the risks of surgery.[14] PCI has rapidly expanded as a viable option for patients with coronary artery disease in many settings; however, whether PCI has a consistent role for patients with low EF has yet to be established. The primary aim of the current study is to provide outcomes for both short- and long-term mortality and readmissions for propensity matched CABG and PCI cohorts in patients with reduced EF.

METHODS

Study Population

Our institution's database yielded a total of 2000 coronary revascularization procedures in patients with reduced EF. Perioperative data and long-term outcomes were retrospectively gathered from a prospectively maintained cardiac surgical database. The institutional review board approved use and analysis of the database. All patients with coronary artery disease and reduced EF requiring revascularization from 2011 to 2018 were included. Additional inclusion criteria were all patients with isolated CABG and in the PCI cohort: presence of 3-vessel coronary disease (≥70% stenosis in all 3 major coronary vessels), 2-vessel coronary disease with ≥70% stenosis in 2 major coronary vessels, including the proximal left anterior descending artery, and left main coronary stenosis ≥50% severity. The preferred mode of therapy for patients with multivessel disease and reduced EF was CABG unless these were patients were not seen by surgeons at our institutions first or they were turned down by surgeons for frailty or being extreme risk for surgery. Exclusion criteria included prior CABG, staged revascularization, and presenting with ST-segment elevation MI. Liver disease implied patients with a history of cirrhosis, elevated bilirubin, or 3 times greater than normal liver enzymes.

Statistical Analysis

Baseline patient demographic characteristics were compared between CABG and PCI cohorts. For continuous variables, *t* test or Mann-Whitney *U* test was used and χ^2 test (or Fisher exact test when 25% cell has expected number <5) was used for categorical variables. All baseline characteristics were assessed in the univariate Cox proportional hazard model of time to death, time to major adverse cardiac and cerebrovascular event (MACCE), and time to revascularization via separate analysis.

Overall mortality was calculated using Kaplan-Meier estimation and overall readmission using cumulative incidence function (CIF) estimation. The log-rank test was used for overall mortality and Gray test was used for overall readmission. The other variables in postprocedure outcomes were calculated using the χ^2 test and report proportion. McNemar test was used for the short-term outcome comparison after propensity score matching. In the instance of multiple readmissions for the same patient, time to the first readmission was used in the model. For readmission, cause-specific hazard (95% confidence interval) was calculated using CIF with death as a competing risk both in univariate and multivariable models. Significant covariables were adjusted in the multivariable models of time to death and readmission separately. Long-term survival and hospital readmissions were compared for each group with the use of Kaplan-Meier curves and CIF was used to generate a curve for long-term readmissions, respectively. The log-rank test was used to compare 1- and 5-year survival. Cox regression analysis was performed to identify baseline characteristics that are associated with MACCE, which included death, MI, stroke, and repeat revascularization. The treatment effect of repeat revascularization was evaluated with the subdistribution model. A subgroup analysis for comparison between groups, including mortality, readmissions, and adverse events was performed for patients with diabetes mellitus (eg, insulin-dependent patients).

For risk adjustment, propensity matching was performed. The matched set was created by greedy matching algorithm (1:1 nearest neighbor matching without replacement, caliper = 0.2 of the standard deviation of the logit propensity score) The difference in propensity score between 2 groups is less than or equal to the caliper width. Finally, we checked the balance of 2 cohorts based on standardized mean difference (SMD). For SMD <10%, the matched population is well balanced. SMD <15% is within an acceptable range for matching. After matching, stratified Cox regression was used (stratified by pairs), which considers the matched cohort in a pairwise manner. Numerous baseline variables were used in the propensity score regression model including race, age, gender, body mass index, body surface area, current smoking status, chronic obstructive pulmonary disease, diabetes, dialysis, hypertension, hyperlipidemia, liver disease, cancer history, peripheral artery disease, cerebrovascular disease, heart failure, MI, prior PCI, cardiac symptoms on presentation, kidney function, number of diseased vessels, and completeness of revascularization with no significant differences between PCI and CABG cohorts. Histogram plots before (Figure E1) and after propensity matching (Figure E2) show adequately risk adjusted patient cohorts. Proportional hazard assumption was tested by Schoenfeld residuals.

RESULTS

Baseline Characteristics

Unadjusted baseline patient characteristics can be found in Table E1. There was no difference in mean left ventricular EF for PCI versus CABG (35.0% vs 35.0%; $P = .77$) (Table 1). All baseline characteristics were risk adjusted with propensity matching. The majority of patients were receiving dual antiplatelet therapy (PCI 93% and CABG 96%) before the revascularization procedure. In the total unadjusted patient population, 400 out of 1153 (34.7%) CABG procedures were performed off-pump.

Postprocedure Outcomes

Unadjusted postoperative outcomes can be found in Table E2. Following propensity matching, 30-day mortality was not significantly different for PCI versus CABG (6.17% vs 4.94%; $P = .49$) (Table 2). Over a median follow-up of 3.23 years, mortality was significantly higher for the PCI group (37.4% vs 21.3%; $P < .001$). Thirty-day readmissions (24.1% vs 12.9%; $P = .001$), all-cause readmissions (24.1% vs 12.9%; $P = .001$), and cardiac readmissions (20.4% vs 11.1%; $P = .001$) were significantly higher for the PCI cohort. There was no difference between cohorts for the frequency of stroke events (3.09% vs 2.47%; $P = .63$). MACCE occurrence (41.4% vs 23.8%; $P < .001$) and need for repeat revascularization (6.45% vs 2.59%; $P = .02$) was significantly higher in the PCI cohort. A total of 15 out of 20 (85%) patients in the PCI cohort required repeat revascularization with CABG and 8 out of 8 (100%) of patients in the CABG cohort required repeat revascularization with PCI. A subanalysis for patients with diabetes showed that insulin-dependent patients who underwent PCI had a significantly higher mortality (59.7% vs 39.2%; $P = .007$) and higher MACCE (58.4% vs 36.5%; $P = .007$), including higher MI (11.7% vs 2.7%; $P = .03$), although overall readmissions (66.22% vs 36.4%; $P = .003$) were significantly higher in the CABG cohort (Table E3).

Survival and Readmission Analysis

The results of multivariable models for predictors of death, readmission, and adverse events can be found in Tables 3 through 5. The most significant variables associated with mortality on cox regression included prior

TABLE 1. Baseline characteristics after propensity matching

Variables	PCI (n = 324)	CABG (n = 324)	SMD
LVEF	35.00 (26.00-43.00)	35.00 (28.00-43.00)	0.05
Race			
White	296 (91.36)	297 (91.67)	0.01
Black	21 (6.48)	21 (6.48)	0.00
Other	7 (2.16)	6 (1.85)	0.02
Age	71.00 (61.00-79.00)	70.00 (62.00-76.00)	0.10
Female	109 (33.64)	92 (28.40)	0.10
BMI	28.00 (25.00-32.00)	29.00 (26.00-33.00)	0.05
BSA	2.00 (2.00-2.00)	2.00 (2.00-2.00)	0.00
Current smoker	72 (22.22)	79 (24.38)	0.05
COPD	72 (22.22)	71 (21.91)	.007
Diabetes	176 (54.32)	179 (55.25)	0.02
Dialysis	17 (5.25)	15 (4.63)	0.03
Hypertension	286 (88.27)	284 (87.65)	0.02
Hyperlipidemia	273 (84.26)	279 (86.11)	0.05
Liver disease	21 (6.48)	17 (5.25)	0.05
Cancer	57 (17.59)	57 (17.59)	0.00
PAD	70 (21.60)	66 (20.37)	0.03
CVD	72 (22.22)	72 (22.22)	0.00
HF	112 (34.57)	111 (34.26)	.006
MI	179 (55.25)	199 (61.42)	0.13
Prior PCI	117 (36.11)	109 (33.64)	0.05
Cardiac presentation			
No symptoms or angina	58 (17.90)	61 (18.83)	0.06
Unlikely ischemia	10 (3.09)	4 (1.23)	0.01
Stable angina	37 (11.42)	37 (11.42)	0.06
Unstable angina	112 (34.57)	121 (37.35)	0.00
Non-STEMI	107 (33.02)	101 (31.17)	0.04
GFR	63.00 (45.00-78.00)	64.00 (50.00-80.00)	0.05
Creatinine	1.00 (1.00-1.00)	1.00 (1.00-1.00)	0.03
No. of diseased vessels			
2	98 (30.25)	97 (29.94)	0.01
3	224 (69.14)	226 (69.75)	0.01
Unknown	2 (0.62)	1 (0.31)	
STS PROM (%)	N/A	2.01 (0.93-4.85)	N/A

Values presented as n (%) and median (interquartile range) for categorical and continuous variables, respectively. *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass grafting; *SMD*, standard mean difference; *LVEF*, left ventricular ejection fraction; *BMI*, body mass index; *BSA*, body surface area; *COPD*, chronic obstructive pulmonary disease; *PAD*, peripheral artery disease; *CVD*, cerebral vascular disease; *HF*, heart failure; *MI*, myocardial infarction; *STEMI*, ST elevated myocardial infarction; *GFR*, glomerular filtration rate; *STS PROM*, Society of Thoracic Surgeons predicted risk of mortality; *N/A*, not available.

TABLE 2. Postprocedure outcomes after propensity matching

	PCI (n = 324)	CABG (n = 324)	*P* value
Mortality			
30-d	20 (6.17)	16 (4.94)	.49
Overall	121 (37.35)	69 (21.30)	<.001
Readmission			
30-d	78 (24.07)	42 (12.96)	.001
Overall	78 (24.07)	42 (12.96)	.001
Cardiac readmission	66 (20.37)	36 (11.11)	.001
Heart failure readmission	26 (8.02)	17 (5.25)	.16
MACCE*	134 (41.36)	77 (23.77)	<.001
Stroke event	10 (3.09)	8 (2.47)	.63
MI event	25 (7.72)	6 (1.85)	.001
Repeat revascularization	20 (6.45)	8 (2.59)	.02

Values presented as n (%). *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass grafting; *MACCE*, major adverse cardiac and cerebrovascular event; *MI*, myocardial Infarction. *Composite of death, MI, stroke, and repeat revascularization.

liver disease (hazard ratio [HR], 1.61; 95% CI, 1.20-2.14; *P* = .001), dialysis (HR, 2.38; 95% CI, 1.61-3.52; *P* < .001), and diabetes (HR, 1.57; 95% CI, 1.28-1.92; *P* < .001) (Table 3). Patients who underwent CABG (HR, 0.57; 95% CI, 0.44-0.73; *P* < .001) had significantly reduced hazard for postoperative death. The PCI cohort had significantly reduced 1-year (81.2% vs 89.2%; *P* = .005) and 5-year (57.2% vs 76.8%; *P* < .001) survival compared with the CABG cohort (Figure 1). The long-term cumulative incidence of hospital readmission was significantly higher in the PCI cohort (*P* = .0003) (Figure 2).

TABLE 3. Cox regression for mortality

Multivariable	Hazard ratio (95% confidence interval)	*P* value
CABG (reference: PCI)	0.57 (0.44-0.73)	<.001
Age	1.04 (1.02-1.05)	<.001
Black (reference: White)	0.59 (0.37-0.92)	.02
Complete revascularization	0.79 (0.63-0.99)	.04
Prior liver disease	1.61 (1.20-2.14)	.001
Hyperlipidemia	0.75 (0.57-0.98)	.04
Previous CVD	1.33 (1.05-1.60)	.01
COPD	1.42 (1.15-1.75)	.001
Dialysis	2.38 (1.61-3.52)	<.001
Diabetes	1.57 (1.28-1.92)	<.001
Previous PAD	1.61 (1.31-1.96)	<.001
Previous PCI	1.23 (1.01-1.51)	.04
Pre GFR	0.99 (0.988-0.997)	.006
LVEF	0.98 (0.97-0.99)	<.001

CABG, Coronary artery bypass grafting; *PCI*, percutaneous coronary intervention; *CVD*, cardiovascular disease; *COPD*, chronic obstructive pulmonary disease; *PAD*, peripheral artery disease; *GFR*, glomerular filtration rate; *LVEF*, left ventricular ejective fraction.

TABLE 4. Competing risk* for readmission using cumulative incidence function

Multivariable	Hazard ratio (95% confidence interval)	*P* value
CABG (reference: PCI)	0.51 (0.37-0.71)	<.001
Black (reference: White)	0.48 (0.26-0.86)	.01
Age	1.03 (1.01-1.04)	.001
BMI	0.97 (0.95-0.99)	.01
Diabetes	2.11 (1.61-2.77)	<.001
Dialysis	2.17 (1.06-4.45)	.04
Prior PAD	1.70 (1.30-2.24)	<.001
Prior cancer	1.74 (1.31-2.31)	<.001
Previous liver disease	1.82 (1.25-2.67)	.002
COPD	1.69 (1.28-2.24)	<.001

CABG, Coronary artery bypass grafting; *PCI*, percutaneous coronary intervention; *BMI*, body mass index; *PAD*, peripheral artery disease; *COPD*, chronic obstructive pulmonary disease. *Death is used as a competing risk in this model.

Multivariable regression analysis for competing risk for readmission (Table 4) identified diabetes (HR, 2.11; 95% CI, 1.61-2.77; *P* < .001], dialysis (HR, 2.17; 95% CI, 1.06-4.45; *P* = .04), and previous liver disease (HR, 1.82; 95% CI, 1.25-2.67; *P* = .002] as the most significant predictors of readmission. Patients who underwent CABG had significantly reduced overall readmission risk (HR, 0.51; 95% CI, 0.37-0.71; *P* < .001). For the CABG cohort, long-term mortality was higher for patients that underwent off-pump coronary bypass, compared with on-pump CABG (34.5% vs 22%; *P* = .047).

TABLE 5. Cox regression for major adverse cardiac and cerebrovascular events (MACCEs)

Multivariable	Hazard ratio (95% confidence interval)	*P* value
CABG (reference: PCI)	0.48 (0.39-0.58)	<.001
Black (reference: White)	0.62 (0.41-0.93)	.02
Age	1.03 (1.02-1.04)	<.001
Prior liver disease	1.59 (1.21-2.09)	<.001
Hyperlipidemia	0.68 (0.53-0.88)	.003
COPD	1.47 (1.21-1.78)	<.001
Dialysis	2.21 (1.50-3.25)	<.001
Prior CVD	1.25 (1.02-1.52)	.03
Diabetes	1.63 (1.34-1.97)	<.001
Prior cancer	1.41 (1.13-1.75)	.002
Prior PCI	1.34 (1.11-1.63)	.003
BMI	0.98 (0.97-0.99)	.04
GFR	0.99 (0.991-0.999)	.01
LVEF	0.98 (0.97-0.99)	<.001

CABG, Coronary artery bypass grafting; *PCI*, percutaneous coronary intervention; *COPD*, chronic obstructive pulmonary disease; *CVD*, cerebral vascular disease; *BMI*, body mass index; *GFR*, glomerular filtration rate; *LVEF*, left ventricular ejective fraction.

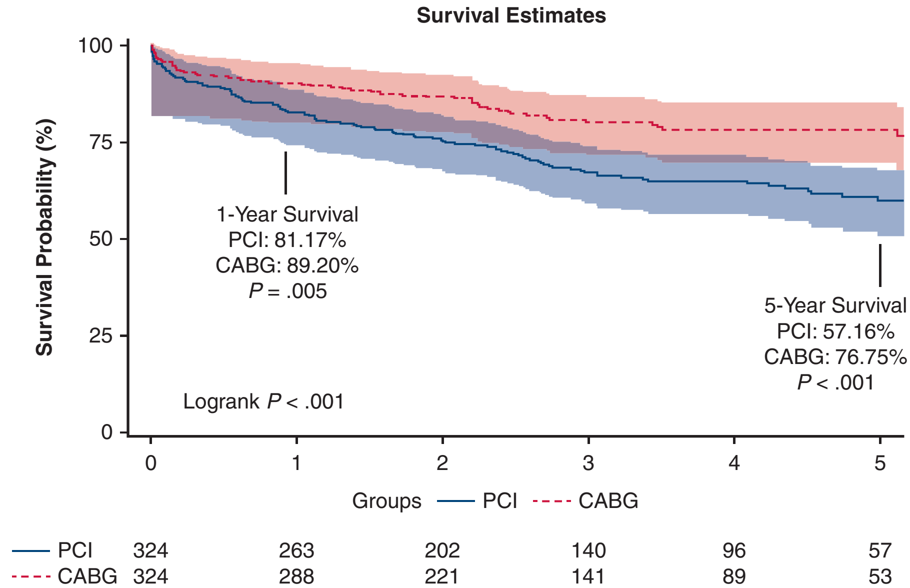

FIGURE 1. For propensity score matched cohorts, the percutaneous coronary intervention (*PCI*) cohort had significantly reduced 1-year (81.2% vs 89.2%; $P = .005$) and 5-year (57.2% vs 76.8%; $P < .001$) survival compared with the coronary artery bypass grafting (*CABG*) cohort.

Multivariable Regression Analysis for Adverse Events

Surgical revascularization was associated with significantly reduced risk of MACCE (Figure 3). Freedom from MACCE was significantly higher in the CABG cohort at 1 year (87.0% vs 74.4%; $P < .001$) and 5 years (74.0% vs 54.5%; $P < .001$) (Figure 4). The most significant predictors of MACCE occurrence included chronic obstructive pulmonary disease (HR, 1.47; 95% CI, 1.21-1.78; $P < .001$), dialysis (HR, 2.21; 95% CI, 1.50-3.25; $P < .001$), and diabetes (HR, 1.63; 95% CI, 1.34-1.97; $P < .001$) (Table 5). Patients who underwent CABG (HR, 0.48;

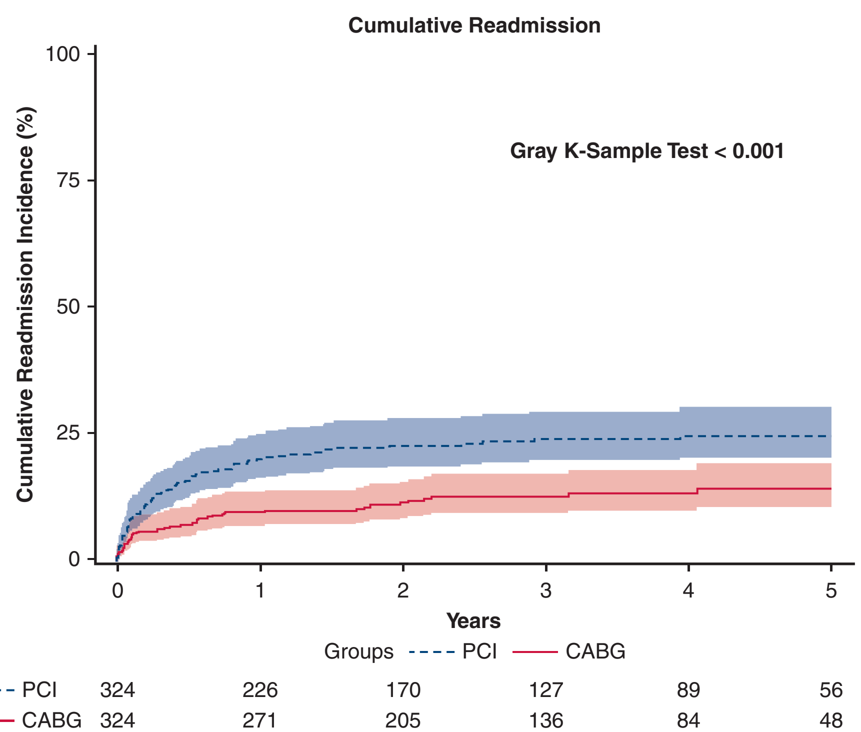

FIGURE 2. For propensity score-matched cohorts, the long-term cumulative incidence of hospital readmission was significantly higher in the percutaneous coronary intervention (*PCI*) cohort ($P = .0003$). *CABG*, Coronary artery bypass grafting.

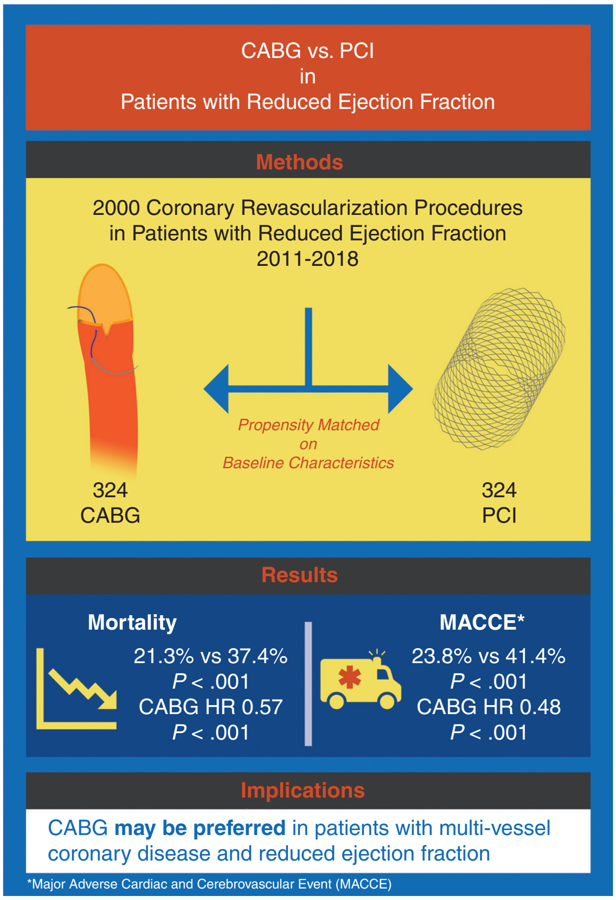

FIGURE 3. Surgical revascularization with coronary artery bypass grafting (*CABG*) was associated with significantly reduced risk of long-term mortality (Hazard ratio [*HR*], 0.57; (95% confidence interval [CI]; 0.44-0.73); P < .001] and major adverse cardiac and cerebrovascular events (*MACCE*) (HR, 0.48; 95% CI, 0.39-0.58; P < .001), compared with percutaneous coronary intervention (*PCI*).

95% CI, 0.39-0.58; P < .001) had significantly less hazard for MACCE occurrence. The competing risk of repeat revascularization (ie, CIF) was significantly lower for the CABG cohort (univariable HR, 0.47; 95% CI, 0.28-0.79; P = .0045).

Subanalyses for Patients With EF 35% to 50% and EF <35%

A total of 1226 patients had EF from 35% to 50% and 774 patients had EF <35%. Following propensity matching, patients who underwent PCI in the 35% to 50% EF cohort (Table E4) had higher mortality (32% vs 16.2%; P = .005), readmission (20.3% vs 12.2%; P = .03), and MI event (7.11% vs 2.54%; P = .03). Patients who underwent PCI in the <35% EF (Table E5) had higher mortality (41.6% vs 28.9%; P = .06) and competing risk for repeat revascularizations (8.5% vs 2.19%; P = .03). Patients who underwent PCI had significantly worse freedom from long-term MACCE in both the EF 35% to 50% (Figure E3) and EF <35% (Figure E4) cohorts.

DISCUSSION

In this large, single-center study, we report propensity matched outcomes for PCI versus CABG in patients with reduced preoperative left ventricular EF. Our outcomes show that procedural mortality (30-day) was not significantly different between cohorts, indicating that CABG can be performed with no additional operative mortality risk. However, the PCI cohort had significantly increased mortality on long-term follow-up. Furthermore, the occurrence of MACCE and the need for repeat revascularization was significantly higher in the PCI cohort. Both 30-day and all-cause readmissions were higher in the PCI cohort. In addition, cardiac-related readmissions were significantly higher in the PCI cohort, which is not surprising given the higher rates of MI and repeat revascularizations in PCI patients on long-term follow-up.

Patients with low EF undergoing cardiac surgery have an established increased operative mortality risk compared with patients with normal EF.[15] Low-EF cardiac surgery patients have a heightened risk of postoperative complications, including, but not limited to, pneumonia, sepsis, low cardiac output syndrome, stroke, atrial fibrillation, endocarditis, deep sternal wound infection, and acute renal failure.[16-21] Recent literature has shown that patients with low EF who underwent CABG have worse outcomes compared with patients with normal EF, including increased short- and long-term mortality.[16,22-24] Nonetheless, clinicians are faced with the decision as to the best means of revascularizing CAD patients with low EF. PCI has been reported as a viable option for this patient population.[25] However, the decision to perform PCI versus CABG for low-EF patients is controversial and comparative studies are relatively limited.

In a recent, large meta-analysis[26] comparing patient outcomes for CABG versus PCI, patients with preoperative LV systolic dysfunction who had PCI with drug-eluting stents had a higher risk of all-cause mortality, cardiac mortality, repeat revascularization, and MI. Although, rates of postoperative stroke were similar between CABG and PCI. The current study results are similar, with no difference in postoperative stroke between cohorts and significantly higher rates of MI, need for repeat revascularization, and all-cause long-term mortality in the PCI cohort. Other recent meta-analyses comparing CABG and PCI in low-EF patients corroborate these findings, showing a significant survival benefit in CABG patients.[27,28] However, these findings are not universal and proponents of PCI in lieu of CABG for this patient population cite comparable long-term survival.[11,12] Recent statewide registry data[12] showed commensurate long-term survival with a lower stroke rate in the PCI cohort; however, the PCI group had significantly

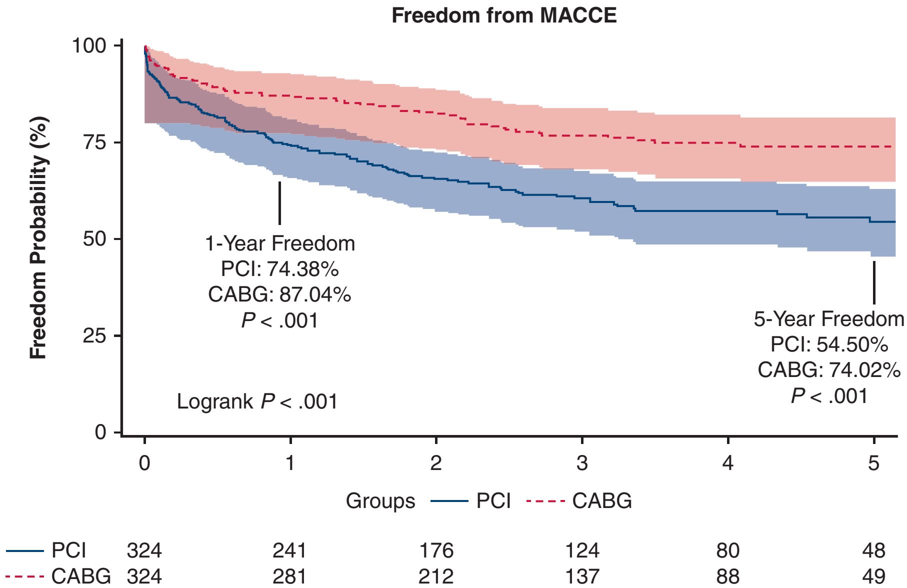

FIGURE 4. For propensity score matched cohorts, freedom from major adverse cardiac and cerebrovascular events (*MACCE*) was significantly higher in the coronary artery bypass (*CABG*) cohort at 1 year (87.0% vs 74.4%; $P < .001$) and 5 years (74.0% vs 54.5%; $P < .001$). *PCI*, Percutaneous coronary intervention.

higher risk of MI and repeat revascularization on follow-up. The higher MI and repeat revascularization rates, which are often reported and confirmed by the current study, have important implications for long-term outcomes and hospital readmissions. Our outcomes indicate that the PCI cohort has a significantly higher number of long-term all-cause readmissions and cardiac readmissions, which is likely related to significantly higher rates of MI requiring repeat revascularization in the PCI cohort. Given these findings, preoperative decision making is critical to identify the risks and benefits of PCI versus CABG in patients with complex coronary artery disease and multidisciplinary cardiac teams, including cardiologists and surgeons, play a pivotal role in determining the appropriate revascularization procedure.

Limitations

The current study is limited by confounding and selection bias, inherent to retrospective study design. There is a chance that a small percentage of hospital readmissions were lost to capture due to patients being readmitted to outside centers. Our database is maintained by trained research staff, although human error in data collection and analysis is possible. Despite propensity matching being performed for risk-adjustment, there may still be some baseline differences between the populations that were not accounted for. Patients in the PCI cohort may have had increased baseline risk due to heightened comorbidities and frailty; although this effect was partially mitigated by matching, selection bias was likely. Moreover, we did not have long-term echocardiographic follow-up in this patient population to report on contractile recovery. Finally, Society of Thoracic Surgeons predicted risk of mortality was not available for the PCI cohort.

CONCLUSIONS

The current study indicates that in patients with CAD and reduced EF, CABG yields better long-term survival, lower readmission rates, reduced MACCE, and fewer repeat revascularizations. Furthermore, CABG can be performed with equivalent stroke risk compared with PCI, indicating that for this patient population CABG may be the preferred method of revascularization.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://aats.blob.core.windows.net/media/20AM/Presentations/PCI%20versus%20CABG%20in%20Patients%20with%20Red.mp4.

Conflict of Interest Statement

Dr Kilic serves on the Medtronic medical advisory board. Dr Gleason serves on the Abbott medical advisory board. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: percutaneous, CABG, PCI, low EF

Discussion

Presenter: Dr Ibrahim Sultan

Dr John D. Puskas *(New York, NY)*. Good morning, and congratulations to Dr Sultan and his colleagues from the University of Pittsburgh Medical Center on their study that addresses an important question, namely whether coronary artery bypass grafting (CABG) imparts superior survival and freedom from major adverse cardiac and cerebrovascular events (MACCE) compared to multivessel percutaneous coronary intervention (PCI) in patients with left ventricular ejection fraction (LVEF) <50%. They've analyzed an institutional database over 7 years, including patients who had either multivessel PCI by a single-stage approach or isolated CABG. They identified 324 propensity-matched pairs, and demonstrated that the baseline characteristics are well balanced, with a median LVEF of 38%.

While 30-day mortality was similar between groups, overall mortality during a median 3.2 years follow-up was significantly higher for PCI at 37%, versus CABG at 21% with a significant *P* value. Total and cardiac-related repeat hospitalizations during follow-up were approximately twice as frequent in the PCI group as in the CABG group. Myocardial infarction occurred in 7.7% of PCI patients during follow-up, and in 1.8% of CABG patients—a more than 3-fold difference in favor of CABG, with a highly significant *P* value. Similarly, MACCE and repeat revascularization were approximately twice as frequent after PCI as after CABG. Multivariate analysis confirmed these results generating hazard ratios of 0.52 for mortality, 0.5 for MACCE, and 0.35 for repeat revascularization in CABG versus PCI.

Of course, these results are music to the ears of coronary surgeons, and are consistent with a very recent report from Ontario by Sun and colleagues published in *JAMA Cardiology* online just a couple weeks ago. Those Canadian investigators retrospectively reviewed the Ontario provincial database, selected data from patients with multivessel coronary disease and LVEF <35% who underwent PCI or CABG over an 8-year period ending in 2016. They found a total of approximately 12,000 patients, used propensity matching on 30 baseline characteristics, and generated almost 2400 propensity-matched pairs, demonstrating a CABG hazard ratio of 0.62 for mortality, 0.71 for cardiac mortality, 0.5 for MACCE, 0.27 for repeat revascularization, and 0.31 for repeat hospitalization for myocardial infarction, CABG compared with PCI. Of course, all of these were statistically significant and consistent with the findings from the University of Pittsburgh Medical Center study presented today.

So, Dr Sultan, I have 4 questions and will ask them 1 at a time.

Why were patients who had multivessel PCI by a staged approach, which is very commonly used in multivessel disease, excluded from your study? Including patients who had multivessel PCI by a staged approach would have certainly changed the ratio of PCI to CABG in your initial sample population of all revascularization procedures. Could that exclusion criteria have introduced selection bias or other confounding into your retrospective trial?

Dr Ibrahim Sultan *(Pittsburgh, Pa)*. Thank you, Dr Puskas. I really appreciate your summary and your questions. The reason we excluded those patients is because a lot of times those patients are not necessarily intended to be treated as staged PCI, and it is challenging to tell that retrospectively. Perhaps the plan could have been to stent the left anterior descending artery in a certain patient and follow the circumflex disease or right coronary disease medically, and not necessarily treat that. However, at a later time if the patient were to experience myocardial infarction or a persistent angina, then that patient may end up getting PCI again. That was a big confounding factor that we wanted to avoid. We wanted to try to keep the groups as similar as possible. That was the primary reason we wanted to go with a single-stage approach.

Dr Puskas. Second question. What definition of myocardial infraction was used for PCI and for CABG? Was it the same definition for early periprocedural infarcts as for later follow-up infarctions during prolonged follow-up? Did the definition that was chosen favor CABG? Of course, you report a threefold higher rate of myocardial infarction in PCI than in CABG, which is frankly unusual. Especially early on when we see a periprocedural cardiac enzyme release that's higher in PCI than in CABG, we wonder about the definition used or some kind of selection bias, because that is an unusual finding.

Dr Sultan. Yeah, I think there's definitely selection bias. In fact, I think particularly in the periprocedural setting because biochemical markers are not consistently measured for post-CABG patients. I think a lot of those patients were left out. I don't think that that's a good representative of what the difference is in periprocedural myocardial infarction, and we didn't really focus on that in the manuscript either.

However, myocardial infarctions in follow-up were determined based on universal definition—biochemical and electrocardiogram evidence—that is what was used. We corresponded that with the diagnosis codes when the patients were admitted.

Dr Puskas. Very good. Third, are there any other biases that you think might have been influencing the result of your study? In particular, could the heart team at University of Pittsburgh Medical Center have systematically assigned more sturdy or hardy patients to CABG, and less hardy or more frail patients to PCI? Your propensity score matching was on 16 characteristics that did not include specific metrics of frailty. Is this another potential source of selection bias? Again, I note that your 30-day mortality was numerically higher in the PCI group than in the CABG group, not significant from a statistical point of view, but it is unusual that 30-day mortality would be higher in the PCI group than in the CABG group in a PCI versus CABG comparison. We expect to see that over a longer-term follow-up, but rarely do we see that at 30 days. Is this evidence of unbalanced or unadjusted selection bias?

Dr Sultan. Yeah, I completely agree. I think there's definitely a selection bias. Frailty was not appropriately coded in our data sets and that's why we do not utilize it, and I think that's a huge confounding factor that would allow us to not necessarily pick the frail patients for CABG. I think that's number 1.

The other thing that's not accounted for are targets. For instance, if the surgeons believed that the targets were poor and the patient may not get complete revascularization, that's another group of patients which may have been diverted toward PCI. I think what we've done over the past year is, any patient who is considered high-risk, which may be because of severely reduced ejection fraction or a variety of other baseline factors is then discussed within the team of surgeons themselves who are not part of the patient's care who then take a look at the patient's angiogram and clinical characteristics, and then make an independent adjudication of whether or not that patient should really have CABG or PCI to really minimize these kind of confounding errors.

Dr Puskas. Don't get me wrong. I personally am very much in favor of assigning more frail patients to PCI and more sturdy patients to coronary bypass. I think that that parses out the relative risk and benefit appropriate among our patients and that 30-day outcome from your study may indicate that your heart team is doing its job.

Last question: in conclusion, Dr Sultan, I think your data are compelling. Are they compelling enough to change referral patterns in clinical practice at University of Pittsburgh Medical Center? If so, then by what mechanism would that change occur? And if not, why not, and what should then be done? Congratulations and thank you.

Dr Sultan. Thank you, Dr Puskas. This started off as a sort of a quality improvement internal audit for us for the heart team. This has now launched into multiple research questions and manuscripts. We've looked at majority of subsets with patients who had multivessel disease, not just the reduced ejection fraction, but patients who had diabetes, patients from a gender perspective, from an ethnicity perspective, socioeconomic perspective, and of course multi-arterial versus third-generation stent. From every single subset, CABG appears to have a survival benefit for overall survival and for MACCE. I do think referral patterns may change from primary cardiologists. I think there's a much more vigorous discussion because I think it's 1 thing for us to read a manuscript from another institution and make judgments on that or give that information to patients, but when it's our own patients that we have taken care of and we know what those results look like, I think we're much more honest with ourselves and I think that goes a long way.

Dr Marc Ruel *(Ottawa, Ontario, Canada).* Ibrahim and John, I thought this was an excellent discussion. It adds to the weight of evidence that we increasingly have gained regarding the role of CABG versus PCI in revascularization of coronary artery disease patients with depressed ejection fraction.

In this regard, there's definitely a selection of patients that may occur, and as such it is possible that surgery patients might be more cherry-picked than patients who are relegated to PCI. One way that we can methodologically address this was utilized in our *JAMA Cardiology* piece—and I think, Ibrahim, that this might be something feasible within your University of Pittsburgh Medical Center database: it was to examine falsification end points. Essentially, this method helps you decipher whether patients are frailer in 1 group versus another. For instance, are events that are not mechanistically related to revascularization occurring more frequent in 1 group versus another?

Louise Sun, Mario Gaudino, Rob Chen, and I compared readmissions for pneumonia or for hip fractures between the 2 groups over the long-term. Adding support to our conclusions, we found that readmissions for those occurrences over a median of 5.2 years were similar in incidence between the PCI and CABG groups, adding credibility to the significant differences seen with regard to major adverse cardiac events. Do you think that you could examine falsification end points within your own dataset?

Dr Sultan. Yes, we've looked at overall hospital readmissions, not just cardiac, and not just heart failure. So, interestingly the PCI readmissions are higher. We haven't really parsed out the exact reasons why, but the most common reason does end up being pneumonia or some sort of respiratory complication; that's how it's coded in our data set. So yes, we have definitely looked at that and we've noticed that the hospital readmissions over 5 years are significantly higher in the PCI group.

Dr Ruel. That would suggest that your PCI patients were sicker patients at baseline, unfortunately.

Dr. Sultan. Absolutely.

ADULT

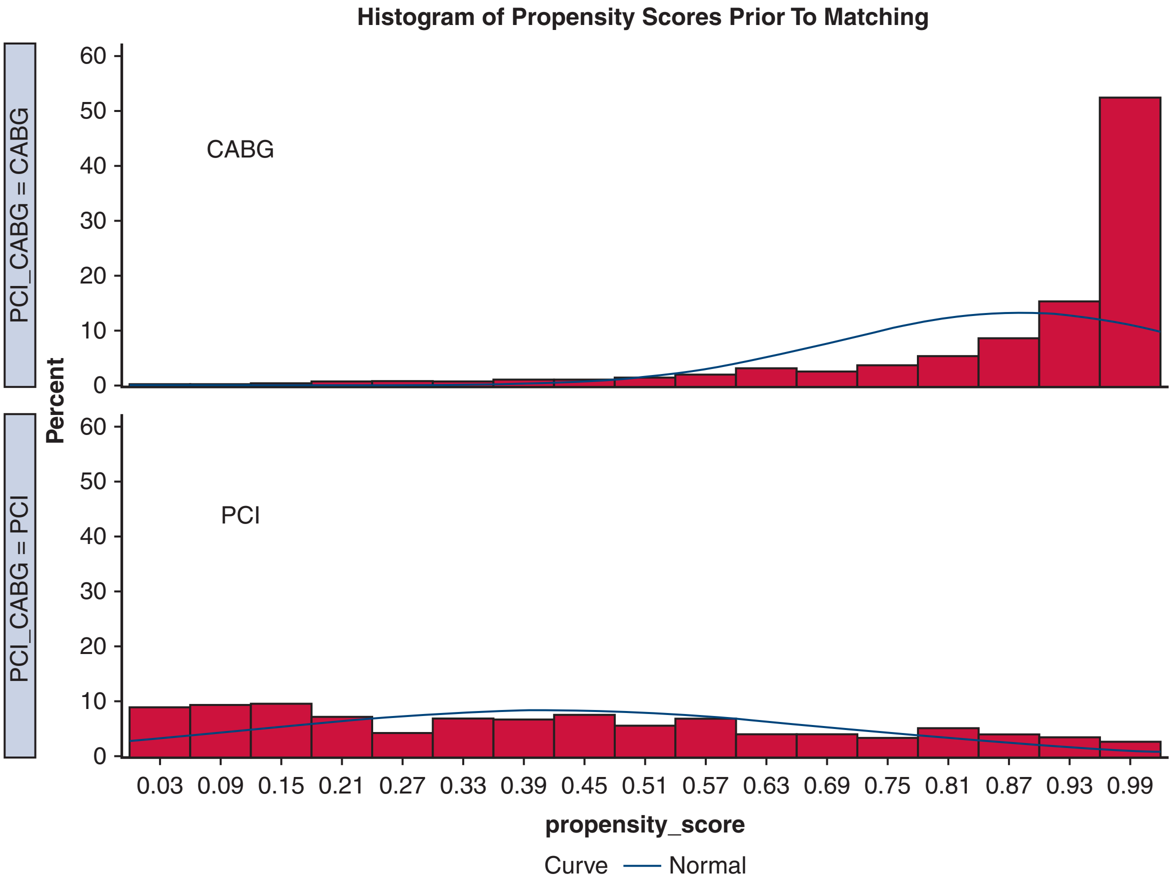

FIGURE E1. Histogram of propensity scores prior to matching. *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass grafting.

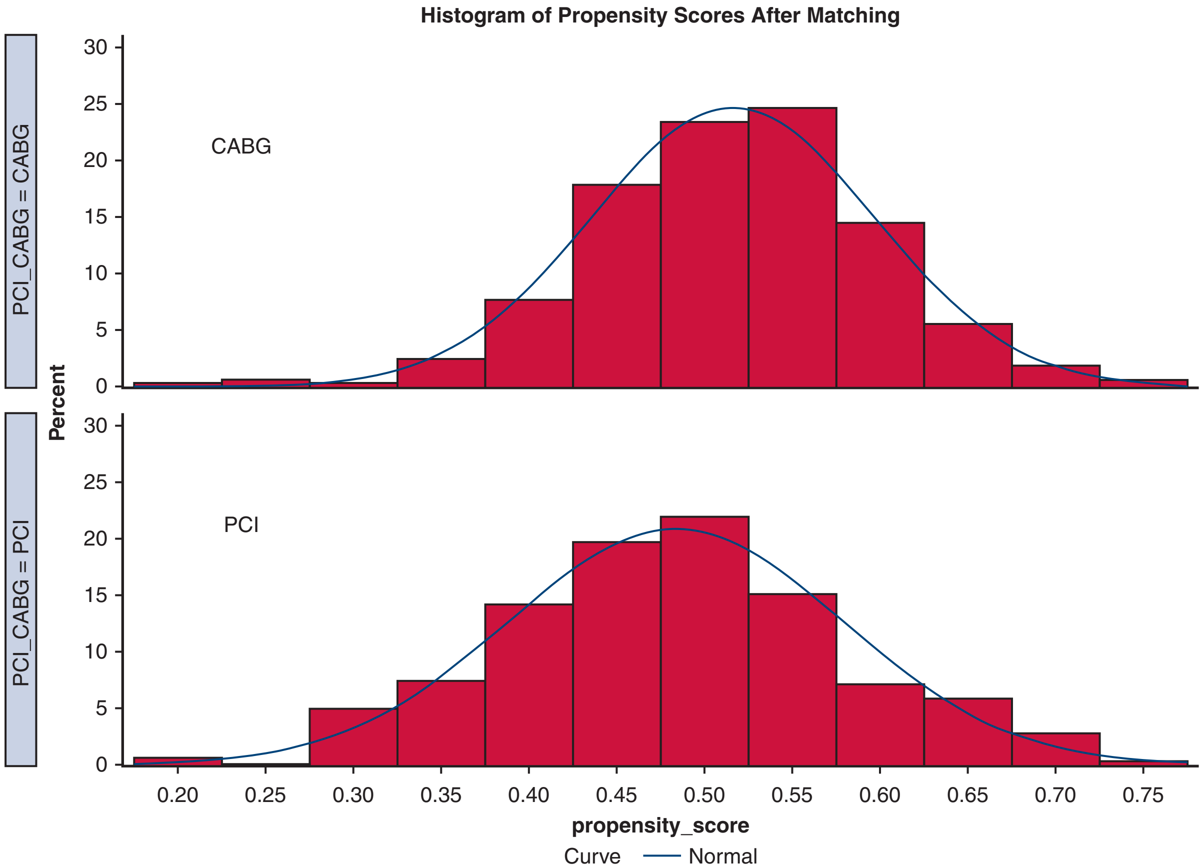

FIGURE E2. Histogram of propensity scores after matching. *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass grafting.

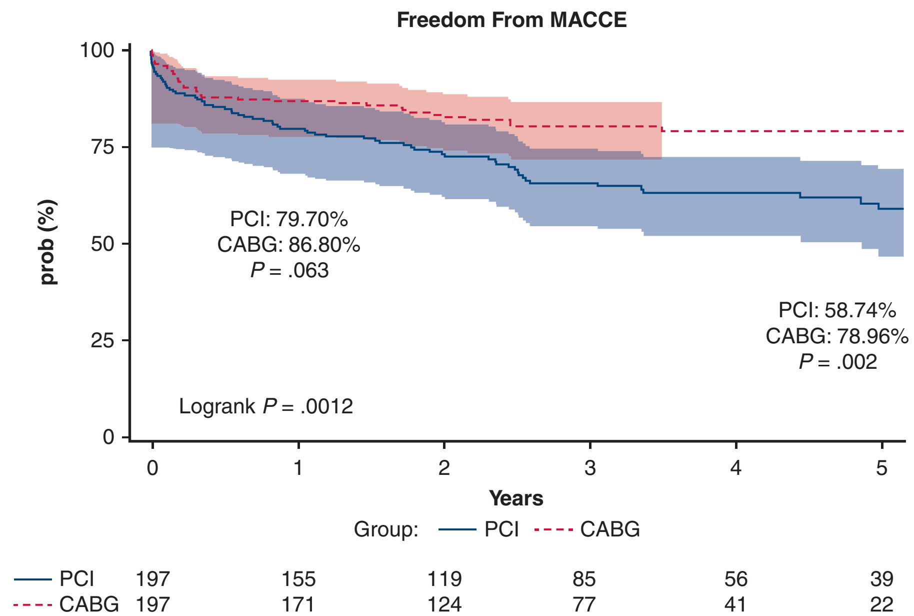

FIGURE E3. Freedom from major adverse cardiac and cerebrovascular event (*MACCE*) in patients with ejection fraction (EF) 35% to 50%. *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass grafting.

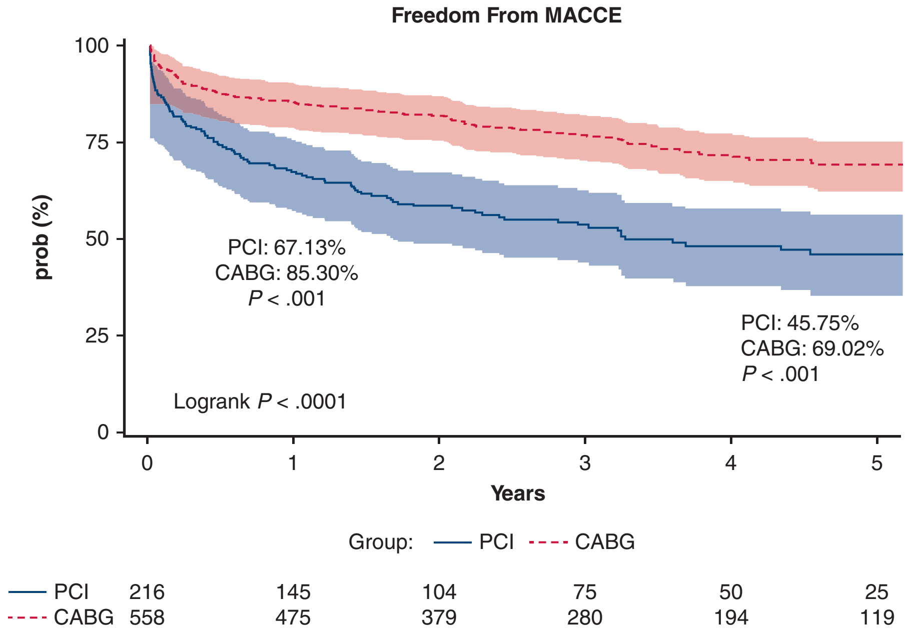

FIGURE E4. Freedom from major adverse cardiac and cerebrovascular event (*MACCE*) in patients with ejection fraction (EF) <35%. *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass grafting.

TABLE E1. Unadjusted baseline patient characteristics

Characteristic	PCI	CABG	SMD
LVEF	35.00 (25.00-43.00)	38.00 (30.00-45.00)	0.26
Race			
White	409 (91.50)	1434 (92.34)	0.03
Black	31 (6.94)	82 (5.28)	0.07
Other	7 (1.57)	37 (2.38)	0.07
Age (y)	72.00 (62.00-80.00)	66.00 (59.00-74.00)	0.41
Female	157 (35.12)	375 (24.15)	0.24
BMI	28.00 (25.00-33.00)	30.00 (26.00-33.00)	0.10
BSA	2.00 (2.00-2.00)	2.00 (2.00-2.00)	0.13
Current smoker	99 (22.15)	453 (29.17)	0.16
COPD	93 (20.81)	388 (24.98)	0.10
Diabetes	233 (52.13)	812 (52.29)	.003
Dialysis	22 (4.92)	54 (3.48)	0.07
Hypertension	390 (87.25)	1386 (89.25)	0.06
Hyperlipidemia	354 (79.19)	1389 (89.44)	0.28
Liver disease	24 (5.37)	120 (7.73)	0.10
Cancer	86 (19.24)	204 (13.14)	0.17
PAD	86 (19.24)	376 (24.21)	0.12
CVD	83 (18.57)	367 (23.63)	0.12
HF	152 (34.00)	357 (22.99)	0.24
MI	197 (44.07)	1248 (80.36)	0.81
Prior PCI	146 (32.66)	442 (28.46)	0.09
Cardiac presentation			
No symptoms or angina	76 (17.00)	210 (13.52)	0.10
Unlikely ischemia	24 (5.37)	6 (0.39)	0.30
Stable angina	48 (10.74)	114 (7.34)	0.12
Unstable angina	136 (30.43)	469 (30.20)	.005
Non-STEMI	163 (36.47)	659 (42.43)	0.12
GFR	61.00 (43.00-76.00)	70.00 (54.00-88.00)	0.37
Creatinine	1.00 (1.00-1.00)	1.00 (1.00-1.00)	0.16
No. of diseased vessels			
2	154 (34.45)	275 (17.71)	0.39
3	284 (63.54)	1226 (78.94)	0.35
Unknown	9 (2.01)	1 (0.06)	
Complete revascularization	117 (26.17)	1239 (79.78)	1.27

Values are presented as n (%) and median (interquartile range) for categorical and continuous variables, respectively. *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass grafting; *SMD*, standard mean difference; *LVEF*, left ventricular ejection fraction; *BMI*, body mass index; *BSA*, body surface area; *COPD*, chronic obstructive pulmonary disease; *PAD*, peripheral artery disease; *CVD*, cerebral vascular disease; *HF*, heart failure; *MI*, myocardial infarction; *STEMI*, ST elevated myocardial infarction; *GFR*, glomerular filtration rate.

TABLE E2. Unadjusted postprocedure outcomes

Outcome	PCI	CABG	*P* value
30-d mortality	34 (7.61)	49 (3.16)	<.001
Mortality	177 (39.60)	293 (18.87)	<.001
30-d readmission	106 (23.71)	174 (11.20)	<.001
Free of readmission	341 (76.29)	1379 (88.80)	<.001
Readmission	106 (23.71)	174 (11.20)	<.001
Cardiac readmission	88 (19.69)	138 (8.89)	<.001
Heart failure readmission	37 (8.28)	70 (4.51)	.002
Stroke event	14 (3.13)	27 (1.74)	.07
MI event	33 (7.38)	29 (1.87)	<.001
MACCE*	192 (42.95)	324 (20.86)	<.001
Revasc (1824 available data)	23 (5.39)	36 (2.58)	.004

Values are presented as n (%). *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass grafting; MI, myocardial infarction; MAACE, major adverse cardiac and cerebrovascular events; *Revasc*, repeat revascularization. *Stroke, MI, or death.

TABLE E3. Postprocedure outcomes for patients with insulin-dependent diabetes

Outcome	PCI (n = 77)	CABG (n = 74)	*P* value
Mortality			
Overall	46 (59.74)	29 (39.19)	.007
Readmission			
Overall	28 (36.36)	49 (66.22)	.003
Cardiac readmission	53 (68.83)	45 (60.81)	.30
Heart failure readmission	37 (48.05)	31 (41.89)	.45
MACCE*	45 (58.44)	27 (36.49)	.007
Stroke event	2 (2.60)	4 (5.41)	.44
MI event	9 (11.69)	2 (2.70)	.03
Repeat revascularization	3 (4.00)	3 (4.35)	1.00

Values are presented as n (%). *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass grafting; *MACCE*; major adverse cardiac and cerebrovascular event; *MI*, myocardial infarction. *Composite of death, MI, and stroke.

TABLE E4. Postprocedure outcomes for patients with ejection fraction of 35% to 50%

	After propensity score matching		
	PCI (n = 197)	CABG (n = 197)	*P* value
Mortality			
30-d	8 (4.06)	6 (3.05)	.59
Overall	63 (31.98)	32 (16.24)	.005
Readmission			
30-d	40 (20.30)	24 (12.18)	.03
Overall	40 (20.30)	24 (12.18)	.05
Cardiac readmission	30 (15.23)	19 (9.64)	.09
Heart failure readmission	10 (5.08)	7 (3.55)	.46
MACCE	70 (35.53)	37 (18.78)	<.001
Stroke event	5 (2.54)	4 (2.03)	1.00
MI event	14 (7.11)	5 (2.54)	.03
Repeat revascularization	10 (5.40)	6 (3.41)	.34

Values are presented as n (%). *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass grafting; *MACCE*; major adverse cardiac and cerebrovascular event (composite of death, MI, and stroke); *MI*, myocardial infarction.

TABLE E5. Postprocedure outcomes for patients with ejection fraction <35%

	After propensity score matching		
	PCI (n = 149)	CABG (n = 149)	*P* value
Mortality			
30-d	11 (7.38)	9 (6.04)	.64
Overall	62 (41.61)	43 (28.86)	.06
Readmission			
30-d	38 (25.50)	25 (16.78)	.07
Overall	38 (25.50)	25 (16.78)	.07
Cardiac readmission	33 (22.15)	24 (16.11)	.19
Heart failure readmission	17 (11.41)	12 (8.05)	.33
MACCE	69 (46.31)	45 (30.20)	.004
Stroke event	6 (4.03)	5 (3.36)	.76
MI event	8 (5.37)	4 (2.68)	.24
Repeat revascularization	11 (8.50)	3 (2.19)	.03

Values are presented as n (%). *PCI*, Percutaneous coronary intervention; *CABG*, coronary artery bypass grafting; *MACCE*; major adverse cardiac and cerebrovascular event (composite of death, MI, and stroke); *MI*, myocardial infarction.