Coronary Bypass Versus Percutaneous Revascularization in Multivessel Coronary Artery Disease

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Background. This study focused on contemporary outcomes after coronary artery bypass graft (CABG) surgery versus percutaneous coronary intervention (PCI) in patients with multivessel coronary artery disease (MVCAD).

Methods. This was a propensity-matched retrospective, observational analysis. Patients with MVCAD who underwent CABG or PCI between 2010 and 2018 and for whom data were available through the National Cardiovascular Data Registry or The Society of Thoracic Surgeons Adult Cardiac Surgery Database were included. The primary outcome was overall survival. Secondary outcomes included freedom from inpatient readmission and freedom from repeat revascularization.

Results. Of the initial 6,163 patients with MVCAD, the propensity-matched cohort included 844 in each group. The estimated 1-year mortality was 11.5% and 7.2% ($p < 0.001$) in the PCI and CABG groups, respectively, with an overall hazard ratio for mortality of PCI versus CABG of 1.64 (95% confidence interval [CI], 1.29 to 2.10; $p < 0.001$). The overall hazard ratio for readmission for PCI versus CABG was 1.42 (95% CI, 1.23 to 1.64; $p < 0.001$). The overall hazard ratio for repeat revascularization for PCI versus CABG was 4.06 (95% CI, 2.39 to 6.91; $p < 0.001$). Overall major adverse cardiovascular events and individual outcomes of mortality, readmission, and repeat revascularization all favored CABG across virtually all major clinical subgroups.

Conclusions. This contemporary propensity-matched analysis of patients undergoing coronary revascularization for MVCAD demonstrates a significant mortality benefit with CABG over PCI, and this benefit is consistent across virtually all major patient subgroups. Futures studies are needed reflecting routine practice to assess how best to approach shared decision making and informed consent when it comes to revascularization decisions in any patient with MVCAD.

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The choice of coronary artery bypass graft (CABG) surgery versus percutaneous coronary intervention (PCI) among patients with multivessel coronary artery disease (MVCAD) or left main coronary artery disease (CAD) continues to be challenging. In the bare metal stent era, several trials showed CABG to be a superior strategy to PCI in such patients [1–5], and although that benefit has been attenuated with drug-eluting stents (DES), it nonetheless remains [6–8]. Nonetheless, several studies have noted a marked shift over the last 15 years from CABG to PCI as the revascularization strategy of choice [9–15]. This shift has been related to data from randomized trials demonstrating an equivalence in long-term survival between patients treated with CABG and those who underwent PCI, albeit at the expense of a greater need for repeat revascularization in PCI-treated patients [4-6, 16–18]. Although these data are highly informative, clinicians may be extending the use of PCI to a broader population than those patients studied in these trials, thereby underusing CABG [9, 19]. Recent data show that CABG has a mortality benefit over PCI in patients with MVCAD, particularly among patients with complex CAD or diabetes [20, 21]. Overall, data from both randomized and observational studies suggest that CABG should be preferred over PCI in patients with MVCAD [4, 20–24], and these data are reflected both in US and European guidelines, which recommend CABG for patients with three-vessel or two-vessel disease with proximal left anterior descending CAD (class I); however, the US guidelines still recommend PCI as an option of uncertain benefit (class IIb) in this population [25, 26]. Both sets of guidelines favor CABG over PCI in the population

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with diabetes mellitus and MVCAD. Nonetheless, there are obvious reasons for patients to prefer PCI over CABG, and these reasons, combined with several recent observational registries suggesting improved long-term mortality with DES [27, 28], have helped to drive increased use of PCI in the treatment of patients with MVCAD.

There have been few studies comparing PCI with CABG in a simultaneous manner in routine clinical practice. Although the American College of Cardiology Foundation and The Society of Thoracic Surgeons Database Collaboration on the Comparative Effectiveness of Revascularization Strategies (ASCERT) study pooled data from the National Cardiovascular Data Registry (NCDR) and The Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database from 2002 to 2007 [16], there is no contemporary update pooling more recent data from the NCDR and STS registries with procedures in the DES era, and the ASCERT study did not evaluate outcomes such as rehospitalization and repeat revascularization. Accordingly, this analysis focuses on contemporary outcomes after PCI or CABG in patients with MVCAD and uses data from the STS and NCDR registries at a large, multihospital health care system.

Patients and Methods

Study Environment

The University of Pittsburgh Medical Center in Pittsburgh, Pennsylvania is a large, multihospital health system with a mix of private practice and academically affiliated providers. Data from the STS and NCDR registries are available from five of the hospitals for PCI and CABG each. This study was approved by a Quality Improvement Institutional Review Board committee.

Study Population

Patients who underwent CABG or PCI between 2010 and 2018 and for whom data were available through the NCDR or STS registries were included. Patients were eligible to be included in the CABG arm if they had isolated CABG and in the PCI arm if they had three-vessel CAD defined by the presence of 70% or greater stenosis in all three major coronary vessels, left main coronary stenosis of 50% or greater severity, or two-vessel CAD defined by the presence 70% or greater stenosis in two major coronary vessels, including the proximal left anterior descending coronary artery. Exclusion criteria included prior CABG, ST-segment elevation myocardial infarction presentation, staged revascularization, and lack of follow-up information.

Outcomes

The primary outcome was mortality, and survival was assessed using the electronic health record and the US Social Security Death Index. Secondary outcomes included freedom from inpatient readmission and freedom from repeat revascularization, excluding staged procedures. Inpatient readmission and repeat revascularization rates were measured on the basis of those events occurring within the University of Pittsburgh Medical Center health system. The 5-year freedom from major adverse cardiovascular events (MACE) was also measured.

Statistical Analysis

Descriptive characteristics are presented as mean ± SD for continuous variables and n (%) for categorical variables; differences were tested using *t* tests for continuous variables and χ^2 tests for categorical variables. Propensity score matching was used to reduce the effect of treatment selection bias. This was done by generating a logistic regression model with age, sex, race, body mass index, smoking status, lung disease, diabetes, dialysis, hypertension, hyperlipidemia, liver disease, cancer, peripheral artery disease, cerebrovascular disease, heart failure, myocardial infarction, prior PCI, cardiac presentation, left ventricular ejection fraction, creatinine, number of diseased vessels, and completeness of revascularization as independent variables and estimating the propensity score of receiving PCI for each patient. PCI-treated patients were then matched 1:1 to CABG-treated patients by using nearest-neighbor matching with a caliper distance of 0.05 in the propensity score. Appropriateness of the match was validated by comparing the descriptive characteristics again in the matched cohort. Differences between groups for the time-to-event outcomes (survival, readmission, repeat revascularization, and composite MACE) are presented using Kaplan-Meier curves and Cox proportional-hazards regression to compare PCI with CABG. No multivariable adjustment was performed because the propensity score–matched cohort purposefully removed known baseline differences between the groups. All statistical analyses were performed using SAS software version 9.4 (SAS Institute, Cary, NC).

Results

Study Cohort

There were 6,163 patients with MVCAD who met eligibility criteria: 1,460 in the PCI group and 4,703 in the CABG group. The propensity-matched cohort included 844 in each group. Table 1 shows the baseline data for the propensity score–matched cohorts. Supplemental Table 1 shows the baseline data for the entire cohort. The remainder of the results are based on the propensity score–matched populations.

The populations were well matched. The mean age was 67.4 ± 11.1 years, with 30.3% female. There were no significant differences in race or body mass index, major risk factors, or cardiac presentation. Mean left ventricular function was 49.4%. Nearly two thirds of the population had three-vessel CAD and approximately one third had two-vessel MVCAD, and the differences in the PCI and CABG groups were small but statistically significant. The stents used represented the most currently used DES, predominantly driven by everolimus-eluting stents in 66% of patients and zotarolimus-eluting stents in 30%. Within the CABG population, 96% had a left internal mammary graft, and 12% had only arterial grafts used.

Table 1. Baseline Characteristics and Revascularization Strategy for Propensity-Matched Cohort

Characteristics	Total (N = 1,688)	PCI (n = 844)	CABG (n = 844)	*p* Value
Age, years	67.4 ± 11.1	67.5 ± 12.0	67.2 ± 10.3	0.519
Sex				0.427
Male	1,177 (69.7)	596 (70.6)	581 (68.8)	
Female	511 (30.3)	248 (29.4)	263 (31.2)	
Race				0.641
White	1,531 (90.7)	766 (90.8)	765 (90.6)	
Black	101 (6.0)	53 (6.3)	48 (5.7)	
Other	56 (3.3)	25 (3.0)	31 (3.7)	
Body mass index, kg/m^2	30.3 ± 6.09	30.2 ± 6.20	30.3 ± 5.99	0.574
Body surface area, m^2	2.00 ± 0.25	2.00 ± 0.25	2.00 ± 0.24	0.787
Current smoker	355 (21.0)	182 (21.6)	173 (20.5)	0.591
Chronic lung disease	320 (19.0)	166 (19.7)	154 (18.2)	0.456
Diabetes	800 (47.4)	397 (47.0)	403 (47.7)	0.770
Dialysis	67 (4.0)	35 (4.1)	32 (3.8)	0.708
Hypertension	1,478 (87.6)	742 (87.9)	736 (87.2)	0.658
Hyperlipidemia	1,457 (86.3)	733 (86.8)	724 (85.8)	0.524
Prior liver disease	85 (5.0)	38 (4.5)	47 (5.6)	0.317
Prior cancer	288 (17.1)	149 (17.7)	139 (16.5)	0.518
Prior PAD	316 (18.7)	161 (19.1)	155 (18.4)	0.708
Prior CVD	343 (20.3)	181 (21.4)	162 (19.2)	0.250
Prior heart failure	276 (16.4)	135 (16.0)	141 (16.7)	0.693
Prior myocardial infarction	765 (45.3)	371 (44.0)	394 (46.7)	0.261
Prior PCI	635 (37.6)	324 (38.4)	311 (36.8)	0.514
Cardiac presentation				<0.001
No symptoms or angina	235 (13.9)	117 (13.9)	118 (14.0)	
Symptoms unlikely ischemic	20 (1.2)	11 (1.3)	9 (1.1)	
Stable angina	238 (14.1)	119 (14.1)	119 (14.1)	
Unstable angina	697 (41.3)	355 (42.1)	342 (40.5)	
Non-STEMI	469 (27.8)	242 (28.7)	227 (26.9)	
Angina equivalent	7 (0.4)	0 (0.0)	7 (0.8)	
Other	22 (1.3)	0 (0.0)	22 (2.6)	
Left ventricular ejection fraction, %	49.4 ± 13.2	49.7 ± 12.7	49.0 ± 13.7	0.275
Creatinine, mg/dL	1.30 ± 1.33	1.33 ± 1.40	1.27 ± 1.25	0.335
Glomerular filtration rate, mL/min/1.73 m^2	68.9 ± 26.7	68.6 ± 27.8	69.3 ± 25.5	0.565
Number of diseased vessels				<0.001
1	23 (1.4)	0 (0.0)	23 (2.7)	
2	602 (35.7)	309 (36.6)	293 (34.7)	
3	1,052 (62.3)	530 (62.8)	522 (61.8)	
Unknown	11 (0.7)	5 (0.6)	6 (0.7)	
Complete revascularization	750 (44.4)	367 (43.5)	383 (45.4)	0.433

Values are mean ± SD or n (%).

CABG = coronary artery bypass graft; CVD = cardiovascular disease; PAD = peripheral arterial disease; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

Complete revascularization was included in the propensity-matched model and was not different between the PCI and CABG groups.

Survival Analysis

The mean follow-up duration was 2.84 ± 1.84 years and 2.45 ± 1.67 years in the PCI and CABG groups, respectively. Figure 1 shows the Kaplan-Meier curve for 5-year freedom from mortality. The estimated 30-day mortality was 2.3% and 2.5% ($p = 0.75$) in the PCI and CABG groups, respectively. The estimated 1-year mortality was 11.5% and 7.2% ($p < 0.001$) in the PCI and CABG groups, respectively. The overall hazard ratio for mortality with PCI versus CABG was 1.64 (95% confidence interval [CI], 1.29 to 2.10; $p < 0.001$). Supplemental Figure 1 shows the Kaplan-Meier curve for the entire cohort and reveals no major differences in comparison with the propensity-matched cohort results.

Freedom From Readmission

Figure 2A shows the Kaplan-Meier curve for 5-year freedom from any readmission. Overall, there were 437

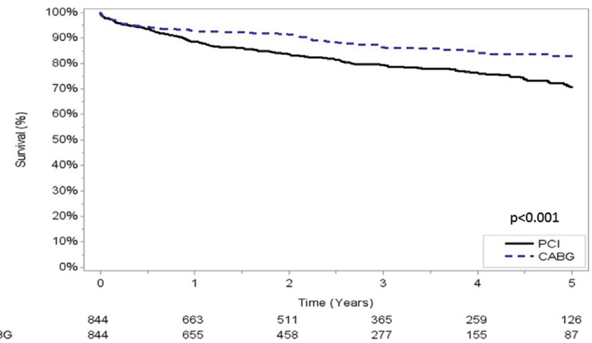


Fig 1. *Survival in patients with multivessel coronary artery disease after percutaneous coronary intervention (PCI) versus coronary artery bypass graft (CABG) in a propensity-matched cohort.*

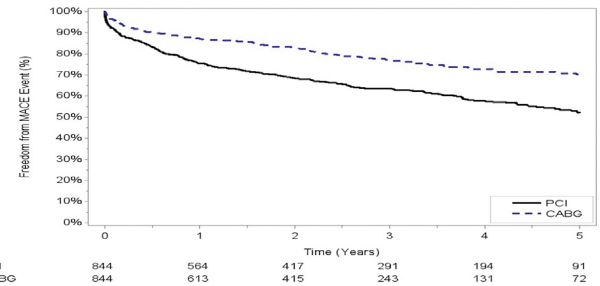


Fig 3. *Freedom from major adverse cardiovascular events (MACE; mortality, myocardial infarction, stroke, repeat revascularization) in patients with multivessel coronary artery disease in a propensity-matched cohort. (CABG = coronary artery bypass graft; PCI = percutaneous coronary intervention.)*

unique patients with inpatient readmissions in the PCI group and 315 in the CABG group over the 5-year follow-up. The estimated 1-year readmission rates were 38.4% and 28.1% ($p < 0.001$) in the PCI and CABG groups, respectively. The hazard ratio for readmission for PCI versus CABG was 1.42 (95% CI, 1.23 to 1.64; $p < 0.001$). Supplemental Figure 2A shows the Kaplan-Meier curve for the entire cohort and reveals no major differences. A total of 52.8% of all readmissions in the PCI group were cardiac readmissions compared with 33.6% within the CABG group.

Freedom From Repeat Revascularization

Figure 2B shows the Kaplan-Meier curve for 5-year freedom from repeat revascularization. Overall, there were 69 events for repeat revascularization in the PCI group and 17 in the CABG group over the 5-year follow-up. The estimated 1-year repeat revascularization rates were 6.7% and 1.0% ($p < 0.001$) in the PCI and CABG groups, respectively. The hazard ratio for repeat revascularization for PCI versus CABG was 4.06 (95% CI, 2.39 to 6.91; $p < 0.001$). Supplemental Figure 2B shows the Kaplan-Meier curve for the entire cohort and the findings are similar.

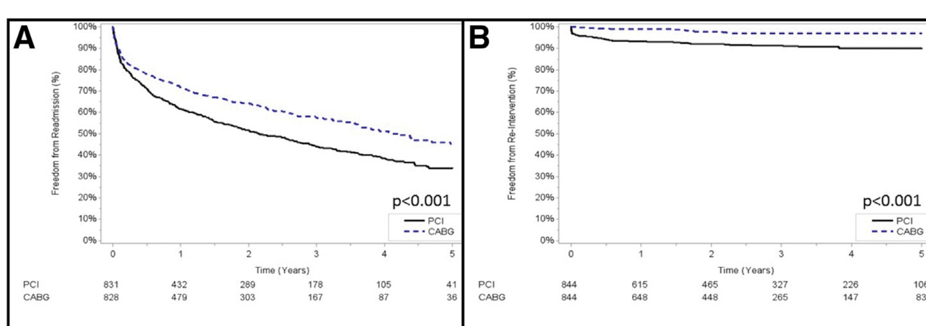
Subgroup Analysis

Figure 3 illustrates the Kaplan-Meier curve for 5-year freedom from MACE, and Figure 4 shows the association between the procedure and overall MACE by subgroups. CABG is consistently favored over PCI for overall MACE. The adjusted subgroup analyses for the overall population (non–propensity-matched) are shown in Supplemental Figures 3 to 5 for the outcomes of mortality, readmission, and repeat revascularization, respectively. CABG was favored for all these individual outcomes over PCI in virtually every subgroup.

Comment

This contemporary propensity-matched analysis of patients undergoing revascularization for MVCAD demonstrates a significant mortality benefit with CABG over PCI across virtually all major patient subgroups. These results are consistent with those of the ASCERT study, which also used data from the STS and NCDR registries [16]. Our results add to the ASCERT study in that ASCERT evaluated outcomes in the early days of DES (2004 to 2008), included only patients 65 years of age and older, and excluded patients with myocardial infarction. The overall 5-year mortality rates are similar. Another observational study from New York State also showed that patients treated with CABG had significantly lower adjusted mortality rates than patients treated with first-generation DES [29]. The current study therefore suggests that the benefits of CABG persist over PCI for patients with MVCAD in the more contemporary DES era. In addition, the current study illustrates that the benefit of CABG over PCI in this population is also reflected by the

Fig 2. *In patients with multivessel coronary artery disease after percutaneous coronary intervention (PCI) versus coronary artery bypass graft (CABG) in a propensity-matched cohort, (A) freedom from readmission and (B) freedom from repeat revascularization.*



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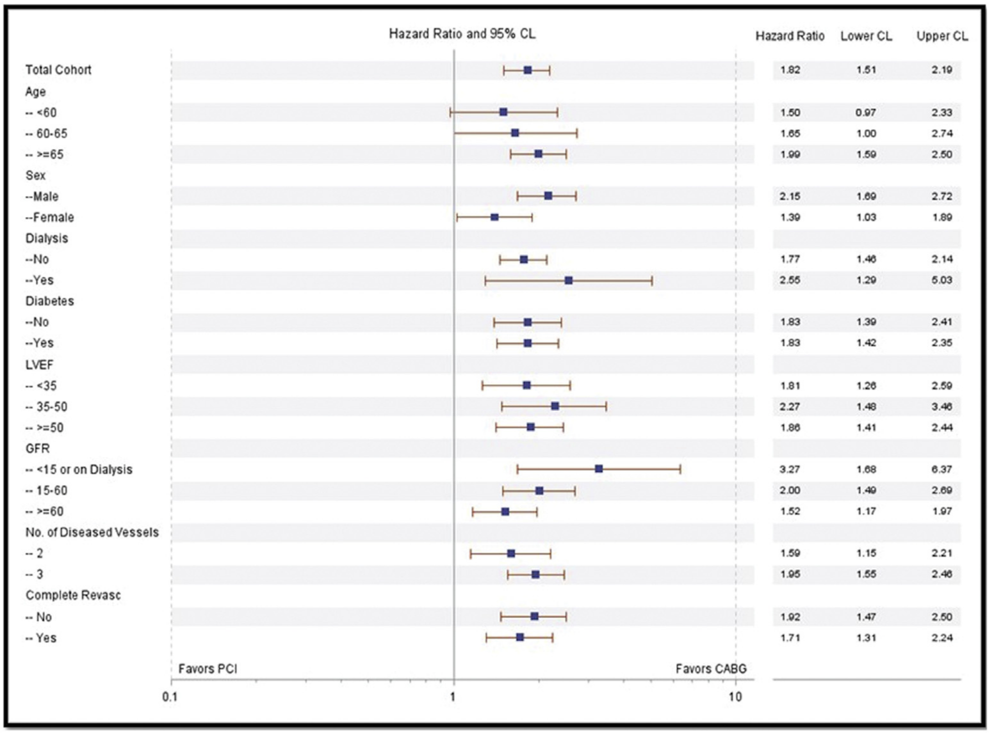

Fig 4. Hazard ratio for major adverse cardiovascular events in patients undergoing percutaneous coronary intervention (PCI) versus coronary artery bypass graft (CABG) across various subgroups in propensity-matched cohort. (CL = confidence limits; GFR = glomerular filtration rate; LVEF = left ventricular ejection fraction.)

lower risk for subsequent revascularization and hospital readmission in the CABG population.

These results from our real-world, contemporary analysis should be contrasted with data from randomized clinical trials. In a recent pooled analysis of 11 randomized trials comparing CABG with PCI, 5-year all-cause mortality was significantly lower after CABG in patients with diabetes but not in those without diabetes [21]. Certainly, several studies have demonstrated the benefit of CABG revascularization over PCI among patients with diabetes, and CABG should be considered the definitive therapy of choice in this important subgroup [30]. However, it is notable that the mortality rates in those trials are lower than the rates observed in our study and other observational studies [16]. The 5-year mortality rates for PCI and CABG from randomized clinical trials are 11.2% and 9.2% [21], respectively, compared with our study, which had 5-year mortality rates of 28% and 18%, respectively, for PCI and CABG. However, in other observational studies, the mortality rates after revascularization have varied [31]. These data suggest that the population of patients in contemporary practice who are undergoing revascularization with MVCAD is different from those participants in randomized trials. For instance, in the SYNergy Between PCI With TAXUS and Cardiac Surgery (SYNTAX) trial, patients were younger, with fewer comorbid conditions [3, 6]. Moreover, our analysis adds to prior studies because it includes 25% to 30% of patients with non–ST-elevation myocardial infarction. This may be an important distinction that contributes to the differing mortality rates.

The shift from CABG to PCI for coronary revascularization has been well established over the last 2 decades [9]. Much of this shift is entirely appropriate, with the dramatic improvements in stents. However, observational and randomized studies of contemporary practice, such as the present analysis, beg the question whether CABG should be more highly considered in the presence of MVCAD regardless of the presence or absence of diabetes or left ventricular dysfunction [20]. In addition, a meta-analysis from the SYNTAX and Randomized Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients with Multivessel Coronary Artery Disease (BEST) trials showed the superiority of CABG over PCI among nondiabetic patients with intermediate or high SYNTAX scores [32].

To navigate the complex issues in decision making for MVCAD, guidelines assign a class IC recommendation for the use of a collaborative heart team approach in the treatment of patients with complex CAD [26]. Nonetheless, the practical and consistent use of the heart team for decision making in MVCAD is lacking [33, 34]. We and others have demonstrated the practical feasibility of a coronary revascularization heart team [33], and, given how significantly the revascularization strategy may affect outcomes, use of the heart team should be considered in all patients with MVCAD according to guidelines. Future studies are needed to formally assess the magnitude of benefit of a heart team approach in revascularization.

Our analysis has limitations. It is an observational study, and, as such, although our propensity matching strategy resulted in well-balanced groups, there remains the potential for unmeasured confounders to have influenced the findings. Although we had considerable data on CAD severity, we acknowledge that the choice of revascularization may have been based on certain angiographic and clinical findings that were not measured or collected, such as chronic total occlusions, presence of extensive coronary calcification, or frailty. For instance, our group has previously shown that patients with high SYNTAX scores are often referred for PCI over CABG after heart team discussion out of frailty concerns [35], but in other cases CABG may have been favored because of the presence of diffuse CAD. Overall, although certain factors may have affected survival negatively in PCI-treated patients, other confounders may have affected survival in CABG-treated patients negatively as well. Further analyses will need to be performed to verify whether our findings are consistent with more complete revascularization, whether by CABG or by PCI. Nonetheless, this issue only further emphasizes the importance of a formal heart team to help with decision making in these patients. Futures studies are needed in contemporary populations that reflect routine practice to assess how best to approach shared decision making and informed consent when it comes to revascularization decisions in any patient with MVCAD.

In conclusion, our findings of contemporary practice demonstrate a significant mortality benefit with CABG over PCI in MVCAD that extends across virtually all major patient subgroups. Our results, if supported by others, strongly advocate for the use of a revascularization heart team to help patients and providers make the best clinical decisions.

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