

# Long-term Outcomes of Percutaneous Coronary Intervention in Patients with Prior Coronary Artery Bypass Grafting

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## ABSTRACT

**Background:** Patients with a prior coronary artery bypass graft (CABG) may have a need for repeat revascularization, which is typically attempted first via percutaneous coronary intervention (PCI) of either a bypass graft or native vessel. Long-term outcomes of native vessel compared with graft PCI after CABG have not yet been explored in a large institution study.

**Methods:** Patients with history of prior CABG who underwent PCI at our institution between 2010-2018 were included. Baseline characteristics and long-term outcomes of up to 5 years were compared between native vessel and bypass graft PCI groups. Cox regression was used to adjust for significant covariates in estimation of risk and calculation of hazard ratios.

**Results:** During the study, 4,251 patients with a prior CABG underwent PCI. Native vessel PCI represented 67.1% ( $N = 2,851$ ) of the cohort. After adjusting for significant covariates, bypass graft PCI compared with native vessel PCI had a higher risk of overall mortality (HR 1.15; 95% CI, 1.04-1.29;  $P < 0.05$ ), all-cause readmission (HR 1.16; 95% CI, 1.1-1.3;  $P < 0.05$ ), readmission for PCI (HR 1.25; 95% CI, 1.13-1.38;  $P < 0.05$ ), readmission for heart failure (HR 1.16; 95% CI, 1.06-1.26;  $P < 0.05$ ), and composite of myocardial infarction and revascularization (HR 1.23; 95% CI, 1.12-1.35;  $P < 0.05$ ).

**Conclusions:** Among patients with prior CABG, bypass graft PCI compared to native vessel PCI was associated with higher risk of adverse long-term outcomes.

## INTRODUCTION

Patients with a prior history of coronary artery bypass grafting (CABG) experience rising rates of graft failure over time, resulting in an eventual need for repeat revascularization [Bianco 2021]. Often, this revascularization is first attempted via percutaneous coronary intervention (PCI) of either a saphenous vein graft (SVG) or a native coronary artery. Some data support PCI of the native vessel over SVG, due to lower associated risk of procedural complications and adverse outcomes [Varghese 2009; Xanthopoulou 2011; Welsh 2010; Brilakis 2011; Bundhoo 2011; Brilakis 2016; Mavroudis 2017; Mulukutla 2019]. Despite this, there is not yet a consensus on the favored form of repeat revascularization, and long-term outcomes of these interventions have not been well evaluated. The aim of this study was to compare long-term outcomes in patients with a history of a prior CABG undergoing PCI of either a native vessel (NV) or SVG, with a focus on mortality, readmissions, and repeat revascularization.

## METHODS

**Study population:** This was a retrospective, observational study that included all patients with a history of prior CABG who underwent PCI at the University of Pittsburgh Medical Center from 2010 to 2018. PCI patients retrospectively were identified from the NCDR CathPCI Registry [Moussa 2013]. It is important to note that this cohort does not represent the reinvention rate for first-time CABG procedures at our institution. Our experience has been published elsewhere, showing good outcomes and a low reintervention rate [Hess 2022; Bianco 2020; Aranda-Michel 2021]. Patients were divided into two groups, by the target vessel of intervention, either NV ( $N = 2,851$ ) or SVG ( $N = 1,335$ ). Interventions of an arterial graft (e.g., left internal mammary artery or radial artery graft,  $N = 65$ ) were included and combined into the SVG group ( $N = 1,400$ ). Patients who underwent PCI of multiple vessels were included, however, patients receiving PCI to both an NV and a bypass graft during the index procedure were excluded. Patients presenting with ST-elevation myocardial infarction and cardiogenic shock were both included, as well as PCI of chronic total occlusions. The majority of our study population received 2nd generation drug eluting stents

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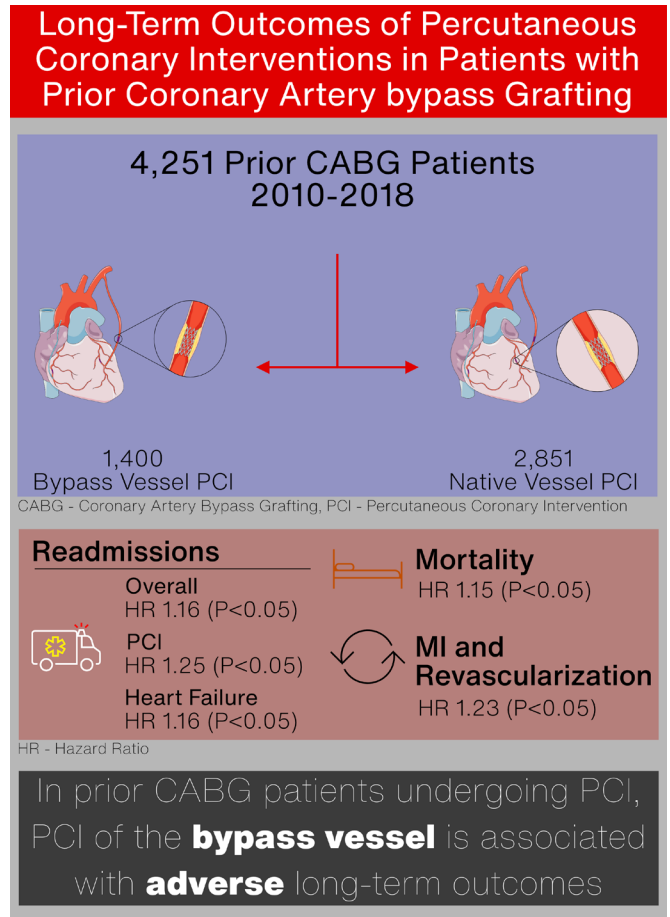
and guideline-directed medical therapy upon discharge. The decision to perform PCI of either an NV or SVG was determined by the interventionalist during the index PCI. Demographics, co-morbid conditions, hospitalization, procedural, and follow-up data all were collected from a systemwide database that included a total of 40 in-system hospitals. The institutional review board approved the use of the data for this study and patient consent was waived due to the anonymized and retrospective use of the data.

**Outcome assessment:** The primary outcome was all-cause mortality. Secondary outcomes included all-cause hospital readmission, readmission for PCI of another target lesion, composite readmission for cardiovascular disease (CVD) or heart failure, and composite readmission for myocardial infarction or repeat revascularization of the same target lesion. Mortality was determined by a combination of social security disability insurance and medical records. Diagnoses and procedures associated with admissions were determined by their respective International Statistical Classification of Disease and Current Procedural Terminology codes acquired from the electronic medical record. Specific diagnoses for cardiac readmissions include, but were not limited to valvular disease, myocardial infarction, heart failure, endocarditis, myocarditis, and cardiac dysrhythmias. Outcomes were stratified by occurrence within 30 days, 1 year, and 5 years of the index PCI.

**Statistical analysis:** Descriptive statistics were presented as mean ± standard deviation for continuous variables and frequency percentage for categorical variables. Unadjusted variables and outcomes were compared using the Anova test and the Chi-square test. Small P-values ( $P < 0.05$ ) indicate statically significant differences between the groups. The primary outcomes were generated on a Kaplan-Meier curve and compared using the log-rank test for 30 days, 1 year, and 5 years. Separate multivariable Cox proportional hazard regression was used for risk-adjusted models to compare outcomes between the two groups.

## RESULTS

**Baseline characteristics:** During the study period, a total of 4,251 patients with prior CABG received PCI. (Graphical Abstract and Figure 1) Of those patients, 2,851 (67.1%) had PCI of a native coronary artery, and 1,400 (32.9%) had PCI of either a saphenous vein or arterial bypass graft. The majority of patients in both groups had a CABG to PCI period of ≥10 years, and there were 24 patients who did not have prior a CABG date available. All patients were followed for up to 5 years. Patient demographics, co-morbid conditions, indication for PCI, years from CABG to PCI, immediate procedural outcomes, and discharge medications are summarized in Table 1. (Table 1) The median age for the NV and SVG groups were 70.0 and 72.1 years, respectively. Compared with patients receiving PCI of an NV, patients undergoing PCI of an SVG were older, less likely to have hypertension and chronic lung disease, and more likely to have a prior MI. Patients in the SVG group were less likely to present with



Graphical Abstract and Figure 1. In prior CABG patients, PCI of the graft vessel is associated with worse long-term outcomes.

stable angina, and more likely to present with unstable angina, NSTEMI, and STEMI. An embolic protection device was utilized in 35% of SVG PCIs. In the NV group, there was a greater amount of complex lesions and a lower rate of the left internal mammary artery to left anterior descending artery graft stenosis.

**Clinical outcomes:** On cumulative incidence analysis, mortality was similar between the SVG and native cohorts at 30 days (3.14% vs. 3.14%,  $P = 0.46$ ) (Supplemental Figure 1) and at 1 year (10.86% vs. 9.05%,  $P = 0.06$ ) (Supplemental Figure 2). (Supplemental Figure 1) (Supplemental Figure 2) However, there was a statistically higher rate of mortality in the SVG group at 5 years (32.0% vs. 26.0%,  $P < 0.001$ ) (Figure 2 and Table 2). (Figure 2) (Table 2) For all-cause readmission, there was no statistical difference at 30 days (10.4% vs. 9.22%,  $P = 0.24$ ). (Supplemental Figure 3) However, the SVG group had a statistically higher rate of all cause readmission at the 1-year (40.1% vs. 34.2%,  $P < 0.001$ ) (Supplemental Figure 4) and 5-year (66.8% vs. 60.5%,  $P < 0.001$ ) (Figure 3) time points. (Supplemental Figure 4) (Figure 3) PCI specific readmissions were similar between the SVG and native cohorts at 30 days (7.36% vs. 8.24%,  $P = 0.30$ ) (Supplemental Figure 5) and at 1 year (22.6% vs. 20.7%,  $P = 0.18$ )

Table 1. Comparison of Baseline Patient Characteristics Between Native Vessel and Bypass Graft Percutaneous Coronary Intervention

	Native (N = 2851)	SVG (N = 1400)	P-value
Age (years)	70.01 ( $\pm$ 10.2)	72.1 (9.89)	<0.000
BMI (kg/m <sup>2</sup> )	30.2 ( $\pm$ 5.98)	29.9 ( $\pm$ 8.72)	0.2114
Female	23.64%	21.29%	0.085
Smoker	15.03%	15.12%	0.8234
Hypertension	95.33%	93.21%	0.00039
Diabetes	48.9%	48.64%	0.8771
Chronic Lung Disease	23.01%	20.50%	0.0642
Dyslipidemia	94.6%	93.86%	0.325
Prior MI	53.17%	57.93%	0.0034
Prior HF	23.92%	25.50%	0.260
Prior PCI	67.73%	64.93%	0.444
Prior Atrial Fibrillation	14.28%	14.86%	0.6125
Prior Malignancy	17.75%	17.93%	0.8851
Current Dialysis	4.45%	4.57%	0.8628
Cardiogenic Shock	1.58%	1.36%	0.5895
Years from CABG to PCI	-	-	<0.0001
≤1	4.52%	1.55%	
1-5	11.34%	2.33%	
5-10	14.00%	5.34%	
≥10	37.21%	23.71%	
CAD Presentation & Symptoms	-	-	<0.0001
No angina	8.19%	3.01%	
Atypical angina	1.81%	0.80%	
Stable angina	15.62%	18.5%	
Unstable angina	26.51%	36.93%	
NSTEMI	12.80%	27.14%	
STEMI	2.14%	5.86%	
Number of stents implanted	-	-	<0.0001
0	10.72%	6.37%	
1	31.84%	18.28%	
2	15.55%	5.67%	
3	5.74%	2.26%	
4	2.28%	0.43%	
5 or more	0.65%	0.21%	
DES type	-	-	<0.0001
First Generation	3.86%	2.36%	
Second Generation	83.20%	79.93%	
ACE Inhibitor	44.18%	44.86%	0.59
Beta Blocker	89.63%	90.34%	0.66
Statin	91.75%	91.41%	0.40
Aspirin	97.49%	97.30%	0.89
Antiplatelet agent	-	-	0.023

Clopidogrel	86.51%	82.99%	
Prasugrel	6.21%	7.33%	
Ticagrelor	7.24%	9.60%	
Ticlopidine	0.04%	0.08%	
CTO	6.17%	1.78%	<0.0001
Segment Thrombus	6.88%	26.61%	<0.0001
Lesion Length (mm)	16 (10-26)	16 (12-28)	<0.0001
Lesion Complexity	-	-	<0.0001
High	37.50%	21.92%	
Low	29.57%	11.01%	
LIMA-LAD stenosis	22.8 (±40.6)	35.0 (±44.5)	<0.0000

Values are median (standard deviation) or %. ACE, angiotensin converting enzyme; BMI, body mass index; CABG, coronary artery bypass graft; CAD, coronary artery disease; CTO, chronic total occlusion; DES, drug eluting stent; HF, heart failure; LAD, left anterior descending; LIMA, left internal mammary artery; MI, myocardial infarction; NSTEMI, non-ST elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST elevation myocardial infarction; SVG, saphenous vein graft

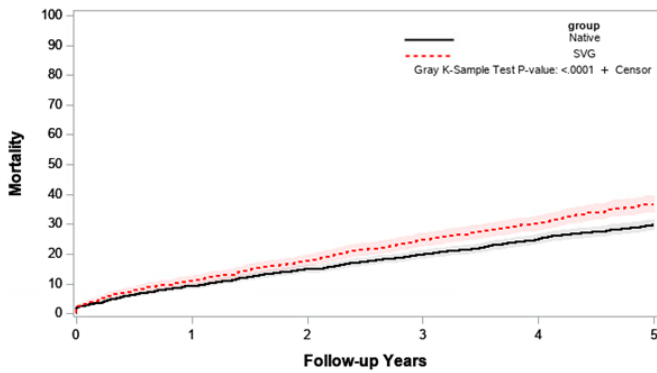


Figure 2. Cumulative incidence of mortality at 5 years. Mortality in % of total group. SVG, saphenous vein graft

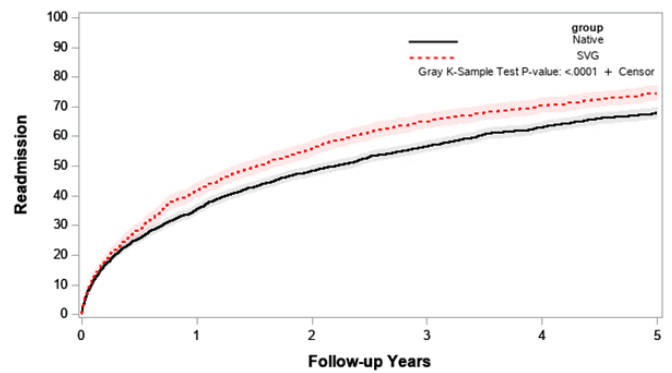


Figure 3. Cumulative incidence of readmission at 5 years. Readmission in % of total group. SVG, saphenous vein graft

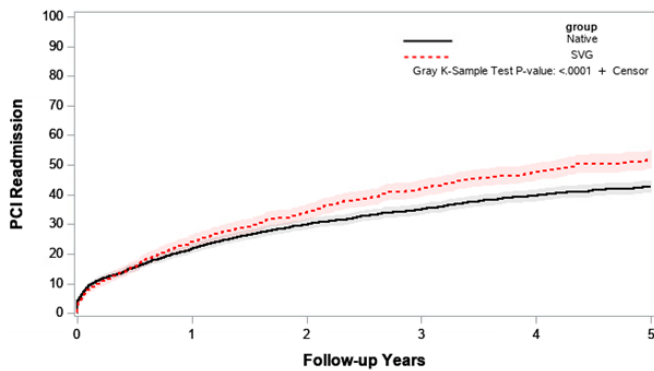


Figure 4. Cumulative incidence of PCI readmission at 5 years. Readmission in % of total group. PCI, percutaneous coronary intervention; SVG, saphenous vein graft

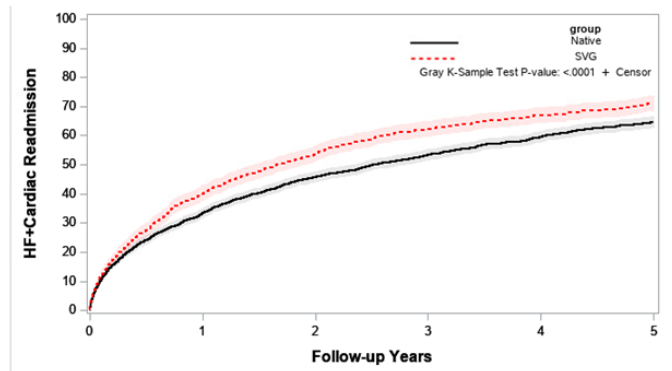


Figure 5. Cumulative incidence of HF and cardiac readmission at 5 years. Readmission in % of total group. HF, heart failure; SVG, saphenous vein graft

(Supplemental Figure 6) follow up. (Supplemental Figure 5) (Supplemental Figure 6) The SVG cohort had a statistically higher rate of PCI readmission at 5 years (42.3% vs. 36.1%,  $P < 0.001$ ). (Figure 4) The composite endpoint of CVD and

heart failure readmission was similar between cohorts at 30 days ( $P = 0.16$ ). (Supplemental Figure 7) This end point was statistically higher in the SVG cohort at 1 year ( $P < 0.001$ ) (Supplemental Figure 8) and 5 years (63.1% vs. 57.0%,  $P <$

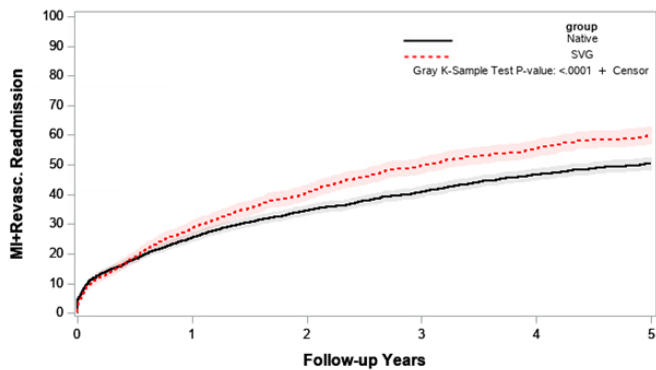
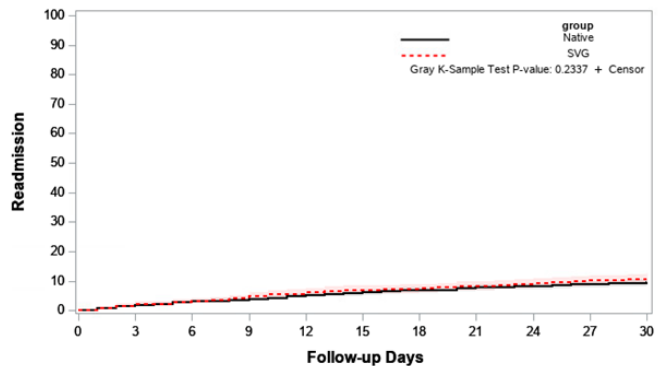
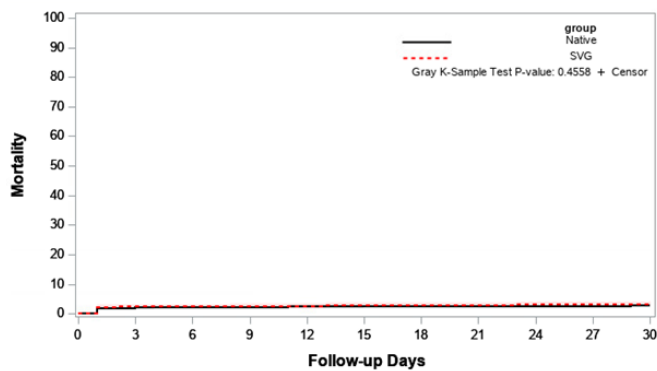


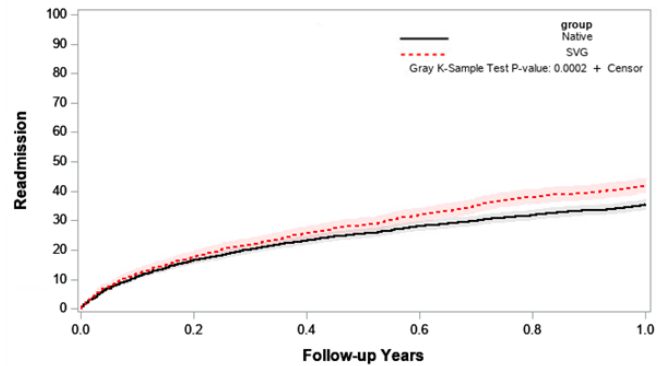
Figure 6. Cumulative incidence of MI and revascularization readmission at 5 years. Readmission in % of the total group. MI, myocardial infarction; SVG, saphenous vein graft



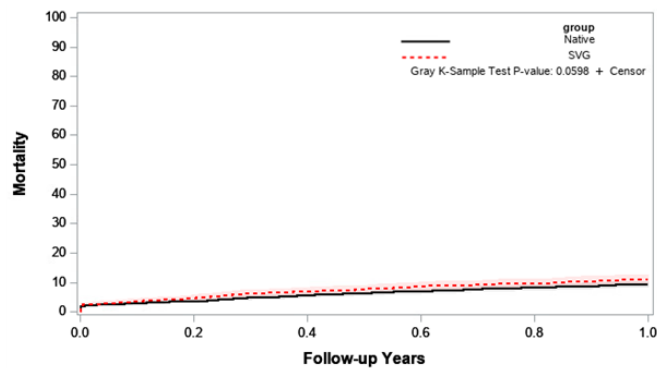
Supplemental Figure 3. Cumulative incidence of readmission at 30 days. Readmission in % of the total group. SVG, saphenous vein graft



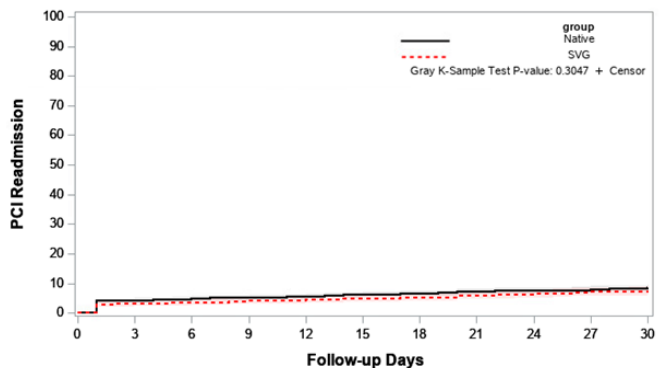
Supplemental Figure 1. Cumulative incidence of mortality at 30 days. Mortality in % of the total group. SVG, saphenous vein graft



Supplemental Figure 4. Cumulative incidence of readmission at 1 year. Readmission in % of the total group. SVG, saphenous vein graft



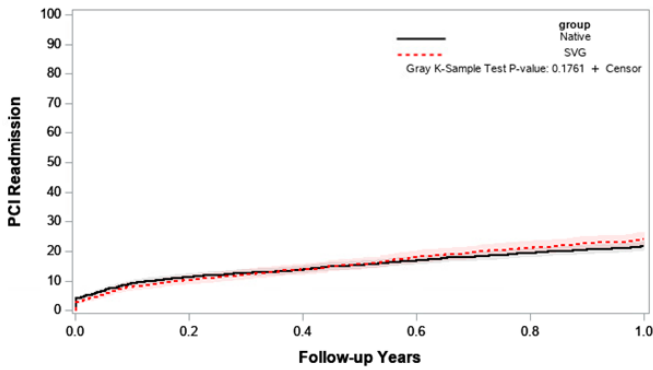
Supplemental Figure 2. Cumulative incidence of mortality at 1 year. Mortality in % of the total group. SVG, saphenous vein graft



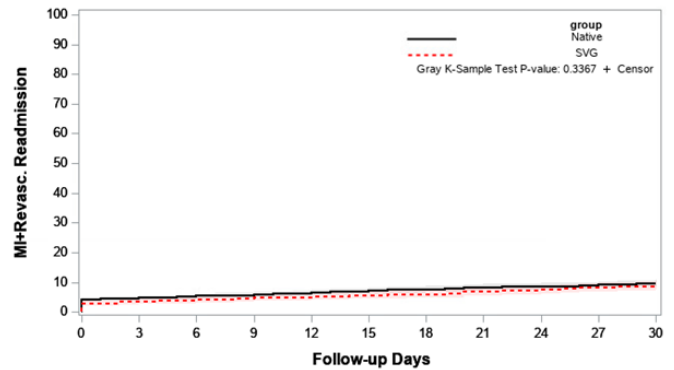
Supplemental Figure 5. Cumulative incidence of PCI readmission at 30 days. Readmission in % of the total group. PCI, percutaneous coronary intervention; SVG, saphenous vein graft

0.001). (Supplemental Figure 8) (Figure 5) Need for repeat revascularization was similar between cohorts at the 30-day ( $P = 0.34$ ) (Supplemental Figure 9) and 1-year ( $P = 0.06$ ) (Supplemental Figure 10) time points. (Supplemental Figure 9) (Supplemental Figure 10) The SVG cohort had a statistically higher rate of repeat revascularization at 5 years (50.2% vs. 42.8%,  $P < 0.001$ ). (Figure 6)

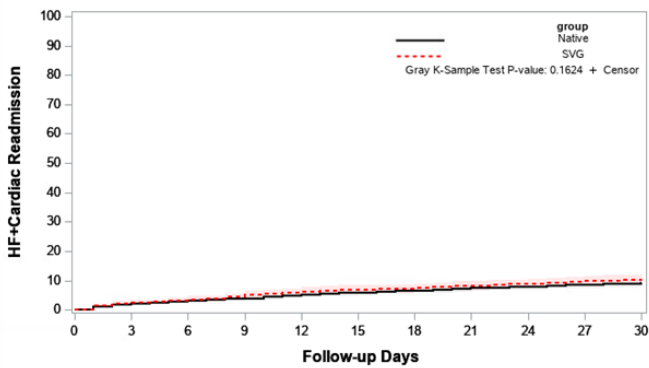
On Cox regression analysis, after adjusting for significant covariates, patients who received PCI of SVG compared to PCI of a NV were associated with higher rates of mortality (HR 1.15; 95% CI, 1.04-1.29;  $P = 0.01$ , Table 3), all-cause readmissions (HR 1.16; 95% CI, 1.1-1.3;  $P = 0.0005$ , Table 4), readmissions for PCI of another lesion (HR 1.25; 95% CI, 1.13-1.38;  $P < 0.0001$ ) (Supplemental Table 1), composite



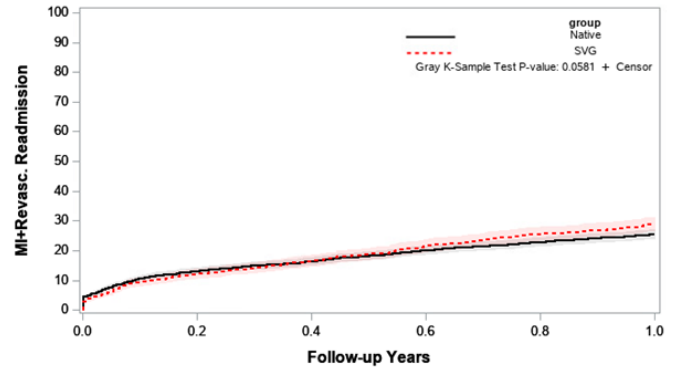
Supplemental Figure 6. Cumulative incidence of PCI readmission at 1 year. Readmission in % of the total group. PCI, percutaneous coronary intervention; SVG, saphenous vein graft



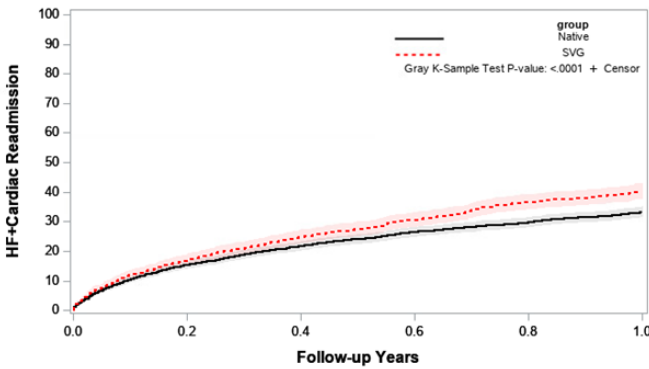
Supplemental Figure 9. Cumulative incidence of MI and revascularization readmission at 30-days. Readmission in % of the total group. MI, myocardial infarction; SVG, saphenous vein graft



Supplemental Figure 7. Cumulative incidence of HF and cardiac readmission at 30 days. Readmission in % of the total group. HF, heart failure; SVG, saphenous vein graft



Supplemental Figure 10. Cumulative incidence of MI and revascularization readmission at 1-year. Readmission in % of the total group. MI, myocardial infarction; SVG, saphenous vein graft



Supplemental Figure 8. Cumulative incidence of HF and cardiac readmission at 1 year. Readmission in % of the total group. HF, heart failure; SVG, saphenous vein graft

CVD and heart failure readmissions (HR 1.16; 95% CI, 1.06-1.26;  $P < 0.0001$ ) (Supplemental Table 2), and composite MI and repeat revascularization readmissions (HR 1.23; 95% CI, 1.12-1.35;  $P < 0.0001$ ) (Supplemental Table 3). (Table 3) (Table 4) (Supplemental Table 1) (Supplemental Table 2) (Supplemental Table 3)

## CONCLUSION

In a multi-hospital observational study at our institution, we found that among a large population of patients with a history of prior CABG, PCI of a bypass graft compared with PCI of a native coronary artery was associated with a higher long-term risk of mortality, revascularization, and readmissions for PCI and heart failure. After adjusting for significant covariates, such as patient demographics, cardiovascular comorbidities, clinical presentation, and time from CABG to PCI, our primary outcomes were all significant 5 years after index PCI. The findings from this study add to the current breadth of data available that primarily favors native vessel PCI over bypass graft PCI due to higher rates of adverse long-term outcomes [Xanthopoulos 2011; Brilakis 2016; Mavroudis 2017].

Among patients with a history of prior CABG, our data shows that the rate of SVG occlusion increase yearly, rising as high as 50% after 1-year post-CABG (Figure 6). When patients present with graft failure, treatment strategies include medical therapy, PCI, and redo CABG [Brilakis 2014; Aranda-Michel 2020]. According to the 2011 American College of Cardiology Foundation/American Heart Association/



Table 2. Comparison of Outcome Incidence Between Native Vessel and Bypass Graft Percutaneous Coronary Intervention

Outcomes	Native	SVG	P-value
<b>Mortality</b>			
5 years	26.03%	32%	0.000
1 year	9.05%	10.86%	0.06
30 days	2.74%	3.14%	0.45
<b>Readmission</b>			
5 years	60.47%	66.79%	0.0001
1 year	34.2%	40.14%	0.0001
30 days	9.22%	10.36%	0.2388
<b>PCI Readmission</b>			
5 years	36.06%	42.29%	0.000
1 year	20.73%	22.57%	0.1683
30 days	8.24%	7.36%	0.3158
<b>CVD &amp; HF Readmission</b>			
5 years	56.96%	63.14%	0.0001
1 year	32.13%	38.50%	0.000
30 days	8.91%	10.21%	0.1693
<b>MI Readmission + Revascularization</b>			
5 years	42.76%	50.21%	0.000
1 year	24.34%	27.21%	0.04
30 days	9.44%	8.57%	0.3586

Values are %. CVD, cardiovascular disease; other abbreviations as in Table 1.

Society for Cardiovascular Angiography and Interventions (ACC/AHA/SCAI) Guidelines, PCI is favored over CABG when there is the limited ischemic area, suitable PCI targets, a patent graft to the LAD, poor CABG targets, and comorbid conditions [Levine 2011]. Additionally, PCI often is preferred, due to the high risk of major adverse cardiovascular events (MACE) associated with redo-CABG procedures [Mavroudis 2017]. The approach to revascularization in patients with a history of prior CABG includes PCI of either a native vessel or surgically implanted bypass graft (SVG or arterial), both associated with clinical and technical challenges for the proceduralist. SVG interventions represent about 6% of all PCIs performed in the U.S. but are also associated with a peri-procedural risk of distal embolization and high rates of re-stenosis at follow-up. Compared with SVGs, arterial grafts have better long-term patency rates, and PCI of arterial grafts carries a lower associated risk of periprocedural complications, despite being a significantly less common procedure. The majority of PCIs performed in prior CABG patients (approximately two-thirds) involve a native coronary artery. Despite native coronary lesions in prior CABG patients often being characterized as calcified, tortuous, and chronic total occlusions (CTO), several studies have shown favorable outcomes comparing PCI of native vessels to PCI of SVGs [Xenogiannis 2019].

In 2011, a retrospective observational study in Greece that included 190 patients with prior CABG receiving PCI of either a graft or native vessel (graft PCI group,  $N = 88$ ) found higher incidence of MACE, cardiac death, and repeat revascularization among the graft PCI group, with a median follow up of 28 months. Additionally, graft PCI was independently associated with higher risk of MACE (HR 2.84; 95% CI, 1.45-5.57;  $P = 0.002$ ) [Xanthopoulou 2011]. Bundhoo et al. retrospectively studied 161 patients with prior CABG undergoing PCI (62.7% native vessel) at two centers in the United Kingdom and found higher incidence of MACE and target vessel revascularization in the graft PCI group, with a mean follow up after PCI of  $13.5 \pm 4.8$  months [Bundhoo 2011]. In a large, national cohort of 11,118 veterans with prior CABG undergoing PCI between 2005 and 2013, Brilakis et al. compared outcomes between PCI of grafts and native vessels (73.4% native vessel) during a median follow up of 3.11 years and found graft PCI to have significantly higher rates of mortality, MI, and repeat revascularization [Brilakis 2016]. In the prospective, multi-center ADAPT-DES study (Assessment of Dual Antiplatelet Therapy with Drug-Eluting Stents), the outcomes of 8,582 subjects with prior CABG undergoing PCI (4.7% SVG PCI) were compared, and SVG PCI was associated with a higher 2-year risk of MACE, ischemia-driven target vessel revascularization, and stent thrombosis [Redfors

Table 3. Hazard Ratio for Mortality

	HR	CI	P-value
SVG*	1.30	(1.17-1.45)	<0.0001
SVG*†	1.15	(1.04-1.29)	0.01

\*Reference: Native Vessel. †Adjusted for age, gender, race, BMI, diabetes, current dialysis, hypertension, chronic lung disease, prior valve surgery, prior malignancy, prior HF, prior atrial fibrillation, CAD presentation and symptoms, years from CABG to PCI. CI, confidence interval; HR, hazard ratio; other abbreviations as in Table 1.

Table 4. Hazard Ratio for Readmission

	HR	CI	P-value
SVG*	1.19	(1.1-1.29)	<0.0001
SVG*†	1.16	(1.1-1.30)	0.0005

\*Reference: Native Vessel. †Adjusted for age, gender, race, BMI, diabetes, current dialysis, hypertension, chronic lung disease, prior valve surgery, prior malignancy, prior HF, prior atrial fibrillation, CAD presentation and symptoms, years from CABG to PCI. Abbreviations as in Tables 1 and 3.

2017]. Comparatively, an observational study in China by Liu et al. of 157 diabetic patients with prior CABG undergoing PCI (native vessel group, N = 113), found no significant difference in the incidence of MACE, cardiac death, MI, or revascularization between the two groups, during a median follow up of 45±18 months [Liu 2019].

To our knowledge, our study is one of the largest of its kind to evaluate and show a significant difference in long-term outcomes with 2,700 (63.5%) patients reaching the 5-year follow-up mark, and the remaining 1,551 participants having a mean follow up of 41±10.4 months. Our findings were consistent with the majority of prior studies of similar design and study populations [Xanthopoulou 2011; Bundhoo 2011; Brilakis 2016; Mavroutis 2017; Redfors 2017]. Of note, there was no significant difference in early post-PCI incidence of mortality between SVG and native vessel groups (30 days and 1 year), which is also consistent with findings from a recent observational study of 18,369 prior CABG patients presenting with NSTEMI for PCI [Shoaib 2018]. As forementioned, SVG PCI is associated with high rates of restenosis at follow up [Xenogiannis 2019], and current guidelines recommend against revascularization of chronic SVG lesions (Class III, level of evidence C) [Levine 2011], thus, greatly limiting therapeutic options and significantly increasing mortality rates. PCI of native coronary lesions in prior CABG patients present their own challenges, however, with new-age advanced PCI techniques for access and atherectomy, the feasibility of these procedures is improving among this population and becoming preferred by operators [Xenogiannis 2019]. The results from our study further support the decision to pursue

PCI of a native coronary artery over a bypass graft, when revascularization is indicated and feasible, due to favorable long-term outcomes among this large population of patients with a history of prior CABG. As a consideration, future areas of study should include direct comparisons between CTO PCI vs. SVG PCI and also PCIs grouped by their respective epicardial coronary territory.

**Limitations:** Our study consists of several limitations. This was not a randomized control trial, thus, allowing for limitations of traditional observational retrospective studies. Despite adjusting for several significant covariates, this study is subject to a degree of selection bias. Although this study was conducted in a single medical system, procedures were performed by many different clinicians at several hospitals in our network, thus, PCI results and decision of target vessel will vary. Additionally, there is a chance of unmeasured confounders that could have affected hospitalizations and follow-up outcomes. The SVG cohort had a larger presentation of STEMI/NSTEMI compared with the native vessel cohort. This could affect long-term outcomes, despite a similar 30-day and 1-year survival, biasing results [Bianco 2021]. Additionally, a total of 1551 patients (36.4% of study population) did not reach the 5-year follow-up mark, decreasing the power of our long-term outcomes. Compared with the amount of SVG patients, the total of included arterial graft patients who underwent PCI was near negligible at <5%. Lastly, we could not adjust for medication adherence, or improvement of comorbidities over time, such as better control of hypertension, diabetes, weight loss, etc.

## CONCLUSIONS

In a large, retrospective observational study of prior CABG patients in our multi-hospital medical system, compared with PCI of a native vessel, PCI of bypass grafts are associated with higher risk of long-term mortality, readmissions, and revascularization. This data further supports the preference to perform PCI of a native coronary artery over a bypass graft, when feasible, in prior CABG patients presenting with indication for revascularization.

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