ABSTRACT

OBJECTIVES The aim of this study was to examine the frequency, associations, and outcomes of native coronary artery versus bypass graft percutaneous coronary intervention (PCI) in patients with prior coronary artery bypass grafting (CABG) in the Veterans Affairs (VA) integrated health care system.

BACKGROUND Patients with prior CABG surgery often undergo PCI, but the association between PCI target vessel and short- and long-term outcomes has received limited study.

METHODS A national cohort of 11,118 veterans with prior CABG who underwent PCI between October 2005 and September 2013 at 67 VA hospitals was examined, and the outcomes of patients who underwent native coronary versus bypass graft PCI were compared. Logistic regression with generalized estimating equations was used to adjust for correlation between patients within hospitals. Cox regressions were modeled for each outcome to determine the variables with significant hazard ratios (HRs).

RESULTS During the study period, patients with prior CABG represented 18.5% of all patients undergoing PCI (11,118 of 60,171). The PCI target vessel was a native coronary artery in 73.4% and a bypass graft in 26.6%: 25.0% in a saphenous vein graft and 1.5% in an arterial graft. Compared with patients undergoing native coronary artery PCI, those undergoing bypass graft PCI had higher risk characteristics and more procedure-related complications. During a median follow-up period of 3.11 years, bypass graft PCI was associated with significantly higher mortality (adjusted HR: 1.30; 95% confidence interval: 1.18 to 1.42), myocardial infarction (adjusted HR: 1.61; 95% confidence interval: 1.43 to 1.82), and repeat revascularization (adjusted HR: 1.60; 95% confidence interval: 1.50 to 1.71).

CONCLUSIONS In a national cohort of veterans, almost three-quarters of PCIs performed in patients with prior CABG involved native coronary artery lesions. Compared with native coronary artery PCI, bypass graft PCI was significantly associated with higher incidence of short- and long-term major adverse events, including more than double the rate of in-hospital mortality. (J Am Coll Cardiol Intv 2016;9:884–93) © 2016 by the American College of Cardiology Foundation.
It is widely believed that native coronary arteries should be the preferred target of percutaneous coronary intervention (PCI) in patients with prior coronary artery bypass graft (CABG) surgery, if technically feasible, because native coronary artery PCI appears to be associated with better short- and long-term outcomes compared with bypass graft PCI. However, there are limited data to substantiate this belief (1-6).

We previously reported that patients with prior CABG undergoing PCI between 2004 and 2009 in the National Cardiovascular Data Registry (NCDR) CathPCI Registry represented 17.5% of the total PCI volume (300,902 of 1,721,046) during that period (7). The PCI target was a native coronary artery in 62.5% and a bypass graft in 37.5%: saphenous vein graft (SVG) (104,678 [34.9%]), arterial graft (7,517 [2.5%]), or both arterial graft and SVG (718 [0.2%]). Compared with patients undergoing native coronary artery PCI, those undergoing bypass graft PCI had higher risk characteristics and more procedural complications (7). However, clinical practice has evolved since, and prior analyses were limited to periprocedural and inhospital outcomes, which are known to be worse in patients who undergo bypass graft interventions. The impact of target vessel on long-term outcomes has received limited study (3,4,6).

The goals of the present study were to: 1) determine the frequency of prior CABG among veterans undergoing PCI in the Veterans Affairs (VA) system; 2) examine the target vessel (native coronary artery vs. SVG vs. arterial graft) in those patients; and 3) compare the immediate post-procedural and long-term outcomes after PCI in native coronary arteries versus coronary bypass grafts.

METHODS

STUDY DESIGN, SETTING, AND POPULATION. We performed a retrospective study of a national cohort of post-CABG veterans who underwent PCI at 67 VA PCI centers from October 1, 2005, through September 30, 2013. For patients who underwent multiple procedures during the study period, the first PCI was defined as the index procedure, and outcomes were assessed through September 30, 2014.

DATA SOURCE. The VA Clinical Assessment, Reporting, and Tracking (CART) program is a national clinical quality improvement program among VA

From the 1VA North Texas Healthcare System and University of Texas Southwestern Medical Center, Dallas, Texas; 2VA Eastern Colorado Health Care System, Denver, Colorado; 3University of Colorado, Denver Anschutz Medical Campus, Aurora, Colorado; 4Colorado Cardiovascular Outcomes Research Consortium, Denver, Colorado; 5San Diego VA Healthcare System, San Diego, California; 6Durham VA Medical Center and Duke University, Durham, North Carolina; 7Minneapolis VA Healthcare System and University of Minnesota, Minneapolis, Minnesota; 8University of Michigan, Ann Arbor, Michigan; 9San Francisco VA Medical Center and University of California, San Francisco, San Francisco, California; 10Atlanta VA Medical Center and Emory University, Atlanta, Georgia; and the 1VA Boston Healthcare System, Brigham and Women’s Hospital, and Harvard Medical School, Boston, Massachusetts. Dr. Brilakis has received consulting and speaking honoraria from Abbott Vascular, Asahi, Boston Scientific, Elsevier, Somahlution, St. Jude Medical, and Terumo; and has received research support from InfraRedx and Boston Scientific; and his spouse is an employee of Medtronic. Dr. Garcia is a recipient of a career development award (1IK2CX00699-01) from the VA Office of Research and Development. Dr. Garcia is a consultant for Surmodics. Dr. Rao is a consultant for Medtronic. Dr. Armstrong is a consultant for Abbott Vascular, Medtronic, Merck, and Spectranetics. Dr. Bhatt is a member of the advisory boards of Cardax, Elsevier Practice Update Cardiology, Medscape Cardiology, and Regado Biosciences; is a member of the boards of directors of the Boston VA Research Institute, the Society of Cardiovascular Patient Care; is chair of the American Heart Association Get With the Guidelines Steering Committee; is a member of the data monitoring committees of the Duke Clinical Research Institute, the Harvard Clinical Research Institute, the Mayo Clinic, and the Population Health Research Institute; has received honoraria from the American College of Cardiology (senior associate editor, Clinical Trials and News, ACC.org), Belvoir Publications (editor-in-chief, Harvard Heart Letter), the Duke Clinical Research Institute (clinical trial steering committees), the Harvard Clinical Research Institute (clinical trial steering committee), HMP Communications (editor-in-chief, Journal of Invasive Cardiology), the Journal of the American College of Cardiology (guest editor, associate editor), the Population Health Research Institute (clinical trial steering committee), Slack Publications (chief medical editor, Cardiology Today’s Intervention), WebMD (continuing medical education steering committees); is deputy editor of Clinical Cardiology; has received research funding from Amarin, AstraZeneca, Bristol-Myers Squibb, Eisai, Ethicon, Forest Laboratories, Ischemia, Medtronic, Pfizer, Roche, Sanoﬁ, and The Medicines Company; is a site co-investigator for Biotronik and St. Jude Medical; is a trustee of the American College of Cardiology; and has conducted unfunded research for FlowCo, PLX Pharma, and Takeda. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. The views expressed in this paper are those of the authors and do not necessarily reﬂect the position or policy of the U.S. Department of Veterans Affairs or the U.S. government.

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catheterization laboratories (8). It uses a software application for medical record documentation of key patient and procedural data for all procedures conducted at the VA catheterization laboratories nationwide. The software is embedded within the VA electronic health record, allowing linkage to longitudinal outcome data. Moreover, it is also linked to fee-based data to account for veterans who receive non-VA care. CART data elements are standardized according to the American College of Cardiology’s NCDR CathPCI Registry (9). A dedicated staff provides continuous monitoring, maintenance, and updating of the application. Quality checks of CART data are periodically conducted for completeness and accuracy. Additional details of CART and the validity, completeness, and timeliness of the CART data have been previously described (10).

**EXPOSURE VARIABLE.** The primary exposure variable of interest was the PCI target vessel during index PCI. Patients were divided between those undergoing native coronary artery versus bypass graft PCI. Patients undergoing PCI of both a native coronary artery and a bypass graft were considered to be part of the bypass graft PCI group. First-generation drug-eluting stents (DES) were defined as paclitaxel-eluting or sirolimus-eluting stents, and second-generation DES were defined as everolimus-eluting or zotarolimus-eluting stents.

**OUTCOME ASSESSMENT.** Outcomes assessed included both short-term (procedure-related in-laboratory complications) and long-term (mortality, myocardial infarction [MI], revascularization) outcomes:

1. Procedure-related in-laboratory complications: We assessed the incidence of death, periprocedural

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**FIGURE 1** Outline of Patient and Lesion Selection for the Present Study

![Diagram](image1.png)

CABG = coronary artery bypass grafting; CART = Clinical Assessment, Reporting, and Tracking; PCI = percutaneous coronary intervention; SVG = saphenous vein graft.

**TABLE 1** Number of Patients Within Time Intervals Where Date of Coronary Artery Bypass Graft Surgery Was Known, Classified According to Type of Vessel Treated

<table>
<thead>
<tr>
<th>Time Interval</th>
<th>Native Coronary Artery PCI</th>
<th>Bypass graft PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–1 yr Post-CABG</td>
<td>266 (67.9%)</td>
<td>126 (32.1%)</td>
</tr>
<tr>
<td>1–5 yrs Post-CABG</td>
<td>892 (65.3%)</td>
<td>473 (34.7%)</td>
</tr>
<tr>
<td>5–10 yrs Post-CABG</td>
<td>611 (63.5%)</td>
<td>351 (36.5%)</td>
</tr>
<tr>
<td>&gt;10 yrs Post-CABG</td>
<td>834 (60.2%)</td>
<td>551 (39.8%)</td>
</tr>
</tbody>
</table>

Values are n (%). The date of prior CABG was available for 4,104 patients (37.0% of the cohort). CABG = coronary artery bypass graft surgery; PCI = percutaneous coronary intervention.
MI, no-reflow, dissection, perforation, and acute target vessel closure. The treating physician directly entered this information into CART as a discrete data elements (10).

2. MI: We used the VA national patient care database to assess the occurrence and timing of MI hospitalizations that were on the basis of validated inpatient primary International Classification of Diseases, Ninth Revision, discharge diagnosis codes (10). A random sample of patients with MI also underwent individual chart review to validate this outcome in accordance with the third universal definition of MI (11). Codes for MI hospitalizations during the first 14 days after PCI discharge date were subsequently disregarded because a review of cases showed that most of these codes were related to the index hospitalization.

3. All-cause mortality: The VA vital status file was used to assess mortality outcome. This file has 98.3% sensitivity and 97.6% exact agreement with dates compared with the National Death Index (12).

4. Repeat revascularization: The VA national database was queried for cases of revascularization. Revascularization was defined by the identification of repeat PCI (from CART data or administrative procedure codes) or CABG (from administrative procedure codes) in the data following the index PCI (or final visit of a staged set of PCIs) that was used in the analysis.

STATISTICAL ANALYSIS. Comparison of baseline characteristics and in-laboratory complications between the native coronary and bypass graft PCI groups was performed using Fisher exact tests for each categorical or dichotomous variable and Mann-Whitney-Wilcoxon nonparametric tests for continuous variables. Generalized estimating equation logistic regression was used to examine parameters associated with performing native coronary PCI. Cox regression models with stent type and target vessel type as predictors and a random-effects term for hospital (frailty) were used to estimate hazard ratios for variables of interest that may affect outcomes. Adjustment was performed for 48 covariates, including baseline patient characteristics and pharmacology regimens (Online Table 1). Log-minus-log plots of survival, \( \ln(-\ln(S)) \), were produced to evaluate the proportional hazards assumption between treated vessel type. We used the product-limit method to determine Kaplan-Meier curves for event-free survival and compared the 2 groups using the log-rank test.

For all analyses reported, \( p \) values are 2-sided, and \( p \) values <0.05 were considered to indicate statistical significance. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina). The Institutional Review Board at the VA Eastern Colorado Health Care System approved this study.

RESULTS

PATIENT POPULATION. During the study period, a total of 74,027 PCIs were performed in 60,171 patients nationwide in the VA health care system, of whom 11,118 (18.5%) were prior CABG patients (22 patients who underwent PCI to both a SVG and an arterial graft were excluded) (Figure 1). A total of 16,440 lesions were treated in patients with prior CABG and were located as follows: native coronary artery (n = 12,073 [73.4%]), SVG (n = 4,114 [25.0%]), and arterial graft (n = 253 [1.5%]). The proportion of PCIs performed on bypass grafts relative to native vessels increased as a function of time elapsed after CABG (Table 1, Figure 2).

BASELINE CHARACTERISTICS. The patient characteristics, procedural indications, and procedural outcomes are summarized in Table 2. The median age was 65.5 years (IQR: 61.0 to 73.3 years), 99% were men, and 84% were white. Compared with patients
TABLE 2  Comparison of Baseline Patient Characteristics of Patients With Prior Coronary Bypass Graft Surgery Undergoing Percutaneous Coronary Artery Intervention Classified According to the Treated Vessel

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Native Only (n = 7,469)</th>
<th>Bypass Grafts (n = 3,346)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>65 (61-72)</td>
<td>67 (62-75)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Men</td>
<td>99%</td>
<td>99%</td>
<td>0.03</td>
</tr>
<tr>
<td>White race</td>
<td>84%</td>
<td>85%</td>
<td>0.11</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>95%</td>
<td>96%</td>
<td>0.02</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>96%</td>
<td>96%</td>
<td>0.24</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>54%</td>
<td>58%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ever smoked</td>
<td>60%</td>
<td>56%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior MI</td>
<td>50%</td>
<td>50%</td>
<td>0.626</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>53%</td>
<td>47%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>33%</td>
<td>35%</td>
<td>0.06</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>11%</td>
<td>11%</td>
<td>1.00</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>29%</td>
<td>32%</td>
<td>0.002</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>21%</td>
<td>24%</td>
<td>0.007</td>
</tr>
<tr>
<td>Dialysis</td>
<td>3%</td>
<td>3%</td>
<td>0.802</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>26%</td>
<td>23%</td>
<td>0.001</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>30 (27-34)</td>
<td>30 (26-33)</td>
<td>0.011</td>
</tr>
<tr>
<td>Depression</td>
<td>36%</td>
<td>33%</td>
<td>0.004</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>22%</td>
<td>19%</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Laboratory tests

| Total cholesterol (mg/dl) | 155 (134-181) | 156 (135-185) | 0.042 |
| LDL cholesterol (mg/dl)  | 85 (68-106)   | 85 (68-108)   | 0.253 |
| HDL cholesterol (mg/dl)  | 36 (31-43)    | 36 (31-42)    | <0.001 |
| G1omerular filtration rate (ml/min/1.73 m²) | 71 (59-87) | 69 (56-84) | <0.001 |

Presentation

| Symptoms | <0.001 |
| Stable angina | 36% | 24% |
| ACS: unstable angina | 28% | 28% |
| ACS: NSTEMI | 16% | 28% |
| ACS: STEMI | 3%  | 5%  |
| Other | 5%  | 5%  | 0.221 |

Years from CABG to PCI | 2.17 (0.81-4.24) | 2.29 (0.67-5.58) | 0.091 |

Values are median (interquartile range) or %.

ACS = acute coronary syndrome(s); HDL = high-density lipoprotein; LDL = low-density lipoprotein; MI = myocardial infarction; NSTEMI = non-ST-segment elevation acute myocardial infarction; STEMI = ST-segment elevation acute myocardial infarction; other abbreviations as in Table 1.

who underwent native coronary artery PCI, those who underwent bypass graft PCI were older, more likely to have diabetes mellitus and chronic kidney disease, and more likely to have depression and obstructive sleep apnea. High-density lipoprotein cholesterol was low (median <40 mg/dl) in all patient groups. Patients who underwent native coronary artery PCI were more likely to present with stable angina and less likely to present with acute coronary syndromes.

On multivariate logistic generalized estimating equation analysis several other parameters were
associated with bypass graft PCI (odds ratio [OR] >1 is more likely to receive graft bypass PCI), including right coronary artery stenosis >70% (OR: 0.09; 95% confidence interval [CI]: 0.07 to 0.13), left main stenosis >50% (OR: 0.07; 95% CI: 0.04 to 0.12), pre-PCI TIMI (Thrombolysis In Myocardial Infarction) grade 3 flow (OR: 0.77; 95% CI: 0.65 to 0.90), high-risk lesion (OR: 2.11; 95% CI: 1.74 to 2.55), diabetes (OR: 1.14; 95% CI: 1.03 to 1.26), presentation with ST-segment elevation acute MI (OR: 1.62; 95% CI: 1.24 to 2.11), and glomerular filtration rate (OR: 0.98; 95% CI: 0.97 to 0.99 per 5-U increase).

PROCEDURAL CHARACTERISTICS. Table 3 describes baseline procedural characteristics in the 2 study groups. Compared with patients who underwent bypass graft PCI, those who underwent native coronary artery PCI were more likely to undergo PCI of a chronic total occlusion, to have TIMI flow grade 3 both before and after PCI, and to receive glycoprotein IIb/IIIa inhibitors but less likely to receive an intracoronary balloon pump. Most bypass graft target lesions were located at the body of the graft. An embolic protection device was used in 26.3% of SVG PCIs. Most patients (77.8%) received at least 1 DES, whereas 19.6% received at least 1 bare-metal stent. Bypass graft PCI patients were less likely to receive DES relative to native vessel PCI patients (65% vs. 72%; p < 0.01).

CLINICAL OUTCOMES. Procedure-related in-laboratory complications. All reported procedure-related in-laboratory complications are presented in Table 4. Patients undergoing bypass graft PCI had higher in-hospital mortality (1.79% vs. 0.83%; adjusted OR: 6.6; 95% CI: 0.7-60.0; p < 0.001), procedural complications (OR: 0.4; 95% CI: 0.3-0.7), presentation with high-risk flow (OR: 0.77; 95% CI: 0.65 to 0.90), diabetes (OR: 0.94% vs. 0.13%, adjusted OR: 2.1; 95% CI: 0.6 to 7.0), and cardiogenic shock (OR: 0.36% vs. 0.3%; adjusted OR: 7.0; 95% CI: 4.8 to 10.3), periprocedural MI (OR: 1.00% vs. 0.36%; adjusted OR: 2.3; 95% CI: 1.1 to 4.7), and cardiogenic shock (OR: 0.36% vs. 0.13%, adjusted OR: 2.1; 95% CI: 0.6 to 7.0), though lower risk for coronary dissection (0.94% vs. 2.08%; adjusted OR: 0.4; 95% CI: 0.3 to 0.7).

FOLLOW-UP OUTCOMES. Outcomes, including the composite outcomes (death, MI, and revascularization), occurred in fewer than 50% of patients during the follow-up period. The median follow-up duration was 3.11 years. During the first year post-PCI, the overall incidence rates of death, MI, and coronary revascularization were 6.7%, 4.3%, and 22.8%, respectively, increasing to 14.4%, 8.6%, and 31.3%, respectively, at 3 years and to 19.4%, 10.2%, and 33.7% at 5 years (Table 5, Figure 3). The incidence of adverse events was higher during the early post-PCI period and subsequently decreased (Figure 3).
hazard ratio: 1.61; 95% CI: 1.43 to 1.82), and repeat revascularization (adjusted hazard ratio: 1.60; 95% CI: 1.50 to 1.71) (Table 5, Figure 3).

**DISCUSSION**

To the best of our knowledge, this is the largest study performed to date examining the long-term outcomes of patients with prior CABG who underwent bypass graft versus native coronary artery PCI. Bypass graft PCI was significantly less frequent than native coronary artery PCI, was performed in patients who had more comorbidities, and was independently associated with worse acute and long-term outcomes.

In our study, approximately 1 in 5 patients (18.5%) undergoing PCI between 2005 and 2013 within the VA system had prior CABG, which is similar to the
proportion observed in the NCDR between 2004 and 2009 (17.5%) (7). There was a higher percentage of a native vessel as the PCI target in the present study compared with the NCDR (73.4% vs. 62.5%), but bypass grafts were more likely to be the PCI target vessel with increasing time after CABG in both cohorts, consistent with the accelerated pace of late SVG failure (13,14). Nearly all target bypass grafts were SVGs, a reflection of the excellent outcomes achieved with use of the internal mammary arteries as conduits (13).

In the present study, patients who underwent bypass graft rather than native coronary PCI were older, had more comorbidities, and were more likely to receive bare-metal stents, which may in part explain the worse clinical outcomes in this patient group. Although statistical adjustment may be imperfect in retrospective studies, our multivariate analyses confirmed that bypass graft (essentially SVG) PCI was significantly associated with worse outcomes. SVG lesions are often degenerated, complex lesions that may predispose to distal embolization. Indeed, SVG PCI was associated with higher risk for no-reflow and periprocedural MI in our study, even though embolic protection devices are used more commonly in the VA system (38%) (15) compared with general practice, as reported by the NC DR (22%) (16,17). Similar findings were reported in prior studies (3), including in patients with ST-segment elevation acute MI: in the APEX-AMI (Assessment of Pexelizumab in Acute Myocardial Infarction) trial in patients with prior CABG who presented with ST-segment elevation MI, TIMI flow grade 3 was achieved less often in bypass grafts (67% vs. 88%), and bypass graft PCI patients had higher 90-day mortality (19% vs. 5.7%) compared with native artery PCI patients (5).

Even with use of DES (14) (including second-generation DES) (18), repeat revascularization is higher after SVG compared with native coronary artery PCI (Figure 3), likely because of higher rates of inflammation and thrombus formation (19). Moreover, intermediate SVG lesions have high rates of progression and failure (20,21), leading to increased need for repeat revascularization (4). Rates of MI were also higher among patients undergoing SVG PCI in our study, which could reflect the increased likelihood of SVG stent failure to present as an acute coronary syndrome or as complete occlusion (22). Patients who underwent SVG PCI were less likely to receive DES, which could be due to safety concerns (higher mortality was observed with DES in the RRIS C [Reduction of Restenosis in Saphenous vein grafts With Cypher sirolimus-Eluting Stent] trial [23] but not in subsequent studies [24,25]) and more comorbidities, potentially raising concerns about the feasibility of long-term dual-antiplatelet therapy in these patients.

Our study is the largest of its kind performed to date on long-term outcomes after PCI of native versus bypass graft PCI in patients with prior CABG. An NC DR analysis of 300,902 patients with prior CABG who underwent PCI between 2004 and 2009 showed that bypass graft PCI was associated with higher in-hospital mortality (adjusted OR: 1.22; 95% CI: 1.12 to 1.32) (7). Similar findings were observed by Bundhoo et al. (4), who demonstrated 3-fold higher target vessel revascularization with SVG versus native coronary PCI (15% vs. 4.9%; p = 0.031) and by Xanthopoulou et al. (6), although outcomes were similar in a study by Varghese et al. (3).

The improved short- and long-term outcomes observed suggest that native coronary arteries should be the preferred PCI target vessels for patients with prior CABG, whenever possible. Although it is not known if the advantage of native coronary PCI will be affected if the native lesions selected are of higher complexity than in this study, contemporary PCI equipment and techniques (26) have increased the rate of successful revascularization for complex lesions, such as chronic total occlusions (27,28). Use of femoral access may facilitate such procedures, compared with radial access (29).

STUDY LIMITATIONS. First, it was an observational retrospective study and not a prospective randomized-controlled trial and hence was subject to all the limitations of observational studies. Second, the choice of PCI target was at discretion of the operator, and the clinical characteristics of the 2 groups of patients were significantly different. Although multivariate analyses were performed, there remains a possibility that unmeasured confounders accounted for some of the variability in inhospital outcomes after native coronary artery or bypass graft PCI. Third, there was no core laboratory assessment of patients’ angiograms and composite assessments of the coronary anatomy. Fourth, most included patients were men, limiting extrapolation to women, although most patients with prior CABG are men. Women have smaller diameter coronary arteries and as a result could have higher restenosis and repeat revascularization rates. Fifth, some veterans may not have had all follow-up evaluations and procedures performed within the VA system, potentially leading to underestimation of their risk for subsequent events. Sixth, underreporting of embolic protection device use and of some complications might
have occurred, although this would be unlikely for severe complications, such as perforation. Seventh, the use of embolic protection devices was relatively low (26.3%), yet it was higher than in the NCDR (21.2%) (30). Potential reasons for the low frequency of embolic protection use include cost, technical complexity, limited familiarity with use of those devices, inability to protect certain (such as distal anastomotic lesions) with currently available devices, and skepticism about their benefits, especially when other embolization prevention strategies, such as vasodilator administration and stent undersizing, are used (31).

**CONCLUSIONS**

Bypass graft PCI was significantly less frequent than native coronary artery PCI in patients with prior CABG, was performed in patients who had more comorbidities, and was associated with 30% higher mortality, 61% higher risk for MI, and 60% higher risk of comorbidities, and was associated with 30% higher risk for repeat revascularization during long-term follow-up. Until randomized clinical trials are performed comparing PCI in bypass grafts with native target vessels, native coronary arteries remain the target vessel of choice, when they are amenable to PCI.

**REFERENCES**


KEY WORDS bypass graft, coronary bypass graft surgery, percutaneous coronary intervention

APPENDIX For a supplemental table, please see the online version of this article.