Three-Year Outcomes Associated With Embolic Protection in Saphenous Vein Graft Intervention
Results in 49,325 Senior Patients in the Medicare-Linked National Cardiovascular Data Registry CathPCI Registry

J. Matthew Brennan, MD, MPH; Wesam Al-Hejily, MD; David Dai, PhD; Richard E. Shaw, PhD; Marina Trilesskaya, MD; Sunil V. Rao, MD; Emmanouil S. Brilakis, MD, PhD; Kevin J. Anstrom, PhD; John C. Messenger, MD; Eric D. Peterson, MD, MPH; Pamela S. Douglas, MD; Michael H. Sketch Jr, MD

**Background**—Information is limited on contemporary use and outcomes of embolic protection devices (EPDs) in saphenous vein graft interventions.

**Methods and Results**—We formed a longitudinal cohort (2005–2009; n=49,325) by linking National Cardiovascular Data Registry CathPCI Registry to Medicare claims to examine the association between EPD use and both procedural and long-term outcomes among seniors (65+ years), adjusting for clinical factors using propensity and instrumental variable methodologies. Prespecified high-risk subgroups included acute coronary syndrome and de novo or graft body lesions. EPDs were used in 21.2% of saphenous vein grafts (median age, 75; 23% women) and were more common in acute coronary syndrome (versus non–acute coronary syndrome; 22% versus 19%), de novo (versus restenotic; 22% versus 14%), and graft body lesions (versus aortic and distal anastomosis; 24% versus 20% versus 8%, respectively). EPDs were associated with a slightly higher incidence of procedural complications, including no reflow (3.9% versus 2.8%; P<0.001), vessel dissection (1.3% versus 1.1%; P=0.05), perforation (0.7% versus 0.4%; P=0.001), and periprocedural myocardial infarction (2.8% versus 1.8%; P<0.001). By 3 years, death, myocardial infarction, and repeat revascularization occurred in 25%, 15%, and 30% of cases, respectively. EPD use was associated with a similar adjusted risk of death (propensity score–matched hazard ratio, 0.96; 95% confidence interval, 0.91–1.02), myocardial infarction (propensity score–matched hazard ratio, 1.00; 95% confidence interval, 0.93–1.09), and repeat revascularization (propensity score–matched hazard ratio, 1.02; 95% confidence interval, 0.96–1.08) in the overall cohort and high-risk subgroups.

**Conclusions**—In this contemporary cohort, EPDs were used more commonly among patients with high-risk clinical indications, yet there was no evidence of improved acute- or long-term outcomes. Further prospective studies are needed to support routine EPD use. *(Circ Cardiovasc Interv. 2015;8:e001403. DOI: 10.1161/CIRCINTERVENTIONS.114.001403.)*

**Key Word:** embolic protection devices

In the early era of saphenous vein graft (SVG) stenting, the periprocedural risk of major adverse clinical event (MACE) was ≈17%, including a 15% risk of periprocedural myocardial infarction (MI). In this setting, the adjunctive use of embolic protection devices (EPDs) significantly reduced the risk of distal embolization, no reflow, and periprocedural MI, thereby leading to a class I (level of evidence B) indication in the most recent American College of Cardiology Foundation/American Heart Association/Society for Cardiovascular Angiography and Interventions coronary intervention guidelines. Despite the advantages of EPDs, these devices can increase the time and complexity of graft interventions and may be associated with an increased risk of distal vessel dissection.

See Editorial by Waksman and Koifman

In the contemporary era, the incidence of both no reflow and periprocedural MI in the setting of SVG intervention has decreased substantially through aggressive preprocedural platelet inhibition and important modifications in both procedural techniques and device characteristics. In this setting, the necessity of embolic protection has been questioned.

© 2015 American Heart Association, Inc.
WHAT IS KNOWN
- Embolic protection devices (EPDs) have been associated with reduced risk of distal embolization, no reflow, and periprocedural myocardial infarction. However, EPDs have not been tested in contemporary practice.
- EPDs may increase the time and complexity of graft interventions and may be associated with an increased risk of distal vessel dissection.

WHAT THE STUDY ADDS
- We found that EPDs were used more commonly among patients with high-risk clinical indications.
- We found no acute- or long-term benefit to routine EPD use in contemporary vein graft percutaneous coronary intervention, despite adjustment for differences in patient characteristics.
- The select use of EPDs in high-risk graft interventions may still be warranted.

a result, the routine use of EPDs is uncommon at most centers in the United States.

In this analysis, we sought to evaluate the safety and effectiveness of EPDs in contemporary practice, using a representative Medicare-linked cohort of patients from National Cardiovascular Data Registry CathPCI Registry. Results were tested in the overall cohort and among important clinical subgroups (eg, by clinical setting, previous lesion treatment, and graft segment), as well as among hospitals with routine EPD use (>50% of SVG percutaneous coronary intervention [PCI] cases) versus no EPD use.

Methods
Study Population
The CathPCI Registry, a joint initiative of the American College of Cardiology Foundation and the Society for Cardiovascular Angiography and Interventions, collects baseline, procedural, and inhospital outcome data of patients undergoing cardiac catheterization from >1000 hospitals in the US. Standardized data definitions that are publicly available (https://www.ncdr.com/webncdr/cathpci/home/datacollection), and the data quality is routinely audited (https://www.ncdr.com/webncdr/cathpci/home/dataquality).

To create a longitudinal study cohort, 92,576 SVG PCI cases were identified among seniors (265 years old) treated at 1048 hospitals participating in the CathPCI Registry (January 2005 to December 2009). We excluded patients who were treated with the Guardwire, Proxis, Percusurge, and TriActiv devices because these devices represented a small minority (<1%) of EPD use in this contemporary practice. We excluded patients who were treated with the Guardwire, Proxis, Percusurge, and TriActiv devices because these devices represented a small minority (<1%) of EPD use in this contemporary practice. We excluded patients who were treated with the Guardwire, Proxis, Percusurge, and TriActiv devices because these devices represented a small minority (<1%) of EPD use in this contemporary practice. We excluded patients who were treated with the Guardwire, Proxis, Percusurge, and TriActiv devices because these devices represented a small minority (<1%) of EPD use in this contemporary practice. We excluded patients who were treated with the Guardwire, Proxis, Percusurge, and TriActiv devices because these devices represented a small minority (<1%) of EPD use in this contemporary practice.

We excluded those without linkage to Medicare records (n=31,540; 34%) and those patients not enrolled in Medicare fee-for-service programs (n=2831). Using the first available CathPCI Registry record as the index admission, 49,325 patients with a Medicare claims linkage (at 1001 hospitals) were identified for inclusion in our final study cohort.

The Duke University Medical Center Institutional Review Board granted a waiver of informed consent and authorization for this study.

Clinical Follow-Up
Inhospital clinical outcomes and adverse events were ascertained using registry records (https://www.ncdr.com/webncdr/cathpci/home/datacollection), whereas death and rehospitalization events (MI and repeat revascularization) were ascertained to 3 years using Medicare denominator and inpatient claims files with the following International Classification of Diseases, Ninth Revision, Clinical Modification codes in the primary position: MI: 410.x1; repeat revascularization: 36.00, 36.06, 36.07, 36.09, and 36.10–36.19.

Statistical Analysis
Baseline patient and procedural characteristics were summarized as counts and percentages for categorical variables and medians (with 25th and 75th percentiles) for continuous variables. Characteristics were stratified by stent type, and differences were compared for categorical variables using the Pearson χ² test or a rank-based group mean score statistic for continuous variables (equivalent to the Kruskal–Wallis test for ≥3-level comparisons and Wilcoxon signed-rank test for 2-level comparisons). Statistical significance was defined as a P value of ≤0.05. All analyses were performed at the Duke Clinical Research Institute using SAS statistical software (version 9.1, SAS Institute, Cary, NC).

Periprocedural adverse events (including no reflow, vessel dissection, perforation, perioperative MI, and inhospital mortality) were compared across treatment groups (EPD versus no EPD) using a logistic regression model for risk adjustment in the overall cohort and in each of the following patient subgroups: (1) clinical presentation (acute coronary syndrome [ACS] versus no ACS), (2) previous lesion treatment (de novo versus in-stent restenosis), and (3) graft segment (aortic anastomosis versus graft body versus distal anastomosis).

Figure 1. Study population. Initial study population (including exclusions) through the final study population of the Medicare-linked National Cardiovascular Data Registry (NCDR) CathPCI Registry saphenous vein graft (SVG) percutaneous coronary intervention (PCI) cohort.
Variables included in the regression model included patient age, sex, race (white, black, and other), body mass index, glomerular filtration rate, smoking history, previous MI, valve surgery, or PCI; history of diabetes mellitus, hypertension, dyslipidemia, congestive heart failure, renal failure, chronic lung disease, coronary artery disease, or peripheral artery disease; New York Heart Association class, ejection fraction, ejection fraction missing, number of diseased vessels, complete total occlusion, PCI status, intra-aortic balloon pump insertion before laboratory visit, time since coronary artery bypass graft surgery (eg, graft age), stent diameter, procedural thrombolysis in MI (TIMI) flow, and percent angiographic stenosis.

The cumulative incidence rates for rehospitalization events were estimated using the Gray–Fine method. In addition, Kaplan–Meier estimates are provided for reference in the Data Supplement. Unadjusted hazard ratio (HR) estimates were calculated using a Cox proportional hazards model. Propensity matching was used to balance observed differences in baseline patient risk. In this case, the propensity score model represented the estimated probability of EPD use, conditioned on the patient-level variables listed above. Propensity score–matched (PM) cohorts were created using the Greedy 5 Digit Matching Algorithm. After PM, the distribution of estimated propensity scores for cases involving EPDs closely matched those for patients without EPDs. Adjusted event rates and HRs comparing each pair of device types were calculated among paired patients who had similar propensity scores. Interactions were formally evaluated in the PM cohort by including an interaction term and indicator variable in the Cox proportional hazards model for clinical presentation, previous lesion treatment, and graft segment (as explained above).

Hospital-Level Treatment Preference Analysis
Because EPDs may be selectively used in higher risk vessels and lesions, the risk for confounding by treatment selection persists despite (1) adjustment for patient comorbidities, clinical status, and graft age and diameter and (2) stratification by clinical presentation, previous lesion treatment, and graft segment. In this sensitivity analysis, we hypothesized that observed (and unobserved) patient and lesion characteristics may be more fully balanced through a comparison of clinical outcomes at hospitals that used EPDs routinely (in ≥50% of SVG PCI cases, high-EPD use hospitals) versus those that do not use EPDs (0% use in SVG PCI cases, no EPD use hospitals). After adjusting for residual differences in case mix, observed differences in clinical outcomes would be expected to reflect either a less biased effect of EPD use or the effect of adjunctive procedural or postprocedural differences in patient care.

To accomplish this analysis, clinical outcomes for patients at high-EPD use hospitals were compared with those at no EPD use hospitals using a Cox proportional hazards model, conditioned on the variables included in the propensity score models (as explained above).

Results
Population Characteristics
During the study interval, 49,325 patients from 1001 hospitals underwent SVG stenting and were linked to Medicare claims, including 10,432 (21%) with EPD use (Figure 1)—a proportion that was stable across the study interval. A minority of hospital centers (n=56 centers; 5.6%) used an EPD in ≥50% of SVG stent cases, and nearly one-third (n=315 centers) used no EPDs for vein graft interventions during this interval (Figure 2). The use of EPDs was higher among ACS versus non-ACS cases (22% versus 19%), de novo versus restenotic lesions (22% versus 14%), and graft body versus aortic anastomosis versus distal graft/anastomosis lesions (24% versus 22% versus 8%).

The median age of this Medicare-linked cohort was 75 years (25th to 75th percentile; interquartile range, 70–80 years); 75% were men and 33% were diabetic (Table 1). The median graft age was 12.2 years (interquartile range, 8.2–16.4) and was similar across EPD and no EPD cases (12.7 versus 12.0 years). Overall, the baseline comorbidities of patients with SVG PCI with adjunctive EPD use were similar to those in whom an EPD was not used (Table 1). Compared with no EPD cases, those involving EPD use occurred more often in the setting of non–ST-segment–elevation MI or high-risk unstable angina (59% versus 54%; P=0.01) but less often in the setting of primary PCI for ST-segment–elevation MI (3% versus 5%; P<0.001). Incomplete TIMI flow before PCI was less common among EPD cases (TIMI 0, 5% versus 9%; TIMI 1, 10% versus 14%; TIMI 2, 22% versus 25%; P<0.001 for each comparison). Lesion length was greater among EPD (versus no EPD) cases (median, 18 mm versus 15 mm; P<0.001), and vessel diameter was slightly larger (mean, 3.6 mm versus 3.3 mm; P<0.001). Although preprocedural clopidogrel was used slightly more often in EPD cases (83% versus 80%; P<0.001), both glycoprotein IIb/IIIa inhibitors (37%) and a single stent (59%) were used with similar frequency (P=not significant for both).

![Figure 2](https://example.com/figure2.png)
### Table 1. Patient and Procedural Characteristics

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>EPD (n=10,432)</th>
<th>No EPD (n=38,893)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y (median, IQR)</td>
<td>75 (70–80)</td>
<td>75 (70–80)</td>
<td>0.01</td>
</tr>
<tr>
<td>Women, %</td>
<td>23</td>
<td>25</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CV risk factors/history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>89</td>
<td>88</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus, insulin</td>
<td>15</td>
<td>15</td>
<td>0.6</td>
</tr>
<tr>
<td>Smoking (current/recent)</td>
<td>11</td>
<td>10</td>
<td>0.04</td>
</tr>
<tr>
<td>eGFR (median, IQR)</td>
<td>62 (48–76)</td>
<td>62 (48–76)</td>
<td>0.05</td>
</tr>
<tr>
<td>CHF</td>
<td>23</td>
<td>22</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEF, % (median, IQR)</td>
<td>50 (40–59)</td>
<td>50 (40–60)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Procedural characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable angina</td>
<td>14</td>
<td>15</td>
<td>0.02</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>42</td>
<td>41</td>
<td>0.09</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>25</td>
<td>21</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>STEMI</td>
<td>4</td>
<td>6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Other</td>
<td>15</td>
<td>17</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Any ACS</td>
<td>72</td>
<td>68</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TIMI flow, pre-PCI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>5</td>
<td>9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1 or 2</td>
<td>32</td>
<td>39</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3</td>
<td>63</td>
<td>52</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. of stents, 1</td>
<td>59</td>
<td>59</td>
<td>0.7</td>
</tr>
<tr>
<td>Multivessel PCI</td>
<td>14</td>
<td>16</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vein graft age, y</td>
<td>13 (9–17)</td>
<td>12 (8–16)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>De novo lesion</td>
<td>93</td>
<td>89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Graft segment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic</td>
<td>20</td>
<td>20</td>
<td>0.09</td>
</tr>
<tr>
<td>Graft body</td>
<td>73</td>
<td>61</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Distal</td>
<td>6</td>
<td>19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>83</td>
<td>80</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GP IIb/IIIa inhibitor</td>
<td>37</td>
<td>37</td>
<td>0.2</td>
</tr>
</tbody>
</table>

ACSM indicates acute coronary syndrome; CHF, congestive heart failure; CV, cardiovascular; eGFR, estimated glomerular filtration rate; EPD, embolic protection device; GP IIb/IIIa, glycoprotein IIb/IIIa inhibitor; IQR, interquartile range; LVEF, left ventricular ejection fraction; NSTEMI, non–ST-segment–elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment–elevation myocardial infarction; and TIMI, thrombolysis in myocardial infarction.

Acute and 3-Year Outcomes (EPD Versus No EPD)

Procedural success was similar among EPD (versus no EPD) cases (96.0% versus 95.4%); however, unadjusted rates of procedural complications were slightly more common among EPD cases (Table 2), including no reflow (3.9% versus 2.8%; P<0.001), dissection (1.3% versus 1.1%; P=0.05), perforation (0.7% versus 0.4%; P=0.001), and periprocedural MI (2.8% versus 1.8%; P<0.001). After risk adjustment, each of these periprocedural adverse events was more common among patients treated with EPD (versus no EPD) in the overall cohort and among most high-risk subgroups (ACS, de novo lesion, and graft body lesion; Table 2). Inhospital mortality was rare (1.1%) without a significant difference in risk across treatment groups (before or after risk adjustment), and the 30-day composite risk of death, MI, or repeat revascularization was 5.5% (P=0.1 across treatment groups).

By 3 years, post PCI, a MACE (death, MI, or repeat revascularization) occurred in 52% of patients, including death in 25%, MI in 15%, and repeat revascularization in 30%. No differences in the unadjusted or adjusted 3-year risks of death (PM HR, 0.96; 95% confidence interval [CI], 0.91–1.02), MI (PM HR, 1.00; CI, 0.93–1.09), or repeat revascularization (PM HR, 1.02; CI, 0.96–1.08) were observed for patients treated with versus without an EPD (Table 3). This finding was independent of clinical settings (ACS and non-ACS) and graft segment (aortic anastomosis, graft body, or distal graft/anastomosis; P values for interaction tests were not significant for each end point and indication). A significant interaction for the risk ofrehospitalization for MI was observed by previous treatment status (in-stent versus de novo; P interaction=0.04); however, EPD use was not associated with a significant reduction in the adjusted 3-year risk of MI for either de novo (PM HR, 1.05; CI, 0.96–1.14) or in-stent lesions (PM HR, 0.80; CI, 0.62–1.02).

Hospital-Level Treatment Preference Analysis

Patients treated at high-EPD use hospitals (n=2483; 56 hospitals) versus no EPD use hospitals (n=5523; 315 hospitals) were similar across most baseline characteristics, yet high-EPD use hospitals treated a higher proportion of patients with non–ST-segment–elevation MI (29% versus 20%; P<0.001) and ST-segment–elevation MI (7% versus 6%; P=0.03). Preprocedural clopidogrel use was high across both groups (80% overall), yet the use of a glycoprotein IIb/IIIa inhibitor was lower among high-EPD use hospitals (34% versus 41%; P<0.001). The TIMI 3 flow at the time of first angiogram was greater among those treated at high-EPD use hospitals (63% versus 39%; P<0.001), and the lesion length was slightly longer (20 versus 18 mm; P=0.02). Across high-EPD use versus no EPD use hospitals, the incidences of procedural no reflow (3.3% versus 2.7%; P=0.1) and dissection (1.2% versus 1.0%; P=0.4) were similar, but the risk of perforation (0.6% versus 0.3%; P<0.001) and periprocedural MI (3.1% versus 1.1%; P<0.001) was higher. At high-EPD use hospitals, the use of most evidence-based medications was higher at discharge, including β-blockers (89% versus 81%; P<0.001), angiotensin-converting enzyme inhibitors (55% versus 47%; P<0.001), and statins (88% versus 82%; P<0.001).

The risk of death, MI, or repeat revascularization by 30 days was 5.8% in this cohort, and no difference in this composite end point was observed to 3 years across high-EPD use versus no EPD use hospitals (HR, 1.06; CI, 0.98–1.14). After adjustment for differences in case mix, patients treated at high-EPD use hospitals experienced a lower 3-year risk of death (adjusted HR, 0.84; CI, 0.75–0.94) but similar risks of both MI (adjusted HR, 1.04; CI, 0.89–1.21) and repeat revascularization (adjusted HR, 1.04; CI, 0.93–1.16).

Discussion

This study represents the largest-ever real-world evaluation of the safety and effectiveness of adjunctive EPD use in the
Table 2. Comparison of Unadjusted and Adjusted Procedural Outcomes in High-Risk Subgroups With EPD vs No EPD

| Table 2. Comparison of Unadjusted and Adjusted Procedural Outcomes in High-Risk Subgroups With EPD vs No EPD |
|---|---|---|---|---|---|---|---|
| | No Reflow | Dissection | Perforation | Perioperative MI | Inhospital Mortality |
| | n | Adjusted OR (95% CI) | %* | Adjusted OR (95% CI) | %* | Adjusted OR (95% CI) | %* | Adjusted OR (95% CI) |
| Overall | EPD 10432 | 3.9 | 1.38 (1.21–1.57) | 1.3 | 1.22 (1.01–1.47) | 0.7 | 1.63 (1.24–2.13) | 2.8 | 1.22 (1.04–1.44) | 1.1 | 0.90 (0.74–1.09) |
| | No EPD 38893 | 2.8 | 1.1 | | | | | | | |
| ACS | EPD 7481 | 4.3 | 1.29 (1.12–1.48) | 1.4 | 1.19 (0.96–1.47) | 0.6 | 1.46 (1.06–2.01) | 2.8 | 1.04 (0.94–1.38) | 1.3 | 0.94 (0.76–1.16) |
| | No EPD 26523 | 3.4 | 1.2 | | | | | | | |
| De novo | EPD 9702 | 4.0 | 1.33 (1.17–1.52) | 1.3 | 1.25 (1.03–1.52) | 0.7 | 1.74 (1.32–2.30) | 2.8 | 1.21 (1.03–1.43) | 1.1 | 0.92 (0.75–1.13) |
| | No EPD 34599 | 2.9 | 1.0 | | | | | | | |
| Graft body | EPD 7650 | 4.3 | 1.33 (1.15–1.54) | 1.3 | 1.25 (1.00–1.57) | 0.8 | 1.69 (1.24–2.32) | 3.0 | 1.22 (1.00–1.48) | 1.1 | 0.81 (0.64–1.02) |
| | No EPD 23651 | 3.2 | 1.1 | | | | | | | |

ACS indicates acute coronary syndrome; CI, confidence interval; EPD, embolic protection device; MI, myocardial infarction; and OR, odds ratio.

*Unadjusted incidences (%) representing the significant differences (P<0.05) across EPD vs no EPD groups.

contemporary treatment of SVG lesions. In this older cohort, thromboembolic complications were rare, and the 30-day risk of MACE (death, MI, or repeat revascularization) was low (5.5%). The use of EPDs was associated with a higher incidence of procedural complications (including periprocedural MI), without an associated reduction in the 3-year risk of death, MI, or repeat revascularization (this was independent of clinical setting, previous lesion treatment, and graft segment). No patient or lesion characteristics were identified for which EPD use conferred a benefit, although we were unable to specifically evaluate EPD effectiveness in severely degenerated or thrombotic grafts. Nevertheless, patients treated at hospitals with high EPD use had a lower associated 3-year risk of mortality after adjusting for differences in case mix, in the setting of a greater use of evidence-based discharge medications.

The US Food and Drug Administration’s approval of contemporary EPDs was based on limited direct efficacy data, and no randomized trial data are available to support the continued use of EPDs in the contemporary era. The use of distal EPDs is technically not possible in distal and many tortuous grafts because their use increases procedural time and complexity, may increase the risk of both distal dissections and device entrapment, and is not tied to additional procedural reimbursement. As a result, EPDs are used in a minority of graft cases, despite a class I American College of Cardiology Foundation/American Heart Association/Society for Cardiovascular Angiography and Interventions recommendation. In this analysis, EPD use was associated with a 39% relative increase in the incidence of no reflow (P=0.001), a 56% relative increase in periprocedural MI, an 18% relative increase in dissection, and a 75% relative increase in perforation, with no decrease in the risk of inhospital mortality or long-term adverse events; these results were independent of clinical presentation, previous treatment, and graft segment. The results observed in our cohort provide an evaluation of the safety and effectiveness of EPDs in a real-world contemporary setting and differ meaningfully from those reported in the Saphenous Vein Graft Angioplasty Free of Emboli Randomized (SAFER) trial, which is the only superiority trial to complete enrollment in this device space. In the SAFER trial (n=801; 1999–2000), patients who were randomized to the PercuSurge GuardWire System experienced a significantly reduced 30-day MACE (death, MI, emergent coronary artery bypass graft surgery, or target lesion revascularization) versus control (9.6% versus 16.5%; P=0.004), with a clear reduction in no reflow or distal cutoff from 9.7% to 4.8% (P=0.02). In contrast to these results, our analysis found the background 30-day incidence of MACE to be 5.5%, with

Table 3. Comparison of 3-Year Clinical Outcomes After Saphenous Vein Graft Percutaneous Coronary Intervention With EPD vs No EPD

| Table 3. Comparison of 3-Year Clinical Outcomes After Saphenous Vein Graft Percutaneous Coronary Intervention With EPD vs No EPD |
|---|---|---|---|---|---|---|---|
| | EPD Cum Inc | No EPD Cum Inc | Unadjusted HR (95% CI) | PM HR (95% CI) | Clinical Setting, Pinteraction | Previous Treatment, Pinteraction | Graft Segment, Pinteraction |
| Death | 25% | 24% | 1.05 (0.99–1.10) | 0.96 (0.91–1.02) | 0.3 | 0.2 | 0.5 |
| MI | 15% | 14% | 1.03 (0.97–1.10) | 1.00 (0.93–1.09) | 0.3 | 0.04 | 0.8 |
| Repeat revascularization | 30% | 30% | 1.00 (0.96–1.05) | 1.02 (0.96–1.08) | 0.5 | 0.2 | 0.9 |

CI indicates confidence interval; Cum Inc, cumulative incidence; EPD, embolic protection device; HR, hazard ratio; MI, myocardial infarction; Pinteraction, P value for interaction test; and PM, propensity score–matched.
no reflow occurring in <3% of no EPD use cases, despite the inclusion of presumably higher risk patients with ACS (ie, non-ST-segment–elevation MI and ST-segment–elevation MI) in the CathPCI Registry cohort. To date, the SAFER trial remains the only randomized comparison of embolic protection versus no embolic protection in vein graft PCI. The Randomized, Controlled Trial of Saphenous Vein Graft Intervention with a Filter-Based Distal Embolic Protection Device (TRAP) trial demonstrated a trend toward reduction in the incidence of MI with (versus without) embolic protection (16.2% versus 10.5%; \( P=0.12 \)), predominantly because of a reduction in moderate large infarction (creatine kinase-MB >5×).17 However, the TRAP trial was terminated early because of slow enrollment. Subsequent trials of EPDs (including those for the FilterWire18 and SpideRx19) have relied on the contemporary relevance of the SAFER control cohort with noninferiority trial designs. Although these studies have demonstrated noninferiority to existing EPD technology, they have not addressed the continued relevance of EPD technology in contemporary practice.

The results presented here challenge both the safety and effectiveness of distal EPDs and question the relevance of existing randomized data in contemporary practice. We hypothesize that advances in preprocedural/intraprocedural medications (including aggressive pre-PCI platelet inhibition and vasodilator20,21), procedural technique (eg, increased direct stenting22), and device deliverability (eg, greater flexibility and smaller crossing diameters), as well as other changes in care, have led to the observed reductions in periprocedural thromboembolic events, rendering distal embolic protection unnecessary in routine clinical practice. Alternatively, it is possible that despite risk adjustment, the increased lesion-level risk associated with EPD use may have obscured an actual benefit of these devices. Nonetheless, the data presented here suggest that further prospective, randomized testing is needed to support the routine use of EPDs.

Although we observed no evidence that EPD use improves clinical outcomes in general practice or among certain high-risk patient and lesion characteristics (ACS clinical presentation and graft body or de novo lesions), the effectiveness of these devices at preventing distal embolization in some specific high-risk clinical situations is not addressed by this analysis. Others have demonstrated the association of high graft degeneration scores, long lesion length, and visible thrombus to an increased risk of no reflow and periprocedural MI.23,24 Furthermore, anecdotal experience has repeatedly demonstrated the use of distal filters for capturing intravascular debris in these cases.25,26 Given the limitations of the CathPCI Registry database, identification of a subset of cases involving these high-risk graft interventions was not possible.

Limitations

Despite the fact that our analysis is the most relevant analysis (to date) of EPD use in contemporary clinical practice, our study has several limitations. First, the comparisons presented here were not randomized; therefore, results may be confounded by unobserved differences in patients, lesions, or procedures across treatment groups. Although the evaluation by treatment preference analysis demonstrated a 3-year reduction in mortality among high-EPD use hospitals, no clinical benefit was apparent in the acute setting (as it was in the SAFER trial), thereby making this reduction in mortality more likely to be the effect of differences in downstream management (eg, discharge medications) than procedural outcomes. Second, because the CathPCI Registry does not follow outcomes beyond hospital discharge, Medicare claims have been used to evaluate long-term outcomes. Although multiple analyses have demonstrated the representativeness of the Medicare-linked CathPCI Registry cohort to the overall Medicare-eligible (>265 year old) CathPCI Registry population, these results may not apply to a younger cohort. However, given the advanced age of many graft failure patients, this limitation is not highly significant. Third, incomplete post-PCI biomarker measurement at CathPCI Registry hospitals may have led to an underestimation of the contemporary incidence of periprocedural MI; nevertheless, the incidence of periprocedural MI observed in our study is similar to that reported in the randomized Death and Events at Long-term follow-up AnalYsis: Extended Duration of the Reduction of Restenosis In Saphenous vein grafts with Cypher stent (DELAYED RRISC) trial (4%);27 the 30-day MACE incidence is similar to that observed in the Is Drug-Eluting-Stenting Associated with Improved Results in Coronary Artery Bypass Grafts (ISAR-CABG) trial (4.3%);28 and the differential effect of any potential underascertainment on the comparative outcomes presented here is unknown. Fourth, adjunctive glycoprotein IIb/IIIa inhibitors were used in more than one-third of the cases included in our study. There is no clear benefit to routine glycoprotein IIb/IIIa inhibition in vein graft PCI; however, the risk of bleeding is greater when contemporary dosing regimens are combined with a transfemoral approach.2 The effect of glycoprotein IIb/IIIa inhibition on the overall incidence of adverse events reported here is unclear, although this effect is unlikely to have confounded the primary treatment comparison because the use of glycoprotein IIb/IIIa inhibitors was equally distributed across the treatment groups. Finally, although the center-level analysis provides important additional insight, the use of the hospital center as an instrumental variable has not been validated and results should be interpreted with the recognition that other process measures may have driven observed differences in outcomes. Together, these limitations emphasize both the hypothesis generating nature of this observational analysis and the need for a contemporary randomized trial of embolic protection in vein graft PCI. Given the enrollment difficulties observed in the TRAP trial, this may be an ideal setting for a pragmatic, registry-based clinical trial.28

Conclusions

In conclusion, we have observed no benefit to routine EPD use in contemporary vein graft PCI—indeed, independent of clinical presentation, previous treatment, and graft segment; however, the select use of EPDs in high-risk graft interventions may still be warranted. Ultimately, the data presented here compel the performance of further randomized evaluations of EPDs in contemporary practice.
Acknowledgments

We would like to thank Erin Hanley, MS, for her editorial contributions to this article. E. Hanley did not receive compensation for her assistance, apart from her employment at the institution where this study was conducted.

Sources of Funding

This work was supported internally by the Duke Clinical Research Institute, Durham, NC.

Disclosures

Dr Brillard received consulting/speaker honoraria from Abbott Vascular, Asahi, Boston Scientific, Elsevier, Somonnlation, St Jude Medical, and Terumo and research support from Guerbet and InfrARedx; his spouse is an employee of Medtronic. Dr Peterson received institutional grant support from American College of Cardiology, American Heart Association, Eli Lilly, and Janssen Medical, and Terumo and research support from Guerbet and Institute, Durham, NC.

assistance, apart from her employment at the institution where this article. E. Hanley did not receive compensation for her contributions to this article. E. Hanley did not receive compensation for her assistance, apart from her employment at the institution where this study was conducted.

7

References


Three-Year Outcomes Associated With Embolic Protection in Saphenous Vein Graft Intervention: Results in 49,325 Senior Patients in the Medicare-Linked National Cardiovascular Data Registry CathPCI Registry


Circ Cardiovasc Interv. 2015;8:
doi: 10.1161/CIRCINTERVENTIONS.114.001403

Circulation: Cardiovascular Interventions is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2015 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-7640. Online ISSN: 1941-7632

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circinterventions.ahajournals.org/content/8/3/e001403

Data Supplement (unedited) at:
http://circinterventions.ahajournals.org/content/suppl/2015/03/04/CIRCINTERVENTIONS.114.001403.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Interventions can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Interventions is online at:
http://circinterventions.ahajournals.org//subscriptions/
Supplemental Figure Legends

**Supplemental Figure 1. Three-year Kaplan Meier for Myocardial Infarction**

This figure displays the three-year Kaplan Meier rates for myocardial infarction for patients with and without EPD.

EPD indicates embolic protection device; KM, Kaplan Meier; yrs, years

**Supplemental Figure 2. Three-year Kaplan Meier for Revascularization**

This figure displays the three-year Kaplan Meier rates for revascularization for patients with and without EPD.

EPD indicates embolic protection device; KM, Kaplan Meier; yrs, years
Supplemental Figure 1

3yr KM for Myocardial Infarction:
EPD, 17.3%
No EPD, 16.1%
p-value=0.3

Supplemental Figure 2

3yr KM for Revascularization:
EPD, 33.3%
No EPD, 32.8%
p-value=0.9