Diagnosis and Therapeutic Procedures

Embolic Protection Devices

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Manipulation of atherosclerotic lesions with wires, catheters, balloons, stents, and other intravascular devices during invasive procedures releases atherosclerotic plaque, resulting in distal embolization. This plaque debris leads to no or slow flow as a result of a multitude of factors, including mechanical obstruction of macrovascular and microvascular channels, local platelet adhesion, platelet activation, and thrombosis attributable to release of tissue factors and microvascular spasm by release of thromboxane. The clinical manifestation of this shower of atherosclerotic debris depends on the characteristics: the amount of debris, the size of particles, and the sensitivity of the organ perfused. Distal embolization during percutaneous coronary intervention (PCI) results in decreased distal perfusion, leading to myocardial ischemia or infarction. Manipulation of the aortic arch during coronary, cerebral, or valvular procedures can cause microembolization to the cerebral circulation that may manifest as a transient ischemic attack or stroke. Distal embolization is seen during intervention of all vascular beds, including peripheral, renal, and mesenteric arteries, but the clinical manifestation varies and depends on the sensitivity of the organ perfused and the metric used to assess end-organ damage.

Embolic protection devices (EPDs) prevent or reduce plaque debris from reaching the distal bed and thereby have the potential to reduce adverse clinical events. They are commonly used in saphenous vein graft (SVG) interventions and during carotid artery stenting procedures. They are also being tested in other vascular beds such as the renal arteries, but their utility at reducing clinically significant outcomes in these vascular beds has yet to be established. Hyperlinked to this article is a video demonstrating the use of EPDs. Downloadable slides about EPD are available in the online-only Data Supplement.

Types of EPDs

EPDs can be divided into 3 distinct types based on their mechanism of operation: distal occlusion aspiration devices, distal filters, and proximal occlusion aspiration devices.

Distal Occlusion Aspiration Devices

Distal occlusion aspiration devices contain an inflatable occlusion balloon mounted on a hypotube (online-only Data Supplement, slide 23: Distal Protection–GuardWire). The balloon is passed several centimeters distal to the lesion and is inflated to obstruct antegrade flow with a carbon dioxide–filled syringe. This low-pressure balloon dilatation has been found not to increase the risk of restenosis, attesting to its safety.1 The hypotube is used as the interventional guide wire for the balloon angioplasty or stenting. These devices work by occluding flow to create a column of stagnant blood that traps plaque debris and soluble debris that are subsequently removed with an aspiration catheter (Export or FlushCath catheter). The balloon is subsequently deflated and antegrade flow reestablished. The PercuSurge GuardWire (6F; Medtronic, Minneapolis, MN) and TriActiv system (7F or 8F; Kensey Nash Corp, Exton, PA) are example of devices that work on this principle.

The advantages of this class of EPDs are the ability to capture debris <100 μm and soluble vasoactive mediators with unlimited debris capture. However, there is potential for embolization to occur during the wiring and device-crossing phase, ischemia during balloon occlusion, and limited contrast opacification. Aspiration may not remove all particles, and the possibility of shunting debris into proximal side branches exists. The inability to tailor the choice of guide wire to the procedural requirements is also a potential limitation (Table 1).

Distal Embolic Filters

Distal embolic filters have a filter bag mounted at the distal part of a 0.014-in guide wire (online-only Data Supplement, slides 13–15: Equipment). The device is advanced through the guide catheter with the filter bag in a collapsed state in a delivery sheath (3.2F) and is deployed 2.5 to 3.0 cm distal to the lesion. The guide wire is used as the interventional guide wire for the balloon angioplasty or stenting. The filter bags have pore sizes of 100 to 110 μm; thus, the devices are effective at filtering particles >100 to 110 μm but maintaining antegrade perfusion. However, data have shown that the size of the debris trapped by the filters is identical to those of the distal occlusion/aspiration systems,2 which is likely attributable to a reduction in functional pore size caused by clumping or stranding of particles across the filter pores.3 The filter bag with the
accumulated plaque debris is later retrieved with a retrieval catheter (4.2F–4.9F) after the procedure. The Spider (eV3; MedNova, Abbott, Abbott Park, IL; online-only Data Supplement, slides 14 and 15: Equipment), the FilterWire (Boston Scientific; online-only Data Supplement, slide 13: Equipment), and the Interceptor Plus Coronary Filter System (Medtronic Vascular, Santa Rosa, CA) are examples of devices that work on this principle. These are compatible with a 6F guide catheter.

The advantages of this class of EPDs are the ability to maintain antegrade perfusion and contrast opacification during the procedure. However, there is still potential for distal embolization to occur during the wiring and device-crossing phases. Additional limitations include the large-diameter delivery sheath required for delivery of these devices, the inability to filter soluble vasoreactive substances, the lack of unlimited debris trapping (limited by filter bag size), embolization of debris during the retrieval phase, and the inability to tailor the choice of guide wire to the procedural requirements. Disadvantages include ischemia during balloon occlusion and limited contrast opacification (Table 1).

### Proximal Occlusion Aspiration Devices

Proximal occlusion devices have a guiding catheter with an inflatable balloon tip that is inflated proximal to the lesion, thereby occluding antegrade flow during the interventional procedure (online-only Data Supplement, slide 21: Proximal EPD–Proxis Device). These devices create a column of stagnant blood containing debris, which is later aspirated via the guiding catheter. The Proxis (7F; St. Jude Medical, Minneapolis, MN) is an example of a device that works on this principle (currently not in production). Similar devices are used for embolic protection during carotid artery stenting (Gore Flow Reversal, Gore & Associates; Mo.Ma Ultra proximal cerebral protection device, Medtronic, Inc).

The advantages of these devices are the establishment of protection before any devices have crossed the lesion, potentially complete recovery of particles of all sizes and vasoreactive substances, ability to use them for lesions without a distal landing zone, unlimited debris trapping and retrieving potential, and ability to tailor the choice of guide wire to the procedural requirements. Disadvantages include ischemia during balloon occlusion and limited contrast opacification (Table 1).

### Indications for EPDs

#### SVG Intervention

SVG intervention is associated with a 15% to 20% incidence of major adverse cardiac events, particularly related to distal embolization. This may be related to the plaque characteristics of SVG. Studies have shown that degenerated vein grafts have more friable, lipid-rich plaque than native coronary arteries; are diffuse and concentric with thin or absent fibrous cap with superimposed thrombus; and thus have a great propensity for distal embolization. The Saphenous Vein Graft Angioplasty Free of Emboli Randomized (SAFER) trial showed a 42% reduction in 30-day major adverse cardiac event rates in patients randomized to the distal occlusion balloon (GuardWire) compared with conventional stenting over a guide wire without embolic protection in patients undergoing SVG intervention, which led to US Food and Drug Administration approval of this device and changed the standard of care for SVG intervention. Other studies have subsequently compared newer devices with the GuardWire (Table 2), and they have been found to be noninferior to the reference standard. The use of distal EPDs during SVG PCI is a Class I indication per the American College of Cardiology/American Heart Association/Society for Cardiac Angiography and Interventions PCI guidelines. Other types of embolic protection/prevention during SVG intervention have been tested and have failed such as the use of polytetrafluoroethylene (PTFE)-covered stents in the Randomized Evaluation of PTFE Covered Stent in Saphenous Vein Grafts (RECOVERS) trial, in which the PTFE stent showed no benefit over bare metal stents with an increase in nonfatal myocardial infarction. In addition, the routine use of glycoprotein IIb/IIa receptor blockers during PCI of SVG has not been shown to be beneficial at reducing major adverse cardiac events. Intracoronary calcium channel blockers, adenosine, and nitroprusside are commonly used to treat the no-reflow phenomenon caused by distal embolization but have not been shown to prevent embolization per se.

Routine use of EPDs in patients undergoing SVG PCI is therefore recommended except perhaps for the treatment of aorto-ostial lesions or for in-stent restenosis, in which the plaque is more fibrocalcific or composed of smooth muscle cells with a consequent reduced propensity for distal embolization and the no-reflow phenomenon. In addition, direct stenting has been reported to be associated with a reduction in creatine kinase-MB and troponin release during SVG
and this strategy, in combination with routine EPD use for all eligible patients, may be useful in reducing the risk of cardiovascular morbidity. However, an analysis of 19,546 SVG PCI procedures from the American College of Cardiology National Cardiovascular Data Registry showed that EPD use is extremely low (22%) despite national and international guidelines.

### Native Coronary Artery Intervention

Much of the evidence for the use of EPDs in native coronary arteries is from trials in patients with ST-segment–elevation myocardial infarction (STEMI; Table 3). In patients with STEMI, the no-reflow phenomenon during PCI is likely the result of distal embolization and is a poor prognostic sign. Unlike the positive results of trials in SVG intervention, trials in STEMI have failed to demonstrate any beneficial effect of routine embolic protection on myocardial reperfusion or clinical outcomes (Table 3). The reason for poor performance of EPDs in the setting of primary PCI in STEMI could be promotion of distal embolization by passage of the guide wire and device during EPD deployment, insufficient capture of debris, and side-branch embolization. Use of proximal protection as a means to overcome distal embolization during EPD deployment was also not effective in the Proximal Embolic Protection in Acute Myocardial Infarction and Resolution of ST-Elevation (PREPARE) trial. In fact, long-term (15 months of follow-up) results of the Drug Elution and Distal Protection in ST Elevation Myocardial Infarction (DEDICATION) trial seem to suggest that the routine use of EPDs in patients with STEMI is associated with an increased incidence of stent thrombosis and clinically driven target lesion/vessel revascularization. It is therefore reasonable to conclude that there is currently no role for routine EPD use during primary PCI in patients with STEMI, although manual aspiration may be beneficial in this setting.

### Carotid Artery Stenting

Distal embolization during carotid artery stenting is common, occurring in the vast majority of patients, and may be more common than during carotid endarterectomy. Nonrandomized studies have suggested that EPD use during carotid stenting reduced the incidence of death or stroke at 30 days by at least half. In the magnetic resonance imaging substudy of the International Carotid Stenting Study (ICSS) trial, new ischemic lesions were 3 times more common in the stenting group than in the endarterectomy group after treatment. Nonrandomized studies have suggested that EPD use during carotid stenting is effective in preventing cerebral ischemia during stenting. It is not clear whether this was attributable to embolization during deployment of EPDs.
Table 3. Major Trials of Embolic Protection Devices for ST-Segment–Elevation Myocardial Infarction Involving the Native Coronary Arteries

<table>
<thead>
<tr>
<th>Trial</th>
<th>Device</th>
<th>Patients, n</th>
<th>Primary End Point</th>
<th>Result, %</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal occlusion device</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EMERALD (26)</td>
<td>GuardWire Plus vs conventional</td>
<td>501</td>
<td>ST-segment resolution at 30 min</td>
<td>63.3 vs 61.9</td>
<td>0.78</td>
</tr>
<tr>
<td></td>
<td>guide wire</td>
<td></td>
<td>Infarct size</td>
<td>12.0 vs 9.5</td>
<td>0.34</td>
</tr>
<tr>
<td>Tahk et al (27)*</td>
<td>GuardWire Plus vs conventional</td>
<td>116</td>
<td>TIMI grade 3 flow</td>
<td>96 vs 81</td>
<td>0.016</td>
</tr>
<tr>
<td></td>
<td>guide wire</td>
<td></td>
<td>TMP grade 3</td>
<td>65 vs 38</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hyperemic average peak velocity</td>
<td>39.2±16.7 vs 30.6±10.8 cm/s</td>
<td>0.014</td>
</tr>
<tr>
<td>MICADO (28)</td>
<td>GuardWire Plus vs conventional</td>
<td>167</td>
<td>No reflow</td>
<td>4 vs 3</td>
<td>0.73</td>
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<tr>
<td></td>
<td>guide wire</td>
<td></td>
<td>TIMI grade 3 flow</td>
<td>80 vs 76</td>
<td>0.182</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>TMP grade 3</td>
<td>58 vs 44</td>
<td>0.054</td>
</tr>
<tr>
<td>Ochala et al (29)</td>
<td>GuardWire Plus vs abciximab</td>
<td>120</td>
<td>TIMI grade 3 flow</td>
<td>89 vs 89</td>
<td>NS</td>
</tr>
<tr>
<td>ASPARAGUS (30)</td>
<td>GuardWire Plus vs conventional</td>
<td>329</td>
<td>TIMI grade 3 flow</td>
<td>77 vs 78</td>
<td>0.73</td>
</tr>
<tr>
<td></td>
<td>guide wire</td>
<td></td>
<td>TMP grade 3</td>
<td>25.2 vs 20.3</td>
<td>0.26</td>
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<tr>
<td>Distal filter device</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PROMISE (31)</td>
<td>FilterWire EX vs conventional</td>
<td>200</td>
<td>Maximum adenosine-induced flow</td>
<td>34±17 vs 36±20 cm/s</td>
<td>0.46</td>
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<tr>
<td></td>
<td>guide wire</td>
<td></td>
<td>velocity</td>
<td></td>
<td></td>
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<tr>
<td>UpFlow MI (32)</td>
<td>FilterWire EZ vs conventional</td>
<td>100</td>
<td>TIMI grade 3 flow</td>
<td>88.2 vs 93.9</td>
<td>NS</td>
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<tr>
<td></td>
<td>guide wire</td>
<td></td>
<td>TMP grade 3</td>
<td>68.1 vs 66</td>
<td>NS</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>ST-segment resolution at 60 min</td>
<td>9.4 vs 10.7</td>
<td>NS</td>
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<tr>
<td>DEDICATION (33,34)</td>
<td>FilterWire vs conventional PCI</td>
<td>626</td>
<td>ST-segment resolution at 90 min</td>
<td>72 vs 76</td>
<td>0.29</td>
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<tr>
<td>PREMIAR (35)</td>
<td>SpiderRX vs conventional PCI</td>
<td>140</td>
<td>ST-segment resolution at 60 min</td>
<td>60 vs 60</td>
<td>0.99</td>
</tr>
<tr>
<td>Proximal occlusion device</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PREPARE (36)</td>
<td>Proxis vs conventional PCI</td>
<td>284</td>
<td>Complete ST-segment resolution at 60 min</td>
<td>80 vs 72</td>
<td>0.14</td>
</tr>
</tbody>
</table>

ASPARAGUS indicates Aspiration of Liberated Debris in Acute Myocardial Infarction With GuardWire Plus System; DEDICATION, Drug Elution and Distal Protection During Percutaneous Coronary Intervention in ST Elevation Myocardial Infarction trial; EMERALD, Enhanced Myocardial Efficacy and Removal by Aspiration of Liberated Debris; MICADO, Multicenter Investigation of Coronary Artery Protection With a Distal Occlusion Device in Acute Myocardial Infarction; PREPARE, Proximal Embolic Protection in Acute Myocardial Infarction and Resolution of ST-Elevation; PREMIAR, Protection of Distal Embolization in High-Risk Patients With Acute ST-Segment Elevation Myocardial Infarction; PROMISE, Protection Devices in PCI Treatment of Myocardial Infarction for Salvage of Endangered Myocardium; TIMI, Thrombolysis in Myocardial Infarction; TMP, Thrombolysis in Myocardial Infarction myocardial perfusion; and UpFlow MI, Use of Protective FilterWire to Improve Flow in Acute Myocardial Infarction study.

*No difference in major adverse cardiac events at 6 months.

Distal Filter Devices: Equipment and Deployment Technique

Equipment

Distal filter devices (such as the SpiderFX) are composed of a capture wire and a catheter. The capture wire is composed of a nitinol mesh filter with a distal floppy tip mounted on a 190-cm or a convertible 320/190-cm PTFE-coated 0.014-in stainless steel wire preloaded through the delivery end of the catheter (online-only Data Supplement, slide 14: Equipment). The catheter is a dual-ended catheter, with a delivery end (green) and a recovery end (blue) at the opposite ends of the catheter (online-only Data Supplement, slide 15: Equipment). Similarly, the FilterWire is composed of a protection wire that is a 190/300-cm PTFE-coated 0.014-in steerable guide wire with a spring coil distal tip, a 110-μm filter bag, a delivery sheath, and a retrieval sheath (online-only Data Supplement, slide 13: Equipment).

Technique

After appropriate antiplatelet therapy as per individual/institutional practice and anticoagulation with either heparin or bivalirudin, a 6F or larger guide catheter is used to engage the coronary ostium. With the Spider system, the lesion is crossed with a standard 0.014-in guide wire. The landing zone for the filter should preferably be 2.5 to 3.0 cm distal to the lesion site. The vessel is measured at this site, and an appropriately sized filter device is chosen to ensure that it is neither undersized (inadequate vessel wall apposition, resulting in embolization of debris) nor oversized (vessel wall damage or slow/no reflow).

Under sterile conditions, remove the EPD components with the hoop from the packaging. Hold the catheter at the distal tip, and submerge only the filter in heparinized saline to wet it and to remove air. Pull the capture wire proximally until the filter portion stops in the clear segment of the catheter. Flush through the distal tip with heparinized saline until all the air is removed and saline passes from the primary wire exit port. Gently apply pressure to the primary wire exit port and continue flushing until all the air is removed and saline passes from the capture wire exit port. After crossing the lesion with a standard 0.014-in guide wire, load the distal tip of the EPD catheter (green) onto the proximal part of the guide wire. Gently bend the catheter at the primary wire exit port to allow the primary guide wire to exit easily. Advance the catheter over the primary guide wire to exit the lesion site.
wire past the lesion until the radiopaque marker at the distal tip of the delivery end is at least 4 to 5 cm beyond the distal edge of the lesion. Fix the catheter in this position, and then withdraw the primary guide wire, leaving the delivery catheter with the capture wire in place. With the catheter fixed with one hand, gently advance the capture wire until the distal radiopaque marker band on the filter aligns with the radiopaque marker on the catheter distal tip. Under fluoroscopy, ensure that the proximal radiopaque marker band is at least 2 cm distal to the lesion treated. If not, advance the unit as a whole until the desired position is reached. Fix the capture wire with one hand, and gently pull back the catheter to expose and deploy the filter. Remove the catheter from the patient.

After completion of PCI with the capture wire used as the primary guide wire, use the recovery end of the catheter (4.2F–4.9F) to remove the filter. Flush the distal tip of the recovery end (blue) to remove all the air until saline passes from the capture wire exit port. Load the recovery end of the catheter, and advance it until the distal tip of the radiopaque marker aligns with the proximal radiopaque marker band on the filter. Gently advance the recovery end over the filter until the proximal portion of the filter is inside the catheter (partial enclosure recovery) or until all radiopaque markers on the filter are within the catheter (full enclosure recovery). Carefully remove the catheter and the capture wire together as a unit. Open the hemostasis valve on the guide catheter to allow the EPD catheter to exit and to flush any thrombus that may have escaped into the guide catheter.

The deployment of FilterWire is similar, except the protection wire serves as the guide wire and a conventional guide wire is not used before deployment of the FilterWire. Briefly, submerge the filter and distal tip of the delivery sheath in heparinized saline, and capture the filter by pulling it into the sheath. Place the peel-away introducer sheath over the spring tip, and insert into the hemostasis valve of the guiding catheter and advance. Peel the sheath introducer off, and advance both the wire and delivery sheath together to the end of the guide catheter. Now attach a torque to the protection wire, and steer the wire using the torque with one hand while advancing the sheath with the second. Advance the filter and deploy a minimum of 3.0 cm distal to the lesion. Advance the torque to the hemostasis valve and tighten. Holding this in place, pull back and remove the delivery sheath by peeling it away. The filter is now ready for use. Retrieval is similar to the description above.

**Proximal Occlusion Aspiration Devices: Equipment and Deployment Technique**

The Proxis catheter (currently not in production in the United States) consists of a short, flexible catheter attached to a hypotube catheter shaft (compatible with a 7F guide; (online-only Data Supplement, slide 21: Proximal EPD–Proxis Device). The catheter has a short distal circumferential balloon at the tip and a more proximal balloon within the guide. The proximal end of the catheter has a built-in standard Y adaptor with a hemostasis valve for guide wire and device entry, a Luer connection for aspiration, and an additional Luer connection for the sealing balloon inflation device. The device needs at least a 10-mm landing zone.

After appropriate antiplatelet therapy as per individual/institutional practice and anticoagulation with either heparin or bivalirudin, a 7F guide catheter is used to engage the coronary ostium. The Proxis catheter is advanced through the guide catheter into the proximal portion of the SVG. Once the position of the distal tip of the catheter is verified and found to be satisfactory, the sealing balloon is inflated with the push of a button using the push-button carbon dioxide inflation device, which deploys the balloon to the proper pressure (∼2–3 atm). The antegrade flow in the graft ceases, and the interventional guide wire is then advanced through the catheter and is used to cross the lesion. Balloon angioplasty and stenting are performed. At the end of the procedure or intermittently during the procedure, the column of stagnant blood is aspirated with the aspiration syringe attached via the Luer connection. The device also has an optional 6F infusion catheter that can be used to infuse heparinized saline and thus promote retrograde flow and aspiration.

**Conclusions**

Distal embolization is common during all interventional endovascular procedures in atherosclerotic vasculature. The use of EPDs has been shown to substantially reduce the risk of major adverse cardiovascular events in patients undergoing SVG PCI and is therefore a Class I indication. However, the actual use of these devices in real-world clinical practice is surprisingly low. EPDs are routinely used in carotid stenting and are being tested for peripheral and renal artery interventions.

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