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STATE-OF-THE-ART PAPERS

Distal Myocardial Protection During Percutaneous Coronary Intervention

When and Where?

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The discrepancy between angiographic success and microvascular perfusion has been recognized for some time. In the face of an open artery, the degree of microvascular perfusion determines post-infarct prognosis. Despite successful epicardial recanalization, tissue perfusion may be absent in up to 25% patients with acute myocardial infarction. Historically associated with saphenous vein graft intervention, embolization is increasingly recognized in native coronary arteries, particularly in patients undergoing primary percutaneous coronary intervention (PCI). With more than two million PCI procedures performed worldwide each year, there is enormous interest in protecting the left ventricular myocardium from embolization during PCI. This article reviews the evidence for distal myocardial protection and discusses the relative merits of the different available techniques. (J Am Coll Cardiol 2005;46:1434–45) © 2005 by the American College of Cardiology Foundation

Distal protection devices (DPDs) were first introduced for cerebral protection during carotid artery stenting (CAS) (1). In this setting, registries have demonstrated that use of DPDs may halve the combined end point of stroke or death (2,3).

Although angiographic evidence represents only the tip of the embolization iceberg during percutaneous coronary intervention (PCI), even this occurs in up to 15% patients undergoing primary PCI (4). Angiographic indicators of embolization such as corrected Thrombolysis In Myocardial Infarction (TIMI) frame count and myocardial blush grade (MBG), as well as rapidity of ST-segment resolution, are highly predictive of clinical and functional outcome (5,6).

That these phenomena are a manifestation of embolization, rather than de novo thrombus formation, is borne out by histological data showing, during elective PCI, emboli comprised of mucopolysaccharide components and necrotic cores (6–11). Vulnerable plaque morphology, namely disruption or thinning of the fibrous cap, overlying thrombus, and increased lipid content are associated with complications from endovascular procedures (12,13). High plaque macrophage content and plasma matrix metalloproteinase 9 (MMP9) levels may predict embolization during PCI, possibly due to thinning of the fibrous cap by MMP9 secreted by plaque macrophages (14). In addition to mechanical obstruction, the local response to embolization may contribute to myonecrosis (15–19).

It is thus not surprising that emboli are resistant to antiplatelet medication. Although use of glycoprotein (GP) IIb/IIIa inhibitors has contributed to improved success rates with PCI, intervention in saphenous vein grafts (SVG) and in native vessels with high intraluminal thrombus burden continues to be hampered by thromboembolic events.

TYPES OF DEVICES

Available devices fall into four categories (Table 1):

Distal filtration devices
Distal occlusion devices
Proximal occlusion devices
Thrombus extraction devices

The devices with widest evidence base in each category are the EZ-FilterWire (Boston Scientific, Natick, Massachusetts), the GuardWire (Medtronic AVE, Santa Rosa, California), Proxis (Velocimed, Maple Grove, Minnesota), and X-Sizer (EndiCOR Medical, San Clemente, California) systems, respectively. This review will therefore concentrate predominantly on these systems.

The FilterWire system (Fig. 1) incorporates a nonocclusive filter (pore size 110 μm) in the shape of a windsock, mounted on a nitinol loop, and fixed on its own guidewire, which is deployed through a 3.2-F delivery sheath. The nitinol loop self-expands to fit vessels 3.5 to 5.5 mm in diameter, and intervention performed over the wire. Finally, the device is captured using a 4-F retrieval sheath. Other filtration devices work similarly.

The GuardWire temporary occlusion-aspiration system (Fig. 2) consists of a guidewire incorporating a central inflation lumen, to which an elastomeric balloon is attached. This has a 2.8-F crossing profile, and injection of diluted contrast results in balloon inflation (2.5- to 5.0-mm or 3.0- to 6.0-mm diameter), arresting anterograde flow. Intervention is performed over the wire, and liberated debris trapped proximal to the balloon aspirated through a 5-F monorail

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Abbreviations and Acronyms

AMI = acute myocardial infarction
ACS = acute coronary syndromes
CAPTIVE = CardioShield Application Protects During Transluminal Intervention of Vein Grafts by Reducing Emboli
CAS = carotid artery stenting
DPD = distal protection device
GP = glycoprotein
MACE = major adverse cardiac event
MBG = myocardial blush grade
MMP9 = matrix metalloproteinase 9
PCI = percutaneous coronary intervention
PRIDE = PRotection During Saphenous Vein Graft Intervention to Prevent Distal Embolization
SAFE = Saphenous Vein Graft Angioplasty Free of Emboli trial
SAFER = Saphenous Vein Graft Angioplasty Free of Emboli Randomized trial
SVG = saphenous vein graft

Export Aspiration catheter. The balloon is then deflated and flow restored.

The Proxis system incorporates a sealing balloon that is deployed upstream of the stenosis to create a stagnant column of blood in which intervention is performed (Fig. 3). Protection is thus in place before any device crosses the lesion. The device is 7- or 8-F guide compatible, and protects vessels 2.5 to 5 mm in diameter. The stent is delivered through the Proxis system, and flow is reversed, aspirating debris, before the sealing balloon is deflated, restoring flow.

The X-Sizer system (Fig. 4) consists of a 1.5- or 2.0-mm stainless steel helical cutter in a protective housing connected to a 4.5- or 5.5-F dual-bore catheter shaft containing the guidewire and vacuum/extraction lumens. The catheter shaft is linked to a handheld control module and vacuum bottle in which debris is collected. Activating the control unit simultaneously activates the helical cutter, which extends 1 mm beyond the protective housing, rotating at ~2,100 rpm and initiates the vacuum, resulting in tissue maceration, excision, and aspiration.

USE IN ACUTE CORONARY SYNDROMES (ACS)

Table 2 shows the trials employing DPD in ACS (trial acronyms explained in Table 3). There have been concerns that DPD use during primary PCI might delay reperfusion. The first study using the FilterWire in primary PCI showed that successful DPD positioning was achieved in 89% of

Table 1. Embolic Protection and Thrombectomy Devices Available or in Development

Filter-Based Systems	Distal Occlusion-Aspiration Systems	Thrombectomy Devices	Proximal Balloon Occlusion-Flow Reversal Systems
EZ-FilterWire (EPI, Boston Scientific) -fixed to its own guidewire -3.2-F crossing profile -110 μm pores -6-F guide-compatible	GuardWire (Medtronic) -2.8-F crossing profile -7-F guide-compatible	X-Sizer (Endicor) -4.5- or 5.5-F crossing profile -6- or 8-F guide-compatible -compatible with any guidewire	Proxis (Velocimed) -7/8-F guide-compatible -compatible with any guidewire
Spider and Microvena Trap (eV3, Minneapolis, Minnesota) -monorail system -Heprotec coating prevents thrombin build-up -3.2- and 2.9-F crossing profiles -6F guide-compatible	TriActiv system (Kensey Nash)	AngioJet (Possis)	Kerberos Rinspirator/Protection device (Kerberos)
Angioguard (Cordis) -100 μm pores -7-F guide-compatible		Hydrolyzer (Cordis)	Parodi Anti-embolization device (ArteriA)
Cardioshield and Neuroshield (Mednova/Abbott, Galway, Ireland)		Rescue (Boston Scientific) -4.5-F crossing profile -7-F guide-compatible	MO.MA occlusion system (Invatec, Brescia, Italy)
Rubicon (Rubicon Medical Corp.) -100 μm pores -fixed to its own guidewire -2-F crossing profile -6-F guide-compatible			
Interceptor (Medtronic AVE) -100 μm pores -6-F guide-compatible		Pronto (Vascular Solutions) -7-F guide-compatible	
		Diver (Invatec, Brescia, Italy) -3.8-F crossing profile -6-F guide-compatible	

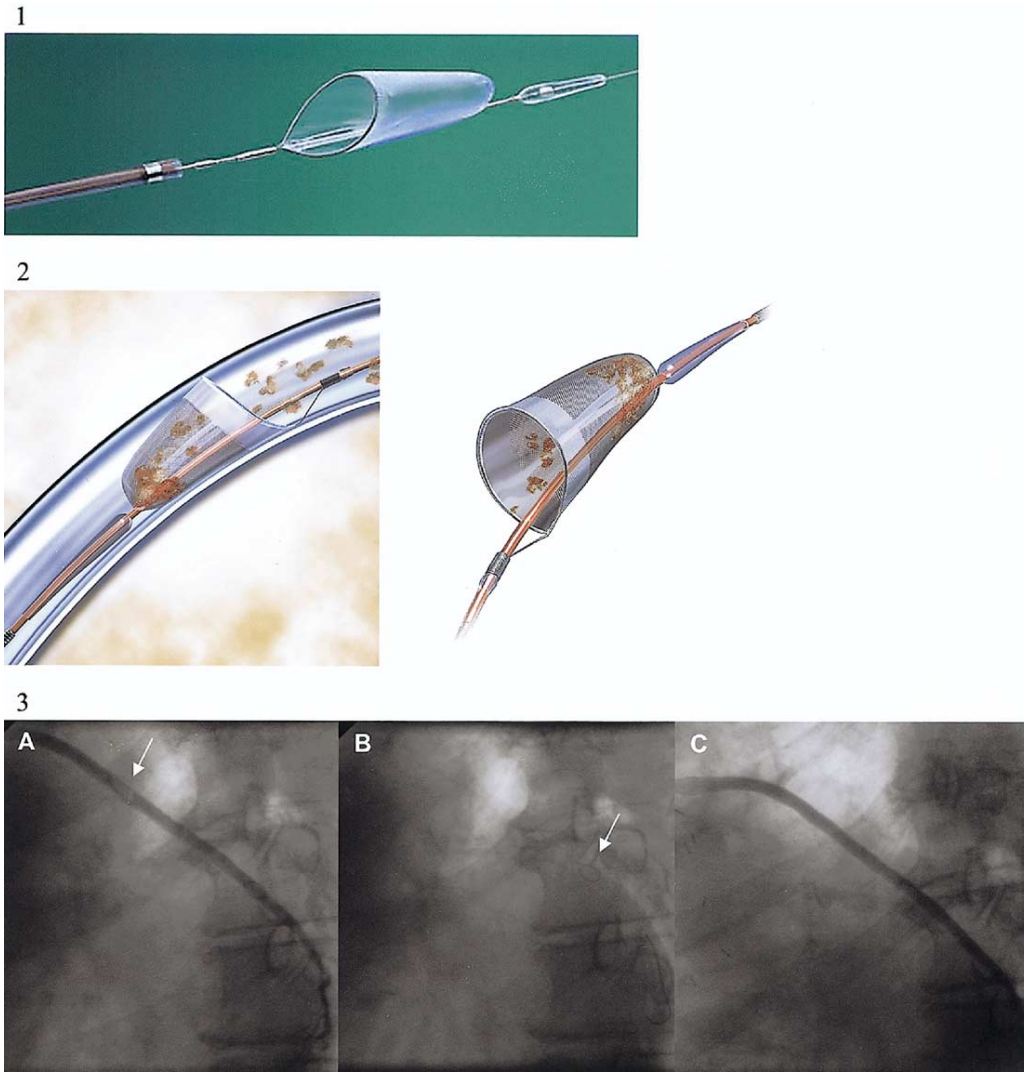

Figure 1. The FilterWire system. **(Panel 1)** The polyurethane porous membrane filter attached to a nitinol loop. **(Panel 2)** The filter is deployed distal to the lesion, and the nitinol loop self-expands to fit the vessel upon retraction of the delivery sheath. **(Panel 3)** Saphenous vein graft containing thrombus, seen as intraluminal filling defect **(A)**, treated with percutaneous coronary intervention using FilterWire protection **(B)**, achieving a good result after stenting **(C)**.

patients in ≤10 min (6). Compared to historical controls, FilterWire use improved final angiographic characteristics and left ventricular performance. Among the several limitations of this study, final TIMI flow grade <3 in 85% of patients in the control group may have lead to overestimation of the benefit of the DPD.

A small study using the GuardWire in patients with angiographic "high-burden thrombus" undergoing primary PCI showed improved flow and MBG, but this did not translate into a reduction in 30-day major adverse cardiac events (MACE) (20). The EMERALD study was the first large randomized trial to evaluate the GuardWire in patients with acute myocardial infarction (AMI). Although the device markedly reduced the incidence of angiographic slow/no-reflow, there was no significant overall effect on ST-segment resolution or infarct size. Preliminary results from the first 188 patients undergoing PCI using the GuardWire in the RUBY registry have suggested that direct device delivery was possible in 87% cases, with favorable angiographic and electrocardiogram characteristics and low clinical event rates. In the PROMISE study, use of the FilterWire-EX in patients undergoing primary PCI did not improve reperfusion and did not reduce infarct size compared with usual care.

There are no data on the safety or efficacy of proximal occlusion systems in AMI.

X-Sizer thrombectomy was first assessed in a small randomized study of patients with suspected intracoronary thrombus (21). Although the study failed to show a benefit on final angiographic characteristics, creatine kinase-MB, or 30-day MACE, X-sizer pretreatment was associated with more rapid normalization of epicardial flow and, in patients

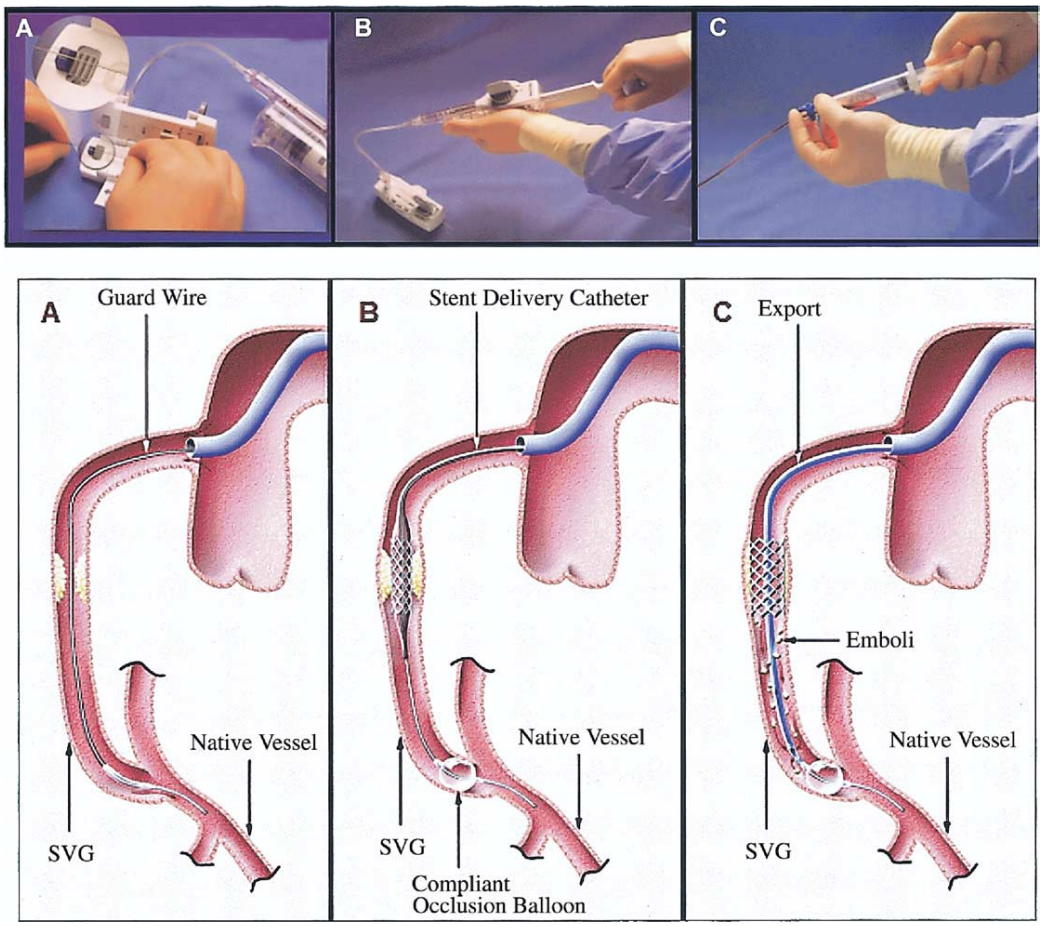

Figure 2. The GuardWire system. **Upper panel** corresponds to **lower panel**: the GuardWire, used to cross the lesion, is inserted into the MicroSeal Adapter **(A)**, connected to the EZ Flator, which is inflated to occlude the vessel **(B)**. Debris is aspirated using the Export Aspiration catheter **(C)**. SVG = saphenous vein graft.

with ST-segment elevation myocardial infarction, more rapid ST-segment resolution. The study was underpowered to detect a benefit in clinical parameters. In AMI patients with angiographic evidence of thrombus (22), thrombectomy significantly improved pre-PCI flow, post-procedural MBG, and ST-segment resolution, but this was not reflected in hard clinical end points, and the device failed to traverse the lesion in 9% of patients.

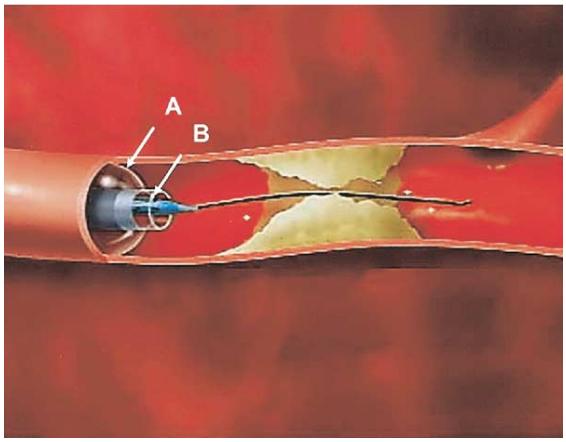

Figure 3. The Proxis system is delivered through a guiding catheter, and the sealing balloon **(A)** is inflated proximal to the stenosis, arresting flow, and debris aspirated through the Proxis system **(B)**.

In the VeGAS-2 study, the AngioJet thrombectomy device (Possis, Minneapolis, Minnesota) was compared with intracoronary urokinase infusion (23). Although thrombectomy was technically successful and reduced in-hospital MACE, the results were clouded by subsequent studies demonstrating worse outcomes with urokinase than with placebo in patients with thrombotic lesions undergoing PCI (24). The disappointing results of the AIMI study, presented at Transcatheter Cardiovascular Therapeutics (TCT) 2004, showed that AngioJet use paradoxically increased infarct size.

There seem to be no data to suggest that routine use of any DPD system is beneficial in patients with ACS undergoing PCI. However, it may be hard to show the benefit of protection against embolization that undoubtedly happens during angioplasty for AMI. In a prothrombotic milieu, thrombi may form on the downstream (low pressure) side of the protection device and embolize. Furthermore, fragmen-

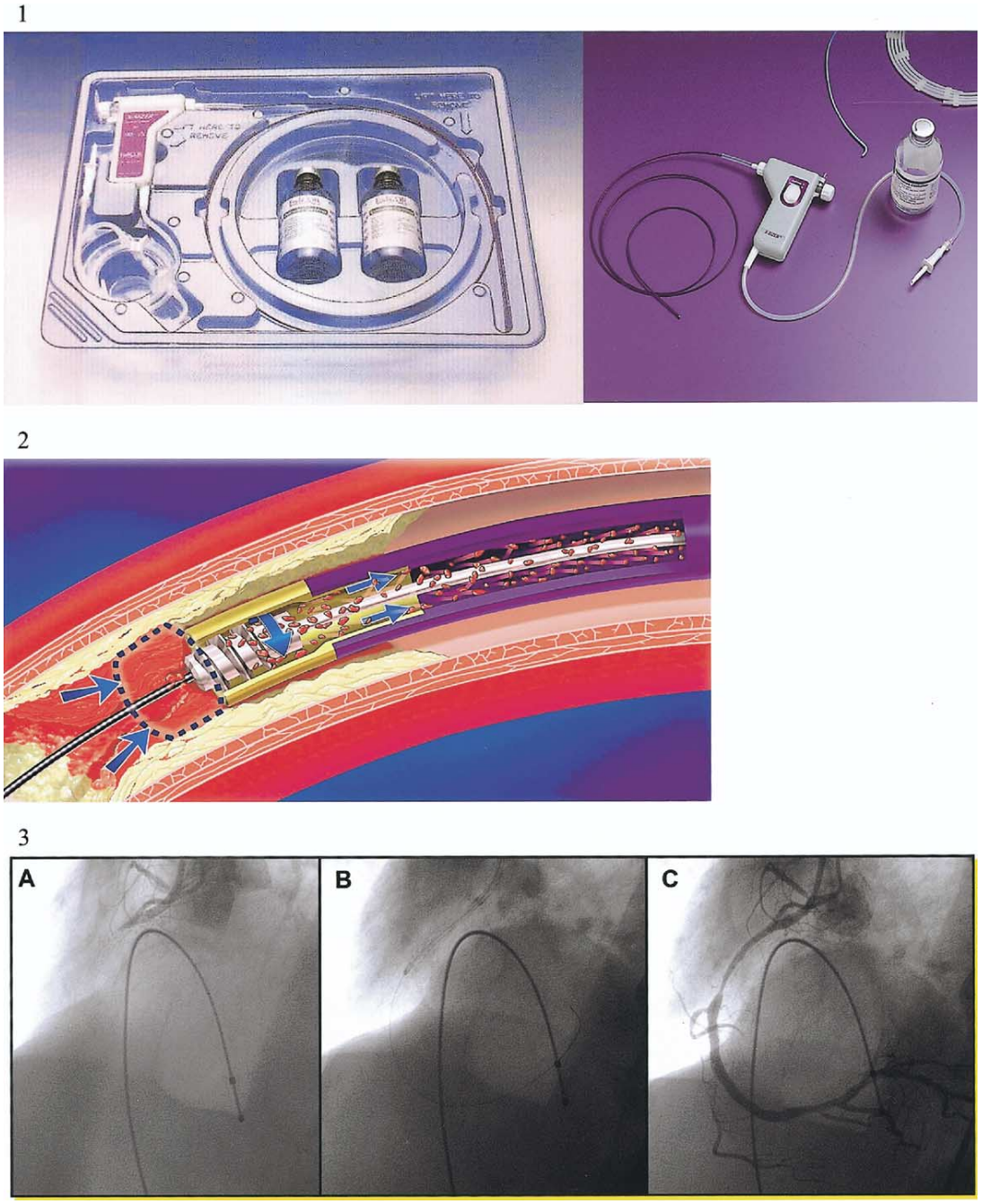

Figure 4. The X-Sizer thrombectomy system comes ready to assemble in a tray **(panel 1)**. Schematic of mechanism of action **(panel 2)**. **Panel 3** shows angiogram of right coronary artery proximally occluded by thrombus **(A)**, X-sizer thrombectomy device in situ **(B)**, and angiographic appearance after thrombectomy **(C)**.

tation of large thrombi by GP IIb/IIIa inhibitors or thrombolysis may result in small particles that pass through the filter. Lastly, in contrast to the cholesterol emboli released in SVG intervention, the consequence of embolization during AMI is not a fait accompli, because thrombotic platelet emboli may subsequently be lysed in the distal myocardial bed, without sequelae. Thus, the significance of embolization during AMI may depend on the nature of the embolic material and integrity of endogenous thrombolytic response

USE IN SVG

Pathophysiology. Saphenous vein graft interventions carry a 20% risk of MACE, predominantly AMI, and significant risk of no-reflow (25). The protection offered by GP IIb/IIIa inhibitors during native vessel PCI has not been mirrored in SVG intervention (26,27), reflecting the differing composition of plaque in these settings; SVG plaques tend to be cholesterol-rich, with relatively low calcium

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