EDITORIAL COMMENT

Aspirating and Filtering Atherothrombotic Debris During Percutaneous Coronary Intervention*

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The coronary “no-reflow” phenomenon can occur during reperfusion of an infarct artery or after percutaneous coronary intervention (PCI) (1). It represents inadequate myocardial perfusion despite epicardial coronary artery patency and can be caused by reperfusion injury, embolization of atherosclerotic or thrombotic debris, or ischemia-induced microvascular damage from endothelial cell injury, leukocyte plugging of capillaries, myocardial cell edema, free oxygen radical generation, and microvascular spasm. Persistent no-reflow is associated with a high incidence of myocardial infarction (MI) and the risks of congestive heart failure and death.

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Multiple pharmacological and device therapies have been developed in an attempt to protect the myocyte from microvascular injury. Thrombectomy and embolic protection devices (EPDs) are used to reduce the risk of distal atherothrombotic embolization during primary PCI and saphenous vein graft (SVG) PCI. Although these devices increase procedure time and complexity, radiation exposure, and cost, they would become routine adjunctive therapy if they could be shown to reduce the risk of MI, congestive heart failure, and death.

Myocyte Protection by Device Therapy

Thrombectomy devices. Thrombectomy devices avoid the need to initially cross the target lesion with a device and reduce the thrombus burden before PCI. Thrombectomy catheter systems that mechanically disrupt and aspirate intravascular thrombus have proven disappointing and included the AngioJet rheolytic system (Possis Medical Inc., Minneapolis, Minnesota), the X-Sizer mechanical thrombectomy system (eV3, Inc. Plymouth, Minnesota), and the Rinspiration system (Kerberos Proximal Solutions, Cupertino, California). More promising results have been seen with simple thrombus aspiration catheters. The Rescue PT system (Boston Scientific, Maple Grove, Minnesota) and the thrombus vacuum aspiration catheter (TVAC) (Nipro, Osaka, Japan) are aspiration catheters that employ a proximal vacuum pump with a collection bottle. Manual thrombus aspiration with a syringe can be performed through a guide catheter or the central lumen of the Export (Medtronic Vascular, Santa Rosa, California), Diver CE (eV3), and Pronto (Vascular Solutions, Inc., Minneapolis, Minnesota) aspiration catheters. Thrombus aspiration can help define the stenosis and facilitate a strategy of direct stenting during primary PCI, but catheter lumen size might limit aspiration of large thrombus mass. Although thrombectomy catheters can decrease thrombus burden, they do not protect against distal embolization during the subsequent PCI procedure.

EPDs. There are two types of EPDs: filter devices and occlusion-aspiration devices. Distal embolic filter devices maintain distal perfusion and allow injection of contrast medium during PCI while trapping most particulate debris. Limitations include need for a suitable landing zone, frequent need to predilate the lesion to allow passage of the filter device, embolization during passage of the device distal to the lesion, failure to prevent embolization into side branches proximal to the filter, possible trauma to the vessel, and failure to trap particles <100 μm. Embolic filters include the FilterWire-EZ (Boston Scientific), the SpideRX protection device (eV3), and the Interceptor Plus Coronary Filter System (Medtronic Vascular).

Proximal and distal occlusion-aspiration devices suspend antegrade flow during the intervention. The stagnant column of blood containing particulate debris and humoral mediators is aspirated before distal occlusion and restoration of flow. Disadvantages include poor vessel opacification during the procedure and distal ischemia while occlusion is maintained. The Proxis embolic protection system (St. Jude Medical, St. Paul, Minnesota) is a proximal occlusion device. It protects all distal side branches, but the requirement of a proximal landing zone precludes its use in very proximal lesions. Distal occlusion devices include the PurcuSurge GuardWire (Medtronic Vascular) and the TriActive system (Kensey Nash, Exton, Pennsylvania). They share the limitations of the distal filter devices noted previously, with the exception of trapping smaller particles.

Primary PCI

Despite successful epicardial coronary artery reperfusion with primary PCI, impaired myocardial reperfusion persists
in 30% of patients and is suggested by slow coronary blood flow, abnormal myocardial blush grade, or persistent ST-segment elevation. Smaller studies with thrombectomy catheters and EPDs have shown encouraging results in improving microvascular reperfusion (better coronary flow, myocardial blush grade, and ST-segment resolution) after primary PCI (2,3), but larger studies (>200 patients) have not (4,5). Despite frequent recovery of atherothrombotic debris and a decrease in angiographic embolization rates, there has been no evidence to suggest that these interventions reduce myocardial infarct size, reinfarction, or mortality (2,3).

Besides the previously described limitations of the devices, limitations of the trials include small sample sizes, mean ischemic times >4 h, and the inclusion of low-risk lesions (patent arteries, circumflex and branch arteries) and low-risk patients (30-day mortality <3%). Therefore, it was with great interest and some surprise that the TAPAS (Thrombus Aspiration during Percutaneous Coronary Intervention in Acute Myocardial Infarction Study) trial recently reported improved reperfusion and clinical outcomes with a strategy of manual thrombus aspiration through the Export catheter and direct stenting irrespective of clinical and angiographic characteristics (6,7). Importantly, the TAPAS trial was a single-center study conducted by superb interventionalists in 1,071 patients, and the mean time-to-treatment of 3 h was a least 1 h faster than in previous studies. In this issue of *JACC: Cardiovascular Interventions*, the TAPAS trial investigators report a cohort study with 2 manual thrombus aspiration catheters: the Diver catheter (internal lumen 0.062 inches) and the Export catheter (internal lumen 0.041 inches) (8). There were no differences in successful thrombus aspiration, Thrombolysis In Myocardial Infarction flow, myocardial blush grade, ST-segment elevation resolution, retrieved particle size, or clinical outcomes despite the difference in catheter lumen diameter. The question remains whether the potential benefit with this aspiration strategy is due to thrombectomy alone or thrombectomy plus direct stenting (6,7,9).

**SVG PCI**

Compared with coronary artery interventions, SVG PCI is associated with increased risk for morbidity and mortality. The major factor is distal embolization of atherothrombotic debris resulting in no-reflow and periprocedural MI. Risk can be estimated by angiographic estimates of plaque volume and SVG degeneration (10) and by the presence of thrombus. A pooled analysis of 5 randomized clinical trials demonstrated no reduction in risk with glycoprotein (GP) IIb/IIIa inhibitors administered during SVG PCI (11).

The American College of Cardiology/American Heart Association/Society for Cardiovascular Angiography and Interventions 2005 guideline update for PCI gives a class Ib recommendation for the use of EPDs during SVG PCI when technically feasible (12). Likewise, the European Society of Cardiology Guidelines for PCI gives EPDs a class Ib recommendation for SVG PCI (13). Interestingly, a review of the published reports reveals only 1 randomized controlled trial with 801 patients that enrolled 8 years ago. The SAFER (Saphenous vein graft Angioplasty Free of Emboli Randomized) trial demonstrated a reduction in the composite end point of death, MI, emergency bypass surgery, or target lesion revascularization at 30 days with the GuardWire device versus conventional guidewire use (14). Subsequent EPDs have only been tested against an active control group in noninferiority comparisons (15-17). As with GP IIb/IIIa inhibitor therapy in native coronary interventions, the major benefit has been in decreasing periprocedural MI measured by biomarker release; no impact on 30-day Q-wave MI or mortality rates has been suggested, and there are no data on long-term survival. Although all would agree that it is desirable to prevent periprocedural MI, the relationship between periprocedural MI and long-term prognosis might be more by association than causality (18). Because patients undergoing coronary artery bypass graft surgery often have a large atherosclerotic burden, decreased ventricular function, and significant co-morbidities, there are many other factors that contribute to their prognosis, with the strong possibility that embolization during SVG PCI is a surrogate marker of increased overall risk.

In this issue of *JACC: Cardiovascular Interventions*, the AMEthyst (Assessment of the Medtronic AVE Interceptor Saphenous Vein Graft Filter System) study investigators report the successful results of another noninferiority comparison trial that will probably lead to Food and Drug Administration approval of another EPD (19,20). However, before we consider using these devices routinely, it is important to recognize that anatomic exclusions might be present in one-half the cases and EPDs are currently used in only one-quarter of SVG PCI (21). One explanation for the difference between eligibility and use is that many SVGs perfuse branch arteries or small areas of myocardium, so the interventionalist might be choosing the faster, easier procedure. Also, only an internal mammary artery graft to the left anterior descending artery has been shown to improve long-term prognosis, so optimal medical therapy is another treatment option for severely degenerated SVGs.

**Conclusions**

At the present time, routine use of mechanical protection devices during primary PCI cannot be recommended. However, manual thrombus aspiration is an attractive concept that is easy, fast, and deserves further investigation in multicenter trials focusing on patients with large infarct
arteries occluded by thrombus who present early for primary PCI.

Selective use of EPDs in SVG PCI is reasonable, but event rates after SVG PCI have decreased in recent years (19). Better patient selection, more frequent pretreatment with statins and clopidogrel, more aggressive use of intragraft vasodilator administration before and after PCI, better stents, and adoption of a direct stenting strategy with 1 balloon inflation and only 1 stent suggests to me that enough equipoise exists to ethically support a randomized clinical trial of EPD versus conventional guidewire use in the current interventional cardiology era.

Although there are no randomized trials proving benefit for EPDs with carotid stenting, it seems intuitively obvious that any intervention that prevents embolism to the brain should be employed. However, the heart is a more forgiving organ, and the importance of distal embolization into a 4-h-old infarct zone or down an SVG into a distal branch artery is less clear. Only 1 positive randomized trial supporting reduction in major adverse cardiac events exists for each potential indication. One is a single-center study, and the other is 8 years old. I believe more randomized, controlled clinical trial data are needed before we add routine aspiration thrombectomy to primary PCI or routine EPDs to SVG PCI.

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