Advances in Embolic Protection Devices

Will improvements in EPD design lead to safer carotid artery stenting procedures?

BY SAMIR K. SHAH, MD; NAVEEN BALASUNDARAM, MD; AND DANIEL G. CLAIR, MD

Internal carotid artery stenting (CAS) has become an increasingly tenable alternative to carotid endarterectomy for occlusive disease in high-risk patients. Although CAS is advantageous in several respects relative to endarterectomy, both show risk for embolic stroke.[1,2] Despite the absence of any form of embolic protection during initial CAS experiences, the potential for embolism during wire manipulation of the plaque with continuous antegrade blood flow is intuitively evident.[3] In fact, one would expect that the number of emboli produced during CAS would be substantially higher than that produced by carotid endarterectomy, and indeed, this has been shown in several studies.[4,5] Although the clinical significance of emboli remains to be clarified (patients appear to tolerate some emboli as documented by transcranial Doppler or diffusion-weighted imaging [DWI] without sequelae[6,7]), it is likely that a reduction in distal embolization would improve the safety of CAS.

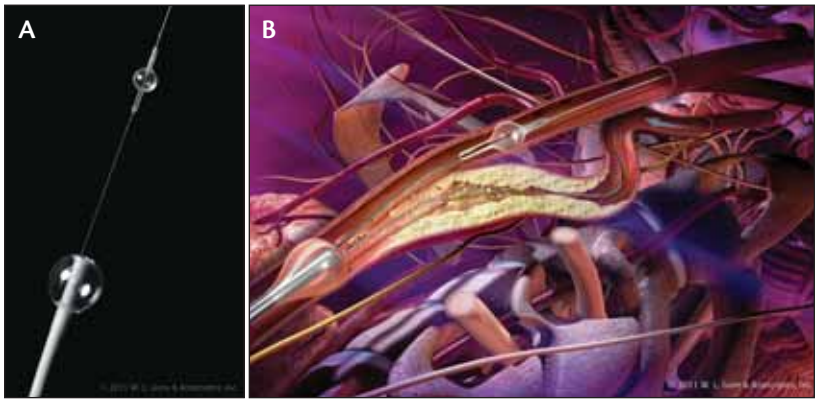

Figure 1. GORE® Flow Reversal System (W. L Gore & Associates [Gore], Flagstaff, AZ). Ex vivo view (A). The larger proximal balloon occludes the common carotid artery, while the distal balloon occludes the external carotid artery. In situ depiction of common and external carotid occlusion and flow reversal (B).

EMBOLIC PROTECTION DEVICES

Since the initial description of an embolic protection device (EPD) in 1990 by Theron et al, there have been numerous technological advances.[8] Currently, three broad categories of EPDs exist: proximal occlusion devices, distal occlusion devices, and filters (Table 1).

Proximal Occlusion Devices

Proximal occlusion devices represent the most recent evolution in EPDs and include the Mo.Ma Ultra (Medtronic Invatec, Frauenfeld, Switzerland) and the GORE® Flow Reversal System (Figure 1), which produce flow stasis and flow reversal, respectively. The Mo.Ma device uses balloon occlusion of the common carotid and external carotid arteries to achieve cessation of blood flow before angioplasty and stenting. The GORE® Flow Reversal System additionally establishes a filtered arteriovenous shunt between the common carotid and femoral vein to produce flow reversal.

The principal advantage of proximal occlusion devices is the avoidance of plaque disruption (provided the lesion begins distal to the origin of the external carotid artery) during EPD placement. The GORE® Flow Reversal System has the added benefit of actively removing particulate matter. Given that these devices sit proximally to the target lesion, there are no relevant landing zone requirements. Disadvantages include the need to separately place two balloons, a slightly larger 9- to 9.5-F compatibility, and potential intolerance to flow cessation.

Distal Occlusion Devices

Distal occlusion devices attempt to prevent embolization via balloon occlusion of the internal carotid artery distal to the lesion. The only currently available device is the GuardWire system (Medtronic, Inc., Minneapolis, MN). The device is 6-F compatible and is available with two balloon

TABLE 1. TECHNICAL DETAILS OF SELECTED EPDs

Type of Protection Device	Device Name	Manufacturer	Landing Zone (mm)	Pore Size (µm)
Proximal occlusion	Mo.Ma Ultra	Medtronic Invatec	–	–
	GORE® NPS	W. L. Gore & Associates	–	–
Distal filter	FilterWire EZ	Boston Scientific Corporation	13.4	110
	Emboshield Nav[6]	Abbott Vascular	19–22.5	140
	RX Accunet	Abbott Vascular	15.1	150
	SpiderFX	Covidien	17.3	50–300
	FiberNet	Medtronic, Inc.	15	< 40
	GORE® Embolic Filter	W. L. Gore & Associates	9[a]	100
	Angioguard RX	Cordis Corporation	5.9	100
Distal occlusion	GuardWire	Medtronic, Inc.	–	–

[a]*No landing zone recommendation provided in the Instructions for Use.*

sizes to occlude vessels with 2.5- to 5-mm and 3- to 6-mm diameters; crossing profiles are 0.028 inches and 0.036 inches, respectively.

The balloon is equipped with a 2.5-cm nitinol distal tip and is advanced past the lesion and inflated using a 0.014-inch wire inflation system. The inflation device is then detached from the balloon and wire, which are used to complete the intervention. After stent placement, an aspiration catheter is advanced over the wire to evacuate debris before balloon retrieval. The aspiration catheter can also be used to flush debris from the "dead end" of the internal carotid artery below the inflated balloon into the external carotid artery, but this risks embolism via external to internal carotid collaterals.

Clear advantages of distal occlusion devices include a low crossing profile and a minimal 4.5-mm landing zone for the occlusion balloon. The need to traverse the lesion before intervention, mandatory use of aspiration, risk of embolism past the balloon, interference with visualization of the lesion, injury to the distal carotid artery, and intolerance to flow occlusion constitute its principal disadvantages.

Filter Devices

Filter devices are the most common EPD type and are available in a broad variety of specifications (Figure 2). Many filter EPDs come attached to a moldable wire tip and wire body, whereas some may be advanced over a 0.014-inch wire that has traversed the lesion. Filter details range widely with regard to several specifications: crossing profile, landing zone length, and pore size. Crossing profile ranges from 1.7 F (FiberNet, Lumen Biomedical, Inc., Plymouth, MN) to 3.9 F (Angioguard Rx, Cordis Corporation, Bridgewater, NJ). The majority of filters can be primarily advanced past the lesion without angioplasty; if needed, the lesion can be predilated with a low-profile angioplasty balloon, although this risks embolism. In addition to the smallest crossing profile, the FiberNet filter also has a short landing zone (15 mm). Although pore size typically ranges from 100 to 140 µm, devices with substantially smaller (FiberNet, 40 µm) and larger pores (SpideRX [Covidien, Mansfield, MA],167–209 µm) are available.

Assessment of flow before filter retrieval is mandatory, as diminished flow may indicate clogging of the device with embolized debris. This requires aspiration of the debris and reassessment of flow to avoid embolism during retrieval. Persistent flow limitations may be due to arterial spasm, which can be treated with injection of a vasodilator (eg, nitroglycerin). Filter devices are easy to deploy, do not interfere with lesion visualization, and maintain antegrade blood flow. However, they also suffer from some disadvantages: the need to cross the lesion before implementation of protection, embolism through the filter both during the intervention and during recapture, and the need for a nontortuous landing zone. Absence of the latter may make performance of the procedure impossible and can allow embolism between the vessel wall and the filter when coaptation of the filter to the vessel wall is inadequate.

EFFECTIVENESS

There have been numerous studies establishing the safety of individual devices (Table 2). Nonetheless, it is difficult to arrive at any robust conclusions regarding the relative effectiveness of particular EPDs because of differences among studies with respect to patient comorbidities, degree of carotid stenosis and symptomatology, carotid stents, operator experience, and other factors that could feasibly affect outcomes. The ideal test to determine EPD effectiveness would be a comprehensive comparative randomized trial involving multiple EPDs;

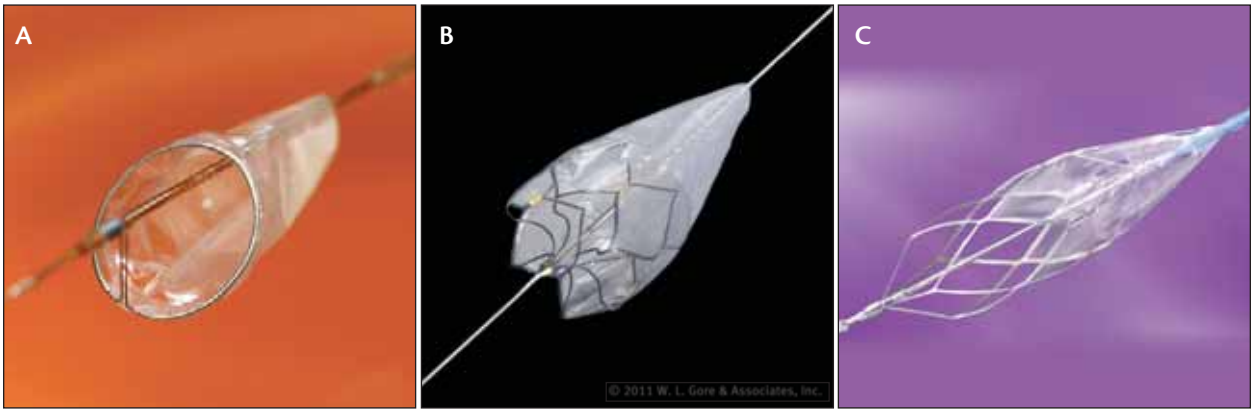

Figure 2. Filter EPDs. FilterWire EZ (A), GORE® Embolic Filter (B), and RX Accunet embolic protection system (C).

regrettably, there is no such study. To make matters worse, as stated previously, knowledge regarding the number and size of emboli required to produce clinical sequelae is lacking.

More problematic is the absence of clear evidence of the general effectiveness of EPDs. No clinical trial has shown improved outcomes from EPD use despite the instinctive sense that they must improve safety. Macdonald et al compared 15 CAS patients who underwent treatment with the Emboshield filter (Abbott Vascular, Santa Clara, CA) with 15 patients who underwent unprotected CAS, using DWI magnetic resonance imaging and transcranial Doppler signals as surrogates for stroke.[7] There was a statistically greater number of signals consistent with embolism on transcranial Doppler in patients with filter placement than in those without. Similarly, there was an increased, but statistically nonsignificant, number of new white lesions indicating emboli on DWI in patients with EPD. The increased number of emboli in EPD patients was generated during filter installation and retrieval.

A similar randomized study by Barbato et al using the RX Accunet embolic protection system (Abbott Vascular) in 35 patients found that there was no statistical difference in the number of lesions detected by DWI between the EPD and non-EPD cohorts.[6] Both of these studies have a number of weaknesses—most importantly, the small sample size and the use of proxy imaging measurements instead of actual clinical stroke. The latter point cannot be overemphasized, and one must be cautious when interpreting the clinical significance of these findings. Whether or not these potential drawbacks are limited to filter devices or extend to all current EPDs is unknown. Some studies have suggested reduced embolism with distal occlusion[9] or proximal occlusion devices relative to filters.[10]

It is important to be mindful that filter use may not be as protective as once thought and has the potential to paradoxically increase embolic phenomena. Despite these issues, most agree that the use of embolic protection is mandatory, and evidence for this comes from several sources. First, the capture rate for visible debris in filters is very high and has been noted at 60% when evaluated by Sprouse et al.[16] Second, experimental ex vivo assessments of

TABLE 2. SELECTED EPD TRIALS

Device	Trial	Number of Patients	30-Day Stroke	30-Day MI/Stroke/Death
Mo.Ma Ultra	ARMOUR[11]	262	2.3%	2.7%
GORE® Flow Reversal System	EMPIRE[12]	245	2.9%	3.7%
Angioguard/Angioguard XP	SAPPHIRE[2]	167	3.6%	4.8%
Accunet	ARCHER[13]	581	5.5%	8.3%
GuardWire	MAVERIC I/II[14]	498	4.2%	5.4%
FiberNet	EPIC[15]	237	2.1%	3%

Abbreviations: MI, myocardial infarction.

EPDs reveal that they all trap debris typically released during CAS.[17,18] Finally, large registries that have compared outcomes with and without protection have found significant reductions in neurologic events among patients who were treated with EPDs.[19-21] It is unclear whether data that do not support the use of these devices reflect a failure of the device, some problem with the devices inducing embolization, or the inability of the devices to trap microparticles. In this regard, the use of proximal protection has the distinct advantages of protected lesion crossing, trapping of debris of all sizes, and no injury beyond the area being protected.

A thoughtful paradigm for choosing EPD type has been outlined by Schneider and Ansel.[22] Briefly, these authors recommend the use of proximal protection in the setting of complex lesions and in those with limited cerebral reserve, filters in the setting of poor collaterals, and a device of the interventionist's choice in situations that do not fall into any of these categories. What is perhaps most important in the performance of CAS is the understanding that adequate experience with every available device is unattainable, and each interventionist should choose one proximal protection system and one distal protection system (filters most commonly) to achieve familiarity and develop a procedural routine. This will limit intraprocedural complications related to deployment and use problems.

CONCLUSION

Embolic stroke remains one of the principal risks of CAS. EPDs attempt to reduce this risk via proximal or distal occlusion or filtration. Although seemingly obvious, evidence regarding the effectiveness of EPD use and of the superiority of one EPD over another is lacking, and we are unlikely to ever see randomized data regarding the use of these devices. Further study is needed to clarify the role of EPDs during CAS. For example, what are the implications of embolic debris below the threshold of filter trapping? Are symptomatic and elderly patients more susceptible to microembolic debris (as an explanation for increased neurologic events in these patient groups)?

Advances in CAS are likely to continue and will be related to the systems used to introduce equipment into the carotid artery, embolic protection, and stent design. Of all of these areas, the majority of advancements to date have been in the design of EPDs, which are now specifically engineered for CAS. I believe that CAS has been made safer because of these advances, and further iterations of these devices will likely lead to continued improvements in the safe performance of this procedure. One can easily envision the day when performance of CAS will be the primary method of treating carotid disease because of successful efforts to limit neurologic sequelae as is already being seen in the development of EPDs. ■

Samir K. Shah, MD, is with the Department of Vascular Surgery, The Cleveland Clinic Foundation in Cleveland, Ohio. He has disclosed that he has no financial interest related to this article.

Naveen Balasundaram, MD, is with the Department of Vascular Surgery, The Cleveland Clinic Foundation in Cleveland, Ohio. He has disclosed that he has no financial interest related to this article.

Daniel G. Clair, MD, is Chair of the Department of Vascular Surgery, The Cleveland Clinic Foundation in Cleveland, Ohio. He has disclosed that he is a paid consultant to Endologix, Inc., Minnow Medical, Boston Scientific Corporation, and Medtronic, Inc. Dr. Clair may be reached at (216) 444-3857; claird@ccf.org.

1. Barnett HJ, Taylor DW, Eliasziw M, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. N Engl J Med. 1998;339:1415-1425.
2. Yadav JS, Wholey MH, Kuntz RE, et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. N Engl J Med. 2004;351:1493-1501.
3. van der Vaart MG, Meerwaldt R, Reijnen MM, et al. Endarterectomy or carotid artery stenting: the quest continues. Am J Surg. 2008;195:259-269.
4. Crawley F, Clifton A, Buckenham T, et al. Comparison of hemodynamic cerebral ischemia and microembolic signals detected during carotid endarterectomy and carotid angioplasty. Stroke. 1997;28:2460-2464.
5. Jordan WD Jr, Voellinger DC, Doblar DD, et al. Microemboli detected by transcranial Doppler monitoring in patients during carotid angioplasty versus carotid endarterectomy. Cardiovasc Surg. 1999;7:33-38.
6. Barbato JE, Dillavou E, Horowitz MB, et al. A randomized trial of carotid artery stenting with and without cerebral protection. J Vasc Surg. 2008;47:760-765.
7. Macdonald S, Evans DH, Griffiths PD, et al. Filter-protected versus unprotected carotid artery stenting: a randomised trial. Cerebrovasc Dis. 2010;29:282-289.
8. Theron J, Courtheoux P, Alachkar F, et al. New triple coaxial catheter system for carotid angioplasty with cerebral protection. AJNR Am J Neuroradiol. 1990;11:869-874; discussion 75-77.
9. Rubartelli P, Brusa G, Arrigo A, et al. Transcranial Doppler monitoring during stenting of the carotid bifurcation: evaluation of two different distal protection devices in preventing embolization. J Endovasc Ther. 2006;13:436-442.
10. Schmidt A, Diederich KW, Scheinert S, et al. Effect of two different neuroprotection systems on microembolization during carotid artery stenting. J Am Coll Cardiol. 2004;44:1966-1969.
11. Ansel GM, Hopkins LN, Jaff MR, et al. Safety and effectiveness of the Invatec Mo.Ma proximal cerebral protection device during carotid artery stenting: results from the ARMOUR pivotal trial. Catheter Cardiovasc Interv. 2010;76:1-8.
12. Clair DG, Hopkins LN, Mehta M, et al. Neuroprotection during carotid artery stenting using the GORE flow reversal system: 30-day outcomes in the EMPIRE clinical study. Catheter Cardiovasc Interv. 2011;77:420-429.
13. Gray W, Hopkins L, Yadav S. Protected carotid stenting in high-surgical-risk patients: the ARCHER results. J Vasc Surg. 2006;44:258-268.
14. Higashida RT, Popma JJ, Apruzzese P, Zimetbaum P. Evaluation of the Medtronic Exponent self-expanding carotid stent system with the Medtronic Guardwire temporary occlusion and aspiration system in the treatment of carotid stenosis: combined from the MAVERIC (Medtronic AVE Self-Expanding Carotid Stent System With Distal Protection in the Treatment of Carotid Stenosis) I and MAVERIC II trials. Stroke. 2009;41:e102-e109.
15. Myla S, Bacharach JM, Ansel GM, et al. Carotid artery stenting in high surgical risk patients using the FiberNet embolic protection system: the EPIC trial results. Catheter Cardiovasc Interv. 2010;75:817-822.
16. Sprouse LR 2nd, Peeters P, Bosiers MJ. The capture of visible debris by distal cerebral protection filters during carotid artery stenting: is it predictable? J Vasc Surg. 2006;41:950-955.
17. Ohki T, Roubin G, Veith FJ, et al. Efficacy of a filter device in the prevention of embolic events during carotid angioplasty and stenting: an ex vivo analysis. J Vasc Surg. 1999;30:1034-1044.
18. Muller-Hulsbeck S, Jahnke T, Liess C, et al. In vitro comparison of four cerebral protection filters for preventing human plaque embolization during carotid interventions. J Endovasc Ther. 2002;9:793-802.
19. Wholey MH, Al-Mubarak N, Wholey MH. Updated review of the global carotid artery stent registry. Catheter Cardiovasc Interv. 2003;60:259-266.
20. Roubin GS, New G, Iyer SS, et al. Immediate and late clinical outcomes of carotid artery stenting in symptomatic and asymptomatic carotid stenosis: a 5-year prospective analysis. Circulation. 2001;103:532-537.
21. Zahn R, Mark B, Niedermaier N, et al. Embolic protection device for carotid artery stenting: better results than stenting without protection? Eur Heart J. 2004;25:1550-1558.
22. Schneider PA, Ansel G. How do I select cerebral protection devices today? J Cardiovasc Surg. 2010;51:873-883.