The balance of evidence for carotid artery stenting with cerebral protection

Key words: carotid artery; stenting; protection devices

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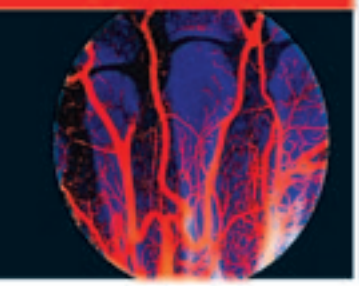


Dr Colombo obtained his MD from the University of Milan, followed by residency at Milan and New York, chief residency at New York and fellowships at the University of California at Irvine and State University of New York in Syracuse. Dr Colombo has devoted time and effort throughout his distinguished career to defining the indications and limitations of coronary stenting. He pioneered the concept of adequate stent deployment during coronary interventions and defined the role of intravascular ultrasound in this setting, and contributed to redefining adequate anticoagulation after coronary stenting. Dr Colombo has published extensively in prestigious cardiology journals, is active in many medical societies and is on the Editorial Board of all major cardiovascular journals. He is recognised worldwide as an authority in interventional cardiology.

Abstract

Although endarterectomy is today considered the gold-standard therapy for the treatment of carotid artery stenosis, the approach is not free of complications. Carotid artery stenting (CAS) has rapidly emerged as an equivalent alternative to surgery for the treatment of extracranial carotid artery disease. Percutaneous stenting is accomplished at the expense of an increased incidence of microemboli. These emboli are associated with a higher neurological complication rate and are also recognised as a potential cause of periprocedural stroke during carotid endarterectomy (CEA). Numerous embolic protection devices are being evaluated as an adjunct to CAS including (1) occlusion balloons, (2) distal filters, and (3) retrograde flow devices. The filter devices are the more promising since they offer the ability to trap embolic debris while maintaining distal cerebral perfusion. They also allow angiographic monitoring of the angioplasty and stent placement concomitant with protection. Their use during CAS has reduced the rate of periprocedural acute cerebral ischaemic complications, thus enhancing the safety of the percutaneous approach, which can therefore be carried out with good results even in high-risk patients. Recently published non-randomised data suggested that unprotected CAS carries a 3.9 times higher risk than the protected CAS for 30-day rate of stroke than of CAS with cerebral protection. Despite the absence of solid scientific data based on randomised trials, carotid filters for cerebral protection have become the standard of care in CAS. Whether this practice underscores the future of protection devices for CAS remains to be seen.

Carotid artery stenting

CAS became a standard percutaneous approach to treating carotid stenosis and, because of the achievement of optimal immediate angiographic results, has emerged as an alternative to CEA. Although CEA is today considered the gold-standard therapy for the treatment of carotid artery stenosis, the approach is not free of complications. In the North American Symptomatic Carotid Endarterectomy Trial Collaborators (NASCET) study, 5.8% of patients suffered from perioperative stroke and death and it was also reported that subgroups of patients at high risk had mortality and morbidity at a rate up to 18%.[1]

Several studies have reported an acceptable rate of immediate complications (particularly in patients at high surgical risk), and good long-term results after CAS.[2,3] However, compared with the surgical approach, percutaneous stenting is accomplished at the expense of an increased incidence of microemboli, as shown by transcranial Doppler monitoring.[4] These emboli are associated with a higher neurological complication rate[5] and are also recognised as a potential cause of periprocedural stroke during CEA.[6,7] Most of the emboli occur during the manipulation of the atheromatic plaque[8] and especially during stent post-dilation.

Protection devices in CAS

A number of non-randomised studies have reported on the safety and feasibility of protection devices in the setting of CAS.[9–11] Protection devices have the potential to reduce the incidence of carotid debris and therefore the intracranial emboli, thus rendering percutaneous treatment of extracranial carotid disease safer (Figure 1).

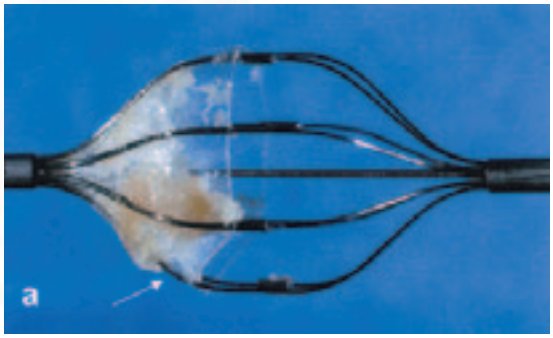
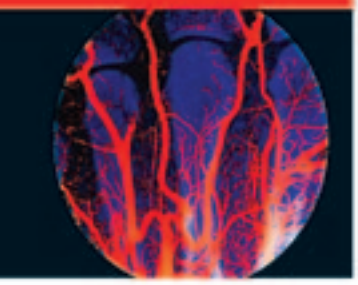


Figure 1. Thrombotic material captured by a Cordis Angioguard™ device. Arrow points to a fold in the plastic membrane which occurred during the retrieval of the protection system.

The balance of evidence for carotid artery stenting with cerebral protection *continued*

Antonio Colombo and Ioannis Iakovou



Very recently, the Endarterectomy Versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis (EVA-3S) Trial reported the results on the first 80 patients randomised in the CAS arm of the study.[12] Unprotected CAS carried a 3.9 times higher risk than the protected CAS for 30-day rate of stroke than of CAS with cerebral protection. This result, despite not being based on a randomised comparison of unprotected *versus* protected CAS, suggests that the use of cerebral protection devices during CAS reduces periprocedural strokes.[12] However, it is worth noting that a substantial number of patients treated without protection developed a stroke, not during the procedure, but during the first 30 days after, suggesting that the lack of a protection device is an unlikely cause. Furthermore, despite their proven safety and effectiveness, these devices are not without complications. Recently, Cremonesi *et al*. reported a 0.9% rate of technical complications (i.e. dissection of the internal carotid artery, or trapped guide wire needing surgical 'bail-out' intervention) during CAS with cerebral protection.[13]

Numerous embolic protection devices are being evaluated as an adjunct to CAS (Figure 2).

The 3 main categories of protection devices are: (1) occlusion balloon, (2) distal filters, and (3) retrograde flow devices. The technical characteristics of the most widely used carotid protection devices are shown in Table 1 and discussed in depth in the accompanying article by Bernhard Reimers. The filter devices are the more promising since they offer the ability to trap embolic debris while maintaining distal cerebral perfusion. They also allow angiographic monitoring of the angioplasty and stent placement concomitant with the protection. Their recent introduction has lowered the rate of periprocedural acute cerebral ischaemic complications, thus enhancing the safety of the percutaneous approach, and therefore enabling it to be carried out with good results even in high-risk patients.[9]

Using protection devices reduces stroke and death rate

In a recent report, Eckert and Zeumer highlighted that current data indicate protected CAS to have a combined stroke and death rate of 2.0%, whereas that of unprotected CAS is 3.2%.[14] Additionally, in a review of patients included in a variety of single-centre studies from 1999 to 2002, Kastrup *et al*. compared

Device	Size	Crossing profile	Flexibility	Flow limiting	Capture/ asp	Pore diameter
Angioguard™ XP	4 → 8 mm	0.042–52”	++	no	0.066”	100 µ
PercuSurge™	3 → 6 mm	0.036”	+++	yes	0.070”	no pore
Mednova™ gen III	4 → 6 mm	0.042–51”	++	no	0.084”	140 µ
Mednova™ gen IV	small/large	0.038”	++	no	0.084”	120 µ
Accunet™	4.5 – 7.5mm	0.045–48”	++	no	0.071”	115 µ
Trap™	2.5 → 7.0 mm	0.042”	++	no	0.066”	200 µ
EPI EZ™	3.5 → 5.5 mm	0.042”	++	no	0.055”	110 µ
SPIDER™	3.0 – 7.0 mm	0.038”	++	no	0.054 – 63”	80 µ
Rubicon™	4.0 – 6.0 mm	0.028–36”	++	no	0.047”	100 µ

Table 1. Technical features of current protection devices

2357 patients with protected CAS to 839 patients with unprotected CAS and reported that the combined stroke and death rate within 30 days was 1.8% in CAS with protection *versus* 5.5% in CAS without protection.[15]

Furthermore, Wholey *et al*. considered a world registry on CAS and described an initial 4.2% perioperative stroke and death rate among 1596 patients without distal protection; this was reduced to a remarkable 1.7% with the availability of distal protection in 771 consecutive procedures.[16] Recently, Reimers *et al*. presented a large series of 750 patients from a multicentre registry of CAS.[17] These data showed a 98% success rate in positioning a filter (79% of procedures), a distal occlusive balloon (18%), or a proximal protection system (3%). A low incidence of device-related complications was observed (1.1%) and none resulted in neurological symptoms. Moreover, the cumulative 30-day rate of stroke and death was 3.8% in symptomatic patients compared with the approximate 6–8% rate after endarterectomy in the symptomatic patients of the carotid surgery trials.[18]

Conclusion

Intriguingly, and despite the absence of solid scientific data based on randomised trials, carotid filters for cerebral protection have become the standard of care in CAS. Whether this practice underscores the future of protection devices for CAS remains to be seen. For the time being, all evidence seems to point to the direction of carefully incorporating these devices into the armamentarium of percutaneous treatment of extracranial carotid disease. Irrespective of the evidence obtained from the upcoming and ongoing trials regarding the use of cerebral protection, CAS (with cerebral protection) is being rapidly established as an alternative to CEA – despite the lack of data from large, prospective, randomised trials.

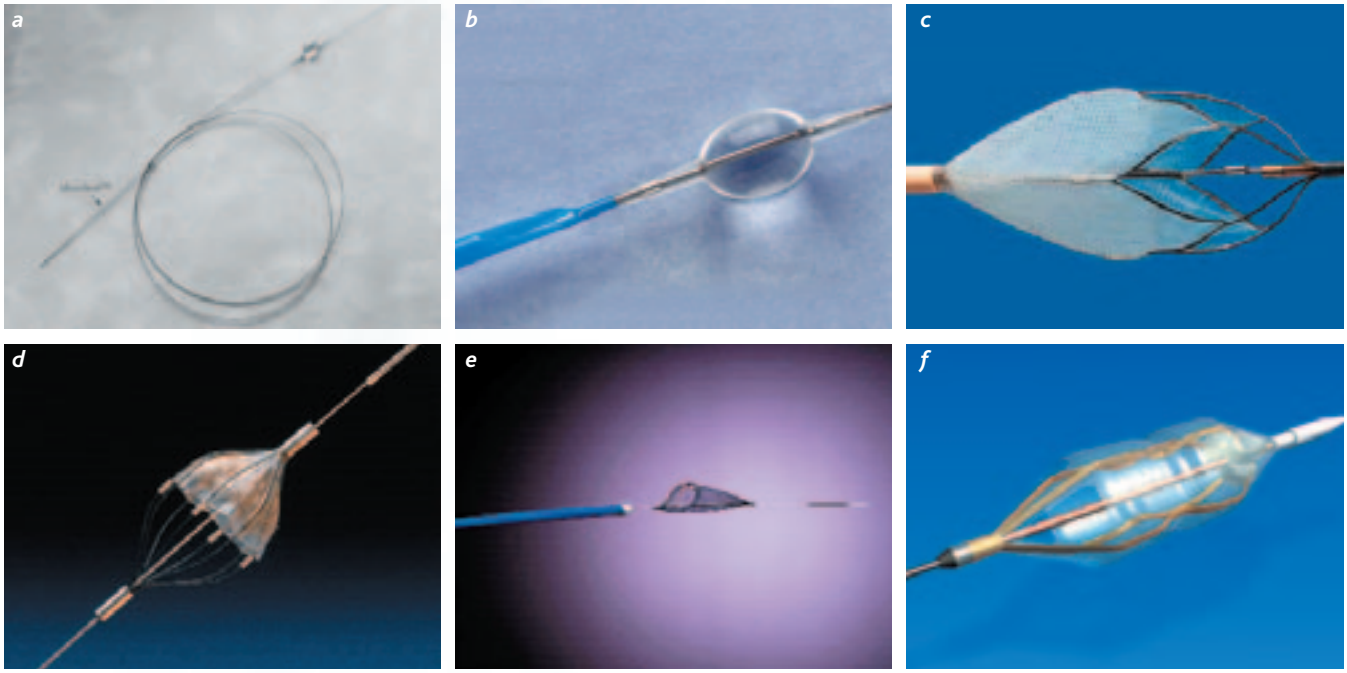


Figure 2. Carotid protection systems: (a) the PercuSurge, GuardWire, (b)distal balloon occlusion system (Medronic, Santa Rosa, CA); (c) the SPIDER filter with nitinol basket (ev3, Plymouth, MN); (d) The Neuroshield-Mednova filter with porous polyurethane membrane (Abbott, Galway, Ireland); (e) the Accunet filter basket (Guidant, Santa Clara, CA); and (f) the Angioguard filter with porous polyurethane membrane (Cordis, Miami, FL).

The balance of evidence for carotid artery stenting with cerebral protection *continued*

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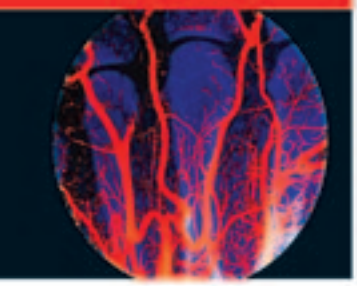

Key Learning

- Carotid artery stenting (CAS) offers an alternative to carotid endarterectomy for treating carotid stenosis
- Percutaneous stenting is associated with an increased incidence of microemboli and hence a higher neurological complication rate
- Devices including occlusion balloons, distal filters and retrograde flow devices are available to protect the cerebral circulation from microemboli
- Filter devices have advantages of:
  - trapping debris
  - maintaining distal cerebral perfusion
  - enabling angiographic monitoring of the angioplasty and stent placement
  - reducing periprocedural acute cerebral ischaemic complications
- Published data suggest protected CAS has a 3.9 times lower risk for the 30-day rate of stroke compared with unprotected CAS
- Carotid filters for cerebral protection are the standard of care in CAS, despite a current lack of supporting data from randomised trials

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