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CAROTID MASTERCLASS

What Practical Factors Guide the Choice of Stent and Protection Device during Carotid Angioplasty?☆

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The importance of angioplasty and stenting in the treatment of carotid artery disease cannot be underestimated. Successful carotid stenting does not only depend of the operator's skills and experience, but also an adequate selection of cerebral protection devices and carotid stents can help avoiding neurological complications. A broad spectrum of carotid devices is currently on the market and since all have their assets and downsides, it is virtually impossible to acclaim one specific device as being the best. The individual characteristics of each specific protection system or stent may make it an attractive choice in one circumstance, but render it a less desirable option in others situations. The applicability depends primarily on the arterial anatomy and the specific details of the lesion being treated. But certainly, personal preferences and familiarity with a specific device may legitimately influence the decision to choose one over another.

Keywords: Carotid artery stenting; Embolic protection device; Carotid stent; Endovascular therapy.

Introduction

Carotid angioplasty and stenting (CAS) is increasingly being performed for the treatment of severe carotid disease.[1–5] Despite this trend, however, data from the two largest and most recently published EVA-3S[6] and SPACE randomised trials[7] failed to demonstrate non-inferiority for CAS over CEA. Nevertheless, other publications suggest that with growing experience and the development of dedicated CAS technology, CAS can be performed safely and efficiently.[2,8]

The number of dedicated CAS devices now commercially available (stents and embolic protection devices (EPD)) has increased considerably over the last few years and has resulted in a bewildering array of interventional options available to modern day CAS practitioners. This variety in products makes individual treatment strategies difficult to generalise as no single device possesses all of the optimal features to treat all types of carotid plaques and patients.[9]

The aim of this paper is to review the principles of device selection in contemporary CAS practice.

Embolic Protection Devices

All commercial EPD systems can be classified under three main groups, each with its own working principle (Fig. 1) and include; (1) distal occlusion balloon protection (DOB), (2) distal filter protection (DF) and (3) proximal occlusion devices (POD).

Distal occlusion balloon protection

Distal occlusion devices (Table 1) evolved following earlier developmental research by Theron[10] in 1996. A balloon is inflated in the internal carotid artery (ICA) between the lesion and the brain so as to

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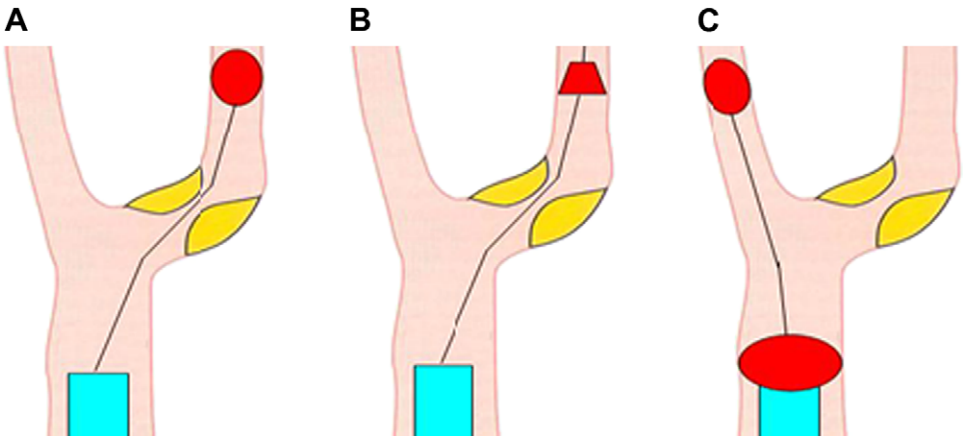

Fig. 1. Working principle of A) distal occlusion balloons (DOB); B) distal filters (DF); and C) proximal occlusion devices (POD).

temporarily prevent blood flow to the brain. Consequently, athero-thrombotic debris cannot enter the cerebral vasculature during the actual procedure. Prior to deflation and restoration of flow, any debris is aspirated and then flushed into either the external carotid artery (ECA) or out of the body through a sheath in the common carotid artery (CCA).

The main advantages of DOB protection devices (compared to other EPDs) include their low crossing profile and higher flexibility which facilitate overall device delivery. However, complete occlusion of the distal ICA may be potentially dangerous in patients with insufficient cerebral collateralisation. Although cerebral oxygenation can be maintained by intermittent distal balloon deflation, this will inevitably compromise the quality of cerebral protection. Another important disadvantage of complete ICA occlusion, is that angiographic assessment of the target lesion is not possible during balloon inflation within the carotid stenosis.

Distal filter device protection

Distal filter systems function like an umbrella which is opened in the ICA between the target lesion and the brain, in order to capture any debris during the CAS procedure (Table 2). This debris is then removed at following successful angioplasty and stent placement. DFs can either be mounted on a guide wire, or with their own dedicated delivery and retrieval system.

Most Interventionists consider the DF protection principle as being, intuitively, the most attractive. This is because there is maintenance of cerebral perfusion during CAS and angiographic assessment of the carotid lesion remains possible throughout all stages of the procedure. DF thrombosis may occur during the intervention, but its prevalence can be reduced by ensuring full heparinisation. In the event of complete DF blockage by embolic debris/thrombus, a few rescue options are available. The debris/thrombus can be removed by DF aspiration, or the device can be simply retrieved. After retrieval, the procedure is either restarted with another protection device or continued 'unprotected'.

Table 1. Specifications of the commercially available distal occlusion device

EPD	Manufacturer	Characteristic	Lesion crossing profile (″)
PercuSurge GuardWire	Medtronic Vascular, Santa Rosa, CA, USA	Manual aspiration	0.036

Proximal occlusion devices

Proximal occlusion systems utilise two compliant balloons which are sequentially inflated within the proximal CCA and the ECA (Table 3). This double balloon inflation creates either a 'no-flow' or a reversed-flow pattern within the ICA, thus preventing debris embolising to the brain. PODs are especially attractive as complete cerebral protection is established before crossing the lesion with guide wires or stent delivery systems.

However, the procedural steps required to maneuver the POD into the CCA and ECA are more laborious compared with other EPDs. In addition, occlusion of the ICA and CCA prevents blood flow to the brain and (as with the DOB principle), patients with inadequate collateralisation will be vulnerable to cerebral ischaemia. Intermittent deflation of the distal balloon

Table 2. Specifications of the commercially available distal filter devices

EPD	Manufacturer	Characteristic	Pore size (μm)	Lesion crossing profile (F)	Available filter diameters (mm)
RX Accunet	Abbott Vascular, Redwood City, CA, USA	Concentric	125	3.5–3.7	4.5, 5.5, 6.5, 7.5
Emboshield Pro	Abbott Vascular, Redwood City, CA, USA	Eoncentric, bare wire	120	2.8–3.2	Small = 2.5–4.8 mm Large = 4.0–7.0 mm
FilterWire EZ	Boston Scientific Corp, Natick, MA, USA	Eccentric	110	3.2	One size fits all
Angioguard	Cordis, Miami Lakes, FL, USA	Concentric	100	3.2–3.9	4, 5, 6, 7, 8
SpideRX	ev3, Plymouth, MN, USA	Eccentric	Variable	3.2	3, 4, 5, 6, 7

between the different steps of CAS may restore cerebral oxygenation, but will inevitably compromise the efficacy of the protection.

Recent EPD developments

The Twin-One device (Minvasys, Genevilliers, France) evolved from the concept of temporary occlusion of the distal internal carotid.[10] The system combines an angioplasty catheter pre-loaded with a DOB. The system is designed to be used whilst performing dilation after CAS has been performed as, according to its inventors, this is the only phase of the procedure requiring embolic protection. The latter concept is key to understanding this device but it remains a topic of considerable debate.

Another recently launched device is the FiberNet (Lumen Biomedical, Plymouth, MN). This is the first EPD to incorporate both a filter and an occlusion device in one system. The system consists of a 3-dimensional expandable Polyethylene Terephthalate (PET) fiber-based filter, which expands radially and is mounted onto a 0.014″ wire and retrieval catheter. The system can capture particles as small as 40 microns without compromising flow. Upon completion of the CAS-procedure, the retrieval catheter is advanced over the wire, and positioned just proximal to the expanded filter. There are two focal suction steps required for this filter. The first focal suction is at the base of the filter to remove any material that may be loosely bound to the filter. The second focal suction is performed while the device is being retrieved. Contained and captured emboli are removed by focal suction through the retrieval catheter and also by their retention within the filter fibers.[11]

Table 3. Specifications of the commercially available proximal occlusion devices

EPD	Manufacturer	Characteristic	Flow pattern	Introducer sheath profile (F)
NPS	W. L. Gore & Associates, Flagstaff, AZ, USA	Separate CCA and ECA balloon	Reversed flow	9F
Mo.Ma	Invatec, Roncadelle, Italy	CCA and ECA balloon mounted on same catheter	No flow	8F

EPD selection guidelines

Determining which EPD to use begins with assessment of the intracerebral circulation. In the absence of adequate cerebral collateralisation, it is probably preferable to use a filter protection device as they preserve blood flow to the brain. Although the protective balloons in DOB and POD devices can be temporarily deflated, it is our opinion that this is a laborious technique which confers suboptimal protection and an increased risk of procedural embolisation and stroke.

Second, the access site needs to checked. Patients presenting with tortuous iliac arteries or a type III aortic arch require low-profile, flexible protection systems as the target carotid lesion is going to be difficult to reach. As DOBs have crossing profiles comparable to those of guidewires, they are always steerable and flexible enough to pass through tortuous vessels. Only small-profile, flexible DFs can negotiate tortuous access vessels and (due to their large calibre) POD devices are not to be recommended in this situation.

The third key to device selection is good knowledge of the anatomy and morphology of the carotid

lesion. Severely stenosed and irregular lesions (including near-occlusions) can be treated with most EPD devices currently available. However, if a DF protection device is preferred, it is important to select low-profile, soft-tipped, flexible device as they are less traumatic and less likely to cause complications. Similarly, where a severely angulated ICA is anticipated, PODs are probably the preferred option because it is not necessary to cross the lesion. However, if a DOB or DF system is preferred, ensure that it is either highly steerable and flexible or, alternatively, straighten the ICA using the 'buddy-wire' technique.

Should the ICA distal to the lesion be too tortuous or there is too little space between the lesion site and the cerebrum, distal protection systems cannot be used because of a lack of space to 'land' the filter. In this situation, PODs are the preferred option. Soft plaque lesions are probably more dangerous because they have a greater tendency to embolize. Therefore, undue trauma to the plaque surface must be minimised. This is obviously not a problem when a POD is used. However, caution must be exercised in this situation should the Interventionist prefer to use a DOB or DF device Here only low-profile, soft-tipped, flexible devices should be selected.

Evidence?

As only small differences in complication rates for the varying protection devices are to be expected, hard data from randomized controlled trials are currently not (and probably never will be) forthcoming. In a recent non-randomised comparison by El-Koussy et al, they did find (using diffusion-weighted magnetic resonance imaging (DW-MRI)) a non-significant trend toward fewer embolic events after CAS with POD versus DF protection. Both the total number of new lesions, as well as the volume of consistent (relevant) new lesions, was non-significantly lower in the POD group.[12] These DW-MRI differences did not, however, result in any difference in clinical outcome between the two types of EPD. The latter observation was also corroborated in a subanalysis of the Belgian Italian Carotid (BIC) Registry, which concluded that none of the observed differences in 30-day event rates could be attributed to EPD selection. Interestingly, many of the observed differences were largely attributable to the choice of stent used in conjunction with the EPD.[13]

Carotid Stents

All commercially available self-expanding carotid stents (Table 4) are composed of either nitinol (a nickel–titanium alloy) or stainless steel (a cobalt alloy). In general, nitinol stents are constructed from a single laser-cut. The only exception is the NexStent, which is laser-cut from a nitinol sheet and coiled into a tube-like form. The overlap area of the coiled structure shrinks or grows as it is placed in larger or smaller diameter vessels. Once deployed in the body, nitinol stents rely on their thermal memory to achieve their predefined shape. The only available stainless steel stent is the Carotid Wallstent which is woven from a single piece of cobalt alloy wire into a tubular structure. The stent is delivered in a retractable sheath and it relies on a spring-like action to expand, once the sheath is withdrawn.

Table 4. Specifications of the commercially self-expanding carotid stents

Stent	Manufacturer	Design	Free cell area (mm^2)	Tapering
Carotid Wallstent Monorail	Boston Scientific Corp, Natick, MA, USA	Woven closed-cell cobalt-chromium tube	1.08	Self-tapering
Exponent RX	Medtronic Vascular, Santa Rosa, CA USA	Laser-cut open-cell nitinol tube	6.51	Self-tapering
NexStent Monorail	Boston Scientific Corp, Natick, MA, USA	Laser-cut closed-cell nitinol coiled sheet	4.70	Self-tapering
Precise Carotid Stent	Cordis, Miami Lakes, FL, USA	Laser-cut open-cell nitinol tube	5.89	Self-tapering
Protégé RX	ev3, Plymouth, MN, USA	Laser-cut open-cell nitinol tube	10.71	Straight or Shouldered tapered
RX AccuLink Carotid Stent	Abbott Vascular, Redwood City, CA	Laser-cut open-cell nitinol tube with longitudinal spines	11.48	Straight or Conical tapered
X-Act	Abbott Vascular, Redwood City, CA	Laser-cut closed-cell nitinol tube	2.74	Straight or Conical tapered
Crystallo Ideale	Invatec, Roncadelle, Italy	Laser-cut closed-cell nitinol tube	Varying smaller at mid portion, larger at stent ends	Straight or Conical tapered

Scaffolding

Besides the material used to manufacture the stent, many other design characteristics need to be considered when choosing the most appropriate stent for the patient. While with carotid endarterectomy (CEA) the complete plaque is removed from the patient, following CAS it obviously remains in the artery. The stent struts compress the dilated plaque material and it is the actual mesh design of the stent that has to then guarantee that no debris is dislodged through the stent interstices. Accordingly, the stent's scaffolding properties (defined as the amount of support given to the vessel wall by the stent) are of major importance in order to minimise the risk of embolic complications.

The 'free cell area' is the best accepted method to describe the scaffolding potential of carotid stents. From the results of the BIC Registry,[14] we learned that stents with a smaller free cell area are better at containing plaque material behind the struts resulting in significant differences in event rates compared to stents with large free cell areas. These differences in outcome were more pronounced among symptomatic patients.

Another often used classification for stent design is the binary ''open'' and ''closed'' cell design one, in which the differentiation is made by the number and arrangement of bridge connectors. In closed cell stents the adjacent ring segments are connected at every possible junction, while in open cell stents not all of the junction points are interconnected. Fig. 2 shows that an open-cell design might insufficiently scaffold a plaque in particularly tortuous arteries as the stent cells open on the concave surface of any bend. This will then predispose to protrusion of plaque after CAS and an increased risk of embolisation to the brain.

''Open'' and ''closed'' cell design stents have been evaluated in a number of early publications which looked at the association between stent design and outcome. Most concluded that patients treated with closed-cell stents had significantly lower 30-day stroke, death, and TIA event rates compared with those treated with open-cell-designed stents.[16] This has more recently been corroborated by a recent subanalysis of the SPACE study data.[7] However, Wholey has suggested that this classification may be an over-simplification giving the example that a closed cell stent with a diameter of 1,000 μm is more likely to be responsible for plaque prolapse and embolization than an open cell of 500 μm.[15] He concluded that cell size and surface area coverage was more important.

Flexibility

The flexibility of a stent is defined as its ability to conform to vessel tortuosity during deployment. In terms of flexibility, closed cell stents, both nitinol and stainless steel, do not perform as well as their open cell counterparts. This is because in closed-cell stents the adjacent ring segments are connected at every possible junction with flexible bridge connectors and only a limited degree of flexion between adjacent rings is possible. In the open-cell stent, not all junction points are interconnected and this therefore allows much more movement between adjacent ring segments and a better conformability to tortuous anatomy. Accordingly, the flexion benefits of an open-cell design are offset by less scaffolding uniformity, while the scaffolding benefits of a closed-cell design are offset by poorer flexion and conformability.[15] If placed in a tortuous carotid, closed-cell stents tend to alter the vessel's original curve. If it is not placed accurately, the insertion of a less flexible closed-cell stent can result in kinking of the carotid vessel just distal of the implanted stent (Fig. 3).

One company (Invatec) has recently developed a new stent design which incorporates varying sizes of free cell area at the mid segment and both distal edges of the stent (Crystallo Ideale). This should provide a compromise between achieving adequate scaffolding at the lesion site along with improved flexibility at the stent edges.

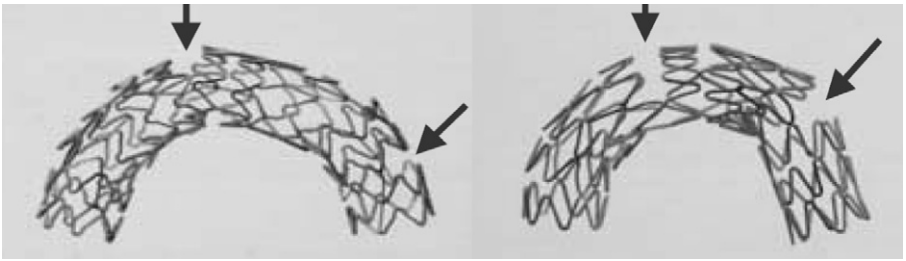

Fig. 2. Larger open-cell-designed stents insufficiently scaffold vulnerable lesions in tortuous anatomy.[15]

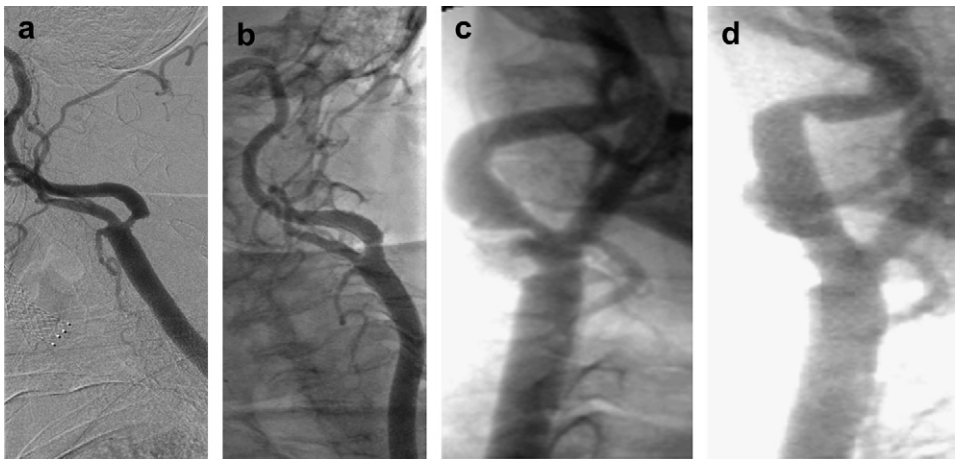

Fig. 3. Stent selection for tortuous carotid lesions a) pre- and b) post-procedural angiography of CAS with open cell nitinol stent (Precise) preserving original anatomy and c) pre- and d) post-procedural angiography of CAS with closed cell Cobalt Chromium alloy stent (Carotid Wallstent) causing kinking of the artery distal of the lesion.

Vessel wall adaptability

Vessel wall adaptability describes the ability of a carotid stent to adjust itself to the tapered anatomy of the region. Although it is typical for a nitinol tube-like stent to convert to its predetermined shape when exposed to body temperature, this is not always achievable. In an attempt to better comply with the carotid anatomy, tapered stents have been developed. These are characterized by a smaller stent diameter at the distal end compared to the proximal end. There are two types of tapered stents: the conical (Acculink, X-Act) and the shouldered tapered stents (Protégé). In the first, there is a gradual decrease in diameter from the proximal to the distal end, whereas in the second, there is a short transition zone in the midsegment of the stent. The coiled nitinol sheet configuration of the NexStent allows the stent to adapt nicely to the change in diameter. The stent overlap will differ from the proximal to the distal stent end. The Precise is claimed to be self-tapering because the different rings interact independently with the vessel wall.

The woven mesh structure of stainless steel stents allows the stent to adjust its diameter to the width of the vessel lumen. This ensures optimal vessel wall adaptability. Final implanted stent length depends on the diameter of the lumen at the site of deployment. If the lesion involves the CCA and the ICA, the stent has to cover the carotid bifurcation completely. Flow disturbances in the ICA occur if the stent is positioned in the bulb.[17] In our experience, a significant mismatch in diameter between the ICA and the CCA (e.g., 5 to 10 mm, respectively) occurs in only 10 to 15% of cases. In these cases, it is recommended that a shouldered tapered stent such as the Protégé should be selected. If appropriately sized and exactly positioned with its shoulders in the bulb, its diameter adapts best to the original vessel diameter changes.

Stent selection guidelines

In light of the findings of the BIC Registry[13,14] along with awareness that once the EPD is removed, the stent remains the only protection against brain-embolization, plaque scaffolding should be the prime determinant in selecting a carotid device. For example, all symptomatic patients and those patients presenting with a highly echogenic lesion (Grey Scale Median > 25)[18] should receive a stent with an as low free cell area as possible.

If the selection of a stent with high scaffolding capacities might potentially compromise the maintenance of the vessel's initial anatomy (e.g. increase the potential risk of causing a distal kink or significant mismatch in proximal and distal diameter), the authors would recommend performing a CEA. Selecting a more flexible stent with less scaffolding in order to achieve an optimal angiographic result after CAS, could expose the patient to an increased risk of post-procedural cerebral embolization.

Conclusion

Following publication of the SPACE[7] and EVA-3S[6] results, it is our opinion that in addition to needing more experienced Interventionists, there is still a need for better designed CAS devices, especially stents. This is because it remains our contention that it is the stent's scaffolding capacity that is of major importance

in preventing procedural events and the current generation of stents with good scaffolding properties are compromised by insufficient flexibility. Future stent design improvements should focus primarily on combining improved scaffolding and flexibility.

Until that time, we would recommended that the number of different EPDs and stents used in an individual's CAS practice should be relatively limited and that he/she should become more intimately acquainted with each of their 'pros and cons'. Finally, it is essential that in symptomatic patients and those patients with vulnerable plaque, the choice of EPD and stent must focus on atraumatic instalment.

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