Summary

✓ Cerebral protection devices offer a new approach to reducing the risk of stroke and death in patients undergoing carotid angioplasty with stenting (CAS).

✓ Nine studies have examined the efficacy of cerebral protection devices, by comparing the incidence of procedure-related stroke and death to that of CAS without protection, and to surgical endarterectomy. Few of the studies were of high quality.

✓ Overall, the differences in the incidence of procedure-related stroke and death were not statistically significant among patients who underwent CAS without protection, compared to those who received CAS with protection, or to those who underwent endarterectomy.

✓ Complications reported with the use of cerebral protection devices are minor and transient.

✓ CAS with cerebral protection may offer a safe and efficacious alternative to endarterectomy in symptomatic, high risk patients with severe carotid artery disease. Evidence to support the use of CAS with cerebral protection devices in asymptomatic patients who have severe carotid artery stenosis, is unavailable.

The Technology

During the past five years, cerebral protection (or distal embolic protection) devices have emerged as an approach to reduce the risk of procedure-related stroke in patients undergoing carotid angioplasty with stenting (CAS), for severe carotid artery occlusive disease (CAOD). CAOD occurs when a carotid artery becomes clogged with fatty deposits that form a plaque along the inner lining of the vessel wall. Over time, pieces of plaque break off and become lodged in a smaller branch of the artery, blocking the supply of oxygen-rich blood to a part of the brain. This results in the sudden death of healthy brain tissue in that area (stroke). The build-up of fatty deposits, which narrow the artery enough to restrict blood flow to the brain, may also cause a stroke.

During CAS, a small puncture is made in the femoral artery. Catheters, wires, and a balloon are inserted and guided to the affected area of the carotid artery. The balloon is inflated to widen the artery, and allow for the delivery and placement of an expandable mesh stent. Once deployed, the stent is implanted in the arterial wall to keep the artery open.

Several clinical trials have suggested that there are promising long-term benefits with CAS, but its use has been limited by a high (6%) incidence of procedure-related stroke and death within 30 days of treatment. These adverse events occur when plaque particles dislodge during the procedure (when the artery is dilated or the stent is deployed).

Cerebral protection devices have been developed to prevent these complications. These devices trap dislodged plaque particles, which are later removed through one of the catheters used to perform the CAS procedure. Each of the three types of devices uses a different approach to cerebral protection: distal balloon occlusion, distal filter, and flow reversal (retrograde or proximal occlusion).

In distal balloon occlusion, a “balloon-on-a-wire” catheter is passed through the target area of the carotid artery, where the balloon is...
Early clinical experiences with prototype cerebral protection systems began in the mid to late 1990s. The devices and the techniques for safely and effectively using them have since been modified. Despite the rapid evolution of all three devices, the filter approach has received the greatest level of clinical enthusiasm, partly because of its capacity to trap particles while permitting continuous blood flow. Filter devices have generally been viewed as being less complex than the other classes of devices, and as being more simple to use.

### Regulatory Status

Several manufacturers are producing the different types of cerebral protection devices. Three devices have been approved for sale in Canada (Table 1).

### Patient Group

In patients with severe CAOD, the diameter of the affected carotid artery has been reduced by >70%. These individuals may experience symptoms, the first of which is typically a transient ischemic attack (TIA). TIAs are neurological events with the signs and symptoms of a stroke (e.g., weakness or numbness on one side of the face or body, changes in vision, confusion, dizziness, and slurred speech). These symptoms last for a short period of time – typically <1 hour – though some may remain for...
<24 hours. TIAs occur when blood flow to the brain is temporarily interrupted. Within one year of diagnosis, the risk of stroke among symptomatic and asymptomatic patients is approximately 13% and 5% respectively.14

Current Practice

The standard treatment for severe CAOD is carotid endarterectomy (the surgical removal of plaque from inside the artery through an incision in the neck). For some patients, however, the risks of surgery outweigh the procedure’s benefits.15 These high risk patients often have additional health conditions, such as hypertension, diabetes, heart disease, kidney problems, or lung disease. Non-surgical treatment options include cholesterol-lowering drugs, antithrombotic medications, and CAS.16 Before the development of cerebral protection devices, few patients underwent CAS. Access is also limited by the availability of clinical specialists who are trained in performing CAS, and in using cerebral protection devices.17

The Evidence

Nine studies18-26 comparing CAS with cerebral protection to CAS without cerebral protection, or CAS with cerebral protection to endarterectomy were identified (Table 2). Eight of the nine studies reported events occurring within 30 days of treatment.18,20-26 The types and classes of cerebral protection devices used varied across studies, as did the characteristics of patients involved (e.g., elderly populations, high risk populations) and the specific outcomes measured. Overall, the strength of the evidence presented was fair (when evaluated against accepted quality criteria).27 For these reasons, data from the studies could not be combined to calculate pooled incidence rates.

Of the nine studies, six provided information on technical success.19,20,22-25 The rate at which the cerebral protection device was successfully deployed and retrieved ranged from 95.6% to 100%.

Studies comparing CAS with cerebral protection to CAS without cerebral protection

Across all studies, the 30-day incidence of stroke and death was higher among patients who were treated with CAS alone than among those who received CAS with cerebral protection. With one exception,24 these differences were not statistically significant.

Studies comparing CAS with cerebral protection to endarterectomy

None of the four studies reported a statistically significant difference in the 30-day incidence of death, major stroke, or myocardial infarction between treatment groups (CAS with cerebral protection, and endarterectomy).18,21-23 In one study, the incidence of minor stroke within 30 days was found to be significantly higher among patients who received CAS with cerebral protection.22

Adverse Effects

The complications that arise from using cerebral protection devices include transient spasm (contraction) of the artery (2.9% to 7.9% of patients), blood flow impairment (2.7% to 13% of patients), and arterial wall injury (one patient).19 In one case, the device became stuck in the stent, and surgery was required to remove it. None of these adverse events had lasting effects.

Administration and Cost

The estimated cost of a cerebral protection device is C$2,000.28 No economic analyses comparing CAS with protection to CAS without protection have been published. It is expected that cost differences will be approximately equal to that of the cerebral protection device, because the treatments are otherwise very similar (JM Finlay, Capital Health Region, Edmonton, Alberta: personal communication, 2005 March 6). Published economic analyses of endarterectomy versus CAS with cerebral protection, in the US, have found the latter to cost approximately C$2,500 more per patient.29 The added equipment-related costs (stent and cerebral protection device) were not offset by the savings arising from a shorter hospital stay.
## Table 2: Studies comparing CAS with cerebral protection to CAS without cerebral protection, or CAS with cerebral protection to endarterectomy

<table>
<thead>
<tr>
<th>Authors; Cerebral Protection Device</th>
<th>Patients (characteristics and number)</th>
<th>Study Design</th>
<th>Main Results</th>
</tr>
</thead>
</table>
| Diethrich et al.; GuardWire | • CAS with cerebral protection 40  
• CAS without cerebral protection 50  
• endarterectomy 100  
• patient characteristics not provided | clinical series | Combined incidence of CVA and TIA within 30 days: CAS with cerebral protection 12.5%, CAS without cerebral protection 22.5%, endarterectomy 3%* |
| Castriota et al.; various (unspecified) | • CAS with cerebral protection 150  
• CAS without cerebral protection 125  
• high risk for surgery  
• >50 years old  
• asymptomatic or symptomatic  
• ≥75% stenosis | non-concurrent cohort study | Combined incidence of major or minor stroke, or TIA unreported; procedural complications: CAS with cerebral protection 1.3%, CAS without cerebral protection 4.0%* |
| Macdonald et al.; NeuroShield (Gen. II and III) | • CAS with cerebral protection 73  
• CAS without cerebral protection 75  
• ≥70% stenosis | concurrent cohort study | Combined incidence of death, and major or minor stroke within 30 days: CAS with cerebral protection 10.7%, CAS without cerebral protection 2.7%, CAS without cerebral protection 6.7%* |
| CARESS Steering Committee; GuardWire Plus | • CAS with cerebral protection 143  
• endarterectomy 254  
• asymptomatic with ≥75% stenosis  
• symptomatic with ≥50% stenosis | non-randomized controlled trial | Combined incidence of death and stroke within 30 days: CAS with cerebral protection 2.1%, endarterectomy 4.0%.* Incidence of myocardial infarction within 30 days: CAS with cerebral protection 0.0%, endarterectomy 0.8%* |
| Castriota et al.; NeuroShield, AngioGuard | • CAS with cerebral protection 53  
• endarterectomy 110  
• asymptomatic or symptomatic  
• ≥70% stenosis | non-concurrent cohort study | Incidence of major stroke within 30 days: CAS with cerebral protection 3.8%, endarterectomy 1.8%.* Incidence of minor stroke within 30 days: CAS with cerebral protection 7.5%, endarterectomy 0.0%* |
| Yadav et al.; AngioGuard, AngioGuard XP | • CAS with cerebral protection 167  
• endarterectomy 167  
• asymptomatic with >80% stenosis  
• symptomatic with >50% stenosis  
• high risk for surgery | randomized controlled trial | Incidence of death within 30 days: CAS with cerebral protection 1.2%, endarterectomy 2.5%. Incidence of myocardial infarction within 30 days: CAS with cerebral protection 2.4%, endarterectomy 6.1%. Incidence of stroke within 30 days: CAS with cerebral protection 2.0%, endarterectomy 3.1%* |
| Zahn et al.; unspecified | • CAS with cerebral protection 668  
• CAS without cerebral protection 815  
• asymptomatic with ≥80% stenosis  
• symptomatic with ≥70% stenosis | clinical series | Combined incidence of death and stroke within 30 days: CAS with cerebral protection 2.1%, CAS without cerebral protection 4.9%* |
| McKevitt et al.; GuardWire, NeuroShield, AngioGuard, FilterWire EX, Parodi AES | • CAS with cerebral protection 97  
• CAS without cerebral protection 150  
• symptomatic with >70% stenosis | clinical series | Combined incidence of death and disabling stroke within 30 days: CAS with cerebral protection 2.1%, CAS without cerebral protection 4.0%* |
| Mas et al.; GuardWire, Emboshield, Filter Wire EX, AngioGuard | • CAS with cerebral protection 58  
• CAS without cerebral protection 15  
• failure to perform CAS 6  
• excluded due to stroke before CAS 1  
• symptomatic with ≥70% stenosis | clinical series | Combined incidence of stroke or death within 30 days: CAS with cerebral protection 10.3%, CAS without cerebral protection 26.7%* |

*difference not statistically significant; †difference is statistically significant; ‡statistical significance unreported.
Concurrent Developments

In 2004, the first studies of another approach to CAS were published. The procedure, called transcervical occlusion and protective shunting (TOPS), involves making a small incision at the base of the neck, inserting a tiny tube into the common carotid artery, and connecting it to a second tube placed in the internal jugular vein. The carotid artery is then clamped below the arterial tube, creating blood flow reversal. Any plaque particles freed during the procedure become trapped in a filter between the arterial and venous tubes. The early results of the TOPS studies appear promising, with technical success rates of 100%, and no patients experiencing procedure-related stroke or death.

Rate of Technology Diffusion

As awareness of cerebral protection devices grows among high risk CAOD patients, the demand for CAS with protection is expected to increase. Preferences for minimally invasive procedures that avoid the need for recovery from a sizeable neck incision are likely to steer even non-high risk patients away from carotid endarterectomy (Finlay JM: personal communication, 2005 Mar). Nevertheless, the rate of diffusion of cerebral protection devices into routine clinical practice will likely be driven by the availability of specialists who are trained to perform the procedure, and by the coverage of the cerebral protection device cost by health care systems.

Several controlled trials are comparing CAS with cerebral protection devices to endarterectomy, including Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE), which focuses on the Angioguard protection device; Performance and Safety of the Medtronic AVE Self-Expandable Stent in Treatment of Carotid Artery Lesions (PASCAL), which focuses on the Guardwire Plus system; and ACT 1, which uses the Emboshield embolic protection system.

The Carotid Revascularization Endarterectomy versus Stenting Trial (CREST), which uses the AccuNet cerebral protection system, is a phase III trial that includes nine participating Canadian centres. Results from CREST are expected to be available in 2007.

Implementation Issues

According to a US report, physicians in several specialties (e.g., interventional radiologists, cardiologists, vascular surgeons) may perform this procedure. The learning curve and training requirements will vary for each specialty.

In high risk patients who have severe CAOD, the evidence suggests that CAS with cerebral protection may offer an effective alternative to endarterectomy. Clinicians may soon face the need to modify their practice in response to patients’ awareness of and preference for this minimally invasive option (Finlay JM: personal communication, 2005 Mar). It may no longer be appropriate to manage patients who are unable to undergo surgery with drug therapy only.

The anticipated increased demand for CAS with cerebral protection could have a significant impact on the health care system. Potential long-term savings through the prevention of stroke, and associated treatment and rehabilitation costs, may initially be overshadowed by the need to revise budgets and reallocate resources to cover increased procedural costs. In addition, the number of specialists performing CAS in a particular health region may no longer be enough to handle patient volumes (Finlay JM: personal communication, 2005 Mar). Hospitals may also need to reorganize their angiography suite (catheterization laboratory) schedules to accommodate more CAS procedures.
References


Cite as: Stafinski T and Menon D. *Cerebral protection devices for use during carotid artery stenting* [Issues in emerging health technologies issue 78]. Ottawa: Canadian Coordinating Office for Health Technology Assessment; 2005.

***************

CCOHTA appreciates comments from its reviewers.

Reviewers: Robert Côté MD FRCPC, McGill University, Montréal QC, Mayank Goyal MD FRCPC, University of Ottawa, Ottawa ON.

Production of this report is made possible by a financial contribution from Health Canada's Health Care Strategies and Policy, federal, provincial and territorial partnership grant program.

CCOHTA takes sole responsibility for the final form and content of this report. The statements, conclusions and views expressed herein do not necessarily represent the view of Health Canada or any provincial or territorial government.

The Canadian Coordinating Office for Health Technology Assessment (CCOHTA) is funded by Canadian federal, provincial and territorial governments. (www.ccohta.ca)