Ischemic Cerebral Lesions after Carotid Surgery and Carotid Stenting

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Objectives. To evaluate the risk of new ischemic cerebral lesions after carotid endarterectomy and carotid stenting and their clinical significance.

Methods. Prospective and non-randomized single-center study including 121 patients with symptomatic and asymptomatic significant carotid stenosis. 60 patients were treated by surgery and 61 treated by carotid stenting. Stenting was restricted to patients at high risk for surgery. Neurological examination and Diffusion-Weighted Cerebral Magnetic Resonance (DW-MRI) were performed before and after each procedure. The presence, location and volume of new cerebral lesions were determined.

Results. In the surgical group, 2 minor strokes were registered. DW-MRI showed new lesions in 7 patients (11.6%). All except one were located in the ipsilateral anterior circulation.

In the stenting group, 1 minor stroke and 1 occurrence of quadranopsia were registered. DW-MRI showed new lesions in 26 patients (42.6%). 10 of these patients (38.4%) had lesions in the contralateral hemisphere and 7 patients (26.9%) in the posterior circulation.

Deficits are found in patients with higher lesion volumes.

Conclusions. Cerebral ischemic lesions are significantly \( p < 0.0001 \) more frequent after carotid stenting than after endarterectomy. The majority of these lesions have no immediate clinical implication, but more specific tests are needed to evaluate their exact significance.

Keywords: Carotid artery; Stent; Endarterectomy; Magnetic resonance imaging.

Introduction

In the last decade, several randomized prospective studies1,2 have unequivocally demonstrated that carotid endarterectomy (CEA) significantly reduces the incidence of stroke in patients with symptomatic and asymptomatic extracranial carotid disease.

Therefore, CEA has rapidly been considered as the standard of care because of its effectiveness and safety.3

More recently, carotid angioplasty and stenting (CAS) has been proposed as an alternative for patients at high risk for surgery. Initially, the success of CAS was limited by a rather high rate of neurological events, mainly related to cerebral embolization; post-procedural neurological complication rates as high as 10% were reported at that time.5 Recently, significant improvement of the endovascular techniques emerged and the rate of neurological events has decreased, particularly with the use of protective devices.6 Recent non-randomized trials evaluating the safety of CAS with embolic protection devices in a broad-risk population report satisfactory 30-day stroke and death rates.7

However, CAS seems to carry a significant rate of microembolisation during the procedure, leading to subclinical cerebral infarction, as reported by some authors8,9 and by our team.10 The aim of this study is to define this phenomenon more precisely and to evaluate its clinical consequences.

Materials and Methods

Patient population and selection

We performed a single-centre, prospective, non-randomized study in order to evaluate periprocedural
embolic events in patients undergoing carotid endarterectomy and carotid stenting for cerebrovascular disease. Our indications for treatment were internal carotid artery stenosis of 70% or more in symptomatic patients, or stenosis of 80% or more in asymptomatic patients. Our policy was to restrict the indications of carotid stenting to patients presenting a high surgical risk, defined as presenting at least one of the following criteria: NYHA functional class III/IV, cardiac surgery within 6 weeks, severe pulmonary disease, age > 80, hostile neck (previous radical neck surgery or radiation therapy) or restenosis after CEA.

The incidence of these risk factors is described in Table 1. Many patients had more than one risk factor. All patients were fully informed about the technical aspects and risks of the procedure, as well as the possible extra costs.

60 patients underwent 60 endarterectomies over a period of 16 months and 61 patients underwent protected carotid stenting over a period of 36 months.

Patient mean age was 70 years (range 51–86 years) in the surgical group and 73.5 years (range 50–92 years) in the stenting group.

68 percent of the procedures were performed to treat symptomatic internal carotid stenosis in the surgical group (stroke, n = 20; transient ischemic attack (TIA), n = 11; amaurosis fugax, n = 10) and 34 percent (stroke, n = 6; TIA, n = 14; amaurosis fugax, n = 1) in the stenting group.

The degree of carotid stenosis and the presence of contralateral occlusion were similar in both groups.

Degree of stenosis, plaque morphology at color Doppler ultrasound and clinical status in both groups are detailed in Table 2.

The pre- and post-procedural work-up for each patient included:

- Assessment of the degree of carotid stenosis and of its morphology by color Doppler ultrasound.
- Neurological examination performed by an independent neurologist the day before and after the procedure.
- Diffusion-Weighted MRI (DW-MRI) examination performed 24 hours before the procedure and within 72 hours after it by a radiologist blind to the clinical evolution of the patient.
- Clinical and color Doppler ultrasound follow-up scheduled at 1 month, 6 months and then annually.

The study was approved by the Ethical Review Board from our University. Informed Consent was obtained from all patients.

**CEA procedure**

Carotid endarterectomy was performed by experienced vascular surgeons under general anesthesia. All patients received 0.5 mg heparin/kg intravenously before clamping. A shunt was systematically used. The endarterectomy was performed in standard fashion; the arteriotomy was closed with a pericardial patch (Vascu-Guard — Synovis).

There was no systematic peroperative control of the carotid endarterectomy.

Antiplatelet therapy (aspirin 160 mg/d) was started in all patients before surgery and continued for life.

**CAS procedure**

The CAS procedure was performed under local anesthesia via percutaneous transfemoral access by a team consisting of one of the vascular surgeons and an interventional radiologist, both having an excellent experience in endovascular procedures. Patient monitoring and management were ensured by an anesthesiologist. A bolus of 5000 units of heparin was administered intravenously. Clopidogrel (75 mg) was given at least 3 days before the procedure. A 4F catheter was introduced for selective cannulation of the common carotid artery and angiography was performed in the lateral, anteroposterior and oblique planes so as to visualize the severity of the stenosis and the intracerebral vasculature. An 6F long sheath was then positioned in the common carotid artery and the protective filter (EZ-Boston Scientific for 52 patients/Spider-EV3 for 9 patients) was passed through the internal carotid artery stenosis and deployed at the base of the skull. The internal carotid artery stenosis was dilated using a 3 or 3.5 mm diameter balloon (Gazelle-Boston Medical) before stenting, if it was judged too tight to allow passage of the stent. A monorail Carotid Wallstent (Boston Scientific) was deployed and dilated to minimize residual stenosis (the length and diameter of the stents more frequently used were as follows: 30/7, n = 10; 30/9, n = 18; 40/9, n = 14; 40/7, n = 5). The filter was recaptured.

Table 1. Criteria of high surgical risk in the stenting group (series of 61 patients)

<table>
<thead>
<tr>
<th>Criteria</th>
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<tr>
<td>NYHA functional class III/IV</td>
<td>28</td>
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<tr>
<td>Cardiac surgery within 6 weeks</td>
<td>19</td>
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<tr>
<td>Severe pulmonary disease</td>
<td>1</td>
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<tr>
<td>Age &gt; 80</td>
<td>17</td>
</tr>
<tr>
<td>Hostile neck</td>
<td>9</td>
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<tr>
<td>Restenosis after CEA</td>
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and macroscopic inspection determined the number and size of debris captured. Ipsilateral cervical and intracranial carotid angiography was performed to assess technical success and exclude distal cerebral embolization. A puncture site closure device was used in all cases (Angioseal-St Jude Medical). Antiplatelet medication consisted in Clopidogrel (75 mg) for 2 months and aspirin (160 mg) for life.

**Diffusion-weighted cerebral magnetic resonance (DW-MRI)**

All DW-MRI examinations were performed on a 1.5T MR system (Intera, Philips Medical System, Netherlands) using a standardized protocol including a FSE-FLAIR sequence and a EPI-SE diffusion-weighted sequence. The DW imaging sequence consisted of initial T2-weighted acquisition without application of the diffusion-sensitizing gradients (DG). Thereafter a similar acquisition with simultaneous application of the DG in the three orthogonal directions was performed at \( b = 1000 \text{ s/mm}^2 \). A set of 24 axial transverse images in similar slice location were obtained for both sequences of the same examination. Neuroradiologists independently rated the DW trace images for the presence of acute ischemic parenchymal damage. Lesions were quantified using the following scoring system: number of lesions, location (anterior/posterior circulation, cortical/subcortical/deep areas, ipsi/controlateral to the carotid stenosis), lesion size (<5 mm, 5–10 mm, >10 mm). The volume of each lesion (ml) was measured and a total lesion volume calculated for each patient.

**Color Doppler ultrasound**

All carotid lesions were detected and imaged by color Doppler ultrasound with an ATL 5000 (Philips Medical, Netherlands), using high-frequency probes (4–7 MHz or 5–12 MHz).

**Statistical analysis**

The data were analysed using a chi-square test and Fischer’s exact test.

**Results**

**Clinical results**

In the surgical cohort, 2 minor strokes were registered: one contra-lateral arm paresis and one contra-lateral lower limb paresis. Both patients recovered after 6 weeks.

One patient presented myocardial ischemia, which was treated medically, and another suffered from vocal cord paralysis. One Parsonage-Turner syndrome was noted 10 days after surgery.

Among 61 patients undergoing protected carotid stenting, one occurrence of quadranopsia and one of hemiparesis, both of which resolved within 4 weeks, were registered. Locally, one groin hematoma was noted.

**DW-MRI results**

The DW-MRI results are depicted in **Table 3**.

7 patients in the surgical group (11.6%) and 26 patients in the stenting group (42.6%) presented new DW-MRI lesions. This difference is statistically significant (\( p < 0.0001 \)).

There was no correlation between the clinical preoperative status or the degree of stenosis and the incidence of brain lesions.

We also didn’t find any correlation between the plaque morphology as assessed by the preprocedural...
color Doppler ultrasound and the new DW-MRI lesions (Table 4).

The location of the lesions in the surgical group was ipsilateral in 6 out of the 7 cases, whereas in the stenting group 10 out of the 26 patients who embolised did so in the contra-lateral hemisphere (6 patients only in the contralateral hemisphere and 4 patients in both hemispheres).

All the new lesions were located in the anterior circulation in the surgical group, whereas 7 of the 26 new lesions in the stenting group were localised in the posterior circulation.

We retrospectively analysed whenever it was possible technical conditions like aortic arch morphology, common carotid angulation and tortuosity, duration of procedure, but didn’t find any correlation between these elements and the embolisation rate.

There was also no correlation between the presence of debris in the filter and the incidence of brain lesions.

The four patients who presented a clinical deficit all had a greater lesion volume (0.4 ml and 8.6 ml in the surgical group and 2 ml and 4.7 ml in the stenting group) than the others (mean lesion volume of deficit-free patients: 0.34 ml in the surgical group and 0.42 ml in the stenting group).

The distribution of the lesion volumes in the stenting group is depicted in Table 5.

During a mean follow-up of 7.4 months in the stenting group, 1 occlusion occurred and 6 non-significant stenoses (50%) were noted.

### Discussion

The results of CAS have rapidly improved over time, and recent controlled series show very low post-procedural complication rates (combined stroke and death rate about 2.1–2.8%), comparing favourably with carotid endarterectomy. However, the superiority of the endovascular approach still needs to be evidenced and several randomised studies are in progress. Microembolisation during CAS has already been reported by several authors and by our team. The sensitivity and specificity of DW-MRI now detect ischemic areas as small as 0.01 ml and actually enable the observers to detect a rate of post-procedural new ischemic lesions in 20 to 40% of patients. Fortunately, the vast majority of them do not present any clinical neurological deficit. We chose to apply the same protocol of DW-MRI before and after CEA during the same period. Our results clearly show a statistically significant lower rate of microembolisation in the surgical group (11.6% versus 42.6%), whereas the clinical results were comparable.

We agree that the two groups were not comparable considering the preoperative neurological and clinical status: there was more symptomatic patients in the surgical group and the stented patients were more frail.

However, our conclusions regarding the fact that stenting is more embogenic than surgery remain valid since the group treated by stenting, comprising less symptomatic patients, carried theoretically a lesser risk of embolisation than the surgical group.
Should the two groups have been strictly identical, the difference in the rate of embolisation should have been probably even more striking.

The reason for this difference can be found in the principle of the technique itself. Whereas access to the vessels during surgery simply requires a gentle, no-touch dissection, access to the common carotid via a sheet during CAS can sometimes be tedious and cumbersome, especially if the origin of the head vessels forms a sharp angle with the aortic arch. In another study, we have previously demonstrated a higher rate of ipsilateral lesions in the case of a sharp aortic angle.

Even the introduction of a guide-wire or catheter into the arch may be deleterious: the detection of a significant number of hits by transcranial Doppler, as well as neurological deficits, have been reported after diagnostic angiogram of the arch, cardiac catheterization or extracorporeal circulation. In our study, a majority of the lesions are found in the contralateral hemisphere (6 cases out of 26), in both hemispheres (4 cases out of 26), or in the posterior circulation (7 cases out of 26).

Once the common carotid is catheterized via the sheet, the risk of embolisation is present when crossing the lesion and deploying the stent. While the risk connected with the second step can theoretically be lowered by protective devices, the risk associated with the first one remains, especially when dealing with tight lesions and soft plaques.

We didn’t find in our study any correlation between the plaque morphology as assessed by the preprocedural color Doppler ultrasound and the new lesions detected at DW-MRI. The reason for this is probably because the evaluation of the plaque concerned more the degree of stenosis than its nature and it is possible that the potential of embolisation was not accurately estimated. In particular, we didn’t performed specific echolucency assessment like the gray-scale median measurement. Furthermore, the number of patients treated is probably too small up to now to evidence statistically any correlation between the plaque morphology as assessed by the preprocedural color Doppler ultrasound and the lesions detected at DW-MRI. The reason for this difference can be found in the comparatively small number of patients treated in our series.

In conclusion, post-procedural DW-MRI revealed significantly more frequent and diffuse ischemic lesions after protected CAS than after CEA in our series. Future studies are needed in order to demonstrate whether these lesions are associated with cognitive dysfunction and to determine the embolic potential of plaques and retrospectively to better classify their risk.

The clinical significance of cerebral embolisation need to be discussed. One could argue that there is no point in elaborating on this phenomenon, since the vast majority of the lesions are clinically silent. However, basic post-procedural clinical examinations give no information regarding possible deterioration of cognitive function related to their presence.

Deficits following embolisation seem to be directly related to its intensity. Patients who presented a deficit had a greater total lesion volume than the others, whereas the aspect of the microlesions themselves was identical. Therefore, quantification of microembolisation by DW-MRI could be used as a marker to evaluate the embolic potential of plaques and retrospectively to better classify their risk.

References


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