Hemodynamic Effect of Carotid Endarterectomy

Torben Schroeder, Henrik Sillosen, and Hans C. Engell

Cerebral blood flow was measured by the intravenous xenon-133 technique at rest and during cerebral vasodilation with acetazolamide in 32 patients before and after uncomplicated carotid endarterectomy. The results were compared with the internal carotid artery perfusion pressure measured during surgery. A significant improvement in side-to-side cerebral blood flow asymmetry occurred in 6 patients studied at baseline and in 11 patients during provoked cerebral vasodilation. These patients all belonged to a group of 14 patients who, in addition to a severe stenosis of the internal carotid artery, presented a reduction in cerebral perfusion pressure of at least 20%. No improvements occurred in 18 patients with no or only minor reduction in perfusion pressure, irrespective of the degree of stenosis.

These findings indicate an improved perfusion reserve following carotid endarterectomy in most patients with marked reduction in perfusion pressure, whereas only some of these patients will experience an improvement in baseline cerebral blood flow. (Stroke 1987;18:204-209)
was 13 weeks (range, 7–132 weeks) for strokes and 7 weeks (range, 1 day–32 weeks) for TIA's.

Preoperative computer tomography (CT scan) showed no signs of infarction in 18 patients. A hypodense area, taken as an infarction, was seen in the ipsilateral hemisphere in 12 patients and bilaterally in 2. Ipsilateral infarction was seen in 11 of 16 (69%) stroke patients and in 3 of the 16 (19%) patients who had experienced TIA's only. Three (38%) patients of Group 1 and 11 (46%) patients of Group 2 had ipsilateral infarction.

**CBF Measurements**

All patients were studied 1–5 days prior to surgery and again within the first postoperative week (median, 5 days after surgery). Late postoperative studies were carried out in 11 patients (median, 77 days after endarterectomy). Each CBF study consisted of 2 measurements performed with the patient in supine position in a quiet room. After baseline measurement, 1 g of acetazolamide was given i.v., and 20 minutes later the CBF measurement was repeated.

CBF was measured with the i.v. xenon-133 technique using a mobile 10-detector unit (Novo Cerebrograph 10a). Five detectors were positioned over each region of the middle cerebral artery (MCA). After bolus injection of 10–20 mCi xenon-133 in saline into an antecubital vein, the clearance was recorded throughout 11 minutes. Air samples were drawn continuously from a tight-fitted face mask for estimation of the arterial blood pressure was registered with each study.

Data were analyzed according to a bicompartamental model including a correction term for the air passage artifact. This method of reducing the influence of radiation originating from air passages made it possible to utilize the entire clearance curve. CBF was expressed by a noncompartmental flow index, calculated as the monoexponential slope between 30 and 90 seconds of the deconvoluted clearance curve times the blood-to-tissue partition coefficient, $k$, set to 1.0 ml/g.

In each study the 5 regional flow values were averaged as the hemispheric CBF, and the relative side-to-side asymmetry was calculated as the difference between CBF in the asymptomatic, contralateral and the symptomatic, ipsilateral hemisphere as percent of mean CBF. Reproducibility studies with this equipment have shown that changes in hemispheric CBF from one study to another exceeding ± 9 ml/100 g/min and changes in side-to-side asymmetry exceeding ± 7% are significant at the 5% level. Correction for CO$_2$ changes was not performed.

**Intraoperative Measurements**

Endarterectomy was performed under halothane anesthesia at hypocapnia with an arterial P$_{CO_2}$ of 30 ± 3 mm Hg (± SD). Before clamping of the ICA, blood pressures across the stenosis were measured through a 21 G cannula connected via manometer line to a pressure transducer (Siemens Elema E33). We calculated a cerebral perfusion pressure index (CPPI) as the ratio of the distal mean pressure to the proximal mean pressure (Figure 1). The ICA mean pressure was also measured after ICA clamping (stump pressure). For reference, direct radial artery blood pressure was recorded. Blood flow through the ICA was measured before and after reconstruction by an electromagnetic flowmeter (Nycton 372).

**Statistical Methods**

Differences between 2 samples were compared with the Wilcoxon or Mann-Whitney rank test. When 3 samples were analyzed, the Newman-Keuls multiple range test was applied. Differences between proportions were compared with Fisher's exact test and $\chi^2$ test. Correlation was assessed by means of the Spearman coefficient of rank correlation, $r$. All tests were performed two-tailed. Since each subset of results involved 3–6 comparisons, the Bonferroni method was applied to each subset, taking account of multiplicity. For convenience, significance was taken as $p<0.01$ throughout the study. The calculations were performed on a Digital PC 350 computer.

**Results**

**Clinical Results**

None of the patients developed postoperative neurological complications. In patients with frequent TIA’s up to the time of surgery, the attacks stopped after endarterectomy. Of the 11 patients with persistent preoperative neurological deficits only 1 improved clinically within the first postoperative week.

**ICA Pressure and Flow**

The 8 patients of Group 1, with < 50% ICA stenosis, all had high CPPI's, averaging 0.97 (range, 1.0–0.94), and the ICA flow did not change significantly after endarterectomy (Table 1). In Group 2 CPPI's were significantly lower ($p<0.001$), averaging 0.72, but a great scatter was noticed (range, 1.0–0.36). After endarterectomy ICA flow doubled in this group ($p<0.001$). Among patients of Group 2, the CPPI was not significantly correlated with the degree of ICA stenosis ($p = -0.3; p>0.1$).

Seven of 14 (50%) patients with CPPI below 0.8 had
Table 1. Internal Carotid Artery Pressure and Blood Flow

<table>
<thead>
<tr>
<th></th>
<th>Group 1:</th>
<th>Group 2:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;50%</td>
<td>&gt;50%</td>
</tr>
<tr>
<td>(n = 8)</td>
<td></td>
<td>(n = 24)</td>
</tr>
<tr>
<td>Cerebral perfusion pressure index</td>
<td>0.97 ± 0.02</td>
<td>0.72 ± 0.20</td>
</tr>
<tr>
<td>Stump pressure (mm Hg)</td>
<td>59 ± 14</td>
<td>52 ± 25</td>
</tr>
<tr>
<td>ICA flow before reconstruction (ml/min)</td>
<td>173 ± 46</td>
<td>92 ± 75</td>
</tr>
<tr>
<td>ICA flow after reconstruction (ml/min)</td>
<td>165 ± 41</td>
<td>203 ± 124</td>
</tr>
</tbody>
</table>

Vol 18, No 1, January–February 1987

Table 2. Arterial Blood Pressure and End-tidal Carbon Dioxide Tension

<table>
<thead>
<tr>
<th></th>
<th>BP</th>
<th>Pco2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preoperative (n = 32)</td>
<td>Postoperative within 1 week (n = 32)</td>
</tr>
<tr>
<td>Baseline</td>
<td>105 ± 15</td>
<td>102 ± 15</td>
</tr>
<tr>
<td>Acetazolamide</td>
<td>105 ± 11</td>
<td>106 ± 12</td>
</tr>
</tbody>
</table>

Baseline vs. acetazolamide: not significant for blood pressure; p < 0.001 for Pco2.
Pre vs. postoperatively: not significant for blood pressure or Pco2.
Values are mean ± SD mm Hg.
Table 3. Hemispheric CBF and Side-to-Side Asymmetry Measured Prior to and Within 1 Week After Carotid Endarterectomy in 32 Patients

<table>
<thead>
<tr>
<th>Group 1 (n = 8): stenosis &lt;50%</th>
<th>Group 2 (n = 24): stenosis &gt;50%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td><strong>Baseline</strong></td>
</tr>
<tr>
<td>Operated side</td>
<td>39 ± 8</td>
</tr>
<tr>
<td>Contralateral</td>
<td>40 ± 8</td>
</tr>
<tr>
<td>Asymmetry</td>
<td>1 ± 4</td>
</tr>
<tr>
<td>Acetazolamide</td>
<td></td>
</tr>
<tr>
<td>Operated side</td>
<td>60 ± 5</td>
</tr>
<tr>
<td>Contralateral</td>
<td>61 ± 7</td>
</tr>
<tr>
<td>Asymmetry</td>
<td>2 ± 4</td>
</tr>
</tbody>
</table>

Values are mL/100 g/min CBF and % asymmetry, mean ± SD.
*p < 0.01; †p < 0.001 compared with the preoperative results.

zolamide, and in all cases these improvements were maintained at the time of the late study. Thus, although hemispheric CBF seemed to return to preoperative levels, the relative flow gain in terms of diminished side-to-side asymmetry was maintained both at baseline conditions and following vasodilation (Table 4).

Discussion

In an early study Engell et al.8 reported an increase in ICA flow to be the main hemodynamic effect of carotid endarterectomy. The concomitant changes in CBF were less pronounced, indicating a redistribution of cerebral blood supply. Yet, patients with a minimal ICA flow due to subtotal ICA occlusion showed a marked CBF increase just after reconstruction. Similar results were reported by Sundt et al.,5 whereas others have not been able to demonstrate any change in CBF measured immediately after surgery.10,14 Measurements of CBF days to weeks after surgery have also rendered conflicting results. Some found no change,12,13 while others reported a moderate to marked increase.14-16

In the present study a minor though significant increase in hemispheric CBF was observed within the first postoperative week. However, this improvement was largely unrelated to the degree of preoperative hemodynamic impairment, and in the late studies the global flow increase had disappeared or diminished considerably (Table 4). A temporary increase in CBF has also been reported following extra-intracranial (EC-IC) bypass surgery17,18 and may be what remains of the transient cerebral hyperemia reported immediately following endarterectomy.19,20 Also, the hemodilution observed in the present study may in part account for a global flow increase,21 though no correlation was found between decrease in hemoglobin and increase in CBF.
Table 4. Hemispheric CBF and Side-to-Side Asymmetry Measured Before, 1 Week, and 2 Months After Carotid Endarterectomy in 11 Patients

<table>
<thead>
<tr>
<th></th>
<th>Preoperative</th>
<th>Early</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operated side</td>
<td>38 ± 8</td>
<td>45 ± 12*</td>
<td>41 ± 7</td>
</tr>
<tr>
<td>Contralateral</td>
<td>39 ± 8</td>
<td>45 ± 11</td>
<td>40 ± 7</td>
</tr>
<tr>
<td>Asymmetry</td>
<td>5 ± 9</td>
<td>1 ± 3</td>
<td>0 ± 3</td>
</tr>
<tr>
<td><strong>Acetazolamide</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operated side</td>
<td>54 ± 11</td>
<td>67 ± 14†</td>
<td>60 ± 12</td>
</tr>
<tr>
<td>Contralateral</td>
<td>59 ± 9</td>
<td>67 ± 14</td>
<td>60 ± 13</td>
</tr>
<tr>
<td>Asymmetry</td>
<td>9 ± 14</td>
<td>0 ± 4*</td>
<td>0 ± 2*</td>
</tr>
</tbody>
</table>

Values are ml/100 g/min CBF and % asymmetry, mean ± SD. *p < 0.01, †p < 0.001 compared with the preoperative results.

Although no overall difference in end-tidal Pco2 or blood pressure occurred between the pre- and postoperative studies, individual variation may contribute to the marked variation in global CBF generally observed in repeated studies, thus making the postoperative changes in absolute flow values difficult to interpret. The side-to-side asymmetry, being considerably more reproducible, provides a more specific measure of the hemodynamic changes. In this study a significant improvement of baseline asymmetry was observed in 6 patients, all having at least a 20% reduction of perfusion pressure. Using xenon-133 inhalation and tomography, Vorstrup et al.22 found a relative increase of CBF in the low-flow area in only 2 of 14 patients who underwent carotid endarterectomy. Similar results are reported in a recent study from the same group.23 These data suggest an unchanged baseline CBF in the majority of cases, in agreement with the original perioperative findings of Boyesen.24 Improvements of baseline CBF indicating a reversible perioperative state of hypoperfusion, during which maximal vasodilation had occurred, may be expected in only approximately 10% of the patients. The 2 patients in the present series with orthostatic TIA’s belonged to this subgroup as indicated by the disappearance of orthostatic symptoms after endarterectomy. One of these patients demonstrated within the first postoperative week a mild but definite improvement in a previous neurologic deficit. Such immediately reversible deficits are reported only occasionally. However, Spetzler et al.25 have recently been able to directly correlate low MCA perfusion pressure with the occurrence of neurologic improvement after EC–IC bypass surgery.

As the existence of a state of reversible hypoperfusion would strengthen the indication for carotid endarterectomy, it is of importance to identify such cases. Measurements of CBF during baseline conditions provide no information on flow capacity.26 A unilateral reduction in CBF, manifested as a side-to-side asymmetry, may indicate a restricted blood supply. More often though, it reflects a diminished metabolic demand due to ischemic tissue damage.27 Studies of cerebral blood volume or cerebral metabolic rate by positron emission tomography have been proposed for identification of patients with hypoperfusion.27,28 However, these techniques are more complicated than enhancing the hemodynamic effect of localized arterial disease by the use of a potent vasodilator. For this purpose we have used the carbonic anhydrase inhibitor acetazolamide as originally proposed by Lassen.29 In a previous study we have found that most patients with severely reduced perfusion pressures could be identified by considering the enhancement of side-to-side asymmetry after cerebral vasodilation with acetazolamide.30 These results are given further support in the present study by the finding of a significant correlation in the preoperative measurements between asymmetry enhancement and CPPI and by the lack of correlation between asymmetry enhancement and CT infarction.

Although no untoward effects of acetazolamide were observed in this study, the potent and long-lasting action makes acetazolamide less suitable for further studies during the hyperemia of the early postoperative period. Instead, inhalation of 5% CO2, though more cumbersome to administer, can be recommended for future studies as it induces a vasodilation of the same order of magnitude as 1 g of acetazolamide, but can be withdrawn immediately.31

The change in vasoreactivity after endarterectomy has been reported in two earlier studies.11,16 both pointing to an increased reactivity in patients with severe stenotic lesions, but containing too few observations to allow statistical verification. Halsey et al.32 studied CBF and CO2 vasoreactivity after EC–IC bypass. They concluded that the surgery did not affect the resting CBF, but did augment the collateral reserve in those patients in which it had been most severely impaired by the arterial lesion. In the present series a significant improvement occurred in the group of patients with stenoses of 50% or more, provided they also had an impaired collateral supply as defined by a CPPI below 0.7 (Figure 3). Thus, no increase in perfusion reserve can be expected in patients with no or only minor reduction of perfusion pressure, irrespective of the degree of ICA stenosis.

It may be questioned whether the difference seen between patients could in part be due to the presence of infarcted brain tissue. Since the time between the latest stroke and surgery was 13 weeks on average and at least 7 weeks, it appears unlikely that results ascribed to surgery were simply caused by resolution of luxury perfusion or diastasis. Moreover, in patients with infarction on CT scan the CBF asymmetry was improved only if CPPI was reduced as well. This clearly indicates that improvement of perfusion reserve was related to the degree of hemodynamic compromise rather than the presence of CT infarction.

In the present study we used the ratio of distal to proximal blood pressure measured before clamping of the vessels as an indication of cerebral perfusion pressure. Since pressures were measured during halothane anesthesia and hypocapnia, the pressure reduction across the ICA stenosis was systematically underestimated.33 On the other hand, conditions were approxi-
mately equal for all patients. The influence of anesthesia and hypocapnia therefore do not invalidate the interpretation of our results.

Though an immediate beneficial effect of an increased perfusion reserve is not apparent in most cases, it should be kept in mind that the two pathophysiological mechanisms thromboembolism and hypoperfusion are not mutually exclusive. Areas of brain tissue functioning on a marginal perfusion appear to be more susceptible to the effect of microembolism. Hence, patients with a severely reduced cerebral perfusion pressure represent a group most likely to benefit from carotid endarterectomy, although they may carry a greater risk of postoperative neurologic complications.

References

Key Words • carotid artery surgery • cerebrovascular circulation • perfusion reserve • acetazolamide
Hemodynamic effect of carotid endarterectomy.
T Schroeder, H Sillesen and H C Engell

Stroke. 1987;18:204-209
doi: 10.1161/01.STR.18.1.204

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/18/1/204