Cognitive Function Remains Unchanged After Endarterectomy of Unilateral Internal Carotid Artery Stenosis Under Local Anaesthesia

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Objective. To assess changes in cognitive function and affective state following carotid endarterectomy (CEA) for high-degree unilateral internal carotid artery stenosis.

Methods. In 33 patients, a CEA was performed under local anaesthesia for a high-grade unilateral stenosis of the internal carotid artery (group A). Twenty-five patients underwent surgery for peripheral arterial occlusive disease under regional anaesthesia served as controls (group B). Patients with neurological deficits due to previous strokes or dementia were excluded. Intelligence level was assessed preoperatively. Cognitive tests were applied preoperatively and postoperatively (3–5 days after surgery) and after 4 months follow-up. Confounding factors, including anxiety and depression, were checked through questionnaires and interviews.

Results. No perioperative neurological complication occurred following CEA. Patients in group A showed a significant postoperative deterioration only in one sub-test. There was no significant change in anxiety and depression during follow up. The control group B had no significant changes in cognitive test performance. Anxiety improved significantly postoperatively, but increased again at the end of the study. There was no significant difference between the groups over time.

Conclusion. Cognitive function does not change following CEA of a unilateral internal carotid stenosis.

Keywords: Carotid endarterectomy; Local anaesthesia; Cognition.

Introduction

Latest results from the ‘Asymptomatic Carotid Surgery Trial’ have shown a significant benefit regarding stroke risk reduction following carotid endarterectomy (CEA) in asymptomatic high-degree internal carotid artery (ICA) stenosis, at least in individuals younger than 75 years of age.1 In addition to the established indication for CEA in symptomatic patients, prophylactic carotid surgery now can be justified, provided that the perioperative combined mortality and stroke rate does not exceed 3%.2

However, the impact of an ICA stenosis and any subsequent CEA on cognitive function remains a matter of debate.3,4 Whereas increased postoperative brain perfusion might improve cognition, patients might also suffer from cerebral emboli during surgery5 or uncontrolled global ischaemia during carotid cross-clamping which could cause strokes but also could separately lead to deterioration of cognitive performance. If this were true, the advantage of CEA for stroke prevention would have to be balanced against potential cognitive impairment, in particular in asymptomatic patients.

In 1998, a review of the literature identified various methodological problems for evaluation of perioperative changes in cognitive function.6 This explains why it is so difficult to assess the real effect of CEA. Most importantly, the majority of studies lack appropriate control groups undergoing a comparable treatment and the same testing. Moreover, they do not address the potential influence of coexisting affective disorders or the impact of general anaesthesia. To date, only a single study has taken such problems into consideration. This study found preoperative cognitive impairment in patients with high-degree ICA stenosis, without a history of stroke compared to healthy controls, but no specific benefit of CEA, because
Patients who underwent femoral endarterectomy also showed some postoperative cognitive improvement. The results were corrected for mood changes. However, CEA patients had both uni- and bilateral carotid disease including contralateral ICA occlusion, and in control patients the degree of ICA stenosis was not assessed at all. In that investigation, CEA was performed under general anaesthesia whereas in the study reported here local anaesthesia was used, to further examine whether perioperative changes seen in cognitive function could be directly attributed to the fact that an ICA stenosis had been removed.

**Patients and Methods**

The Institutional Ethics Committee condoned this study. All patients gave informed consent to the study. From April 2001 until October 2002 a total of 33 patients (group A) who underwent CEA for high-degree (>70%) ICA stenosis were included in this study. The degree of stenosis was defined according to NASCET criteria if angiography was performed preoperatively. Otherwise it was assessed by duplex ultrasonography.

A contralateral high-degree ICA stenosis or ICA occlusion were exclusion criteria, in order to ensure a study group homogeneity with respect to cerebral perfusion conditions. Patients with previous strokes or other permanent neurological or psychiatric diseases influencing cognitive function also were excluded from the study. Thus, only asymptomatic patients or those who had experienced transitory ischaemic attacks were included.

The operation was performed under local, cervical anaesthesia which ensured that any impact of narcotics in case of general anaesthesia on cerebral function was eliminated. Patients remained awake during the operation enabling a clinical supervision of their neurological status. Only if hemispheric deficits occurred or if the patients became unconscious during temporary carotid cross-clamping, an intraluminal shunt was inserted to maintain sufficient cerebral perfusion. Depending on the anatomical situation either a standard endarterectomy followed by Dacron-patchplasty or an eversion endarterectomy was performed.

The control group consisted of 25 patients (group B) suffering from peripheral arterial occlusive disease in whom a bypass procedure was performed for revascularization also under local, peridural anaesthesia. Preoperatively, the presence of a high-degree ICA stenosis was ruled out by Doppler examination.

Therefore, as both groups underwent comparable treatment and presented comparable vascular risk factors the main difference is given by the fact that cerebral perfusion was restored after removal of the ICA stenosis.

All patients were controlled for cardiac arrhythmias as an alternative source of cerebral emboli and other neurologically relevant concomitant diseases.

Dementia was ruled out by mini-mental state examination (MMSE) at a cut-off score of 24. Multiple choice vocabulary test B provided information about general intelligence level.

Cognitive tests were chosen to examine various representative brain functions. Parallel test versions were used randomly for repeated tests to avoid practice effects. For evaluation of working and short-term memory letter number span (LNS) was used. Trail-making test version B (TMT-B) examined visual and motor coordination (by time measurement in seconds) whereas the auditory verbal learning test (AVLT) assessed verbal learning and memory. This latter test is divided into sub-tests noticing the scoring at several time points: after the 1st trial (AVLT-1), 5th trial (AVLT-5), after a short delay (AVLT-SD) and after a longer delay of 30 min (AVLT-LD). Finally, recognition is checked (AVLT-R).

The occurrence of anxiety and depression was checked through self-rating questionnaires (hospital anxiety and depression scale: HADS) and additional interviews (Hamilton depression scale: HAM-D). Since, impending amputation in case of advanced perfusion impairment might be associated with a state of depression and/or fear, which could falsify the results of cognitive testing, patients with critical limb ischaemia were not included in the control group.

The tests were performed in constant, undisturbed environment on the day before surgery, 3–5 days postoperatively and after a median of 4 months follow-up (range 3–10 months). Patients, particularly the controls, were reluctant to undergo follow-up examinations so that several attempts had to be undertaken to arrange appointments. At follow up the patency of both ICAs was assessed by Doppler ultrasound. Additionally, any other meaningful somatic or psychological event with potential consequences on cognition or affection was recorded.

For statistical analysis SPSS 11.0 software was used. All data are expressed as mean and standard deviation (SD). After having confirmed parametric distribution, basic demographic data and test results at baseline were compared between the groups with a T-test for independent samples. Alternatively, the chi-square test or Fisher’s exact test were applied as appropriate.
MANOVA with measurement occasions (preoperatively, postoperatively, follow-up) as the within-subject factors were used followed by within-subject contrasts comparing cognitive function over time for both treatment groups separately. A group factor was introduced to compare test performance in patients undergoing CEA (group A) or peripheral arterial reconstruction (group B). Further covariates were added to check for possible age effects and the impact of the affective status on cognitive function. Differences were considered significant at a level of $p < 0.05$.

Results

Perioperatively, no new neurological deficit occurred after CEA (left sided in 17 patients and right sided in 16 patients). Also all peripheral bypass operations were performed without major complications. Patients in groups A and B were similar regarding basic demographic data, except for age as patients undergoing CEA were significantly older ($68 \pm 8$ versus $62 \pm 11$ years), $p = 0.01$. Baseline MMSE-scores, intelligence level scores and the number in employment were similar in both groups (Table 1).

Postoperatively, one patient in group A and two patients in group B did not attend for further follow up. At the end of the study a further five CEA patients and six bypass surgery patients were lost to follow-up. The patients lost to follow up did not differ from the remaining patients who completed the study in terms of demographic characteristics or primary test performance.

Group A

Cognitive tests

Compared to baseline performance, the patients undergoing CEA showed worse postoperative test results in most cognitive tests, with partial recovery at later follow-up examination. In some tests a continuous decline was observed over the study period. Only in a single test did patients improve at follow-up compared to baseline testing. In none of the other tests was the preoperative level reached again at the end of the study. However, these differences were statistically significant only in AVLT-LD, pre versus postoperative testing ($p = 0.004$) and between preoperative versus follow-up testing ($p < 0.01$) (Table 2).

Tests for affective state

Depression was diminished postoperatively, but tended to increase again at follow-up. Anxiety decreased continuously over time so that the overall level of affective symptoms was lower at follow-up examination than preoperatively. None of these trends were statistically significant (Table 2).

Group B

Cognitive tests

In contrast to group A, the controls achieved improved test scores postoperatively in the majority of tests throughout follow up, but none of the changes were statistically significant (Table 3).

Tests for affective state

Patients undergoing surgery for arterial occlusive disease also presented with less anxiety and depression postoperatively. However, an aggravation of depression and anxiety was noticed at follow-up examination with higher HADS-anxiety scores than baseline, pre versus postoperative testing ($p = 0.01$) and postoperative versus follow-up testing ($p = 0.02$) (Table 3).

Group comparison

Preoperative baseline scores of groups A and B were not statistically different in any of the tests, regarding either cognition or the affective state. Test results over time of both patient groups were compared to evaluate the independent impact of carotid surgery. Significant interactions between treatment and cognitive performance over time were found in two sub-tests (AVLT-SD, AVLT-LD). Since, patients undergoing CEA were significantly older, age was added as a covariate. Primary group analysis showed significant changes regarding the affective state as indicated by HADS-anxiety in patients in group B which was introduced as a second covariate. After further adjustment for

<table>
<thead>
<tr>
<th>Table 1. Basic data</th>
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</thead>
<tbody>
<tr>
<td>Group A (N = 33)</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Sex (male/female)</td>
</tr>
<tr>
<td>Education (primary/middle/high school)</td>
</tr>
<tr>
<td>Verbal IQ</td>
</tr>
<tr>
<td>MMSE</td>
</tr>
<tr>
<td>Employed/unemployed</td>
</tr>
</tbody>
</table>

T-test for independent samples, chi-square test or Fisher’s exact test when appropriate.
HADS-anxiety changes there were no differences between groups A and B (Table 4).

**Discussion**

Factors influencing cognitive function

The literature regarding cognition after CEA is so heterogeneous that no definitive conclusions can be drawn. Irvine analysed 22 studies of which 15 reported an improvement of cognitive function, but seven demonstrated an impairment. In 16 out of 28 relevant papers reviewed by Lunn CEA was followed by an improved cognitive test performance. In the remaining 12 studies no substantial change was found. However, the vast majority of these publications suffer from poor methodology. First patients with and without neurological defects have been assessed using the same protocol. Second, natural processes of spontaneous brain repair might be underestimated compared to the effect of carotid surgery, although especially in younger patients the prognosis of cognitive functioning following an ischaemic event is rather favourable. To avoid such factors, in this study only patients without any permanent deficit and presenting an unilateral ICA stenosis were included. The presence of a contralateral ICA stenosis or even occlusion might have continuously compromised cerebral perfusion and cognition. In addition, the patients underwent CEA under local anaesthesia. Therefore, any potential impact of narcotics was avoided. The absence of a control group, like in one of the latest publications, furthermore limits the significance of previously reported changes in test performance. When selecting an appropriate control population, vascular risk factors must be considered.

Table 2. Test results in group A (patients undergoing CEA)

<table>
<thead>
<tr>
<th>Test</th>
<th>Preoperative (N=33)</th>
<th>Postoperative (N=32)</th>
<th>Follow-up (N=27)</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>LNS</td>
<td>13.2±2.9</td>
<td>13.6±2.5</td>
<td>12.7±3.1</td>
<td>1.29</td>
<td>0.30</td>
</tr>
<tr>
<td>AVLT-1</td>
<td>4.5±1.9</td>
<td>4.5±1.5</td>
<td>4.4±1.4</td>
<td>0.14</td>
<td>0.87</td>
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<tr>
<td>AVLT-5</td>
<td>10±2.3</td>
<td>9.0±2.2</td>
<td>9.4±2.2</td>
<td>3.30</td>
<td>0.06</td>
</tr>
<tr>
<td>AVLT-SD</td>
<td>9.5±2.3</td>
<td>9.0±2.3</td>
<td>8.7±2.1</td>
<td>2.45</td>
<td>0.11</td>
</tr>
<tr>
<td>AVLT-LD</td>
<td>8.2±2.4</td>
<td>6.4±2.9</td>
<td>6.9±2.6</td>
<td>8.67</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>AVLT-R</td>
<td>12.3±2.1</td>
<td>11.5±2.6</td>
<td>11.2±3.4</td>
<td>3.24</td>
<td>0.06</td>
</tr>
<tr>
<td>TMT-B</td>
<td>136.8±47.8</td>
<td>141.2±80.6</td>
<td>130.9±39.8</td>
<td>0.26</td>
<td>0.77</td>
</tr>
<tr>
<td>HAM-D</td>
<td>4.9±6.2</td>
<td>4.4±4.8</td>
<td>4.7±4.8</td>
<td>0.39</td>
<td>0.68</td>
</tr>
<tr>
<td>HADS depression</td>
<td>3.8±3.4</td>
<td>3.3±2.7</td>
<td>3.2±3.2</td>
<td>1.41</td>
<td>0.26</td>
</tr>
<tr>
<td>HADS anxiety</td>
<td>5.3±3.4</td>
<td>4.0±3.5</td>
<td>3.7±3.2</td>
<td>2.92</td>
<td>0.07</td>
</tr>
</tbody>
</table>

* MANOVA: significant within-subject contrast between: pre and postoperative testing (p<0.01); preoperative and follow-up testing (p<0.01).

Table 3. Test results in group B (patients undergoing peripheral bypass)

<table>
<thead>
<tr>
<th>Test</th>
<th>Preoperative (N=25)</th>
<th>Postoperative (N=23)</th>
<th>Follow-up (N=17)</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>LNS</td>
<td>13.0±3.5</td>
<td>13.0±2.9</td>
<td>13.3±3.6</td>
<td>0.03</td>
<td>0.97</td>
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<tr>
<td>AVLT-1</td>
<td>4.4±1.4</td>
<td>4.6±1.5</td>
<td>5.5±1.6</td>
<td>3.44</td>
<td>0.07</td>
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<tr>
<td>AVLT-5</td>
<td>9.5±2.5</td>
<td>10.0±2.3</td>
<td>9.9±2.7</td>
<td>0.61</td>
<td>0.56</td>
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<tr>
<td>AVLT-SD</td>
<td>8.6±2.8</td>
<td>9.3±2.8</td>
<td>9.9±3.1</td>
<td>2.01</td>
<td>0.18</td>
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<tr>
<td>AVLT-LD</td>
<td>7.3±3.7</td>
<td>6.5±3.3</td>
<td>8.4±3.6</td>
<td>1.88</td>
<td>0.20</td>
</tr>
<tr>
<td>AVLT-R</td>
<td>11.5±2.5</td>
<td>9.9±3.0</td>
<td>11.6±5.6</td>
<td>1.22</td>
<td>0.33</td>
</tr>
<tr>
<td>TMT-B</td>
<td>130.3±52.3</td>
<td>109.0±42.4</td>
<td>103.8±35.3</td>
<td>2.53</td>
<td>0.12</td>
</tr>
<tr>
<td>HAM-D</td>
<td>3.94±6.4</td>
<td>3.6±3.2</td>
<td>3.1±2.8</td>
<td>0.74</td>
<td>0.50</td>
</tr>
<tr>
<td>HADS depression</td>
<td>3.2±3.3</td>
<td>2.6±3.2</td>
<td>3.1±2.2</td>
<td>2.70</td>
<td>0.11</td>
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<tr>
<td>HADS anxiety</td>
<td>4.4±3.2</td>
<td>3.2±2.6</td>
<td>5.0±3.4</td>
<td>4.79</td>
<td>0.03</td>
</tr>
</tbody>
</table>

* MANOVA: significant within-subject contrast between: pre and postoperative testing (p<0.01); postoperative and follow-up testing (p<0.02).
as they are associated with a gradual decline in cognitive function. In a large cohort study of 1500 men Elwood found, that ‘subjects with evidence of cardiac or peripheral disease have a significant reduction in cognitive function equivalent to about 4 or 5 years of additional age’. Consequently, patients undergoing spine or urologic surgery, but without evidence of atherosclerosis or patients not undergoing a surgical procedure are unsuitable as controls. We used peripheral arterial disease patients receiving surgery under regional anaesthesia as controls.

Test composition

Testing only a single brain function would be insufficient to capture postoperative cognitive changes. On the other hand, too large a collection of tests could be tiring leading to worse test results, particularly in older populations. We chose a selection of tests focusing on memory and coordination lasting approximately 45 min. These tests also have been used in other studies making the results and conclusions more comparable.

In many of previously published studies neither anxiety nor depression were ruled out, despite the fact that both the disease and the operation were associated with a stroke risk. Even minor mood changes might adversely influence motivation and performance in neuropsychological tests.

Test results

Baseline test results did not differ between the patient groups indicating that they were comparable, although one would have expected better cognitive performance in the significantly younger controls. However, the intelligence level and occupation rate, partly representing their daily degree of mental activity, was similar in the two groups.

There was little indication of significant cognitive decline after CEA, a significant decline having been identified in only one sub-test. This suggests that CEA is not associated with important changes in cognitive function.

Patients in group B tended to obtain better test results over time without showing any impairment directly after surgery. However, these differences in test performance were not statistically significant.

The affective status patients undergoing peripheral reconstruction showed a significant change in anxiety with particular increase from postoperative to follow-up testing which might represent the continuous fear of disease progression and ultimate amputation. After CEA an opposite (but not statistically significant) trend was observed, perhaps reflecting the relief from the individual stroke risk. Interestingly, the operation itself was not associated with an elevated level of anxiety which one could have expected in conscious patients undergoing serious surgery.

Further multivariate analyses, which have been applied in this study, compare test results between the groups by considering the development over time. Significant differences with subject to CEA or bypass surgery were sporadically detected. However, there were no significant differences after correction for the covariates age and anxiety which were differently pronounced in both treatment groups indicating that changes in test performance are not independently associated with surgery itself.

This kind of analysis is useful in assessing neuropsychological changes, as the level of baseline performance is taken into account as a point of reference.

Bossema et al. analysed data in a similar way comparing two patients groups (CEA versus femoral endarterectomy) with time of testing as covariate. They found improvement in some cognitive tests within the first postoperative year, which, however, did not differ between the two groups. Furthermore, both surgical groups performed worse at baseline compared to healthy volunteers, which reinforces the necessity for appropriate control groups in neuropsychological testing. This study also concluded that there was no cognitive benefit following CEA. Both the Boesma study and our own are limited by small sample size.

Outlook

Some authors claim that by eliminating the source of cerebral emboli future cognitive impairment will be prevented, so that it is reasonable to do additional late follow-up examinations in order to recognize a potential improvement or at least stabilization of cognition over a period of several years: confounding factors would be difficult to identify. When reviewing publications stating an improvement of cognition following CEA, it seems like at least a sub-group of patients with multivessel disease (in particular if the contralateral ICA is occluded) or functional proof of exhausted cerebrovascular reserve benefit from carotid surgery in neuropsychological terms because under these circumstances overall cerebral perfusion would gain more from CEA, so that relative changes in cognition might be greater and clinically more pronounced. For these reasons it is important to
continue and expand cognitive testing in patients with carotid disease under well defined conditions.

Conclusions

There are no significant variations in perioperative cognitive function after CEA and no differences compared to a control group. Patients undergoing CEA for a unilateral ICA stenosis can expect no change compared to a control group. Patients undergoing cognitive function after CEA and no differences There are no significant variations in perioperative

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References


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