Impact of Microembolism and Hemodynamic Changes in the Brain During Carotid Endarterectomy

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Background and Purpose Monitoring of carotid endarterectomy with electroencephalography and transcranial Doppler ultrasonography provides instantaneous information about hemodynamic changes and embolic signals. However, a relation between these findings and intraoperative infarcts has not yet been demonstrated.

Methods In this study we compared preoperative and postoperative computed tomographic scans (58 patients) or magnetic resonance imaging (40 patients) of the brain, assessed by two independent observers, to detect intraoperative infarcts, and we related any such new lesions to the findings of intraoperative monitoring.

Results In the computed tomography series one intraoperative infarct occurred, with corresponding clinical deficits. In the magnetic resonance group four patients developed new lesions that occurred intraoperatively, all of which were clinically silent. There was a significant relation between the number of embolic signals during the surgical dissection of the carotid artery and the occurrence of intraoperative infarcts (P<.005). Three of the four infaracts were of the lacunar type; the fourth patient had a border-zone infarct, associated not only with many embolic signals but also with low flow during cross-clamping. There were no demonstrable ultrasound side effects on brain tissue.

Conclusions Embolic signals detected by transcranial Doppler monitoring in the dissection phase of carotid endarterectomy show a significant relation to new ischemic lesions and therefore are potentially harmful. The phenomenon should alert the vascular surgeon. (Stroke. 1994;25:992-997.)

Key Words • carotid endarterectomy • tomography, x-ray computed • magnetic resonance imaging • ultrasonics

The occurrence of transient ischemic attacks of the brain or eye in patients who have ipsilateral carotid artery stenosis with an angiographically documented linear diameter reduction of at least 70% is now an established indication for carotid endarterectomy (CEA). The next challenge for surgeons and physicians is to make the operation safer, in particular to avoid intraoperative and postoperative stroke. Determinants of these complications have been studied in terms of "static" risk factors before the operation but have not yet been systematically related to dynamic events during the actual CEA procedure.

In our institute CEA is performed with intraoperative monitoring by means of electroencephalography (EEG) and transcranial Doppler ultrasonography (TCD). EEG shows the electric activity of the cortex and is sensitive to changes in the metabolism of neurons. Originally we used only EEG changes during test clamping of the carotid artery as a criterion for the selective use of a shunt. Deeply located lacunar ischemic lesions, however, were usually not detected by intraoperative EEG monitoring. Moreover, a computed tomography (CT) study showed that more than 50% of cerebral infarcts during CEA were probably of thromboembolic origin.

Detection of embolic signals in the middle cerebral artery (MCA) during CEA is easily achieved with TCD recording. From previous studies we concluded that this technique has the potential to detect embolic signals as well as hemodynamic changes during CEA. The occurrence of intraoperative embolic signals without any clinical sequelae in the majority of our patients raised a fundamental question about the clinical relevance of this phenomenon. If the effects of the detected embolic signals in CEA cannot be demonstrated by means of neurological examination postoperatively, such effects might be shown by sensitive neuroimaging techniques. In the past 15 years CT has been the most common tool in the demonstration of cerebral lesions in clinically manifest or silent brain ischemia. The introduction of magnetic resonance (MR) imaging has made it possible to detect in a very early phase even smaller ischemic cerebral lesions, both in the cortex and the deep white matter. Recently new subcortical white matter hyperintensities on T2-weighted MR images have been described after therapeutic balloon occlusion of the internal carotid artery for unclippable giant aneurysms. Preoperative and postoperative MR scanning of the brain in patients who undergo CEA therefore seemed the most appropriate method for detecting evidence of cerebral ischemia caused by thromboembolism or hemodynamic changes during CEA.

It has been assumed that TCD is a harmless diagnostic instrument. However, during monitoring of CEA...
with TCD a pulsed ultrasound beam is continuously insonated on the MCA. The ultrasound beam passes a sector of the ipsilateral hemisphere from the cortex to the basal ganglia. Thus, an extensive part of the brain is insonated for a period of 1 to several hours. At present there have been no reported adverse effects from TCD monitoring, but sensitive neuroimaging studies have not been systematically applied. The current study was undertaken to answer the following questions: (1) Does cerebral microembolization, detected by TCD monitoring during CEA, result in ischemic damage? (2) Do hemodynamic changes, detected by TCD and EEG monitoring during cross-clamping, result in ischemic lesions? (3) Does postoperative cerebral CT or MR imaging have the potential to detect small, new ischemic brain lesions after CEA, and which method is the most sensitive? (4) Does long-standing TCD monitoring during CEA have any harmful effect on brain tissue as seen on CT or MR imaging?

**Subjects and Methods**

Altogether 98 patients underwent CEA with TCD monitoring and preoperative and postoperative brain imaging. In the CT study we investigated 58 patients (47 men and 11 women; mean age, 63 years [range, 43 to 82 years]). All these patients underwent CT scanning of the brain before and 3 to 5 days after surgery. These 58 patients were part of a larger group of 130 patients described elsewhere. Ten of these 58 patients underwent CEA in combination with a coronary bypass operation. Thirty-nine patients (67%) showed recent carotid artery symptoms (amaurosis fugax, transient ischemic attacks, or minor ischemic stroke), and 19 patients were asymptomatic. All CT scans were performed on a Philips Tomoscan TX, with contiguous slices of 5- or 6-mm thickness, parallel to the supraorbital-meatal line.

In the RR study we enrolled 40 consecutive patients (31 men and 9 women; mean age, 60 years [range, 54 to 87 years]). Thirty patients (75%) had transient ischemic attacks or amaurosis fugax, and 10 patients were asymptomatic. All patients underwent CEA without concomitant coronary bypass surgery. All MR scans were performed on a Philips Gyroscan T5, with a 0.5-T superconducting magnet. After a T-weighted spin-echo scout view, axial T2-weighted spin-echo images were made with a repetition time of 2335 milliseconds and echo times of 30 and 90 milliseconds. The scans were made with a slice thickness of 6 mm, a slice gap of 0.6 mm, and a field of view of 230 mm. We followed the same MR protocol in the postoperative studies and made every attempt to use an identical slice angulation.

All patients underwent a detailed neurological examination before and after the operation, as soon as the level of consciousness was appropriate. In the event that the patient's preoperative neurological status was unchanged, the procedure was considered uncomplicated. New cerebral deficits were recorded as intraoperative stroke; complications that developed within 3 months after the first postoperative examination were classified as postoperative. Preoperative duplex scanning and digital subtraction angiography of both carotid and vertebral arteries were performed in all patients. The methods of intraoperative EEG and TCD monitoring have been described elsewhere. We applied an EME TC 2-64 TCD with an IMP monitoring transducer. The ultrasound beam of this system was focused at a depth of 60 mm, and in the focal point the sample volume had a length of 10 mm (axial resolution) and a width of 5 mm (lateral resolution). In the present study the sample volume was located at a depth of 45 to 60 mm, and the pulse repetition frequency was 4.96 kHz. The transmitted intensity control setting varied between 75% and 100%. This refers to in situ intensities of 87 to 116 mW/cm² (spatial peak-temporal average). However, this is only an estimation because the exact attenuation and refocusing of the ultrasound beam by the human skull during the monitoring procedure are not known. A continuous video recording of the spectral waveforms and the audio Doppler signals was made from intubation until the end of anesthesia. We recorded peak flow velocity, pulsatility index, blood pressure, anesthetics used, and surgical manipulations. Special attention was paid to the occurrence of embolic signals in the Doppler spectrum according to the criteria described by Spencer and Russell et al. We measured the number of embolic signals semiquantitatively: (1) <10 isolated signals and (2) ≥10 isolated signals or complex signals. This was performed in three different phases of the operation: (1) during dissection of the artery until cross-clamping, (2) at release of the cross-clamps after closure of the arteriotomy, and (3) in the event of shunting, during the introduction and removal of the Javid shunt. In cases of doubt the tapes were reviewed immediately after surgery (C.J., R.G.A.A.). All surgical procedures were uniform. Shunting was performed selectively on the basis of EEG and TCD criteria as described in earlier reports. Anesthesia was given with nitrous oxide and halothane 0.25% to 0.50% to avoid a depth of anesthesia that would interfere with reliable EEG monitoring.

All CT scans were independently interpreted by two radiologists. When new lesions were suspected on the postoperative scan, a separate committee made an independent judgment on the scans. The films were mixed with those of other patients as part of another study regarding interobserver agreement in the classification of CT-proven infarcts. The MR scans were assayed by two radiologists who independently counted hypertense lesions in both hemispheres, brain stem, and cerebellum without knowledge of the preoperative or postoperative status or the side of operation. In the event of disagreement, a third neuroradiologist was consulted. For the comparison of data we used Fisher's exact tests. We considered values of P<.05 to be significant. The interobserver agreement was calculated by means of kappa statistics.

**Results**

**Computed Tomographic Study**

In the group of 58 patients who underwent preoperative and postoperative CT scanning, one ipsilateral border-zone infarct occurred intraoperatively, with the corresponding clinical deficits. At test clamping, this patient showed a severe (>70%) reduction of blood flow velocities in the MCA but no EEG asymmetry. She was not shunted, and only a few (<10) embolic signals were noticed at release of the cross-clamps. A second patient developed a transient postoperative deficit after many embolic signals during release of the cross-clamps, without a new infarct on the postoperative CT scan.

In this part of the study, no silent ischemic lesions were found, although there were embolic signals during the phase of dissection of the artery in 10 patients and at release of the cross-clamps in 39 patients. In 19 of these 49 patients there were more than 10 embolic signals. The remaining 9 patients of the 58 had embolic signals (always <10) during other moments of the operation: in 3 patients during the introduction or removal of a shunt and in 6 during closure of the wound.

Five patients developed delayed postoperative infarcts on the side of surgery. All these infarcts were confirmed by CT. It should be emphasized that CT scanning was performed only in patients who showed embolic signals during surgery or new neurological deficits. Excluding hemorrhage and transient ischemic attack, the combined intraoperative and postoperative
ischemic stroke rate in the whole series was 6 of 130 patients.4

**Magnetic Resonance Study**

Of the 40 patients who underwent preoperative and postoperative MR scanning, 3 patients showed transient ischemic symptoms immediately after the operation, with complete recovery within 6 to 36 hours and without new lesions on the MR scan. One patient (Fig 1; patient A) developed a delayed ischemic stroke on the operated side 11 days after surgery. A postoperative duplex examination on day 11 revealed an occlusion of the external carotid arteries and a subtotal stenosis of the internal carotid arteries.

The two radiologists reached agreement in 39 patients (κ=0.9). In 4 patients they agreed on a new ischemic lesion, and in 35 they agreed on no change. In 1 scan they disagreed, even on repeated assessment, after which a third radiologist decided that there were no new lesions. The four new lesions occurred in the ipsilateral hemisphere, and all were without clinical symptoms. Three lesions were small, deeply located infarcts (lacunes; Fig 2). In the fourth patient the infarct was in a subcortical border-zone area (Fig 1; patient A). Eight days after the MR scan was made this patient developed a manifest stroke (see above).

**Embolic Signals**

The Table shows the semiquantitative counting of embolic signals in the three different phases of the operation. Three of the 40 patients showed no embolic signals and no new lesions on the MR scan. Embolic signals were noticed in the remaining 37 patients. The occurrence of more than 10 embolic signals during any phase of the operation was significantly associated with the appearance of new MR lesions (P=.01). During dissection of the carotid arteries, 14 patients showed embolic signals. Nine of these 14 patients had fewer than 10 embolic signals and no new MR lesions. The remaining 5 had more than 10 embolic signals, 3 of whom showed a new silent MR lesion on the side of surgery (P<.005). One of these 3 patients was patient A, who had the border-zone infarct.

At release of the cross-clamps, 19 patients showed embolic signals, in 13 cases fewer than 10. One of these 13 patients had a new MR lesion, but this patient had also exhibited more than 10 embolic signals during dissection. The 6 remaining patients had more than 10 embolic signals after release of the cross-clamps, 1 of whom showed a new lesion (P=.5). Of all 19 patients who had embolic signals during release of the clamps, 3 had transient ischemic symptoms (P=.1) without a new lesion on the scan. Only 1 of these 3 patients had shown more than 10 embolic signals after cross-clamp release (P=.7).

In this part of the study 13 patients were shunted, and none of these patients had new MR lesions. Three of the shunted patients showed no embolic signals at all. In 7 patients fewer than 10 signals and in 3 patients more than 10 embolic signals were noticed during insertion of the shunt. Two of these 13 patients showed transient symptoms after the operation (P=.2).

**Hemodynamics**

Electroencephalographic asymmetry during test clamping was associated with a reduction of blood flow velocities by more than 70% in 11 patients. One patient developed EEG asymmetry but no significant reduction
Occurrence of New Hyperintense Lesions In the Ipsilateral Hemisphere on Postoperative Magnetic Resonance Imaging of the Brain and Data of Intraoperative Monitoring in 40 Patients

<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>New Lesion (n=4)</th>
<th>No New Lesion (n=36)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Embolic signals</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>4</td>
<td>33</td>
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<tr>
<td>≥10 at any time</td>
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<td>.01</td>
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<tr>
<td>During dissection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>0</td>
<td>9</td>
<td>.3</td>
</tr>
<tr>
<td>≥10</td>
<td>3</td>
<td>2</td>
<td>&lt;.005</td>
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<tr>
<td>On cross-clamp release</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>1</td>
<td>12</td>
<td>.6</td>
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<td>1</td>
<td>5</td>
<td>.5</td>
</tr>
<tr>
<td>During shunt insertion or removal (n=13)</td>
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<td>7</td>
<td>.4</td>
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<tr>
<td>Hemodynamics</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>EEG asymmetry on cross-clamping</td>
<td>1</td>
<td>11</td>
<td>.7</td>
</tr>
<tr>
<td>&gt;70% reduction of MCA blood flow velocity on cross-clamping</td>
<td>2</td>
<td>10</td>
<td>.3</td>
</tr>
</tbody>
</table>

EEG indicates electroencephalographic; MCA, middle cerebral artery.
*This patient also had >10 embolic signals during dissection.
†One patient showed both EEG asymmetry and >70% reduction; the other patient also showed >10 embolic signals during dissection (patient A; see "Results").

Discussion

Ischemic complications during CEA appear in almost every series reported in the literature. These complications can present as a transient cerebral deficit without new lesions on neuroimaging, a permanent cerebral deficit attributable to a new infarct on neuroimaging, or as a clinically silent lesion shown on CT or MR imaging. Whatever their clinical or radiological manifestations, the causes of these ischemic cerebral complications are either hemodynamic insufficiency during cross-clamping of the carotid artery or thromboembolism from the atheromatous lesion in the carotid artery.

Hemodynamic compromise of a cerebral hemisphere on cross-clamping of the carotid artery is especially encountered in patients with a poor collateral circulation and an exhausted vasomotor reserve. In a previous study we described the relation between severe EEG asymmetry and the reduction of MCA peak blood flow velocities by 70% or more.4 One patient in the CT series with a severe reduction of blood flow velocities but without severe EEG asymmetry was not shunted and developed transient dysphasia and on CT showed two small infarcts in the subcortical white matter of the MCA, which is the region of the MCA in the Sylvian fissure and the surrounding tissue in the frontal and temporal lobes. Within this beam area, no new CT or MR lesions were noticed. The mean duration of TCD monitoring was 90 minutes (range, 55 to 140 minutes). After surgery there were no complaints of local pain at the site of the TCD transducer. On inspection, no skin discolorations or burns were seen in the transducer area.

Safety Considerations

All new MR lesions occurred in the subcortical white matter and outside the area of the ultrasound beam, which is the region of the MCA in the Sylvian fissure and the surrounding tissue in the frontal and temporal lobes. Within this beam area, no new CT or MR lesions were noticed. The mean duration of TCD monitoring was 90 minutes (range, 55 to 140 minutes). After surgery there were no complaints of local pain at the site of the TCD transducer. On inspection, no skin discolorations or burns were seen in the transducer area.

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danger of embolization by micro air bubbles or formed elements at this stage of the operation. Moreover, the conclusions we draw from this series are based on the occurrence of intraoperative lesions that were silent and not on clinically manifest infarcts.

On the assumption that microemboli are the cause of the new MR lesions, it is interesting to highlight the anatomic appearance of these lesions. In the event of thromboembolism, one would expect cortical, wedge-shaped infarcts in the territory of an artery or an arterial branch. However, no such infarcts occurred in this study. In patient A (Fig 1), subcortical white matter hyperintensities were seen in a border-zone area. This particular patient had evidence of hemodynamic insufficiency during cross-clamping on TCD and was shunted. Additionally, the TCD monitor detected more than 10 embolic signals during dissection and fewer than 10 embolic signals after release of the cross-clamps. It must be emphasized that microembolization into a hemodynamically compromised hemisphere will contribute to ischemia in the territories with the lowest perfusion (watershed areas). The same assumption probably holds true for a heavily embolized hemisphere that subsequently suffers a hemodynamic insult. The hemodynamic vulnerability of patient A was further demonstrated by extension of the border-zone infarct on day 11 as a result of subtotal internal carotid restenosis. Three other patients with new lesions showed small, rounded subcortical lesions, which looked like lacunes (Fig 2). Although lacunar infarcts have traditionally been attributed to lipohyalinosis of small vessels, often associated with hypertension, recent evidence suggested the possibility of a thromboembolic cause for some lacunar infarcts.\(^{19,20}\) In our patients with new lesions, it is very unlikely that small-vessel disease leading to the formation of lacunes had developed in a perioperative period of 3 to 5 days. Hemodynamic factors did not contribute to the development of all new subcortical lesions, because two of the four patients with new lesions had no evidence of hemodynamic insufficiency during the entire operation. Moreover, if hemodynamic insufficiency during cross-clamping was demonstrated by EEG or TCD, the rapid introduction of a shunt immediately restored the circulation. Therefore, our findings support a thromboembolic pathogenesis of at least some infarcts of the lacunar type developing during CEA. Similar lesions were described by Awad et al\(^{16}\) after therapeutic balloon occlusion of the intracranial part of the internal carotid artery for giant aneurysms. In view of the occlusion procedure they performed, they attributed these lesions to hemodynamic factors. However, thromboembolism could not be excluded in these patients.

The safety of intraoperative TCD monitoring is of paramount importance because of the prolonged exposure of the brain to ultrasound in this technique. Therefore, we scrutinized the preoperative and postoperative scans for morphological changes that might reflect adverse effects of ultrasound exposure. Other than the morphological changes of thromboembolic origin outside the area of the ultrasound beam, no other new lesions were demonstrated on either the CT or MR scans. Moreover, no skin changes or burns occurred at the site of the transducer in any of the patients. Therefore, in the particular setting of intraoperative TCD monitoring with a mean duration of 90 minutes of ultrasound energy transmission into the brain, no cerebral lesions were revealed in the region of the ultrasound beam. The estimated intracranial intensities were supplied by Eden Medical Electronics Group. They were defined by taking into account a worst-case value of 40% loss of acoustic energy by reflection of the bony skull.\(^{22,23}\) Although our conclusion in regard to safety is reassuring, the number of patients in this study is relatively small. With a sample size of 98 patients and a 5% significance level, the true incidence of alterations in brain morphology could in reality have been as high as 3% and still have been undetected.\(^{24}\) Therefore, more follow-up studies must be performed to evaluate any possible negative impact on brain morphology after prolonged exposure to ultrasound.

In summary, our study suggests that TCD monitoring during CEA can alert the surgeon not only to hemodynamic phenomena (low flow) but particularly to thromboembolism from the atheromatous lesion. This may help to make the procedure safer. Of course, our findings do not apply to strokes developing hours or days after the operation (approximately one third of all perioperative strokes\(^{8}\)).

Acknowledgments

We would like to thank Dr H.L.J. Tanghe, neuroradiologist from the University Hospital Dijkzigt, Rotterdam, the Netherlands, who interpreted the MR scans as an independent referee, and Mrs J. Pitt, London, England, for the textual correction of the manuscript.

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Stroke. 1994;25:992-997
doi: 10.1161/01.STR.25.5.992

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