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Stroke From Carotid Endarterectomy: When and How to Reduce Perioperative Stroke Rate?

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Objectives: *to analyse four years of CEA with respect to the underlying mechanisms of perioperative stroke and the role of intraoperative monitoring in the prevention of stroke.*
Patients and Methods: *from January 1996 through December 1999, 599 CEAs were performed in 404 men and 195 women (mean age: 65 years, range: 39–88). All operations were performed under general anaesthesia using computerised electroencephalography (EEG) and transcranial Doppler (TCD). Any new or any extension of an existing focal cerebral deficit, as well as stroke-related death were registered. Perioperative strokes were classified by time of onset (intraoperative or postoperative), outcome (minor or major stroke), and side (ipsilateral or contralateral). Stroke aetiology was assessed intraoperatively by means of EEG, TCD, completion arteriography or immediate re-exploration, and postoperatively by duplex sonography, computerised tomography (CT) or magnetic resonance imaging (MRI) of the head.*
Results: *perioperative stroke or death occurred in 20 (3.3%) patients. In four operations stroke was apparent immediately after surgery. Mechanisms of these strokes were ipsilateral carotid artery occlusion (1) and embolisation (3). In 16 patients stroke developed after a symptom-free interval (2–72 h, mean 18 h) due to occlusion of the internal carotid artery on the side of surgery (9). Other mechanisms were: contralateral occlusion of the internal carotid artery (1), postoperative hyperperfusion syndrome (1), intracerebral haemorrhage (1), and contralateral ischaemia due to prolonged clamping (1). In three procedures the cause was unknown.*
Conclusions: *in our experience most strokes from CEA developed after a symptom-free interval and mainly due to thromboembolism of the operated artery. We suggest the introduction of additional TCD monitoring during the immediate postoperative phase.*

Key Words: Carotid endarterectomy; Stroke; Perioperative monitoring.

Introduction

NASCET and ECST have demonstrated clear benefits of carotid endarterectomy (CEA) in patients with severe carotid artery stenosis in the prevention of stroke.[1,2] However, the absolute benefit of CEA is limited by the morbidity and mortality of the procedure itself, particularly the risks of stroke and death. Although a risk profile for cerebral complications was recently published,[3] the actual pathophysiological mechanisms of stroke from CEA often remain unclear. About 20 mechanisms have been proposed, mainly categorised into ischaemia from carotid artery clamping, intraoperative and postoperative thrombosis and embolism, and intracerebral haemorrhage.[4] In agreement with Radak *et al.*[5] we believe it is important to distinguish between intraoperative and postoperative stroke. The differentiation between stroke that is apparent in the recovery room and stroke that develops after a symptom-free interval can lead to a better understanding of the underlying mechanisms and, thus, may have important clinical implications.

In our institution, the use of intraoperative computerised electroencephalography (EEG) during CEA was evaluated in 1989.[6] With regard to the detection of intraoperative major stroke the results were promising. However, the detection of intraoperative minor stroke was unreliable. In the study of Krul *et al.*[7] we showed that in 69% of these minor strokes embolism was the likely cause, but these embolic events were not detected by our EEG expert system. Transcranial Doppler (TCD) is the only modality that can provide direct information about the appearance of microemboli during CEA. Made audible in the operation theatre, the embolic signals can warn the surgeon in time as to

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which manipulation causes embolism and, thus, he or she can try to adopt a technique that avoids further embolisation. With respect to intraoperative haemodynamics, EEG and TCD give complementary information about metabolic state of the cerebral cortex and blood flow velocities in the ipsilateral middle cerebral artery, respectively. After the introduction and standardisation of TCD monitoring during CEA in our institution, three important changes were noticed: (1) the rate of intraoperative embolism decreased, (2) the use of an indwelling shunt increased, and (3) the intraoperative stroke rate declined from 4.8% to 1%.[8] However, it was disappointing to observe that our monitoring programme had not altered our postoperative stroke rate.

A more profound understanding of the present causes of perioperative stroke might be the key in further prevention of stroke from CEA, possibly resulting in additional monitoring measures. Therefore, the purpose of the present study was to examine the pathogenesis of perioperative stroke and the role of cerebral function monitoring in the prevention of these strokes.

Materials and Methods

Patients

From a prospective computerised database the records of all patients undergoing CEA of the internal carotid artery from January 1996 through December 1999 were analysed. Patients with a CEA in combination with coronary artery bypass surgery as well as patients undergoing surgery of the carotid artery for non-atherosclerotic disorders were excluded. In patients who underwent a second CEA (ipsilaterally or contralaterally), only one operation was analysed in this study. If both operations were uneventful, the first operation was included. In case of one CEA with and one without complications, the former was included.

Preoperative patient characteristics

Age, gender, medical history and preoperative cerebral symptoms were documented. Symptomatic patients were classified according to the most severe symptom (amaurosis fugax < transient ischaemic attack < minor stroke). Preoperative evaluation included neurological examination and assessment of ipsilateral and contralateral internal artery stenosis by duplex sonography and digital arteriography. Before surgery, a computerised tomography (CT) scan or magnetic resonance image (MRI) of the head was performed in all patients.

Carotid endarterectomy

All patients were operated under general anaesthesia using nitrous oxide and halothane or isoflurane, and were mechanically ventilated. Carotid endarterectomy was performed in a standardised way. Surgery was executed by an experienced vascular surgeon or by a specialist vascular trainee under supervision. Before cross-clamping intravenous heparin (5000 IU) was administered; protamine reversal was not used. All patients were given 100 mg aspirin daily preoperatively which was continued postoperatively. Duplex was performed 3 months after surgery.

Intraoperative monitoring

Intraoperative brain function monitoring was based on simultaneous EEG and TCD monitoring that have been discussed elsewhere in detail.[9,10] In summary, all patients underwent computerised EEG monitoring with fronto-parietal and temporo-occipital leads. In addition, TCD monitoring of the ipsilateral middle cerebral artery blood flow velocities was possible in 90% of the operations. Patients were selectively treated with intra-arterial shunting (Javid shunt) on the basis of EEG and TCD criteria mentioned in these reports. In patients at risk for a hyperperfusion syndrome based on intraoperative TCD monitoring variables,[11] blood pressure was closely monitored and controlled with medication intraoperatively immediately after declamping and postoperatively on the medium care unit or surgical ward.

Outcome

Postoperatively, patients were assessed by the vascular surgeon in the operating theatre and later in the recovery area. In the case of possible cerebral deficit the patient was examined by a neurologist. In the analyses, we focused on the occurrence of ischaemic and haemorrhagic stroke and stroke-related death within 7 days after surgery. Cerebral deficits persisting for more than 24 h were regarded as stroke. Transient cerebral deficits were not included in this study. Perioperative strokes

were classified by time of onset (intraoperative or postoperative), outcome (minor or major stroke) and side (ipsilateral or contralateral to the side of surgery). The severity of stroke was graded according to the modified Rankin scale.[12] Cerebral deficit that was noticed immediately after the operation was defined as intraoperative. Delayed cerebral deficit that appeared after a symptom-free interval was classified as postoperative. We correlated the onset of cerebral symptoms with specific operative and monitoring events (carotid artery dissection, clamping and declamping, shunting, EEG asymmetry, TCD detected cerebral embolism and important changes of MCA blood flow velocities). Furthermore, the pathogenesis of these strokes was assessed by completion arteriography or by means of intraoperative findings on immediate re-exploration of the carotid artery, and postoperatively by duplex sonography, TCD, head CT or MRI. All these forms of quality control assessment were only performed in patients with possible stroke from CEA. We considered re-exploration an option when a CT-scan has ruled out cerebral haemorrhage and re-operation can be carried out within 3 h after onset of symptoms. For logistic reasons this was not possible in all patients. Routine postoperative TCD monitoring to evaluate the possible impact of microemboli during the first hours after surgery on clinical outcome was not done.

Statistical analysis

Fisher's exact test and Student *t*-test were used to test the differences of clinical and operative variables between the groups of patients with and without postoperative stroke. $p<0.05$ was considered statistically significant.

Results

A total of 599 CEAs were studied (Table 1). Perioperative stroke occurred in 20 (3.3%). Patients with a perioperative stroke showed more severe contralateral carotid artery disease; specifically, a subtotal stenosis (90–99%) of the contralateral internal carotid artery ($p=0.01$). This may be why an indwelling shunt was used more often in this group ($p=0.03$).Three patients died from their stroke, resulting in a mortality rate of 0.5%. During the four years of analysis, two patients underwent two CEAs of which one was eventful.

Table 1. Clinical and operative characteristics of the non-stroke and stroke groups.

	Non-stroke $n=579$	Stroke $n=20$	*p*-value
Male gender	378 (65%)	17 (85%)	0.09
Mean age (years)	65 (39–88)	68 (52–82)	0.27
Clinical presentation			
Ischaemic stroke	168 (29%)	7 (35%)	0.62
Asymptomatic	131 (23%)	8 (40%)	
Contralateral ICA			
Subtotal stenosis (90–99%)	39 (6.7%)	5 (25%)	0.01
Occlusion	103 (18%)	7 (35%)	0.07
Shunt used	174 (30%)	11 (55%)	0.03
Patch used	259 (45%)	11 (55%)	0.37

ICA = internal carotid artery.

Intraoperative stroke

Four ipsilateral strokes (0.7%) were immediately apparent on waking from anaesthesia; two minor and two major strokes. In two operations, TCD detected multiple microembolism was the probable cause of cerebral deficit. In one operation a macroembolus blocked the MCA blood flow velocities. In this patient, the postoperative CT scan showed a hyperdense artery sign in the MCA mainstem. In the fourth operation, there was ipsilateral thrombotic occlusion of the operated artery.

Postoperative stroke

In sixteen (2.7%) operations stroke appeared after a symptom-free interval of between 2 h and three days (mean 18 h). Thirteen strokes developed within the first 24 h. Neurological outcome was a minor stroke in 7 operations and a major stroke in 9 operations. Fourteen of these strokes developed ipsilaterally to the side of surgery. One minor and one major stroke appeared contralaterally. In 13 of these 16 operations it was possible to determine the most probable cause: ipsilateral occlusion of the operated arteries (9), occlusion of the contralateral internal carotid artery (1), intraoperative hypoperfusion related to prolonged clamping due to shunting difficulties (1), postoperative hyperperfusion syndrome (1), and intracerebral haemorrhage (1). In 3 operations (all minor strokes) it was not possible to pinpoint the causes of cerebral deficit.

Of the 20 CEAs that resulted in a stroke, Table 2 shows the most probable causes of cerebral deficit. Information about contralateral internal carotid artery stenosis, the use of a shunt or patch, and intraoperative findings at re-exploration are also summarised. In the

Table 2. Preoperative and intraoperative characteristics, time of onset, and causes of perioperative stroke, and outcome in 20 eventful CEAs.

Onset	Contralat. stenosis	Shunt	Patch	Time of cause onset (h)	Re-expl.	Outcome
I	90	No	Yes	0 embolisation	No	Minor stroke
I	30	Yes	No	0 embolisation	Yes	Minor stroke
I	50	Yes	No	0 embolisation	Yes	Major stroke
I	100	Yes	No	0 occlusion	Yes	Major stroke
P	100	No	No	24 occlusion	No	Minor stroke
P	100	Yes	Yes	72 occlusion	No	Minor stroke
P	100	Yes	Yes	7 occlusion	Yes	Major stroke#
P	0	No	Yes	48 occlusion	No	Major stroke
P	40	No	Yes	4 occlusion	No	Major stroke
P	80	No	No	9 occlusion	No	Major stroke#
P	100	Yes	Yes	3 occlusion	Yes	Major stroke
P	100	Yes	Yes	2 occlusion	Yes	Major stroke#
P	90	No	Yes	19 occlusion	No	Major stroke
P	90	Yes	No	2 HPS	No	Major stroke
P	90	No	Yes	32 haemorrhage	No	Major stroke
P	100	Yes	No	6 clamp time	No	Major stroke (contralateral)
P	90	Yes	Yes	18 contralat. occl.	No	Minor stroke (contralateral)
P	0	No	No	18 unknown	No	Minor stroke
P	90	Yes	Yes	24 unknown	No	Minor stroke
P	0	No	No	24 unknown	No	Minor stroke

I = intraoperative; P = postoperative; contralat. stenosis = degree of stenosis of contralateral internal carotid artery; HPS = postoperative hyperperfusion syndrome; # = death due to stroke; contralat. occl. = occlusion of the contralateral internal carotid artery; contralateral = stroke contralaterally to the side of surgery.

group of 20 patients with intraoperative or postoperative cerebral deficit, a CT-scan of the head was performed in 19 cases. Postoperative angiography, duplex scanning of the carotid arteries or TCD-monitoring were performed in 12 cases. Six patients were reoperated at the onset of neurological symptoms (3 intraoperative and 3 postoperative). In 4 cases re-exploration confirmed an acutely thrombosed endarterectomy site and revision was performed successfully. One of these 4 thrombotic occlusions was caused by a technical error and in three cases no evidence of technical error was found. In the remaining two patients re-exploration showed a mural thrombus in one, suggesting intraoperative embolisation as the cause. Unfortunately, in this patient TCD monitoring was not possible due to a poor acoustic window. In the last patient a patent vessel was found at re-exploration.

At three months, duplex follow-up of 579 non-stroke patients revealed an asymptomatic occlusion of the operated artery in 5 cases (0.9%). In the remaining patients all operated carotid arteries were found patent.

Discussion

The present study evaluated the causes of perioperative stroke (intraoperative and postoperative) from CEA. We observed that during carotid surgery with intraoperative computerised EEG and TCD monitoring intraoperative stroke only occurred in 4 out of 599 (0.7%) procedures. In contrast, a postoperative stroke was assessed in 16 operations (2.7%). In 9 out of the 16 (56%) postoperative strokes an occlusion of the operated artery was found. Moreover, in an additional 5 patients an asymptomatic occlusion of the operated artery was found with duplex sonography at three months after an uneventful CEA. Two patients (0.3%) developed symptoms of a postoperative hyperperfusion syndrome, one with and one without an intracerebral haemorrhage. Finally, 2 patients developed a stroke of the contralateral hemisphere. In one patient this was an intraoperative major stroke due to a difficult shunting procedure with prolonged clamping time. In the other patient, a tightly stenosed contralateral internal carotid artery completely occluded symptomatically one day after surgery.

Several reports have shown that the introduction of standardised TCD monitoring during CEA results in a decrease of the intraoperative stroke rate.[13–15] We share the opinion of these investigators that surgeons can be guided by the "embolic signals" and accordingly can adapt their technique to prevent a serious outcome. Moreover, in the course of TCD monitoring, it became apparent that microembolism occurring during dissection and wound closure

showed a statistically significant association with perioperative stroke.[16] Since the introduction of intraoperative TCD monitoring in our institution in 1990, the intraoperative stroke rate from CEA declined from 4.8% in the late eighties[6,7] to 0.7% in this study.

With respect to postoperative stroke, probably the most devastating cerebral complication is the so-called postoperative hyperperfusion syndrome often resulting in intracerebral haemorrhage and death. Dalman *et al.*[11] have shown that TCD monitoring can reliably identify patients who are at risk. With strict postoperative control of hypertension the incidence of symptomatic hyperperfusion after CEA decreased from 2.1% in the early nineties[17] to 0.3% in this study.

A more frequent cause of postoperative stroke from CEA is thrombus formation at the endarterectomy and clamping sites coupled with an increasing cerebral embolic load. This often results in an occlusion of the operated artery.[18–21]

Spencer *et al.*[22] first observed that TCD detected cerebral microemboli that occur during the first hours after CEA may be associated with postoperative cerebral deficit. More recently, several studies[23–25] revealed that a small proportion of patients (5–10%) who underwent CEA showed sustained cerebral embolisation, with a maximum rate of embolism during the first postoperative hours. Moreover, Cantelmo *et al.*[26] demonstrated that multiple cerebral microemboli during the immediate postoperative phase were statistically significantly associated with new, clinically silent ischaemic lesions on MRI of the brain made after surgery. TCD monitoring in the early postoperative course of CEA has the potential to identify patients at high risk of postoperative embolic stroke. There is a strong association between embolic rates exceeding 50 microemboli per hour and focal postoperative ischaemic deficit.[23,25] Moreover, the administration of Dextran-40 in the selected group of patients significantly reduced the risk of carotid thrombosis and cerebral embolic burden and, finally, resulted in a postoperative stroke rate of 0%.[27]

The present study presents several limitations. Cerebral deficit was primarily assessed by a vascular surgeon and a neurologist was consulted only in patients with possible postoperative neurological complications. Therefore, it is reasonable to assume that some minor signs and symptoms of cerebral deficit were missed. Second, in 3 out of 20 CEAs that resulted in a postoperative minor stroke we were not able to find a plausible explanation for the underlying pathophysiological mechanisms. Third, postoperative TCD monitoring could not be of help because it was not routinely performed in our patients. Thus, there is only indirect evidence that postoperative thrombosis and occlusion resulted in a significant embolic burden and postoperative stroke.

In conclusion, intraoperative EEG and TCD monitoring has shown to be effective in the prevention of intraoperative ischaemic and haemorrhagic stroke. In contrast, postoperative thrombus formation and occlusion still complicated CEA in a significant number of patients. In the present study of 599 CEAs, we found 10 symptomatic (1 intraoperative and 9 postoperative) and 5 asymptomatic occlusions of the operated artery, i.e. in 2.5%. If TCD monitoring during the first hours after CEA has the ability to identify carotid thrombosis prior to the occurrence of carotid artery occlusion and cerebral deficit, this will be an important additional clinical application of this technique.

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