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Frequency, Clinical Significance and Course of Cerebral Ischemic Events after Carotid Endarterectomy Evaluated by Serial Diffusion Weighted Imaging

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Objectives. *Neurological deficit defines the outcome of Carotid Endarterectomy (CEA) that is mainly caused by cerebral ischemia. Diffusion-weighted imaging (DWI) is a sensitive method for demonstrating even small ischemic lesions. The aim of this study was to evaluate the frequency, clinical significance and course of ischemic lesions after CEA using serial DWI.*
Methods. *DWI was performed within 1 day before and after CEA in 88 patients. Postoperative lesions were analyzed by their quantity, volume and distribution. To differentiate temporary ischemia from definite cerebral infarction (blood brain barrier disruption) all patients with a positive postoperative DWI were reexamined with contrast-enhanced T1-MRI 7–10 days after the procedure. All patients were examined by a neurologist within 2 days before and after CEA.*
Results. *Two patients showed a postoperative neurological deficit. Postoperative DWI revealed ipsilateral ischemic lesions in 15 patients. In seven of these patients a brain infarction was diagnosed on the T1-MRI during follow-up. A significant correlation between the number of DWI lesions ($p = 0.031$) as well as the volume of DWI lesions ($p = 0.023$) and definite infarction was found. Symptomatic patients preoperatively showed significantly more DWI lesions ($p = 0.036$) and cerebral infarcts ($p = 0.003$).*
Conclusion. *DWI is a sensitive method of demonstrating ischemic events after CEA. The number and volume of DWI lesions after CEA are highly predictive of brain infarction.*

Key Words: Magnetic resonance imaging; Diffusion-weighted imaging; Carotid endarterectomy; Cerebral infarction; Stroke; Carotid stenosis.

Introduction

The main purpose of Carotid Endarterectomy (CEA) is the prevention of stroke. The benefit of CEA depends on low morbidity and mortality rates.[1,2] Cerebral embolization and hypoperfusion are the major causes of perioperative neurological deficits.[3–5]

Using diffusion-weighted imaging (DWI) cerebral ischemic lesions caused by microembolism and hypoperfusion can be detected with a high accuracy and soon after the event.[6,7] Therefore, DWI is superior to conventional spin echo t2-weighted and FLAIR sequences.[8] In animal models DWI lesions were visible within 5–15 min;[9,10] in humans DWI lesions could be seen within less than an hour after stroke.[11] Most of the DWI lesions seen after CEA are clinically silent and transient,[12] but some of them develop into infarctions within days and are then detectable with conventional MRI. A correlation between the volume of DWI lesions and the neurological outcome after a first stroke has been described[8] and neuronal damage even after early DWI recovery in the rat model was found.[13] The importance of DWI lesions after CEA is still matter of debate as the majority of the patients lack a neurological deficit.[12,14,15] However, until now the transition of DWI lesions after CEA into infarction[16] has not been evaluated.

Our study aimed to analyze the frequency, volume and number of lesions after CEA using serial DWI and follow-up contrast-enhanced T1-MRI.

Materials and Methods

From a series of 116 consecutive patients treated between May 2000 and July 2002, three patients with Crescendo-TIA, two cases with progressive stroke and

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seven patients with claustrophobia were excluded. Sixteen patients were excluded because no preoperative or postoperative DWI was available. Therefore 88 patients (32 female, 56 male) with a median age of 67 years (range 46–90) were included in this prospective study and underwent CEA for asymptomatic ($n = 48$) and symptomatic ($n = 40$) high-grade carotid artery stenosis. Stenosis were evaluated by color-coded duplex sonography following ECST-criteria in all patients[17] and additionally with diagnostic carotid angiography in two patients. In symptomatic patients, the indications for surgery were transient ischemic attacks (TIA) in 15 cases, transient monocular blindness (TMB) in eight cases, prolonged reversible ischemic neurological deficit (PRIND) in one case, and previous cerebral infarction in 16 cases. In cases of TIA or TMB, patients underwent anticoagulant therapy and were operated within 3 days after the first symptomatic event. In case of PRIND patients were anticoagulated and surgery was performed as soon as blood brain barrier disruption was no longer detectable. All patients were treated with acetylsalicylic acid with 100 mg daily (Fig. 1).

The procedure was performed under normotensive, normocapnic, general anesthesia. As a standard procedure a thrombendarterectomy with routine shunting was performed using a size-compatible BARD®-Shunt (IMPRA, Inc. Tempe, USA). The arteriotomy was routinely closed with a pre-clotted Dacron patch (Hema Carotid Patch Knitted And Knitted Ultrathin™, Intervascular, La Ciotat Cedex, France). The median clamping time was 159 s (range: 60–385 s) for shunt insertion and 174 s (80 440 s) for shunt removal and restoration of flow.

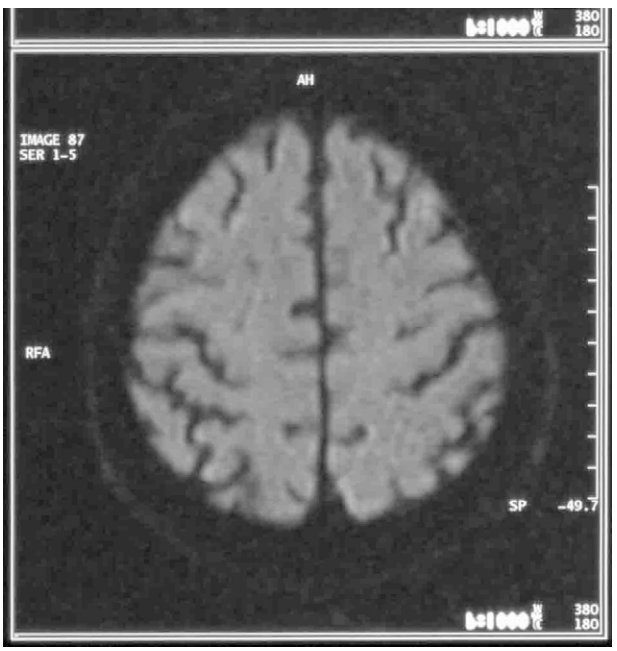

Fig. 1. DWI before CEA in a patient with symptomatic high-grade stenosis of the left carotid artery.

MRI was performed using a 1,5 T whole body imaging system (Magnetom Symphony Quantum gradient, Siemens Medical Systems, Germany) with a dedicated head coil. DWI was performed within 1 day before and after CEA. The whole brain DWI was carried out with an isotropic echo-planar sequence with b-values of 0, 500 and 1000 s/mm^2, TR 4006 ms, TE 83 ms, number of averages two, slice thickness 4–6 mm, 128×128 matrix size and 220×220 mm^2 field of view. Sagittal, coronal and transverse views were obtained. All MRI results were reviewed by two experienced neuroradiologists, without knowledge of the vascular status and the side of operation and blinded to each other findings. An acute lesion on DWI was only diagnosed if an increased signal intensity was visible on two planes, if a corresponding decreased signal intensity was detected in the apparent diffusion coefficient (ADC)-image and if both neuroradiologists agreed on their DWI findings.

If a new lesion was detected in postoperative DWI, T1-weighted spin-echo images (TR/TE: 548/14,0) with and without gadolineum were performed 7–10 days after the procedure. A blood brain barrier disruption was judged to represent a definite infarction. Volume size was obtained by measuring all three planes. All patients underwent a detailed neurological examination within 2 days before and after the procedure by a neurologist. All patients gave written informed consent for the study.

Statistical Analysis

Statistical analysis was performed in cooperation with the Institute of Medical Statistics and Epidemiology of the Technical University of Munich. All calculations were carried out using SPSS (version 11.0). The Chi-square-test was used to analyze the relationship between MRI findings and asymptomatic/symptomatic stenosis. The nonparametric Wilcoxon rank sum test was used for comparison of postoperative DWI lesion volume, postoperative DWI lesion number and evidence of brain infarction at the follow-up investigation. A value of $p < 0.05$ was considered statistically significant (Fig. 2).

Results

After CEA two patients, both symptomatic preoperatively, showed neurological deficits. The deficits

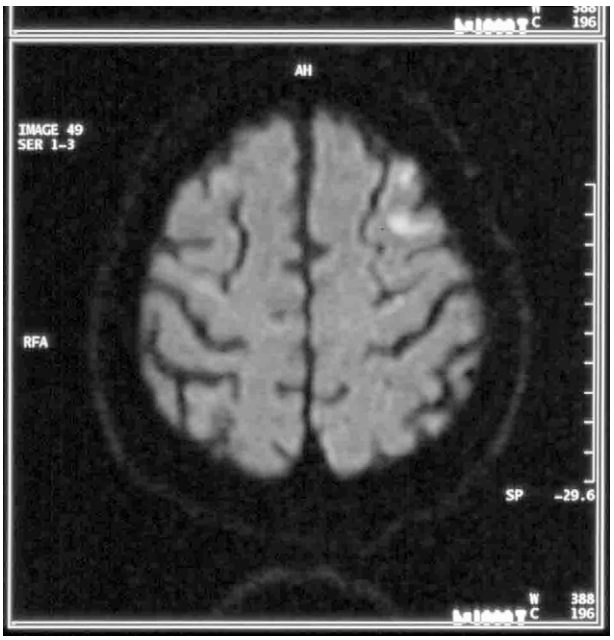

Fig. 2. DWI performed in the same patient 24 h after surgery with a cortical DWI lesion in the left frontal middle gyrus.

occurred within 6 h of the operation and on the hemisphere ipsilateral to the operated side. One patient developed a Broca's aphasia and one patient an incomplete right hemiparesis. The patient with the hemiparesis showed six DWI-lesions with a total volume of 1.42 ml and the patient with the aphasia showed one DWI-lesion with a size of 6 ml (see Table 1). Both patients were referred to the stroke-unit. In both patients the neurological deficit was persistent. Three patients underwent reoperation because of postoperative bleeding. None of the patients in the study died.

Preoperative DWI was performed in all patients. Ten patients showed pathological changes in the preoperative DWI. Eight of the 40 preoperative symptomatic patients and two of the 48 preoperative asymptomatic patients showed new ischemic lesions. These two patients underwent diagnostic carotid angiography prior to DWI. Fifteen patients showed new ischemic lesions after CEA (Table 1). All lesions occurred ipsilateral to the operated side, none contralateral. All lesions showed territorial character, none were found in the watershed region. Six patients had a single and three patients had two dot-shaped lesions. Six patients showed more than two dot-shaped lesions. One patient developed a territorial lesion with embolic occlusion of a branch of the middle cerebral artery.

Fourteen of the 15 patients with positive DWI were examined with contrast-enhanced T1-MRI. One patient with a positive DWI was lost during follow-up. Seven patients had transient DWI lesions and showed no pathological findings in T1-MRI. In seven patients an ipsilateral infarction with blood brain barrier disruption was seen with the ischemic areas corresponding to the areas of the DWI lesions. In all cases the size of the infarction was comparable to the size of the initial DWI lesion. We observed a significant correlation between the number of lesions in DWI ($p = 0.031$) as well as the volume of the lesions ($p = 0.023$) and the occurrence of definite brain infarction on follow-up MRI. Five of the six patients with more than two lesions showed brain infarction while only two of the nine patients with a singular or two dot-shaped lesions showed infarction (Fig. 3).

All patients with a DWI lesion volume of 0.34 ml or more developed brain infarction, compared to only two of the nine patients with a volume less than 0.34 ml. The patients with neurological deficits developed one large infarction in one case and six

Table 1. Patients with positive DWI after CEA: lesion number, lesion volume, radiological and clinical impact regarding brain infarction.

Patient	DWI lesions (*n*)	DWI lesion volume (ml)	Brain-infarction contrast-enhanced MRT	Neurological deficit
1	1	0.01	Negative	Negative
2	1	0.01	Negative	Negative
3	1	0.01	Negative	Negative
4	1	0.02	Negative	Negative
5	2	0.06	Negative	Negative
6	1	0.08	Positive	Negative
7	2	0.1	Positive	Negative
8	4	0.15	Negative	Negative
9	1	0.17	Lost in follow up	Negative
10	2	0.2	Negative	Negative
11	4	0.34	Positive	Negative
12	5	1.17	Positive	Negative
13	6	1.4	Positive	Negative
14	6	1.42	Positive	Positive
15	Territorial	6	Positive	Positive

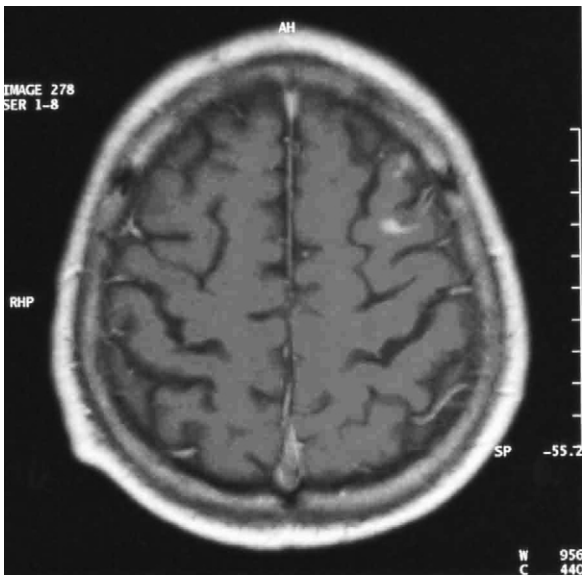

Fig. 3. Contrast-enhanced T1-MRI in the patient 8 days after surgery with a blood brain barrier disruption in the same localization.

dot-shaped infarctions in the other case. These patients showed the largest ischemic volume on DWI (see Table 1).

In 10 (25%) of the preoperative symptomatic patients DWI lesions were observed and 6 (15%) developed brain infarction. In contrast 5 (10.4%) of the preoperative asymptomatic patients showed DWI lesions and none of them developed infarction. The correlation between a symptomatic stenosis and a DWI-lesion ($p = 0.036$) as well as a symptomatic stenosis and a postoperative brain infarction was significant ($p = 0.003$). There was no correlation between the grade of the stenosis and the occurrence of DWI lesions or infarction. We did not find a correlation between lesions detected on DWI preoperatively and postoperatively.

Discussion

In the past, various methods have been used for the detection of clinically evident and silent ischemia after CEA. Studies using CT scanning 5–6 days after the procedure demonstrated new cerebral infarctions in 0–8.8% of patients.[18–20] In studies using conventional MRI such as T1- and T2-weighted spin-echo or FLAIR-sequences, the rate of detected lesions after CEA was up to 24%.[21–23] Recent developments in the diagnostic accuracy of MRI using DWI-techniques have substantially improved the rapidity and quality of the diagnosis of cerebral ischemia with a sensitivity of 92% and a specificity of 100%.[6,24] DWI lesions after CEA ipsilateral to the procedure have been found in 0–33% of patients.[12,14,15]

DWI is a reliable method for the detection of acute ischemic brain lesions and is superior to CT and conventional MRI.[6] In animal models DWI lesions appear as soon as 5[9] to 15 min[10] after ischemia. In humans with ischemic stroke, DWI lesions are detectable within 1 h.[11] DWI changes after stroke appear within 24 h in nearly all patients and disappear within 10–14 days.[24] Most of the lesions are seen as infarctions by conventional follow-up MRI.

Therefore, we chose DWI for the detection of acute ischemic lesions in our study. Based on the findings of Burdette et al.[24] DWI was scheduled within 1 day after the procedure.

We observed new postoperative DWI lesions in 15 (17%) cases ipsilateral to the side of surgery. All lesions appeared embolic and none showed watershed infarction. As we observed no correlation between preoperative and postoperative DWI lesions, the clinical usefulness of preoperative DWI remains questionable. However, in our study design preoperative DWI was necessary to reveal the procedure-related lesions. The percentage of postoperative DWI lesions in our study was comparable to the study of Müller.[12] However, in previous studies the clinical importance of postoperative DWI lesions remained unclear since these lesions were mostly silent and seldom correlated with neurological deficits. None of the authors examined the clinical course of the lesions by follow-up contrast-enhanced T1-MRI.

Within the group of patients with positive DWI after CEA we found gadolinium-enhancement representing brain-infarction detected by follow-up MRI in 7 (46.6%) patients.[16] The question of whether potential therapies (e.g. antiplatelet therapy, anticoagulation or statins) might reduce the positive DWI rate or attenuate progression to subsequent infarction will require further studies.

It is still a matter of debate whether DWI lesions seen after CEA correspond exclusively to infarcted brain tissue or whether they also indicate reversibly ischemic brain tissue.[12] We observed a significant correlation between the number of lesions in DWI ($p = 0.031$) as well as the volume of the lesions ($p = 0.023$) and the occurrence of brain infarction with blood brain barrier disruption in follow-up MRI. These findings indicate that stroke severity correlates with DWI lesion size, confirming the results found in spontaneous stroke.[25] Normalization of the DWI does not necessarily imply that the tissue is normal. In regions of rapid and complete recovery of the DWI after temporary occlusion of the middle cerebral artery in rats, structural damage of the neurones could be found.[13]

It is conceivable that these 'silent' DWI lesions may explain the neuropsychological and cognitive dysfunction observed in some patients after CEA.

Symptomatic carotid stenoses are associated with a higher perioperative risk of stroke than asymptomatic stenoses. Similarly, we found a significant higher incidence for DWI lesions ($p = 0.036$) and brain infarction ($p = 0.003$) in symptomatic stenoses as compared to asymptomatic stenoses in our investigation. This may reflect the higher fragility of the plaque in symptomatic carotid artery disease. After stenting of the carotid artery ipsilateral DWI lesions occur more often as compared to CEA.[26,27] Assuming that any loss of brain tissue impairs the result of carotid artery reconstruction DWI including volumetric evaluation, as an objective and sensitive method, should be included into future multicenter studies of CEA vs stenting.

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