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ORIGINAL COMMUNICATION

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Neuropsychological consequences of endarterectomy and endovascular angioplasty with stent placement for treatment of symptomatic carotid stenosis

A prospective randomised study

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Abstract *Background and purpose* Previous studies compared carotid endarterectomy (CEA) and carotid artery stent placement (CAS) for treatment of symptomatic carotid artery stenosis. Whereas most previous studies showed both treatment modalities to be associated with a comparable risk of periprocedural cerebrovascular complications, these previous studies have shown significantly more microemboli and significantly more lesions in diffusion-weighted MR imaging after CAS compared to CEA. The clinical relevance of these differences remains unknown. We therefore compared the neuropsychological consequences of CAS and CEA and additionally measured the S100β protein, a marker of cerebral damage. *Methods* A total of 48 patients with symptomatic carotid artery stenosis greater than 70 % (according to ECST criteria) were enrolled and 45 patients participated in the follow-up. The patients were randomly assigned for CEA (24 patients) or CAS (21 patients). S100β protein values were evaluated 2 hours before the procedure, as well as one and two hours thereafter. Patients were assessed before treatment, and again 6 and 30 days after treatment using a comprehensive neuropsychological test battery. *Results* Patients of the CAS and the CEA groups did not significantly differ in terms of age, gender, education, degree of carotid artery stenosis, cerebrovascular symptoms and vascular risk factors. Following previously used criteria, a cognitive change in patients was assumed to have occurred when there was a decline of more than one standard deviation in two or more tests assessing various cognitive domains. Six days and 30 days after the treatment both groups showed a comparable number of patients with cognitive changes compared to baseline. There were no significant differences in S100β protein values. *Conclusion* These results provide some reassurance that CAS is not associated with greater cognitive deterioration than CEA is.

Key words stroke · carotid artery stenosis · endarterectomy · stent placement · neuropsychology

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Introduction

Severe symptomatic carotid artery stenosis holds a 26 % cumulative risk for ipsilateral stroke within a two-year period [2]. Since it has been shown that carotid endarterectomy (CEA) dramatically decreases the risk of a recurrent stroke, this procedure has become standard therapy for symptomatic arteriosclerotic carotid artery stenosis. Treatment of symptomatic arteriosclerotic carotid artery stenosis by endovascular techniques, such as percutaneous transluminal angioplasty (PTA) and carotid angioplasty with stent placement (CAS) is a form of therapy that prevents minor complications of CEA such as cranial or superficial nerve injury, wound complications and the possible side effects of a general anaesthesia. The significance of CAS in the treatment of symptomatic severe carotid is still a matter of debate since one large study failed to prove non-inferiority of CAS compared with CEA for the periprocedural complication rate [35]. However, a second recent study has shown lower rates of severe complications at 1 and 6 months after CEA compared to CAS [29]. Several studies have reported significantly more cerebral microembolisms after PTA and CAS in comparison to CEA as demonstrated by transcranial Doppler sonography [9, 10]. Diffusion-weighted MR imaging (DWI) showed significantly more lesions after PTA and CAS compared to CEA [23, 24, 32, 36]. Previous investigators suggested that these lesions lead to a cognitive decline but the clinical correlates of these lesions are still controversial. One study investigated the effects of PTA in comparison to CEA in the cognitive domain of patients with a symptomatic carotid stenosis of more than 70 %. They reported no significant differences between these procedures 6 weeks and 6 months after the intervention [10]. The present investigation extended this study by investigating the possible clinical consequences of a higher rate of microembolism in CAS in two ways: First we investigated the effects of CAS and CEA in the cognitive domain using a neuropsychological test battery 6 days after treatment because we suspected that clinical correlates of microembolism occur in the CAS group shortly after the intervention. Furthermore second neuropsychological testing took place 30 days after the intervention to examine the long-term effects of both techniques. An additional step was to measure the S100β protein values as previous studies had demonstrated that the gliofibrillar S100β protein is a valuable biochemical marker of early brain damage [13, 20, 21, 31]. Our hypothesis is that cerebral microembolism leads to more brain lesions after CAS compared to CEA and therefore S100β protein should be increased in the CAS group because it correlates with cognitive deterioration.

Methods

Patients

Forty-eight patients were consecutively recruited for CEA or CAS. Three patients were lost to follow-up, so the study group consisted of 45 patients. We collected clinical symptoms and the vascular risk factors of each patient as shown in Table 1. The degree of carotid stenosis was evaluated by duplex sonography using ECST criteria [12]. Inclusion criteria were severe symptomatic carotid stenosis ≥ 70 %, clinical signs and symptoms related to the carotid stenosis within the previous 180 days, age > 50 years, a modified ranking scale from 0 to 3 [41] and written consent to participate in the study. All patients were randomly selected for either the CAS or the CEA procedure as part of this stent-protected percutaneous angioplasty versus carotid endarterectomy study (SPACE) [35].

Patients underwent testing and CEA or CAS at the University Medical Centre Kiel, Germany. The protocol was approved by the local ethical committee at Kiel University and all of the patients gave their informed consent prior to participating.

One of the first steps was to assess hand preference using Annetts Test of handedness [1]. In each group one left-handed patient was detected. For further comparison of the two groups we applied the "Mehrfach-Wahl-Wortschatz-Test" (MWT-B), a vocabulary test that correlates significantly with premorbid intelligence [27].

Procedure

Prior to treatment all patients received low molecular-weight heparin (enoxaparin) subcutaneously, 100 mg aspirin and 75 mg Clopidogrel as tablets once a day for at least 3 days. Cognitive functions were evaluated at baseline (48–72 hours before CEA or PTA), and two times in the follow-up period: 6 days after CEA or CAS and 30 days after CEA or CAS. Blood samples for measurements of S100β protein were collected from the brachial vein at baseline (2 hours before the CEA or CAS) and 1 and 2 hours after final catheter placement in the CAS group as well as 1 and 2 hours after skin suture in the CEA group.

Table 1 Demographics, clinical symptoms and vascular risk factors in the percutaneous transluminal angioplasty and the carotid endarterectomy groups

	CAS (n = 21)	CEA (n = 24)	
Age	67.8 (6.5)	67.1 (7.7)	NS
Gender (female/male)	8/13	9/15	NS
Education, yrs	10.4 (2.0)	9.6 (1.2)	NS
Premorbid intelligence[1]	115.9 (14.3)	110.4 (14.9)	NS
Handedness (right/left)	20/1	23/1	NS
Clinical symptoms			
Side of treatment (right/left)	10/11	10/14	NS
TIA	14	12	NS
Stroke	7	12	NS
Motor/sensory/sensorimotor/ Amaurosis fugax/cognition	7/2/5/ 4/2	7/5/7/ 2/3	NS
NIHSS[2]	0.14 (0.5)	0.88 (1.8)	NS
Degree of ICA stenosis [%][3]	82.4 (7.5)	82.1 (9.7)	NS

[1] Premorbid intelligence was estimated using a German vocabulary test ("Mehrfach-Wahl-Wortschatz-Test", Lehr 1995)
[2] National Institutes of Health Stroke Scale
[3] Degree of carotid stenosis revealed by Doppler sonography using the ECST criteria [12]
Values are mean (SD) or number of patients

Neuropsychological evaluation

Signs and symptoms of depression were assessed using the Beck Depression Inventory (Beck 1961). Neuropsychological testing examined functions in the cognitive domains memory, attention, executive function and motor skills. Memory was assessed with Rey's Auditorial Verbal Learning Test (RAVLT) [28]. The number of words recalled after the first presentation of a 15-word list and the interference list were summed up to record a patient's short-term memory. The free recall after 20 minutes were used to assess long-term memory abilities. Parallel versions of the word list were used at random. For nonverbal memory we used Complex Figure Tests (CFT). The Rey-Osterrieth Figure and the Taylor Figure [28] were each applied in a pseudo-random balanced order before treatment and 30 days after treatment. Results of the immediate and 20-minute delayed recall were scored. To test attention, we applied the Paced Visual Serial Addition Test (PVSAT) [18] in which the subjects were instructed to add 32 randomised pairs of digits, i. e. each digit was added to the digit immediately preceding it. The numbers 1–9 were presented on a PC screen at the rate of one digit every two seconds. The percentage of correct additions was calculated. Additionally we applied the Trail-making Test parts A and B. In this test patients connect consecutive numbers as fast as possible (part A) and then alternate between number and letters on part B [28]. The time it took to carry out the test was measured. Moreover we applied a shortened version of the Stroop Test (Regard 1981). The patients were presented a sheet of paper on which the words "blue", "yellow", "green" and "red" were printed in incongruent ink colours. In the first run participants read out loud the colour of the ink, ignoring the name of the words. In the second run participants read the name of the words ignoring the ink colour [28]. We measured the total reading time under both conditions. Executive functions were tested at each visit with one-minute verbal fluency tests including two semantic and two phonemic categories [28]. The categories were pseudo-randomised each time, taking "male first names", "female first names", "animals", "countries", "professions" and "plants" for semantic categories and the first letters "M", "N", "L", "D", "K" and "B" for phonemic fluency. Categories and letters appeared in a pseudo-random balanced order during the visits. The sum of all runs was scored. For the Random Number Generation Task (RNGT), subjects were instructed to randomly generate a series of 100 numbers by continually choosing a digit 1–10. This was accompanied by a tone (1 Hz). The concept of randomness was explained using standard procedures [43]. The total time taken to generate 100 items was noted. The series of digits that was analysed by the Evans Random Number Generation Index is a first-order measure of randomness. This index varies between 0 and 1; the higher the Evans index, the less random the series. Furthermore, we calculated the total counting score. This index measures the tendency to count in ascending or descending series in steps of 1 and 2. Subjects with higher counting scores are unable to suppress a habitual counting tendency which reflects cognitive inflexibility [43]. Motor skills were assessed using the Purdue Pegboard Test [28]. Patients placed pegs into the appropriate slot with the preferred hand in the first run and the other hand in the second run. Each test lasted 30 seconds. In the Finger-tapping Task (FTT) patients were presented with a button box and had to use their index finger to press and release a button as fast as possible within a 10-second period. Two practice trails were given before the patients began 5 blocks of 10-second tapping using their dominant hand. In successive trials patients tapped first with the index finger of the non-dominant hand and then with both index fingers in an alternating fashion. Trials of each condition (dominant hand, non-dominant hand and alternate finger-tapping) were summed up.

S100β protein measurement

Serum S100β protein was analysed using a two-sided immunoradiometric assay kit (S100 electrochemiluminescence immunoassay, Roche Eclia 1010/2010 and modular analytics E170, Roche Diagnostics GmbH, D-68298 Mannheim)

Carotid angioplasty with stent placement (CAS)

The procedure was performed under local anaesthesia via percutaneous transfemoral or transbrachial access with a long sheath (SuperArrowflex 6 French, Arrow International, Reading, PA, USA). The sheath was advanced coaxially by catheter and guidewire into the common carotid artery. The sheath was flushed continuously with saline (1000 IU heparin per litre). After introduction of the sheath a maximum dose of 8000 IU heparin was administered intravenously to achieve an activated clotting time of 250–350 seconds. At the beginning of the procedure 0.1 mg atropine was given subcutaneously to prevent bradycardia. For stent placement fluoroscopy and the roadmap technique was used. After placing the sheath in the CCA the stenosis was passed with a micro-guidewire (Choice PT Extra Support 0.014 inch, Boston). Monorail systems were used for balloon dilatation and stent delivery. The stenosis was predilated when primary passage with the stent delivery system was not possible. Only Carotid Wall Stents (Boston Scientific Corp., Natick, MA, USA) were used. Available sizes were 5x30, 7x30 or 9x40 mm. The suitable size was estimated from angiography, depending on the vessel diameter and location of the stenosis. After stenting and angioplasty the final result was documented angiographically with two intra- and extracranial projections.

Carotid endarterectomy (CEA)

All operations were performed under general anesthesia by two surgeons. An incision was made along the anterior border of the sternocleidomastoid muscle and dissection was carried through the platysma and deep into the jugular vein. The branches of the internal jugular vein crossing the carotid artery were ligated and divided and vessel loops were gently placed around the common carotid and external carotid arteries. Before carotid clamping, 4000 to 9000 units of heparin were administered, and the patient's systolic blood pressure was elevated to approximately 150 to 170 mm Hg. An arteriotomy incision was made on the common carotid artery extending into the bulbous portion of the internal carotid artery. The incision extended superiorly until it was above all areas of ulceration. The endarterectomy was performed in a standardized manner with the use of electroencephalography. When electroencephalographic changes indicated possible cerebral ischemia (prolongation of frequency or reduction of amplitude) while the carotid arteries were being clamped despite induced hypertension, a Pruitt-Inahara shunt was placed. After removal of the carotid plaque, the arteriotomy was closed with a patch (VascuGuard® Biovascular Inc., St. Paul, MN, U. S. A.). After declamping, final fluoroscopy was performed in every case. Depending on the amount of blood loss, protamine sulphate was given to partially neutralize the heparin.

Statistical analysis

Chi-square tests were performed to compare variables such as clinical symptoms in cross tables. Independent *t*-tests were performed to compare baseline characteristics. Using the Kolmogorov-Smirnov Goodness-of-fit Test we examined the normality of distribution of each of the pre-procedural neuropsychological test results. The results of the Stroop Test and the trials of RAVLT were not normally distributed. Square root transformation rendered these test results a normal distribution.

We adopted the conventional definition of neuropsychological deficit that has been used by previous studies examining cognitive changes after PTA, CEA and cardiac surgery [10, 39]. A cognitive change was assumed if the pre- to post-treatment difference in two or

more tasks assessing various cognitive domains exceeded more than one standard deviation. To answer the question as to how many patients cognitively declined, the standard deviation (SD) of each neuropsychological test of the pre-procedural assessment based on all patients was calculated. The decline should be detected in tests that assessed different cognitive domains as described in Tables 2 and 3. Additionally we separately summed up the number of patients who showed an improvement in neuropsychological performance for each treatment modality to assess various possible beneficial effects of CAS and CEA on cognitive functioning. In another step we calculated a standardized score by calculating a change score (pre-procedural test performance – post-procedural test performance) divided by the test specific pre-procedural SD for each patient. This pre-procedural SD was calculated on the basis of all patients of the study. These scores reflect the relative change in performance. If appropriate we changed the algebraic sign so that positive changes reflect an improvement and a negative algebraic sign indicates deterioration in test performance. Moreover we summed up standardized change scores of all tests and compared CAS and CEA patients in a one-way ANOVA of variance. This sum of all standardised change scores was also correlated with the S100β protein values at baseline, 1 and 2 hours after the procedure (Spearman correlation analysis). Finally we compared the S100β protein values of the patients that showed significant cognitive deterioration with the rest of the patients regardless of the treatment modality (ANOVA with repeated measurements) to determine if S100β protein is a biomarker that is able to predict cognitive decline in the follow-up.

Results

Demographics, clinical symptoms and vascular risk factors showed no significant differences between the CAS

Table 2 Data of the neuropsychological assessment before, 6 days and 30 days after treatment, grouped by cognitive function and tests. Values are mean (SD)

Cognitive function and tests	Procedure	Pre-procedure	After 6 days	After 30 days
Short Term Verbal Memory				
RAVLT	CAS	39.2 (7.4)	Not investigated	38.9 (8.5)
Sum of correct recalls of run 1 to 7	CEA	42.3 (8.0)		41.7 (8.3)
Long Term Verbal Memory				
RAVLT	CAS	12.8 (1.8)	Not investigated	13.0 (1.9)
Free recall after 30 min	CEA	12.8 (1.9)		13.1 (1.8)
Long Term Nonverbal Memory				
Complex Fig. Test,	CAS	12.8 (3.1)	Not investigated	15.0 (2.9)
Score of 20 min recall	CEA	13.0 (2.4)		14.3 (2.9)
Concentration				
PVSAT	CAS	63.8 (19.2)	70.8 (24.0)	76.6 (20.0)
Percentage correct	CEA	61.3 (25.4)	68.8 (22.0)	71.6 (20.6)
Visuomotor Tracking				
Trail-making Test A, s	CAS	48.3 (23.5)	53.0 (30.3)	47.8 (23.7)
	CEA	55.2 (22.1)	53.8 (23.5)	48.9 (18.8)
Trail-making Test B, s	CAS	122.7 (49.9)	111.2 (55.6)	115.4 (62.9)
	CEA	136.0 (67.7)	147.4 (72.6)	124.5 (64.6)
Response Selection				
Stroop reading time, s	CAS	11.7 (2.7)	13.5 (2.6)	15.1 (5.1)
	CEA	14.0 (7.7)	13.8 (3.8)	15.1 (8.0)
Stroop reading time interference	CAS	35.5 (9.8)	36.6 (12.0)	33.4 (10.6)
condition, s	CEA	37.4 (12.6)	37.1 (10.8)	34.4 (9.7)
Verbal Fluency				
Sum of semantic and phonematic	CAS	59.2 (15.1)	55.3 (16.2)	57.7 (16.2)
verbal fluency	CEA	58.3 (16.3)	58.6 (21.1)	60.8 (14.2)
Cognitive Flexibility				
Random number generation	CAS	97.9 (96.5)	100.6 (99.1)	81.7 (53.0)
Total counting score	CEA	101.7 (57.5)	94.8 (50.7)	74.1 (38.6)
Motor Tasks				
PP-Test dominant	CAS	10.7 (2.7)	11.3 (3.3)	11.4 (3.0)
30 s run	CEA	10.7 (3.4)	11.3 (3.1)	11.1 (3.2)
PP-Test non-dominant	CAS	9.9 (3.5)	11.6 (8.6)	10.3 (3.6)
30 s run	CEA	9.5 (2.9)	9.0 (3.0)	9.7 (3.4)
Finger-tapping	CAS	199.9 (23.8)	192.2 (34.2)	191.4 (33.0)
dominant, sum of 4 runs	CEA	193.7 (24.1)	189.5 (26.4)	188.3 (27.9)
Finger-tapping non-	CAS	175.6 (21.1)	174.7 (22.3)	173.9 (23.7)
dominant, sum of 4 runs	CEA	166.9 (24.6)	167.5 (25.6)	163.6 (27.7)
Altern. finger-tapping,	CAS	204.7 (39.3)	193.9 (51.2)	187.3 (45.3)
sum of 4 runs	CEA	191.6 (45.8)	194.6 (60.4)	183.9 (68.2)
Depression				
Beck Depression	CAS	4.0 (3.8)	Not investigated	4.3 (4.2)
Inventory, sum score	CEA	6.2 (6.1)		7.2 (9.1)

RAVLT Rey's Auditorial Verbal Learning Test; *TMT* Trail-making Test; *PP* Test Purdue Pegboard Test

Table 3 Standardized Change Scores 6 and 30 days after treatment grouped by cognitive functions. Positive scores indicate improvement and negative scores indicate deterioration

	6 days after treatment			30 days after treatment		
Cognitive Function and Test	CAS	CEA	P (2-tailed)	CAS	CEA	P (2-tailed)
Short Term Verbal Memory						
RAVLT 1st run	na	na		–0.04	–0.06	0.92
Long Term Verbal Memory						
RAVLT Recall after 30 Min.	na	na		0.20	0.17	0.94
Long Term Nonverbal Memory						
Complex Figure Test Recall after 20 min	na	na		0.84	0.46	0.21
Concentration						
PVSAT	0.43	0.19	0.23	0.21	0.24	0.90
Visuomotor Tracking						
TMT A	–0.16	–0.24	0.76	–0.14	0.03	0.60
TMT B	–0.14	–0.42	0.62	0.10	–0.12	0.51
Response Selection and Attention						
Stroop Reading time	–0.22	–0.19	0.57	–0.28	0.04	0.20
Stroop reading time interference	–0.24	–0.26	0.93	–0.06	0.05	0.66
Executive functions						
Verbal Fluency						
Semantic Verbal Fluency	0.02	–0.22	0.49	–0.09	–0.05	0.34
Phonematic Verbal Fluency	0.16	0.8	0.71	0.03	0.07	0.92
Cognitive Flexibility Random Number Generation						
Total Counting Score	0.21	0.36	0.52	–0.5	0.15	0.28
Motor Tasks						
PP Test, Dom. Hand	0.14	0.11	0.90	0.17	0.14	0.89
PP Test, Non-dom. Hand	0.08	0.03	0.80	0.44	–0.25	0.21
FTT Dom. Hand	–0.36	–0.23	0.68	–0.32	–0.18	0.65
FTT Non-dom. Hand	–0.07	–0.14	0.79	–0.04	0.03	0.8
Alternating FTT	–0.40	–0.18	0.50	–0.25	0.07	0.29
Depression						
Beck Depression Inventory	na	na		–0.01	–0.02	0.96

RAVLT Rey's Auditorial Verbal Learning Test; *TMT* Trail-Making-Test; *PP Test* Purdue Pegboard Test; *FT* Finger Tapping Test

and the CAE groups (Table 1). One patient suffered a minor stroke after CEA, one patient suffered from a superficial facial nerve injury after CEA and one patient developed an aneurysm of the femoral artery after CAS. The mean duration of surgery was 84.1 min (SD 20.9 min) and the mean duration of cross-clamp was 19.5 min (SD 6.1 min). A contralateral carotid artery stenosis was found in 7 patients who underwent CAS (mean degree of the stenosis was 60 %, SD 10 %) and in 10 patients who underwent CEA (mean degree of the stenosis 73 %, SD 19 %).

One patient of the CAS group and two patients of the CEA group did not take part in the first follow-up consultation. For technical reasons we were not able to assess the finger-tapping test in 3 patients of the CAS and 4 patients in the CEA group at the first and third consultations and in 4 patients on the second visit. The random number generation task could not be performed for technical reasons in one patient of the CAS group and in one patient of the CEA group on day 6. One patient of the CEA group was not able to reproduce and recall the CFT before or after surgery and one patient of the CAS group refused to take the PVSAT at visit 1. In 17 patients of the CAS group and in 20 patients of the CEA group blood samples were collected.

A comparison of the test results of the pre-procedural assessment demonstrated no significant differences between the CEA and the CAS groups.

Neuropsychological changes 6 days after the treatment compared to baseline performance (Table 2)

In two or more tests of the various cognitive domains four patients of the CAS group (21 %) and four patients of the CEA group (19 %) showed cognitive deterioration (Fig. 1A). In contrast, 3 patients in the CAS (14 %) group

and 6 patients in the CEA group (25 %) improved in 2 or more tasks in different cognitive domains. However, none of these comparisons reached statistical significance. Comparison of the standardized change scores showed no significant differences between the CEA and the CSA groups. A one-way ANOVA demonstrated no significant difference between the CAS and the CEA groups in the sum of all standardized change scores.

Neuropsychological changes 30 days after the treatment compared to baseline performance (Table 2)

Using the same tests that had been applied 6 days after treatment, the analysis of the neuropsychological results 30 days after treatment identified 2 patients in the CAS group (10 %) and 4 patients of the CEA group (17 %) who met the criteria for cognitive decline. Including the memory tests, which were conducted before the intervention and 30 days after treatment, 5 patients in the CAS group (24 %) and 6 patients in the CEA group (25 %) demonstrated impairments (Fig. 1B). Five patients of the CAS group (24 %) and 7 patients of the CEA group (29 %) showed improved test performance in two or more tasks assessing various cognitive abilities. The standardized change scores are shown in Table 3. We found no significant differences in standardized change score between the CAS and CEA groups (Table 3). Furthermore, the analysis of the sum of the standardized change scores showed no significant group differences.

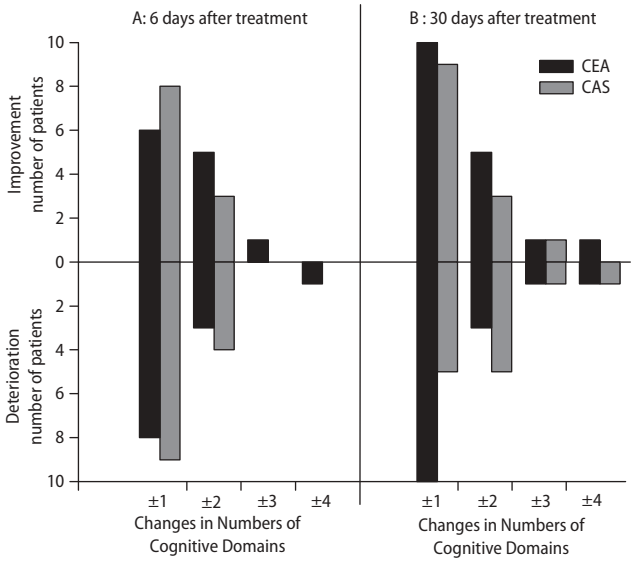

Fig. 1 The number of patients that showed changes in cognitive performance from baseline (pre-procedural assessment) are presented: 6 days after the treatment (**A**) and 30 days (**B**) after the procedure (filled bars for CEA, grey bars for CAS). Bars represent the number of patients who showed a change of more than one SD from baseline in one (± 1) to four (± 4) cognitive functions. Ascending bars represent the number of patients who showed improved performance; descending bars represent the number of patients who demonstrated deterioration in task performance. Note that the test battery 30 days after the treatment (**B**) included memory tasks that were not part of the test battery of day 6 after the treatment (**A**). Therefore a comparison between bars in **A** and **B** is not reasonable

Evaluation of the S100β protein values

Fig. 2 shows the time course of the S100β protein values in both groups. A one-way ANOVA with the within-subject-factor-S100β-protein value (pre-treatment, 1 and 2 h after treatment) and the between-subjects-effect group (CAS and CEA) showed no significant effect for factor and group. A correlative analysis between the change in the S100β values and the standardized change score of day 6 and day 30 from baseline did not reveal any significant correlation. This lack of correlation was found in the CAS group, the CEA group and a combination of both. A comparison of the S100β protein values between the patients who developed cognitive impairment, irrespective of the therapeutic procedure (CAS or CEA), demonstrated no higher S100β values 2 hours after the treatment.

Discussion

The principal aim of our investigation was to find significant differences comparing the neuropsychological changes after CAS and CEA. We did not find significant differences compared to baseline between CAS and CEA regarding neuropsychological deterioration 6 days and 30 days after the treatment. Six days after treatment 21 % of the patients in the CAS group compared to 19 % of patients in the CEA group showed deterioration in two or more tests assessing various cognitive domains. Thirty days after the procedure we found a cognitive decline in

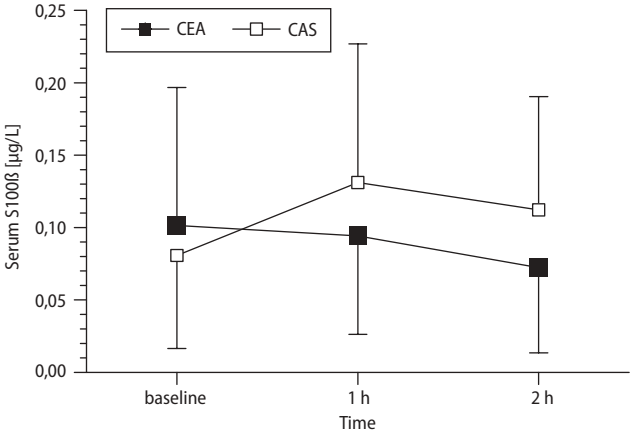

Fig. 2 Graph showing S100ß values (mean ± 1 SD) for the CEA (closed squares) and the CAS groups (open squares) at baseline, 1 and 2 hours after the procedure

24% of the CAS patients and 25% of the CEA patients. These results are in agreement with the report of Crawley et al. using the same evaluation criteria and demonstrating cognitive deterioration in a comparable proportion of patients 6 weeks and 6 months after PTA or CEA [10]. Our study extends this observation by two findings: First, we demonstrate that in the early course of treatment (assessment 6 days after the procedure) CAS and CEA did not have different outcomes in the cognitive domain. Second, we tested the cognitive sequelae after CAS, whereas Crawley investigated the effect of PTA on the cognitive domain. Despite the absence of significant differences between the CAE and the CAS groups in the cognitive domain, our limited number of patients and our statistical design is not suitable for proving equality between both treatment modalities.

A series of studies documented a significantly higher proportion of microemboli after CAS as compared to CEA [5, 9, 10, 26, 32, 37, 40]. In addition, DWI lesions on MRI were significantly more frequent after CAS compared to CEA [19, 23, 24, 32, 36, 37, 40]. One limitation of our study is the lack of post-procedural MRI data and the lack of periprocedural microembolic counts by Doppler sonography. But it has been hypothesised that structural changes after CAS are clinically silent because they are located in non-eloquent brain areas causing no or only a transient neurologic deficit [3]. Neuropsychological assessment may discover discrete abnormalities after CAS, but we were not able to show this hypothesised cognitive impairment. A recent study by Haupt et al. demonstrated the reversibility of DWI lesions after CAS [19]. Possibly these DWI lesions do not correspond to vascular lesions and, as a consequence, the lesions may not be responsible for a neurological and a neuropsychological deficit. Although most researchers favour the hypothesis that microemboli are the cause of neurological and neuropsychological signs and symptoms after CAS [8, 15, 19, 30], our results argue against this hypothesis. There may be other causes such as hemodynamic or metabolic stressors occurring after both CAS and CEA that account for a mild cognitive decline. This interpretation is in line with a recent study that showed neuropsychological dysfunction in the absence of structural evidence for cerebral ischemia after uncomplicated CEA [22]. Our results also lead to the conclusion that general anesthesia associated with CEA does not explain the cognitive impairment because the CAS group suffered from cognitive impairments to the same extent.

There are no clear guidelines for judging significant improvement in performance after successful revascularization of a carotid stenosis. We applied the same criteria to the evaluation of improvement as for deterioration in test performance, namely a change of more than one SD compared to baseline performance in 2 or more tests assessing different cognitive functions. Of the patients, 14% showed an improvement in cognitive functioning 6 days after CAS and 25% of the patients improved after CEA. The test results after day 30 showed an improvement of 24% and 29%, respectively. Both comparisons were not significantly different. Only a minority of studies in this field showed improved cognitive functions after successful carotid revascularization [4, 7]. In rare cases a critical ipsilateral cerebral hypoperfusion might cause cognitive dysfunction which can be reversed after successful carotid revascularization. In our study it is more likely that the improvement in cognitive function is the result of a practice effect and not the direct effect of recovered cerebral circulation.

We measured the S100β protein soon after the intervention and found no significant differences between the CAS and the CAE groups. The lack of correlation between S100β values and cognitive impairments after CEA was also found by other authors [11, 14, 17, 33, 38], whereas Connolly et al. described a relation between elevated S100β values and cognitive deterioration after CEA [8]. These divergent results might be the consequence of S100β measurements at different points of time after the procedure, different neuropsychological test batteries and different treatment modalities. Nevertheless, protein S100β has many desirable characteristics of a biochemical marker (low molecular size, high organ specificity and a high degree of solubility [6, 16, 25, 34, 42]) and patients with cardiac arrest without detectable brain damage showed increased S100β values [6]. The sensitivity and specificity of S100β in detecting small brain lesions is not known and therefore our results are preliminary at this point.

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