Vascular Specialist International
Vol. 33, No. 4, December 2017
pISSN 2288-7970 • eISSN 2288-7989
Check for updates

Original Article

Neuropsychological Outcome One Year after Carotid Revascularization: A before-and-after Study

Laura Casas-Hernanz[1,2], Maite Garolera[3], Dolors Badenes[1], Salvador Quintana[4], Susana Millán[5], Noemi Calzado[1], Jorge de Francisco[1], Josep Royo[6], and Miquel Aguilar[1]

[1]Servei de Neurologia, Hospital Universitari Mútua Terrassa, Barcelona, [2]Departament de Psiquiatria i de Medicina Legal, Universitat Autònoma de Barcelona, Barcelona, [3]Neuropsychological Unit, Hospital of Terrassa-Consorci Sanitari de Terrassa, Barcelona, [4]Servei de Medicina Intensiva, Hospital Universitari Mútua Terrassa, Barcelona, [5]Unitat d'Urgències, Hospital Plató, Barcelona, [6]Servei de Cirurgia Vascular, Hospital Universitari Mútua Terrassa, Barcelona, Spain

Purpose: The aim of our study was to determine the clinical profile of patients considered cognitive 'responders' to surgery in order to establish clinical variables associated with a favorable cognitive performance.

Materials and Methods: A total of 70 patients were included in the study. A well-validated, comprehensive standardized neurocognitive battery of tests of about 2 hours was administered. Patients were examined twice, 1-week before surgery and 1-year postoperatively. The criterion to be included in the 'responder' group was the following: to obtain a positive difference between post-revascularization and pre-revascularization neuropsychological assessment ≥1 standard deviation in ≥2 tests.

Results: Twenty-seven patients (38.6%) were cognitive responders to treatment. In bivariate analysis between responders and non-responders, presence of atrophy (P=0.003), small vessels (P=0.577), symptoms (P=0.046), and age (P=0.030) were the factors statistically significant. When comparing cognitive performance before and after carotid revascularization, significant differences were observed in semantic fluency with a lower performance after 12 months (P=0.004, d=0.29), and in the Language index (Repeatable Battery for the Assessment of Neuropsychological Status) (P=0.005, d=0.34).

Conclusion: Patients without neurological symptoms, of a younger age and without atrophy and white matter small vessel lesions are better cognitive responders 1-year after carotid revascularization.

Key Words: Endarterectomy, Carotid stenosis, Angioplasty, Cognition, Neuropsychological tests

Received September 2, 2017
Revised November 7, 2017
Accepted November 24, 2017

Corresponding author: Laura Casas-Hernanz
Servei de Neurologia, Hospital Universitari Mútua Terrassa, Plaça del Dr. Robert 5, Terrassa 08221, Barcelona, Spain
Tel: 34-669867621
Fax: 34-937860300
E-mail: lauracasass@gmail.com
Conflict of interest: None.

Vasc Spec Int 2017;33(4):146-155 • https://doi.org/10.5758/vsi.2017.33.4.146

INTRODUCTION

Stroke is one of the most frequent causes of neuronal damage since it affects about 16 million people per year and has an accumulated prevalence of 60 million cases [1]. Stroke recurrence is about 33% in the first 5 years after the first stroke [2]. Stenosis of the extracranial carotid artery is one of the most frequent causes of ischemic cerebrovascular strokes. In fact, subjects with severe atherosclerosis of both carotid arteries have an increased risk of developing subsequent strokes [3], and subsequent brain hypoperfusion can lead to cerebral atrophy, dementia or cognitive impairment [4]. Several studies evaluating cognition in subjects with carotid artery stenosis suggest a relationship between brain hypoperfusion and cognitive impairment [5].

On the other hand, it is known that transient cerebral ischemia associated with carotid artery stenosis can lead to white matter ischemic lesions, which in turn lead to an increased risk of cognitive impairment [6,7]. Interestingly, some studies have described the presence of cognitive impairment independently of the presence of white matter brain lesions, suggesting that carotid artery stenosis is causing cognitive impairment by itself and is thus a variable leading to cognitive impairment independent of other causative factors [8,9].

Carotid revascularization including carotid endarterectomy (CEA) and carotid artery stenting (CAS) is routinely performed in subjects with carotid artery stenosis to prevent further strokes [10]. The hypothesis is that, in addition to preventing further strokes, carotid revascularization could improve pre-surgical cognitive status owing to the restoration of normal brain blood perfusion. However, the conclusions of different studies are unclear. Some studies reported that restoration of normal brain blood perfusion improves cognitive performance [11] whereas others did not find such improvement. An explanation for the lack of post-surgical cognitive improvement could lie in intra-operatory complications, such as global brain ischemia after clamping the carotid artery [12].

Other studies have tried to identify whether carotid revascularization can improve certain cognitive functions depending on the side of the body operated on; this is based on the idea that brain blood perfusion would improve ipsilateral cognitive functions. However, the results of studies searching for differences in cognitive profile according to the operated side are not consistent [13].

Taking all this into account, it appears that different factors exist that could play a factor in the resulting cognitive state following carotid revascularization. It would be interesting to be able to recognize those variables that could identify 'responders' and 'non-responders' on a cognitive level, and thereby optimize treatment.

The aim of our study was to determine the clinical profile of patients considered cognitive 'responders' to surgery in order to establish clinical variables associated with a favourable cognitive performance. A secondary objective was to evaluate via a battery of neuropsychological tests, the cognitive profile of patients with carotid stenosis before and after one year of revascularization. Also, the potential influence of neurological symptoms (asymptomatic vs. symptomatic) and the side of carotid revascularization (right internal carotid artery [RICA] vs. left internal carotid artery [LICA]) on cognitive outcome was evaluated. To this purposes, a prospective cohort study was designed in which patients with carotid stenosis treated surgically completed a neurocognitive test battery before and after one year of revascularization.

MATERIALS AND METHODS

1) Subjects

This was a prospective observational study with sequential inclusion of subjects. Seventy patients who underwent carotid revascularization were included between July 2005 and December 2009 from the Vascular and Endovascular Unit of the Hospital Universitari Mútua Terrassa. The study was approved by the Review Board and Ethics Committee of Mútua Terrassa University Hospital (study no. EO/0806). All participants signed the informed consent.

Patients with carotid stenosis eligible for carotid revascularization were included in the trial. The patients were assessed by Doppler ultrasound of the carotid bifurcation, and magnetic resonance angiography of the supra-aortic branches. All patients had an angiography prior to surgery. The degree of stenosis was defined as mild (0%-50%), moderate (50%-70%), and severe (more than 70%) according to criteria of the European Carotid Surgery Trial. All patients with no contraindications underwent a brain magnetic resonance imaging (MRI) scan (Symphony 1.5T; Siemens, Erlangen, Germany) with the following sequences: T1, T2, FLAIR and diffusion. In subjects for whom MRI was not possible (pacemaker or claustrophobia) a computed tomography (CT) brain scan (Somatom Sensation 16; Siemens) was performed. MRI/CT images were visually evaluated by both a neurologist and a neuroradiologist with experience in neuroimaging of cerebrovascular disease. Each patient was scored with a qualitative scale as follows: no atrophy, presence of cortical atrophy, subcortical atrophy, or both. According to the presence of small cerebral infarcts, the patients were stratified into the following groups: no infarcts, leukoaraiosis, subcortical white matter small infarcts, or both. With regard to large cerebral infarcts, patients were classified as having cortical or subcortical large strokes, both or no large infarcts at all. Patients were also classified as having a stroke on the basis of the presence of a relevant neurologic deficit during more than 24 hours, a transient ischemic attack (TIA) during less than 24 hours, as well as non-hemispheric symptoms (dizzy spells, vertigo or other symptoms typical of vertebral-basilar transient ischemia) or no symptoms at all.

The exclusion criteria as follows: severe aphasia or dementia (Mini-Mental State Examination [MMSE] ≤20), severe non-ischemic sensory deficits (severely impaired vision

https://doi.org/10.5758/vsi.2017.33.4.146

or hearing), and non-ischemic neurologic or psychiatric diseases that could interfere in cognitive assessment according to Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) [14].

Patients were examined twice at the outpatient clinics of the hospital, 1-week before surgery and 1-year postoperatively. At the first assessment, subjects were asked about their level of education, medical and psychiatric history and alcohol and tobacco use. A subject was classified as a smoker if she/he was a current cigarette smoker or quit cigarette smoking during the year before the first assessment. Subjects were specifically questioned about their medical history of other pathologies, such as myocardial infarction or coronary artery surgery and vascular risk factors, risk factors, which are associated with a greater probabiliy of suffering vascular disease. In our study we took into account hypertension, hyperlipidemia, diabetes mellitus and smoking.

2) Study procedures

① Neuropsychological and functional assessment

A well-validated, comprehensive standardized neurocognitive battery of tests of about 2 hours was administered. The battery of tests included the MMSE as a measure of global cognitive function, and tests evaluating the different cognitive domains. The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) is recognized as a useful tool to rapidly screen neuropsychological status and to help make a decision to perform CEA in terms of premorbid cognitive status [15]. This test assesses five domains of cognitive function: Immediate Memory, Visuospatial/constructional, Language, Attention, and Delayed Memory. Scoring has been well standardized in age groups with a mean score of 100 and standard deviation (SD) of 15 points. Attention was assessed by a forwards digit span (list of numbers that a person can repeat in correct order immediately after presentation) and Trail Making Test (TMT)-A, which consists in connecting a set of numbers in the correct order. We used Grooved Pegboard for manual dexterity and bimanual coordination and Ideomotor Praxia to assess the ability to carry out common tasks on command. Working memory was assessed by the Backward Digit Span (list of numbers that a person can recall in reverse of the presented order). Language tests included the Boston Naming Test for denomination (name the pictures), and for

Table 1. Description of the neurocognitive test battery

Test	Neuropsychological variable	Cognitive domain
MMSE	MMSE total score	Immediate and delayed memory, attention, language and visuospatial skills
RBANS	Immediate memory index Visuospatial index Language index Attention index Delayed memory index	Immediate and delayed memory, attention, language and visuospatial skills
Corsi block	Total blocks forwards Total blocks backwards	Attention and visual working memory
Grooved Pegboard Test	Right hand (time) Left hand (time)	Psychomotor speed
Boston Naming Test	Total score	Language (denomination)
Token Test	Total score	Language (auditory comprehension)
Ideomotor apraxia	Praxis right hand Praxis left hand	Praxia
COWAT	Total score (F+A+S)	Executive functioning (fonemic fluency)
Semantic fluency		Executive functioning (semantic fluency)
TMT	TMT-A time TMT-B time	Psychomotor speed and executive functioning
Stroop test	Stroop inhibition subtest	Executive functioning (susceptibility to interference)
Tower of London	Total correct score	Executive functioning (planning)

MMSE, Mini-Mental State Examination; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; COWAT, controlled oral word association test; TMT, Trail Making Test.

comprehension the Token test. Executive functions were evaluated using the TMT-B, which consists of connecting a set of letters and numbers in the correct order. The Stroop Color and Word Test was used to evaluate the ability to inhibit automatic cognitive processes. Subjects must name the ink color instead of the printed color. In addition, other tests were assessed, such as: Category Verbal Fluency (subjects have to say as many animals as possible), Phonological Verbal Fluency (subjects have to say as many words as possible beginning with letters F, A, S), and the Tower of London in order to study deficits in planning. The test consists of 2 boards with beads and 3 colored disks. The examiner uses the disks and the boards to present the examinee with problem-solving tasks. The cognitive domains that were evaluated and the variables derived from each test are detailed in Table 1. Neuropsychological tests were administered in a quiet environment in the hospital. The Spanish normative data on score adjustment for age and education, and the normality cutoff scores (95% of the lower tolerance limit of the normal population distribution) were followed for each of the tests [16].

② Vascular assessment

Patients were considered candidates for carotid revascularization, CEA or CAS procedures, after being individually evaluated on regular criteria in an expert committee composed of neuroradiologists, vascular surgeons and neurologists. Performing CEA was reasonable and appropriate for asymptomatic patients with carotid stenosis ≥70% at low risk for surgery and symptomatic patients with 50% to 70% stenosis at low risk for surgery. On the other hand, CAS was reasonable and appropriate for symptomatic patients with carotid stenosis ≥70% at high risk for surgery. The criteria followed for considering a patient as either CEA or CAS candidate were the following: medical situation of the patient and medical comorbidity. The presence of fatty components and/or thrombus within the probable carotid plaque, in addition to the presence of severe carotid tortuosity or calcification, were considered as strong criteria to support CEA [17]. Both types of procedures were performed by highly experienced vascular surgeons. The patients were continuously monitored during the procedure by transcranial Doppler and by direct neurological assessment while they were awake.

3) Statistical analysis

Descriptive analysis was conducted. Continuous variables were described with mean and standard deviation, and categorical variables with frequencies and percentages. To assess the change between neurocognitive battery tests before and after treatment, Student's t-test for paired data were performed. This analysis was also used in different subgroups depending of the presence or absence of symptoms and carotid revascularization side. Additionally, we calculated the effect size (d) to measure the magnitude of the differences found [18]. The following cut-off scores were applied: 1.10 to <1.45, very large effect; 0.75 to <1.10, large effect; 0.40 to <0.75, medium effect; 0.15 to <0.40, small effect.

According to pre- and post-surgery cognitive performance, the sample was divided into responders and non-responders. The criterion to be included in the "responder" group was the following: to obtain a positive difference between post-revascularization and pre-revascularization neuropsychological assessment, ≥1 SD in ≥2 tests according to the protocol previously reported [19]. Pre- and post-surgery comparison of neuropsychological battery test in responders and non-responders groups were performed using Student's t-test for paired data.

In order to assess what factors are related with responsiveness to treatment, a bivariate analysis was performed comparing age, gender, comorbidity variables, presence of symptoms, carotid revascularization side and MMSE between the 2 groups. Categorical variables were compared with the chi-square test or the Fisher's exact test, and continuous variables with the Student's t-test for independent samples. Those variables related with response to carotid surgery in the bivariate analysis with P-value <0.1 were entered into a binary logistic regression model to determine the best predictor model of response to treatment.

In all analysis P-value less than 0.05 were considered as statistically significant. Analysis were performed with IBM SPSS Stastistic ver. 19.0 software (IBM Co., Armonk, NY, USA).

RESULTS

From the initial 105 recruited subjects, 6 did not agree to participate in the study and 6 were excluded because of severe global aphasia. From the initial 93 patients included with the pre-surgery cognitive assessment after a year, twenty-three patients could not be evaluated for different reasons (9.9% did not comply with the follow-up, 5.4% suffered severe strokes (not periprocedural, strokes during the 12 months follow-up) that hindered their neuropsychological assessment, 3.2% died and 2.2% were not surgically treated). A total of 70 patients were included in the study. The study population was primarily male (77.1%) with a mean age of 72 years. The mean preprocedural degree of stenosis in our cohort was classified as severe in 54.3% for RICA and 51.4% for LICA. Ten patients (14.3%) had un-

https://doi.org/10.5758/vsi.2017.33.4.146

dergone revascularization on contralateral carotid artery previously, and 4 patients (5.7%) presented a MMSE <26 before revascularization. Fifty-three patients underwent the CEA procedure and 17 underwent CAS. No significant differences in demographic factors or neuropsychological profile were observed between patients undergoing CEA or CAS. The mean (SD) time of ischemia was 8.5 (2.5) minutes. Saphenous vein was used in 80% of cases for closure and Dacron in the remaining 20% (for patients with ischemia of lower limbs or severe venous insufficiency). Perioperative complications occurred in 3 cases (hematoma in 1, TIA in 1, and acute pulmonary edema in 1) but all patients recovered. During the 12 months follow-up period, no patients experienced ocular transient ischemic attack, hemipsheric TIA, or stroke. The characteristics of the study population are summarized in Table 2.

Table 2. Description of the study population

Variable	Patient (n=70)
Age (y)	72.17 (9.15)
Sex	
Male	54 (77.1)
Female	16 (22.9)
Educational level	6.20 (4.5)
Right-handedness	67 (95.7)
MMSE	26.39 (3.52)
Neurological symptoms	
Asymptomatic[a]	31 (44.3)
Symtomatic[b]	39 (55.7)
Side of intervention	
RICA	37 (52.9)
LICA	33 (47.1)
RICA stenosis	
Mild	1 (2.7)
Moderate	5 (13.5)
Severe	31 (83.8)
LICA stenosis	
Mild	2 (6.1)
Moderate	1 (3.0)
Severe	30 (90.9)
RICA contraltural stenosis	
Mild	20 (54.1)
Moderate	11 (29.7)
Severe	6 (16.2)
LICA contraltural stenosis	
Mild	16 (48.5)
Moderate	10 (30.3)
Severe	7 (21.2)

Values are presented as number (%). Mild stenosis severity (0%-50%), moderate stenosis severity (50%-70%), severe stenosis severity (+70%).
MMSE, Mini-Mental State Examination; RICA, right internal carotid artery; LICA, left internal carotid artery.
[a]No hemispheric symptoms or no symptoms at all; [b]Transient ischemic attack or stroke.

Neuroimaging results revealed that 47.6% of patients had no atrophy, 28.6% showed cortical atrophy, 4.8% subcortical atrophy, and 19% cortical-subcortical atrophy. Additionally, 14.3% presented cortical lesions, 15.9% subcortical lesions, and 9.5% cortical-subcortical lesions. Periventricular small vessel lesions were found in 17.5% of patients, white matter lesions in 7.9% of patients, and 30.2% presented lesions in both areas. Forty-four percent of patients were free of small vessel lesions.

Twenty-seven patients (39%) were classified as cognitive responders to treatment (having improved over the SD in at least 2 tests). The Token Test, Grooved Pegboard Test, Ideomotor Apraxia and the Attention and Language RBANS indexes revealed clear differences between the 2 groups, with responders performing better in these tests (Table 3).

In bivariate analysis between responders and not responders, presence of atrophy (P=0.003), small vessels (P=0.577), symptoms (P=0.046), and age (P=0.030) were the factors statistically significant (Table 4). When we developed a logistic regression model including all the variables found to be significantly associated with response only the presence of atrophy remains as independent factor in the multivariate analysis (odds ratio, 4.24; 95% confidence interval, 1.41-12.76; P=0.010), probably due to sample size. There were no significant differences in the distribution of vascular risk factors between the groups of responders and non-responders at baseline. After 1-year, the distribution of vascular risk factors had not changed.

The cognitive performance of patients before (T0) and after 12 months (T1) of carotid revascularization is summarized in Table 5. Neuropsychological assessment revealed that patients with carotid stenosis achieved a lower basal performance in attention, phonetic fluency and bimanual coordination when they were compared to those of norm-groups coinciding with age and education. When comparing cognitive performance before and after carotid revascularization, significant differences were observed in semantic fluency with a lower performance after 12 months (P=0.004, d=0.29), and in the Language index (RBANS) (P=0.005, d=0.34). Both were significantly poorer 1-year after carotid revascularization. No other significant differences were observed.

When patients were divided according to the presence of neurological symptoms, the symptomatic group showed reductions in Language scores, measured by RBANS Lan-

Table 3. Comparison of responders and non-responders before (T0) and after (T1) treatment in neurocognitive test battery

Test	Responder (n=27)			Non-responder (n=43)		
	T0	T1	P-value	T0	T1	P-value
MMSE	27.22 (3.35)	27.67 (2.88)	0.167	26.02 (3.43)	25.83 (4.04)	0.637
Immediate memory (RBANS)	80.63 (17.75)	82.74 (16.20)	0.385	70.57 (15.21)	69.88 (17.80)	0.747
Visuospatial (RBANS)	110.27 (14.64)	116.42 (14.34)	0.009	98.46 (18.92)	100.56 (21.36)	0.460
Language (RBANS)	93.00 (10.42)	94.00 (9.86)	0.487	90.74 (11.41)	83.02 (14.64)	0.001
Attention (RBANS)	72.08 (16.74)	75.35 (18.01)	0.065	65.18 (17.29)	63.68 (16.04)	0.396
Delayed memory (RBANS)	82.85 (22.94)	86.00 (20.30)	0.272	73.02 (17.28)	72.43 (18.46)	0.814
TMT-A	9.15 (3.80)	8.77 (3.38)	0.818	7.82 (3.41)	7.56 (3.29)	0.555
TMT-B	8.56 (3.07)	9.06 (2.92)	0.579	8.36 (2.97)	8.36 (2.20)	1
Token	8.00 (2.17)	9.31 (2.65)	0.005	8.20 (3.81)	7.74 (2.52)	0.453
Corsi blocks forwards	9.33 (2.60)	10.41 (3.06)	0.096	9.45 (2.78)	9.05 (2.67)	0.251
Corsi blocks backwards	9.67 (2.40)	10.33 (2.52)	0.209	10.38 (3.39)	9.70 (3.05)	0.114
Stroop C[a]	9.86 (3.66)	9.18 (2.77)	0.387	9.27 (4.18)	8.35 (3.80)	0.073
Boston Naming	6.15 (3.40)	6.70 (3.79)	0.304	5.15 (3.29)	4.95 (3.19)	0.526
Semantic fluency	15.48 (5.63)	16.00 (4.94)	0.484	14.95 (5.22)	12.14 (4.57)	0.000
Phonetic fluency	6.64 (2.85)	6.84 (2.85)	0.569	6.70 (3.34)	6.00 (3.57)	0.041
Praxis right	14.07 (2.68)	14.66 (1.73)	0.359	14.13 (2.60)	13.18 (3.61)	0.035
Praxis left	14.07 (2.68)	14.74 (1.34)	0.161	14.26 (2.55)	13.61 (3.30)	0.104
Grooved right	3.96 (4.34)	5.74 (4.65)	0.023	3.70 (4.20)	3.09 (4.18)	0.139
Grooved left	4.63 (4.19)	5.79 (4.65)	0.047	3.52 (4.01)	2.39 (3.11)	0.054
Tower of London[b]	9.04 (2.79)	9.00 (3.36)	0.956	9.92 (2.95)	8.77 (2.77)	0.095

Values are presented as number (%). MMSE and Semantic Fluency scores are raw scores. RBANS indexes are age- and education-corrected standard scores (mean: 100, standard deviation: 15). All other tests are presented as scaled scores.
MMSE, mini-mental state examination; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; TMT, Trail Making Test.
[a]Interference score, [b]total correct score.

Table 4. Bivariate analysis between responders and non-responders

Variable	Responder (n=27)	Non-responder (n=43)	P-value
Male	21 (77.8)	33(76.7)	0.920
Hypertension	18 (66.7)	36 (83.7)	0.098
Dyslipemia	16 (59.3)	24 (55.8)	0.777
Diabetes mellitus	9 (33.3)	17 (39.5)	0.601
Coronary artery disease	8 (29.6)	14 (32.6)	0.797
COPD	0 (0)	4 (9.3)	0.154
Smoking habit- smokers (absence)	6 (22.2)	9 (20.9)	0.636
Neurological symptoms (abcense)	16 (59.3)	15 (34.9)	0.046
Side of intervention (RICA)	14 (51.9)	23 (53.5)	0.894
Type of intervention (CEA)	21 (77.8)	32 (74.4)	0.750
Atrophy (absence)	16 (69.6)	14 (35)	0.003
Small vessels lesions (absence)	14 (60.9)	24 (60.0)	0.577
Leukoaraiosis (absence)	14 (60.9)	14 (35.0)	0.003
Age	68.89 (10.87)	74.23 (7.29)	0.030
Educational level	7.41 (5.13)	5.44 (4.02)	0.078
MMSE	27.22 (3.35)	25.86 (3.56)	0.116

Values are presented as number (%).
COPD, chronic obstructive pulmonary disease; RICA, right internal carotid artery; CEA, carotid endarterectomy; MMSE, Mini-Mental State Examination.

https://doi.org/10.5758/vsi.2017.33.4.146

Table 5. Comparison of patients before (T0) and after (T1) treatment in neurocognitive test battery

Test	T0	T1	P-value	d
MMSE	26.49 (3.43)	26.55 (3.72)	0.833	0.01
Immediate memory (RBANS)	74.51 (16.86)	74.91 (18.20)	0.800	−0.02
Visuospatial (RBANS)	103.18 (18.17)	106.91 (20.32)	0.055	−0.19
Language (RBANS)	91.62 (11.04)	87.32 (13.98)	0.005	0.34
Attention (RBANS)	68.17 (17.26)	68.73 (17.76)	0.654	−0.00
Delayed memory (RBANS)	76.87 (20.11)	77.74 (20.19)	0.645	−0.04
TMT-A	8.40 (3.61)	8.08 (3.36)	0.444	0.09
TMT-B	8.48 (2.98)	8.79 (2.65)	0.622	−0.10
Token	8.11 (3.19)	8.41 (2.67)	0.467	−0.10
Corsi blocks forwards	9.40 (2.69)	9.62 (2.89)	0.523	−0.07
Corsi blocks backwards	10.08 (3.01)	9.97 (2.83)	0.744	0.03
Stroop C[a]	9.54 (3.92)	8.73 (3.36)	0.070	0.22
Boston naming	5.55 (3.35)	5.66 (3.52)	0.715	−0.03
Semantic fluency	15.16 (5.35)	13.63 (5.05)	0.004	0.29
Phonetic fluency	6.67 (3.11)	6.36 (3.28)	0.208	0.09
Praxis right hand	14.11 (2.61)	13.80 (3.05)	0.414	0.10
Praxis left hand	14.18 (2.59)	14.08 (2.71)	0.728	0.03
Grooved right hand	3.83 (4.22)	4.41 (4.57)	0.196	−0.13
Grooved left hand	4.02 (4.08)	3.93 (4.19)	0.824	0.01
Tower of London[b]	9.49 (2.88)	8.88 (3.05)	0.218	0.20

Values are presented as number (%).
MMSE and Semantic fluency scores are raw scores. RBANS indexes are age- and education-corrected standard scores (mean [M]: 100, standard deviation [SD]: 15). All other tests are presented as scaled scores (M:10, SD: 3).
MMSE, Mini-Mental State Examination; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; TMT, Trail Making Test.
[a]Interference score, [b]Total correct score.

guage index (P=0.023) and in semantic fluency (P=0.014). The performance of the remaining tests remained otherwise stable (data not shown). For the asymptomatic group there were differences in visuospatial tasks as measured by the RBANS Visuospatial index (P=0.003) and in psychomotor speed as measured by the Grooved Pegboard test (P=0.041), where the asymptomatic group significantly improved after 12 months in both measures (data not shown).

When patients were divided according to the side of the carotid revascularization (RICA vs. LICA), the RICA group showed improvement in visuospatial tasks as measured by the RBANS Visuospatial index (P=0.018), but showed reductions in inhibition, measured by Stroop C (P=0.049). After 12 months, there were also some differences in the LICA group showing reductions in language scores, measured by RBANS Language index (P=0.005) and in semantic fluency (P=0.001). The performance of the remaining tests remained otherwise stable (data not shown).

DISCUSSION

Carotid revascularization is a surgical procedure widely used for the prevention of strokes. However, the effects of carotid revascularization on patient's cognition are unclear. The aim of our study was to evaluate cognition changes in patients one year after a carotid revascularization procedure using an extensive battery of standardized neuropsychological tests. We decided to use both therapeutic techniques, CEA and CAS, because the majority of the studies we reviewed did not show significant differences between the 2 procedures at a cognitive level [20]. Our findings indicate that only language showed a slight worsening 12 months after carotid revascularization, as observed in other studies [21,22]. Studies that found an improvement in attention, memory or executive functions [3,6,23] or a deterioration in global cognition or in specific subtests after intervention [24] were generally performed at an early post-surgery stage, only 1 to 3 months after carotid revascularization. Like many authors, we support the idea that longer term assessments of cognition changes can avoid the effect of confounding factors, such as test learning time, residual effect of anesthesia, and post-surgical mood alterations [21].

With regard to the factors associated with response, we found that the absence of atrophy and of white matter small vessel lesions was also predictive of good response to surgery after 12 months, supporting again the hypothesis that the brain ischemia associated with carotid stenosis causes subtle brain structural abnormalities [7]. Additionally, it can cause brain ischemic stress and increase the risk of cognitive impairment. However, analyses of response predictors revealed that only visuospatial capacity may be useful as part of an algorithm for the prediction of therapeutic outcome.

Since there is controversy over how previous strokes can influence the cognitive outcome of carotid revascularization, we included patients with previous strokes in our study. Our results suggest that the presence of previous neurological status did not affect the cognitive profile after carotid revascularization as reported by other groups [3,7,24,25]. We can hypothesize that the presence of microstrokes or the type of carotid plaque are more determinant of cognitive performance before carotid revascularization [26], or, as Bakker et al. [27] suggested, that carotid occlusion or contralateral flow circulation may be of more importance than TIA or stroke in the cognitive prognosis before carotid revascularization. However, other groups found differences in pre-CEA neurological status, though based on different selection criteria than our sample. Only one study compared the performance between 3 groups: subjects with carotid stenosis and TIA; subjects with stroke; and subjects with peripheral vascular disease, but they were not assessed until 9 months after the cerebrovascular event [28].

Patients without neurological symptoms showed an improvement in visuospatial functioning after carotid revascularization, which was not observed in symptomatic patients. In addition, patients with neurological symptoms revealed poorer results in language functions after the intervention. Our results are consistent with previous studies showing that symptomatic patients had poorer results in the left hemisphere tasks 3 months after CEA [29], supporting the hypothesis that symptomatic patients can suffer a higher ischemic stress during carotid revascularization and, as a result, are at higher risk of having cognitive deterioration. Our results also agreed with previous studies in which patients who responded to carotid revascularization showed improvement in language, attention and praxis scores.

Previous studies found that patients with left carotid stenosis show poorer basal performance in frontal cognitive tasks than patients with right carotid stenosis, as reported previously [30]. Similarly, results were poorer in LICA patients in comparison with RICA one year after carotid revascularization [24], with an increased deterioration observed showing that cerebrovascular ischemic episodes that involve the left carotid vascular territory are associated with greater risk of cognitive impairment and were more likely to have vascular dementia [30]. This results correspond to the fact that left hemisphere is the language dominant hemisphere in 98% of right-handed people, and it seems more vulnerable to vascular damage than the right hemisphere. When comparing within groups, LICA patients present poorer cognitive results after one year. The restoration of blood supply to the brain is hypothesized to be more beneficial to the functions mediated by the ipsilateral hemisphere on the side of the operation rather than on the contralateral side [24], and this may explain the RICA finding at T1.

One of the limitations of our study was the absence of neuroimaging data after carotid revascularization. Therefore, no follow-up on the changes in brain structure was possible. Additional limitations were that, of course, there was no control group and the sample size was limited. In future studies, it would be interesting to add other related variables (as depression status, apolipoprotein E gene study, or type of anesthesia) as these variables would improve the quality of our study. Expanding this study to other hospitals with a larger sample size would help to confirm our results.

In conclusion, the present results indicate that patients without neurological symptoms, of a younger age and without atrophy and white matter small vessel lesions are better cognitive responders one year after carotid revascularization. Our results argue in favor of incorporating cognitive testing in future clinical trials and in practices related to carotid artery stenosis, because this information may be useful when selecting patients who could benefit from carotid revascularization.

ACKNOWLEDGEMENTS

The authors are grateful to all of the participants who volunteered for this study. We also thank Unitat de Recerca de Neurologia team for their assistance with recruitment, and Marta Pulido, PhD, for editing the manuscript and editorial assistance.

This study was supported by a grant from the Fundación Mútua Madrileña.

https://doi.org/10.5758/vsi.2017.33.4.146

REFERENCES

1) Mukherjee D, Patil CG. Epidemiology and the global burden of stroke. World Neurosurg 2011;76(6 Suppl):S85-S90.
2) Elneihoum AM, Göransson M, Falke P, Janzon L. Three-year survival and recurrence after stroke in Malmö, Sweden: an analysis of stroke registry data. Stroke 1998;29:2114-2117.
3) Fearn SJ, Hutchinson S, Riding G, Hill-Wilson G, Wesnes K, McCollum CN. Carotid endarterectomy improves cognitive function in patients with exhausted cerebrovascular reserve. Eur J Vasc Endovasc Surg 2003;26:529-536.
4) Muller M, van der Graaf Y, Algra A, Hendrikse J, Mali WP, Geerlings MI; SMART Study Group. Carotid atherosclerosis and progression of brain atrophy: the SMART-MR study. Ann Neurol 2011;70:237-244.
5) Balestrini S, Perozzi C, Altamura C, Vernieri F, Luzzi S, Bartolini M, et al. Severe carotid stenosis and impaired cerebral hemodynamics can influence cognitive deterioration. Neurology 2013;80:2145-2150.
6) Bossema ER, Brand N, Moll FL, Ackerstaff RG, van Doornen LJ. Does carotid endarterectomy improve cognitive functioning? J Vasc Surg 2005;41:775-781.
7) Soinne L, Helenius J, Tikkala I, Saimanen E, Salonen O, Hietanen M, et al. The effect of severe carotid occlusive disease and its surgical treatment on cognitive functions of the brain. Brain Cogn 2009;69:353-359.
8) Mathiesen EB, Waterloo K, Joakimsen O, Bakke SJ, Jacobsen EA, Bønaa KH. Reduced neuropsychological test performance in asymptomatic carotid stenosis: The Tromsø study. Neurology 2004;62:695-701.
9) Romero JR, Beiser A, Seshadri S, Benjamin EJ, Polak JF, Vasan RS, et al. Carotid artery atherosclerosis, MRI indices of brain ischemia, aging, and cognitive impairment: the Framingham study. Stroke 2009;40:1590-1596.
10) Halliday A, Mansfield A, Marro J, Peto C, Peto R, Potter J, et al.; MRC Asymptomatic Carotid Surgery Trial (ACST) Collaborative Group. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. Lancet 2004;363:1491-1502.
11) Heyer EJ, Adams DC, Solomon RA, Todd GJ, Quest DO, McMahon DJ, et al. Neuropsychometric changes in patients after carotid endarterectomy. Stroke 1998;29:1110-1115.
12) Heyer EJ, Gold MI, Kirby EW, Zurica J, Mitchell E, Halazun HJ, et al. A study of cognitive dysfunction in patients having carotid endarterectomy performed with regional anesthesia. Anesth Analg 2008;107:636-642.
13) Bossema E, Brand N, Moll F, Ackerstaff R, van Doornen L. Testing the laterality hypothesis after left or right carotid endarterectomy: no ipsilateral effects on neuropsychological functioning. J Clin Exp Neuropsychol 2007;29:505-513.
14) American Psychiatric Association, Teton Data Systems (Firm); Task Force on DSM-IV. Diagnostic and statistical manual - text revision (DSM-IV-TRim, 2000). 4th ed. Washington, DC: American Psychiatric Association. 2000.
15) Randolph C, Tierney MC, Mohr E, Chase TN. The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS): preliminary clinical validity. J Clin Exp Neuropsychol 1998;20:310-319.
16) Peña-Casanova J, Blesa R, Aguilar M, Gramunt-Fombuena N, Gómez-Ansón B, Oliva R, et al. Spanish Multicenter Normative Studies (NEURONORMA project): methods and sample characteristics. Arch Clin Neuropsychol 2009;24:307-319.
17) Demarin V, Zavoreo I, Kes VB. Carotid artery disease and cognitive impairment. J Neurol Sci 2012;322:107-111.
18) Cohen J. Statistical power analysis for the behavioral sciences. New York: Psychology Press; 1988.
19) Lezak MD. Neuropsychological assessment. 3rd ed. New York, Oxford: Oxford University Press; 1995.
20) Paraskevas KI, Lazaridis C, Andrews CM, Veith FJ, Giannoukas AD. Comparison of cognitive function after carotid artery stenting versus carotid endarterectomy. Eur J Vasc Endovasc Surg 2014;47:221-231.
21) Feliziani FT, Polidori MC, De Rango P, Mangialasche F, Monastero R, Ercolani S, et al. Cognitive performance in elderly patients undergoing carotid endarterectomy or carotid artery stenting: a twelve-month follow-up study. Cerebrovasc Dis 2010;30:244-251.
22) Ogasawara K, Yamadate K, Kobayashi M, Endo H, Fukuda T, Yoshida K, et al. Postoperative cerebral hyperperfusion associated with impaired cognitive function in patients undergoing carotid endarterectomy. J Neurosurg 2005;102:38-44.
23) Fukunaga S, Okada Y, Inoue T. Neuropsychological changes in patients with carotid stenosis after carotid endarterectomy. Eur Neurol 2006;55:145-150.
24) Mononen H, Lepojärvi M, Kallanranta T. Early neuropsychological outcome after carotid endarterectomy. Eur Neurol 1990;30:328-333.
25) Heyer EJ, DeLapaz R, Halazun HJ, Rampersad A, Sciacca R, Zurica J, et al. Neuropsychological dysfunction in the absence of structural evidence for cerebral ischemia after uncomplicated carotid endarterectomy. Neurosurgery 2006;58:474-480.
26) Rocque BG, Jackson D, Varghese T, Hermann B, McCormick M, Kliewer M, et al. Impaired cognitive function in patients with atherosclerotic carotid

stenosis and correlation with ultrasound strain measurements. J Neurol Sci 2012;322:20-24.

27) Bakker FC, Klijn CJ, Jennekens-Schinkel A, van der Tweel I, Tulleken CA, Kappelle LJ. Cognitive impairment in patients with carotid artery occlusion and ipsilateral transient ischemic attacks. J Neurol 2003;250:1340-1347.

28) Rao R, Jackson S, Howard R. Neuropsychological impairment in stroke, carotid stenosis, and peripheral vascular disease, A comparison with healthy community residents. Stroke 1999; 30:2167-2173.

29) Brand N, Bossema ER, Ommen Mv Mv, Moll FL, Ackerstaff RG. Left or right carotid endarterectomy in patients with atherosclerotic disease: ipsilateral effects on cognition? Brain Cogn 2004;54:117-123.

30) Lin JH, Lin RT, Tai CT, Hsieh CL, Hsiao SF, Liu CK. Prediction of poststroke dementia. Neurology 2003;61:343-348.

https://doi.org/10.5758/vsi.2017.33.4.146