International Journal of Cardiology 176 (2014) 478–483

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Cerebral microemboli and neurocognitive change after carotid artery stenting with different embolic protection devices

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ARTICLE INFO

Article history:
Received 26 April 2014
Accepted 28 July 2014
Available online 12 August 2014

Keywords:
Cerebral microembolism
Neurocognitive function
Carotid artery stenting

ABSTRACT

Objectives: Proximal cerebral protection devices have been developed as an alternative to filter protection devices for reducing neurological complications during carotid artery stenting (CAS). The aim of the present study was to evaluate the frequency of silent cerebral embolism after CAS using different cerebral embolic protection devices and the impact of silent cerebral embolism on neurocognitive function.

Methods: One hundred consecutive patients who underwent CAS were enrolled. The patients were randomized to either proximal balloon occlusion or filter protection. Neurocognitive tests were performed before and six months after CAS. Cerebral embolisms were evaluated with diffusion-weighted magnetic resonance imaging (DW-MRI).

Results: The number and volume of new ischemic lesions found with DW-MRI were higher in the filter protection group than in the proximal balloon occlusion group. According to our definition, nine (21%) patients in the balloon occlusion group and 16 (36%) patients in the filter protection group showed neurocognitive decline, and ten (23%) patients in the balloon occlusion group and four (9%) patients in the filter protection group showed neurocognitive improvement (NS). Regarding the group of patients with new cerebral ischemic lesions on DW-MRI, neurocognitive decline occurred in 14 (31%) of 45 patients with DW-MRI lesions and 11 (26%) of 43 patients without DW-MRI lesions (NS).

Conclusion: Neurocognitive outcome after CAS is unpredictable; both neurocognitive decline and improvement can occur. In this study, the proximal balloon occlusion system significantly decreased cerebral microemboli during CAS compared to filter protection. Cerebral microembolism was not found to be associated with neurocognitive decline.

1. Introduction

High-grade stenosis of the carotid artery, even when asymptomatic, is associated with cognitive impairment [1]. Treating carotid artery stenosis with carotid endarterectomy (CEA) can improve cognitive function [2]. Carotid artery stenting (CAS) with various protection devices has become an acceptable alternative to endarterectomy in the treatment of symptomatic stenosis or asymptomatic severe stenosis, especially in patients with high surgical risks [3–5]. However, the major drawback of this technique is that it can be complicated by cerebral embolism, which usually remains clinically silent. Periprocedural cerebral embolic events are associated with a high rate of patient morbidity and can lead to cognitive impairment [6]. Although cerebral protection devices reduce the risk of perioperative apparent stroke during CAS [7,8], the rate of procedure-related silent cerebral embolic events remains high, and the risk depends on the type of protection used [9].

Diffusion-weighted magnetic resonance imaging (DW-MRI) is highly sensitive and specific in the diagnosis of cerebral microemboli [10]. However, evidence suggesting that these microemboli might damage the brain is still unclear [11–14]. Neuropsychological tests are designed to diagnose brain damage or impairment. In this study, we prospectively investigated the impact of type of cerebral protection method on silent cerebral embolism and the impact of silent cerebral embolism on neurocognitive function.

2. Methods

We prospectively enrolled 100 consecutive patients who underwent CAS in two different institutions. Internal carotid artery stenosis was diagnosed using carotid duplex ultrasonography with the following Doppler criteria: peak systolic velocity

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http://dx.doi.org/10.1016/j.ijcard.2014.07.241
0167-5273/

(PSV) >125 cm/s; internal carotid artery (ICA) to common carotid artery (CCA) PSV ratio >2; and stenosis diameter >50%. The patients were randomized to either the proximal balloon occlusion or filter protection system group, with equal numbers allocated to each cerebral protection method (Fig. 1). CAS was performed by two experienced interventional cardiologists. The study protocol was approved by the local ethics committee, and written informed consent was obtained from all of the patients.

2.1. Inclusion and exclusion criteria

Inclusion criteria were ICA stenosis >80% in asymptomatic patients and >60% in symptomatic patients. The degree of stenosis diameter was calculated according to the European Carotid Surgery Trial method [15]. Exclusion criteria included 1) stroke within one month prior to the procedure; 2) previous major stroke; 3) total occlusion of the ICA or external carotid artery (ECA); 4) "string sign" stenosis of the ICA; 5) stenosis of the contralateral ICA >50%; 6) contraindications for antiplatelet agents; 7) severely tortuous and calcified aortic arch vessels; 8) contraindication for MRI; 9) inability to read; 10) previous atrial fibrillation; and 11) Mini-Mental State Examination (MMSE) score <24 points.

2.2. CAS procedure

Clopidogrel (75 mg/day) and aspirin (100 mg/day) were administered for at least seven days before CAS. During the procedure, intravenous heparin (100 IU/kg of body weight) was administered to maintain an activated clotting time of 250–300 s. CAS was performed using a proximal balloon occlusion system (Mo.Ma; Invatec, Roncadelle, Italy) or filter-type distal protection device (Emboshield NAV6; Abbott, Santa Clara, CA). After the embolic protection device was inserted, lesions were treated with a hybrid design carotid stent. All stents were dilated with 5.0- or 5.5-mm balloons. All of the patients were prescribed aspirin (100 mg daily) for life and clopidogrel (75 mg daily) for three months after the procedure.

2.3. Cranial MRIx

Prior to the CAS procedure, all of the patients underwent cranial MRI scans performed with a 1.5 Tesla scanner with the following parameters: T1-weighted sequence (repetition time [TR] 535 ms; echo time [TE] 10 ms; 16 slices; slice thickness 5 mm; field of view [FOV] 230 mm); T2-weighted sequence (TR/TE: 3000/60 ms; 16 slices; slice thickness 5 mm); FLAIR sequence (TR/TE: 5400/100 ms; 16 slices; slice thickness 5 mm; matrix size 256 × 256; reduced acquisition 90%); and DWI (RT/RE: 8000/100 ms; 16 slices; slice thickness 5 mm; gap 1 mm; FOV 230 mm; matrix size 128 × 128; reduced acquisition 75%). DWI scans were acquired with three different b values: 0, 500, and 1000 s/mm^2. After the CAS procedure, 93 patients underwent DW-MRI. The number and volume of new ischemic lesions were evaluated with DWI. Acute ischemic lesion was diagnosed by DWI when increased signal intensity was seen on either axial or coronal DWI images and confirmed on the apparent diffusion coefficient. Two radiologists analyzed each DWI lesion separately by measuring its volume. Quantification of cerebral infarct lesion volume was performed using image analysis software (FuncTool; GE Medical Systems, Milwaukee, WI).

2.4. Neuropsychological assessment

The cognitive battery included eight neuropsychological tests to assess cognitive skill. Global cognitive functioning was assessed with the MMSE to exclude pre-existing cognitive impairment. The following tests were also administered: Rey Auditory Verbal Learning Test, forward and backward digit span tests, Trail Making Test (TMT) A and B, verbal fluency test (animals category), Stroop Color and Word Test, and Rey Complex Figure Test (Table 1). The neuropsychological tests were administered the day before the CAS procedure and six months after the procedure. The test results were analyzed using the reliable change index (RCI), which was first described by Jacobson and Traux [16] and designed to determine whether or not the change in a patient's score on a test of cognitive function is statistically significant. In the current study, RCI was computed using a modification suggested by Hageman and Arrindell [17], calculated as $RCI = (X_{post} - X_{pre})\, r_{dd} + (M_{post} - M_{pre})\,(1 - r_{dd})/(r_{dd})^{1/2}\,(2S_E^2)^{1/2}$ where X_{pre} = pretreatment score, X_{post} = post-treatment score, M_{pre} = mean of sample at pretreatment, M_{post} = mean of sample at post-treatment, r_{dd} = reliability of difference scores, and S_E = standard error of the estimate. The standard error of the mean was computed as $S_E = S\sqrt{1-r}$, where S = standard deviation at pretreatment and r = internal consistency reliability coefficient. The patients were then separated into three groups based on their RCI scores: reliable decline (RCI < −1.96), no reliable change (RCI between −1.96 and +1.96), and reliable improvement (RCI < +1.96). Neurocognitive decline or improvement were defined as RCI score <−1.96 or >+1.96, respectively, on two or more tests assessing different cognitive domains [18].

2.5. Statistical analysis

Statistical analyses were performed using SPSS, version 20.0 (SPSS, Chicago, IL). The normality of distribution of the neuropsychological tests was examined using the Kolmogorov–Smirnov test. Group comparisons were made using the independent samples *T* test and chi-square test. Two-sided P values <0.05 were considered significant.

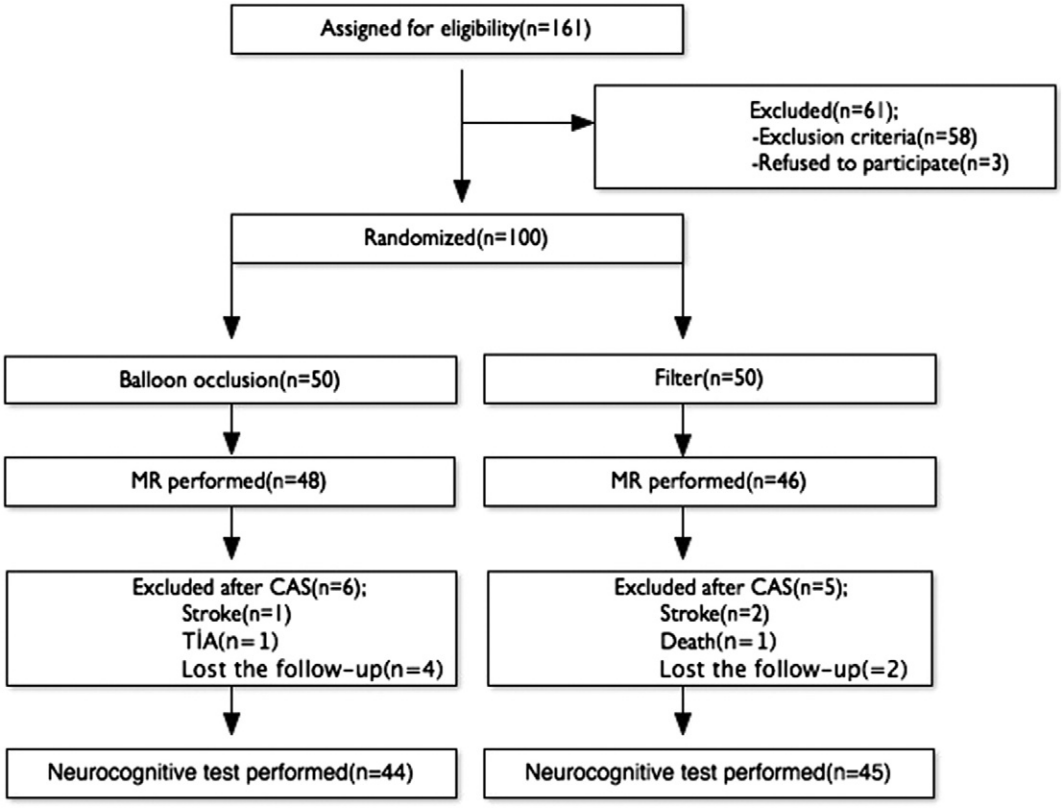

Fig. 1. Flow chart of patient enrollment.