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Cognitive Outcomes 3 Months after Unilateral Carotid Stenting: A Preliminary Study

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Background: Percutaneous transluminal angioplasty with stenting (PTAS) has become a treatment option for severe carotid stenosis. The goal of our study was to determine retrospectively neurocognitive outcome 3 months after unilateral stent-protected carotid angioplasty. Methods: Nine patients who underwent stent-protected angioplasty for symptomatic (n=7) or asymptomatic (n=2) high grade carotid stenosis were investigated. Patients were performed pre-stenting MRI, and the neuropsychological tests were performed both before and 3 month after stent placement. Results: Three months after stenting, we found no change or deterioration of cognitive outcomes in 5 of 9 patients (55%) and prominent cognitive improvement in 4 of 9 patients (45%) for memory, visuospatial function, and frontal executive function. Conclusions: Our study showed that 3 months after PTAS cognitive functioning did not change in most patients significantly. For some patients, however, significant improvement were confirmed in clinical and in neuropsychological test. The reasons for these differences are unclear, but we suggest that it may depend on variable factor; symptomatic, education, right vs. left and the combined ipsilateral intracranial stenosis.

Key Words: *Carotid stenting, Cognitive outcome*

INTRODUCTION

Internal carotid artery atherosclerosis is a major cause of ischemic stroke and also can induce impairment of cognitive functioning[1-3, 13]. The prevention of stroke in patients with high-grade stenosis traditionally has been carried out by carotid endarterectomy (CEA) of the stenotic segments of the artery[6]. The use of percutaneous endovascular methods to treat significant carotid stenosis has gained much attention during the last years[4, 5]. As a consequence, percutaneous transluminal carotid angioplasty (PTA) and stent placement is now being investigated as an alternative to CEA. Studies of patients with extracranial internal carotid artery stenosis undergoing CEA have shown impaired preoperative neuropsychological performance. These studies have also shown that restoration of blood flow after endarterectomy correlated with cognitive improvement[6, 15, 16]. Although there has been increasing adoption of endovascular stent placement of the cervicoreberal vessels as a less-invasive alternative to open surgery, the benefit of these new techniques in relation to cerebral perfusion and cognition has been controversy[4, 5]. The goal of the present study was to determine long-term neurocognitive outcome in patients after unilateral percutaneous transluminal angioplasty with stenting (PTAS) surgery. We compared pre and postinterventional cognitive performances.

MATERIALS AND METHOD

Subjects

Between February 2005 to February 2007, 22 patients with angiographical-proven severe (70-99%) extracranial internal carotid artery stenosis underwent stent placement. Of the 22 patients with stent placed, 18 were elective and 4 were urgent (withn 14 days of patient presentation). Of the 18 patients with elective PTAS, 9 patients were performed follow-up neuropsychological test at 3 month after unilateral carotid stenting. Remained 9 patients showed the transient ischemic attack (TIA) or stroke after stent placement (2 patients), acute MI (1 patient), severe disability affecting neuropsychological tests (3 patients) and follow-up loss (3 patients). These investigation was performed retrospectively by review of medical record.

MRI

Cerebral MRI was performed with a Philips Gyroscan 1.5 T scanner using sagittal T1-weighted (T1W1) spin echo (SE) sequence (repetition time [TR]/echo time [TE] 374/15 milliseconds, section thickness 6.0 mm, intersection gap 1.0 mm) and an axial and a coronal T2W SE sequences (TR/TE 2,229/20 to 90 milliseconds, section thickness 6.0 mm, intersection gap 0.6 mm). All MRI scans were read independently by two radiologists.

Surgical procedure

In 9 patients, 5 patients were performed PTAS in the left carotid artery and 4 patients in the right. Stent implantations were performed by two neuroradiologist. Interventions were undertaken via a trans femoral access with placement of an 8-F sheath under local anesthesia. The selective angiography (in at least 2 planes) of the carotid artery and its intracranial branches were performed to establish a road map for intraprocedural guidance and assessment. A gold-tip guidewire was passed into the ICA distally, and a Bijou balloon was placed at the site of the stenosis for primary dilation. And then the catheter was exchanged before deploying a Wallstent (Schneider, Bulach, Switzerland), which had been sized based on a reference diameter measured from the selective angiogram. Stent deployment was followed by dilation within the stent using a 5- to 6-diameter ballon catheter. After stenting, selective angiography in at least 2 planes was done to evaluate the local result and to examine the intracranial arteries with respect to changes in hemodynamics and embolization. Standardized antiplatelet therapy was prescribed in all patients.

Neuropsychological assessment

Follow-up examinations were performed at 3 months after stenting. At that time, none of the 9 patients reported a neurological event and examination revealed no neurological change after stenting. The patients received identical neuropsychometric assessment being used before stenting. All patients were subjected to SNSB-D form (Dementia version of the Seoul Neuropsychological Screening Battery) test. The SNSB contains tests for attention, visuospatial function, verbal and visual memory function, language-related function, and frontal and executive functions. These tests include the digit span (forward and backward) for attention (total score=17), the Korean version of the Boston Naming Test (Kim and Na, 1999) and written calculations (three items each for addition, subtraction, multiplication, and division, with 1 point for each correct item) for language& related function (total scores=27), the Rey-Osterrieth Complex Figure Test (RCFT) copying (total score=36), time and place orientation, free recall, delayed recall trials and recognition scores of Seoul Verbal Learning test (SVLT) and RCFT immediate, 20-min delayed recall trials and recognition scores for memory (total score=150). Impersistence, contrasting program, Go, No-go test, Fist-edge-palm test, luria loop, phonemic and semantic Controlled Oral Word Association Test, and the Stroop Test

Table 1. Basline characteristics of cases of stents placed for unilateral extracranial carotid severe stenosis

Patient No.	Age (yr)	Sex	Clinical diagnosis				Stent side	Vascular risk factor				
			Educational year (yr)	TIA	Str	Asym		HTN	DM	SM	Hyper -lipid	CHD
1	74	M	1			+	R	+	−	−	+	−
2	79	F	1		+		L	+	−	−	−	+
3	67	F	6		+		L	−	+	+	+	+
4	63	M	2			+	R	+	+	−	−	−
5	64	M	1	+			L	−	−	+	+	−
6	65	M	16		+		L	+	+	+	+	−
7	61	M	9		+		R	+	−	+	−	+
8	68	M	12		+		L	+	−	−	−	−
9	67	F	6		+		R	+	−	−	−	−

L indicates left; R, right; HTN, hypertension; DM, Diabetes mellitus; SM, smoking; CHD, coronary heart disease; TIA, transient ischemic attack; Str, stroke; Asym, asymptomatic.

(word and color reading of 112 items in 2 min) for frontal executive function (total score=70).

Data analysis

Demographic and clinical data of the patients were obtained by interview with patient or chart review. The neuropsychological changes between pre-and post-stenting were compared by nonparametric independent-T test (Wilcoxon signed rank test).

RESULTS

Demographic features of the subjects

Demographic features of participants are shown in Table 1. Severe stenosis of ICA was in left for 5 patients and right for 4. The mean age of the patients was 67.56 yr (SD±5.66 yr, range 61 and 79 yr). The gender of patients was male for 6 patients and female for 3. The average length of education was 6.11 yr (SD±5.33 yr, range 1 and 16 yr). Clinical manifestations were minor stroke for 6 patients, TIA for 1, and asymptomatic for 2. The vascular risk factors and comorbidities included arterial hypertension (7 patients), diabetes mellitus (3 patients), tobacco use (4 patients), hyperlipidemia (4 patients) and coronary heart disease (3 patients).

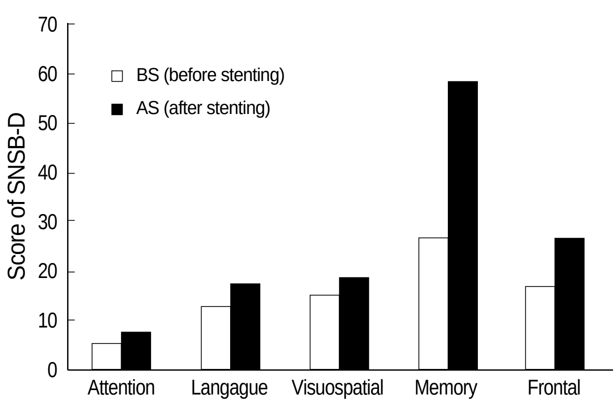

Fig. 1. Comparison of the scores of each cognitive domain between pre and poststenting SNSB-D tests in four patients with poststent cognitive improvement. Prominent improvement of measurement scores was observed in the memory domain.

MRI and angiography

Seven of the 9 patients had MR ischemic lesions, 4 of 7 patients showed the lesion confined to the subcortical white matter lesion, 1 confined to cortical lesion and 2 showed lesions of combined cortical and subcortical area (Fig. 2). Patients with combined controlateral ICA stenosis were 4 of 9 patients (44%) and patients with mild to moderate ipsilateral intracranial artery stenosis were 3 of 9 patients (33%) (Table 2).

Table 2. MRI and angiographic findings of cases of stents placed for unilateral extracranial carotid severe stenosis

Patient No.	MR lesion	Acom	No. of pcom	Ipsilateral intracranial stenosis	Controlateral ICA stenosis
1	–	–	1	–	+
2	+	+	1	+	+
3	+	+	2	–	–
4	–	+	0	+	+
5	+	+	2	–	–
6	+	+	2	–	–
7	+	–	0	–	–
8	+	+	2	–	+
9	+	+	2	+	–

The circle of Willis (COW) anatomy in each case is indicated by the presence or absence of anterior communicating artery (Acom), number of posterior communicating arteries (Pcom), ipsilateral intracranial artery stenosis and contralateral carotid stenosis.

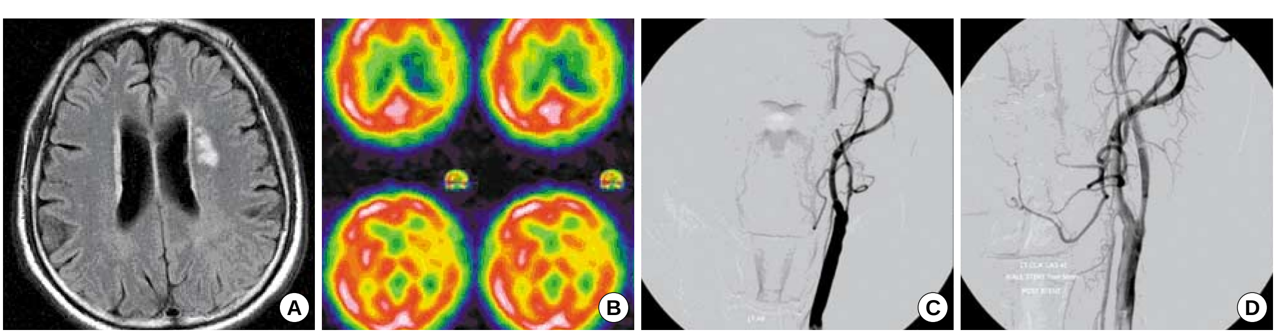

Fig. 2. Images obtained in patient 3, (A) FLAIR image showing small ischemic lesions in the left deep white matter area. (B) Brain SPECT showed hypoperfusion on the left fronto-temporo-parietal area. (C) Carotid angiogram showing severe stenosis of the proximal internal carotid artery and (D) DSA after stent placement.

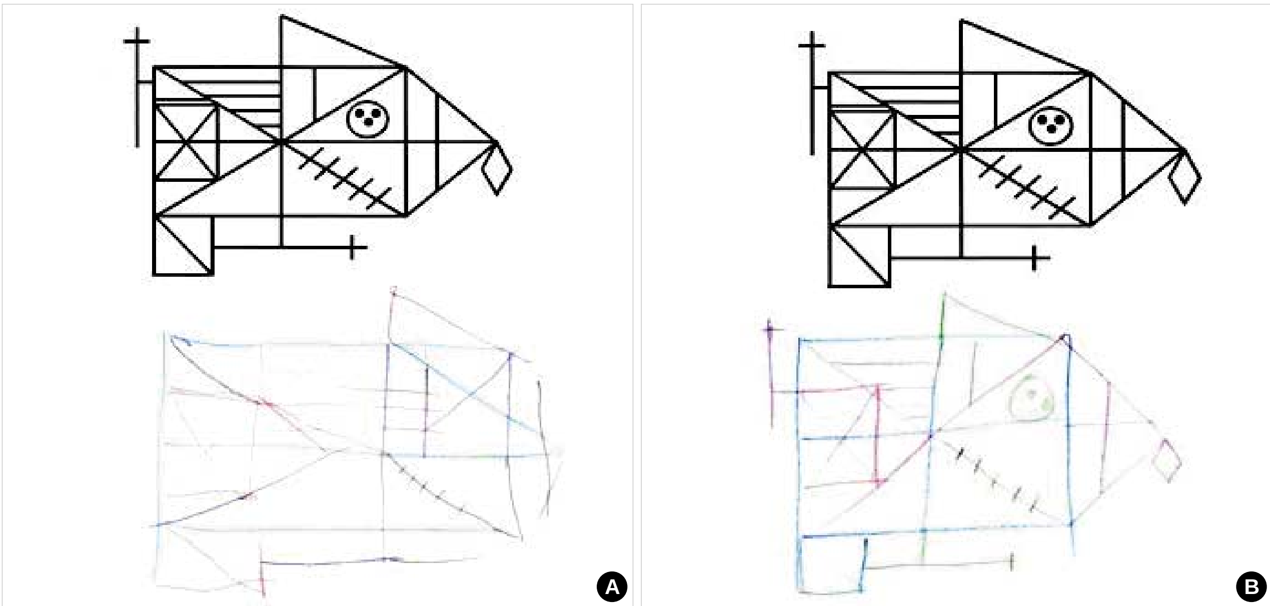

Fig. 3. Rey-Complex Figure prestenting (A), poststenting (B) of patient 6.

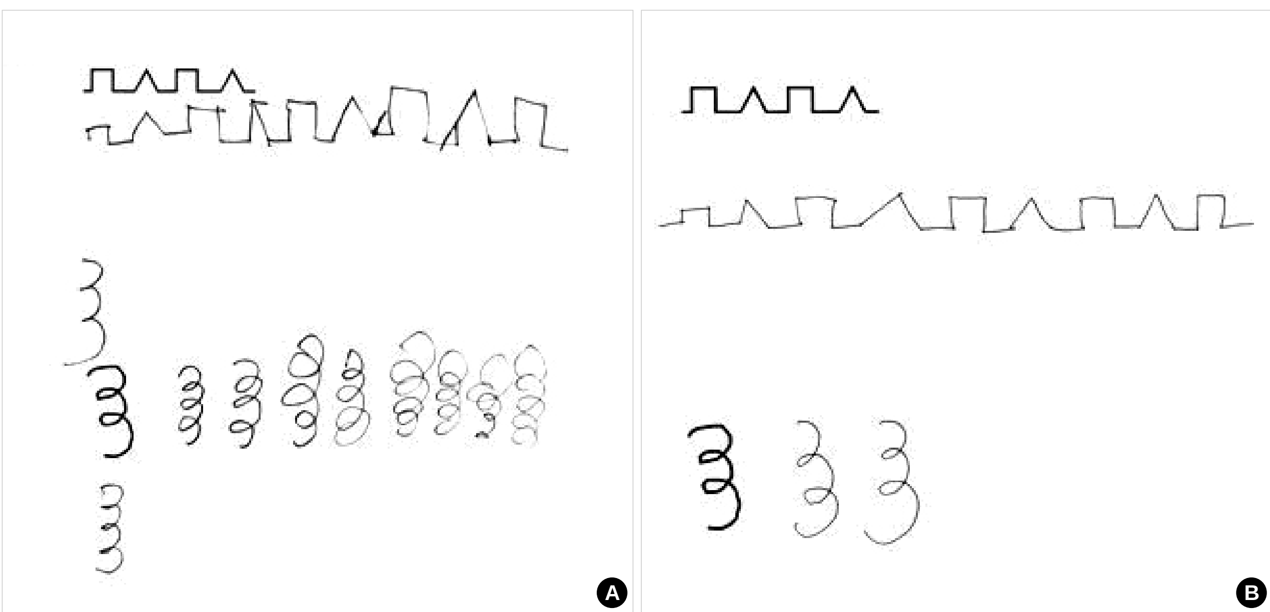

Fig. 4. Alternating sqaure and triangle and luria loop test, prestenting (A), poststenting (B) of Paitnet 7.

Neuropsychological assessment

On baseline neuropsychological assessment, all 9 patients had cognitive deficits more than two domains of attention, language function, frontal executive function, memory or visuospatial function. Frontal executive dysfunctions were found in all patients. Three of 9 patients had cognitive deficit on two cognitive domains, two showed cognitive deficit on three cognitive domains, and the other four patients showed dysfunction of all five cognitive domains. Nonparametric independent t-tests detected no statistical significant differences for pre- and poststenting scores in each neuropsychological variables. Individually different outcomes for neuropsychological test, however, were showed in each patient. Cognitive improvements were observed in four patients (Patient 3, 6, 7, 8), no change in four patients (Patient 1, 4, 5, 9) and deterioration in one patient (Patient 2) were displayed. Among the neuropsychological domains, in four

Table 3. Prestenting and poststenting scores for each neuropsychological test

Patient No	1		2		3		4		5		6		7		8		9		*p*
Test time	BS	AS	BS	AS	BS	AS	BS	AS	BS	AS	BS	AS	BS	AS	BS	AS	BS	AS	
Attention (17)	10	11	8	6	4	6	7	7	7	8	4	8	7	5	7	12	8	9	0.197
Langague and related function (27)	21	22	17	15	10	11	15	14	22	10	21	27	12	14	9	18	17	20	0.701
Visuospatial function (36)	25	19.5	29.5	1	24.5	25.5	24.5	24	25.5	27.5	17.5	30	15	13.5	3.5	6	18.5	22	0.468
Memory (150)	48	53.5	42	36	23.5	53.5	78	70	44	44	22.5	86	38	59	23	34.5	27	33	0.102
Frontal executive function (70)	44	28	36	21	10	12	54	52	45	41	10	35	25	31	23	29	30	33	0.895
Total	148	145	132.5	78	72	108	178.5	167	143.5	130.5	75	186	98	122.5	66.5	99.5	100.5	117	0.000

BS indicates before stenting; AS, after stenting, *p* value assessed by nonparametric independent t test.

patients having showed the cognitive improvement, improvement of memory was most prominent rather than other domains (Fig. 1). One patient revealed definite improvement for visuospatial function test and three patients, improvement for frontal executive dysfunction (Fig. 3, 4). Table 3 showed pre and poststenting score in each neuropsychological measure for nine patients.

DISCUSSION

This study documented changes of pre- and 3 months poststenting cognitive function in 9 patients following unilateral carotid angioplasty with stent placement for unilateral carotid stenosis. Our study showed that 3 months after PTAS cognitive functioning did not significantly change in most patients. Four patients with cognitive improvement had left side carotid stenting rather than right (three of four, 75%), symptomatic clinical stroke manifestation, presence of MR lesion and collateral circulation (four of four, 100%) and relatively high educational level (mean 9.8 yr vs 3 yr) rather than patients with poor or unchanged cognitive outcome. Among the all cognitive domains, prominent improvement of measurement scores was observed in the memory domain. One patient with marked deterioration of cognition had ipsilateral intracranial artery stenosis and controlateral carotid stenosis.

Several sutides have indicated improvement of intellectual functions after reconstructive operation on the severe ICA stenosis[6]. Other studies suggested that the improvement might be related to the laterality of the operation, being more marked in verbal tests in patients with left ICA operation and in visuospatial tests in patients with right ICA operation[9, 10, 16-18]. However, there has been a few report of a relationship between carotid stenting and cognitive function[5, 6]. These studies reported similar findings compared with our results. Interesting question is the cause of neurocognitive improvement/deterioration after PTAS in some patients. One could think of the presence or absence of hemodynamic ischemia, microembolisms during ballon inflation or the poststenting restenosis to be responsible for the observed cognitive change in patients with severe ICA stenosis[11, 12]. Unfortunately, small sample size in this investigation and absence of follow-up SPECT or MRI and angio study did not allow us to trackle this question. However, each single patient tell something about the factors affecting prognosis. The mechanism of each presumptive factor affecting poststenting cognitive outcomes are unclear, however, we suggest that it may depend on variable factor; symptomatic, education level, right vs. left and combined ipsilateral intracranial stenosis in our investigation.

The limitation of our study is small sample size, practice effect due to 3-month test-retest and no control data by validated neuropsychological test. A further study to investigate these questions will be necessary to predict the outcome of the carotid stenting more precisely.

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