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ORIGINAL RESEARCH

Effect of Carotid Artery Stenting on Cognitive Function in Patients With Carotid Artery Stenosis: Preliminary Results

A.S. Turk
I. Chaudry
V.M. Haughton
B.P. Hermann
H.A. Rowley
K. Pulfer
B. Aagaard-Kienitz
D.B. Niemann
P.A. Turski
R.L. Levine
C.M. Strother

BACKGROUND AND PURPOSE: Stenosis of the carotid artery may be a cause of reduced cognitive performance that can be ameliorated with placement of a stent. The goal of this study was to measure cognitive performance and speed of psychomotor performance prospectively before and after carotid stent placement.

MATERIALS AND METHODS: Patients referred for stent placement for a unilateral carotid artery stenosis were enrolled in the study. Neuropsychologic testing was performed with a Mini-Mental State Examination, an extended mental status examination, a subjective cognitive status measure, and a psychomotor performance test for speed. The severity of the stenosis was measured on angiograms performed before stent placement. Three months after stent placement, CT angiograms were performed and the neuropsychologic testing was repeated. Differences in neuropsychologic test scores before and after stent placement were calculated and tested for significance with a Student *t* test.

RESULTS: Seventeen patients with a single unilateral carotid stenosis of more than 50% completed the study. Stenosis of the carotid artery averaged 80% before treatment and 18% after treatment. After stenting, the scores from the extended mental status examination improved significantly. The scores from the subjective cognitive status measure also improved. No significant change was noted in the scores from the Mini-Mental State Examination or in the speed of psychomotor performance.

CONCLUSION: Carotid stent placement in patients with a unilateral stenosis of the carotid artery resulted in significant improvement in cognitive test scores in this highly selected patient group. Further studies are needed to confirm these preliminary observations.

There are more than 750,000 patients with new or recurrent stroke in the United States each year, with as many as 25% related to significant cerebrovascular stenoses.[1] In addition, progressive cognitive decline among patients with cerebrovascular stenosis may be an even greater problem than the actual stroke, but it is not a widely recognized symptom and has yet to be adequately addressed in any study. Patients with carotid stenosis have been shown to have significantly poorer scores on cognitive tests than matched control subjects.[2-6] Evidence is accumulating that revascularization of a carotid stenosis may improve cognitive performance.[7-13] Subjective evaluation of patients who had stent placement of the carotid or vertebrobasilar system suggests improved cognitive function after treatment.[8] Objective measures evaluating the speed of cognitive functioning improved in 1 group of 10 patients studied before and after stent placement.[9] Endarterectomy in patients with carotid stenosis resulted in improved scores on psychomotor and cognitive tests[10] but can result in cognitive decline if operative ischemia is encountered.[14] Additional studies are needed to confirm the effect of carotid stenosis and stent placement on cognition. The goal of this study was to prospectively measure objective and subjective cognitive performance and speed of completing psychomotor tests in patients undergoing carotid stent placement.

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From the Departments of Radiology (A.S.T., I.C., V.M.H., H.A.R., K.P., B.A.-K., D.B.N., P.A.T., R.L.L., C.M.S.), Neurosurgery (A.S.T., B.A.-K., D.B.N.), and Neurology (B.P.H., H.A.R., R.L.L.), University of Wisconsin Hospital and Clinics, Madison, Wis.

Please address correspondence to Aquilla S. Turk, DO, 600 Highland Ave, CSC E3/372, Madison, WI 53792. E-mail: as.turk@hosp.wisc.edu

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Materials and Methods

We asked patients who were referred to the neuroendovascular service for stent placement of a unilateral carotid stenosis between July 2005 and December 2006 to participate in the study. The institutional review board approved the study, and we obtained written consent from each patient. Initial selection of the patients was performed with CT angiogram (CTA), and conventional cerebral angiograms were performed in anticipation of carotid stent placement.

Inclusion criteria included recent (within 30 days of the date of procedure) CTA of the head and neck, evidence of an isolated stenosis of 1 carotid artery of more than 50% confirmed with conventional angiography, age older than18 years, and selection by the treating vascular disease specialist as a suitable candidate for stent placement. Exclusion criteria included evidence of other significant stenosis (>50%) in the major arteries of the head or neck, evidence of a previous large stroke or cerebral infarction on MR or CT of the head, a history of previous subarachnoid or cerebral hemorrhage, rapidly evolving symptoms or other reason for emergency stent placement, uncontrolled hypertension or hypotension, angina, or evidence of a spontaneous or traumatic carotid dissection. A neuroradiologist and neuroendovascular physician reviewed the CT and CTA studies to determine that the patients met criteria for enrollment.

Neuropsychologic testing was performed before stent placement. Cognitive performance and speed of psychomotor processing were measured by a trained research assistant (K.P.), supervised by an experienced neuropsychologist (B.P.H.). An objective measure of cognitive performance was obtained with the Repeatable Battery for the Neuropsychological Status (RBANS).[15,16] The total score and scores for the domains of immediate memory (list learning, prose), visuospatial/constructional (spatial orientation, construction), language (naming, fluency), attention (digit span, digit symbol), and delayed memory (verbal, visual) were recorded. Scores were normalized for

Neuropsychologic test scores at baseline and follow-up

3-Month Follow-Up of Proximal and Distal Unilateral Carotid Stenosis	Baseline	3 Months After Stenting	*P* Value of Difference
Objective Screening Measures of Mental Status			
RBANS total score	80.4 (9.3)	85.6 (10.8)	.004*
Immediate memory	80.4 (11.8)	87.3 (14.1)	.04*
Visual/constructional	80.5 (14.0)	83.1 (13.8)	.32
Language	92.3 (6.4)	95.1 (7.9)	.08
Attention	86.9 (12.4)	92.5 (13.5)	.05*
Delayed memory	85.1 (15.9)	89.1 (15.3)	.28
MMSE	28.1 (2.1)	28 (1.6)	.91
Subjective Test of Cognition			
IQCODE	−1.9 (2.5)	1.1 (4.1)	.04*
Speed-based psychomotor test			
Trail A	41.5 (11.3)	41.1 (14.0)	.88
Trail B	40.1 (11.8)	42.3 (11.9)	.39

Note:—RBANS indicates Repeatable Battery for the Neuropsychological Status; MMSE, Mini-Mental State Examination; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly: Trail A, Trail Making Test A; Trail B, Trail Making Test B.
* Statistically significant difference.

age, sex, ethnicity, and level of education with a score of 100 and a standard deviation of 15 for the index group. The Mini-Mental State Examination (MMSE), which has poor sensitivity to episodic memory performance,[17,18] was obtained for comparison. The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), a brief 16-item informant-completed questionnaire, was used as a subjective assessment of changes in cognitive function.[19-21] The speed of psychomotor processing was measured by means of the Trail Making Test, Part A and Part B, which require simple and complex visuomotor tracking and which are used often in patients with cerebrovascular disease.

At conventional angiography, the severity of carotid stenosis on each side was measured on the angiogram in accordance with the criteria of the North American Symptomatic Carotid Endarterectomy Trial. If the stenosis did not exceed 50% on 1 side only, or if the interventionalist elected to discontinue the procedure, the patient was excluded from the study. All patients were treated with clopidogrel (Plavix) before and for at least 3 months after stent placement. All patients were treated with aspirin before stent placement and continuously after stent placement.

Imaging with CTA was performed routinely at baseline and at 3 months after stent placement. The CTA was inspected for evidence of restenosis or the presence of any new strokes after stent placement. Of the 17 patients, 6 presented with strokes, 7 with transient ischemic attacks (TIAs), and 4 were asymptomatic.

We compared neuropsychologic test scores at baseline and at 3 months after stent placement, and we tested differences for significance with a paired Student *t* test and significance set at .05. The differences in the scores for left and right carotid stenoses were tested with a Student *t* test of the means. We tested for significance the correlation of the RBANS score and presence of a perfusion abnormality with the severity of stenosis using the Spearman correlation coefficient. We performed all statistical analyses with SPSS version 14 (SPSS, Chicago, Ill).

Results

We initially enrolled 25 patients into the study. All patients had symptomatic carotid stenosis of more than 50% manifested by TIAs or previous small strokes or an asymptomatic carotid stenosis of more than 80%. Of the 25 patients, 5 were subsequently excluded because stent placement was not performed because the stenosis at the time of angiography did not conform to the enrollment criteria (>50% stenosis on 1 side, without a tandem lesion and <50% on the contralateral side), so stent placement was not performed. Two additional patients who declined poststenting neuropsychologic testing were excluded. One patient was found to have colon cancer between initial presentation and the scheduled procedure, and treatment was not performed.

For our study, we analyzed the results in 17 patients. The mean age of the patients was 71 years (range, 60–91 years) with 15 men and 2 women. Of the 17 patients, 15 had stenosis of the proximal internal carotid artery, and 2 had stenosis of the distal internal carotid artery. The severity of stenosis of these patients averaged 80% (range, 55%–95%). The stenosis was left sided in 59% and right sided in 41% of patients. After stent placement, the severity of the stenosis averaged 18% (range, 0%–50%). No periprocedural adverse clinical events were noted.

The total scores for the RBANS before stent placement averaged 80 and, after stent placement, increased significantly to 86 ($P = .004$). The RBANS domains of immediate memory, visual/construction, language, attention, and delayed memory scores increased after stent placement (Table). For 3 of the domains, the increase was significant ($P \leq .05$), and for 2 of the domains, the increase was not significant. The MMSE did not significantly change from baseline in the patients after stent placement. The scores from the subjective cognitive test (IQCODE) increased significantly from −1.9 initially to +1.1 after placement of a stent ($P = .04$). The scores from the speed-based psychomotor test (Trails A and B) increased, but not by a significant amount.

Before stent placement, the scores from the RBANS tended to be lower in patients with greater severity of stenosis. Patients with left-sided stenosis had a baseline RBANS score of 81.2, and after stent placement the average increase was 2.4. The patients with right-sided stenosis had slightly lower baseline RBANS scores of 79.3, and the average increase was 5.6 after stent placement. There were no significant differences in baseline RBANS scores between patients with left-sided and those with right-sided stenoses ($P = .7$).

Discussion

In our study, patients before stent placement had, on average, a total RBANS score of 80, which compares with the index score of 100 for age-, sex-, and education-adjusted norms for the group or 105 or higher on average for normal adult men.[15] A score of 80 is approximately 1 standard deviation below the average for age, which suggests a pattern of mild but relatively diffuse cognitive impairment. The scores for RBANS increased significantly after stent placement. The scores for the subjective test (IQCODE) of cognition also increased significantly. Significant changes were not found in the scores from MMSE or in speed-based psychomotor tests.

The results in our study agree with the results from previous reports that have shown improvements in cognitive function in patients treated with stent placement or surgery for carotid artery stenosis. Patients treated surgically for carotid artery stenosis have been shown to increase their neuropsychologic test scores and/or psychomotor speed.[7,10,12,13] Patients treated with stent placement had an increase in subjective cognitive function, as we have demonstrated previously.[8] Our patients did not show an improvement in speed of performing psychomotor tests, in contrast to the results of Grunwald et al.[9] The difference may be because of the smaller number of cases in that study, a larger proportion of patients with right-sided carotid artery stenosis, or different neuropsychologic tests used to measure speed.

There were no declines in any individual scores on RBANS in our patient group. Some reports on carotid endarterectomy have shown declines in cognition to be associated with chronic ischemia, increasing age, and the presence of diabetes.[14,22,23] Significant cognitive improvements in our study were demonstrated irrespective of age or the presence of diabetes. The significant increase in the scores for the subjective tests suggests a clinically evident change in objective measures, though this result was relatively modest.

We found no significant change in the test results on MMSE or correlation of the laterality of the lesion and cognitive outcomes. In a large, retrospective cardiovascular health study involving 4373 patients, an effect on the MMSE was found in 32 patients with a left-sided carotid stenosis of more than 75%, when other factors were controlled for.[6] The size of our sample was probably insufficient to detect a difference in the laterality of the stenosis. Furthermore, the MMSE is a test designed to measure cognitive function in the dominant hemisphere, with poor ability to evaluate the nondominant hemisphere.[24-26]

In our study, as in a previous study, 76% of patients with lesions of the anterior circulation had a perfusion abnormality at presentation, and all resolved with treatment.[8] Significant cognitive improvements after stent placement were seen in patients irrespective of the presence of a baseline perfusion abnormality, though this finding is limited because only 24% of patients were without perfusion abnormalities at presentation. Perfusion abnormalities were present in patients with a higher average degree of vessel stenosis. There was no correlation between the severity of stenosis and the amount of improvement in cognitive performance as measured by the RBANS test.

Because, to our knowledge, there has not been a significant study of the incidence of cognitive dysfunction in patients with carotid artery stenosis, it is speculative as to the degree to which stent placement for carotid artery stenosis might improve cognitive function in this population. In our experience, it is not unusual for patients (or their family members) in whom carotid artery stenosis has been treated by angioplasty or angioplasty and stent placement to spontaneously make comments such as "things seem much clearer since my procedure." When one considers the frequency of significant hemispheric perfusion defects in subjects with "asymptomatic" carotid artery stenosis, it seems quite reasonable that there may be subclinical cognitive dysfunction in some of them that could be reversible when normal perfusion is restored. Further study in larger populations with careful neuropsychologic testing both before and after treatment will be required to add clarity to this question.

Our study had limitations. No control group was included, though patient scores after treatment were compared with scores in the same patient before treatment. This limitation may be significant because it is impossible to predict the degree to which spontaneous cognitive improvement after a stroke or TIA occurs. The patients were highly selected to minimize the confounding effects of other cerebrovascular stenoses or treatments. The number of patients who fit our criteria was small, but statistical significance was achieved. The number of patients who were excluded after enrollment was large. Although we made an effort to perform neuropsychologic testing in a remote controlled clinical environment before the date of surgery, we believe that depressed baseline cognitive performance could have been related to emotional duress or presenting symptoms. Exclusions were made because patients failed to meet criteria for study inclusion after enrollment or did not wish to continue neuropsychologic testing. The role of practice effects on the improvement of scores cannot be evaluated objectively but in previous studies has not been a significant factor.[27]

Our prospective study shows that stent placement for selected patients with carotid stenosis improves cognitive function. This study is unique in that both objective and subjective measures of cognitive performance were obtained. It demonstrated that this patient population exhibits diminished baseline scores in neuropsychologic performance that improve significantly with stent placement. Stent placement has already been demonstrated to reduce the risk for stroke in selected patients.[28-32] The inclusion of cognitive deficit as an ancillary criterion for carotid stent placement warrants further evaluation.

Conclusion

Our study shows that patients with carotid stenosis of more than 50% show improved cognitive function after carotid stent placement. The improvement was measured in objective, extended mental status examinations and in subjective cognitive tests. It was not measured by the MMSE or by tests of psychomotor speed. Further work in this area with larger patient populations is needed to confirm these preliminary findings.

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