Biomedical Research 2016; 27 (2): 429-433

ISSN 0970-938X
www.biomedres.info

Cognitive outcome after carotid artery stenting in patients with cerebral ischemia.

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Abstract

Background: **Chronic cerebral hypoperfusion may lead to cognitive decline in patients with chronic stenosis or occlusion of the cervicocerebral vessels, and the effects of stent placement on neurocognitive function have been controversial.**
Methods: **A series of 105 patients, who were identified with arterial stenosis or occlusion and abnormal cerebral perfusion in the area of the stenotic vessel based on computed tomography (CT) angiography or magnetic resonance angiography (MRA) and magnetic resonance (MR) or CT perfusion were selected to investigate. A battery of neuropsychological tests, including the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA), were assessed 1 week before and 90 days after the cervicocerebral vessel stenting, or conventional angiography without intervention.** ***Results:*** **Patients were subdivided into 2 groups (n=83 carotid artery stents [CAS]); no intervention (n=22) serving as a control group. Significant improvements in MMSE (CAS 23.9 [4.9] vs 25.4 [4.7] for before vs after the procedures; *P*<0.01) and in MoCA (CAS 19.9 [6.4] vs 22.0 [6.0] for before vs after the procedures; *P*<0.01) were observed in the intervention groups. Orientation, delayed recall and abstraction were also improved.**
Conclusions: **Successful cervicocerebral vessel stenting improve cognitive function in patients with cervicocerebral vessels stenosis or occlusion with a corresponding perfusion abnormality.**

Keywords: Arterial stenosis, Carotid stenting, Brain perfusion, Neurocognitive function.

Accepted November 26, 2015

Introduction

Impaired cognitive function is often reported in patients with carotid artery stenosis or occlusion. As is known to all, there is an independent risk factor for the progression of mild cognitive impairment (MCI) to dementia which is carotid stenosis [1, 2, 3]. Cerebral emboli and hypoperfusion which play key roles in this process can be improved by angioplasty [4, 5]. Most of the studies that have evaluated cognitive functions before and after carotid endarterectomy (CEA) or carotid artery stenting (CAS) have reported either improvement or no change in cognition [6-13].

The purpose of this study is to investigate the effect of CAS on neurocognitive function in patients with stenosis or occlusion of the cervicocerebral vessels and objective hypoperfusion.

Materials and Methods

Patients

A total of 105 patients aged 40 to 80 years with carotid artery stenosis or occlusion were consecutively selected from the Department of cerebral vascular Neurosurgery, Huanhu Hospital, Tianjin, China from March 2011 to December 2011. All patients had persistent neurologic symptoms, including transient ischemic attacks, dizziness or stroke. The score of modified Rankin Scale was 0-2. Cervicocerebral vessel stenosis or occlusion was documented by computed tomography angiography (CTA) or magnetic resonance angiogram (MRA). Objective perfusion abnormalities corresponding to the area of the stenotic or occluded vessel were documented by magnetic resonance (MR) perfusion; except for 10 patients who were evaluated by CT perfusion because of a contraindication to magnetic resonance imaging. All of the excluded patients presented an ischemic stroke in previous 14 days, catheter-based techniques, arteriovenous malformation, or aneurysm, history of previous bleeding disorder, plan to carry out any operation within 1 month, life expectancy is less than 1 year, aphasia, right-sided hemiparesis, marked depression or a mental disorder, who were unable to comply with the study assessment or with a concomitant cognitive impairment, including Alzheimer's disease and other dementia related to degenerative disease Table 1.

Treatment process

We use baseline CTA or MRA to assess the presence of vascular stenosis or occlusion, which allowed risk stratification before conventional angiography.

We use the North American Symptomatic Carotid Endarterectomy Trial (NASCET) for cervical carotid lesions and the Warfarin and Aspirin Symptomatic Intracranial Disease (WASID) criteria for evaluation of the stenotic vessels using conventional angiograms before and after endovascular treatment [14, 15].

Pretreatment of aspirin and clopidrogel were taken to all participants for more than 5 days if they were not already taking these medications. Technical success was defined as a less than 30% residual stenosis after the stent implantation; while, in patients with a stenosis more than 90%, the residual stenosis was extended to approximately 60% in order to reduce the risk of hyperperfusion syndrome postoperatively [16]. During CAS, distal protection devices were used to avoid distal cerebral emboli.

Brain perfusion follow up

Magnetic resonance or CT imaging perfusion data were analyzed on an advanced workstation (SyngoMMWP VE27A, SIEMENS; Advantage 4.2, GE Healthcare). Cerebral blood volume (CBV), cerebral blood flow (CBF), time to peak (TTP) and mean transit time (MTT) were calculated. We divided the brain perfusion into three levels by using a qualitative grading system: 0, the perfusion situation is normal and complete; 1, hypoperfusion were presented by low CBF, delayed TTP, increased MTT, decreased flow, but the CBV is still normal or elevated; or 2, hypoperfusion with declined CBV. At least one level decline of the grading system is considered to be an improvement in perfusion after recanalization [17].

Neurocognitive function evaluation

A series of cognitive tests were assessed in the week before and 120 days after the intervention or conventional angiogram without intervention. A cognitive function evaluation was performed by an independent clinical neurologist, who was blinded to the outcome of the intervention. Functional assessments, including activities of daily living (ADL) and the Barthel Index were used. Cognitive assessments that included the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA) were used.

MMSE is one of the most influential screening tool for cognitive impairment currently; however it does not contain much capacity to test frontal/executive or visuospatial functions and abstraction. Also, MMSE is not sensitive to mild cognitive impairment [18, 19]. In the evaluation of mild cognitive impairment, Montreal cognitive assessment (MoCA) scale as a simple and brief screening tool with high sensitivity for subtle cognitive impairment is superior to the MMSE scale [20-22]. Compared to MMSE, MoCA adds more frontal lobe testing items which reflect the visual space and executive function; it appears that MoCA could be recommended as more appropriate tool for the assessment of cognitive changes in patients with carotid stenosis.

Informed written consent was obtained from all subjects and their relatives. The medical ethics committee of Huanhu Hospital approved this study.

Statistical Analysis

Continuous data are presented as means (SD). Discrete data are presented as counts and percentages. Analysis of variance (ANOVA) was used to compare differences for continuous and normally distributed data, and Chi-square analyses were done for categorical data among the 2 groups (CAS and CTR). Significant main effects in ANOVA were followed up with two-tailed t-tests for post hoc pairwise comparisons. Paired continuous data were compared by the Wilcoxon signed rank sum test. Pearson's correlation coefficients were used to assess the correlation between the change in brain perfusion and the changes in neuropsychological test results. A two-sided P-value <0.05 was considered as a statistically significant difference. Statistical analyses were performed using SPSS 16.0 for Windows (SPSS, Inc., Chicago, IL, USA).

Results

Technical success was achieved in all 105 patients. One patient with a left internal carotid artery occlusion (ICAO) were excluded, because of a small, nonfatal ipsilateral temporal lobe hemorrhage 2 days after successful CAS owing to the complication of right-sided hemiparesis. During the perioperative period, there were no neurologic or vascular complications noted in the remaining 104 patients. After 3 months follow-up, no patients had a new ischemic event according to independent neurologic examination.

Patients were subdivided into 2 groups as follows: CAS (n=83) and routine medical therapy with no intervention for arterial stenosis or occlusion (CTR or control group; n=22). Control group included 14 of them with carotid stenosis or occlusion, and 3 of them with middle artery stenosis or occlusion, and 5 of them with multiple artery stenosis or occlusion. All these control patients gave up stenting because of the potential risk of the interventions after conventional angiograms.

Patients' baseline clinical characteristics and neurocognitive status were similar between the 2 groups. The preprocedural scores from ADL and the results of neuropsychological tests results were similar among 2 groups. The score of MoCA was between 9 and 28. However the score of MMSE was between 11 and 30, including 8 patients with normal score [5].

Table 2 shows neurocognitive scores at baseline and 90 days after the procedures in CAS. Significant improvements in MMSE (CAS 23.9 [4.9] vs 25.4 [4.7] for before and after the procedures; P<0.01), and MoCA (CAS 19.9 [6.4] vs 22.0 [6.0]; for before and after the procedures; P<0.01) were observed. In comparison, there were no significant changes in any test parameters at follow-up in the CTR group. The scores for orientation, delayed recall, abstraction, visuospatial and executive functions, attention and calculation were increased in the CAS group.

Conclusion

Our study suggests that patients harboring carotid artery stenosis or occlusion with a corresponding hypoperfusion derive a cognitive benefit from cerebral revascularization when properly selected for stenting. This study supports the theory that reversal of the hemodynamic disorder may reverse cognitive impairment.

Discussion

In our series of patients, all showed a mild decline in cognition based on MoCA scores and had objective cerebral ischemia suggested from MR or CT hypoperfusion. But based on MMSE scores, 8 patients showed normal (30 score) before intervention. These results indicated MoCA is more sensitive than MMSE on subtle cognitive

Table1. *Baseline characteristics of patients according to different procedures.*

	CAS n=83	**CTR n=22**	**P-value**
Age (years)	64.0 (8.3)	61.7 (9.8)	0.000
Female (%)	14.7	28.6	0.088
Lower education level (≤ 6 years) (%)	32.4	19.0	0.68
Hypertension (%)	76.5	76.2	0.939
Diabetes mellitus (%)	26.5	33.3	0.602
Hyperlipidemia (%)	38.2	33.3	0.940
Prior ischemic stroke (%)	79.4	76.2	0.867
Coronary artery disease (%)	41.2	14.3	0.197
Smokers (%)	76.5	61.9	0.605
Daily alcohol consumption (%)	42.9	52.2	0.578
Body mass index	25.1 (2.5)	25.1 (2.9)	0.480
Hachinski index	3.8 (1.1)	4.1 (2.1)	0.739
MMSE	23.9 (4.9)	25.7 (2.7)	0.155
MoCA	19.9 (6.4)	22.0 (3.9)	0.312
ADL	26.5 (11.5)	28.5 (14.0)	0.837
HAM-D	5.9 (3.8)	7.0 (3.7)	0.654

Data are presented as mean (SD) or number (%).
Abbreviations: ADL, activities of daily living; CAS, carotid artery stenting; CTR, controls; HAM-D, Hamilton-depression; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment.

Table 2. *Neuropsychologic test scores at baseline and follow-up.*

	CAS-B	**CAS-F**	**CTR-B**	**CTR-F**
MMSE	23.9 (4.9)	25.4 (4.7)**	25.7 (2.7)	25.8 (3.0)
Orientation	8.7 (2.1)	9.2 (1.5)*	9.3 (0.9)	9.3 (0.9)
Attention and calculation	2.9 (1.9)	3.6 (1.7)**	3.8 (1.4)	3.8 (1.4)
Registration	2.9 (0.2)	3.0 (0.2)	3.0 (0.2)	3.0 (0.2)
Delayed recall	1.2 (0.9)	1.6 (1.0)*	1.0 (1.0)	1.1 (0.9)
Language and construction	7.1 (1.2)	7.1 (1.3)	8.7 (0.8)	8.7 (0.8)
MoCA	19.9 (6.4)	22.0 (6.0)**	22.0 (3.9)	22.1 (4.1)
Visuospatial/executive	3.2 (1.6)	3.5 (1.5)*	3.7 (1.4)	3.7 (1.4)
Attention	4.8 (1.5)	5.1 (1.5)	5.3 (1.0)	5.3 (1.0)
Delayed recall	1.6 (1.6)	2.1 (1.7)**	1.5 (1.1)	1.6 (1.2)
Naming	2.9 (0.4)	2.8 (0.4)	3.0 (0.2)	3.0 (0.2)
Language	1.4 (0.8)	1.6 (0.8)	1.9 (0.7)	1.9 (0.7)
Abstraction	1.3 (0.7)	1.6 (0.7)**	1.3 (0.9)	1.3 (0.8)
Orientation	4.8 (1.7)	5.2(1.3)*	5.3 (1.0)	5.3 (1.0)

Data are presented as mean (± SD).
*The scores at follow up vs baseline P<0.05.
**The scores at follow up vs baseline P<0.01.
Abbreviations: ADL, activities of daily living; CAS-B, carotid artery stenting-baseline; CAS-F, carotid artery stenting-follow-up; CTR-B, controls-baseline; CTR-F, controls-follow-up; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment.

impairment related to vessel stenosis.

After 3 months of follow-up, CAS treatment group showed neurocognitive improvement according to MMSE and MoCA scores. Global cognitive improvements including orientation, delayed recall, abstraction, visuospatial and executive functions, attention and calculation were observed in the CAS group. This also suggests that MoCA is more suitable to assess the cognitive changes than MMSE, especially for the frontal function.

Several studies have confirmed cerebrovascular stenosis was associated with poorer cognitive performance [23-26]. Others have shown cognitive improvement in patients after carotid endarterectomy [27-30]. However, the effects of carotid stenting on cognitive outcome are controversial [31, 32]. The main factor that may contribute to the diversity in cognitive responses is the detrimental effects of procedural emboli [33-36]. CAS can be widely used in high-risk patients with carotid stenosis because of the development of intervention materials and neuroimaging techniques, especially the distal protection device for cerebral embolism. The safety and effectiveness of CAS has been confirmed by clinical studies [37, 38], and cognitive improvement after CAS has been reported in the several studies [6-13]. Our study also confirmed the safety and effectiveness of CAS. At 3 months follow-up, none of the CAS patients had a new ischemic event.

There were limitaions to this study. Some of the cases underwent CT perfusion (n=10) and most cases underwent MR perfusion (n=94). Most of the stenting cases did not have poststenting perfusion images. Finally, this study included a relatively small population of patients, with only 3 months of follow-up. The control patients were not selected randomized; most of them selected routine medical therapy because of the risk of stenting.

Funding

The project was supported by Tianjin Science and Technology Support Programs (Fundings Number: 12ZCZDSY02900 and 12ZCZDSY01600), Science and technology project of Tianjin Municipal Health Bureau(Funding Number: 11KG117) and Tianjin Natural Science Foundation(Funding Number: 13JCYBJC21300).

References

1. Fergenbaum JH, Bruce S, Spence JD, Lou W, Hanley AJ, Greenwood C. Carotid atherosclerosis and a reduced likelihood for lowered cognitive performance in a Canadian First Nations population. Neuroepidemiology 2009; 33: 321-328.
2. Silvestrini M, Viticchi G, Falsetti L, Balucani C, Vernieri F, Cerqua R. The role of carotid atherosclerosis in Alzheimer's disease progression. J Alzheimers Dis 2011; 25: 719-726.
3. Li J, Wang YJ, Zhang M, Xu ZQ, Gao CY, Fang CQ. Vascular risk factors promote conversion from mild cognitive impairment to Alzheimer disease. Neurology 2011; 76: 1485-1491.
4. Goessens BM, Visseren FL, Kappelle LJ, Algra A, van der Graaf Y. Asymptomatic carotid artery stenosis and the risk of new vascular events in patients with manifest arterial disease: the SMART study. Stroke 2007; 38: 1470-1475.
5. North American Symptomatic Carotid Endarterectomy Trial C. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. N Engl J Med 1991; 325: 445-453.
6. Cheng Y, Wang YJ, Yan JC, Zhou R, Zhou HD. Effects of carotid artery stenting on cognitive function in patients with mild cognitive impairment and carotid stenosis. Exp Ther Med 2013; 5: 1019-1024.
7. Feliziani FT, Polidori MC, De Rango P, Mangialasche F, Monastero R, Ercolani S. Cognitive performance in elderly patients undergoing carotid endarterectomy or carotid artery stenting: a twelve-month follow-up study. Cerebrovasc Dis 2010; 30: 244-251.
8. Grunwald IQ, Papanagiotou P, Reith W, Backens M, Supprian T, Politi M. Influence of carotid artery stenting on cognitive function. Neuroradiology 2010; 52: 61-66.
9. Lal BK, Younes M, Cruz G, Kapadia I, Jamil Z, Pappas PJ. Cognitive changes after surgery vs stenting for carotid artery stenosis. J Vasc Surg 2011; 54: 691-698.
10. Lin MS, Chiu MJ, Wu YW, Huang CC, Chao CC, Chen YH. Neurocognitive improvement after carotid artery stenting in patients with chronic internal carotid artery occlusion and cerebral ischemia. Stroke 2011; 42: 2850-2854.
11. Takaiwa A, Hayashi N, Kuwayama N, Akioka N, Kubo M, Endo S. Changes in cognitive function during the 1-year period following endarterectomy and stenting of patients with high-grade carotid artery stenosis. Acta Neurochir (Wien) 2009; 151: 1593-1600.
12. Ortega G, Alvarez B, Quintana M, Ribo M, Matas M, Alvarez-Sabin J. Cognitive improvement in patients with severe carotid artery stenosis after transcervical stenting with protective flow reversal. Cerebrovasc Dis 2013; 35: 124-130.
13. Raabe RD, Burr RB, Short R. One-year cognitive outcomes associated with carotid artery stent placement. J Vasc Interv Radiol 2010; 21: 983-988.
14. Chimowitz MI, Kokkinos J, Strong J, Brown MB, Levine SR, Silliman S. The Warfarin-Aspirin Symptomatic Intracranial Disease Study. Neurology 1995; 45: 1488-1493.
15. Paulson GW, Kapp J, Cook W. Dementia associated with bilateral carotid artery disease. Geriatrics 1966; 21: 159-166.
16. van Mook WN, Rennenberg RJ, Schurink GW, van Oostenbrugge RJ, Mess WH, Hofman PA. Cerebral hyperperfusion syndrome. Lancet Neurol 2005; 4: 877-888.
17. Group TEIBS: Failure of extracranial-intracranial arterial bypass to reduce the risk of ischemic stroke. Results of an international randomized trial. The EC/IC Bypass Study Group. N Engl J Med 1985; 313: 1191-1200.
18. Nasreddine ZS, Phillips NA, Bedirian V, Charbonneau S, Whitehead V, Collin I. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc 2005; 53: 695-699.

19. Tombaugh TN, McIntyre NJ. The mini-mental state examination: a comprehensive review. J Am Geriatr Soc 1992; 40: 922-935.

20. Meyer JS, Okayasu H, Tachibana H, Okabe T. Stable xenon CT CBF measurements in prevalent cerebrovascular disorders (stroke). Stroke 1984;15: 80-90.

21. Martinic-Popovic I, Lovrencic-Huzjan A, Demarin V. Assessment of subtle cognitive impairment in stroke-free patients with carotid disease. Acta Clin Croat 2009; 48: 231-240.

22. Popovic IM, Lovrencic-Huzjan A, Simundic AM, Popovic A, Seric V, Demarin V: Cognitive performance in asymptomatic patients with advanced carotid disease. Cogn Behav Neurol 2011; 24: 145-151.

23. Hamster W, Diener HC. Neuropsychological changes associated with stenoses or occlusions of the carotid arteries. A comparative psychometric study. Eur Arch Psychiatry Neurol Sci 1984; 234: 69-73.

24. Linfante I, Hirsch JA, Selim M, Schlaug G, Caplan LR, Reddy AS. Safety of latest-generation self-expanding stents in patients with NASCET-ineligible severe symptomatic extracranial internal carotid artery stenosis. Arch Neurol 2004; 61: 39-43.

25. Mathiesen EB, Waterloo K, Joakimsen O, Bakke SJ, Jacobsen EA, Bonaa KH. Reduced neuropsychological test performance in asymptomatic carotid stenosis: The Tromso Study. Neurology 2004; 62: 695-701.

26. O'Brien JT, Erkinjuntti T, Reisberg B, Roman G, Sawada T, Pantoni L. Vascular cognitive impairment. Lancet Neurol 2003; 2: 89-98.

27. Dardik A, Minor J, Watson C, Hands LJ. Improved quality of life among patients with symptomatic carotid artery disease undergoing carotid endarterectomy. J Vasc Surg 2001; 33: 329-333.

28. Hemmingsen R, Mejsholm B, Vorstrup S, Lester J, Engell HC, Boysen G. Carotid surgery, cognitive function, and cerebral blood flow in patients with transient ischemic attacks. Ann Neurol 1986; 20: 13-19.

29. Sinforiani E, Curci R, Fancellu R, Facchinetti P, Mille T, Bono G. Neuropsychological changes after carotid endarterectomy. Funct Neurol , 2001; 16: 329-336.

30. Kelly MP, Garron DC, Javid H: Carotid artery disease, carotid endarterectomy, and behavior. Arch Neurol 1980; 37: 743-748.

31. De Rango P, Caso V, Leys D, Paciaroni M, Lenti M, Cao P. The role of carotid artery stenting and carotid endarterectomy in cognitive performance: a systematic review. Stroke 2008; 39: 3116-3127.

32. Ghogawala Z, Westerveld M, Amin-Hanjani S. Cognitive outcomes after carotid revascularization: the role of cerebral emboli and hypoperfusion. Neurosurgery 2008; 62: 385-395.

33. Braekken SK, Reinvang I, Russell D, Brucher R, Svennevig JL. Association between intraoperative cerebral microembolic signals and postoperative neuropsychological deficit: comparison between patients with cardiac valve replacement and patients with coronary artery bypass grafting. J Neurol Neurosurg Psychiatry 1998; 65: 573-576.

34. Crawley F, Stygall J, Lunn S, Harrison M, Brown MM, Newman S. Comparison of microembolism detected by transcranial Doppler and neuropsychological sequelae of carotid surgery and percutaneous transluminal angioplasty. Stroke 2000; 31: 1329-1334.

35. Grunwald IQ, Supprian T, Politi M, Struffert T, Falkai P, Krick C. Cognitive changes after carotid artery stenting. Neuroradiology 2006; 48: 319-323.

36. Sylivris S, Levi C, Matalanis G, Rosalion A, Buxton BF, Mitchell A. Pattern and significance of cerebral microemboli during coronary artery bypass grafting. Ann Thorac Surg 1998; 66: 1674-1678.

37. Safian RD, Bresnahan JF, Jaff MR, Foster M, Bacharach JM, Maini B. Protected carotid stenting in high-risk patients with severe carotid artery stenosis. J Am Coll Cardiol 2006; 47: 2384-2389.

38. Zahn R, Ischinger T, Hochadel M, Zeymer U, Schmalz W, Treese N. Carotid artery stenting in octogenarians: results from the ALKK Carotid Artery Stent (CAS) Registry. Eur Heart J 2007; 28: 370-375.

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