

Correlation between carotid stenosis and cognitive impairment

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Abstract

Background Severe internal carotid artery stenosis significantly affects the cognitive function of patients, but the effect of different degree and different side of stenosis on cognitive function was still controversial. This study aims to investigate the correlation between different degrees and different sides of internal carotid artery stenosis and cognitive impairment.

Methods There were 34 patients with internal carotid stenosis and 31 controls without stenosis who underwent CTA, DSA, memory scale and modified WCST. Stenosis group was divided into mild stenosis group (n=15) and moderate-severe stenosis group (n=19) according to the degree of stenosis, and was divided into left stenosis group (n=24) and right stenosis group (n=10) according to the sides. Overall vascular examination results, cognitive function scores were computed and analysed.

Results Stenosis group and no-stenosis group did not differ in age, education level, BMI, hyperlipidemia, gender, hypertension, diabetes, smoking drinking and right-handedness. Stenosis group had worse memory scale and modified WCST scores for cognitive function. There were statistically significant differences in memory scale and modified WCST scores between mild stenosis group, moderate-severe stenosis group and no-stenosis group, but no differences between mild stenosis group and moderate-severe stenosis group, no differences between left stenosis group and right stenosis group.

Conclusions Internal carotid artery stenosis affects the cognitive function represented by memory and executive ability significantly.

Background

The incidence of cerebrovascular disease is increasing with the changes of human lifestyle, diet and environment. In the early survey, the rate of intracranial arterial stenosis in Chinese people over 60 years old reached 5.9%~6.9% [1], which can be divided into symptomatic stenosis and asymptomatic stenosis according to clinical manifestations, not only manifested as somatic functional symptoms, but also manifested as non-somatic functional symptoms, which cannot be ignored. According to the scope of vascular blood supply, the frontal temporal lobe and other areas closely related to cognitive function may be affected by cognitive function after ischemia, which may be related to small-vessel disease, decreased cerebral perfusion and pathological changes of neurons and white matter connection fibers.

Vascular cognitive impairment (VCI) [2] is an important subgroups of mild cognitive impairment (MCI) [3, 4], including caused by vascular pathological changes of any level of cognitive impairment, range from the subjective cognitive decline and dementia [2]. Patients with VCI have delayed response and high levels of dysfunction, such as attention, planning, organization, and monitoring, as well as memory impairment, behavioral abnormalities, and depression, other neurological manifestations such as asymmetrical reflexia, dysphonia, Parkinson's disease, rigidity, or urinary incontinence. The course of the disease depends on the type, extent, and location of the underlying cerebrovascular involvement, which is defined to be both MCI diagnostic and vascular based.

Digital subtraction angiography(DSA) is the "gold standard" for the diagnosis of cerebrovascular diseases[5]. Contrast agents are injected into the target blood vessel, and subtraction, enhancement and reimaging are processed by computer to obtain clear pure blood vessel images and real-time display of angiography. CT angiography(CTA) is the rapid injection of contrast agent into the vein of the subject, and it can quickly obtain a large number of thin layer images during the peak period of intravascular contrast agent, and adopt special reconstruction method to display the anatomical details of the vessels, which takes less time, and can replace DSA in the diagnosis of carotid stenosis[6]. Therefore, DSA and CTA were used in this study to evaluate the vascular status of patients. The Wisconsin card sorting test(WCST)[7] is the most commonly used executive function test that evaluates the ability to form abstractions, transform and maintain classifications, and apply feedback. Memory assessment and modified WCST were used to assess the cognitive function of patients.

As for the relationship between vascular stenosis and cognitive function, many studies[8–11] have shown that the treatment of vascular stenosis can improve patients' cognitive function, and the literature has shown that angioplasty, STA-MCA bypass and stent implantation can improve cognitive function to varying degrees. However, the degree of vascular stenosis requiring surgical treatment was severe, and there were few studies on the cognitive impairment caused by different degrees of vascular stenosis. This study was designed to understand the correlation between internal carotid artery stenosis and cognitive function, to deeply understand the correlation between internal carotid artery stenosis at different degrees and different sides and cognitive dysfunction. In order to provide a reference for the diagnosis and treatment of diseases in clinical work, and provide a reference for the further study on the mechanism of cognitive impairment caused by vascular stenosis.

Methods

Patients

This study was a prospective study of patients with stenosis (stenosis group) and no stenosis(no-stenosis group). A total of 65 patients receiving CTA or DSA examination in the department of neurology in a hospital in Sichuan province were included in the study, including 32 females and 33 males. The inclusion criteria were as follows:1) There were no self-reported symptoms and signs of central nervous system dysfunction,including cerebral parenchymal infarction in or old lacunar cerebral infarction in the head CT or MRI,but not in the thalamus,frontal lobe or temporal lobe and other cognition-related parts;2) cerebrovascular CTA or DSA examination was performed for various reasons during hospitalization;3) there was no Transient Ischemic Attack (TIA) or acute cerebral infarction in 3 months;4) non-illiteracy,non-color blindness, education level and vision can cooperate to complete the memory assessment scale and WCST card assessment;5) informed consent of all participants. The exclusion criteria were as follows:1) Patients with cognitive dysfunction caused by neurodegenerative diseases such as Alzheimer's disease(AD) and frontotemporal dementia;2) head CT or MRI indicated intracranial space occupying lesions or hydrocephalus,etc.;3) neuropsychiatric diseases (such as mental diseases, encephalitis, Parkinson's disease, epilepsy, demyelinating disease, neurosyphilis, and brain trauma) that can lead to

cognitive impairment have been clearly diagnosed;4) severe liver and kidney insufficiency,cardiopulmonary insufficiency,hypoglycemia,decreased thyroid function,folic acid and vitamin B12 deficiency and other systemic diseases;5) long-term use of sedative and hypnotic drugs or patients with special history of alcohol abuse and drug abuse that affect cognition.

This study was approved by the local Ethics Committee.Written informed consent was obtained from each participant.

Methods

Cerebrovascular examination

1) CTA:GE Discovery CT750 HD was adopted. Scanning parameters: layer thickness 0.625mm, spacing 0.625mm, 120kv, intelligent mAs;

2) DSA: GE Innova 3100 digital vascular subtraction imaging system was used;3) Diagnostic criteria: According to NASCET[12] standards:0~29% was mild, 30~69% was moderate, and 70~99% was severe.

Cognitive testing

Memory scale and modified WCST were used to assess the patient's cognitive function. Testing was conducted by the person who has received formal training and proficient in operation. The subjects are evaluated at the same time period, and the surrounding environment remains quiet without interference. The total testing time varied from 15 to 30 minutes because of interindividual variability in completion time for test without specific time limits.

Statistical analysis

SPSS 20.0 software (IBM Corp., Armonk, NY, USA) was used for statistical analyses. Continuous variables such as age,education level,BMI,memory score,modified WCST score were expressed as mean \pm standard deviation(SD) and analysed by Student's test. Categorical values such as gender,hypertension,diabetes,hyperlipidemia,smoking,drinking,right-handedness and other counting data were represented as frequencies(percentage,%). T test with two independent samples was used to compare the measurement data between groups.One-way analysis of variance was used to analyze the data among multiple groups of measurement data.P<0.05 was considered statistically significant.

Results

Clinical characteristics

A total of 65 subjects were included in the study.According to the results of CTA and DSA, the subjects were divided into the stenosis group (n=34) and the no-stenosis group (n=31), the stenosis group was further divided into the mild stenosis group (n=15) and the moderate -severe stenosis group (n=19) according to the stenosis degree, and the stenosis group was divided into the left stenosis group (n=24)

and the right stenosis group (n=10) according to the stenosis side again. When comparing the general clinical data of patients in the stenosis group (n=34) and the no-stenosis group(n=31), t test was used for measurement data, and chi-square test was used for counting data. The results showed that there was no statistically significant difference in age, years of education, BMI, history of hyperlipidemia, gender, history of hypertension, history of diabetes, smoking history, drinking history, and right-handedness between the two groups. The detailed results are presented in Table 1 and Table 2.

Table 1 Distribution of internal carotid artery stenosis in enrolled patients

No-stenosis group (n=31)	Stenosis group (n=34)		Total(n=65)
31	34		65
	Left stenosis group	Right stenosis group	
	24	10	34
	Mild stenosis group	Moderate and severe stenosis group	
	15	19	34

Table 2 Clinical characteristics of control group and stenosis group

Characteristics	Stenosis group (n=34)	No-stenosis group(n=31)	Test value	P value
Age(years)	65.03±7.54	60.16±9.55	1.876 ^a	0.066
years of education (years)	7.35±3.15	8.42±3.15	-1.363 ^a	0.178
BMI	23.25±3.09	24.31±2.28	-1.555 ^a	0.125
history of hyperlipidemia	14[41.2]	17[54.8]	1.213 ^b	0.271
Males	19[55.9]	14[45.2]	0.746 ^b	0.388
history of hypertension	23[67.6]	17[54.8]	1.124 ^b	0.289
history of diabetes	8[23.5]	4[12.9]	1.216 ^b	0.27
smoking history	18[52.9]	10[32.3]	2.829 ^b	0.093
drinking history	14[41.2]	8[25.8]	1.711 ^b	0.191
right-handedness	26[76.5]	30[96.8]	0.259 ^b	0.611

a stands for *t* value and b stands for χ^2 value

Comparison of stenosis group and control group

Memory assessment and WCST scores of stenosis group (n=34) and no-stenosis group (n=31) were compared, and the difference was statistically significant (P<0.05). The detailed results are presented in Table 3.

Table 3 Comparison between stenosis group and control group

Group	Stenosis group (n=34)	No-stenosis group (n=31)	t value	P value
Memory assessment	40.44±19.92	57.77±17.94	-3.672	0.000
WCST scores	6.62±2.84	8.42±1.43	-3.272	0.002

Memory assessment and WCST scores of mild stenosis group (n=15), moderate-severe stenosis group (n=19) and no-stenosis group (n=31) were compared, and the difference was statistically significant (P<0.05). The WCST scores of the mild stenosis group (n=15) and the moderate-severe stenosis group (n=19) were compared, and the statistical analysis showed no statistically significant difference (P>0.05). The detailed results are presented in Table 4 and Table 5.

Table 4 Comparison between mild stenosis group, moderate-severe stenosis group and control group

Group	mild stenosis group (n=15)	Moderate-severe stenosis group (n=19)	No-stenosis group(n=31)	F value	P value
Memory assessment	45.63±16.65	36.34±21.72	57.78±17.94	7.872	0.001
WCST scores	6.80±2.89	6.47±2.88	8.42±1.43	5.080	0.009

Table 5 Comparison between mild stenosis group and moderate-severe stenosis group

Group	mild stenosis group (n=15)	Moderate- severe stenosis group (n=19)	t value	P value
Memory assessment	45.63±16.65	36.34±21.72	1.412	0.165
WCST scores	6.80±2.89	6.47±2.88	0.328	0.745

Memory assessment and WCST scores of left stenosis group (n=24),right stenosis group(n=10) and no-stenosis were compared, and the difference was statistically significant (P<0.05). The WCST scores of the left stenosis group (n=24),right stenosis group(n=10) were compared, and the statistical analysis showed no statistically significant difference (P>0.05). The detailed results are presented in Table 6 and Table 7.

Table 6 Comparison between left stenosis group, right stenosis group and no-stenosis group

Group	left stenosis group (n=24)	right stenosis group(n=10)	No-stenosis group(n=31)	F value	P value
Memory assessment	41.69±19.64	37.45±21.36	57.78±17.94	6.847	0.002
WCST scores	7.25±2.33	5.10±3.48	8.42±1.43	8.962	0.000

Table 7 Comparison between left stenosis group and right stenosis group

Group	left stenosis group (n=24)	right stenosis group(n=10)	t value	P value
Memory assessment	41.69±19.64	37.45±21.36	0.54	0.597
WCST scores	7.25±2.33	5.10±3.48	1.794	0.097

Discussion

This study concluded that no matter mild or moderate- severe internal carotid artery stenosis, no matter left or right stenosis, will lead to cognitive dysfunction. It is also confirmed that the etiology of VCI involves many reasons. For patients with severe cerebrovascular stenosis, vascular lesions are likely to cause ischemic brain injury, such as low perfusion, subcortical small infarction, lacunar infarction, micro infarction, white matter injury may also be related to the occurrence of cognitive impairment. Many studies[8–11] have shown that angioplasty, stenting, endarterectomy, sta-mca bypass and other procedure can improve patients' cognitive function to varying degrees, suggesting that cognitive function may be related to brain attention. In other study[13], CT perfusion(CTP) imaging was performed on patients with carotid artery stenosis at different degrees, and the differences in cerebral perfusion results were analyzed in each group. The results showed that the perfusion parameters regional cerebral blood flow (regional cerebral blood flow(rCBF) regional cerebral blood volume (rCBV), mean transit time (MTT), time to peak (TTP) and delay time (DT)) in the mild and moderate stenosis group had no statistical significance, only severe stenosis group showed decreased perfusion. However, in this study, patients with mild and moderate internal carotid artery stenosis still showed decreased cognitive function, the authors speculate that lacunar infarction, demyelination, arteriolosclerosis, Cerebral Amyloid Angiopathy(CAA), and immune response may be related to cognitive decline, except for the causes of reduced cerebral perfusion. Studies[14] have shown that local innate or adaptive immune responses or the removal of damaged proteins are also important for tissue damage and cognitive impairment. Other literatures[15] have mentioned that pathological changes such as neuronal atrophy, oligodendrocyte and astrocyte changes in white matter are related to cognitive decline, and the related pathological changes need to be further confirmed by animal experiments.

With the changes in human diet, environment and lifestyle, 5.9–6.9%[1] of people over 60 years old in China suffer from intracranial arterial stenosis. In this group of patients, asymptomatic stenosis were more likely to be ignored as a risk factor for stroke. The incidence of MCI is high, and the rate of progression to AD is also high[4]. As we all know, the quality of life of AD patients is low, and the high incidence of AD in the population over 60 years old is also a major burden for society and families, therefore, how to effectively prevent MCI has important social significance. Among the many causes of MCI[16], VCI is an important subgroup[17]. A number of studies[8–11] had shown that treatment of intracranial vascular stenosis significantly improved patients' cognitive function. The results of this study showed that no matter what degree and what kind of lateral stenosis were significantly correlated with cognitive function. Therefore, for patients suffering from high blood pressure, diabetes, hyperlipidemia, cerebral infarction, cerebral hemorrhage, loose white matter, and chronic diseases such as cerebral ischemia[18], should be checked as soon as possible and cerebrovascular, diagnosed with asymptomatic stenosis (especially mild to moderate stenosis overlooked inspection) or symptomatic stenosis, and cognitive function checks (such as MMSE, MoCA, WSCT) found MCI or VCI as soon as possible, in time for the secondary prevention drug therapy or surgery can make people better prognosis. As above, early detection, early diagnosis of cerebral vascular stenosis and cognitive dysfunction, treatment for vascular stenosis (including control risk factors, internal medicine improved drug therapy and surgical intervention[19–20]), the reasonable treatment of cognitive impairment (including neurotrophic drugs, brain metabolism activating agent, antioxidant, acetyl choline enzyme inhibitors, exercise training and vascular risk factors, cognitive control of multimode interference[21, 22]), are likely to reduce the incidence of MCI, reduce the possibility of MCI progression to AD, so as to improve the quality of survival, reduce the burden of society and family.

This study sample size was small, considering the scale examination time adherence, cultural level and other factors, represented by using memory assessment scale and improvement of WCST test patients' cognitive function, unable to detailed understanding of naming, attention, language, abstract thinking, and other cognitive functions, it was not the results of the study in the difference between cerebrovascular stenosis with higher nervous function in the field of every detailed correlation, hoping for a larger sample size, a more reasonable inventory check related research confirms that the correlation of internal carotid artery stenosis with MCI.

Conclusions

Internal carotid artery stenosis significantly affects the cognitive function represented by memory and executive ability. The mild stenosis group and the moderate-severe stenosis group, the left stenosis group and the right stenosis group all significantly affected the cognitive function of the patients.

Abbreviations

VCI Vascular Cognitive Impairment

MCI Mild Cognitive Impairment

DSA Digital Subtraction Angiography

CTA CT angiography

WCST The Wisconsin card sorting test

AD Alzheimer's Disease

rCBF regional Cerebral Blood Flow

rCBV regional Cerebral Blood Volume

MTT Mean Transit Time

TTP Time To Peak

DT Delay Time

CAA Cerebral Amyloid Angiopathy

Declarations

Ethics approval and consent to participate

This study was approved by the ethics committee of The Second People's Hospital of Chengdu. All the patients involved in this study were introduced with the collection and usage of the tissues when they were conscious and had the capacity of independent decision-making. Written consent was obtained directly from each participant that was approved by the ethics committee of The Second People's Hospital of Chengdu.

Consent for publication

Written informed consent for publication was received from all the patients.

Availability of data and material

The dataset analysed are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Yao Huang performed the cognitive testing and wrote the manuscript. Lanying He and Feng Wang contributed with clinical information of the study. Yuanye Ma and Yao Huang carried out the study design. All authors read and approved the final manuscript.

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