

Clinical research of collateral circulation in patients with severe internal carotid artery stenosis

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Abstract: To observe the relationship between collateral circulation with cerebral infarction and neurological deficit in patients with severe internal carotid artery stenosis. 108 patients were selected who are unilateral internal carotid artery severe stenosis and were compared the incidence of cerebral infarction and type of infarction and NIHSS score. Among the 108 patients, 54 patients were first collateral circulation, while 20 patients were cerebral infarction. 35 patients were secondary collateral circulation, while 25 patients were cerebral infarction. 19 patients were without cerebral infarction, while 17 patients were cerebral infarction. The difference of collateral circulation has statistically significant ($P < 0.01$). The difference of cerebral infarction type caused by different collateral circulation was not statistically significant ($P < 0.01$). Neurological function scores of patients were statistically significant who were different collateral circulation ($P < 0.01$). There were significant differences in the incidence of cerebral infarction, the type of cerebral infarction and the neurological deficit of the patients with different collateral circulation. There was obvious in protective effect of cerebral collateral circulation on the brain.

Keywords: Severe internal carotid artery stenosis; Collateral circulation; Acute cerebral infarction; Digital subtraction angiography

Received 24 October 2017, Revised 2 January 2018, Accepted 5 January 2018

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1. Introduction

Ischemic cerebrovascular disease is a disease with high incidence, high disability rate, high recurrence rate and high mortality rate, which is one of the three diseases that seriously endanger the health of the Chinese people. It has aroused extensive attention, and its prevention and control has become a hot topic. The patient's clinical symptoms and treatment outcomes vary widely. Recent studies have found that when one or both sides of the internal carotid artery supply arteries are severely narrowed, the symptoms and types of cerebral infarction vary greatly among patients. Some patients present with cerebral infarction and transient ischemic attack, while some patients present without any symptoms. The establishment of the effective collateral circulation is the key factor, which can reduce the infarct area, improve the prognosis and reduce the risk of recurrence. Therefore, understanding the compensation of collateral circulation has important clinical value. With the development of medical imaging technology, especially the development of DSA, we can accurately evaluate the collateral circulation compensation of cerebral vessels. The purpose of this study was to investigate the relationship between collateral circulation and cerebral infarction and neurological deficits in patients with severe stenosis of unilateral internal carotid artery.

2. Objects and methods

2.1. Objects

A total of 108 patients in the Department of Neurology of Affiliated Hospital of Qingdao

University from June 2015 to May 2017 were enrolled in this study. Among them, there were 86 males and 22 females, aged 37-82 years old, with an average age of 68.2 ± 12.37 years old. They were the patients with severe stenosis at the beginning of the unilateral internal carotid artery who had cerebral infarction, or hemiplegia, partial sensory disorders, dizziness and other symptoms of ischemic cerebrovascular disease recently, and confirmed by DSA.

2.2. Methods

All patients underwent femoral artery puncture by using Seldinger technique. They were confirmed by DSA for severe stenosis at the beginning of the unilateral internal carotid artery with a stenosis of 70%-99%. The NASCET was used to evaluate the severe stenosis of internal carotid artery: Stenosis = $1 - \text{vessel diameter at the narrow place} / \text{distal normal vessel diameter}$ [1]. The brain MRI diffusion weighted imaging (DWI) showed a new onset of cerebral infarction after the onset of the disease, and they were divided according to the location of cerebral infarction, referring to related literature[2]: Regional infarction, watershed infarction (external watershed infarction, internal watershed infarction), perforating regional infarction. For each patient performed DSA, imaging results were read by two interventional physicians over the positional title of associate chief physician by blind method, to assess the collateral circulation of the patients belonging to primary or secondary collateral compensation. The neurological function score was scored by the National Institutes of Health Stroke Scale[3].

Table 1. Relationship between different collateral circulation and cerebral infarction

Group	Number of cases	Is there any cerebral infarction in 3 months?	
		Yes	No
Primary collateral circulation compensation group	54	20	34
Secondary collateral circulation compensation group	35	25	10
No collateral circulation compensation group	19	17	2
Statistic		$\chi^2=19.968$	$P<0.01$

Table 2. the relationship of collateral circulation and the different types of cerebral infarction

Group	Number of cases	Watershed infarction	Regional infarction	Perforating regional infarction
Primary collateral circulation compensation group	20	15	3	2
Secondary collateral circulation compensation group	25	5	15	5
No collateral circulation compensation group	17	2	13	2

2.3. Inclusion and exclusion criteria

Inclusion criteria: (1) patients with severe stenosis in the origin of one side of the internal carotid artery confirmed by DSA, with complete clinical data; (2) The severe stenosis at the beginning of the unilateral internal carotid artery was responsible for the symptoms; (3) The diagnostic criteria of cerebral infarction referred to the < Guidelines for the diagnosis and treatment of acute ischemic stroke in 2014[4].

Exclusion criteria: (1) The symptoms of ischemic cerebrovascular disease were not caused by severe stenosis at the beginning of the unilateral internal carotid artery. (2) Suffering from serious liver and kidney disease, blood system diseases, autoimmune diseases and other basic diseases. (3) The lack of clinical data and have difficulty in the assessment.

2.4. Statistical analysis methods

SPSS 20 software package was used for statistical analysis. The *t test* was used for measurement data. Enumeration data were checked by chi square test. $P < 0.05$, the difference was statistically significant.

3. Results

3.1. The relationship between compensation of different collateral circulation and cerebral infarction

In this study, there were 54 cases of primary collateral compensation, 35 cases of secondary collateral compensation, and 19 cases of no collateral compensation. In patients with primary collateral circulation compensation, 20 patients suffered from cerebral infarction. In patients with secondary

collateral circulation compensation, 25 patients suffered from cerebral infarction. In patients with no collateral circulation compensation, 17 patients suffered from cerebral infarction, $\chi^2=19.968$, $P<0.01$. After the pairwise comparison of the primary and secondary collateral circulation compensation, $\chi^2=10.048$, $P<0.01$, the difference was statistically significant. After the pairwise comparison of the primary and no collateral circulation compensation, $\chi^2=15.461$, $P<0.01$, the difference was statistically significant. After the comparison of the secondary and no collateral circulation compensation, Fisher's exact probability=0.178, the difference was not statistically significant (See in Table 1).

Table 3. Relationship between different collateral circulation and neurological impairment

Group	Number of cases	NIHSS score
Primary collateral circulation compensation group	54	2.91 ±1.17
Secondary collateral circulation compensation group	35	4.77 ±1.83
No collateral circulation compensation group	19	7.21 ±1.44

3.2. Relationship between different collateral circulation compensation and the different types of cerebral infarction

Among the patients with primary collateral

circulation compensation, there were 15 cases of watershed infarction, 3 cases of regional infarction, and 2 cases of perforating regional infarction. Among the patients with secondary collateral circulation compensation, there were 5 cases of watershed infarction, 15 cases of regional infarction, and 5 cases of perforating regional infarction. Among the patients with no collateral circulation compensation, there were 2 cases of watershed infarction, 13 cases of regional infarction, and 2 cases of perforating regional infarction. Fisher's exact probability <0.01 , the difference was statistically significant. After the pairwise comparison of the primary and secondary collateral circulation compensation, Fisher's exact probability <0.01 , the difference was statistically significant. After the pairwise comparison of the primary and no collateral circulation compensation, Fisher's exact probability <0.01 , the difference was statistically significant. After the pairwise comparison of the secondary and no collateral circulation compensation, Fisher's exact probability $=0.721$, the difference was not statistically significant (See in Table 2).

3.3. Relationship between different collateral circulation compensation and neurological impairment

Patients with primary collateral compensation had an NIHSS score of 2.91 ± 1.17 . Patients with secondary collateral compensation had an NIHSS score of 4.77 ± 1.83 . Patients with no collateral compensation had an NIHSS score of 7.21 ± 1.44 . After the pairwise comparison of the primary and secondary collateral circulation compensation, $t = -5.864$, $P < 0.01$, the difference was statistically significant. After the pairwise comparison of the primary and no collateral

circulation compensation, $t = -12.979$, $P < 0.01$, the difference was statistically significant. After the pairwise comparison of the secondary and no collateral circulation compensation, $t = -5.017$, $P < 0.01$, the difference was statistically significant.

4. Typical case analysis

4.1. Primary collateral circulation compensation

The patient was male and aged 69 years old. He was admitted to the hospital because of paroxysmal dizziness for 2 months, accompanied by left limb weakness and 3 days of active failure. DSA showed severe stenosis at the beginning of the right internal carotid artery. The intracranial angiography showed no development of the right anterior cerebral artery. Contralateral internal carotid angiography showed the opening and compensation of anterior communicating artery for the right anterior cerebral artery. MRI showed new cerebral infarct in right inner watershed and near the lateral ventricle, see Figure 1.

4.2. Secondary collateral circulation compensation

The patient was male and aged 74 years old. He was admitted to the hospital because of paroxysmal dizziness for 10 years and aggravation for 1 month. DSA showed severe stenosis at the beginning of the left internal carotid artery. The intracranial angiography showed blurred development of the left anterior cerebral artery and insufficient blood flow. Vertebral artery angiography showed the compensation of leptomeningeal branch of left posterior cerebral artery for the supply area of left anterior cerebral artery. The MRI of the patient showed a new infarct in the left frontal lobe, see Figure 2.

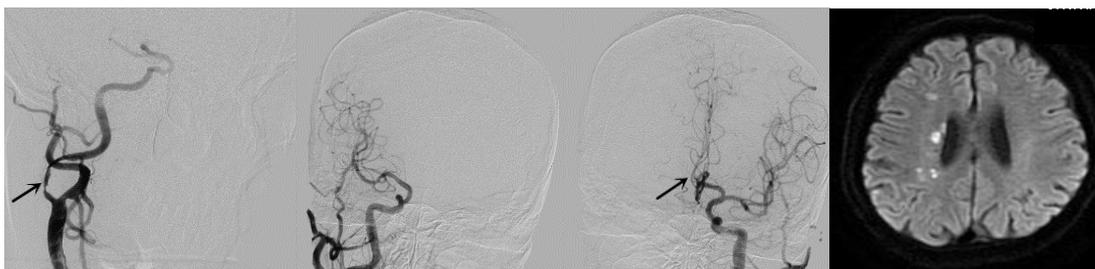


Figure 1. MRI for new cerebral infarct in right inner watershed and near the lateral ventricle.

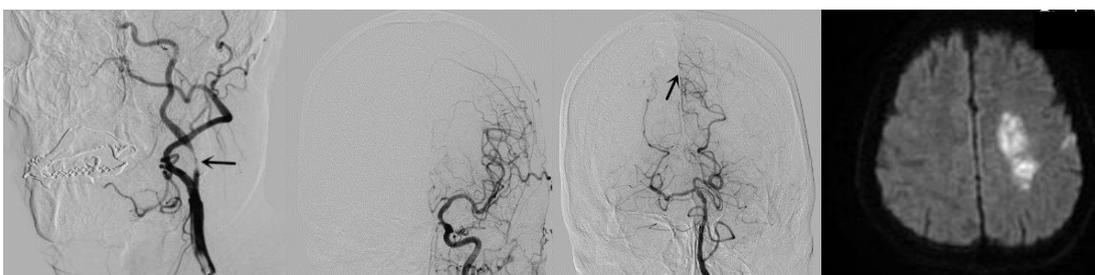


Figure 2. MRI for a new infarct in the left frontal lobe.

5. Discussion

The internal carotid artery is one of the important supply arteries of the brain, and the severe stenosis of the internal carotid artery is one of the main causes of ischemic cerebrovascular disease. We found in clinical practice that when one side of the internal carotid artery started severe stenosis, and even bilateral severe stenosis occurred in the internal carotid artery, there could be severe cerebral ischemia symptoms such as extensive cerebral infarction, and there can also be no symptoms. Some scholars thought that the important reason was because of the difference in the formation of collateral circulation of each patient[5]. The collateral is the adjacent structure of the blood vessel. There are collateral vessels in various parts of the body. The collateral compensation of cerebral vascular system is divided into three levels: (1) Primary collateral compensation refers to the Willis'circle composed of the anterior communicating artery, posterior communicating artery, end of the internal carotid artery, A1 segment of anterior cerebral artery and other components. (2) Secondary collateral compensation refers to that the external carotid artery provide compensation for the internal carotid artery system through the ophthalmic artery and the middle meningeal artery, or intracranial leptomeningeal collateral artery makes it the intracranial vessels compensate for each other. (3) Tertiary collateral circulation refers to that Intracranial new vessels form the compensation[6-7]. It is because the collaterals of each person are different, leading to different clinical symptoms. Among them, the opening of Willis'circle is the most important, and the related research is also more [8]. When the Willis'circle is intact, primary collateral compensation is the first to open, mainly the anterior communicating artery or the posterior communicating artery to supply the affected side. If primary collaterals cannot meet the need for perfusion, or because of the variation of Willis'circle, primary collateral compensation cannot be provided. Due to the presence of collateral anastomoses between the internal carotid artery and the external carotid artery, as well as a large number of anastomoses between the cerebral hemisphere and cerebellar pia mater, the secondary branches open immediately. The degree of openness is closely related to primary collateral compensation and is time dependent. Because of its limited compensatory capacity, the secondary collateral opening is a sign of hemodynamic impairment, which is closely related to the severity of clinical symptoms[9].

The assessment of cerebrovascular collateral circulation is divided into structural and functional assessment[10-11]. The collateral circulation is assessed by means of TCD, CTA, MRA, DSA, and so on. The DSA is an invasive method, and there are various side effects, but DSA is still the current gold standard for assessment of collateral circulation[12], and the accuracy of collateral circulation assessment is

significantly higher than that of CTA, MRA, TCD, etc. Therefore, this study used DSA to assess collateral circulation compensation in patients.

In this study, there were significant differences between the opening of collateral circulation and the incidence of cerebral infarction and the types of cerebral infarction. Collateral circulation is an independent risk factor of cerebral infarction[13]. The more collateral circulation is, the more effective it is to maintain the perfusion of ischemic penumbra. The survival time of the brain tissue is increased, and the infarct size is smaller[14-15].

Yuh reported that brain tissue of ischemic penumbra after cerebral infarction mainly rely on collateral protection. The more the collateral circulation is, the lighter the clinical symptoms are[16]. In this study, the incidence of infarction in patients with primary collateral circulation was lower than in patients with secondary collateral circulation and no collateral circulation. The patients with primary collateral circulation were mainly watershed infarction. The patients with secondary collateral circulation and no collateral circulation were mainly regional infarction. Then, Cassot[17] established the primary collateral compensatory blood supply model, and found that the size of the anterior communicating artery diameter significantly affected the perfusion pressure of the cerebral blood vessels in the ischemic region, which proved the important role of primary collateral compensation. Muller[18] found that when the secondary collateral circulation opened to supply the blood to the brain, intracranial hypoperfusion was indicated. The symptoms of patients were significantly worse than those in patients with primary collateral circulation.

In this study, NIHSS scores were scored within one week after admission. At present, the main treatment of cerebral infarction is recanalization of the vessels. Collateral circulation provides blood flow to the brain tissue that blocks the supply of blood to the arteries. If cerebral ischemia rapidly promotes the establishment of collateral circulation and microvascular formation in ischemic tissue, it will be important for the protection of ischemic tissue and the recovery of neurological function after ischemia[19]. It shows that good collateral compensation plays an important role in improving the blood perfusion and protecting the nerve function of the brain in the affected side of the internal carotid artery stenosis.

To sum up, the effective collateral circulation especially the primary collateral circulation can significantly reduce the incidence of cerebral infarction in patients with severe stenosis of internal carotid artery and reduce the severity of infarction. Collateral circulation also plays an important role in the protection of nerve function. However, due to the heterogeneity of population (Asian population and Caucasian population), the difference of risk factors in the enrolled patients, the nature of atherosclerotic plaques and the limitations of various means of

inspection, the preliminary results of this study still need to be further.

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