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Original Article

Therapeutic effect of carotid artery stenting versus endarterectomy for patients with high-risk carotid stenosis

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Abstract: Objective: To investigate therapeutic effect of carotid artery stenting versus endarterectomy for patients with high-risk carotid stenosis. Methods: A total of 130 carotid stenosis patients at high-risk of stroke were randomly divided into stenting group and endarterectomy group, including 65 patients in each group. The patients in the endarterectomy group underwent endarterectomy and those in the stenting group received carotid artery stenting for treatment. Results: After operation, carotid intima-media thickness (IMT), plague areas and carotid artery resistance indexes in both groups decreased significantly, and the carotid artery peak blood flow velocities increased significantly and had significant differences with that before operation ($P < 0.05$). After operation, total cholesterol (TC), triglyceride (TG) and low density lipoprotein (LDL) values in two groups all significantly decreased, and intragroup and intergroup differences were statistically significant ($P < 0.05$). Postoperative three months of followed-up found that the mortality rate in stenting group was 1.5% and that in the endarterectomy group was 9.2%; the mortality rate in the stenting group was significantly lower than the endarterectomy group ($P < 0.05$). Conclusion: Compared with carotid endarterectomy, application of carotid artery stenting can effectively promote patency of blood flow in the carotid artery, and exertion of its effect is related to lowering lipid and lowering inflammatory factor expression.

Keywords: Carotid stenosis, endarterectomy, vascular stenting, resistance index, blood lipids, inflammatory factor

Introduction

Carotid stenosis is an important cause of stroke and has become the leading cause of adult disability today [1]. A survey shows that now about a quarter of the incidence of stroke is related to carotid atherosclerotic stenosis, which is a clinically important high-risk disease [2]. At present, a study shows that presence of carotid stenosis, severity, progression situation and shedding of atheromatous embolus all play important roles in the pathogenesis of stroke [3]. Lowering blood lipids and expanding blood vessels are helpful to prevent the occurrence and development of carotid stenosis, thereby reducing the incidence of stroke. Currently clinical interventions for high-risk carotid stenosis mainly include drug treatment, surgical operation and interventional treatment [4]. Among them, drug treatments were used for anti-platelet aggregation, anticoagulation, lowering blood lipids, lowering blood pressure, controlling blood sugar, etc. and can effectively relieve symptoms, but do not significantly improve the pathological stenosis [5]. In interventional and surgical treatments, currently carotid endarterectomy (CEA) is used as the classic operation for treating carotid stenosis and preventing stroke, and with the increase of carotid stenosis detection rate, its application gradually increases; surgery has become the gold standard of treating severe carotid stenosis, however, it can cause some trauma to patients, leading to postoperative inflammation, such as increase of C reactive protein (CRP) level [6, 7]. In recent years, with the rapid development of minimally invasive interventional technique, carotid artery stenting (CAS) has become a safe and effective means for treating carotid stenosis [8]. Therefore, this study has specially compared the prognostic effects of carotid endarterectomy and stenting in high-risk carotid stenosis patients.

Materials and methods

Study subjects

From September 2011 to November 2013, patients at high-risk of stroke who were hospitalized in our hospital were selected, and inclusion criteria were: Meeting the diagnostic criteria for patients at high-risk of stroke; angiographically confirmed carotid stenosis (common carotid artery trunk and (or) bifurcation and (or) the initial segment of the internal carotid artery) and the degree of stenosis ≥ 50%; consent of a patient and his (her) relative; expected survival of more than one month; existence of complete follow-up data. Exclusion criteria were: A patient with abnormal heart, liver, kidney and other functions; dropouts during the study; pregnant and postmenopausal women. The selected patients included 67 males and 53 females; the youngest one was 46 years old and the oldest one was 78 years old with average of 60.52 ± 6.53 years old; concomitant diseases were: 56 cases of hypertension, 32 cases of diabetes, 23 cases of hyperlipidemia; mean body mass index (BMI) was 23.29 ± 2.89 kg/m^2; average years of education were 13.22 ± 3.08 years; 122 patients were accompanied with carotid atherosclerotic plaques. According to the principle of randomly drawing lots, the patients were divided into the stenting and the endarterectomy group, including 65 patients each group, and there was no statistically significant difference in gender, age, comorbidities, disease status, BMI and years of education between two groups ($P > 0.05$).

Treatment regimen

The endarterectomy group: The patients underwent endarterectomy for treatment. Cervical plexus local anesthesia or general anesthesia was performed. An incision in the neck was selected to expose the carotid artery. A plastic tube was inserted into both ends of the blocked carotid artery so as to ensure blood to run into the brain during stripping the atherosclerosis plaque. Next, endarterectomy was performed. After the atherosclerosis plaque was stripped, the arterial wall was sutured, the bypass tube was withdrawn, and the dacron patch was used to suture the carotid artery. Finally, the skin was sutured and routine drainage was performed.

The stenting group: The patients underwent carotid artery stenting for treatment. Through the femoral artery, Seldinger technique was used to insert a 90 cm 8F long sheath, which coordinated with a 300 cm alternating guide wire and a 125 cm angiography tube to constitute a triangle long sheath system; then, a superhard guide wire was used to send the triangle long sheath system to the site of the carotid stenosis for performing carotid angiography and clarifying the nature of the stenosis part. An appropriate stent was selected. Under the guide of angiography, through the triangle long sheath system the 300 cm alternating guide wire was sent to petrous segment level of the carotid artery and then the stent system was sent to the site of the carotid stenosis. After confirmation of angiography, a self-expanding stent was released.

Symptomatic treatments including antihypertensive, lipid-lowering and sugar-lowering treatments were actively given to all patients; routine oral aspirin was also given, and platelet function was periodically reexamined and according its result, aspirin dose was adjusted; if the efficacy was not good, clopidogrel was added.

Ultrasound observation

Carotid ultrasonography was performed by using an American HD15000-type color ultrasound instrument; frequency of the superficial probe was 6.0-7.5 MHz; the examined sites included bilateral common carotid artery, internal carotid artery. Longitudinal section examination along the blood vessels was performed for measuring and calculating carotid intima-media thickness (IMT) and the plaque's largest area, and the measurement was performed one month before and after operation. Meanwhile, color blood flow signals were used to observe blood filling, and pulsed Doppler was used to measure blood flow spectrum. Sampling volume was placed at the brightest color blood flow in the blood vessel longitudinal section; blood flow spectrum was displayed during continuous three cardiac cycles, and image was frozen for measurement and the average value was taken. The indicators for measurement and calculation included the common carotid artery' carotid artery resistance index and carotid artery peak blood flow velocity, etc., and the measurement was also

Table 1. Comparison of IMT and plaque area before and after operation between two groups

Group	Number of cases (n)	IMT (mm)		Plaque area (%)	
		Before treatment	After treatment	Before treatment	After treatment
Stenting	65	3.94 ± 0.06	0.61 ± 0.04	65.21 ± 3.62	35.96 ± 4.25
Endarterectomy	65	3.95 ± 0.05	0.85 ± 0.10	64.63 ± 4.88	13.96 ± 5.26
t		0.067	6.098	0.189	12.343
P		> 0.05	< 0.05	> 0.05	< 0.05

Table 2. Comparison of carotid artery resistance index and carotid artery peak blood flow velocity before and after operation in two groups

Group	Number of cases (n)	Resistance index (mm)		Peak blood flow velocity (cm/s)	
		Before treatment	After treatment	Before treatment	After treatment
Stenting	65	0.76 ± 0.08	0.62 ± 0.08	62.45 ± 11.28	66.98 ± 10.23
Endarterectomy	65	0.76 ± 0.19	0.73 ± 0.10	62.43 ± 9.54	64.99 ± 8.34
t		0.034	5.409	0.056	5.343
P		> 0.05	< 0.05	> 0.05	< 0.05

performed one month before and after operation.

Blood indicator detection

The fasting venous blood of all patients was collected for test in the morning at the same time point and the test was performed in the clinical laboratory in our hospital. The tested indicators included total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL) and C-reactive protein (CRP) levels, and their determination was completed by using a Japanese Au640 automatic biochemical analyzer. Meanwhile, all patients were followed up for 6 months for observing prognosis and death situations.

Statistical analysis

SPSS statistical software (version 19.5) was used for statistical analysis, t test and correlation analysis of variance were used for comparison of measurement data and chi-square analysis was used for comparison of enumeration data; $P < 0.05$ illustrated that the difference was statistically significant.

Results

Comparison of IMT and plaque area changes

Before operation, there was no statistically significant difference in IMT and plaque area between both groups. After operation, above values all significantly decreased ($P < 0.05$) and meanwhile the intergroup difference was statistically significant ($P < 0.05$). See **Table 1**.

Comparison of carotid artery resistance index and carotid artery blood flow peak velocity

After operation, carotid artery resistance indexes in both groups decreased significantly, and the carotid artery peak blood flow velocities increased significantly and had significant differences compared with before operation ($P < 0.05$); meanwhile, after operation, comparison of above values in two groups had statistically significant difference ($P < 0.05$). See **Table 2**.

Comparison of lipid changes

After operation, TC, TG and LDL values in two groups all significantly decreased, and intragroup and intergroup differences were statistically significant ($P < 0.05$). See **Table 3**.

Comparison of CRP changes

Determination showed that postoperative serum CRP values in two groups all significantly decreased, while intragroup and intergroup differences were statistically significant ($P < 0.05$). See **Table 4**.

Comparison of follow-up of death situation

Postoperative three months of followed-up found that the mortality rate in the stenting group was 1.5% (1/65) and that in the endarterectomy group was 9.2% (6/65); the mortality

Table 3. Comparison of lipid changes before and after operation between two groups (mmol/L)

Group	Cases (n)	TC		TG		LDL	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Stenting	65	8.62 ± 0.62	4.52 ± 0.65	3.26 ± 0.52	1.34 ± 0.42	4.25 ± 0.22	1.48 ± 0.46
Endarterectomy	65	8.62 ± 0.82	5.12 ± 0.52	3.27 ± 0.11	2.14 ± 0.50	4.26 ± 0.29	2.33 ± 0.56
t		0.034	3.089	0.167	4.232	0.156	4.872
P		> 0.05	< 0.05	> 0.05	< 0.05	> 0.05	< 0.05

Table 4. CRP changes before and after operation in two groups (mmol/L)

Group	Cases (n)	Before treatment	After treatment
Stenting	65	13.64 ± 0.62	5.52 ± 0.65
Endarterectomy	65	13.63 ± 0.52	7.12 ± 0.82
t		0.045	4.560
P		> 0.05	< 0.05

rate in the stenting group was significantly lower than the endarterectomy group (χ^2 = 3.542, P < 0.05).

Discussion

At present, cerebrovascular disease deaths have been ranked first of all diseases in our country. Number of the patients is over three million, among whom the stroke accounts for about 75%. Once cerebral infarction occurs, besides relatively high mortality rate, about 60% of survivors have sequelae of paralysis, aphasia and other severe disabilities, bringing a heavy burden to society and families [9]. An epidemiological survey shows that among stroke patients, about 50% patients have ipsilateral extracranial carotid stenosis and also shows that the occurrence of the disease is related to atherosclerotic lesion at common carotid artery bifurcation [10]. A study in our country shows that carotid stenosis with 50% degree increases stroke risk by 4%, carotid stenosis with 75% degree increases stroke risk by 15%, and carotid stenosis with 85% degree increases stroke risk by 35% six months later and by 46% one year later [11]. With the development of society and economy, popularization of bad lifestyle, the aging of the society as well as increase of hypertension and diabetes and other internal medicine diseases, incidence of carotid stenosis shows a significantly increasing trend [12]. Moreover, carotid stenosis is a progressive disease that can progress to complete carotid artery occlusion or irreversible functional damage, thus early intervention treatment is very important for preventing and slowing progression of carotid stenosis [13].

In treatment aspect, carotid endarterectomy has been recognized up to now as the standard for treating carotid stenosis. The operation mainly completely strips the carotid atherosclerotic plaque restricting blood supply of the brain, therefore, the diseased internal carotid artery restores patency and vitality again, and relatively good results can be achieved; however, its clinical application has a certain degree of trauma for patients, and postoperative luminal stenosis and thrombosis easily occur so that the prognosis and effect are not good [14]. With development of medical technology, the effectiveness of carotid artery stenting has been widely confirmed. Compared with carotid endarterectomy, invasiveness of stenting is smaller, and it is more suitable for patients with severe heart and lung complications and can effectively reduce risk. Moreover, stenting more easily reaches lesion site of carotid stenosis of patients who have undergone operation or radiation therapy, and for patients with stenosis extending to the base of the skull, stenting can be used to perform the same treatment [15, 16]. Before operation, comparison of IMT and plaque area between two groups had no statistically significant difference; after operation, above values all significantly decreased (P < 0.05), while intergroup difference was also statistically significant (P < 0.05). The postoperative carotid artery resistance indexes in two group decreased significantly, while the carotid artery peak blood flow velocities increased significantly and had significant differences compared with preoperative values (P < 0.05) and at the same time postoperative intergroup

comparison of above values had statistically significant difference ($P < 0.05$).

Postoperative three months of followed-up found that the mortality rate in the stenting group was 1.5% and that in the endarterectomy group was 9.2%; the mortality rate in the stenting group was significantly lower than the endarterectomy group ($P < 0.05$), indicating that stenting application can continue to play a role in promoting improvement of blood flow in the carotid artery and expanding the lumen, thereby can improve the prognosis.

In the treatment of carotid stenosis, that blood lipids have been lowered is half the success. Application of stenting improves endothelial function and also can effectively reduce plasma total cholesterol and apolipoprotein B in patients with hypercholesterolemia and mixed lipid metabolism disorder [17]. The results of this study have shown that after operation, TC, TG and LDL values in two groups all significantly decreased and in intragroup and intergroup comparisons ($P < 0.05$). Current inflammation plays an important role in occurrence and development of carotid stenosis; CRP is considered as a strongest indicator among inflammatory markers for predicting carotid stenosis event, and the elevated CRP level is an independent risk factor of carotid stenosis [18, 19]. In this paper, postoperative serum CRP levels in two group all significantly decreased, and meanwhile in intragroup and intergroup comparisons ($P < 0.05$).

In summary, compared with carotid endarterectomy, application of carotid artery stenting can effectively promote patency of blood flow in the carotid artery, and exertion of its effect is related to lowered lipid and lowered inflammatory factor expression.

Disclosure of conflict of interest

None.

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