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*Original Article*

# Comparative efficacy and safety of carotid endarterectomy and carotid angioplasty stenting in the treatment of asymptomaticcarotid artery stenosis

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**Abstract:** Objective: To compare the efficacy and safety of two methods in the treatment of carotid artery stenosis (CAS) and carotid endarterectomy (CEA) in elderly patients with asymptomatic carotid stenosis. Methods: Retrospective analysis method was used to collect 86 gerontal patients diagnosed with asymptomatic carotid artery stenosis (ACAS) in our hospital from January 2011 to January 2015. Then they were divided into two groups, CEA group (n=28) and CAS group (n=58). The patients' hospital day, scores of National Institutes of Health Stroke Scale (NIHSS) before and after treatment, peak systolic blood flow velocity and stenosis of the original stenosisone month, six months and one year before and after treatment, and the incidence rate of ipsilateral stroke, myocardial infarction, cerebral apoplexy, delayed intracranial hemorrhage and death and other endpoints were observed and compared. Results: CEA group of 28 patients with successful recanalization, group CAS recanalization was basically successful in 58 cases. The differences of hospital day and NIHSS scores (≥20) both had statistically significance between two groups after treatment ($P<0.05$). Obvious differences were detected in the degrees of carotid stenosis between two groups before and after treatment by Doppler ultrasound ($P<0.05$). Within one month after treatment, the cumulative incidence of endpoints between two groups had statistically significance ($P<0.05$), from 1 month to 1 year, the cumulative incidence of end point events showed no significant difference ($P>0.05$). The incidence of restenosis in CAS group was higher than that in CEA group. Conclusion: There is no significant difference in the efficacy of gerontal ACAS between CEA group and CAS group. However, CAS is more widely used in clinic for short hospital days, small trauma, fast recovery and high safety.

**Keywords:** Asymptomaticcarotid artery stenosis, carotid endarterectomy, carotid angioplasty stenting

## Introduction

With the ongoing increase in the number of aging population, the proportion of senior citizens in China aged 60 and above has rose 2.93% compared with the fifth national census in 2000, reaching 178 million in the sixth national census in 2010. The incidence of ACAS becomes higher in the senior citizens because of the inconspicuous symptoms and their high incidence of arteriosclerosis. The main cause of ACAS is atherosclerosis, and it can also be seen in the carotid artery dissection, and autoimmune, development and inflammation related vascular lesions [1]. In 1905, Chiari first reported extracranial carotid artery occlusive disease and emphasized that atherosclerosis in carotid artery bifurcation and embolus produced by plaque shedding were the direct causes of ischemic cerebrovascular disease [2]. With the aggravation of carotid artery stenosis, ischemic cerebrovascular disease will develop from transient cerebral insufficiency to cerebral apoplexy, which has been one of the three most common diseases in the world and can easily cause permanent disability [3]. Also, cerebral apoplexy can make gerontal patients bedridden and harm the quality of their lives, along with many complications such as vein thrombosis, pulmonary infectious and bedsore, etc. That is why the therapy of carotid artery stenosis becomes so important. Today CAS and CEA are mainly used in those patients with ACAS, for whose drug conservative treatment is ineffective. Recent studies have found that CEA is the traditional therapy method of extracranial

**Table 1.** General information of CAS group and CEA group

| Clinical features | | CAS group (n=58) | CEA group (n=28) | *P* value |
|---|---|---|---|---|
| Gender | Male | 42 | 21 | 0.07 |
| | Female | 16 | 7 | 0.06 |
| Age | | 66.4±3.7 | 65.1±2.9 | 0.12 |

carotid atherosclerotic stenosis and has become the gold standard in the treatment of symptomatic carotid artery stenosis, while its efficacy in the treatment of ACAS is not as significant as CAS [4]. Some studies, however, indicated that there was no difference in the efficacy of CEA and CAS on ACAS, meanwhile they also found that the postoperative incidence of complications such as restenosis in CAS is higher than CEA. The application of embolic protection device (EPD) greatly improved the safety of CAS and made it possible to be another important therapeutic option except CEA. But for the choice of the two treatment methods, domestic and foreign scholars have different opinions, the corresponding reports are also few. To investigate the efficacy and safety of long-term prognosis of CEA and CAS, the clinical data of 86 gerontal patients diagnosed with ACAS in our hospital from January 2011 to January 2015 were analyzed retrospectively as follows.

## Materials and methods

### *General information*

A total of 86 cases were selected who are gerontal patients with ACAS treated with CEA or CAS in our hospital from January 2011 to January 2015. Inclusion criteria: patients who were treated with physician conservative treatment but ineffective; patients who underwent carotid artery color Doppler ultrasonography to confirm the diagnosis of carotid artery stenosis; patients who aged from 60 to 75; carotid artery stenosis ≥50%; patients without obvious carotid artery stenosis symptoms, such as aphasia, dizzy, amaurosis and limb weakness, etc.; this study was approved by the ethics committee of clinical research, and all the patients signed informed consents in a sober state. Exclusion criteria: patients with heart failure and coronary heart disease with unstable angina pectoris; patients who suffered myocardial infarction or lung disease within half a year; patients with certain anatomical difficulties, such as a higher carotid artery bifurcation position; patients who had previously undergone CAS or CEA or had surgical contraindications; patients with chronic renal failure or combined with internal carotid artery aneurysm.

There were 28 cases in CEA group and 58 cases in CAS group. In CEA group, 21 cases were male and 7 cases were female, aged from 62 to 74 years old with an average of 65.1±2.9 years old. In CAS group, 42 cases were male and 16 cases were female, aged from 60 to 75 years old with an average of 66.4±3.7 years old. There was no significant difference in age and gender between the two groups (P>0.05), as shown in **Table 1**.

### *Treatment methods*

*General treatment in perioperative period:* In CAS group, before operation, the patients were orally given aspirin 100 mg/d and clopidogrel 75 mg/d for three days, fasted for preoperative 6h and done routine preparation for digital subtraction angiography (DSA). The 5000IU heparin was given by intravenous injection during operation, clopidogrel 75 mg/d was given orally for 90 days and aspirin 100 mg/d was given orally for a long term after operation. Patients in CEA group discontinued antiplatelet drugs for three days before operation for preventing intraoperative serious errhysis and kept heparinization with intravenous injection of heparin (0.9-1 mg/kg) during operation. After operation, patients were orally given aspirin 100 mg/d and clopidogrel 75 mg/d for 90 days. All the patients in two groups received long-term oral administration of statins which is used for lipid-lowering and stable plaque after operation.

### *CAS method*

Patients with horizontal position, ECG monitoring, disinfected and draped, were placed 8F arterial sheaths through femoral arteries under local anesthesia. With heparinization, the guiding catheter was sent to the proximal end of carotid artery stenosis with the help of superslip lead, and then patients received DSA to fully understand the stenosis and clear the length and diameter of stenosed vessel to choose appropriate stenting and protection

devices. The umbrella (spider EPD) reached to the siphon segment of internal carotid artery through the stenosis site, and then the appropriate balloons were selected in turn to expand the stenosis site. At this point, it is necessary to pay attention to whether the patients' heart rates >50 times/min. If the patients' heart rates <50 times/min, they should be asked to cough to stimulate sympathetic nerve excitation immediately and at the same time treated with intravenous injection of 0.5 mg of atropine to increase patients' heart rates. When patients had hyperperfusion syndrome, such as headache with nausea and vomiting, elevation of blood pressure and the systolic blood pressure higher than 180 mmHg, they should turn their heads to one side immediately in case of asphyxia by vomit. Meanwhile give close monitoring of vital signs, pupils size and the change of light reflection, the changes of consciousness and the signs of cerebral hemorrhage were observed. At the same time patients were given the lowering blood pressure, reducing cerebral edema and other drugs for symptomatic treatment to make symptoms disappear. After balloon dilatation was completed, the appropriate stenting was selected, and it was required to across the both end of stenosis site at least 5 mm to ensure that the stenting covered all lesions. And then the stenting sheath was withdrawal, the stenting was released completely, and patients were observed whether the stenosis was satisfactory and measured the residual stenosis with positive and lateral angiography. Meanwhile, understand whether the intracranial arteries reduced comparing with the preoperative, the cerebral infarction caused by embolus detachment during the operation procedures was removed, catheters were withdrawn and pressure dressing was performed on puncture points. Patients were carefully observed intraoperative changes of heart rate and blood pressure to symptomatic treatment.

*CEA method*

The changes of cerebral blood flow were monitored continuously by transcranial Doppler during operation. Patients with dorsal decubitus turned their heads to the side without stenosis and exposed the affected side. Under general anaesthesia, with routine disinfection, draped and triangular locating, patients were performed incision along the anterior border of the sternocleidomastoid, freed the subcutaneous tissue, platysma, deep cervical fascia and deep surface of sternocleidomastoid layer by layer, and isolated common carotid artery, external carotid artery and internal carotid artery. Noninvasive blood vessel forceps were used to block the superior thyroid artery, external carotid artery and common carotid artery, without blocking the internal carotid artery. To increase 20-30 mmHg on the basis of original blood pressure before clamping the common carotid artery and remained stable, with intravenous infusion of heparin to ensure cerebral perfusion. Common carotid artery and internal carotid artery were incised longitudinally, the arterial intima and plaque were completely removed, and the internal carotid artery was clamped until the vessel wall was smooth and blood regurgitation was unobstructed. The distal intima was trimmed, vascular lumen was washed with heparin saline, and then the blood vessel wall was continuous stitched. After finishing the suture, the blocking clip of external carotid artery, common carotid artery and internal carotid artery were opened in sequence. If the transcranial Doppler monitoring showed that the middle cerebral artery flow rate increased >150% after opening, then the common carotid artery was blocked partially and gradually opened to prevent excessive perfusion. Reexamination of transcranial Doppler confirmed vascular patency, and the incisions were stitched in turn. Postoperative blood pressure was control strictly.

*Observation indexes*

The hospitalization days of patients were recorded, and NIHSS was used to evaluate the neurological function before and after treatment for seven days [5]. The three levels of mild, moderate and severe stenosis were divided by scores (less than or equal to 10, between 11 and 19, greater than or equal to 20), respectively. The higher the score, the worse the effectiveness. The peak value (cm/s) of contraction inflow velocity in narrow at one month, six months, and one year before and after treatment was measured by Doppler ultrasound, which was adopted to stenosis assessment. The stenosis degree was evaluated by reference to North American Symptomatic Carotid Endarterectomy Trial standard method, steno-

**Table 2.** Comparison of carotid artery position and degree of two groups of patients before treatment (cases)

| Group | Cases | Stenosis position | | | | Stenosis degree | | |
|---|---|---|---|---|---|---|---|---|
| | | Continuity of narrow | Internal carotid artery | Common carotid artery | Bilateral stenosis | Mild | Moderate | Severe |
| CAS group | 58 | 24 | 7 | 9 | 16 | 15 | 35 | 8 |
| CEA group | 28 | 16 | 10 | 7 | 7 | 8 | 16 | 4[a] |

Note: compared with CAS group, [a]P<0.05; stenosis degree was measured by NASCET method.

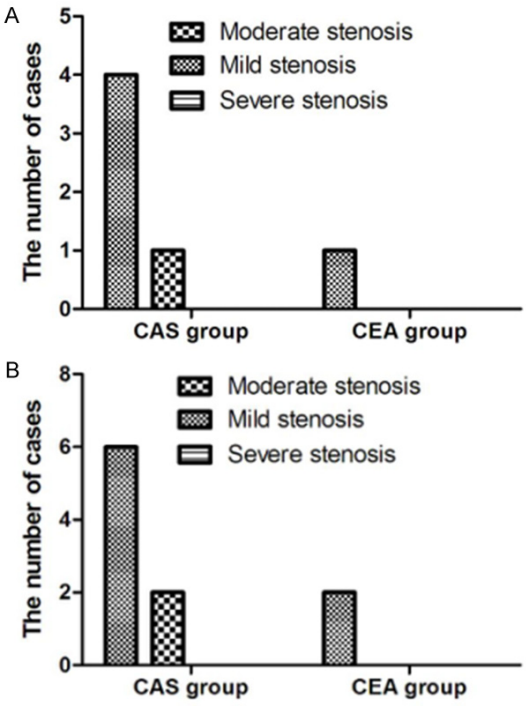


**Figure 1.** A: Comparison of restenosis cases between CAS group and CEA group within 6 months after treatment; B: Comparison of restenosis cases between CAS group and CEA group within 12 months after treatment.

sis rate = (narrow distal normal diameter -the narrowest diameter of narrow distal)/narrow distal normal diameter*100% [6]. The details were as follows: mild stenosis, peak value was less than 150 cm/s and artery diameter reduction was under 30%; moderate stenosis, peak value was between 150 and 200 cm/s and artery diameter reduced from 50% to 75%; severe stenosis, peak value was between 200 and 400 cm/s and artery diameter reduced from 76% to 99%; complete occlusion, peak value was more than 400 cm/s and no blood flow signal in carotid artery. Patients were followed up within one month and one month to one year after treatment, and the follow up included cumulative incidence of primary endpoints, covering ipsilateral stroke, myocardial infarction, cerebral apoplexy, delayed intracranial hemorrhage, death and so on.

*Statistical method*

All data were statistical processed by SPSS 17.0 software package. The measurement data were expressed as mean ± standard deviation ($\bar{x}$±S), and t test was performed. The comparison of the clinical data, the carotid arterystenosis one to twelvemonths after treatment, the cumulative incidence of major endpoints within one year and the grades of NIHSS scores before and after treatment in two groups were detected by $\chi^2$ test. According to the test level of $\alpha$=0.05, P<0.05 indicated that the difference was statistically significant.

## Results

*Comparison of carotid stenosis before and after treatment for 1 month to 1 year*

It was significant difference of the stenosis of carotid artery between the two groups before treatment (P<0.05, see **Table 2**), but there was no re-stenosis in both groups within one month after treatment. At six months, there were four cases of mild stenosis, one case of moderate stenosis in CAS group, and only one case of mild stenosis in CEA group. At one year, there were six cases of mild stenosis, two cases of moderate stenosis in CAS group, and a total of two cases of mild stenosis in CEA group. No severe stenosis was found in two groups within one year after treatment (**Figure 1**).

*Comparison of hospitalization days and NIHSS scores before and after treatment*

The average hospitalization days in the two groups were as follows: CAS group 5.4±1.7 d, CEA group 8.5±3.9 d, there was significant dif-

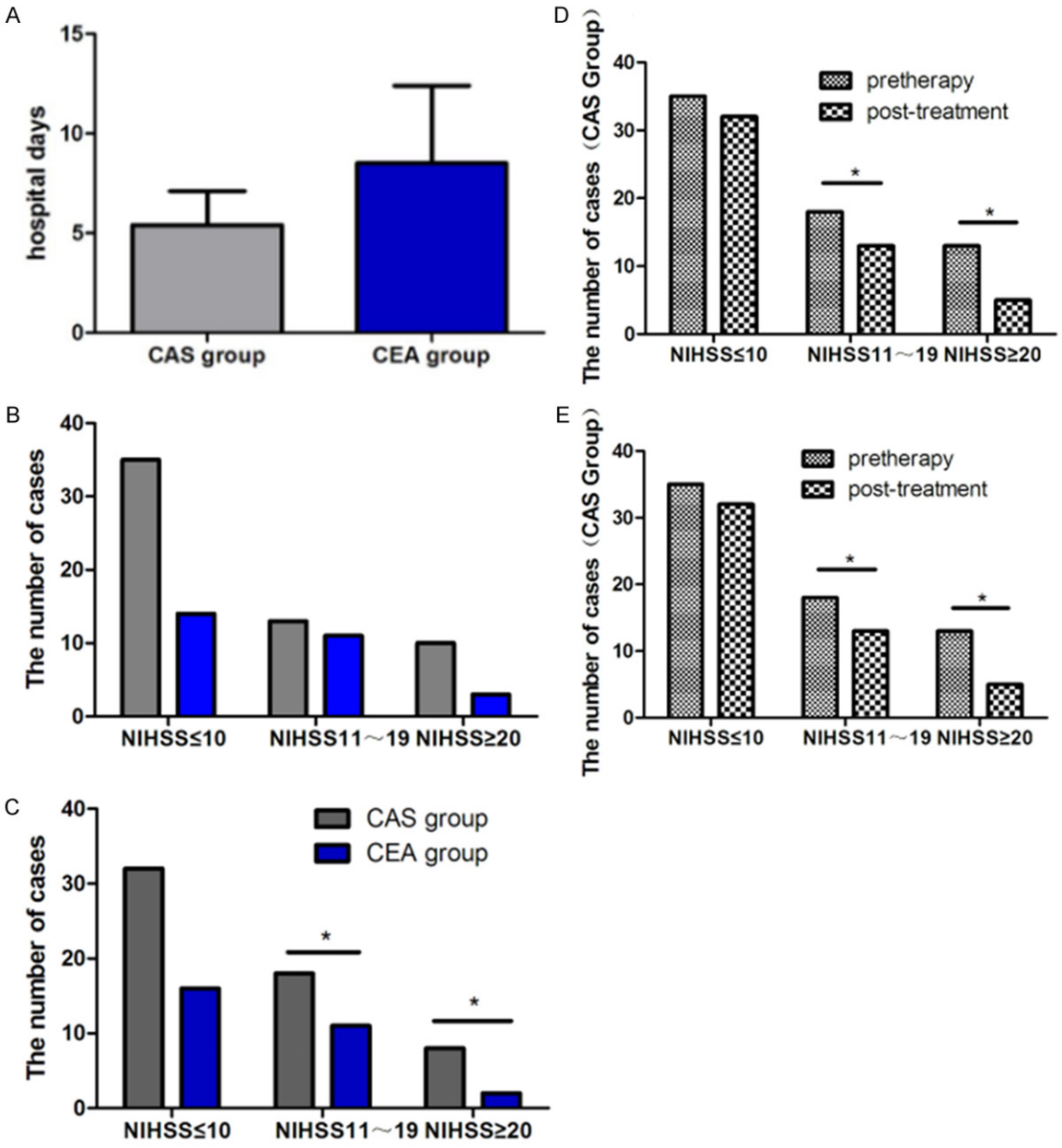


**Figure 2.** A: The comparison of hospitalization days between CAS group and CEA group; B: The NIHSS scores before treatment between the two groups (P>0.05); C: The comparison of NIHSS scores at 7 days after treatment between two groups; when NIHSS scores were greater than or equal to 20, the differences between CAS group and CEA group were statistically significant (*P<0.05); when NIHSS scores were less than 20, the differences between CAS group and CEA group were not statistically significant (P>0.05); D: When the NIHSS scores were more than or equal to 11 before and after treatment, the differences in CAS group were statistically significant (*P<0.05); E: When the NIHSS scores were more than or equal to 11 before and after treatment, the differences in CEA group were statistically significant (*P<0.05).

ference between the two groups in hospital stay (P<0.05); before treatment, the NIHSS score difference between the two groups was not statistically significant. When the NIHSS scores at 7 d before and after treatment were greater than or equal to 20, the differences between the CAS group and CEA group were statistically significant. There was statistical significance in difference between the two groups when NIHSS score at 7 d after treat-

**Table 3.** Cumulative incidence of major cardiovascular events of the patients in the two groups two years aftertreatment (cases, %)

| Primary endpoints | One month after treatment | | One month to one year after treatment | |
|---|---|---|---|---|
| | CAS group | CEA group | CAS group | CEA group |
| Ipsilateral stroke | - | - | 6 (10.3) | 3 (10.7) |
| Cerebral apoplexy | 3 (5.1) | 7 (25.1) | - | - |
| Myocardial infarction | 1 (1.7) | 5 (17.8) | - | - |
| Delayed intracranial hemorrhage | 0 | 1 (3.5) | - | - |
| Death | 2 (3.4) | 4 (14.2) | 8 (13.7) | 4 (14.2) |

ment was greater than or equal to 20 ($P<0.05$). No statistical significance was found in difference between the two groups when NIHSS score was less than twenty ($P>0.05$) (**Figure 2**).

*The incidence of endpoints from one month to one year after treatment*

Within one month after treatment, the cumulative incidence of endpoints such as myocardial infarction, cerebral apoplexy, delayed intracranial hemorrhage and death in CEA group was higher than that in CAS group, the difference was statistically significant ($P<0.05$), without ipsilateral stroke found in two groups. There was no statistical significance in difference from one month to one year between the two groups, as shown in **Table 3** ($P>0.05$).

## Discussion

In 1954, Eastcottreported the world's first case of CEA treatment of carotid artery stenosis, creating a new era of surgical prevention and treatment of ischemic stroke [7]. Both European Carotid Surgery Trial and North American Symptomatic Carotid Endarterectomy Trial had confirmed the important role of CEA in the prevention of ischemic stroke [8]. After several decades of development, the surgical approach has achieved good clinical efficacy and become the standard method for carotid artery stenosis. With the development of neurology intervention, there has appeared a new therapy: CAS. Despite CAS started later, it greatly reduced the occurrence of patients' nerve damage and stroke in the perioperative period and increased the safety of treatment for its needlessness of general anesthesia and small neck incision, less trauma, short hospital stay, quick recovery and other advantages, especially the application of EPD. There were countless studies on the efficacy, advantages and disadvantages of the two treatment methods at home and abroad. However, for the elderly patients with ACAS, how to choose a reasonable treatment has not reached a conclusion yet.

This paper retrospectively collected and analyzed the clinical data of patients with ACAS admitted in our hospital. The patients in two groups were assessed by Doppler ultrasound, the degrees of stenosis were significantly different after 6 months. The rate of restenosis in CAS group was higher than that in CEA group. Considering the possible causes is that each step of CAS in the operation may have the possibility of embolus shedding, and the wire into the blood vessel itself is a stimulus to the blood vessels to make the incidence of restenosis and postoperative stroke were increased. In recent years, there have been two kinds of EPD, one is placed in the distal carotid artery stenosis to prevent the shedding embolus flow to the brain, another is used less, placed balloon in the common carotid artery and external carotid artery so that the blood flow back to the brain will make small embolus rushing to proximal internal carotid artery [9, 10]. Although under the application of the EPD, the CAS will lead to the embolus shedding inevitably. Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) reported that about 1/3 treatment-related complications in 30 days occurred in the venous catheters and other related operations [11]. However, when the patient exists myocardial infarction, heart failure and other factors that increase the risk of surgery, CAS is very important, the results of a foreign randomized controlled trial show that under the premise that the general data has no significant difference in patients, select CEA and CAS with an embolus protection device respectively in treating patients with ACAS, and found that the incidence of postoperative cerebral ischemic

stroke was not significantly different [12]. However, the incidence of cerebral ischemia in CEA group was lower than that in CAS group in patients with symptomatic carotid artery stenosis and the difference was statistically significant [13].

This study showed that the difference of NIHSS score in two groups was meaningless before treatment, when NIHSS score ≥20 points after treatment, the difference was statistically significant ($P<0.05$). When the NIHSS scores before and after treatment were greater than or equal to 11, the differences between CAS group and CEA group were statistically significant ($P<0.05$). It indicated that both CEA and CAS were beneficial for the recovery of patients with nerves injury, whose NIHSS scores were greater than or equal to 11. However, when the NIHSS scores after treatment were more than or equal to 20, the difference of the two groups was statistically significant. CEA was more beneficial than CAS for the recovery of patients with nerves injury when NIHSS scores were more than or equal to 20 points. The score of NIHSS was mainly used to assess the cerebral stroke outcome caused by circulating blood supply disorders, using a score to refine the specific neurological function, the higher the score, the heavier the nerve damage [14]. There are studies showing that NIHSS score can reduce the research error, so it is widely used in cerebral apoplexy related research. The significance of treatment was small in two groups with NIHSS score >20 points, the reason might be the patient's neurological impairment was severe, brain nerve cells were irreversible necrosis, even treated by revascularization, necrotic brain tissue was still unable to restore its normal function in a short term, these patients were mostly doing rehabilitation exercise, but good circulation perfusion was not meaningless, it could create an environment to reproduce nerve cell and connect synapsis [15-17].

In this study, we also found that the average time of hospitalization between the two groups was statistically significant ($P<0.05$), and the incidence of endpoints of CAS group was significantly lower than the CEA group within 1 month, the difference was statistically significant ($P<0.05$). It showed fewer traumas, more repeatedly process, quicker recovery, fewer complications in CAS compared with CEA. Therefore, particularly suitable for those who could not tolerate surgery or who refuse surgery, asymptomatic patients with carotid artery stenosis, postoperative stenosis recurrence, could not reach multiple vascular caused by influence of lesion part in the surgery. This was consistent with the domestic reports [18]. Other studies reported that when the CEA could not treat the high carotid artery stenosis, subclavian artery stenosis, lateral stenosis contralateral occlusion lesions, CEA restenosis, ACAS, combined with severe medical diseases, CAS has significant advantages in the treatment of high-risk surgery patients [19, 20]. But in the study of long-term outcomes of CEA and CAS in treating carotid artery stenosis conducted by Thomas et al, during a more than 10-year follow-up, there was no significant difference between stroke, myocardial infarction, or death and subsequent ipsilateral stroke risk in patients with CAS and CEA in perioperative period. There was no difference in the incidence of postoperative ipsilateral stroke. This was inconsistent with the results of this study.

Because the number of collected cases was too small in this retrospective analysis, it lacks accuracy. The follow-up information of several cases could not be recorded timely due to patient transitions, these patients met the criteria for entering groups but not included in the analysis. There might be selective bias and follow-up time was short. And the observation and comparison of the impact of the endpoints needed to be further improved and studied.

In summary, CEA and CAS are effective therapeutic methods for the treatment of ischemic cerebrovascular disease and have their own advantages, no one can be replaced by another. This paper found that CEA and CAS are effective to cure ischemic cerebrovascular disease, however, CAS was superior to CEA in the treatment of ACAS in gerontal patient and more widely used in clinic for its short hospital days and small trauma. In our actual clinical work for the treatment of patients with carotid artery stenosis, we should base on whether the patient is symptomatic, stenosis parts, the overall nutritional status of the comprehensive assessment, to make a reasonable choice to reduce the incidence of postoperative endpoints of patients, thereby improving the quali-

ty of lives of patients and reducing the social burden.

## Disclosure of conflict of interest

None.

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