

Analysis on risk factors for cerebral hyperperfusion syndrome following carotid angioplasty stenting in the elderly patients with carotid artery stenosis and intervention measures.

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Abstract

Objective: To study the risk factors for Cerebral Hyperperfusion Syndrome (CHS) following Carotid Angioplasty Stenting (CAS) in the elderly patients with carotid artery stenosis and to explore the intervention measures for prevention and treatment of CHS.

Methods: A total of 500 elderly patients with carotid artery stenosis enrolled in our hospital from May 2012 to May 2017 were selected as the objects. They all were treated with CAS, and divided according to presence of CHS into non CHS group (n=482) and CHS group (n=18), general data of patients were compared between the two groups, and independent risk factors were analysed by stratified method.

Results: The Univariate analysis showed that there was statistically significant difference between CHS group and non CHS group in diabetes and postoperative hypertension (P<0.05); but not in age, sex, hypertension, hyperlipidemia, ischemic events, drinking history as well as degree of stenosis (P>0.05). CAS was performed on 532 cases in the two groups, including 18 cases in CHS group and 514 cases in non CHS group. There was no statistically significant difference between the two groups in operative MCA occlusion, operative PCoA opening, symptomatic focus, and operative ACAA1 segment dysgenesis (P>0.05). The stratified analysis showed that postoperative hypertension (OR=7.248, P<0.01) and diabetes mellitus (OR=5.906, P<0.01) were important risk factors for CHS after CAS.

Conclusion: In elderly patients with carotid artery stenosis, those with postoperative hypertension or diabetes history are more prone to CHS following CAS with poor prognosis, which should be controlled and prevented from a variety of perspectives through intervention measures.

Keywords: Elderly, Carotid artery stenosis, Carotid angioplasty stenting, Cerebral hyperperfusion syndrome, Risk factors, Hypertension, Diabetes mellitus.

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Introduction

Carotid stenosis is the stenosis of carotid artery that serves as the main blood vessel from the heart to the brain and other parts of the head. Carotid stenosis is mostly caused by atherosclerotic plaques of the carotid artery, with a high incidence and often occurs in the common carotid bifurcation and the beginning of the internal carotid artery. The main causes of carotid stenosis are atherosclerosis, aortic inflammation and fibromuscular dysplasia; other causes include trauma, arterial torsion, congenital atresia, tumor, artery or periarteritis, and fibrosis after radiotherapy. Carotid artery stenosis is an important cause of ischemic stroke, accounting for 5% to 10%. It is generally treated with Carotid Angioplasty Stenting (CAS), Carotid Endarterectomy (CEA) and internal medicine [1]. Some clinical trials and many retrospective analysis by medical centers show that [2] CAS and CEA both were the main methods for treatment of carotid stenosis in the past decades with better curative effect than

medicine therapy alone. With the development of endovascular interventional treatment in recent years, the safety and effectiveness of CAS have been confirmed by some large-scale randomized controlled trials [3]. However, some patients treated with CAS are prone to such complications as ischemic stroke, immediate hemodynamic changes, acute or subacute thrombosis and Cerebral Hyperperfusion Syndrome (CHS) [4,5]. In particular, CHS, although with low incidence rate, has rapid progress of the condition, which is very easy to induce intracranial hemorrhage and death in patients [6]. Therefore, a comprehensive treatment program should be developed for those with high risk of CHS before CAS is performed on patients with carotid stenosis to prevent and control the occurrence or development of CHS so as to ensure the safety of high-risk patients. This study retrospectively analysed the general data of 500 elderly patients with carotid artery stenosis treated by CAS in our hospital from May 2012 to May 2017,

aiming to find out the main risk factors of CHS after CAS, with the details reported as follows.

Subjects and Methods

Research subjects

A total of 500 elderly patients with carotid artery stenosis enrolled in our hospital from May 2012 to May 2017 were selected as the objects. Among them there were 430 males and 70 females aged 61-79 with an average age of (68.3 ± 3.5 y), including 460 cases of unilateral CAS and 40 cases of bilateral CAS. All patients were diagnosed by color Doppler ultrasound. Inclusion criteria: (1) the degree of residual stenosis after CAS (calculated by NASCET method) was below 30 %; (2) CAS stents were all self-expandable; (3) stent was located in sinus of internal carotid. Exclusive criteria: (1) patients with antiplatelet drug allergy, bleeding tendency or accompanied by malignant tumor or organ dysfunction; (2) patients with incomplete cerebral angiography data and case information; (3) patients simultaneously with posterior circulation stent. The enrolled 500 patients were divided into non CHS group (n=482) and CHS group (n=18) according to presence of CHS.

Research methods

A retrospective analysis was conducted on such baseline data as patient gender, age, history of heart disease, diabetes, hypertension, hyperlipidemia, smoking history, drinking

history, history of stroke, perioperative hemodynamic depression, presence of bilateral CAS and presence of Transient Ischemic Attack (TIA) followed by a record of such characteristics as degree of stenosis in the operative side, presence of operative Middle Cerebral Artery (MCA) occlusion, Operative Posterior Communicating Artery (PCoA) open, asymptomatic lesions, and abnormal development of A1 segment in operative Anterior Cerebral Artery (ACA).

Statistical treatment

All the data were analysed on SPSS 21 software, the measurement data were described as and assessed by t-test, the count data were expressed by percentage (%) and checked by, independent factor was assessed by Man-tel-Haenszel method with hierarchical analysis, $P < 0.05$ suggested that there was statistically significant difference.

Results

Comparison of general data between the two groups

The Univariate analysis showed that there was statistically significant difference between CHS group and non CHS group in diabetes and postoperative hypertension ($P < 0.05$); but not in age, sex, hypertension, hyperlipidemia, ischemic events, drinking history as well as degree of stenosis ($P > 0.05$), as shown in Table 1.

Table 1. Comparison of general data between the two groups ($\bar{x} \pm s$).

Item	CHS group (n=18)	Non CHS group (n=482)	χ^2	P
Age(y)	68.1 \pm 3.5	69.2 \pm 3.2	0.347	0.652
Male	13 (72.22)	417 (86.51)	0.159	0.434
Diabetes	10 (55.56)	64 (13.28)	7.286	0.011
Hypertension	11 (61.11)	296 (61.41)	0.133	0.598
Hyperlipidemia	9 (50.00)	242 (50.21)	0.844	0.325
Drinking history	7 (38.89)	189 (39.21)	0.052	0.877
Smoking history	6 (33.33)	165 (34.23)	0.116	0.659
Heart disease history	5 (27.78)	138 (28.63)	0.552	0.213
Stoke history	5 (27.78)	140 (29.05)	1.066	0.142
Bilateral CAS	2 (11.11)	38 (7.88)	0.084	0.792
Ischemic events				
TIA	5 (27.78)	135 (28.00)	0.098	0.536
Cerebral infarction	9 (50.00)	243 (50.41)	0.065	0.741
Postoperative hypertension	8 (44.44)	150 (31.12)	9.138	0.016
Operative stenosis degree				
50%-69%	7 (38.89)	188 (39.17)	0.019	0.822
70%-99%	9 (50.00)	243 (50.41)	0.122	0.719

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100%	2 (11.11)	51 (10.58)	0.459	0.304
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Comparison of imaging data of cerebral arteries

There was no statistically significant difference between CHS group and non CHS group in operative MCA occlusion, operative PCoA opening, symptomatic focus, and operative

ACAA1 segment dysgenesis (P>0.05), as shown in Table 2. The relevant cerebral artery images of a typical CHS patient (a female aged 69) were shown as Figures 1 and 2.

Table 2. Comparison of cerebral artery imaging in the two groups (n (%)).

Item	CHS group (18 cases)	Non CHS group (514 cases)	χ^2	P
Operative MCA occlusion	3 (16.67)	86 (16.73)	0.178	0.877
Operative PCoA opening	3 (16.67)	88 (17.12)	0.216	0.643
Symptomatic Focus	9 (50.00)	253 (49.22)	0.415	0.529
Operative ACAA1 segment dysgenesis	3 (16.67)	87 (16.92)	0.104	0.812



Figure 1. Preoperative whole brain Digital Subtraction Angiography (DSA) showed that stenosis rate of the right internal carotid sinus was 90%.



Figure 2. Postoperative DSA showed that the stent in patients was well shaped and the stenosis of the right internal carotid artery basically relieved.

The results of stratified analysis on risk factors for CHS

The stratified analysis showed that postoperative hypertension (OR=7.248, P<0.01) and diabetes mellitus (OR=5.906, P<0.01) were important risk factors for CHS after CASS, as shown in Table 3.

Table 3. Results of stratified analysis on risk factors for CHS.

Factor	β	OR	95% CI	P
Diabetes	1.627	5.906	1.911-15.673	0.001
Postoperative hypertension	2.135	7.248	2.406-22.152	0.001

Summary: The univariate analysis showed that there was statistically significant difference between CHS group and non CHS group in diabetes and postoperative hypertension (P<0.05); but not in age, sex, hypertension, hyperlipidemia, ischemic events, drinking history as well as degree of stenosis (P>0.05); CAS was performed on 532 cases in the two groups, including 18 cases in CHS group and 514 cases in non CHS group; there was no statistically significant difference between the two groups in operative MCA occlusion, operative PCoA opening, symptomatic focus, and operative ACAA1 segment dysgenesis (P>0.05); and the stratified analysis showed that postoperative

hypertension (OR=7.248, $P<0.01$) and diabetes mellitus (OR=5.906, $P<0.01$) were important risk factors for CHS after CAS. These results suggested that in elderly patients with carotid artery stenosis, those with postoperative hypertension or diabetes history were more prone to CHS following CAS with poor prognosis, which should be controlled and prevented from a variety of perspectives through intervention measures.

Discussion

CHS, as a deadly complication after CEA, is worth being stressed in intervention of perioperative carotid artery stenosis in Neurosurgery or Vascular Surgery. The key to the treatment of carotid stenosis is to fully understand the risk factors, characteristics and treatment of CHS [7-9]. A foreign study [10] has found that the incidence of CHS following CAS in patients with carotid stenosis ranges from 0.25% to 4.13%. Of the 500 patients selected in this study, 18 patients had CHS, accounting for 3.60%, which is basically consistent with the results of epidemiological surveys at home and abroad.

In recent years, there are many studies on the risk factors for the occurrence of CHS after CAS in patients with carotid stenosis but with no consistent conclusion. It is shown by the study that [11] the risk factors for CHS after CEA include diabetes mellitus, hypertension, coronary artery bypass grafting, low ejection fraction and blood flow factors related to operation techniques. Some studies also suggest that [12] the main risk factors for postoperative infection include diabetes, age >75 y, severe carotid artery stenosis in the operation side, history of stroke, anticoagulant use and operative MCA occlusion. In this study, the Univariate analysis showed significant difference in diabetes and the incidence of postoperative hypertension between the patients with CHS and those without ($P<0.05$), and the results of multivariate analysis showed that diabetes as well as postoperative hypertension were important risk factors of CHS after CAS ($P<0.05$). The OR value of postoperative hypertension was 7.248, suggesting that postoperative hypertension has significantly increased the incidence of CHS.

In this study, among 18 patients with CHS there were 11 cases with preoperative elevation of blood pressure, and after symptomatic treatments of decompressive craniectomy, dehydration as well as anti-hypertension, there is still 1 patient with the blood pressure more than 165 mmHg, who had intracranial hemorrhage and ended up in death. Therefore, after CAS treatment, patient's blood pressure should be closely monitored and those with elevated pressure timely controlled [12]. We believe that in patients with vascular stenosis the elevated blood pressure will cause the increase of cerebral perfusion pressure and thus damage the blood-brain barrier, which has been destroyed before CAS, in this case the liquids in brain will continue to leak to the brain tissue gap, thereby leading to brain edema, and if there occurs rupture of blood vessel in brain, there would be subarachnoid hemorrhage or cerebral hemorrhage, thereby aggravating the patient's condition and even causing death [13]. In this study, there were 5 CHS cases with a stable blood pressure of 90-145mmHg after symptomatic treatment and the symptom of CHS disappeared completely after 2 d. Therefore, if the blood

pressure can be strictly controlled within a certain range, and plus with continuously enhanced cerebral autoregulation, CHS will be much likely to disappear completely, basically in line with the results of related research [14].

At the same time, diabetes mellitus is also an important risk factor for CHS following CAS in patients with carotid stenosis. An epidemiological survey has revealed that [15] patients with diabetes were 2 times more likely to have stroke than those without. In CHS group of this study, there were 10 patients with diabetes before operation, including 2 with intracranial hemorrhage and 1 of them with death, so the mortality rate was moderately high. Related studies suggest that [16] diabetic patients are prone to cerebral vascular lesions. High blood sugar will give rise to oxidative stress reaction, which is easy to damage the vascular endothelial cells with the resulting function disorder, destroyed defense mechanism, increased gap and significantly higher vascular permeability, so patients with carotid artery stenosis and diabetes are more prone to CHS and even intracranial hemorrhage. Therefore, for patients with diabetes or history of carotid artery stenosis and history of stroke which possibly induce CHS, measures should be taken to cautiously prevent CHS after CAS treatment. We hold that following points should be paid attention for CHS prevention: (1) patients with higher blood pressure than pre-treatment in perioperative CAS period should be promptly sent to the ICU with the blood pressure strictly controlled at 90-145 mmHg; (2) the changes of patient vital signs in perioperative period should be strictly monitored followed by a detailed recording and a summary of DSA manifestations; (3) the blood glucose should be controlled in a reasonable range in diabetic patients before treatment with CAS.

However, antiplatelet drugs, age, history of stroke as well as anticoagulants were not discovered in the study as possible risk factors for CHS following CAS in patients with carotid artery stenosis, and according to the Table 2 which reveals cerebral artery imaging, there was no significant difference between the two groups of patients in operative MCA occlusion, operative PCoA opening, symptomatic focus, and operative ACAA1 segment dysgenesis ($P>0.05$), differing from some other research results to a certain degree. It may be related to the smaller sample size of the study. Because the incidence of CHS is moderately low in a small number of subjects, the results of this study is likely to be affected. As a result, further studies can be carried out with expanded sample size to clarify relevant risk factors.

To sum up, in elderly patients with carotid artery stenosis, those with postoperative hypertension or diabetes history are more prone to CHS following CAS with poor prognosis, which should be controlled and prevented from a variety of perspectives through intervention measures.

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