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A Study of the Association Between Carotid Artery Curvature and Intracranial Aneurysms

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Background: Carotid artery curvature is considered a sign of a weak vessel wall, and we hypothesize that a weak vascular wall under the effect of hemodynamics may cause intracranial aneurysms.

Materials and Methods: The general data of 534 patients with aneurysms and 473 control patients were retrospectively analyzed in a case-control study. Carotid artery curvature was characterized as none, tortuosity, kinking, and coiling by computed tomography angiography images. Univariate analysis was performed to determine the degree of carotid artery tortuosity and to analyze the general data between the aneurysm group and the control group, and then, multivariate statistical logistic regression analysis was used to analyze the statistical significance of the univariate analysis. Finally, the correlation between aneurysm-related features and carotid artery curvature was analyzed.

Results: Univariate analysis showed that kinking was significantly related to the occurrence of intracranial aneurysms ($P=0.009$). The results of multivariate regression analysis showed that kinking was an independent risk factor for the occurrence of aneurysms (odds ratio: 1.942; 95% confidence interval: 1.387-2.720 for model 1; odds ratio: 1.995; 95% confidence interval: 1.419-2.805 for model 2). In the analysis of the correlation between the characteristics of intracranial aneurysms and the curvature of the internal carotid artery, there was no correlation between the curvature of the internal carotid artery and the size, location or number of aneurysms, or whether the intracranial aneurysm was ruptured.

Conclusion: Intracranial aneurysms are associated with carotid artery curvature. Kinking of the internal carotid artery may indicate a higher risk for aneurysm formation.

Key Words: intracranial aneurysm, carotid artery curvature, weak vascular wall, pathogenesis, kinking, computed tomography angiography

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An intracranial aneurysm is the most important cause of spontaneous subarachnoid hemorrhage, and its incidence in the population is ∼3%, which places a heavy economic and spiritual burden on the family, society, and the country.[1] In recent years, several clinical and basic studies have been conducted on the etiology of intracranial aneurysms. Current studies have shown that factors such as age, sex, hypertension, arteriosclerosis, and hemodynamic changes may be related to the occurrence of aneurysms, but their specific pathogenesis is still unknown.[2–4]

With the development of imaging technology, carotid artery curvature is considered to be a common carotid artery variation. Studies have found that patients with connective tissue diseases have a higher incidence of carotid artery curvature,[5,6] and the cause may be closely related to the weak arterial wall of patients with such diseases; consequently, carotid artery curvature may also indicate a weak vessel wall.[7] On the basis of this theory, Kim and other researchers found that internal carotid artery curvature is closely related to the occurrence of internal carotid artery dissection aneurysms.[8,9] Considering the common pathogenesis of internal carotid artery dissecting aneurysms and intracranial aneurysms, we speculate that a weak vascular wall under the effect of hemodynamics may show an increased incidence of vascular wall bulging, leading to the occurrence of intracranial aneurysms. The research report on the relationship between internal carotid artery curvature and intracranial aneurysm was relatively late, and it was not reported for the first time until 2017 by Labeyrie et al.[10] On the basis of statistical analysis of digital subtraction angiography of the included patients, the study found that tortuosity of the internal carotid artery was significantly related to intracranial aneurysms. Considering that computed tomography angiography (CTA) is the first choice to detect aneurysms in this region, this article intends to analyze and study the carotid artery morphology of patients with intracranial aneurysms who were admitted to our department, based on CTA findings, and to explore the correlation between carotid artery curvature and intracranial aneurysms.

MATERIALS AND METHODS

The study was approved by the Ethics Committee of Chongqing Medical University. Because of the retrospective nature of this analysis, the IRB granted a waiver of consent.

Inclusion and Exclusion Criteria

Aneurysm Group

The data of patients who visited our department from January 2017 to January 2019 were continuously collected. The inclusion criteria were as follows: (1) patients who were diagnosed with subarachnoid hemorrhage by head CT and intracranial aneurysm by CTA; (2) head and neck CTA that diagnosed an intracranial aneurysm and indicated that the patient had an unruptured aneurysm. According to the inclusion criteria, a total of 578 cases were included in the aneurysm group. The exclusion criteria were as follows: (1) patients who did not undergo cervical vascular CTA examination (17 patients); (2) patients whose neck CTA could not distinguish the degree of carotid artery curvature (9 patients); (3) patients with other vascular diseases (4 patients); (4) patients with traumatic and

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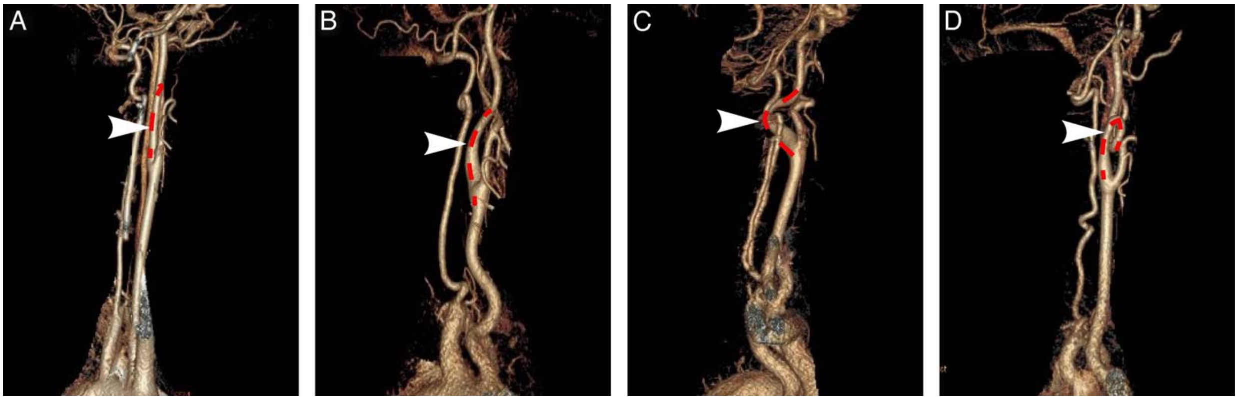

FIGURE 1. Classification of carotid artery curvature: (A) no, (B) tortuosity, (C) kinking, (D) coiling.

infectious aneurysms (2 patients); and (5) patients with serious systemic diseases (12 patients). Eligible patients included 173 males and 361 females.

Control Group

Data were continuously collected from patients in the Department of Neurology in our hospital from January 2017 to January 2019. The inclusion criteria were as follows: (1) patients admitted to the hospital with simple headache or dizziness and (2) patients with improved head and neck CTA test results. According to the inclusion criteria, a total of 550 cases were included in the control group. The exclusion criteria were as follows: (1) patients who did not undergo neck vascular CTA examination (23 patients); (2) patients whose neck CTA could not distinguish the degree of carotid artery curvature (11 patients); (3) patients who underwent head and neck CTA and the findings showed intracranial vascular disease (24 patients); and (4) patients whose cases were complicated with serious medical diseases and other nervous system diseases (19 patients). Eligible patients included 205 males and 268 females.

General data included the patient's age, sex, hypertension history, diabetes history, smoking history, drinking history, history of coronary heart disease, number of aneurysms, aneurysm size, aneurysm rupture status, aneurysm location (anterior circulation or posterior circulation), etc.

Head and Neck CTA Examination

All patients in this study underwent 64-slice spiral CT (GE light speed VCT) for head and neck scans. The patient was placed in the supine position, venous access was established through the median cubital vein, and a high-pressure syringe was used to inject 20 mL contrast agent: UVIX (370 mg I/mL) at a speed of 4 mL/s. The layer thickness was 0.625 mm, and the layer spacing was 0.3 mm. After scanning, the boneless 3DVR reconstructed image was obtained through data processing and image reconstruction. The CTA diagnosis result was determined by 2 experienced radiologists and a neurosurgeon.

CTA Image Analysis of Cervical Blood Vessels

According to the standards of Paulsen, Weibel and Fields, carotid artery morphology was divided into the following 4 types[11,12]: none (no curvature): the deviation of the carotid artery from the vertical line is <15 degrees; tortuosity: the angle between the 2 arterial segments is 90 to 165 degrees; kinking: the angle between the 2 arterial segments is <90 degrees; coiling: 360 degrees appears on the carotid artery segment, with bending of the ring. As shown in Figure 1, the values represent no curvature, tortuosity, kinking, and coiling. Two well-trained investigators classified the carotid artery curvature, and any differing opinions were resolved by consensus.

Statistical Analysis

SPSS 21 software was used for statistical analysis. First, univariate analysis was performed; univariate analysis of categorical variables between groups was performed using the χ^2 test, and univariate analysis of continuous variables was performed using the *t* test. A P-value < 0.05 was considered to be statistically significant. Next, the statistically significant factors from the univariate analysis were incorporated into the multivariate logistic regression analysis model for statistical analysis.

RESULTS

Single-Factor Statistical Analysis Between the Aneurysm Group and the Control Group

Univariate analysis of age, sex, history of hypertension, history of diabetes, history of coronary heart disease, history of smoking, history of drinking, and carotid artery curvature of the aneurysm group and control group showed that there were 135 cases of kinking in patients with aneurysms. There were also 87 cases in the control group, but the incidence of kinking in the aneurysm group was higher than that in the control group, and this difference was statistically significant ($P = 0.009$). In addition, we found that the incidence of tortuosity in the control group was higher than that in the aneurysm group, and this difference was statistically significant ($P = 0.015$). Moreover, we found that the age and sex of the 2 groups were also different (Table 1).

Multivariate Logistic Regression Analysis Between the Aneurysm and Control Groups

To exclude the confounding effects of other factors from the statistical results of the 2 groups, we included age, sex, hypertension, diabetes mellitus, and coronary artery disease in the multivariate logistic regression analysis (Table 2). In the model adjusted only for age and sex (Model 1), carotid kinking was associated with an increased risk of intracranial aneurysms [odds ratio (OR): 1.942; 95% confidence interval (CI): 1.387-2.720], and carotid tortuosity was associated with an attenuated risk of intracranial aneurysms (OR: 0.682; 95% CI: 0.515-0.901). Further adjustments for age, sex, hypertension, diabetes mellitus, and coronary artery disease (Model 2) enhanced the ORs slightly of carotid kinking (OR: 1.995; 95% CI: 1.419-2.805), and reduced the ORs slightly of carotid tortuosity, but the association

TABLE 1. Univariate Analysis of Various Factors Between the Intracranial Aneurysm Group and the Control Group

	Control Group (n = 473), n (%)	Intracranial Aneurysm Group (n = 534), n (%)	t/χ^2	P
Age, mean ± SD	63.1 ± 11.8	56.0 ± 10.8	9.944	< 0.001
Female	268 (56.7)	361 (67.6)	12.811	< 0.001
Hypertension	191 (40.4)	238 (44.6)	1.800	0.180
Diabetes	51 (10.8)	67 (12.5)	0.755	0.385
Coronary heart disease	27 (5.7)	20 (3.7)	2.172	0.141
Smoking	105 (22.2)	126 (23.6)	0.277	0.599
Drinking	101 (21.4)	110 (20.6)	0.086	0.769
Internal carotid artery morphology				
No	36 (7.6)	42 (7.9)	0.023	0.880
Tortuosity	320 (67.7)	322 (60.3)	5.870	0.015
Kinking	87 (18.4)	135 (25.3)	6.924	0.009
Coiling	30 (6.3)	35 (6.6)	0.019	0.891

still remained significant (OR: 0.648 ; 95% CI: 0.489-0.861). Carotid coiling was not associated with intracranial aneurysms, in either Model 1 or Model 2.

Correlation Analysis of Carotid Artery Curvature and Related Features of Aneurysms

In the study of the correlation between carotid artery curvature and aneurysm-related characteristics, we found that there was no correlation between carotid artery curvature, whether the aneurysm was ruptured, number of aneurysms, aneurysm location, or the size of the aneurysm (Tables 3–6).

DISCUSSION

Aneurysmal subarachnoid hemorrhage is a critical condition that develops in neurosurgery. Its mortality rate is as high as 50%, and more than 50% of survivors have long-term neurological dysfunction, which seriously threatens overall health.[13] Scholars, at home and abroad, have conducted many clinical and basic studies on its pathogenesis, but its complex mechanism has not been fully elucidated. This further clarifies the pathogenesis of aneurysms, which will help formulate effective prevention and treatment measures and is a very important aspect of improving human health.

Carotid artery curvature is a common morphological variation of the carotid artery. According to Paulse, Weibel, and Fields' classification standards, internal carotid artery curvature can be divided categorized based on tortuosity, kinking, and coiling.[11,12] Studies have shown that carotid artery curvature may be caused by atherosclerosis, muscle fiber hypoplasia, hypertension, etc., and can cause hemodynamic changes.[14,15] Other studies have shown that tortuosity is mostly related to age, kinking is mostly related to atherosclerosis, and coiling is mostly related to congenital variation.[12] Recent studies have shown that ICA curvature has a higher incidence in patients with connective tissue diseases and is closely related to adverse cardiovascular and cerebrovascular accidents in patients with connective tissue diseases.[7] Because the arterial wall in patients with connective tissue diseases is relatively weak, an increasing number of scholars believe that carotid artery curvature is a sign of a weak vascular wall and is a subclinical vascular disease. Many studies have found that internal carotid artery curvature is associated with certain heart and brain diseases.[16–18] Numerous studies have explored the formation, mechanism and risk factors for internal carotid artery curvature, and its role in the occurrence of other diseases is the latest research focus. The study conducted by Kim et al[9] and Lauric et al[7] found that the incidence of internal carotid artery curvature in the internal carotid artery dissecting aneurysm group was higher than that in the control group. Among the related factors, kinking is closely related to the occurrence of internal carotid artery dissecting aneurysms, which are considered one of the influencing factors of internal carotid artery dissecting aneurysms. Regarding the similar pathogenesis of carotid artery dissecting aneurysms and intracranial aneurysms, we suspect that carotid artery curvature may also be related to the occurrence of intracranial aneurysms.

The Labeyrie PE study also proved the above conjecture.[10] The researchers determined the degree of curvature of the internal carotid artery in patients through digital subtraction angiography and evaluated its correlation with the incidence of aneurysms and its related characteristics. The results showed that cervical artery tortuosity is significantly associated with intracranial aneurysms, although it is not related to the main aneurysm characteristics. The difference between the present study and the Labeyrie PE study is that we used CTA to assess the degree of curvature of the patient's internal carotid artery to analyze the correlation between internal carotid artery curvature and intracranial aneurysm. The final research results are different from those in Labeyrie PE's report.

Consistent with previous studies, this study showed that the proportion of females in the aneurysm group (67.6%) was significantly higher than that in the control group (56.7%), indicating that sex differences are significantly related to the occurrence of intracranial aneurysms ($P < 0.001$). There was no difference in the history of hypertension, diabetes, coronary heart disease, smoking, or drinking between the 2 groups. The incidence of tortuosity, kinking, and coiling in the intracranial aneurysm group was 60.3%, 25.3%, and 6.6%, respectively, and that in the control group was 67.7%, 18.4%, and 6.3%, respectively. The incidence of kinking in the intracranial aneurysm group was significantly higher than that in the control group, and the difference was statistically significant ($P = 0.009$). The incidence of tortuosity in the control group was higher than that in the aneurysm group, and this difference was statistically significant ($P = 0.015$). The incidence of coiling in the 2 groups was not significantly different. Because of the differences in the age, sex or other factor compositions of the 2 groups of patients, to better prove that internal carotid artery curvature is related to the occurrence of intracranial aneurysms, this study included age, sex, hypertension, diabetes mellitus, and coronary artery disease in the multivariate logistic regression analysis. After allowing for the effects of confounding factors on the statistical results, the results showed that kinking was an independent risk factor that increased the occurrence of intracranial aneurysms (OR: 1.942; 95% CI: 1.387-2.720 for model 1; OR: 1.995; 95% CI: 1.419-2.805 for model 2). There are differences between our research results and those of Labeyrie PE.[10] The reasons for the analysis may be related to the ethnicity of the participants, the choice of the control group and the different imaging tools. Next, we discussed the correlation between internal carotid artery curvature and intracranial aneurysm-related features. Unfortunately, whether the intracranial aneurysm was ruptured, number and size of the aneurysms are not related to internal carotid artery curvature. This research result is consistent with Labeyrie PE's research.[10] On this basis, we first studied the correlation between the location of the aneurysm (anterior circulation or posterior circulation) and carotid artery curvature. Unfortunately, there is no obvious correlation between the location of

TABLE 2. Results of Multiple Logistic Regression Analysis Between the Intracranial Aneurysm Group and the Control Group

	Model 1		Model 2	
Internal Carotid Artery Morphology	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***
Tortuosity	0.682 (0.515-0.901)	0.007	0.648 (0.489-0.861)	0.003
Kinking	1.942 (1.387-2.720)	< 0.001	1.995 (1.419-2.805)	< 0.001
Coiling	1.276 (0.750-2.169)	0.368	1.308 (0.765-2.235)	0.327

Model 1: adjusted for age and sex.
Model 2: adjusted for age, sex, hypertension, diabetes mellitus, and coronary artery disease.
CI indicates confidence interval; OR, odds ratio.

TABLE 3. Analysis of the Correlation Between the Internal Carotid Artery Curvature and the Rupture of Intracranial Aneurys

Internal Carotid Artery Morphology	Unruptured Aneurysm (n = 82), n (%)	Ruptured Aneurysm (n = 452), n (%)	χ^2	*P*
Tortuosity	44 (53.7)	278 (61.5)	1.785	0.182
Kinking	26 (31.7)	109 (24.1)	2.118	0.146
Coiling	5 (6.1)	30 (6.6)	0.033	0.856

TABLE 4. Analysis of the Correlation Between the Internal Carotid Artery Curvature and the Number of Intracranial Aneurysms

Internal Carotid Artery Morphology	Single Aneurysm (n = 293), n (%)	Multiple Aneurysms (n = 241), n (%)	χ^2	*P*
Tortuosity	170 (58.0)	152 (63.1)	1.409	0.235
Kinking	79 (27.0)	56 (23.2)	0.972	0.324
Coiling	17 (5.8)	18 (7.5)	0.600	0.439

TABLE 5. Analysis of the Correlation Between Internal Carotid Artery Curvature and Aneurysm Location

Internal Carotid Artery Morphology	Anterior Circulation (n = 450), n (%)	Posterior Circulation (n = 62), n (%)	χ^2	*P*
Tortuosity	277 (61.6)	32 (51.6)	2.251	0.134
Kinking	111 (24.7)	20 (32.3)	1.649	0.199
Coiling	28 (6.2)	5 (8.1)	0.077	0.781

Excluding patients with both anterior and posterior circulation aneurysms, a total of 512 patients were included and divided into anterior circulation group and posterior circulation group according to the location of their aneurysms.

TABLE 6. Analysis of the Correlation Between Internal Carotid Artery Curvature and Intracranial Aneurysms Size

Internal Carotid Artery Morphology	Diameter ≤ 5 mm (n = 259), n (%)	Diameter > 5 mm (n = 275), n (%)	χ^2	*P*
Tortuosity	152 (58.7)	170 (61.8)	0.546	0.460
Kinking	62 (23.9)	73 (26.5)	0.480	0.488
Coiling	152 (58.7)	170 (61.8)	0.546	0.460

the aneurysm and carotid artery curvature. On the basis of this finding, we believe that changes in the kinking of the internal carotid artery may only be related to the occurrence of intracranial aneurysms but not to the development of intracranial aneurysms.

Our research has certain limitations. First, this was a single-center retrospective study. Second, we only evaluated the degree of internal carotid artery curvature. The degree of curvature of the vertebrobasilar artery may have affected our results. Third, this study did not obtain any pathologic data that showed the weakness of the intracranial vascular wall to enhance the scientific nature of our results. The correlation between internal carotid artery curvature and the occurrence of intracranial aneurysms and its underlying mechanisms need to be further confirmed by a larger number of in-depth studies.

CONCLUSION

In summary, although internal carotid artery curvature has no relation to whether the intracranial aneurysm is ruptured, the number, location, and size of the aneurysms, kinking is closely related to the occurrence of intracranial aneurysms. Therefore, changes in internal carotid artery kinking are intracranial factors that affect the occurrence of aneurysms. Patients with aneurysms may have some pathologic factors that cause the intracranial blood vessels to weaken.

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