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The risk factors of intracranial aneurysm rupture and the assessing efficacy of CTA.

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Abstract

Objective: The objective is to apply the Computed Tomographic Angiography (CTA) on assessing the risk factors of intracranial aneurysm rupture, providing the reference for the prevention of intracranial aneurysm rupture.
Methods: 252 intracranial aneurysm rupture patients admitted in our hospital between February 2014-February 2017 were selected for prospective study. The rate of intracranial aneurysm rupture was evaluated and calculated. The univariate analysis was used to evaluate the different clinical characteristics and CTA results of patients with intracranial aneurysm rupture patients, and then the factors with statistical difference were included in Logistic multivariate regression analysis to analyse the risk factors of intracranial aneurysm rupture.
Results: In 252 patients, 45 patients were confirmed as intracranial aneurysm rupture during the surgery, the rate of intracranial aneurysm rupture was 17.86%. Logistic multivariate regression analysis results showed that complicating with hypertension, the diameter of aneurysm ≥ 3.850 mm, the ratio of aneurysm depth to aneurysm neck width (aspect ratio, AR) ≥ 1.448, the ratio of tumor depth to patent artery diameter (size ratio, SR) ≥ 1.388, the ratio of aneurysm area to the patent artery area at aneurysm neck ≥ 1.192, irregular aneurysm wall and the aneurysm locating at posterior communicating artery, internal carotid artery or middle cerebral artery were the independent risk factors of intracranial aneurysm rupture. The age ≥ 60, male patient and complicating with diabetes were the protective factors (P<0.05).
Conclusion: Intracranial aneurysm rupture is closely related to clinical characteristics, aneurysm morphology and location. Based on the baseline characteristics, aneurysm diameter, AR, SR and area ratio in CTA image could be the reliable references of intracranial aneurysm rupture risk.

Keywords: Intracranial aneurysm, Rupture, Risk factor, CT angiography, Evaluation.

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Introduction

Intracranial aneurysm is an acute cerebrovascular disease caused by cystic encephalocele of intracranial arterial wall in Neurosurgery Department [1,2]. It is also the premonitory symptom of subarachnoid hemorrhage, the disability rate and mortality of which are high. Hemorrhage caused by intracranial aneurysm rupture is the main reason of subarachnoid hemorrhage. Therefore, combining with the rapid diagnosis and treatment, accurately assessing the risk of aneurysm rupture and intervening timely is critical for improving the survival rate and prognosis of patients [3-5]. As a simple and non-invasive method, Computed Tomographic Angiography (CTA) is widely applied in the assessment of intracranial aneurysm size, structure and anatomical location. Some researchers also have proposed that the advantage of CTA is hopeful to provide the reference for intracranial aneurysm rupture [6-8]. In this study, 252 intracranial aneurysm rupture patients were included and CTA was applied to assess the risk factors of aneurysm rupture.

Materials and Methods

Objects

252 intracranial aneurysm patients admitted in our hospital during February, 2014-February 2017 were selected as objects for the prospective study. Inclusion criteria: intracranial aneurysm was confirmed by medical imaging and surgery, and there were no criteria of intracranial aneurysm rupture when

included; the clinical data were complete; the patients were informed about this study and accepted CTA voluntarily. Exclusion criteria: the patients were complicated with other hemorrhagic disease or vascular diseases such as hypertensive intracerebral hematoma, arteriovenous fistula, moyamoya disease, facial hemangioma and head trauma; infection or intracranial aneurysm caused by trauma; unconsciousness or unable to cooperate; the patients received vessel clamp or endovascular interventional therapy before inclusion; contrast agent allergy. The age of 252 patients was 24-79 y and the average age was (51.52 ± 11.38 y). There were 167 male patients and 85 female patients. The complications: 161 patients had hypertension, 78 patients had diabetes and 85 patients had hyperlipemia. The Ethics Committee of our hospital approved this study.

Methods

The baseline of patient characteristics: The baselines of patient characteristics were collected, including age, gender, past medical history, family history and personal history. The past medical history included hypertension, diabetes, hyperlipemia, coronary heart disease and polycystic kidney et al, the family history included intracranial aneurysm, subarachnoid hemorrhage, and the personal history included smoking and drinking history.

CTA: The patients in both groups received CTA on the day admitted; the equipment used for the examination was LightSpeed 64 slice CT scanner (GE Healthcare, California, USA). Scanning parameters: the diameter was 64 mm × 0.5 mm, the pitch was 0.641, reconstructed slice thickness was 0.5 mm, the interval was 0.3 mm, the bulb rotation time was 0.5 s/circle, the matrix was 512 × 512; scanning range: from calvarium to the lower edge of atlas; 60-80 ml non-ionic contrast agent iohexol and 100 ml normal saline were injected through cubital vein with speed of 4 ml/s, the threshold was set as 100 Hu at aortic arch. After scanning, the three dimensional image was reconstructed by several methods including multiplane reconstruction, maximal intensity projection and volume rendering technique, ADW 4.5 workstation was applied for image post-processing. In addition to aneurysm location and aneurysm wall, the aneurysm parameters were also assessed including aneurysm depth (H_{max}, the maximal distance from the midpoint of aneurysm neck to aneurysm peak), height (H_p, the vertical distance from aneurysm peak to aneurysm neck plane), aneurysm width (W, the maximal vertical diameter from aneurysm to H_p), aneurysm neck width (N, the maximal vertical diameter from aneurysm neck to H_p), and the diameter of patent artery (D_v). Based on above parameters, the ratio of aneurysm depth to aneurysm neck width (aspect ratio, $AR=H_{max}/N$), the ratio of tumor depth to patent artery diameter (size ratio, $SR=H_{max}/D_v$), the ratio of aneurysm neck width to patent artery diameter (NPR, $NPR=N/D_v$) and the ratio of aneurysm area to the patent artery area at aneurysm neck (area ratio=$H_p \times W/(D_v \times N)$) were calculated.

Diagnosis of intracranial aneurysm rupture: According to the references [9-11], the intracranial aneurysm rupture was diagnosed, the criteria were as the following: the location where subarachnoid hemorrhage is concentrated or the location of hematoma; the ruptured aneurysm indicated by parent artery spasm; surgery results. The rupture rate of 252 patients was calculated.

Analysis of risk factors: The rates of intracranial aneurysm rupture in patients with different clinical characteristics and CTA results were calculated, and the factors with statistical difference were included in Logistics multivariate analysis to conclude the factors that affect intracranial aneurysm rupture.

Statistical analysis

SPSS18.0 (International Business Machines Corp., New York, USA) was used to analyse the clinical data in this clinical study. The numeration data were presented as (n/%) and χ^2 test was used for analysis. The measurement data were presented as ($\bar{x} \pm s$), if the data fit normal distribution t-test was used for analysis and if the data don't fit normal distribution modified t-test was used for analysis. The factors that affected intracranial aneurysm rupture were included in Logistic multivariate analysis, P<0.05 was considered as statistically significant.

Results

The general data of intracranial aneurysm rupture

In 252 patients, 45 patients were confirmed as intracranial aneurysm rupture during the surgery. The rate of intracranial aneurysm rupture was 17.86%.

Univariate analysis

Baseline characteristics: The rates of intracranial aneurysm rupture in patients with different age, gender, hypertension and diabetes were statistically different (P<0.05), as shown in Table 1.

Table 1. *Analysis of intracranial aneurysm rupture in patients with different baseline characteristics (n=252).*

Baseline characteristics		Case number	Case number of intracranial aneurysm rupture (n)	Occurrence rate (%)	P value
Age (Year)	<60	156	36	23.08	<0.05
	≥ 60	96	9	9.38	

Gender	Male	167	23	13.77	<0.05
	Female	85	22	25.88	
Hypertension	Yes	161	39	24.22	0.05
	No	91	6	6.59	
Diabetes	Yes	78	6	7.69	<0.05
	No	174	39	22.41	
Hyperlipemia	Yes	85	15	17.65	0.05
	No	167	30	17.96	
Family history	Yes	34	7	20.59	0.05
	No	218	38	17.43	
Smoking history	Yes	60	11	18.33	0.05
	No	192	34	17.71	
Drinking history	Yes	31	6	19.35	0.05
	No	221	39	17.65	

CTA parameters: The rates of intracranial rupture in patients with different aneurysm diameter, AR, SR, area ratio, aneurysm diameter and irregular aneurysm wall were statistically different (P<0.05), as shown in Table 2.

Table 2. *The relation between CTA parameter and intracranial aneurysm rupture (n=252).*

	CTA parameter*	Case number	Case number of intracranial aneurysm rupture (n)	Occurrence rate (%)	P value
Aneurysm neck	<3.151 mm	173	31	17.92	>0.05
	≥ 3.151 mm	79	14	17.72	
Aneurysm diameter	<3.850 mm	85	8	9.41	<0.05
	≥ 3.850 mm	167	37	22.16	
Dv	<2.081 mm	16	3	18.75	>0.05
	≥ 2.081 mm	236	42	17.80	
AR	<1.448	151	11	7.28	<0.05
	≥ 1.448	101	34	33.66	
SR	<1.388	22	1	4.55	<0.05
	≥ 1.388	230	44	19.13	
Area ratio	<1.192	139	11	7.91	<0.05
	≥ 1.192	113	34	30.09	
Irregular aneurysm wall	Yes	125	38	30.40	<0.05
	No	127	7	5.51	
Aneurysm location	Posterior Communicating artery	89	18	20.22	<0.05
	Internal carotid artery	37	9	24.32	
	Anterior cerebral artery	51	5	9.80	
	Middle cerebral artery	59	12	20.34	
	Posterior cerebral circulation artery	16	1	6.25	

*Note: the mean CTA parameters of 252 were selected as cut-off value.

Logistic multivariate analysis

Logistic multivariate regression analysis results showed that complicating with hypertension, the diameter of aneurysm ≥ 3.850 mm, AR ≥ 1.448, SR ≥ 1.388, the area ratio ≥ 1.192, irregular aneurysm wall and the aneurysm locating at posterior communicating artery, internal carotid artery or middle cerebral artery were the independent risk factors of intracranial aneurysm rupture. The age ≥ 60, male patient, complicating with diabetes were the protective factors (P<0.05), as shown in Table 3.

Table 3. *The multivariate regression analysis of factors that affect intracranial aneurysm rupture.*

Risk factor	β	SE (β)	Wald χ^2 value	P value	OR	95% CI
Age ≥ 60 y	-1.325	0.118	126.086	0.000	0.266	0.211~0.335
Male	-0.399	0.125	10.189	0.000	0.671	0.525~0.857
Complicating hypertension	1.525	0.176	75.078	0.000	4.595	3.255~6.488
Complicating diabetes	-1.683	0.325	26.816	0.000	0.186	0.098~0.351
Aneurysm diameter ≥ 3.850 mm	0.781	0.339	5.308	0.000	2.184	1.124~4.244
AR ≥ 1.448	0.265	0.111	5.700	0.000	1.303	1.049~1.620
SR ≥ 1.388	0.994	0.135	54.213	0.000	2.702	2.074~3.520
Area ratio ≥ 1.192	1.032	0.241	18.337	0.000	2.807	1.750~4.501
Irregular aneurysm wall	2.597	0.582	19.911	0.000	13.423	4.290~42.002
Location at posterior communicating artery/ internal carotid artery/middle cerebral artery	0.891	0.147	36.738	0.000	2.438	1.827~3.252

Discussion

Intracranial aneurysm is prone to locate at posterior communicating artery or anterior communicating artery branch in Willis circle and this area is located around the subarachnoid space [12,13]. Thus, once there is intracranial aneurysm rupture, there is high risk of spontaneous subarachnoid hemorrhage, which causes high mortality and disability rate [4,14,15]. Therefore, risk assessment of intracranial aneurysm rupture in the early stage is critical in determining the surgical regimen and timing.

Previously most of the studies regarding the risk factor of intracranial aneurysm rupture focused on the baseline characteristics of patients [16]. In this study, the results showed that the patients with age ≥ 60 y, male patient and complicating with diabetes had lower risk of intracranial aneurysm rupture, and the patients complicating with hypertension had higher risk of intracranial aneurysm rupture, which is in accordance with the previous studies [17-19]. Compared with young people, older people's cerebrovascular autoregulation ability is relatively slow, which may lead to intracranial aneurysms more likely to rupture in the elderly ones. The main reasons are: Although among the elderly population the compliance and elasticity of artery are decreased and there is high morbidity of aneurysm in elderly population, the risk of rupture is lower. As the age increases the rupture risk is decreased. It is considered that the decreased risk is related to several protective factors such as decreased blood flow and decreased external stimuli [20,21]. In this study, the risk of intracranial aneurysm rupture in male patients was only 0.671 times of female patients, that is to say, the risk in female patients was 1.5 times higher than male patients, which might be related to that most of female patients were in menopausal status, and menopause is considered to be related to increased risk of intracranial aneurysm rupture. This may be related to endocrine factors. Postmenopausal estrogen levels decreased, causing the content of collagen in tissues to reduce, and thus increasing the brittleness of the vessel wall, so the aneurysm is easy to form and develop. There is also study proposes that estrogen-replacement therapy can effectively decrease the rate of intracranial aneurysm rupture [22,23]; in diabetes patients, there are some pathophysiological changes such as glucose, lipid and protein metabolism disorder, the above changes can cause thickening of capillary basement membrane and atherosclerosis which further increases the risk of intracranial aneurysm. Hyperglycemia is conducive to mononuclear cells into the intima and into foam cells, eventually leading to atherosclerosis, contributing to the occurrence of aneurysms, but the role of aneurysm rupture is not clear. However, in this study, complicating with diabetes was the protective factor of intracranial aneurysm rupture, that is to say, although diabetes can increase the occurrence rate of intracranial aneurysm, it can decrease the risk of intracranial aneurysm rupture. This may be related to that diabetes patients have higher self-management awareness, and there is better timing for the early diagnosis and treatment of intracranial aneurysm. Furthermore, the regular diet and exercise of diabetes patients are helpful to the stability of aneurysm, and the complications in diabetes patients can also cause vicious events before intracranial aneurysm rupture, which can also cause error in statistical results [24-27]; hypertension caused thickening of vessel wall, arteriole hyaline change, smooth muscle cell proliferation of vascular wall, and endothelium damage can decrease the tolerance of vascular wall to blood pressure, and repetitive blood pressure fluctuation impact can gradually cause aneurysm rupture [28-30].

Based on the baseline characteristics, the value of CTA parameters in assessing aneurysm rupture risk was discussed. The results showed that aneurysm diameter $\geq$ 3.850 mm, AR $\geq$ 1.448, SR $\geq$ 1.388, area ratio $\geq$ 1.192, irregular aneurysm or the aneurysm located at posterior communicating artery/ internal carotid artery/middle cerebral artery could provide reliable reference for assessing the risk of aneurysm rupture. The above characteristics can not only help to assess the aneurysm itself, but also judge some parameters including the blood volume in aneurysm, blood flow speed and average shear stress within the aneurysm, and further predict the rupture risk based on the patent artery. Besides, Huang et al. [31] found that CTA parameters were independent risk factors from baseline characteristics, thus, CTA parameters combined with patients baseline characteristics can provide more accurate assessment, and further provide a timing and reliable indication for the diagnosis and treatment of intracranial aneurysm.

In conclusion, intracranial aneurysm rupture is closely related to patient age, gender and complication, and CTA parameters can also be applied in predicting the risk of intracranial aneurysm rupture. Thus, the above parameters are hopeful to be applied in predicting the risk of intracranial aneurysm rupture more accurately, however larger sample size is needed to verify the efficacy.

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