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Original Article

Analysis on prognostic factors of patients with ruptured intracranial aneurysms

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Abstract: Background: Intracranial aneurysm (IA) is a common vascular disease which causes neoplastic hyperplasia of cerebral vessels. It is very important to study relevant factors that influence the prognosis of patients with ruptured intracranial aneurysm to guide the clinical treatment of IA. Methods: This study made a retrospective analysis on data of 580 patients with ruptured IA. To screen risk factors that related to the prognosis of ruptured IA, univariate analysis of variance by χ^2 test or Wilcoxon test, and multivariable logistic by multiple logistic regression model were carried out. According to the Glasgow Outcome Scale (GOS) scored, the surgical outcomes were also evaluated. Results: The univariate analysis results showed that Age, headache symptoms, Hunt-Hess classification, onset time of surgery, and surgical approach were the risk factors related to the prognosis of patients with ruptured IA. Multivariable logistic regression analysis results showed that the age (*P=0.021*), Hunt-Hess classification (*P=0.002*). Onset time of surgery (*P=0.019*) and surgical approach ($P \leq 0.003$) were the independent risk factors. Conclusions: The ultimate outcome of the patients with ruptured intracranial aneurysm depend on clinical judgement including accurate comprehensive analysis, the best surgical time, the right surgical method.

Keywords: Ruptured intracranial aneurysm, risk factor, prognosis

Introduction

Intracranial aneurysm (IA) is a common vascular disease in which local vessel abnormal change causes neoplastic hyperplasia of cerebral vessels [1-3]. In clinical, spontaneous subarachnoid hemorrhage (SAH) is taken as the initial symptom [4-6]. Its morbidity ranks the third among patients with cerebrovascular accidents, just after cerebral thrombosis and hypertensive cerebral hemorrhage. But its fatality rate and disability rate are very high [7, 8]. According to the latest research report of Mayo Clinic in 2009, the occurrence rate of unruptured aneurysms is about 2% while the annual morbidity of subarachnoid hemorrhage caused by intracranial aneurysm rupture is about 60~100/100 thousand people.

SAH may result in various pathological changes including cerebral vasospasm, cerebral edema, cerebral infarction and hydrocephalus and the fatality rate is as high as 25%~60%. If not treated well at the first time of hemorrhage, 40% of survivors [9] may have the risk of re-hemorrhage in 3 weeks and the mortality and disability rate of re-hemorrhage will be as high as 80% [10, 11], seriously threatening patients' life. The curative effects of patients with ruptured intracranial aneurysms are influenced by onset severity of patient's condition, timing of treatment, treatment methods, etc [12-16].

Surgical treatment of intracranial aneurysm includes two strategies: one is arterial aneurysm clipping operation. The other is endovascular intervention. The former one is a classic and traditional surgery, which has been regarded as "golden standard" for treating intracranial aneurysm in recent decades [17], while endovascular intervention is a new technology that has been developed in recent 20 years. In recent years, microsurgery clipping and endovascular intervention have been developed and improved continuously, however which one is optimal in safety and effectiveness has not been determined yet.

Therefore, it is very important to study relevant factors that influence the prognosis of patients

Table 1. Analysis on Single Factors that Influence Intracranial Aneurysm Patients' Diagnosis

Influencing factors		Poor prognosis		Good prognosis		*P* value
		Cases	(%)	Cases	(%)	
Gender	Male	40	(16.7)	199	(83.3)	0.474
	Female	65	(19.1)	276	(80.9)	
Age	≤40 years	8	(15.4)	44	(84.6)	0.029
	40-49 years	23	(14.9)	131	(85.1)	
	50-59 years	25	(13.4)	161	(86.6)	
	≥60 years	44	(23.4)	144	(76.6)	
Aneurysmal neck size	Wide (1)	67	(17.8)	309	(82.2)	0.810
	Narrow (2)	19	(20.0)	76	(80.0)	
	Unknown (3)	17	(16.5)	86	(83.5)	
Headache	Yes	79	(15.7)	424	(84.3)	0.000
	No	26	(33.8)	51	(76.2)	
Hunt-Hess	Level I	9	(8.8)	93	(91.2)	0.000
	Level II	31	(13.5)	199	(86.5)	
	Level III	42	(22.5)	145	(77.5)	
	Level IV	16	(34.8)	30	(65.2)	
	Level V	7	(63.6)	4	(37.4)	
Surgical timing	0~3 d	80	(22.3)	278	(77.7)	0.002
	4~10 d	16	(15.5)	87	(84.5)	
	11~14 d	3	(7.1)	39	(92.9)	
	>14 d	5	(6.8)	69	(93.2)	
Surgical way	Craniotomy clipping	82	(20.8)	313	(79.2)	0.015
	Endovascular intervention	23	(12.4)	162	(87.6)	

with ruptured intracranial aneurysm to predicate the development of patients' condition. This study made a retrospective analysis on clinical medical records of 580 patients with ruptured intracranial aneurysms that had been hospitalized in neurosurgery of Weifang People's Hospital and studied prognosis and relevant factors of patients with ruptured intracranial aneurysms to determine relevant factors that may influence prognosis, so as to instruct clinical work and improve clinical rescue level.

Materials and methods

Study objects

580 patients with ruptured intracranial aneurysms that had been hospitalized in neurosurgery of Weifang People's Hospital and had received operative treatment from January 2007 to July 2013 were taken as study objects, of which, there were 239 male cases, 341 female cases; 52 cases younger than 40 years old, 154 cases 40~49 years old, 186 cases 50~59 years old and 188 cases older than 60 years old; 395 cases received craniotomy clipping operation and 185 cases received intravascular interventional operation; 71 cases died after surgery.

Glasgow outcome scale (GOS)

Scores of treatment finality were taken as clinical prognosis evaluation indexes and GOS1~2 was defined as poor prognosis, 3~5 points as good prognosis. Inclusion criteria: (1) Patients who were checked by digital subtraction angiography (DSA) and (or) CT angiography (CTA) and were diagnosed with subarachnoid hemorrhage caused by ruptured intracranial aneurysm; (2) Patients who had typical clinical manifestation and signs of subarachnoid hemorrhage; (3) Patients who were performed craniotomy clipping or endovascular interventional surgery [17]. Exclusion criteria: (1) Patients who were hospitalized due to trauma; (2) Patients who were diagnosed with intracranial aneurysm but not received surgical treatment; (3) Patients who received two kinds of surgery; (4) Patients who were diagnosed with intracranial

Table 2. Multiple Logistic Regression Analysis on Factors Influencing Intracranial Aneurysm Patients' Prognosis

Influencing factor	Regression coefficient	Standard error	*OR*	*P value*	*95% CI*
Patients' age	-1.243	0.512	0.329	0.021	0.144-0.735
Surgical timing	-15.54	0.643	1.826	0.019	1.521-2.103
Hunt-Hess	-20.417	0.939	1.358	0.002	2.531-5.622
Headache	-0.478	0.326	0.614	1.534	0.328~1.151
Surgical way	-0.849	0.283	0.428	0.003	0.246~0.745
Constant	1.054	0.907	2.869		

aneurysm and received surgery but with unruptured intracranial aneurysm.

Statistical methods

SPSS13.0 statistical software was adopted and usage rate and constituent ratio were used to describe materials. Single factor analysis was first conducted on factors that may influence the prognosis of patients with ruptured intracranial aneurysm and χ^2 and rank sum tests were adopted. Factors that had statistical significance in the single factor analysis were analyzed further by multiple logistic regression model and $P<0.05$ was statistically significant.

Results

Analysis on single factors that influence patients' diagnosis

Among 580 patients, 471 patients had a good prognosis and the good prognosis rate was 81.2%. Single factor analysis results indicated that patients' age, headache symptom, Hunt-Hess grading, surgical timing and surgical way are influencing factors that influence prognosis of patients with intracranial aneurysms and the difference had statistical significance ($P<0.05$); patients' gender and aneurysm size are not influencing factors that influence patients' prognosis ($P>0.05$, **Table 1**).

Multiple logistic regression analysis on factors influencing patients' prognosis

Five factors with statistical significance in signal factor analysis were taken out for multiple factor Logistic regression analysis and the results indicated that patients' age (*P=0.021*), Hunt-Hess grading (*P=0.002*), surgical timing (*P=0.019*) and surgical way ($P=0.003$) are independent risk factors that influence prognosis; headache symptom at admission is not an independent risk factor that influence prognosis and the difference had no statistical significance ($P>0.05$, **Table 2**).

Discussions

In this study, 580 patients with ruptured intracranial aneurysms that had been hospitalized in neurosurgery of Weifang People's Hospital and had received operative treatment from January 2007 to July 2013 were taken as study objects and the big sample size is the advantage of this study. By reading relevant literatures, it can be found that there are always disputes about the relation of age and prognosis. By analyzing cases of this group, it indicated that age is the independent risk factor that influences the prognosis of patients with ruptured intracranial aneurysm. Single factor analysis found that the favorable prognosis of patients younger than 40 years old, 40~49 years old, 50~59 years old had no big difference (84.6%, 85.1% and 86.6%), while the favorable prognosis of patients older than 60 years old was only 76.6%. Shirao et al. [18] found that the state of consciousness on admission was evidently related to age. CT examination found that the older the patient is, the bigger the SAH volume will be and the occurrence rate of intraventricular hemorrhage and hydrocephalus increases with aging. Symptomatic vasospasm is more common in the older group, confirming that age is the independent risk factor affecting prognosis. The reason may be due to arterial sclerosis: the vascular elasticity and adaptability decrease with age and their reaction to vascular constriction factors also decrease [19]. With age, the occurrence rate of diabetes, hypertension, cerebrovascular disease, and cardiopulmonary dysfunction disease also increases and these are all important factors that influence patients' prognosis.

Hunt-Hess classification is an index that indicates the risk degree of the disease condition. This study showed that Hunt-Hess classification is an independent risk factor that influences the prognosis. Single factor analysis results indicated that, the higher the grading level is, the lower the favorable prognosis rate of patients will be; especially when it is level V, it is only 37.4%, that is, the higher the Hunt-Hess grading of ruptured intracranial aneurysm is, the poorer the clinical prognosis will be.

Different points by scholars were concluded by reading literatures: (1) Hunt-Hess grading level I and level II had no significant influence on prognosis; (2) for patients with Hunt-Hess low grading (level I, II and some III), there is a low risk of rehaemorrhagia and vasospasm; currently, early operative treatment is suggested and it can evidently improve prognosis [18, 20, 21]; (3) for patients with Hunt-Hess level IV~level V, symptomatic cerebral vasospasm easily appears, with poor prognosis [18]. Multiple factor logistic regression analysis indicated that there was a statistical difference between Hunt-Hess I~II and Hunt-Hess V, there was no statistical significance in difference between III~IV and V, but *p* value of III was 0.06, close to 0.05, and this can better demonstrate the listed points. During the treatment, we found that patients with high Hunt-Hess level should be analyzed comprehensively before deciding the best surgical timing and the treatment plan.

Surgical timing, as one of the factors that affect the prognosis of patients with intracranial aneurysms, has always been the hot spot of the discussion. Most scholars advocate early treatment (in 3 d) to ruptured intracranial aneurysms [20-22]. For intracranial aneurysm patients, early surgical treatment cannot only reduce the risk of bleeding again, but can also eliminate cerebral hemorrhage within the cistern, create conditions for follow-up treatment, and reduce the incidence of vasospasm and severity. Delayed surgery can effectively reduce the intracranial pressure of patients and increase the rate of intraoperative complete clipping, but due to time delay, secondary bleeding rate may increase. Therefore, both of them have advantages and disadvantages.

In this study, multiple-factor logistic regression analysis revealed that surgical timing is an independent risk factor affecting the prognosis of patients with intracranial aneurysms: comparing the prognosis of patients operated at 0~3 d and 4~10 d with that operated after 14 days, the difference had significance statistical significance; the prognosis difference between 11~14 d and >14 d had no statistical significance and OR value was 1.045, which confirmed that >10 d can be the evidence for surgery later stage. Single factor analysis results indicated that prognosis favorable rate at 0~3 d, 4~10 d, 11~14 d and >14 d were separately 77.7%, 84.5%, 92.9% and 93.2%.

The longer the surgical time to the onset time, the higher the favorable rate of prognosis will be. And the favorable rates of prognosis at 11~14 d and >14 d are basically the same and this is different from the point that early surgery should be conducted [23]. The reason may be that the treatment habits of this department for severe patients are that surgery should be conducted as soon as possible after admission, but for patients with lighter disease condition, surgery may be conducted after the disease condition is steady. In the early operative treatment, poor preoperative condition, mechanical stimulation and anesthesia of surgery and will further worsen the brain injury and exacerbate the disease in a short time, which may influence the short-term prognosis of patients.

For middle-stage and later-stage surgery, patients' disease conditions are relatively stable and the adverse impact caused by SAH will be lightened, so surgery during this period will cause little injury to the brain and the surgical safety is evidently increased. Therefore, middle-stage and later-stage surgery have better effects. But considering that rehaemorrhagia may cause death, so as long as patients' basic conditions are permitted, early operative treatment should be conducted, especially patients with preoperative Hunt-Hess level I and II. For patients with Hunt-Hess III, IV, if their clinical conditions are also steady, they can also consider early operative treatment. Treatment plans for patient with level V should be made carefully, because no matter surgery or not, the results are neither ideal.

Currently, the most effective methods for treating intracranial aneurysm are neurosurgical clipping and endovascular intervention [24]. Intraoperative tumor rupture is the biggest risk

of neurosurgical clipping and it is the main reason that results in surgical failure, patients' disability and death [25-27]. With the development and innovation of endovascular intervention and various intervention materials and diversification of intracranial aneurysm intervention ways, endovascular intervention is being widely accepted and approved by its micro- invasiveness, low disability rate and low fatality rate [28]. But six-year follow-up data published by ISAT showed that the arterial aneurysm complete clipping rate of neurosurgical clipping was slightly higher than that of endovascular intervention.

This research showed that the favorable prognosis rate of patients treated by neurosurgical clipping is 79.2% and that of patients treated by intravascular intervention is 87.6%, and the difference had statistical significance, indicating that both operative ways have a certain curative effect but the prognosis effect of intravascular intervention is better. To sum up, neurosurgical clipping and intravascular intervention both have an evident effect on treating intracranial aneurysm, but intravascular intervention has a better curative effect, with a favorable prognosis rate 2.336 times as that of the neurosurgical clipping. Therefore, if the disease condition is allowable, endovascular intervention is a better choice. This study indicated that: for treating patients with ruptured intracranial aneurysm, first analyze their disease condition comprehensively, then determine the time and way of surgery, so as to improve the treatment effect and improve patients' survival quality.

This study still has some shortcomings: (1) The samples are only from one hospital, so there are some biases in hospital. (2) This study is a retrospective analysis, so it is unable to determine the reasons and standards that patients chose these two ways of surgery. The selection of operative ways are mostly decided by doctors based on disease condition of patients and after discussion with family members, therefore, the standard of choosing the operative way needs further study; besides, this study may have lost some information which may not be induced into the influencing factors with statistical significance, so it needs forward-looking multi-center control study, unify the inclusion standard and end point observation indexes and have long-term follow-up visits, only by doing these, a more accurate prognosis model can be established.

Disclosure of conflict of interest

None.

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