Research Square

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Exploring risk factors for intraoperative aneurysm rupture during clipping

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Abstract

Objective To investigate risk factors for aneurysm rupture in intracranial aneurysm clipping (IAC).

Methods Patients admitted for IAC from April 2010 to December 2017 in the Fujita Health University Hospital or the First Affiliated Hospital of Xiamen University were retrospectively reviewed. Clinical parameters were recorded and analyzed using univariate and multivariate analysis. The Hunt-Hess grade was used to assess the preoperative clinical status of patients. Modified Rankin Scale was applied to evaluate the prognosis of patients 6 months after surgery.

Results Univariate analysis showed that the preoperative clinical status ($p = 0.015$) and the preoperative aneurysm rupture ($p = 0.005$) were significantly associated with intraoperative aneurysm rupture (IAR) during clipping. Multivariate logistic regression analysis showed that the preoperative aneurysm rupture was an independent risk factor of IAR ($p < 0.001$, OR = 10.518). There was no significant difference in the prognosis between patients with and without IAR ($p > 0.05$). No significant differences existed on aspects of incidences and time points of rupture in the operations conducted by experienced surgeons compared with that conducted by less-experienced surgeons ($p > 0.05$).

Conclusion Preoperative aneurysm rupture is the independent risk factor for aneurysm rupture during IAC. Intraoperative rupture, if treated properly in time, has no influence on the prognosis of patients receiving IAC. Less-experienced surgeons can also reduce the incidence rate of IAR by strictly controlling surgical indications.

Background

Intraoperative aneurysm rupture (IAR) is one of the most serious complications during intracranial aneurysm clipping (IAC). If not disposed quickly and effectively, IAR would decrease success rate of operations, lead to disastrous consequences, and deteriorate the quality of life in patients after receiving IAC[1 – 3]. It is crucial to take effective measures to prevent IAR. Besides, how to deal with this surgical emergency timely and properly after IAR happened needs more consideration.

In order to prevent rupture, it is necessary to identify the risk factors affecting the incidence of IAR during surgical clipping. Due to the largely different designs of researches, previously reported risk factors for IAR varied widely[4 – 6]. The operative experience of surgeons as a variable was not involved and analyzed in most studies except only a few reports[7, 8]. Based on the evidence from existing literature and our preliminary research results, we took the surgical experience of surgeons into consideration and tried to comprehensively evaluate the risk factors of IAR from the aspects of both patient and surgeons during IAC.

Methods

Research object

All enrolled patients in this study who underwent IAC were separated into two groups according to the different operative surgeons. The surgeries in the experienced group were conducted by two experienced neurosurgeons who possessed accumulated experience for more than 30 years and performed IAC 200 cases per year averagely. This group contained 211 patients with intracranial aneurysm admitted to Fujita Health University Hospital in Japan from April 2010 to March 2011. Assistant operators for the patients with unruptured aneurysm were resident surgeons, while for the cases with ruptured aneurysm, the intraoperative assistants were attending surgeons.

As for the less-experienced group, a total of 120 patients with intracranial aneurysm admitted to the Neurosurgery Department of the First Affiliated Hospital of Xiamen University from November 2011 to December 2017 in China were enrolled. The chief surgeon in this group was fixed, who performed aneurysm surgery for 20 cases per year. The intraoperative assistants in the less-experienced group were resident surgeons of the neurosurgery department.

Clinical data

Clinical data of patients, including name, gender, age, medical history, aneurysm site, aneurysm size, postoperative follow-up and so on (Table 1) were collected from the electronic medical records of Fujita Health University Hospital and the First Affiliated Hospital of Xiamen University. All enrolled patients received craniotomy and microsurgical clipping for intracranial aneurysm.

On admission to hospital, the clinical status of patients was evaluated by the Hunt-Hess grade (H-H grade). Patients with a preoperative H-H grade of 0-3 were classified into well status, while a grade 4-5 was defined as poor status. Surgery performed within 24 hours, 24-72 hours, 4-14 days and more than 2 weeks after admission were defined as ultra-early operation, early operation, mid-phase operation and late-phase operation respectively. The Modified Rankin Scale was used to evaluate the prognosis of patients 6 months after surgery, in which 0-2 scores represented well prognosis, while 3-6 scores were defined as poor prognosis.

Based on maximum diameter measured by CTA or DSA three-dimensional reconstruction, aneurysms were divided into small aneurysms (less than 5mm), medium aneurysms (5 - 15mm), large aneurysms (15 - 25mm), and giant aneurysms (greater than 25mm). According to intracranial location, they could also be classified into paraclinoid aneurysms, supraclinoid segment aneurysms and posterior circulation aneurysms. The time points of intraoperative aneurysm rupture were divided into the following four categories: (1) before incision of dura maters: included the rupture occurred in the process of preoperative positioning, anesthesia, fixing head rack, and craniotomy; (2) preliminary separation phase: referred to the rupture occurred from preliminary separation of subarachnoid space to the exposure of the proximal of the parent artery; (3) aneurysm dissection phase: represented rupture occurred during the further dissection of the aneurysm neck, body and its branches; (4) aneurysm clipping phrase: referred to rupture occurred during the clipping of aneurysm neck.

Statistical analysis

SPSS 22.0 software was used for statistical analysis. Data conforming to normal distribution were expressed as $\bar{X} \pm S$. Categorical variables were represented by number and percentage. Chi-square test or

Fischer's exact test was used to identify the possible risk factors of rupture during IAC. Statistically significant risk factors obtained from univariate analysis were further analyzed using multivariate logistic regression analysis. It was considered statistically significant when $p < 0.05$.

Results

The comparison of general information between the experienced and less-experienced group

There were 211 cases in the experienced group which contained 145 (68.7%) female patients and 66 (31.3%) male patients. A total of 152 (72%) cases were younger than 60 years old. Almost 94.8% of the patients had the well preoperative clinical status. The supraclinoid segment aneurysms accounted for 83.9% of all cases. There were 185 (87.7%) patients with well prognosis, 165 (78.2%) patients with unruptured aneurysm, and 6 (2.8%) patients with intraoperative aneurysm rupture（**Table 1**）.

As for the less-experienced group, a total of 120 patients were included, which contained 51 (42.5%) female patients and 69 (57.5%) male patients. There were 74 (61.7%) cases younger than 60 years old. The well preoperative clinical status was observed in 103 (85.8%) cases. The supraclinoid segment aneurysms occurred in 115 (95.8%) patients. There were 97 (80.8%) patients with well prognosis, 111 (92.5%) patients with ruptured aneurysm, and 13 (10.8%) patients with intraoperative aneurysm rupture（**Table1**）.

There are significant differences between these two groups in the gender ($\chi2$ =4.214, p =0.04), preoperative clinical status ($\chi2$ =7.919, p =0.005), aneurysm location (p =0.003), the rate of ruptured aneurysm ($\chi2$ =153.345，p＜0.001), and intraoperative aneurysm rupture ($\chi2$ =9.025，p =0.004)（**Table1**）.

Risk factors for intraoperative aneurysm rupture

Univariate analysis showed that the gender ($\chi2$ = 0.125, p = 0.723), age ($\chi2$ = 1.003，p = 0.317), operation time (p = 0.353), aneurysm size (p = 0.886) and aneurysm site (p = 0.19) were all not correlated with IAR(**Table4**). A total of 14 patients (4.6%) in the group of well preoperative clinical status and 5 patients (17.9%) in the group of poor preoperative clinical status suffered IAR respectively, which showed significant difference (Fisher test, p = 0.015) (**Table4**). Besides, IAR occurred in 15 cases (9.4%) of patients who had ruptured aneurysms before operation and in only 4 cases (2.3%) of patients with preoperative non-ruptured aneurysms ($\chi2$ = 7.716, p = 0.005) (**Table4**).

The two significant variables (history of aneurysm rupture and preoperative clinical status), as well as the aneurysm site were further included for multivariate logistic regression analysis. The result showed that the history of aneurysm rupture was an independent risk factor influencing the incidence of IAR (*OR* = 10.518, 95% *CI* = 2.389 46.303, $p < 0.001$).

Effect of intraoperative aneurysm rupture on patients' prognosis

For the 303 patients with Hunt-Hess scores of 0-3, there was no significant difference in prognosis between the patients with IAR (poor prognosis rate of 7.1%) and patients without IAR (11.8%). Meanwhile, for the 28 patients with preoperative Hunt-Hess scores of 4-5, no significant difference of prognosis was observed between the patients with IAR (poor prognosis rate of 60%) and patients without IAR (65.2%) (**Table5**).

The association of surgeons' experience with the incidence and time points of rupture in IAC

For patients with preoperatively ruptured aneurysms, as shown in Table 6, the intraoperative rupture rate of aneurysm in the experienced group was 10.9% (5 cases), while in the less-experienced group was 10.8% (12 cases). There was no significant difference in the IAR rate for the patients with preoperative ruptured aneurysms between these two groups ($\chi 2$=0.000，p = 1) (Table6). Concomitantly, for the patients with preoperatively unruptured aneurysm, the IAR rate in the two groups were 0.6 (1 case) and 11.1% (1 case) respectively, with no significant difference (Fisher test, p = 0.101) (**Table6**).

Among the 6 cases with intraoperative ruptured aneurysms in the experienced group, 1 case of rupture occurred in the initial separation process after dura incision (16.7%), 4 cases occurred in the process of aneurysm separation (66.7%), and 1 case occurred in the process of aneurysm clipping (16.7%). In the less-experienced group, a total of 13 cases suffered IAR, among which 1 case of rupture occurred before opening the dura mater (7.7%), 2 cases of rupture occurred in the initial separation process after dura incision (16.7%), 7 cases occurred in the process of aneurysm separation (66.7%), and 3 cases occurred in the process of aneurysm clipping (16.7%). There was no statistically significant difference in the time point of rupture between the two groups (Fisher test, p =0.226) (**Table7**).

Discussion

The difference of the gender between the two groups was most likely due to the limited sample size with no clinical significance. The followings may explain the differences in preoperative clinical status and the occurrence of ruptured aneurysm: In China, few patients received preoperative medical examination for cerebrovascular disease. The detection rate of unruptured aneurysm is low and a large number of patients suffer from intracranial aneurysm with subarachnoid hemorrhage. In Japan, the screening for cerebrovascular disease is widely adopted. When the unruptured aneurysm is detected, the patients can in time receive regular hospital treatment, which explains that a majority of the aneurysms in Japan are not accompanied with subarachnoid hemorrhage. We believe that it is the subarachnoid hemorrhage which leads to the rupture easily during operation and gives rise to the difference between the two groups in the IAR rate.

In this study, the preoperative aneurysm rupture was found to be an independent risk factor for intraoperative aneurysm rupture. Risk of the patients with a history of aneurysm rupture was 10.518 times higher than that of patients without preoperative aneurysm rupture. Causally, previously ruptured aneurysms may have more fragile crevasses, which easily break up during surgical operation. Besides, hemorrhage combining with brain tissue swelling result in higher intracranial pressure, which made the separation of subarachnoid space difficult. What' s more, hemorrhage in the subarachnoid space brings about serious adhesion of tissue, indistinct anatomical layer and blurred surgical vision, which all increase the rate of IAR during clipping. These results were also consistent with previous founding of Leipzig et al.[8] Additionally, in the current clinical work of receiving emergency patients with existing ruptured aneurysms, in order to prevent any possible ruptures again, emergency surgery will be conducted in early even ultra-early stage of hemorrhage for most patients. The higher rate of rupture in patients with preoperative aneurysm rupture may also be related to less-experienced participant doctor and inadequate preparation because of the urgency.

For the preoperative ruptured aneurysm, it is generally recommended that early surgery should be performed to prevent the recurrence of hemorrhage if the patient's condition permits. However, there were inconsistent reports on the incidence of IAR at different time points of operation. A retrospective study conducted by Schramm et al.[9], which included 222 cases underwent IAC, revealed that the incidence of aneurysm rupture in the early-phase operation group (within 72 hours) was nearly 40.2%, which was significantly higher than the 20.7% of the late-phase operation group (72 hours later). The early-phase surgeries were often accompanied with the greatly fluctuant blood pressure, unabsorbed intracranial hemorrhage, obvious swelling of brain tissue and immature repair of aneurysm fiber, which all increased the risk of IAR during clipping. Inversely, Peerless et al.[10] reviewed 1767 cases with posterior- circulation aneurysms and proposed that the incidence of IAR in surgical operations within 7 days after aneurysm rupture was not significantly different from that in the surgeries 14 days later after aneurysm rupture. Meanwhile, Sandalcioglu also suggested that even though the fragile crevasses of ruptured aneurysms increased IAR rate, the tissue adhesion in subarachnoid space made it difficult to separate and expose, which also facilitated IAR. The results of our study suggested that the possibility of IAR was not associated with time points of surgical operation.

Preoperative clinical status was calculated as a risk factor in the present study for IAR through univariate analysis while was not an independent risk factor through multivariate analysis. These results were in consistence with the reports from Sandalcioglu[11]. However, the opposite voice also existed. For clipping ruptured anterior cerebral aneurysms and middle cerebral aneurysms, Inagawa[12] suggested that there was no significant relationship between the preoperative Hunt-Hess grade of patients and the incidence of IAR.

Accumulated evidences[9, 11, 13–15] previously showed that the occurrence of IAR during clipping surgery did not affect the prognosis of patients. However, a few researches, such as the CARAT study conducted by Elijovich[16] retrospectively, revealed that IAR might potentially deteriorate the postoperative recovery of patients. In this study, the prognosis of patients with Hunt-Hess scores of 0–3 and patients with Hunt-Hess scores of 4–5 was analyzed respectively. Results indicated there was no correlation between the prognosis and IAR in both the two groups. In response to these negative results, we tried to make the appropriate explanations as follows: On one hand, due to the limited sample size and only 19 cases of IAR in our study, bias might exist, which would affect the accuracy of analysis. On the other hand, the intraoperative rupture mostly occurred in the process of separating and clipping aneurysms. At this time point of operation, aneurysms had been well exposed. If aneurysms ruptured, hemorrhage usually accumulated in the separated space, rather than penetrating into the brain parenchyma or the deep arachnoid space leading to acute encephalocele. Furthermore, dual aspirator assistance and temporary blocking would be applied after the rupture to avoid uncontrollable fatal bleeding. These also indicated that if IAR was treated properly and promptly, the prognosis of patients would not be aggravated.

Another potential risk factor of IAR, the experience of surgeons, was considered in this study. For clipping the preoperative ruptured aneurysms, the incidence of IAR in operations conducted by the experienced surgeons was similar to that conducted by the less-experienced surgeon. As for clipping preoperative unruptured aneurysms, the difference of IAR rate between experienced and less-experienced surgeons existed, nevertheless with no statistical significance. Irrespective of bias due to sample size, we believed that invasive surgical operation might surely destroy the thin walls of aneurysms regardless of the surgeons' experience. Considering the fact that delicate differences existed, we still extrapolated that the incidence of IAR, especially for preoperatively unruptured aneurysms, could be reduced to some extent during clipping with the accumulation of surgeons' experience. For the less-experienced operators, the incidence of IAR could be decreased by strictly controlling surgical indications and properly selecting patients for IAC.

Previous study had also reported several other risk factors of IAR. Leipzig et al. demonstrated that temporary arterial occlusion could decrease the tension inside the tumor and contribute to the separation and clipping of aneurysms[8], which benefits the decrease of the rate of IAR. Several studies had also revealed that the rate of IAR is significantly associated with the intracranial location of aneurysms[17 – 21]. It is indicated that anterior communicating artery aneurysms have a higher rate of IAR than the middle cerebral artery aneurysms[8,21,22]. Accordingly, we believe that the surgeries of blood blister-like aneurysm in the internal carotid artery, posterior-circulation aneurysm, and giant aneurysm should be conducted by more experienced neurosurgeons.

There are several defects in the present study. First, this is a single-center retrospective study which composes of two groups with differences in gender and preoperative clinical status. Second, several patients with complicated intracranial aneurysm in China might be transferred to the superior hospital to receive surgery, leading to the occurrence of bias. Third, the sample size is still limited to get the precise statistic difference.

Conclusion

Preoperative aneurysm rupture is the independent risk factor for aneurysm rupture during IAC. Intraoperative rupture, if treated properly in time, has no influence on the prognosis of patients receiving IAC. Less-experienced surgeons can also reduce the incidence rate of intraoperative aneurysm rupture by strictly controlling surgical indications.

Declarations

Abbreviations: Intracranial aneurysm clipping (IAC); Intraoperative aneurysm rupture (IAR)
Ethics approval and consent to participate: This study was approved by the Research Ethics Committee of The First Affiliated Hospital of Xiamen University and all patients signed informed consents. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.
Consent for publication: Not applicable
Availability of data and material: The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.
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Authors' contributions: Zhi Zhu and Sifang Chen analyzed and interpreted the patient data, and were major contributors in writing the manuscript. Ningning Song，Weichao Jiang，Xi Chen，Yukui Li ，Fei Xiao，Chaofan Fan， Guowei Tan recorded and collected patients' information, and also participated in writing the manuscript. Sifang Chen and Yoko Kato performed surgeries for most of cases and designed this study. All authors read and approved the final manuscript.
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Tables

Table1. Baseline Characteristics of the 331 Patients Included in the Study

Characteristics	Experienced n（%）	Less-experienced n（%）	P	χ2
Sex			0.04	4.214
Female	66（31.3）	51（42.5）		
Male	145（68.7）	69（57.5）		
Age（y			0.051	3.799
<60	152（72）	74（61.7）		
≥60	59（28）	46（38.3）		
Preoperative status			0.005	7.919
Well	200（94.8）	103（85.8）		
Poor	11（5.2）	17（14.2）		
Location			0.003#	
Paraclinoid aneurysms	28（13.3）	4（3.3）		
Supraclinoid segment aneurysms	177（83.9）	115（95.8）		
Posterior-circulation aneurysms	6（2.8）	1（0.8）		
Size			0.209#	
Small aneurysms	71（33.6）	49（40.8）		
Medium aneurysms	119（56.4）	66（55.0）		
Large aneurysms	18（8.5）	5（4.2）		
Giant aneurysms	3（1.4）	0（0.0）		
Prognosis			0.092	2.841
Well prognosis	185(87.7)	97(80.8)		
Poor prognosis	26(12.3)	23(19.2)		
Preoperative aneurysm rupture			<0.001	153.345
Yes	46（21.8）	111（92.5）		
No	165（78.2）	9（7.5）		
Intraoperative aneurysm rupture			0.004	9.025
Yes	6（2.8）	13（10.8）		
No	205（97.2）	107（89.2）		

#P value derived from the Fisher's exact test.

Table 2. Preoperative Hunt-Hess grade

Preoperative Hunt-Hess grade	Experienced n（%）	Less-experienced n（%）
0	165（78.2）	9（7.5）
I	13（6.2）	30（25.0）
II	16（7.6）	46（38.3）
III	6（2.8）	18（15）
IV	5（2.4）	15（12.5）
V	6（2.8）	2（1.7）

Table 3. Aneurysms location

Location	Experienced n（%）	Less-experienced n（%）
Intracavernous segment aneurysms	5（2.4）	0（0）
Ophthalmic segment aneurysms	18（8.5）	1（0.8）
Superior hypophyseal artery aneurysms	5（2.4）	3（2.5）
Carotid-posterior communicating aneurysms	43（20.4）	53（44.2）
Carotid bifurcation aneurysms	2（0.9）	0（0）
Middle cerebral artery aneurysms	76（36）	27（22.5）
Anterior communicating artery aneurysms	45（21.3）	30（25）
Anterior cerebral artery aneurysms	11（5.2）	5（4.2）
Basilar bifurcation aneurysms	3（1.4）	0（0）
Posterior cerebral artery aneurysms	0（0）	1（0.8）
Posterior inferior cerebellar artery aneurysms	3（1.4）	0（0）

Table 4. Risk Factors for Intraoperative Aneurysm Rupture：Univariate Analysis

Characteristics	Intraoperative aneurysm ruptured n (%)	Intraoperative aneurysm unruptured n (%)	P	χ2
Age，y			0.317	1.003
<60	11（4.9）	215（95.1）		
≥60	8（7.6）	97（92.4）		
Sex			0.723	0.125
Female	6（5.1）	111（94.9）		
Male	13（6.1）	201（93.9）		
Preoperative status			0.015#	-
Well（H-H grade 0-3）	14（4.6）	289（95.4）		
Poor（H-H grade 4-5）	5（17.9）	23（82.1）		
Operation time point			0.353#	-
Ultra-early	7（6.1）	107（93.9）		
Early	9（8.4）	98（91.6）		
Mid-phase	1（1.7）	57（98.3）		
Late-phase	2（3.8）	50（96.2）		
Preoperative aneurysm rupture			0.005	7.716
Yes	15（9.4）	144（90.6）		
No	4（2.3）	168（97.7）		
Location			0.19#	-
Paraclinoid aneurysms	3（15.8）	29（9.3）		
Supraclinoid segment aneurysms	15（78.9）	277（88.8）		
Posterior-circulation aneurysms	1（5.3）	6（1.9）		
Size			0.886#	-
Small aneurysms	8（42.1）	112（35.9）		
Medium aneurysms	10（52.6）	175（56.1）		
Large aneurysms	1（5.3）	22（7.1）		
Giant aneurysms	0	3（1.0）		

#P value derived from the Fisher's exact test.

Table 5. Effect of Intraoperative Aneurysm Rupture on Patients' Prognosis

Characteristics	Well prognosis n（%）	Poor prognosis n（%）	P
H-H grade 0～3			>0.05
Intraoperative aneurysm ruptured	13（92.9）	1（7.1）	
Intraoperative aneurysm unruptured	255（88.2）	34（11.8）	
H-H grade 4～5			>0.05
Intraoperative aneurysm ruptured	2（40.0）	3（60.0）	
Intraoperative aneurysm unruptured	8（34.8）	15（65.2）	

Table 6. The Association of Surgeons’ Experience with the Incidence of Rupture in IAC

Characteristics	Intraoperative aneurysm	Intraoperative aneurysm	P

	ruptured n(%)	unruptured n(%)	
Preoperative aneurysm ruptured			1
Experienced	5(10.9)	41(89.1)	
Less-experienced	12(10.8)	99(89.2)	
Preoperative aneurysm unruptured			0.101
Experienced	1(0.6)	164(99.4)	
Less-experienced	1(11.1)	8(88.9)	

Table 7. The Association of Surgeons’ Experience with the Time Points of Rupture in IAC

	Experienced n(%)	Less-experienced n(%)	P
Time points of intraoperative aneurysm rupture			0.226
Before incision of dura maters	0(0.0)	1(7.7)	
Preliminary separation phase	1(16.7)	2(15.4)	
Aneurysm dissection phase	4(66.7)	7(53.8)	
Aneurysm clipping phrase	1(16.7)	3(23.1)	