Int J Clin Exp Med 2019;12(3):2435-2442
www.ijcem.com /ISSN:1940-5901/IJCEM0089812

Original Article

Comparative research on clamping and interventional embolization on aneurysmal subarachnoid hemorrhage patients and effects on prognosis

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Received December 13, 2018; Accepted January 11, 2019; Epub March 15, 2019; Published March 30, 2019

Abstract: Objective: The aim of this study was to compare the curative effects and prognosis of interventional embolization and clipping craniotomies on aneurysmal subarachnoid hemorrhages (aSAH). Methods: A total of 117 aSAH patients were divided into the intervention group (n=62) with interventional embolization and the clipping group (n=55) with clipping craniotomies. Therapeutic effects and complications were compared, with the Grasse Prognosis Scale referenced. A total of 4 mL of fasting venous blood was extracted at 3 days before and after the operation. Immunoturbidimetry was used to test levels of immunoglobulin G (IgG), immunoglobulin A (IgA), and immunoglobulin M (IgM). Patients were followed up for 5 years and prognosis and survival conditions were recorded. Results: The cure rate of the intervention group was significantly higher than the clipping group (P=0.016). Incidence of complications of the intervention group was lower than the 40.00% of the clipping group (P < 0.001). Three days after surgery, serum levels of IgG, IgA, and IgM of the intervention group were higher than the clipping group (P < 0.050). Compared with the same group, levels of IgG, IgA, and IgM at 3 days before surgery were lower than levels at 3 days after surgery (P < 0.050). Hospitalization time of the intervention group was significantly shorter than the clipping group (P < 0.050). Differences in 5-year survival rates between the two groups were statistically significant, while the intervention rate of the intervention group was significantly higher than the clipping group (P=0.041). Conclusion: Intracranial aneurysm interventional embolization is more effective than clipping craniotomy for aSAH patients. It reduces complications and improves immune capacity, prognosis conditions, and survival rates.

Keywords: Intracranial aneurysm interventional embolization, intracranial aneurysms clipping craniotomy, aSAH, prognosis, IgM

Introduction

Intracranial aneurysms are tumor prominence of the artery walls with local abnormal enlargement in intracerebral artery lumen. They are usually caused by congenital defects of the cerebral artery walls or increased intracavitary pressure. They have become common malignant tumors, worldwide [1, 2]. In cerebrovascular accident diseases, incidence of cerebral aneurysms ranks second, only to cerebral thrombosis and hypertensive cerebral hemorrhages. It may occur in any age group [3]. The most common clinical manifestation of intracranial aneurysms is aneurysmal subarachnoid hemorrhages (aSAH) [4]. aSAH is a critical disease with a high fatality rate [5]. According to statistics, the average mortality rate of patients with aSAH is as high as 30.0%-50.0%. It is also the leading cause of death [6]. Blood vessel ruptures on the surface of the brain and spinal cord and the bottom of the brain cause vasospasms and obstructive hydrocephalus. They also cause aSAH and damage to patients [7]. Therefore, the main method of treatment is intracranial aneurysm clipping craniotomies [8].

However, in recent years, with the development of the disease, traditional craniotomies present a great risk to patients. The long rehabilitation cycle and physical and mental pain make traditional craniotomies difficult to endure [9, 10]. Therefore, new and effective treatments are constantly being researched to treat aSAH. Intracranial aneurysm interventional embolization is an improved treatment method for brain tumors [11]. At present, many studies, at home

and abroad, have shown that intracranial aneurysm interventional embolization has a good application value on aSAH [12-14]. However, there has been little research on therapeutic effects comparisons between intracranial aneurysm interventional embolization and intracranial aneurysms clipping craniotomies. There remains a great controversy over the most suitable method for aSAH.

Therefore, this article compared the clinical effects and prognosis of intracranial aneurysm interventional embolization and intracranial clipping. This article aimed to find a more suitable method for aSAH patients, providing reference and guidance for future clinical diagnosis and treatment of aSAH.

Materials and methods

General information

A total of 117 cases of aSAH patients were collected, including 73 males and 44 females. The ages ranged between 32 to 71 years old, with an average age of (52.68±12.84). After communicating with patients, they were divided into the intervention group (n=62) and clipping group (n=55), according to patient intentions.

Inclusion and exclusion criteria

Inclusion criteria: Clinical manifestations of the patients were in line with aSAH clinical diagnostic guidelines [15]; Patients were diagnosed with aSAH by the Pathology and Imaging Department; Cases conformed to the World Federation of Neurosurgical Societies (WFNS) classification [16] and all cases were IV and V class aSAH; All patients received tumor treatment surgery within 3 days after hospitalization; Patients agreed to cooperate with medical staff; and Case information was complete. Exclusion criteria: Patients with other tumors; Patients with cerebral edema; Severe organ failure patients; Patients with liver and kidney dysfunction; Patients that could not tolerate surgery; Coagulopathy patients; Patients with mental illness; Long-term bedridden patients and patients that could not take care of themselves; Patients with physical disabilities; and Transferred patients. This experiment was approved by the Ethics Committee of Affiliated Hospital of North Sichuan Medical College. All subjects in this experiment provided informed consent.

Methods

Basic treatment methods: Patients were given medicine to lower blood pressure and lower intracranial pressure, as well as anti-angiospasm, anti-infection, blood enriching, fluid replacement, and other basic treatments. All basic treatment and operations were completed by the Senior Chief Physician of the Neurosurgery Department. During the operation, patient real time vital signs were detected. All operations complied, strictly, with aseptic operation principles.

Methods in the clipping group: Patients were in the supine position, receiving general anesthesia with tracheal intubation. Intracranial arteries and aneurysms were examined by vascular ultrasound and surgical approaches were selected. The flap and bone flap were fully separated and the aneurysm was exposed. Normal nerves and blood vessels around the aneurysm were determined, avoiding injuries during the operation. The appropriate aneurysm clip was selected and the tumor neck was clamped at the right position. If there was atheromatous or thrombosis in the aneurysm, blood flow was controlled first. The tumor wall was then cut and the thrombus and atheromatous substances were removed. The tumor neck was narrowed down by electrocoagulation, enabling it to be clipped.

Methods in the intervention group: After CT examination, patient bleeding conditions were determined. Whole-brain vessel angiographies were used to confirm the location and morphological characteristics of the aneurysm. According to patient conditions, the appropriate coil embolization (simple spring coil was preferred) was selected. A routine calcium antagonist was given to patients before the operation. After positioning the aneurysm, the spring coil was delivered to the best position. Thus, the spring coil was tightly packed around the aneurysm cavity until the aneurysm disappeared completely. Appropriate antibiotics were given after the operation.

Observation indexes

Therapeutic effects: Grasse Prognosis Scale (GOS) [17] was taken as evaluation criterion. If the patient recovered normal social activity and occasionally had mild symptoms, results were judged to be excellent. If patients lost part of

their daily living activities, if they could basically take care of themselves, and if there were mild symptoms, results were judged to be good. If the patient lost self-care ability, but he still had self-consciousness, results were judged to be invalid. If the patient completely lost self-care ability and there was no conscious response, then results were judged to be poor. Cure rate = (the number of "excellent patients" + the number of "good patients")/total number × 100%. All curative effect evaluations were carried out in the third month after surgery. Complications included hydrocephalus, cerebral hemorrhages, vasospasms, and other complications. Incidence of complications = number of patients with complications/total number × 100%. Immunization ability: A total of 4 mL of fasting venous blood was extracted, respectively, at 3 days before the operation and 3 days after the operation. All blood samples were placed at room temperature for 30 minutes and centrifuged for 10 minutes (4000 rpm/min). Serum was obtained. Immunoturbidimetry was used to test levels of immunoglobulin G (IgG), immunoglobulin A (IgA), and immunoglobulin M (IgM). Hospitalization time: The total time spent from admission to discharge of the two groups was recorded. Prognosis: Patients were followed up for 5 years by telephone, letters, reexaminations, or visits. The termination time was November 1, 2018, and the termination event was the death of patient. Survival rates of patients in the 5 years were recorded.

Statistical methods

Data were analyzed and processed using SPSS 24.0 statistical software (Beijing Boyi Zhixun Information and Technology Co., Ltd.). Count data are expressed in the form of ratios, including treatment effects and complications. Chi-squared test was used for comparisons between groups. Measurement data are expressed in the form of mean ± standard deviation, including IgG and IgA. Student's t-test was used for comparisons between groups. Survival rates were calculated by the Kaplan-Meier method, while the log-rank test was used for comparisons between groups. Differences are statistically significant when $P < 0.050$.

Results

General data comparison

Comparing the clinical data of the two groups, there were no significant differences in age, weight, BMI, platelet, red blood cells, white blood cell, disease course, gender, residence place, smoking habits, exercise habits, tumor location, and tumor stage ($P > 0.050$). Results proved that the two groups were comparable (**Table 1**).

Therapeutic effects comparison

In the intervention group, 29.03% (18 cases) of patients were excellent, 41.94% (26 cases) of patients were good, 20.97% (13 cases) of patients were invalid, and 8.06% (5) of patients were poor. In the clipping group, 21.81% (12 cases) of patients were excellent, 27.27% (15 cases) of patients were good, 36.36% (20 cases) of patients were invalid, and 14.55% (8) of patients were poor. The cure rate of the intervention group was 70.97%, significantly higher than the 49.09% of the clipping group ($P=0.016$) (**Table 2**).

Complications comparison

In the intervention group, 3.23% (2 cases) of patients had hydrocephalus, 1.61% (1 case) of patients had cerebral hemorrhages, 1.61% (1 case) of patients had cerebral vasospasms, and no patients had cerebral infarction or intracranial infections. In the clipping group, 9.09% (5 cases) of patients had hydrocephalus, 3.64% (2 cases) of patients had cerebral hemorrhages, 21.82% (12 cases) of patients had cerebral vasospasm, 1.82% (1 case) of patients had cerebral infarction, and 3.64% (2 cases) of patients had intracranial infections. Incidence of complications in the intervention group was only 6.45%, significantly lower than the 40% of the clipping group ($P < 0.001$) (**Table 3**).

Immunocompetence comparison

In the intervention group, 3 days before the operation and 3 days after the operation, levels of serum IgG were, respectively, (12.27±4.26) g/L and (9.07±3.15) g/L. Levels of serum IgA were, respectively, (3.18±0.22) g/L and (2.38±0.18) g/L. Levels of serum IgM were, respectively, (2.08±0.39) g/L and (1.22±0.29) g/L. In the clipping group, 3 days before the operation and 3 days after the operation, levels of serum IgG were, respectively, (12.38±4.51) g/L and (7.38±3.57) g/L. Levels of serum IgA were, respectively, (3.12±0.16) g/L and (1.57±0.10) g/L. Levels of serum IgM were, respectively, (2.11±0.34) g/L and (0.85±0.16) g/L. Three days before the operation, there

Table 1. Comparison of clinical data [n (%)]

	Intervention group (n=62)	Clamping group (n=55)	t or X^2	P
Age	53.24±11.54	54.07±12.21	0.378	0.706
Body weight (KG)	78.35±7.16	79.16±8.08	0.575	0.567
BMI	26.35±5.54	27.14±6.16	0.730	0.467
Platelet (× 10^9)	287.62±52.62	279.92±54.03	0.780	0.437
Red blood cell (× 10^{12})	6.23±2.27	6.55±2.05	0.796	0.428
White blood cell (× 10^9)	11.57±3.63	11.87±4.01	0.425	0.672
Course of disease (d)	5.22±1.52	5.07±1.35	0.561	0.576
Gender			0.068	0.794
Male	38 (61.29)	35 (63.64)		
Female	24 (38.71)	20 (36.36)		
Place of residence			0.018	0.892
Town	48 (77.42)	42 (76.36)		
Rural	14 (22.58)	13 (23.64)		
Smoking habits			0.543	0.461
Yes	40 (64.52)	39 (70.91)		
No	22 (35.48)	16 (29.09)		
Sports habit			0.281	0.596
Yes	8 (12.90)	9 (16.36)		
No	54 (87.10)	46 (83.64)		
Tumor location			0.220	0.999
RPCA	14 (22.58)	11 (20.00)		
LPCA	10 (16.13)	9 (16.36)		
RRAA	7 (11.29)	7 (12.73)		
AA	9 (14.52)	8 (14.55)		
ACA	9 (14.52)	9 (16.36)		
MCAA	13 (20.97)	11 (20.00)		
Tumor grading			0.544	0.461
IV	29 (46.77)	22 (40.00)		
V	33 (53.23)	33 (60.00)		

RPCA: Right posterior communicating aneurysm. LPCA: Left posterior communicating aneurysm. RRAA: Right anterior aneurysm. AA: Anterior communicating aneurysm. ACA: Anterior cerebral artery. MCAA: Middle cerebral artery aneurysm.

Table 2. Comparison of treatment effects [n (%)]

	Intervention group (n=62)	Clamping group (n=55)	X^2	P
Excellent	18 (29.03)	12 (21.81)		
Good	26 (41.94)	15 (27.27)		
Invalid	13 (20.97)	20 (36.36)		
Error	5 (8.06)	8 (14.55)		
Cure rate (%)	70.97	49.09	5.846	0.016

were no significant differences in levels of serum IgG, IgA, and IgM between the two groups (P > 0.050). Three days after the operation, levels of serum IgG, IgA, and IgM of the intervention group were significantly higher than the clipping group (P < 0.050). Compared with levels of serum IgG, IgA, and IgM 3 days before the operation, levels of serum IgG, IgA, and IgM 3 days after the operation decreased in both groups (P < 0.050) (**Figures 1**-**3**).

Hospitalization time comparison

Hospitalization time of the intervention group was (20.77± 4.82) days, while the hospitalization time of the clipping group was (26.87±5.94) days. Hospitalization time of the intervention group was significantly shorter than the clipping group (P < 0.050) (**Figure 4**).

Prognosis comparison

Patients were followed up for 5 years, with 112 patients followed up successfully. The followup success rate was 95.73%. In the intervention group, 58 cases were successfully followed up. A total of 54 cases were successfully followed up in the clipping group. The 1-year survival rates, 3-year survival rates, and 5-year survival rates of the intervention group were, respectively, 91.94%, 85.48%, and 80.65%. The 1-year survival rates, 3-year survival rates, and 5-year survival rates of the clipping group were, respectively, 94.55%, 81.82% and 69.09%. The total survival rate of the two groups was statistically significant. The rate of the intervention group was significantly higher than the clipping group (P=0.041) (**Figure 5**).

Discussion

Aneurysmal subarachnoid hemorrhages are a common malignant complication of aneurysms. These hemorrhages are the most serious com-

Table 3. Comparison of complications [n (%)]

	Intervention group (n=62)	Clamping group (n=55)	X^2	P
Hydrocephalus	2 (3.23)	5 (9.09)		
Brain rebleeding	1 (1.61)	2 (3.64)		
Cerebrovascular	1 (1.61)	12 (21.82)		
Brain infarction	0 (0.00)	1 (1.82)		
Intracranial infection	0 (0.00)	2 (3.64)		
Complication rate (%)	6.45	40.00	18.982	< 0.001

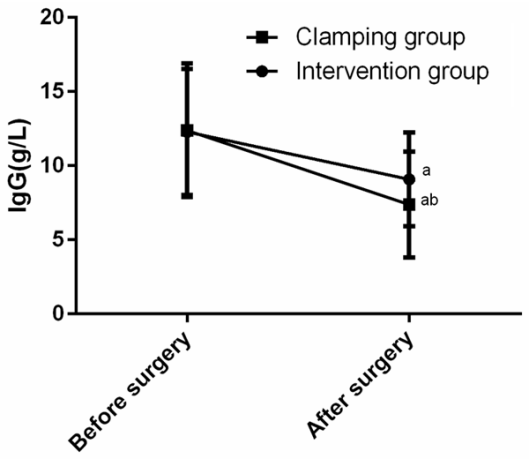

Figure 1. Comparison of serum IgG before and after the operation. Compared with serum IgG of the same group at 3 days before the operation, a represents P < 0.050; Compared with serum IgG of the intervention group at 3 days after the operation, b represents P < 0.050.

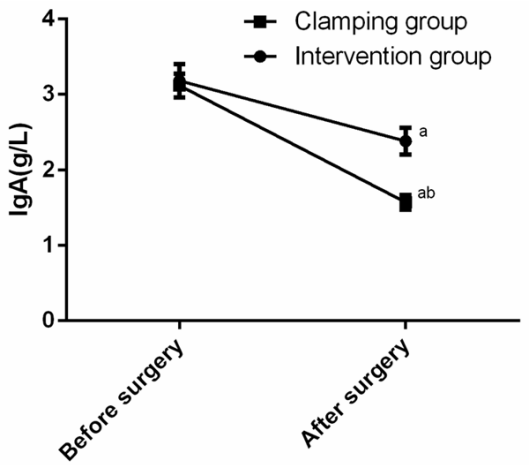

Figure 2. Comparison of serum IgA before and after the operation. Compared with serum IgA of the same group at 3 days before the operation, a represents P < 0.050; Compared with serum IgA of intervention group at 3 days after the operation, b represents P < 0.050.

plications [17]. According to statistics, about 15.0%~25.0% of aneurysm patients have high grade subarachnoid hemorrhages, with mortality rates of aSAH as high as 30.0%~50.0% [18]. Because of the poor prognosis of aSAH, conservative treatment is usually not recommended in clinic. At present, surgical operation remains the main treatment method [19]. With the development of aSAH in recent years, more and more studies, at home and abroad, have shown that aSAH patients usually suffer from different degrees of consciousness disturbance and mild hemiplegia. This may be related to the stimulation of oxygen free factor, endothelin, and invasiveness of surgery [20, 21]. Therefore, the choice of the best surgical procedure for aSAH is not only determinant of the patient's cure conditions, but it is also a major factor that affects prognosis. At present, the main surgical procedures in clinic are intracranial aneurysm interventional embolization and intracranial aneurysms clipping craniotomies. Domestic and foreign studies have been limited to the efficacy of one surgical method. There are few studies comparing differences between the two surgical methods, with few articles concerning patient prognosis. Therefore, this current study compared the therapeutic effects of intracranial aneurysm interventional embolization and intracranial aneurysms clipping craniotomies for treatment of aSAH. Patients were followed up for 5 years, aiming to discover the best surgical method for treatment and prognosis of aSAH patients.

Experimental results showed that the therapeutic effects of the intervention group were better than the clipping group, indicating that intracranial aneurysm interventional embolization is better for grade IV and grade V aSAH patients. The main reason for the differences may be the surgery characteristics of intracranial aneurysm interventional embolization. Intracranial aneurysm interventional embolization has the characteristics of less trauma and quicker recovery. The coil is filled into the aneurysm cavity through a small surgical incision, to slow down velocity of blood flow in aneurysm until the aneurysm completely blocked. The spring coil induces endovascular thrombosis, while the aneurysm neck becomes intima. Th-

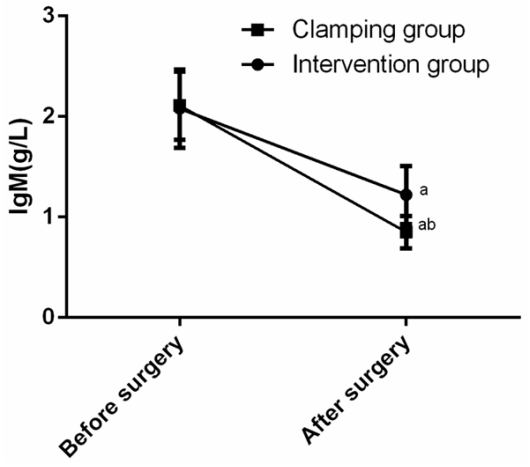

Figure 3. Comparison of serum IgM before and after the operation. Compared with serum IgM of the same group at 3 days before the operation, a represents P < 0.050; Compared with serum IgA of intervention group at 3 days after the operation, b represents P < 0.050.

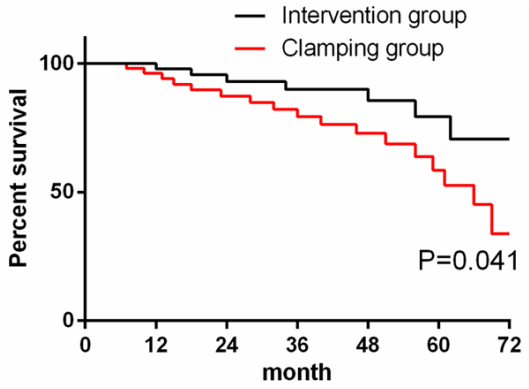

Figure 5. Prognostic survival curve. The 1-year survival rates, 3-year survival rates, and 5-year survival rates of the intervention group were, respectively, 91.94%, 85.48% and 80.65%. The 1-year survival rates, 3-year survival rates, and 5-year survival rates of the clipping group were, respectively, 94.55%, 81.82% and 69.09%. The total survival rate of the intervention group was significantly higher than the clipping group (P=0.041).

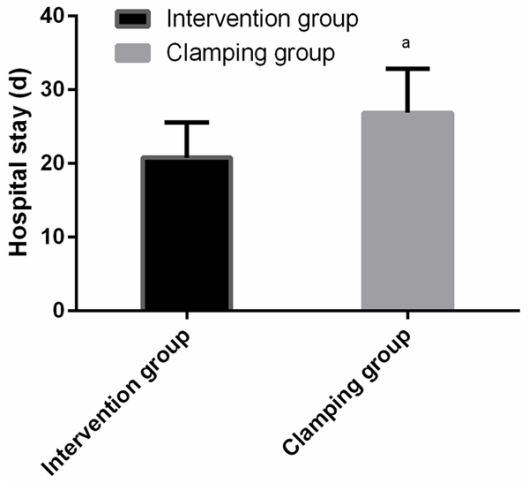

Figure 4. Comparison of hospitalization times. Compared with hospitalization times of the intervention group, a represents P < 0.050.

us, the arterial aneurysm can be treated [22, 23]. The main operation of intracranial aneurysm interventional embolization is in blood vessels, hence the effects on cerebral vessels are small [24]. Additionally, it avoids the invasiveness of the operation and damage to normal and important brain tissues around the tumor. In contrast, although intracranial aneurysm clipping craniotomies have significant curative effects, they cause more damages to patients during surgery because of the large incision [25]. Intracranial aneurysm clipping craniotomies greatly prolong the recovery period. For some deep aneurysms, the integrity of the operation is affected because of unreached incisions. Further comparing complications of the two groups, incidence of complications of the intervention group was significantly less than the clipping group. Results indicate that intracranial aneurysm interventional embolization can effectively reduce complications of patients with grade IV and grade V aSAH. It has been proven that the influencing factors of aSAH complications are related to nitric oxide, endothelin, and oxygen free radicals [26]. In the process of intracranial aneurysm interventional embolization, small incisions can avoid massive hemorrhaging. In addition, vascular exposure time is significantly shorter than intracranial aneurysm clipping craniotomies. Thus, incidence of vasospasms is greatly reduced. In the process of intracranial aneurysm interventional embolization, continuous drainage of the lumbar spine subarachnoid space can greatly improve the absorptive capacity of subarachnoid hematocele. Thus, it can avoid re-blockage caused by hemorrhage accumulation [27]. Comparing hospitalization times between the two groups, hospitalization time of the intervention group was significantly shorter than the clipping group. Intracranial aneurysm interventional embolization could greatly shorten the rehabilitation process. Therapeutic effects of intracranial aneurysm interventional embolization are better than intracranial aneurysm clipping craniotomies.

Both operation methods are traumatic surgeries. They both cause great damage to the body's nerve and immune function. Body injury is mainly manifested as B-cell injury and the most representative factors are IgG, IgA, and IgM [28]. Therefore, to further understand the influence of the two surgical methods on immune function of patients, this study compared the immune factors of the two groups. Results showed that, after surgery, IgG, IgA, and IgM of both groups decreased significantly, but levels of the intervention group were much higher than the clipping group. Results indicate that intracranial aneurysm interventional embolization caused less damage to the immune function of patients with high grade aSAH. To a certain extent, minimally invasive surgery causes less damage to patients than traditional surgery. The long rehabilitation cycle of the clipping group may place patients in poor immune function states for a long time. The consequences are not only complications, but also the recurrence of disease and poor prognosis of patients. According to follow-up studies, survival rates of the clipping group were significantly lower than the intervention group. This indicates that intracranial aneurysm interventional embolization provides a better prognosis for patients with high grade aSAH.

This experiment compared the efficacy of intracranial aneurysm interventional embolization and intracranial aneurysm clipping craniotomies for high grade aSAH patients. However, due to limited experimental conditions, there were some shortcomings. For example, the number of research objects was small. Thus, statistical analysis of large data could not be carried out. In addition, many factors influenced the operation process. Collected data were incomplete and relevant factors could not be analyzed. More follow-up investigations will be conducted and experiments will be improved in the future, aiming to obtain the best experimental results.

In conclusion, the efficacy of intracranial aneurysm interventional embolization is better than intracranial aneurysm clipping craniotomies for patients with high grade aSAH. Intracranial aneurysm interventional embolization can reduce incidence of complications, improve the immune system, and improve patient prognosis.

Disclosure of conflict of interest

None.

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