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Original Article

Comparison of microsurgical clipping with intravascular interventional embolization in the treatment of ruptured aneurysms and risk factors for intraoperative rupture and bleeding

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Abstract: Objective: To investigate the effectiveness of microsurgical clipping compared with intravascular interventional embolization in the treatment of ruptured aneurysms and the risk factors for intraoperative rupture and bleeding. Methods: The data of 116 patients with ruptured aneurysms admitted to the People's Hospital of China Three Gorges University from January 2020 to March 2021 were collected for retrospective analysis. Among them, 61 cases with microsurgical clipping were classified as the control group (CG), and the rest 55 with intravascular interventional embolization were the observation group (OG), and the treatment effects in the two groups were compared. The general conditions of operation (operation time, postoperative hospital stay and intraoperative blood loss) were compared between the two groups. The intraoperative rupture of cerebral aneurysm during operation was counted, and the incidence of complications between the groups was compared. Risk factors affecting intraoperative rupture of cerebral aneurysms were analyzed by logistic regression. Results: The total clinical treatment efficiency was dramatically higher in the OG than that in the CG ($P<0.05$). The operative time, postoperative hospital stays, and intraoperative bleeding were all higher in the CG than those in the OG (all $P<0.001$). There was no statistical difference in the incidence of wound infection, hydrocephalus, and cerebral infarction between the two groups (all $P>0.05$). However, the incidence of intraoperative rupture was markedly higher in the CG than that in the OG ($P<0.05$). Multifactorial logistic regression analysis revealed that history of subarachnoid hemorrhage, history of hypertension, large diameter of aneurysm, irregular morphology, and anterior communicating artery aneurysm were independent risk factors for intraoperative rupture in patients. Conclusion: Intravascular interventional embolization for middle cerebral artery aneurysm rupture is a less invasive procedure with faster recovery time, and history of subarachnoid hemorrhage, history of hypertension, large diameter of aneurysm, irregular morphology, and anterior communicating artery aneurysm are independent risk factors affecting patients with intraoperative rupture.

Keywords: Microsurgical clipping, intravascular interventional embolization, ruptured aneurysms, intraoperative rupture, bleeding

Introduction

Intracranial aneurysms are the most common cause of spontaneous subarachnoid hemorrhage, with an acute and severe onset and often combined with intracranial hematomas, which can suddenly worsen patients' condition and lead to brain herniation with a high rate of disability and mortality [1, 2]. With the continuous improvement in medical care, more and more patients with intracranial aneurysms are being detected [3]. Research has shown [4] that the incidence of middle cerebral artery aneurysms is high, accounting for approximately 30% of all intracranial aneurysms, and that 30-50% of ruptured artery aneurysms are complicated by intracranial hematomas. Most unruptured aneurysms are essentially asymptomatic, and ruptured intracranial aneurysms account for only 1-2% of patients, but they have high rates of death, disability, and rebleeding [5].

Traditional craniotomy for ruptured middle cerebral artery aneurysms is dangerous, traumatic, painful, and has a poor prognosis. It is difficult to completely remove the blood in the subarachnoid space, and it is prone to serious complications such as cerebral vasospasm, which is rarely used in clinical practice [6]. With the development of microsurgery and minimally invasive surgery, there are more methods to treat ruptured middle cerebral artery aneurysms, such as microsurgical clipping and intravascular interventional embolization [7]. Microscopic craniotomy can clearly reveal the tumor and the surrounding tissue structure, completely remove the tumor, and has a high cure rate and a low recurrence rate. But its limitation is that it requires craniotomy, which is very traumatic, and the surgical risk is high [8, 9]. Compared with microscopic craniotomy, the greatest advantage of intravascular interventional embolization is that it is less invasive. Through carotid artery puncture, a flexible spring coil is placed inside the aneurysm using a microcatheter to block blood flow in the aneurysm and prevent re-rupture and bleeding of the aneurysm [10]. Regardless of the treatment option, while there are benefits, the risks are not negligible [11].

Although both treatment modalities have their advantages and limitations, intraoperative aneurysm rupture and acute thrombosis due to stent occur in both treatments. The incidence of intraoperative aneurysm rupture is low, and the prognosis is poor, but there are few reports on the risk factors for the occurrence of intraoperative aneurysm rupture.

In this study, we aimed to analyze the effectiveness of microsurgical clipping versus intravascular interventional embolization in the treatment of ruptured aneurysms and the risk factors for intraoperative rupture and bleeding, to provide a reference for the selection of clinical treatment options.

Materials and methods

Clinical data

The data of 116 patients with ruptured aneurysms admitted to the People's Hospital of China Three Gorges University from January 2020 to March 2021 were collected for retrospective analysis, of which 61 patients with microsurgical clipping were assigned to the control group (CG) and the rest 55 with intravascular interventional embolization were assigned to the observation group (OG). The study was conducted with the approval of the People's Hospital of China Three Gorges University Ethics Committee (2020141).

Inclusion and exclusion criteria

Inclusion criteria: All patients met the WHO criteria for the diagnosis of cerebral aneurysms [12] and patients' aneurysm ruptured and required surgical treatment. Patients underwent surgery within 3 days of onset. Patients had complete clinical data. Patients were 18-75 years old.

Exclusion criteria: Patients had abnormal function of important organs. Patients were combined with coagulation dysfunction or autoimmune system disease. Patients had other types of cerebrovascular lesions. Patients were involved in other treatment protocols during the course of this treatment. Patients were combined with other tumors. Patients were expected to survive for no more than 3 months.

Treatment options

Upon admission, patients were queried about their past medical history and underwent CT and angiography to obtain information on their condition and contraindications. 1) In the control group, the patient was placed supine on the surgical bed, and then general anesthesia was administered by tracheal intubation. The head was immobilized with a frame, the brain tissue was separated through a pterygoid approach, and the subarachnoid pool and subarachnoid space were dissected under a microscope to release cerebrospinal fluid. If blood accumulates in the subarachnoid space, it should be removed promptly, and the patient's physiological indicators should be checked. After the level of cerebrospinal fluid dropped, the aneurysm-carrying artery was exposed, the aneurysm was separated, and the aneurysm was clamped with an aneurysm clip. The vessels and nerves surrounding the lesion were examined to determine the location of the arterial clip. Meninges were sutured tightly for those with preoperative low grading and no significant intraoperative cerebral edema. In those with high preoperative grading and significant cerebral tissue edema, the dura mater was closed by artificial dural reduction sutures, the bone flap was removed to reduce pressure, a drainage tube was placed under the scalp, the scalp was sutured, and the incision was closed. 2) In the OG, general anesthesia, heparin anticoagulation, and catheter flushing with 0.9% sodium chloride solution were administered. The patient was in supine position on the surgical bed. Cerebral angiography was performed through femoral artery cannulation, and the non-ionic contrast agent Onepac was selected to determine the location of the aneurysm and its size, and to measure the diameter and width of the aneurysm. The microcatheter was placed through which aneurysm was located according to the imaging results, and the catheter spring ring was fixed in the lesion area. The catheter was withdrawn, pressure was applied to stop bleeding, and the puncture site was bandaged and disinfected to avoid secondary infection.

Outcome measures

Main outcome measures: The therapeutic effects in the two groups were compared. The general conditions of operation (operation time, postoperative hospital stay and intraoperative blood loss) were compared between the groups. Patients were counted for intraoperative cerebral aneurysm rupture during surgery, and the risk factors affecting intraoperative cerebral aneurysm rupture were analyzed by logistic regression.

Secondary outcome measures: The clinical data and the incidence of complications of both groups were compared.

Efficacy evaluation

Markedly effective: The therapeutic effect was evaluated 1 week after operation. After treatment, the lesion was removed completely, the symptoms such as headache and neck ankylosis disappeared, and the neurological function recovered. Effective: The size of the lesion was significantly reduced, the symptoms were relieved, and the neurological function was improved compared with that before treatment. Ineffective: The lesion volume of the patients changed little or increased, the symptoms were not relieved or further aggravated, and the neurological function was not dramatically improved. Total effective rate = (1 - ineffective/total number of cases) × 100%.

Statistical analysis

SPSS 20.0 software (USA) was used for inter-data variance analysis, and Graphpad 8.0 was used to visualize the data. The measurement results were presented as Mean ± SD (standard deviation), and the data were compared between groups using independent samples t-test. The counting data were assessed using the chi-square test. Risk factors affecting intraoperative rupture in patients were analyzed by logistic regression. Prediction curves for risk factors were plotted using receiver operating characteristic (ROC) curve. Differences were statistically significant when $P<0.05$.

Results

Clinical data

A comparison of the clinical data between the two groups revealed that there were no statistical differences in age, gender, history of subarachnoid hemorrhage, history of hypertension, history of diabetes, cerebrovascular stenosis, maximum diameter of aneurysm, irregular morphology, or anterior communicating aneurysm (all $P>0.05$, **Table 1**).

Efficacy evaluation

Evaluation of the efficacy in the two groups revealed that the overall clinical efficiency after treatment was dramatically higher in the OG than that in the CG ($P<0.05$, **Table 2**).

Comparison of general conditions of surgery

Comparison of the operative time, postoperative hospital stays, and intraoperative bleeding between the two groups demonstrated that the operative time, postoperative hospital stays, and intraoperative bleeding were higher in the CG than those in the OG (all $P<0.001$, **Figure 1**).

Comparison of complications

Statistics on the occurrence of complications in both groups showed that there was no statistical difference in the incidence of wound infection, hydrocephalus, or cerebral infarction between the two groups (all $P>0.05$, **Table 3**). However, the incidence of intraoperative rup-

Table 1. Patients' clinical data

Factors	Control group (n=61)	Observation group (n=55)	x^2/t value	*P* value
Age	51.06±10.53	52.25±12.12	0.565	0.573
Gender			0.864	0.352
Male	33	25		
Female	28	30		
History of subarachnoid hemorrhage			0.075	0.783
Yes	10	8		
No	51	47		
History of hypertension			1.058	0.303
Yes	22	25		
No	39	30		
History of diabetes			0.140	0.708
Yes	18	18		
No	43	37		
Cerebrovascular stenosis			1.424	0.490
No	50	40		
Near-end	5	7		
Far-end	6	8		
Maximum diameter of aneurysm			0.233	0.629
≥10 mm	31	25		
<10 mm	30	20		
Irregular morphology			0.178	0.672
Yes	13	10		
No	48	45		
Anterior communicating aneurysm			1.420	0.233
Yes	11	15		
No	50	40		

Table 2. Efficacy evaluation

Groups	Markedly effective	Effective	Ineffective	Total efficiency rate
Control group (n=61)	24 (39.34%)	27 (44.26%)	10 (16.40%)	51 (83.60%)
Observation group (n=55)	12 (21.82%)	25 (45.45%)	18 (32.73%)	37 (67.27%)
x^2 values				4.214
P value				0.040

ture was dramatically higher in the CG than that in the OG (P<0.05, **Table 3**).

Analysis of risk factors for intraoperative rupture in patients

Patients were divided into an occurrence group and a nonoccurrence group according to their intraoperative rupture. A history of subarachnoid hemorrhage, history of hypertension, cerebral vascular stenosis, large aneurysm diameter, irregular morphology, anterior communicating aneurysm, and treatment regimen were found to be risk factors influencing intraoperative rupture in patients by univariate analysis (**Table 4**). The factors with statistical significance in univariate analysis were then assigned (**Table 5**). A multifactorial logistic regression analysis revealed that history of subarachnoid hemorrhage, history of hypertension, large diameter of aneurysm, irregular morphology, and anterior communicating artery aneurysm were independent risk factors for intraoperative rupture in patients (**Figure 2**). Subsequent prediction by ROC curve denoted that the area under the curve for joint prediction in predicting intra-

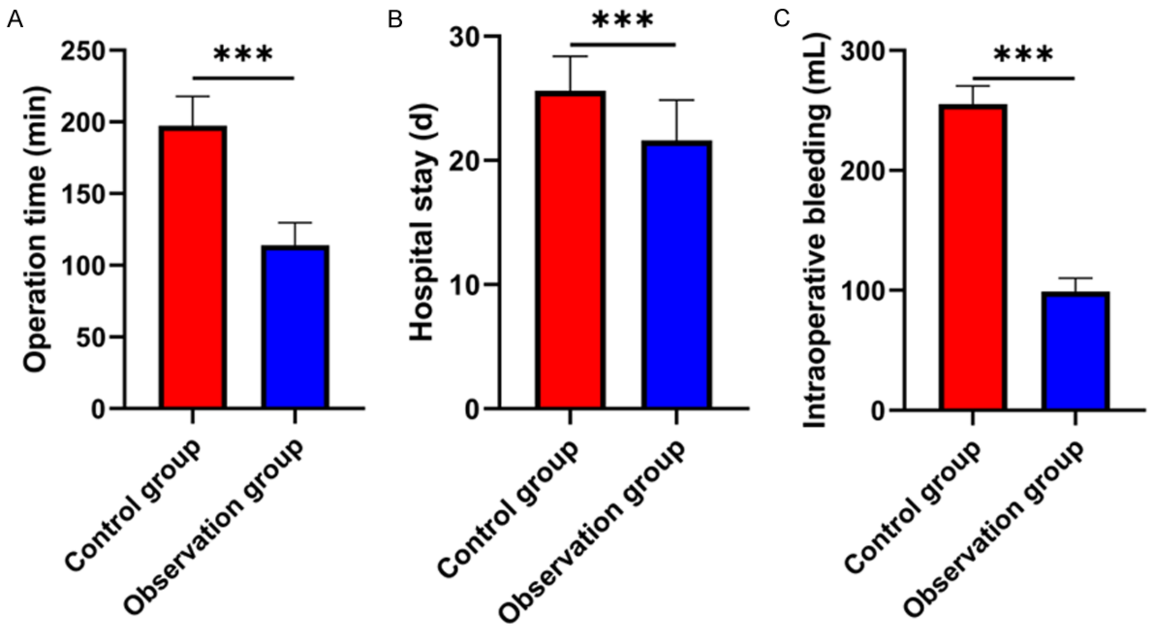

Figure 1. Comparison of general condition of patients undergoing operation. A. Comparison of operation time between patients in the observation and control groups. B. Comparison of length of stay between patients in the observation and control groups. C. Comparison of intraoperative bleeding between patients in the observation and control groups. Note: *** indicates P<0.001.

Table 3. Comparison of complications

Groups	Wound infection	Hydrocephalus	Cerebral infarction	Intraoperative rupture
Control group (n=61)	8	3	3	14
Observation group (n=55)	6	2	5	5
x^2 values	0.132	0.101	0.784	4.056
P value	0.715	0.750	0.375	0.044

operative rupture in patients was 0.953 (**Figure 3**).

Discussion

Currently, there is no uniform understanding of the pathogenesis of middle cerebral artery aneurysm formation and rupture, which may be the result of a combination of genetic factors, acquired degenerative lesions and hemodynamics [13]. Traditional craniotomy for middle cerebral artery aneurysm rupture is dangerous, traumatic, painful, and has poor prognosis. It is difficult to completely remove the blood in the subarachnoid space, which is prone to serious complications such as cerebral vasospasm [14]. With the development of microsurgery and minimally invasive surgery, there are more methods to treat ruptured middle cerebral artery aneurysms, such as microsurgical clipping and intravascular interventional embolization.

Craniotomy is a traditional procedure, which can rapidly open the subarachnoid space and release the bloody cerebrospinal fluid in time, has a high rate of aneurysm neck clipping, and can quickly stop the bleeding. However, the craniotomy is traumatic and has a great impact on brain tissues and neurological function, and it is easy to increase the risk of intracranial infection and cerebrospinal fluid leakage [15, 16]. With the development of minimally invasive technique and the improvement of clinical medical technology, intravascular interventions can reduce tissue trauma, reduce intraoperative bleeding, speed up the recovery process and shorten hospitalization time based on effective clamping of the tumor neck and rapid hemostasis without opening the cranium [17]. In this

Table 4. Univariate analysis of factors affecting intraoperative rupture in patients

Factors	Occurrence group (n=19)	Non-occurrence group (n=97)	x^2/t value	*P* value
Age	48.10±10.46	52.31±11.35	1.497	0.137
Gender			0.556	0.451
Male (n=58)	8	50		
Female (n=58)	11	47		
History of subarachnoid hemorrhage			12.253	<0.001
Yes (n=18)	8	10		
No (n=98)	11	87		
History of hypertension			10.371	0.001
Yes (n=47)	14	33		
No (n=69)	5	64		
History of diabetes			0.358	0.549
Yes (n=36)	7	29		
No (n=80)	12	68		
Cerebrovascular stenosis			6.998	0.030
No (n=90)	11	79		
Near-end (n=12)	5	7		
Far-end (n=14)	3	11		
Maximum diameter of aneurysm			8.560	0.003
≥10 mm (n=56)	15	41		
<10 mm (n=50)	4	56		
Irregular morphology			15.381	<0.001
Yes (n=23)	10	13		
No (n=93)	9	84		
Anterior communicating aneurysm			8.136	0.004
Yes (n=26)	9	17		
No (n=90)	10	80		
Treatment options			4.056	0.044
Microsurgery (n=61)	14	47		
Intravascular interventions (n=55)	5	50		

Table 5. Assignment table

Factor	Assignment
History of subarachnoid hemorrhage	Yes =1; No =0
History of hypertension	Yes =1; No =0
Cerebrovascular stenosis	Yes =0; Near-end =1; Far-end =2
Maximum diameter of aneurysm	≥10 mm =1, <10 mm =0
Irregular morphology	Yes =1; No =0
Anterior communicating aneurysm	Yes =1; No =0
Treatment options	Microsurgery =1; Intravascular interventions =0
Rupture	Ruptured =1; Unruptured =0

study, we compared microsurgical clipping with intravascular interventional embolization for the treatment of ruptured aneurysms. In our study, we found that the overall clinical efficiency after treatment was dramatically higher in the OG than that in the CG. The length of stay, operative time and intraoperative bleeding were all higher in the CG than those in the OG. This indicates that intravascular interventional embolization can be performed intracranially

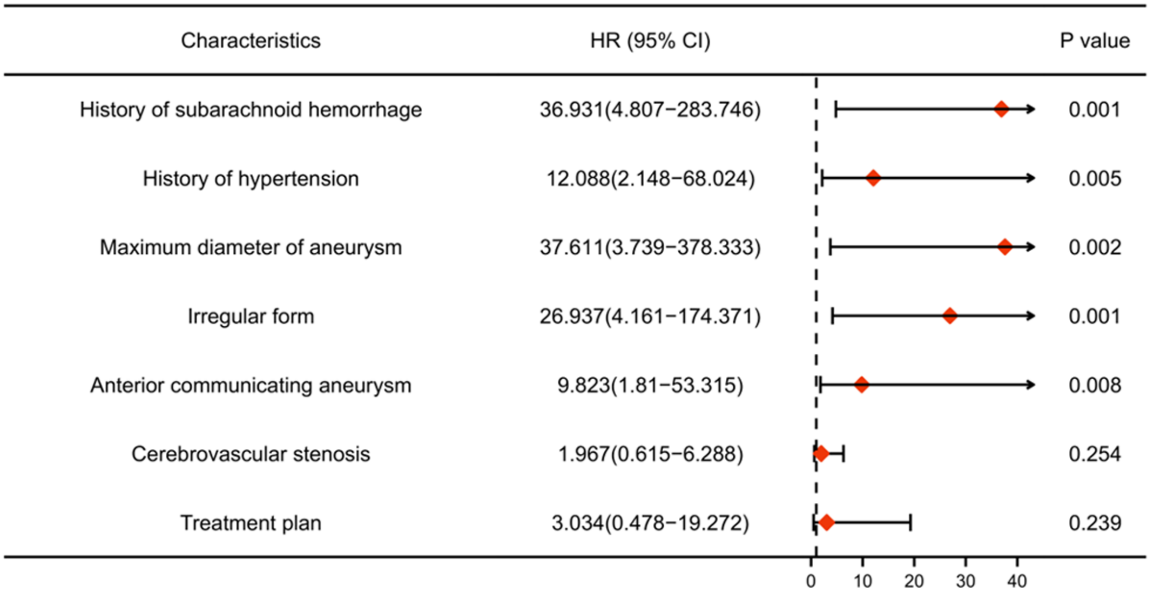

Figure 2. Logistic regression analysis of risk factors affecting vascular rupture in patients.

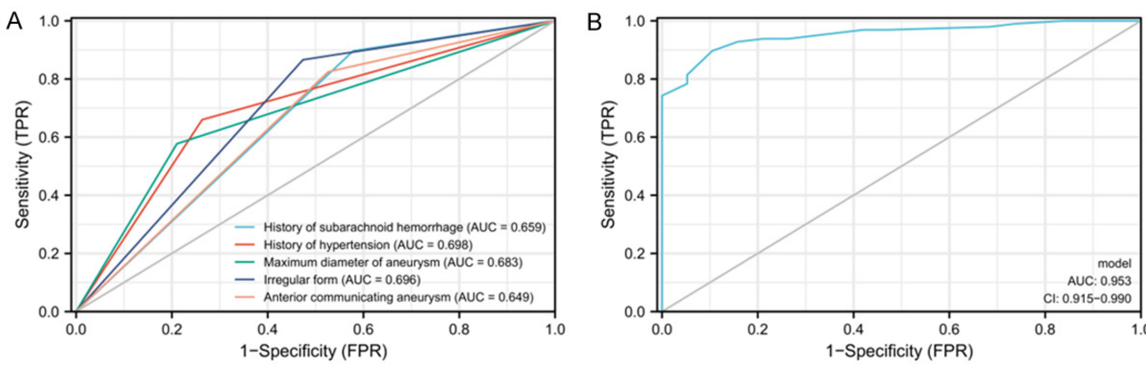

Figure 3. ROC curves of risk factors independently versus jointly in predicting vascular rupture in patients. A. ROC curve of each factor in predicting the vascular rupture in patients. B. ROC curves of combined factors in predicting vascular rupture in patients.

and directly to the lesion, which reduces the trauma caused by the procedure compared to microscopic craniotomy and allows for rapid postoperative recovery. Previously, Liu et al. [18] discovered that intravascular interventional embolization was better to improve the distribution of shear stress on the vessel wall and stabilize vascular blood flow compared to open clamping, achieving better outcomes for patients, which was also confirmed in our study. We believe that this is because microsurgical clipping requires an open cranial operation, which is demanding, complex and traumatic, resulting in longer operative time and hospital stay, and increased intraoperative bleeding. In contrast, intravascular interventional embolization is a minimally invasive procedure with low trauma and high success rate, which can avoid nerve strains and make intracranial aneurysms less likely to rupture after surgery, helping to reduce postoperative complications and control the symptoms of subarachnoid hemorrhage [19, 20].

In addition, we counted the incidence of post-treatment complications in both groups. A difference in intraoperative rupture was found between the two groups, with a dramatically higher incidence in the CG than that in the OG. This suggests that microsurgical clipping increases the chances of intraoperative rupture. To determine the risk factors affecting intraoperative rupture in patients, we also performed regression analysis and found that history of subarachnoid hemorrhage, history of hypertension, large diameter of aneurysm, irregular morphology, and anterior communicating aneurysm were independent risk factors affecting intraoperative rupture in patients. Previous studies have found that patients with a history of explicit subarachnoid hemorrhage have more fragile blood vessels, which does not facilitate surgical treatment of patients [21]. Long-term hypertension causes increased shear stress in the aneurysm wall, thus making it weaker. Inhibition with a relatively slight intraoperative touch can cause rupture of the aneurysm, thus making the surgical operation more difficult [22]. And the larger the diameter of the tumor, the more irregular the morphology of the aneurysm, which can affect the surgeon's judgment during the surgery [23]. The anterior communicating artery aneurysm complex has many vascular variants with complex local anatomical relationships and is one of the most difficult intracranial aneurysms to manage clinically [24]. It has been shown to be the most common site of aneurysm rupture, with approximately 40% of spontaneous subarachnoid hemorrhages occurring from ruptured anterior communicating aneurysms [25]. Therefore, patients should consider the above factors in advance during the surgical selection process to avoid the occurrence of intraoperative vascular rupture in patients.

In this study, we found that microsurgical clipping is less effective than intravascular interventional embolization in treating ruptured aneurysms, and we determined the risk factors for the emergence of intraoperative rupture in patients through logistic regression analysis. Nevertheless, the present study still has some limitations. First, due to the retrospective nature, we failed to follow up the patients, so it was not possible to analyze the factors influencing their survival after both surgical treatments. Second, current study did not validate the results with external data. Finally, the present study was a single-center study, so the data were limited. Hence, we hope to conduct studies with larger sample size involving more clinical centers to refine our findings.

In conclusion, intravascular interventional embolization for middle cerebral artery aneurysm rupture is a less invasive procedure with faster recovery time as compared to microsurgical clipping. History of subarachnoid hemorrhage, history of hypertension, large diameter of aneurysm, irregular morphology, and anterior communicating artery aneurysm are independent risk factors for intraoperative rupture affecting patients with ruptured aneurysms.

Disclosure of conflict of interest

None.

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