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Original Article

Comparison of the effects of microscopic clipping and endovascular embolization on intracranial aneurysms

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Abstract: Objective: To compare the efficacy of microsurgical clipping and endovascular embolization in patients with intracranial aneurysms. Methods: The clinical data of 96 patients with intracranial aneurysms were retrospectively analyzed. According to different treatment options, the patients were divided into two groups: the clipping group and the embolization group. Among them, 45 patients in the clipping group were treated with microsurgical clipping; 51 patients in the embolization group were treated with endovascular embolization. The operative time, postoperative hospital stay, Glasgow Outcome Scale (GOS) score at discharge, complications at 1-year follow-up, recurrence rate, and brain injury related factors in serum before and after surgery were compared. Results: The operative time and postoperative hospital stay in the embolization group were significantly shorter than those in the clipping group, and the differences were statistically significant (both $P<0.05$). The rate of good GOS score in the embolization group was 96.08% when discharged, which was significantly higher than 80.00% in the clipping group. There were no statistically significant differences in the incidence and recurrence rate of cerebral edema and brain nerve injury between the two groups at 1-year follow-up (all $P>0.05$). The levels of soluble protein-100B (S100B protein), matrix metalloproteinase-9 (MMP-9) and superoxide dismutase (SOD) in serum before surgery were compared between the two groups. The differences were not statistically significant (all $P>0.05$). After surgery, serum S100B protein and MMP-9 levels were significantly lower in the embolization group than in the clipping group, and the SOD level was significantly higher than in the clipping group. The differences were statistically significant (all $P<0.05$). Conclusion: Both the microsurgical clipping and endovascular embolization can achieve satisfactory short-term curative effect on intracranial aneurysms, but the latter has little damage to brain tissue and rapid postoperative recovery. It is worth further research and application.

Keywords: Intracranial aneurysm, microsurgical clipping, endovascular embolization

Introduction

In recent years, with the rapid development of neurosurgical imaging technology, the detection rate of intracranial aneurysms increased as well. The intracranial aneurysm is considered to be one of the major risk factors for subarachnoid hemorrhage. The intraluminal pressure of the intracranial aneurysm is greater than the compliance of the vessel wall, lead to abnormal bulging of the vessel wall and the risk of rupture bleeding is large [1, 2]. Regarding the treatment of intracranial aneurysms, microsurgical clipping has been widely used in the past. The curative effect is worthy to be affirmed, but the damage to brain tissue after surgery should not be ignored [3]. In recent years, clinicians have gradually paid attention to the treatment of intracranial aneurysms by endovascular embolization, and more and more cases have been operated. However, there are many disputes about the effect of endovascular embolization and microsurgical clipping on intracranial aneurysms without a unified conclusion. Studies have shown that endovascular embolization in the treatment of intracranial aneurysm led to significantly lower mortality and survival dependence rate than microsurgical clipping. Another study reported that endovascular embolization can hardly make completely embolism, and the residual rate of tumor neck and tumor body is high [4, 5]. Some studies suggest that the efficacy of microsurgical clipping and endovascular embolization in patients with intracranial aneurysms may be related to the degree of surgical invasion of brain tissue. Although microsurgery can clearly show the aneurysm and its surrounding blood vessels, a craniotomy is essential, surgical operation still may have damage to brain tissue and blood vessels [6]. At present, there are few reports on the differences in treatment effects caused by surgical factors of these two surgeries [7].

The present study retrospectively analyzed the clinical data of patients with intracranial aneurysms treated with microsurgical clipping or endovascular embolization in The Second People's Hospital of Deyang City from January 2016 to January 2017. The level of brain injury related factors in serum before surgery, indicators of perioperative period, efficacy and prognosis of the two groups were compared to provide an experimental basis for the selection of treatment strategies for patients with intracranial aneurysms.

Materials and methods

General information

The clinical data of patients with intracranial aneurysms treated with microsurgical clipping or endovascular embolization in the Second People's Hospital of Deyang City from January 2016 to January 2017 are classified into two groups: the clipping group and the embolization group according to different treatment plans. Groups of 45 patients were treated with microsurgical clipping and 51 patients were treated with endovascular embolization.

Inclusion criteria

Patients aged between 18 and 70 years old; with typical clinical manifestations such as sudden headache, disturbance of consciousness, nausea, vomiting, etc.; intracranial aneurysms diagnosed by whole brain digital subtraction angiography (DSA), confirmed as ruptured aneurysms by CT or MRI [8]; Hunt-Hess classification grade I-III [9]; suitable for microsurgical clipping or endovascular embolization; cooperative follow-up and complete clinical data.

Exclusion criteria

Patients with postoperative recurrent intracranial aneurysms; combined with intracranial vascular malformation hemorrhage or severe organ failure; endovascular embolization failure and conversion to craniotomy; follow-up time less than 12 months or incomplete clinical data. This study was reviewed by the Ethics Committee of the Second People's Hospital of Deyang City and all selected patients signed informed consent.

Study methods

The patients in clipping group were treated with microsurgical clipping as follows [10]. First, preoperative imaging examination was made for the patient to confirm the location of intracranial aneurysms. After the gas and intravenous general anesthesia, the patient was placed in a corresponding position with the head fixed. The operative region was routinely sterilized and covered with surgical drapes. After bone flap forming, the scalp and dura were cut and the microscope was placed. The brain pool was opened on the bottom, and the arachnoid around the aneurysm were detached after drainage of cerebrospinal fluid. Therefore, the aneurysm and its anatomical neck were fully exposed. If necessary, the parent artery should be temporarily blocked with blood pressure under control. Then the aneurysm was clipped at an appropriate angle by a suitable aneurysm clip, after that, the incision was closed layer by layer when no active bleeding was found. After the operation, close observation, routine antibiotics to prevent infection and positive symptomatic supportive care were given to the patient.

The patients in embolization group were treated with endovascular embolization as follows [11]. Firstly, the gas and intravenous general anesthesia was given to the patient, followed by routinely sterilization and surgical drape placement. After that, an angiography examination of internal carotid and vertebral artery was performed to the patient through a femoral artery puncture. Then a lateral or oblique radiograph was taken for the diseased vessels. At the same time, a three-dimensional reconstruction was made to confirm the diagnosis, the location, the size and shape of the aneurysm and its relationship with the surrounding blood vessels. Under the guidance of micro-guide wire, the microcatheter was placed into the aneurysm and an appropriate coil was used to embolize the aneurysm. Several angiographies were made for the aneurysm until it became invisible, so that the embolization could be certified to be sufficient and no blood flow of the parent artery was affected. Then the catheter was released with ease and the catheter

Table 1. Comparison of general information in two groups

Group	n	Gender		Age	Hunt-Hess Classification		Duration (d)	Aneurysm diameter (mm)
		M	F		Grade I-II	Grade III-IV		
Clipping	45	19	26	51.42±3.62	32	13	13.25±3.47	10.23±0.47
Embolization	51	22	29	52.41±3.58	35	16	14.36±3.52	10.18±0.45
t/χ^2 value		0.008		1.345	0.070		1.552	0.532
P value		0.928		0.182	0.791		0.124	0.596

Table 2. Comparison of operation time and length of postoperative hospital stay in the two groups

Group	n	Operation time (min)	Postoperative hospital stay (d)
Clipping	45	128.45±21.63	19.47±5.84
Embolization	51	91.36±14.58	14.32±6.79
t value		9.952	3.957
P value		<0.001	<0.001

sheath was left inside. After 6 hours, the catheter sheath was removed with pressure on the femoral artery until there was no active bleeding, after that the puncture point was bound up. The lower limb of the puncture side should be immobilized for 24 hours. After the operation, close observation, routine antibiotics to prevent infection and positive symptomatic supportive care were given to the patient.

Observation indicators

Main outcome indicators: The Glasgow Outcomes Scale (GOS) scores at the time of discharge from the two groups were compared [12]. The evaluation criteria were as follows. 5 points: complete recovery of daily activities, good prognosis; 4 points: mild disability, independent living, work under protection; 3 points: severe disability, conscious, daily care required; 2 points: persistent vegetative state, only minimal response; 1 point: death. Higher GOS score indicates better patient outcome. The GOS score 4 and 5 represent good for patients, the good rate for GOS scores = (number of cases of GOS score of 4 and 5)/total number of cases * 100% [13].

The levels of brain injury related factors in serum before and after surgery were compared between the two groups of patients. Three milliliter of venous blood was collected from the patient's cubital vein 1 day before and 3 days after surgery. Serum was separated by centrifugation at 2,000 r/min for 10 minutes and placed in a test tube, saved at -20°C. The serum S100B protein was detected by ELISA (S100B kit was purchased from CanAg Diagnostics AB Co. Ltd., Sweden) and matrix metalloproteinase 9 (MMP-9) (MMP-9 kit was purchased from R&D Systems Co. Ltd., USA). The Oxide dismutase (SOD) in serum was detected by colorimetric method (SOD kit was purchased from Sigma-Aldrich Co. Ltd., USA), strictly followed the kit instructions.

Secondary indicators

The operative time and postoperative hospital stay were compared between the two groups. The complications and recurrence rates were compared within 1 year's follow-up, complications included cerebral edema and brain injury. Relapse was defined as a DSA reexamination showing a more enlarged neck or body part, or a loosely compressed coil. Recurrence rate = number of relapsed cases/total number of cases * 100%.

Statistical analysis

All data were statistically analyzed using SPSS 22.0 software. Measured data were expressed as mean ± sd, the comparison between groups with normal distribution was performed using independent sample t-test, expressed as t. Measurement data were expressed as percentage, the comparison between groups was performed using χ^2 test or Fisher's exact probability method, expressed as χ^2. P<0.05 indicates that the difference is statistically significant.

Results

Comparison of basic data between two groups of patients

There was no statistically significant difference in basic data such as sex, age, Hunt-Hess classification, duration of disease, and diameter of intracranial aneurysms between patients in the clipping and embolization groups (all P>0.05). See **Table 1**.

Table 3. Comparison of good rate of GOS scores when two groups of patients were discharged (n, %)

Group	n	GOS score					Good rate (%)
		1 point	2 points	3 points	4 points	5 points	
Clipping	45	0 (0.00)	4 (8.89)	5 (11.11)	13 (28.89)	23 (51.11)	80.00
Embolization	51	0 (0.00)	0 (0.00)	2 (3.92)	1 (1.96)	48 (94.12)	96.08
χ^2 value							66.975
P value							<0.001

Note: GOS score, Glasgow Outcome Scale score.

Table 4. Comparison of recurrence rate of intracranial aneurysms and incidence of cerebral edema and cerebral nerve injury in two groups (n, %)

Group	n	Cerebral edema	Cerebral nerve injury	Recurrence
Clipping	45	4 (8.89)	3 (6.67)	5 (11.11)
Embolization	51	3 (5.88)	2 (3.92)	3 (5.88)
χ^2 value		0.030	0.365	0.308
P value		0.863	0.546	0.579

Comparison of operation time and length of postoperative hospital stay in the two groups

The operation time and postoperative hospital stay in the embolization group were significantly shorter than those in the clipping group (P<0.001). See **Table 2**.

Comparison of good rate of GOS scores when two groups of patients were discharged

The GOS score of the embolization group was 96.08% (49/51) when discharged, which was significantly greater than 80.00% (36/45) of the clipping group. The difference was statistically significant (P<0.001). See **Table 3**.

Comparison of recurrence rate and incidence of cerebral edema and cerebral nerve injury in two groups

There was no significant difference in the incidence of brain edema, brain injury, and recurrence rate of intracranial aneurysms between the two groups (P>0.05). See **Table 4**.

Comparison of brain injury related factors in serum before and after surgery in both groups

There was no significant difference in serum S100B protein, MMP-9, and SOD levels between the two groups before surgery (P>0.05). Compared with preoperative levels, postoperative serum S100B protein levels (clipping group: P=0.002; embolization group: P=0.008) and MMP-9 (clipping group: P=0.002; embolization group: P=0.021) in both groups significantly decreased. The SOD level (clipping group: P=0.004; embolization group: P=0.008) in both groups significantly increased. Between the two groups, postoperative serum S100B protein and MMP-9 levels in embolization group were significantly lower than the clipping group, the SOD levels were significantly higher than the clipping group, the difference was statistically significant (all P<0.001). See **Table 5**.

Discussion

The condition of ruptured intracranial aneurysm is very dangerous, and the sum of mortality and disability can reach 60% [14, 15]. Once the intracranial aneurysm is diagnosed, intervention should be taken actively. Some studies have reported that patients with intracranial aneurysms treated with microsurgical clipping could obtain satisfactory results and recover well [16]. With the continuous development of endovascular embolization techniques, studies have shown that patients with endovascular embolization have significantly less risks of mortality in 5 years than that of patients underwent microsurgical clipping [17, 18]. We believe that personalized treatment of different types of patients for intracranial aneurysm treatment is expected to further improve efficacy and safety. The reason is that unreasonable treatment options may increase patients' suffering, and cause iatrogenic damage and aggravated conditions [19].

The advantage of microsurgical clipping in the treatment of intracranial aneurysms is the high rate of tumor neck clipping. Darsaut et al. reported that microsurgical clipping can effec-

Table 5. Comparison of brain injury related factors in serum before and after surgery in both groups

Group	Pre/post-operation	S100B protein (ng/L)	MMP-9 (μg/L)	SOD (μU/L)
Clipping Group	Pre	1.83±0.29	725.41±53.69	68.52±7.34
	Post	1.25±0.25	524.47±42.62	76.14±6.51
	t value	25.115	5.714	15.901
	P value	0.002	0.002	0.004
Embolization	Pre	1.82±0.31	719.84±56.84	68.36±7.29
	Post	0.69±0.13	376.25±31.26	84.14±8.37
	t value	10.873	6.755	3.491
	P value	0.008	0.021	0.008
Pre-comparison between groups	t value	0.163	0.492	0.107
	P value	0.871	0.624	0.915
Post-comparison between groups	t value	14.000	19.580	5.176
	P value	<0.001	<0.001	<0.001

Note: MMP-9, matrix metalloproteinase-9; SOD, superoxide dismutase.

tively prevent rerupture hemorrhage, and at the same time can clear intracranial hematoma and hematocele, and release the mass effect [20]. But microsurgical clipping operation has higher requirements for operating equipment and surgeon, as it is difficult to reveal complex aneurysms or posterior circulation aneurysms, resulting in poor occlusion of such aneurysms [21]. Other studies have shown that complications such as residual aneurysm, brain edema, and brain injury after microsurgical clipping are also common [22]. Tabani et al. considered that limited by the operating space, microsurgical clipping surgery would inevitably damage the nerves and blood vessels distributed around the intracranial aneurysm, as the main cause of postoperative complications [23].

For patients with poor clinical grade, older age and poor physical condition, we believe that the risk of microsurgical clipping is higher and the endovascular embolization is more suitable for them [24]. Through blood vessel puncture techniques, embolization material was placed into the aneurysm to reduce the impact of blood flow on the aneurysm wall, thereby relieving the disease [25]. With the continuous improvement of embolization materials, the effectiveness and safety of intravascular treatment have been significantly improved. Its clinical efficacy is comparable to microsurgical clipping, and even more superior in the treatment of complex aneurysms [26]. The results of this study showed that the good rate of GOS score was 96.08% when discharged in the embolization group, which was significantly higher than that of the clamp group (80.00%). The difference was statistically significant. However, cerebral edema and cerebral nerve injury were followed up for 1 year in both groups. There was no significant difference in the incidence and recurrence rate between the two groups, which was similar to that reported in previous studies, indicating that endovascular embolization is superior to microsurgical clipping in the treatment of intracranial aneurysms [27, 28].

Endovascular embolization in the treatment of intracranial aneurysms was primarily aimed at ensuring embolization, reducing surgical trauma and accelerating postoperative recovery [29]. We believe that endovascular embolization in the treatment of intracranial aneurysms subverted the traditional surgical treatment of intracranial aneurysms by avoiding craniotomy for clinicians. Not only is endovascular embolization comparable to microsurgical clipping in clinical efficacy, but even more effective in the treatment of complex or posterior circulation aneurysms [30-32]. The results of this study showed that the operative time and postoperative hospital stay in the embolization group were significantly shorter than those in the clipping group, indicating that endovascular embolization is less invasive than microsurgical clipping in intracranial aneurysms and more conducive to postoperative recovery. For in-depth analysis, this study used S100B protein, MMP-9 and SOD to assess brain injury. S100B protein reflects endothelial function and disease status [33]. Studies have pointed out that serum S100B protein and MMP-9 levels in patients with intracranial aneurysms are positively correlated with brain injury [34, 35]. In this study, the levels of S100B protein and MMP-9 in serum in the embolization group were significantly lower than those in the clipping group, which might be due to brain injuries caused by craniotomy of the microsurgical clipping and intracranial operation. As an important factor in antagonizing the oxidative stress response in the treatment of intracranial aneurysms, SOD can degrade oxygen free radicals and protect brain tissue. This effect is particularly evident in the brain [36]. Increased serum SOD levels in patients with intracranial aneurysms may reflect the degree of brain protection to some extent. The results of this study showed that serum SOD levels in the embolization group were significantly higher than those in the clipping group, indicating that endovascular embolization treatment had less damage to the brain tissue and better protection of the brain tissue than microsurgical clipping surgery, and facilitated the recovery of postoperative neurological function.

Since this study is a retrospective study with small sample size and short follow-up. Prospective controlled studies with increased sample size and follow-up are needed to obtain more in-depth data and analyze the long-term efficacy of microsurgical clipping and endovascular embolization on intracranial aneurysms.

In summary, both microsurgical clipping and endovascular embolization for intracranial aneurysms can achieve satisfactory short-term efficacy, but the latter has less damage to brain tissue and rapid postoperative recovery. In clinical practice, comprehensive consideration should be given to the choice of treatments based on the actual situation of patients. For old patients with high clinical scale, poor physical condition and complicated or posterior circulation intracranial aneurysms, endovascular embolization may be preferred.

Disclosure of conflict of interest

None.

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