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Safety and Efficacy of Endovascular Treatment for Intracranial Ruptured Aneurysms: Stent-Assisted Coiling *vs*. Single Coiling

Jia L#, Wang J#, Zhang L, Ming LV and Yang X**

Department of Interventional Neuroradiology, Beijing Neurosurgical Institute and Beijing Tian Tan Hospital, China

#These authors contributed equally to this work

Abstract

Background: Patients undergoing endovascular treatment by Stent-Assisted Coiling (SAC) require dual antiplatelet therapy, which may increase the risk of intracranial hemorrhage. Therefore, SAC is controversial in Intracranial Ruptured Aneurysms (IRA).

Objective: To evaluate the effectiveness and safety of treating IRA with SAC versus single coiling.

Methods: We retrospectively analyzed the data from 151 patients with spontaneous subarachnoid hemorrhage resulting from IRA confirmed by digital subtraction angiography who underwent SAC or single coiling therapy in our hospital from January 2017 to December 2017.

Results: There were 152 aneurysms in 151 patients; 64 aneurysms were treated with SAC, while 88 were treated with single coiling. Follow-up angiography showed that the complete occlusion rate in the SAC group was similar to that in the single coiling group (89.7% *vs*. 78.2%, respectively; P=0.08). In addition, the total perioperative complication rate in the SAC group was similar to that in the single coiling group (23.4% *vs*. 19.5%, respectively; P=0.56). During follow-up, the SAC group had a similar incidence of favorable outcomes (modified Rankin Scale score, 0-2) compared with the single coiling group (88.3% *vs*. 83.3%, respectively; P=0.41).

Conclusion: SAC may be as effective and safe as single coiling for IRA.

Keywords: Intracranial ruptured aneurysms; Stent-assisted coiling; Single coiling

Correspondence:

Ming LV, Department of Interventional Neuroradiology, Beijing Neurosurgical Institute and Beijing Tian Tan Hospital, Beijing, 100070, China, Tel/Fax: +8610-59978557;

E-mail: dragontiger@163.com

Yang X, Department of Interventional Neuroradiology, Beijing Neurosurgical Institute and Beijing Tian Tan Hospital, Beijing, 100070, China, Tel/Fax: +8610-59978557;

E-mail: yangxinjian@voiceoftiantan.org

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Introduction

The overall prevalence of aneurysms in Chinese adults aged 37 years to 75 years is as high as 7% [1]. An untreated ruptured aneurysm is at high risk of rebleeding, with a cumulative risk at 4 weeks of 40% without intervention, and re-rupture is associated with a poor prognosis [2]. Therefore, ruptured aneurysms should be treated as quickly as possible.

Endovascular therapy for intracranial aneurysms is a recent development that is gradually replacing surgery because of the advantages of minimal invasiveness and lower rates of morbidity and mortality [3]. However, a lack of permanent support for the coil mass inside the aneurysm may allow the coil to prolapse or migrate. In Stent-Assisted Coiling (SAC), the stent acts as a scaffold across the aneurismal neck, keeping the coils inside the aneurysm [4]. However, SAC is controversial in Intracranial Ruptured Aneurysms (IRA) because of the increased intracranial rebleeding rate secondary to Dual Antiplatelet Therapy (DAT). A retrospective study reported that hemorrhage was 3.4 times more likely to occur in patients with Subarachnoid Hemorrhage (SAH) treated with SAC compared with coiling alone [5]. Thus, the safety of SAC for the treatment of SAH still needs further research. The purpose of the present study was to evaluate the safety and effectiveness of SAC in the treatment of IRA.

Materials and Methods

Study design

This was a retrospective review of our experience treating IRA using SAC or single coiling. This study was approved by the ethics committee of our hospital and was performed in accordance with the guidelines of the Helsinki Declaration.

Table 1: Patients' baseline characteristics.

Characteristics	SAC (n=64)	SC (n=87)	P Value
Age (SD)	55.1 (12.5)	53.2 (12.1)	0.35
Range	27-86	23-85	
Male	25(39.1%)	33(37.9%)	0.89
Symptoms of the patient			
Headache	58 (90.6%)	85 (97.7%)	0.07
Nausea and (or) vomiting	56 (87.5%)	70 (80.5%)	0.25
Disturbance of consciousness	24 (37.5%)	32 (36.8%)	0.93
Epilepsy	6 (9.4%)	11 (12.6%)	0.53
Limb weakness	0 (0%)	2 (2.3%)	0.51
Cranial nerve palsy	3 (4.7%)	4 (4.6%)	1
Aneurysm location			0.93
Anterior circulation	52 (81.3%)	72 (81.8%)	
Posterior circulation	12 (18.8%)	16 (18.2%)	
Aneurysm size (mm)(SD)	5.16 (2.68)	5.19 (2.83)	
Range	1.54 - 17.50	1.59 -13.00	
Aneurysmal morphology			<0.01
Regular shape	24 (37.5%)	58 (65.9%)	
Irregular shape	40 (62.5%)	30 (34.1%)	
Wide-necked aneurysms	53 (82.8%)	38 (43.2%)	<0.01

SD: Standard Deviation; wide-necked aneurysm: dome-to-neck ratio ≤ 2 or a neck diameter ≥ 4 mm; SAC: Stent-Assisted Coiling; SC: Single Coiling

Table 2: Preoperative classifications.

	SAC (n=64)	SC (n=87)	P Value
mRS grade			0.9
1	5 (7.8%)	9 (10.3%)	
2	47 (73.4%)	65 (74.7%)	
3	2 (3.1%)	2 (2.3%)	
4	10 (15.6%)	11 (12.6%)	
HH grade			0.18
I	20 (31.1%)	23 (26.4%)	
II	33 (51.6%)	37 (42.5%)	
III	6 (9.4%)	20 (23.0%)	
IV	5 (7.8%)	7 (8.0%)	
Modified Fisher grade			0.48
I	17 (26.6%)	19 (21.8%)	
II	21 (32.8%)	24 (27.6%)	
III	26 (40.6%)	44 (50.6%)	
GCS grade			0.79
3-5	7 (10.9%)	8 (9.2%)	
6-10	6 (9.4%)	11 (12.6%)	
11-15	51 (79.7%)	68 (78.2%)	

Patient characteristics

A retrospective review of our institutional clinical database identified 279 patients who presented with a diagnosis of SAH resulting from IRA from January 2017 to December 2017. Among this group, 15 patients were not treated due to poor clinical conditions, 91 patients underwent microsurgical clipping, and 173 patients underwent endovascular treatment. Among the 173 patients who underwent endovascular treatment, two underwent pipeline flow diverter therapy, while 171 underwent SAC or single coiling therapy. However, 20 of these 171 patients had dissecting aneurysms and were excluded from the present study. Thus, we retrospectively analyzed the data from 151 patients who underwent endovascular treatment (SAC or single coiling); the cohort comprised 93 women and 58 men (female: male ratio, 1.6:1) with a median age of 54.0 ± 12.2 years (range: 23 years to 86 years). All patients were diagnosed with SAH caused by IRA confirmed by preoperative Computed Tomography (CT) and Digital Subtraction Angiography (DSA). Sixty-four patients with 64 aneurysms were treated with SAC (SAC group), while 87 patients with 88 aneurysms were treated with single coiling (single coiling group). Patient demographic data and clinical characteristics were collected from the medical records and are shown in Table 1.

Imaging diagnosis

SAH was confirmed by CT, and the amount of hemorrhage was evaluated by the modified fisher grade. The detailed aneurysm location was confirmed by DSA; 152 aneurysms were confirmed in 151 patients (one patient had two aneurysms). In the SAC group, 64 aneurysms were confirmed in 64 patients; 52 (81.3%) aneurysms were located in the anterior circulation, while 12 (18.8%) were located in the posterior circulation. In the single coiling group, 88 aneurysms were confirmed in 87 patients; 72 (81.8%) aneurysms were located in the anterior circulation, while 16 (18.2%) were located in the posterior circulation. Wide-necked aneurysms were defined as aneurysms with a dome-to-neck ratio of ≤ 2 or a neck diameter of ≥ 4 mm. There were 91 wide-necked aneurysms; 53 (82.8%) in the SAC group and 38 (43.2%) in the single coiling group. Table 1 and 2 show the details of the aneurysms undergoing endovascular treatment and the amount of hemorrhage.

Endovascular procedure

Endovascular treatment was selected after comprehensive discussion with a multidisciplinary team including neurologists and neurosurgeons. Treatment with SAC or single coiling was decided by the group in accordance with the size, location, and morphology of the aneurysm. All endovascular treatments were performed under general anesthesia by experienced neurointerventionalists. The appropriate stent was chosen in accordance with the sizes of the parent artery and aneurysm; the stents used were Neuroform® (Stryker, Kalamazoo, MI), Solitaire® (ev3, Irvine, CA), Enterprise® (Codman, Raynham, MA), and LVIS® (Microvention, Tustin, CA). In the SAC group, the aneurysms were coiled using the coil-through technique (i.e., the stent was released before the microcatheter was inserted into the aneurysmal sac and passed through the stent interstices) or the jailing technique (i.e., the stent was released after the microcatheter was inserted into the aneurysmal sac). In the single coiling group, the femoral artery was canalized with a suitable sheath before the microcatheter was delivered to the aneurysm using a microguidewire, and the coil was transferred to the aneurysm. The aneurysm was occluded with decreasing sizes of coils with the aim of occluding the aneurysm completely. Angiographic results were classified into three categories in accordance with the immediate postprocedural angiographic findings: 1) complete occlusion, defined as no contrast filling the aneurysmal sac (Figure 1); 2) near-complete occlusion, defined as contrast filling the aneurysmal neck (Figure 2); and 3) incomplete occlusion, defined as contrast filling the aneurysmal sac.

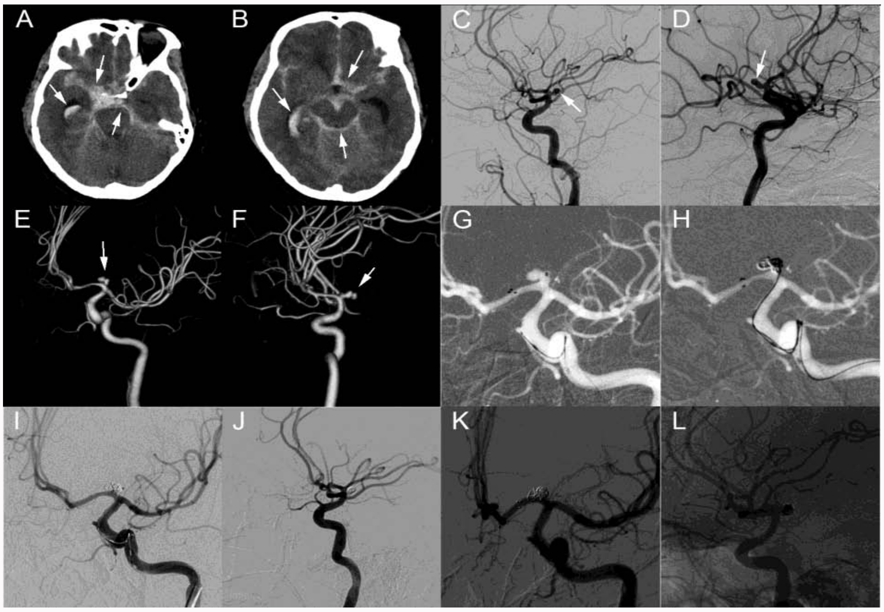

Figure 1: Images from a 49-year-old woman in the stent-assisted coiling group with a saccular aneurysm located in the Anterior Cerebral Artery (ACA). (A-B) Preoperative computed tomographic images showing subarachnoid hemorrhage and intraventricular hemorrhage; modified Fisher grade 3. (C–F) Preoperative angiograms (C and D) and three-dimensional reconstruction (E and F) confirming the saccular aneurysm located in the ACA. (G) Intraoperative road map showing complete release of the Solitaire® stents. (H) Intraoperative road map showing that the coil fills the aneurysm. (I and J) Immediately postoperative angiograms showing a patent parent artery and a completely occluded aneurysm. (K and L) Three-month postprocedural angiograms showing a patent parent artery and a completely occluded aneurysm.

Antiplatelet treatment and anticoagulation

All patients in the SAC group received a loading dose of DAT drugs (300 mg aspirin and 300 mg clopidogrel) at least 2 h before the procedure. The single coiling group did not receive antiplatelet therapy. During the procedure, both the SAC and single coiling groups received intravenous heparin to maintain an activated clotting time of approximately 250 s to 300 s throughout the procedure. For the SAC group, DAT (100 mg of aspirin and 75 mg of clopidogrel daily) was continued for 3 months postoperatively, and aspirin will be continued for life to prevent thrombus formation in the stents.

Statistical analyses

SPSS 25.0 software (IBM Corp., Armonk, NY) was used for all statistical analyses. The Mann-Whitney U test was performed for non-normally distributed continuous variables, while Pearson's correlation or Fisher's exact test was used to compare proportions. All tests were two-sided, and P<0.05 was considered statistically significant.

Results

Patient baseline characteristics

Of the 151 patients, 64 patients with a mean age of 55.1 ± 12.5 years underwent SAC, while 87 patients with a mean age of 53.2 ± 12.1 years underwent single coiling. Most patients were women in both the SAC and single coiling groups (60.9% *vs.* 62.1%, respectively). Mean aneurysm size was 5.16 ± 2.68 mm in the SAC group and 5.19 ± 2.83 mm in the single coiling group. Patient and aneurysm characteristics are summarized in Table 1.

The severity of SAH was classified by the modified Fisher grade. The distribution of the modified Fisher grade did not significantly differ between the SAC and SC groups. The severity of clinical symptoms was classified by the Hunt and Hess grade, modified Rankin Scale (mRS) score, and Glasgow coma scale grade. The distributions of the Hunt and Hess grade, mRS score, and Glasgow coma scale grade did not significantly differ between the SAC and single coiling groups (Table 2).

Adverse events and embolization results

The total perioperative complication rate in the SAC group (23.4%; 15 patients) was similar to that in the single-coiling group (19.5%; 17 patients) (P=0.56). Intraoperative rupture occurred in one patient (1.6%) in the SAC group and four patients (4.6%) in the single coiling group. Two patients (3.1%) died perioperatively in the SAC group, while no patients died in the single coiling group. The frequency of complications was similar in the SAC and single coiling groups. The respective postoperative hemorrhagic rate and ischemic rate were 12.5% (eight patients) and 18.8% (12 patients) in the SAC group, and 6.9% (six patients) and 13.8% (12 patients) in the single coiling group. The postprocedural complete occlusion rate in the SAC group (81.3%) was similar to that in the single coiling group (79.3%; P=0.70) (Table 3).

Clinical and imaging follow-up

Clinical follow-up results were assessed by the mRS score, while imaging follow-up was evaluated by DSA. A total of 138 patients (82.8%) underwent clinical follow-up, with a median follow-up time of 17.1 ± 3.39 months (range: 12 months to 23 months). The follow-up rate was 93.8% (60/64) in the SAC group and 90.0% (78/87) in the single coiling group. There was no significant difference in the incidence of favorable outcomes (defined as mRS ≤ 2) in the SAC group (88.3%) *vs.* the single coiling group (83.3%; P=0.41). Imaging follow-up data were obtained for 136 patients (90.1%), with a median imaging follow-up period of 9.2 ± 3.8 months (range: 3 months to 21 months). The imaging follow-up rate was 90.6% (58/64) in the SAC group and 89.7% (78/87) in the single coiling group, and four

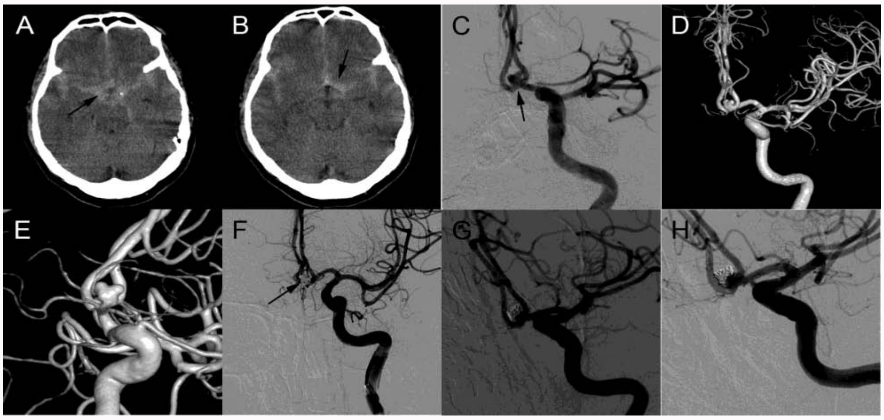

Figure 2: Images from a 48-year-old man who underwent single coiling treatment for a saccular aneurysm located in the anterior cerebral artery (ACA). (A and B) Preoperative computed tomographic images showing subarachnoid hemorrhage and intraventricular hemorrhage; modified Fisher grade 3. (C–E) Preoperative angiograms (C) and three-dimensional reconstruction (D and E) confirming an irregular saccular aneurysm located in the ACA. (F) Immediately postoperative angiograms showing a near-completely occluded aneurysm. (G) Three-month postprocedural angiograms showing contrast media filling the aneurysmal neck. (H) Eight-month postprocedural angiograms showing contrast media filling the aneurysm neck, and no substantial change compared with 3 months postoperatively.

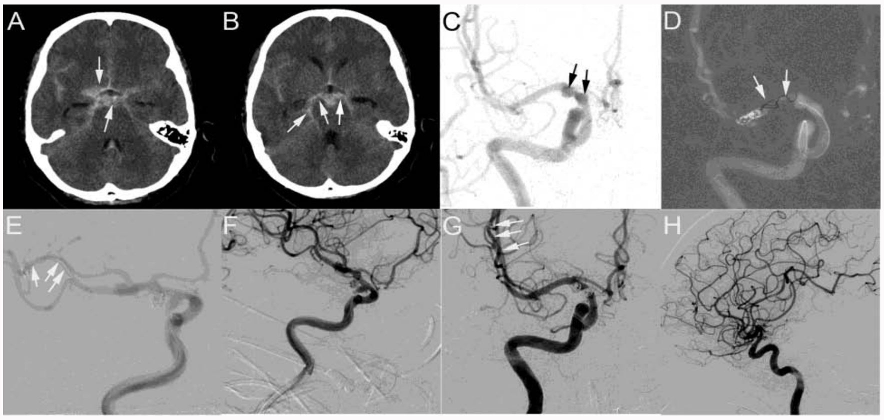

Figure 3: Images from a 63-year-old woman in the single coiling group with two saccular aneurysms located in the posterior communicating artery (PcomA). (A and B) Preoperative computed tomographic images showing subarachnoid hemorrhage; modified Fisher grade 2. (C) Preoperative angiograms confirming two saccular aneurysms located in the PcomA. (D) Intraoperative road map showing coil displacement to the parent artery. (E) After retrieving the two coils with a Solitaire® stent, one coil escaped to the distal middle cerebral artery (MCA). (F) Angiography showing that the branches of the MCA are well-developed without retention of contrast agent, and that the blood supply is not affected. (G and H) Immediately postoperative angiograms showing an unobstructed parent artery and distal MCA and a completely occluded aneurysm.

patients experienced recurrence (defined as increased contrast filling of the aneurysmal sac compared with immediate postprocedural angiographic findings). The recurrence rate was 1.7% (one patient) in the SAC group and 3.8% (three patients) in the single coiling group. The complete occlusion rate in the SAC group (89.7%) was similar to that in the single coiling group (78.2%; P=0.08) (Table 4).

Discussion

Spontaneous SAH from ruptured aneurysms often leads to a variety of complications, such as cerebral infarction, vasospasm, hydrocephalus, and even death [3,6]. Untreated ruptured aneurysms have a high rate of re-rupture, and the mortality rate due to re-ruptured aneurysms and the associated hemorrhage is as high as 59% [7]. The treatment of intracranial aneurysms has progressed over time from craniotomy and clipping to the current endovascular treatment. Endovascular therapy developed from electrothrombosis to occlude saccular aneurysms, which was followed by single coiling therapy, balloon-assisted coiling, and SAC [8]. The advantages of endovascular therapy, such as minimal trauma, have made endovascular therapy the first-line choice for treating intracranial aneurysms. The use of controlled-detachment coils to occlude the aneurysm originated in 1991 [8,9]. Compared with surgery, single coiling has a significantly lower incidence of complications such as angiographic vasospasm and delayed ischemic neurological deficits [10-16]. A recent study found that most IRAs are treated with single coiling and balloon-assisted coiling [17]. However, incomplete occlusion is still a major limitation of single coiling therapy [18]. SAC is a feasible endovascular treatment option for IRAs, but SAC is associated with a mild increase in the postprocedural complication rate [19-21]. Additionally, patients undergoing endovascular treatment by SAC require DAT, which may increase the risk of intracranial hemorrhage. A recent study reported that the early complication rate of SAC in patients with ruptured aneurysms is 10 times higher than that in patients with unruptured aneurysms, with early rebleeding accounting for most mortality [22].

Complications

According to a recent study, coil migration during endovascular treatment of an intracranial aneurysm occurs in 2% to 6% of patients [23]. In the present study, coil displacement during endovascular treatment occurred in one patient in the single coiling group (Figure

Table 3: Comparison of SAC and SC.

	SAC (n=64)	SC (n=87)	P Value
Time (hours)*			0.15
Less than 24	40 (62.5%)	64 (73.6%)	
24 – 72	24 (37.5%)	23 (26.4%)	
Total perioperative complication	15 (23.4%)	17 (19.5%)	0.56
Intraoperative coil migration	0 (0%)	1 (1.1%)	1
Intraoperative rupture	1 (1.6%)	4 (4.6%)	0.4
Intraoperative thrombosis	4 (6.3%)	1 (1.1%)	0.16
Postoperative* hemorrhagic	8 (12.5%)	6 (6.9%)	0.24
Rebleeding	3 (4.7%)	2 (2.3%)	0.65
mRS score*			
1	0	1	
2	1	1	
6	2	0	
Postoperative ischemic *	12 (18.8%)	12 (13.8%)	0.41
Perioperative mortality	2 (3.1%)	0 (0%)	0.19
Acute hydrocephalus	14(21.9%)	17 (19.5%)	0.73
Shunt operation	10(15.6%)	15 (17.2%)	0.79
Immediate angiographic results			0.7
Complete	52 (81.3%)	69 (79.3%)	
Near complete	7 (10.9%)	13 (14.9%)	
Incomplete	5 (7.8%)	5 (5.7%)	

***Time refers to the time from the onset of symptoms to the start of the endovascular procedure.

*Postoperative refers to the time from the completion of the endovascular procedure to patient discharge from the hospital.

*mRS Score refers to the outcome of rebleeding patients at the time of discharge from the hospital.

3), while no coil displacement occurred in the SAC group. This further verified that the stent acts as a scaffold and helps to maintain the coil placement. One study reported an intraprocedural rupture rate of 0% to 16.1% during endovascular treatment of IRA [24]. The rate of intraoperative aneurysmal rupture in the present study was significantly higher in the single coiling group (4.6%) than in the SAC group (1.6%), while the overall incidence of complications was similar in both groups. Hemorrhagic complications reportedly occur in 8% of patients with ruptured aneurysms treated with SAC [19]. The postoperative hemorrhagic complication rate in the present SAC group (12.5%) was significantly higher than that in the single coiling group (6.9%). Our results showed a relatively high incidence of bleeding events in the SAC group, which confirms that DAT increases the risk of bleeding. Thromboembolic events are the most common adverse events in endovascular treatment, with a reported incidence of 2% to 61% [25,26]. In the present study, the incidence of intraoperative thrombosis in the SAC group (6.3%) was significantly higher than that in the single coiling group (1.1%), and the SAC group (18.8%) had a significantly higher incidence of postoperative ischemic events than the single coiling group (13.8%), consistent with the thrombogenicity of stents. Recent studies have reported that regular administration of aspirin has a positive impact on the delayed cerebral ischemia risk and outcome of patients with SAH, without increasing the risk of bleeding [27-29]. Patients with SAC treated endovascularly are routinely prescribed aspirin, which helps to prevent the development of delayed cerebral ischemia.

Table 4: Clinical and imaging follow-up results.

	SAC	SC	P value
Clinical follow-up	n=52	n=73	
mRS			0.51
0-2	45 (86.5%)	60 (82.2%)	
3-6	7 (13.5%)	13 (17.8%)	
ventriculostomy	1 (1.9%)	0 (0%)	
Imaging follow-up	n=50	n=69	
Follow-up angiographic results			
Complete	44 (88.0%)	55 (79.7%)	0.23
Aneurysm recurrence	1 (2.0%)	3 (4.3%)	0.64

SAC: Stent-Assisted Coiling; SC: Single-Coil; mRS: Modified Rankin Scale

Medication

Because of the thrombogenicity of stents, SAC is associated with a high risk of ischemia [30]. Furthermore, SAH triggers the coagulation cascade, leading to a hypercoagulable state with a high tendency for clotting or thrombosis. This is normally a protective mechanism, but is countered by preoperative medication. Antiplatelet drugs are administered to prevent stent thrombosis, but this increases the risk of aneurysmal bleeding, which may increase the risk of aneurysm rupture. The clinical outcomes of SAC for IRA are reportedly affected by antiplatelet administration, but there is little consensus regarding the appropriate and safe timing of the administration of antiplatelet agents [31]. Standardized guidelines for antiplatelet therapy for IRA require further study. A recent study reported that the administration of antiplatelet therapy significantly improves the outcome of patients younger than 60 years, but worsens the outcome of patients older than 60 years [32]. However, some studies report that antiplatelet therapy has a positive impact on patients with SAH [33,34]. Thus, the benefits and risks of antiplatelet drugs remain unclarified, and need to be confirmed by further research. Furthermore, patients need to take antiplatelet drugs for life after SAC therapy, and clinicians should consider this when selecting the treatment plan.

Occlusion rate and follow-up results

The aim of the treatment of ruptured aneurysms is to achieve complete embolization to reduce the occurrence of re-rupture. One study found that patients presenting with ruptured aneurysms had a relatively high incidence of re-rupture from a neck remnant (3.4%), which highlights the importance of achieving complete occlusion of ruptured aneurysms [35]. The complete embolization rate immediately after treatment in the present SAC group (81.3%) was similar to that in the single coiling group (79.3%). Additionally, the follow-up complete embolization rate in the SAC group (89.7%) was similar to that in the single coiling group (78.2%). Previous studies report that the incidence of complete embolization is 20.2% to 89.2% in patients undergoing SAC, and 31.7% to 89.2% in patients undergoing single coiling therapy; however, these results included both ruptured and unruptured aneurysms [36-38]. One study reported that the initial incomplete occlusion rate is higher in the SAC group (64.3%) than in the single coiling group (51.7%) [37]. Our results showed a non-significant tendency for the complete occlusion rate to be higher in the SAC group than the single coiling group. A recent study reported that SAC achieves a significantly higher progressive complete occlusion rate at follow-up and a lower recurrence rate than single coiling [39]. In the present study, the recurrence rate was similar in the SAC group (1.7%) and the single coiling group (3.8%), and the incidence of favorable outcomes was similar in the SAC group (88.3%) and the single coiling group (83.3%) during clinical follow-up. Our results confirm the effectiveness of SAC in the treatment of IRA.

Limitations

The present study had some limitations. First, this was a single-center retrospective study without treatment randomization. The second limitation was the small number of patients and the high lost-to-follow-up rate. The present findings need to be confirmed in a prospective, multicenter, randomized controlled clinical trial with a large sample size.

Conclusion

Stent-assisted coiling may be as effective and safe as single coiling for IRAs.

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