Online April 22, 2020
Journal of Neuroendovascular Therapy 2020; 14: 249–254 DOI: 10.5797/jnet.oa.2019-0086

Original Article

Additional Embolization for Intra-aneurysmal Blood Flow Resumption after Stent-assisted Embolization of Cerebral Aneurysms

Sosho Kajiwara,[1] Masaru Hirohata,[1] Yasuharu Takeuchi,[1] Naoko Fujimura,[2] Shin Yamashita,[3] Yukihiko Nakamura,[4] Aya Hashimoto,[1] and Motohiro Morioka[1]

Objective: Stent-assisted aneurysmal embolization (SAAE) is an effective treatment for aneurysms with a low risk of recurrence. In rare cases, retreatment is necessary due to recanalization of blood flow into the aneurysm. However, only a few studies have reported on retreatment. We examined the efficacy and complications of stent-assisted aneurysm embolization for large or wide-neck aneurysms at our hospital.

Methods: Between July 2010 and June 2018, 293 patients underwent stent-assisted aneurysm embolization at our hospital. Among them, 12 (2 women, 10 men, mean age: 62 years) needed retreatment. We evaluated the initial treatment of these 12 patients, and the methods and results of their retreatment.

Results: Six of the 12 retreated patients were treated using the simple technique. It was possible to treat nine patients (75%) without placing new stents, but three needed additional stents. We were able to guide the microcatheter into the aneurysm using the trans-cell technique even with two overlapping stents. We achieved complete embolism in seven patients (58%), and remnants were observed in the neck in five (42%) patients. No complications were associated with our surgery. We were able to perform follow-up for 10 patients and there was no recurrence.

Conclusion: Embolization should be considered in recurrent cases after the initial stent-assisted coil embolization. We achieved good results and reduced the recurrence rate by selecting the appropriate treatment in each case.

Keywords ▶ stent assist, coil embolization, recanalization, re-aneurysm embolization

Introduction

Stent-assisted aneurysmal embolization (SAAE) has recently been performed as an endovascular technique for large aneurysms, markedly improving the results of treatment.[1)] However, in some cases, intra-aneurysmal blood flow resumption was observed during long-term follow-up. The incidence depended on the type of stent, but was reportedly 5.0%–14.6%.[2)] Of patients with such blood flow resumption, 1.9% required additional treatment.[2)] Adjunctive techniques are required in many cases, but these techniques may be difficult to perform. The level of surgical difficulty and risk of adjunctive techniques are higher than in initial treatments. Few clinical studies have been published regarding additional treatment after SAAE. In this study, we investigated patients after SAAE in whom intra-aneurysmal blood flow resumption required additional treatment.

Materials and Methods

The subjects were 293 patients (294 aneurysms) who had undergone SAAE of cerebral aneurysms in our department between July 2010 and June 2018. SAAE was indicated for patients in whom blood influx into the aneurysm was clear,

[1]*Department of Neurosurgery, Kurume University School of Medicine, Kurume, Fukuoka, Japan*
[2]*Department of Neurosurgery, Fukuokaken Saiseikai Futsukaichi Hospital, Chikushino, Fukuoka, Japan*
[3]*Department of Neurosurgery, Omuta City Hospital, Omuta, Fukuoka, Japan*
[4]*Department of Neurosurgery, Saiseikai Fukuoka General Hospital, Fukuoka, Fukuoka, Japan*

Received: October 3, 2019; Accepted: March 31, 2020
Corresponding author: Sosho Kajiwara. Department of Neurosurgery, Kurume University School of Medicine, 67 Asahi-machi, Kurume, Fukuoka 830-0011, Japan
Email: kajiwara_soushou@med.kurume-u.ac.jp

Table 1 Two hundred and ninety-four aneurysms treated by stent-assisted coil embolization

Sex	
Male	204
Female	90
Age (years)	31–80 (mean: 65.4)
Location	
Anterior circulation	ICA: 168 (57%)
	C1: 47
	C2-3: 85
	C4-5: 36
	Acom.A: 39 (13%)
	MCA (M1-2): 10 (3%)
Posterior circulation	BA: 33 (11%)
	BA tip: 24
	BA-SCA: 1
	Mid-BA: 6
	VA: 41 (14%)
	VADA: 29
	VA-PICA: 7
	other VA: 6
Other	3
Size	
Small	169
Large	114
Giant	11
Surgical procedure	
SA	38
SA & DC	172
SA & BNR	45
SA & DC & BNR	20
Telescopic	19
Stent	
ENTERPRISE or E2	72
LVIS Blue	56
LVIS Jr	91
NEUROFORM ATLAS	58
NEUROFORM EZ	25
Result	
Complete	154
Residual neck	128
Residual aneurysm	12

BA: basilar artery; BNR: balloon neck remodeling; DC: double catheter; PICA: posterior inferior cerebellar artery; SA: stent assist; SCA: superior cerebellar artery; VA: vertebral artery; VADA: VA dissecting aneurysm

those with additional enlargement of the aneurysm, and those with contrast effects in the aneurysmal wall. Respective patients were reviewed, and the treatment procedures and efficacy were evaluated. Of the 293 patients, additional treatment was performed in 12 (13 cerebral aneurysms). For additional treatment, dual antiplatelet therapy (DAPT) (biaspirin at 100 mg/day + clopidogrel at 75 mg/day) was administered orally as a basic therapy. The effects were confirmed using a VerifyNow system (Accumetrics, San Diego, CA, USA). When evaluating the treatment response, patients with an aspirin reaction unit (ARU) level of >550 were regarded as non-responders to aspirin and those with a P2Y12 reaction unit (PRU) level of >230 as non-responders to clopidogrel.[3] When the effects were insufficient, cilostazol at 100 mg/day was added and administered orally. For the 12 patients who required additional treatment, second surgery was performed under general anesthesia. The state of embolization was assessed using Raymond's classification.[4] This study was approved by the ethics review board of our hospital (Application No.: 2019-068).

Results

The characteristics of the study population (293 patients and 294 aneurysms) are presented in **Table 1**. The mean age was 65.4 years (31–80 years). There were 204 males (70.0%). Eighty-five of 168 (57.0%) internal carotid artery (ICA) aneurysms involved the C2-3 area, and 24 of 33 (11.2%) basilar artery (BA) aneurysms involved the BA end. Of 41 (14.0%) vertebral artery (VA) aneurysms, 29 were dissecting aneurysms. The mean aneurysmal size was 8.9 mm (1.5–35 mm). Stent-assisted and double catheter techniques were selected as the surgical procedures for 172 aneurysms (58.5%), accounting for the highest percentage. Enterprise (23.8%), Neuroform (EZ: 8.3%, Atlas: 19.2%), and LVIS (Blue: 18.5%, Jr: 30.1%) stents were used. The state of embolization on initial treatment was evaluated as "complete" in 154 aneurysms (53%) and "residual neck" in 128 (43%). In both "complete" and "residual neck" patients, favorable embolization was achieved. The state of embolization was evaluated as "residual aneurysm" in 12 cases (4.1%).

The mean follow-up period after initial treatment was 39.4 months. In the above population, 12 patients (12/293, 4.1%) (13 aneurysms) required additional treatment. The mean interval from initial to additional treatment was 18.3 months (6–58 months). The mean age of the 12 patients was 62 years (44–80 years). There were 10 males. The reasons for using a stent as an initial treatment included acute rupture in three aneurysms (VADA: 2, ICA [bail out]), the absence of rupture in eight (symptomatic: 1), and recurrence after coil embolization in two patients (**Table 2**). Six aneurysms (3.6%) measured ≤10 mm, 6 (5.2%) measured 10–24 mm, and 1 (9.1%) measured ≥25 mm. The risk of recurrence requiring additional treatment was higher for larger aneurysms. The sites consisted of the ICA in seven aneurysms, BA in three, and VA in three. The mean dome and neck sizes were 9.9 and 7 mm, respectively. The mean dome/neck ratio was 1.4.

The state of embolization of cerebral aneurysms at the completion of initial treatment was evaluated as "complete"

Table 2 Twelve patients (13 aneurysms) in whom recurrence after SAAE required treatment

No.	Sex	Age	Location	Size	1st SAAE		Re-embolization					Follow-up
					Reason	Result	Clinical presentation	Time interval (month)	Procedure	Result	Surgical complication	
1	M	68	BA tip	G	Unrupture	RN	Mass effect	10	DC	C	None	L
2	F	71	IC-PC	S	Unrupture	C	Asymptomatic	27	Simple	C	None	L
3	F	58	ICA C2	L	Unrupture	C	Asymptomatic	8	BNR	C	None	NR
4	M	70	BA tip	L	Recurrence after CE	RN	Asymptomatic	21	Simple	C	None	NR
5	F	80	IC-PC	S	Rupture	RN	Asymptomatic	15	Simple	C	None	NR
6	F	53	VA	S	Unrupture	C	Asymptomatic	12	Telescopic	C	None	NR
7	F	44	VA	L	Rupture	C	Asymptomatic	27	Telescopic	C	None	NR
8	F	65	BA tip	L	Recurrence after CE	RN	Asymptomatic	12	Simple	RN	None	NR
9	F	50	VA	L	Rupture	RN	Asymptomatic	6	BNR + telescopic	RN	None	NR
10	F	70	IC-PC	S	Unrupture	C	Asymptomatic	58	Simple	RN	None	NR
11	F	58	ICA C2	S	Unrupture	RN	Asymptomatic	8	BNR	RN	None	NR
12	F	57	ICA C5	S	Unrupture	C	Asymptomatic	15	Simple	C	None	NR
			ICA C5	L	Unrupture	RN	Asymptomatic	15	Simple	RN	None	NR

Sex—M: male; F: female; Size—S: small; L: large; G: giant; Time interval—1st SAAE to re-embolization procedure; DC: double catheter; BNR: balloon neck remodeling; Result—C: complete; RN: residual neck; RA: residual aneurysm; Follow-up—NR: no recanalization; R: recanalization; L: lost; SA: stent assist; SAAE: stent-assisted aneurysmal embolization; CE: coil embolization

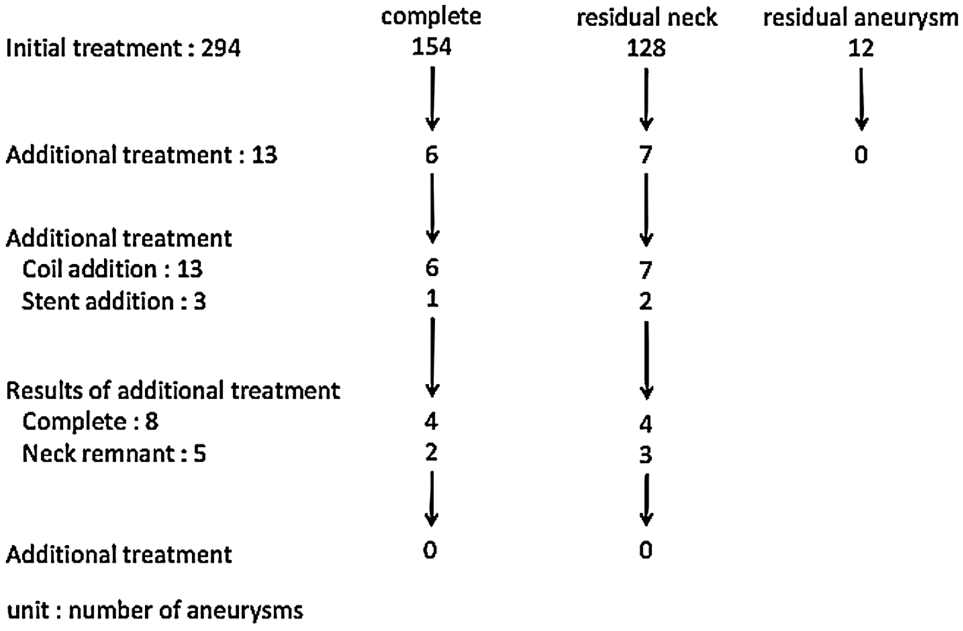

Fig. 1 Course of 13 cerebral aneurysms for which additional treatment was performed

in six aneurysms and "residual neck" in seven patients. Cerebral aneurysms were asymptomatic in 11 patients (12 cerebral aneurysms), but a consciousness disorder related to a partially thrombotic, recurrent giant cerebral aneurysm that compressing the brainstem at the BA end was observed in one patient. Additional treatment for the recurrent cerebral aneurysm was performed using the surgical procedures shown in **Table 2**. The level of surgical difficulty is higher for recurrent cerebral aneurysms than for initial cerebral aneurysms due to complications with stent insertion.

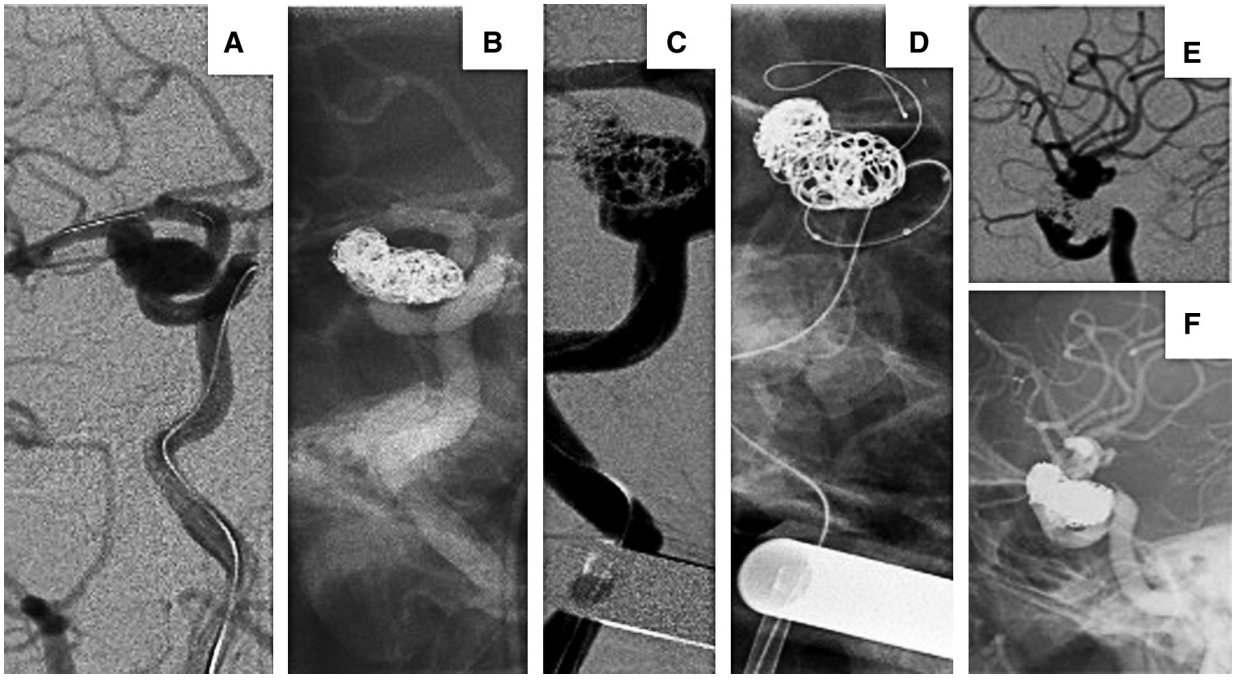

Fig. 2 (**A**) Pre-first treatment. (**B**) Post-first treatment; coil embolization with the double catheter technique after the Enterprise was placed. (**C**) Eight months after initial treatment. (**D**) Additional coil embolization with balloon neck remodeling. (**E** and **F**) Post-second treatment

Therefore, in many cases, it is difficult to adopt an adjunctive technique. As a result of this higher risk, seven aneurysms (54%) required additional treatment using a simple technique alone. It was possible to accomplish treatment without inserting a new stent in 10 cerebral aneurysms (77%); however, three (23%) required the addition of a stent. The results of treatment were evaluated as "complete" in eight aneurysms (62%) and "residual neck" in five patients (38%) (**Fig. 1**). There were no surgery-related complications. Postoperative follow-up has been continued for 10 patients (11 aneurysms). After a mean follow-up of 14.3 months, there has been no recanalization in any patient.

Representative case 1 (Fig. 2)

Case 1 is a 58-year-old female. For the initial treatment of an unruptured, large right ICA aneurysm at the level of C2 (A), an Enterprise (Johnson & Johnson, Raynham, Miami, Florida, USA) was inserted using a double catheter technique (B). After 8 months, cerebral angiography revealed intra-aneurysmal blood flow resumption (C), and additional treatment was conducted. During stent placement, balloon neck remodeling was adopted (D), and a microcatheter SL10 (Stryker, Kalamazoo, MI, USA) was guided into the aneurysm in combination with a CHIKAI14 (Asahi Intecc, Tokyo, Japan) using a trans-cell technique, leading to favorable embolization (E and F). There has been no recurrence during the 6-year follow-up after this additional treatment.

Representative case 2 (Fig. 3)

Case 2 is a 56-year-old female. Saccular and giant fusiform aneurysms of the left ICA (at the level of C5) were detected (A). Two LVIS BLUE stents (Microvention, Tustin, CA, USA) were used, and combined with a telescopic stent such that a portion overlapped. A microcatheter was inserted into the aneurysms using the jail method, and coil embolization was performed (B, C, D). After 15 months, cerebral angiography demonstrated blood inflow into the two aneurysms (E). Adopting a TACTICS (Technocrat Corporation, Kasugai, Aichi, Japan) as a distal access catheter (DAC), a HEADWAY 17 (Micro Vention, TERMO, Tustin, CA, USA) was guided into the aneurysms in combination with a CHIKAI14 (Asahi Intecc) using a trans-cell technique. At the neck of the saccular aneurysm, one LVIS BLUE stent had been inserted, facilitating microcatheter guiding using a trans-cell technique. However, at the neck of the fusiform aneurysm, two LVIS BLUE stents had been inserted, and as a result, microcatheter guiding using a trans-cell technique may have been difficult. However, a HEADWAY 17 was successfully guided in combination with a CHIKAI Black (Asahi Intecc), leading to favorable embolization (F, G). To our knowledge, no other study has

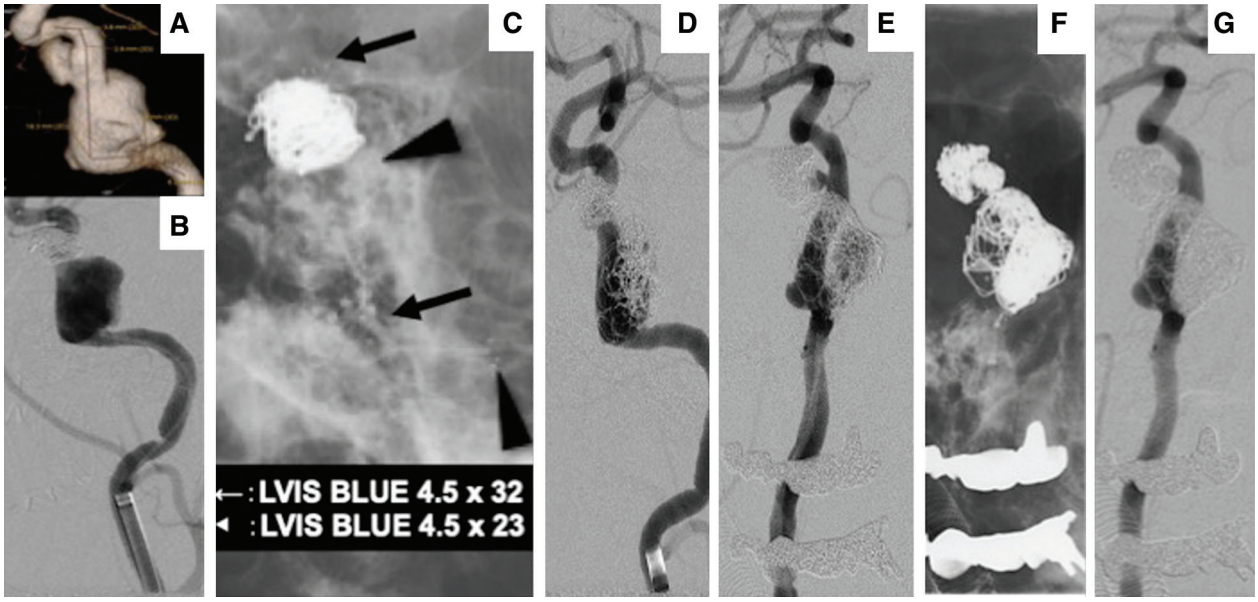

Fig. 3 (**A**) Pre-first treatment. (**B**) Coil embolization of saccular aneurysm. (**C**) A telescopic stent was placed and coil embolization was carried out using a jailed microcatheter. (**D**) Post-first treatment. (**E**) Fifteen months after initial treatment; recanalization of both aneurysms. (**F** and **G**) Post-second treatment

reported microcatheter guiding into aneurysms using a trans-cell technique under two overlapping LVIS BLUE stents as was possible in this case. There has been no recurrence during the 1-year follow-up after treatment.

Discussion

We performed additional treatment for patients with aneurysm recurrence after SAAE. Of 12 patients, 10 were followed-up at the outpatient clinic after surgery. There has been no further recurrence in any patient and the postoperative course has been favorable. When a stent is inserted in the initial treatment, additional treatment is difficult in many cases, and devices that are available for treatments are restricted. A previous study suggested that overlapping stents exhibited flow diversion effects; therefore, their use could be an effective treatment method.[5] However, the risk of thrombotic complications may increase with an increase in the number of stents, that is, metal abundance. The incidence of ischemic complications after treatment with overlapping stents was reported to be 3.2%, and that of intra-stent thrombus formation was 6.4%.[5] According to a computational fluid dynamics (CFD) study, overlapping stents may reduce wall shear stress or velocity.[6] However, stent-strut narrowing makes additional treatment using a trans-cell technique more difficult. In patients with VA dissecting aneurysms (VADAs) and for those in whom it is impossible to guide a microcatheter into the aneurysm using a trans-cell technique, it is necessary to overlap stents. However, simple methods of treatment should be attempted prior to using overlapping stents.

In this study, stent-free treatment was possible in 9 (75%) of the 12 patients. The stent strut of bladed stents is narrower than that of laser-cut stents, making microcatheter guiding using a trans-cell technique more difficult. However, in this study, microcatheter guiding using a trans-cell technique was possible even in the presence of two overlapping bladed stents. When guiding a microcatheter into an aneurysm using a trans-cell technique, the physician must provide support to guide the microcatheter carefully. As DACs, a TACTICS (Technocrat Corporation) and 4.2-Fr FUBUKI (Asahi Intecc, Tokyo, Japan) may be useful.[7,8] When using a DAC, a coaxial, thick guiding catheter is necessary, making operations complex. However, this may improve access to cerebral aneurysms as well as the stability and operability of microcatheters. Therefore, for additional treatment, it is important to guide a DAC to an area adjacent to a target cerebral aneurysm.

Balloon neck remodeling may be an effective treatment method for stent insertion if the size of the balloon or properties of different balloons are considered.

Of the 13 aneurysms, three (23%) were treated using overlapping stents, and the postoperative course has been favorable without recurrence. In the future, ongoing follow-up

of these patients is necessary to provide long-term data of recurrence. In Japan, Pipelines (Medtronic, Irvine, USA) are indicated for large (maximum aneurysmal diameter: 10–25 mm) or giant (maximum aneurysmal diameter: >25 mm), wide-neck (neck length: ≥4 mm) intracranial aneurysms involving the petrous part to superior hypophysial region of the ICA. These cannot be used in patients who have had stent-inserted treatments. Our literature review included a study which reported favorable results when using a Pipeline in patients with posterior circulation aneurysms, dissecting aneurysms,[9] or blood-blister-like aneurysms.[10] However, no study has reported the use of a Pipeline in patients with recurrence after stenting. An overlapping flow diverter may improve the results of treatment, although the level of technical difficulty in using this device is greater.

In 53% of our patients requiring additional treatment, large or giant aneurysms were present. The size of the aneurysm may be associated with recurrence. Wang et al. found that the recurrence rate after stent-assisted coil embolization was lower than after coil embolization in patients with large or giant cerebral aneurysms. In addition, the recurrence rate increased with the aneurysmal size.[11] Furthermore, the most frequent sites of recurrent aneurysms include the ICA and posterior circulation (VA, BA). Recurrence may be associated with cerebral blood flow or dissecting lesions. In this study, the 12 patients had ICA, BA, or VA (3/3: VADA) aneurysms. The dome/neck ratio was 1.4, but there was no significant difference in comparison with patients who did not require additional treatment. However, the aneurysmal height was slightly lower in those requiring additional treatment.

Cases in which recurrence of aneurysms after SAAE require treatment are rare (1.9%–4.1%). In all 12 patients, satisfactory treatment led to favorable results. An ideal approach for the management of these patients is for clinicians to perform initial treatment with the intention of preventing recurrence. In order to increase treatment options for patients with recurrence, further clinical studies and case reports should be completed.

Conclusion

In this study, we investigated the incidence of aneurysm recurrence in patients who had previously received SAAE as well as additional treatments that they may have required. Our results, based on postoperative data and observations, were favorable for no further aneurysm recurrence after additional treatments.

Acknowledgment

We would like to thank Editage (www.editage.com) for English language editing.

Disclosure Statement

We declare no conflict of interest.

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