Acta Neurochirurgica (2024) 166:216
https://doi.org/10.1007/s00701-024-06117-8

ORIGINAL ARTICLE

Safety and efficacy of stent-assisted coil embolization with periprocedural dual antiplatelet therapy for the treatment of acutely ruptured intracranial aneurysms

In-Hyoung Lee[1] · Sung-Kon Ha[1] · Dong-Jun Lim[1] · Jong-Il Choi[1]

Received: 14 January 2024 / Accepted: 4 May 2024

Abstract

Purpose Despite growing evidence for the effectiveness of stent-assisted coil embolization (SAC) in treating acutely ruptured aneurysms, the safety of stent placement in acute phase remains controversial because of concerns for stent-induced thromboembolism and hemorrhagic events attributable to the necessity of antiplatelet therapy. Therefore, we investigated the safety and efficacy of SAC with periprocedural dual antiplatelet therapy (DAPT) compared with the coiling-only technique to determine whether it is a promising treatment strategy for ruptured aneurysms.

Methods We retrospectively evaluated 203 enrolled patients with acutely ruptured aneurysms, categorizing them into two groups: SAC and coiling-only groups. Comparative analyses between the two groups regarding angiographic results, clinical outcomes, and procedure-related complications were performed. A subgroup analysis of procedural complications was conducted on patients who did not receive chronic antithrombotic medications to alleviate their influence before hospitalization.

Results 130 (64.0%) patients were treated using the coiling-only technique, whereas 73 (36.0%) underwent SAC. There was a trend to a higher complete obliteration rate ($p=0.061$) and significantly lower recanalization rate ($p=0.030$) at angiographic follow-up in the SAC group compared to the coiling-only group. Postprocedural cerebral infarction occurred less frequently in the SAC group (8.2%) than in the coiling-only group (17.7%), showing a significant difference ($p=0.044$). Although the ventriculostomy-related hemorrhage rate was significantly higher in the SAC group than in the coiling-only group (26.2% *vs.* 9.3%, $p=0.031$), the incidence of symptomatic ventriculostomy-related hemorrhage was comparable. Subgroup analysis excluding patients receiving chronic antithrombotic medications showed similar results.

Conclusion SAC with periprocedural DAPT could be a safe and effective treatment strategy for acutely ruptured aneurysms. Moreover, it might have a protective effect on postprocedural cerebral infarction without increasing the risk of symptomatic hemorrhagic complications.

Keywords Cerebral aneurysm · Dual antiplatelet therapy · Coil · Stent · Subarachnoid hemorrhage

Introduction

Stent-assisted coil embolization (SAC) for treating unruptured intracranial aneurysms with unsuitable configuration for conventional coiling has been adopted as a safe and effective therapeutic strategy and is extensively used in the endovascular era [14, 37]. Moreover, there is growing evidence for the effectiveness of the SAC technique with a relatively low recurrence rate, even in patients with acutely ruptured intracranial aneurysms [36, 39, 41]. Stent application improves aneurysm occlusion by preventing coil protrusion into the parent artery and facilitating delayed aneurysmal thrombosis caused by the diminishing intra-aneurysmal flow [34]. However, the safety of stent placement in the acute phase remains controversial despite several recent studies showing comparable results regarding the risk of periprocedural complications of SAC, compared with that of the coiling-only technique [4, 25, 36, 38, 41].

The primary concerns for using the SAC technique in acutely ruptured aneurysms include stent-related thromboembolic complications (TECs) and hemorrhagic events

✉ Jong-Il Choi
thlthd@korea.ac.kr

[1] Department of Neurosurgery, Korea University Ansan Hospital, Korea University College of Medicine, Gyeonggi-Do, Korea

Published online: 15 May 2024

attributable to the necessity of periprocedural antiplatelet therapy [4, 25, 32]. Limited premedication of antiplatelet agents and the complexity of the procedure may elevate the risk of thromboembolism leading to cerebral infarction, a significant cause of procedure-related morbidity [16]. Conversely, using antiplatelet agents to mitigate TECs raises fear about rebleeding and additional procedure-related hemorrhagic events during the acute phase. Therefore, an assessment of the potential benefits and harms of SAC requiring antiplatelet therapy is essential to determine whether it is a promising therapeutic option in treating acutely ruptured aneurysms.

The primary goal of the current investigation is to establish the safety and efficacy of SAC with periprocedural dual antiplatelet therapy (DAPT: aspirin and clopidogrel) compared with that of the coiling-only technique for treating acutely ruptured aneurysms. We hypothesized that the angiographic results of the SAC group would be better than those of the coiling-only group, with no significant difference in procedure-related complications.

Methods and materials

Study design

A total of 240 patients with acutely ruptured intracranial aneurysms who were treated by endovascular procedure in two institutions from March 2017 to December 2021 were retrospectively reviewed. All ruptured cerebral aneurysms were confirmed by computed tomography (CT) scan or magnetic resonance image (MRI). The following cases were not included in the analysis: (1) dissecting, infectious, and blister-like aneurysms; (2) aneurysms with other vascular diseases (e.g., arteriovenous malformation and moyamoya disease); (3) aneurysms treated by parent vessel occlusion; (4) staged stent placement; (5) multiple aneurysms, but failed to identify which aneurysm had ruptured; and (6) recanalized aneurysm.

The patient selection process is detailed in Fig. 1. A total of 203 patients have satisfied our inclusion criteria and were included in the current study. Patient demographics on sex, age, comorbidities, and history of antithrombotic medications were documented. Admission Hunt and Hess grade, modified Fisher grade before treatment, aneurysm characteristics (location, maximal diameter, neck size, and dome-to-neck ratio), type of procedure, and time interval between dual antiplatelet loading and stent placement in the SAC group were reviewed from electronic medical records and radiographic data. Ethical approval was obtained from the Institutional Review Board of each participating institution, and the need for informed consent was waived due to the retrospective nature of the study.

Endovascular procedure and medical treatment

In all patients, coiling procedures were performed in the biplane neuro-angiography suite under general anesthesia through transfemoral access. Through flushing lines, systemic heparinization was administered during the procedure to sustain the activated clotting time at least two times at baseline. Additional heparin (50 IU/kg) was administered as an intravenous (IV) bolus injection after adequate protection of the ruptured aneurysm sac to reduce the risk of aneurysmal rebleeding.

After diagnostic digital subtraction angiography (DSA) and 3D rotational angiography were performed, an appropriate therapeutic strategy (simple coiling or SAC) was adopted according to the configuration and geometry of the aneurysms and the origin of the branching vessels. The SAC was generally selected when the aneurysm morphology was unfavorable for simple coiling (e.g., wide-necked aneurysm; neck size >4 mm or dome-to-neck ratio <2), or coiling alone could not guarantee a satisfactory treatment result. It was also considered as a rescue technique when coils protruded into the parent vessel. Flow-diverting stents for treating ruptured aneurysms were not allowed by the insurance system in our country. When the use of a stent was decided, patients were immediately administered a loading dose of 300 mg aspirin and 300 mg clopidogrel either orally or via a nasogastric tube. After the procedure, dual antiplatelet (100 mg aspirin and 75 mg clopidogrel) medication was maintained for at least 3 months.

The majority of the SAC procedure was performed using the jailing technique; however, in some cases, a trans-strut technique was used. The following self-expandable stents were used in SACprocedures: Neuroform Atlas ($n=50$; Stryker Neurovascular), Enterprise ($n=12$; Codman Neurovascular), and Solitaire AB ($n=11$; Covidien). All aneurysm embolizations were conducted using various detachable platinum coils, according to the attending interventional neurosurgeon's discretion.

Angiographic evaluation and clinical assessment

The degree of immediate aneurysm occlusion was assessed on the final DSA and classified using the Raymond-Roy scale [30]. Angiographic follow-up results were determined by comparing DSA 1 year after endovascular treatment with the immediate occlusion degree and categorized into three types as follows: 1) complete obliteration, no contrast filling within the aneurysm; 2) stability, unchanged or decreased contrast filling within the aneurysm; and 3) recanalization, increased contrast filling within the aneurysm sac. Angiographic follow-up was

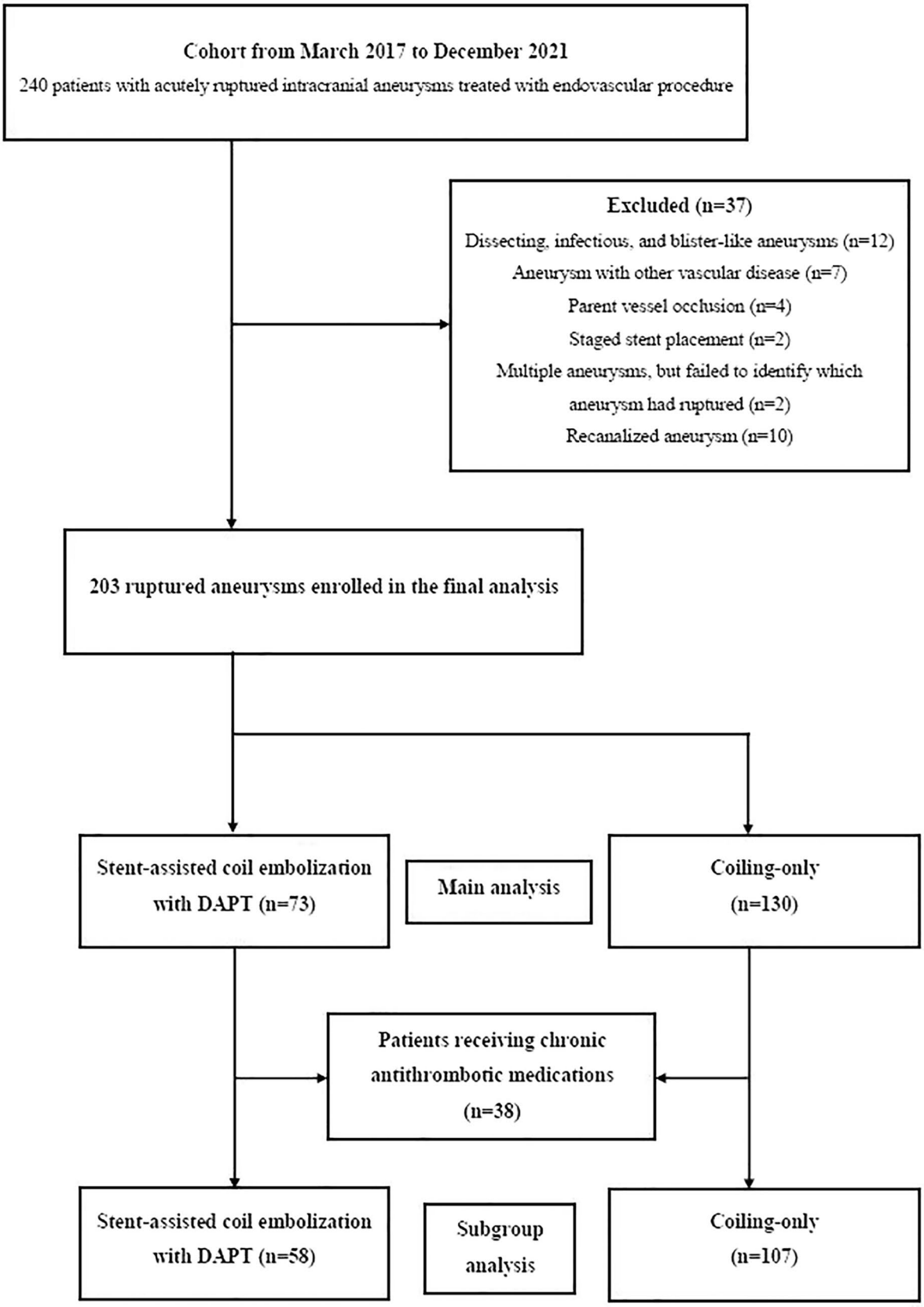

Fig. 1 Flowchart of patient enrollment. DAPT, dual antiplatelet therapy

conducted earlier when the morphology of the implanted coil mass had undergone visible change suggestive of recanalization on plain skull radiographs obtained within the follow-up period.

Every patient underwent an initial clinical follow-up assessment at the time of discharge, and follow-up visits for surviving patients were scheduled at 3, 6, and 12 months. Clinical outcomes were assessed by interventional neurosurgeons using the modified Rankin Scale (mRS) score. Favorable functional outcomes were defined as mRS 0–2, whereas unfavorable outcomes were defined as mRS ≥ 3.

Procedure-related complications

All complications related to the procedure that occurred during the perioperative period were recorded. Intraprocedural complications such as aneurysm rupture and thrombosis were documented based on the angiographic evidence during the procedure. Postprocedural complications, including aneurysm rebleeding, cerebral infarction, and vasospasm, were assessed on appropriate brain imaging (CT or MRI) performed in cases where the patient's clinical condition deteriorated after the procedure. Postprocedural cerebral infarction was defined as the presence of diffusion restriction in diffusion-weighted MRI or a new hypodense lesion noted on CT scan, accompanied by acute neurologic deficits casually related to the cerebral infarction (Fig. 2) [22]. Small punctate ischemic lesions detected on diffusion-weighted MRI were excluded, because these areas were likely the result of tiny air emboli or thrombi unintentionally introduced during the coiling procedure [24]. Parenchymal hypodensity that resulted from intracerebral hemorrhage or ventriculostomy was not regarded as cerebral infarction. Clinical vasospasm was defined as significant development of neurological deterioration combined with angiographic evidence on DSA [24, 33].

In patients with hydrocephalus or increased intracranial pressure treated by external ventricular drainage (EVD) or ventriculoperitoneal shunt, ventriculostomy-related hemorrhage, defined as occurring along the catheter tract, was evaluated on the subsequent postoperative follow-up non-contrast CT. Ventriculostomy-related hemorrhage was classified as symptomatic if it required additional surgical intervention or was associated with neurological deterioration (Fig. 3) [15].

Statistical analysis

All data are presented as mean $\pm$ standard deviation or median with interquartile range for continuous variables and as a frequency for categorical variables, where appropriate. Comparative analyses between SAC and coiling-only groups regarding baseline characteristics, clinical variables, angiographic results, clinical outcomes, and procedural complications were performed. A subgroup analysis of procedural complications was conducted on patients who were not prescribed chronic antiplatelet or anticoagulation medications to clarify the risks and benefits of periprocedural dual antiplatelet administration. Student's t-test or Mann–Whitney U test was used to analyze continuous variables. Categorical variables were analyzed using the chi-squared test or Fisher's exact test. All statistical analyses were conducted using SPSS 25.0 software (IBM Corp., Armonk, NY, USA). Variables with a p value < 0.05 were considered statistically significant.

Results

Patient and aneurysm characteristics

During the study period, the endovascular procedure was performed to treat 240 patients with ruptured aneurysms.

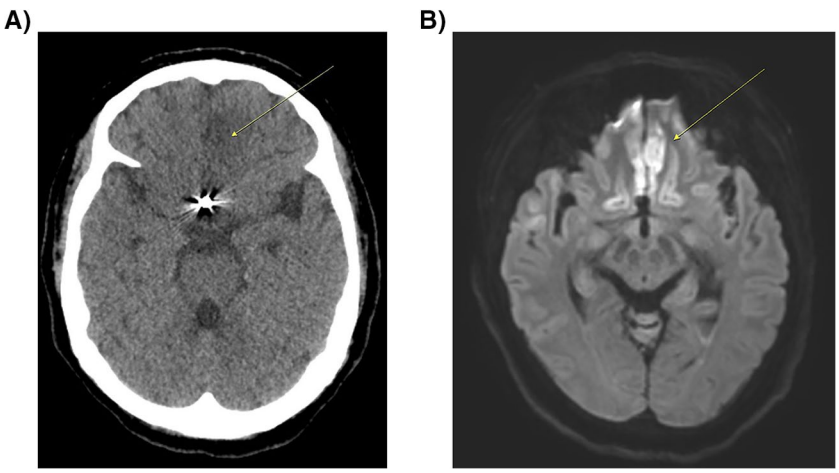

Fig. 2 An example of cerebral infarction after endovascular coiling demonstrating hypodense lesions noted on CT (**A**) and the presence of diffusion restriction on diffusion-weighted MRI (**B**). CT, computed tomography; MRI, magnetic resonance image

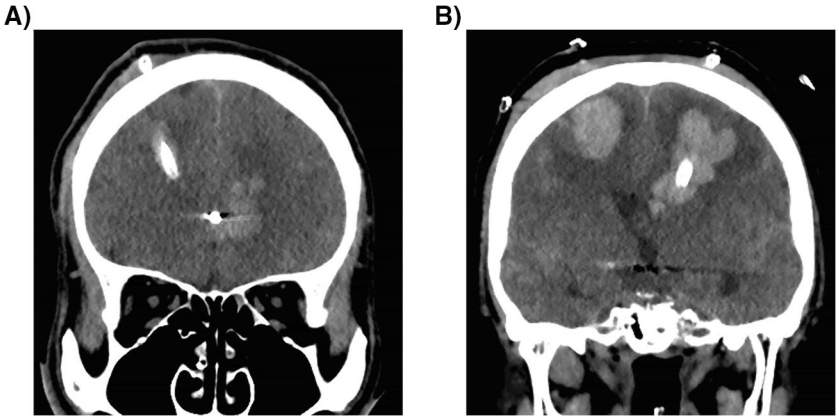

Fig. 3 Representative images of asymptomatic ventriculostomy-related hemorrhage (**A**) and symptomatic ventriculostomy-related hemorrhage (**B**) on brain CT scans. (**A**) Asymptomatic ventriculostomy-related hemorrhage occurred after placing an external ventricular catheter in the patient who underwent SAC for an acutely ruptured aneurysm at the left anterior cerebral artery A2-3 junction. (**B**) Bilateral symptomatic ventriculostomy-related hemorrhage was observed following subsequent ventricular catheter exchange after conventional coiling for the acutely ruptured aneurysm at the anterior communicating artery. The patient developed a new neurological deficit: motor aphasia. CT, computed tomography; SAC, stent-assisted coil embolization

Of them, 203 consecutive patients with 203 ruptured aneurysms met the inclusion criteria and were enrolled. Of these aneurysms, 130 (64.0%) were treated using the coiling-only technique, while 73 (36.0%) were treated with SAC (Fig. 1). Table 1 summarizes the differences in patient and aneurysm characteristics when comparing the two groups. No significant differences were found in both groups, except for the aneurysm profile. The SAC group had a wider neck diameter (4.9 ± 2.5 mm *vs.* 3.2 ± 1.6 mm, $p < 0.001$) and lower dome-to-neck ratio (1.1 ± 0.1 *vs.* 1.7 ± 0.2, $p < 0.001$) than that of the coiling-only group.

Angiographic results and clinical outcomes

The angiographic results and clinical outcomes are displayed in Table 2. No significant difference was found in the immediate aneurysm occlusion degree classified using the Raymond-Roy scale between the two groups. A total of 173 (85.2%) patients underwent 1-year angiographic follow-up, including 64 (87.7%) patients in the SAC group and 109 (83.8%) in the coiling-only group. The angiographic follow-up revealed differences between the two groups, with a trend toward a higher complete obliteration rate ($p = 0.061$) and significantly lower recanalization rate ($p = 0.030$) in the SAC group.

At discharge, 57 patients (78.1%) in the SAC group and 90 patients (69.2%) in the coiling-only group achieved favorable outcomes, which were comparable while it trended toward significance ($p = 0.165$). 183 patients who survived at discharge underwent clinical follow-up for at least 12 months. The Clinical outcomes at 12 months were comparable in both groups ($p = 0.353$).

Perioperative procedure-related complications

Intra-/postprocedural complications, except for cerebral infarction, were comparable between the SAC and coiling-only groups. Cerebral infarction occurred in six patients (8.2%) in the SAC group and in 23 patients (17.7%) in the coiling-only group, representing a significant difference ($p = 0.044$). For surgery-related complications, we compared the occurrence of ventriculostomy-related hemorrhage and symptomatic ventriculostomy-related hemorrhage between the two groups. Of all patients, 58 underwent 117 ventriculostomies (42 in the SAC group and 75 in the coiling-only group). The rate of ventriculostomy-related hemorrhage was significantly higher in the SAC group than in the coiling-only group (26.2% *vs.* 9.3%, $p = 0.031$). However, we noted that the rates of symptomatic ventriculostomy-related hemorrhage were comparable ($p = 0.926$) (Table 3).

Subgroup comparison analysis of perioperative procedure-related complications was additionally performed between SAC and coiling-only groups on patients who were not administered chronic antiplatelet or anticoagulation therapy. Similar to the total cohort analysis, cerebral infarction occurred more frequently in the coiling-only group ($p = 0.042$). Also, the rate of symptomatic ventriculostomy-related hemorrhage was comparable between the two groups, although ventriculostomy-related hemorrhage occurred more frequently in the SAC group ($p = 0.025$) (Table 4).

Table 1 Patient and aneurysm characteristics

	SAC (n = 73)	Coiling-only (n = 130)	*p*-value
Male	26 (35.6)	46 (35.4)	0.974
Age, year, mean (SD)	55.8 ± 13.8	56.2 ± 12.5	0.816
Medical history			
Hypertension	39 (53.4)	69 (53.1)	0.962
Diabetes mellitus	9 (12.3)	17 (13.1)	0.879
Coronary heart disease	8 (11.0)	16 (12.3)	0.776
Smoking history	6 (8.2)	11 (8.5)	0.953
Antiplatelet prior to hospitalization	11 (15.1)	16 (12.3)	0.581
Anticoagulant prior to hospitalization	4 (5.5)	8 (6.2)	0.846
Hunt-Hess grade			
I	3 (4.1)	6 (4.6)	0.867
II	39 (53.4)	65 (50.0)	0.641
III	13 (17.8)	26 (20.0)	0.705
IV	15 (20.5)	26 (20.0)	0.926
V	3 (4.1)	7 (5.4)	0.689
Modified Fisher grade			
1	11 (15.1)	18 (13.8)	0.812
2	29 (39.7)	48 (36.9)	0.695
3	23 (31.5)	42 (32.3)	0.907
4	10 (13.7)	22 (16.9)	0.547
Aneurysm location			
ACoA	17 (23.3)	36 (27.7)	0.495
PCoA	25 (34.2)	43 (33.1)	0.866
MCA	12 (16.4)	17 (13.1)	0.514
ICA	8 (11.0)	14 (10.8)	0.967
ACA	3 (4.1)	5 (3.8)	0.927
PC	8 (11.0)	15 (11.6)	0.901
Aneurysm profile, mean (SD)			
Aneurysm diameter, mm	5.4 ± 2.7	5.3 ± 2.6	0.814
Neck diameter, mm	4.9 ± 2.5	3.2 ± 1.6	**< 0.001***
Dome-to-neck ratio	1.1 ± 0.1	1.7 ± 0.2	**< 0.001***
Time interval between dual antiplatelet loading and stent placement	110.7 ± 48.0	N/A	

Data are presented as numbers (percentages) unless otherwise indicated. *Statistically significant

SAC, stent-assisted coil embolization; SD, standard deviation; IQR, interquartile range; ACoA, anterior communicating artery; PCoA, posterior communicating artery; MCA, middle cerebral artery; ICA, internal carotid artery; ACA, anterior cerebral artery; PC, posterior circulation

Discussion

The present study indicated that SAC significantly reduces the recanalization rate and might improve the progressive complete obliteration rate compared to the coiling-only technique in treating acutely ruptured aneurysms. In terms of safety, SAC was associated with a higher occurrence of ventriculostomy-related hemorrhage than the coiling-only technique. This difference may be attributed to the requirements of periprocedural antiplatelet medication; however, we found that the rates of symptomatic ventriculostomy-related hemorrhage were comparable. In addition, contrary to concerns about stent-related TECs, postprocedural cerebral infarction occurred more frequently in the coiling-only group. These results suggest that (1) SAC with periprocedural DAPT is a safe and effective therapeutic option for treating acutely ruptured aneurysms compared to the coiling-only technique, and (2) periprocedural dual antiplatelets routinely administered to patients using stents are potentially efficacious in reducing the risk of postprocedural cerebral infarction.

Complete coil embolization in wide-necked aneurysm cases is technically challenging, as unstable framing coils tend to prolapse into the parent artery, potentially leading to migration or thrombus formation. Placing a stent across

Table 2 Angiographic results and clinical outcomes

	SAC ($n=73$)	Coiling-only ($n=130$)	p-value
Immediate aneurysm occlusion			
Raymond scale I	46 (63.0)	76 (58.5)	0.527
Raymond scale II	25 (34.2)	50 (38.5)	0.553
Raymond scale III	2 (2.7)	4 (3.1)	0.892
Follow-up angiographic results**			
Complete obliteration	47/64 (73.4)	65/109 (59.6)	0.061
Stability	10/64 (15.6)	18/109 (16.5)	0.879
Recanalization	7/64 (10.9)	26/109 (23.9)	**0.030***
Clinical outcome at discharge			
Favorable outcome (mRS score 0–2)	57 (78.1)	90 (69.2)	0.165
mRS score 3–6	16 (21.9)	40 (30.8)	
Clinical outcome at 12 months***			
Favorable outcome (mRS score 0–2)	61/66 (92.4)	103/117 (88.0)	0.353
mRS score 3–6	5/66 (7.6)	14/117 (12.0)	

Data are presented as numbers (percentages) unless otherwise indicated. *Statistically significant. **Angiographic follow-up was available for 64 patients (87.7%) in the SAC group and 109 patients (83.8%) in the coiling-only group. ***Excluding patients who died at discharge

SAC, stent-assisted coil embolization; mRS, modified Rankin Scale

Table 3 Perioperative procedure-related complications

	SAC (n = 73)	Coiling-only (n = 130)	p-value
Intraprocedural complications			
Intraprocedural rupture	2 (2.7)	3 (2.3)	0.850
Intraprocedural thrombosis	3 (4.1)	4 (3.1)	0.701
Postprocedural complications			
Aneurysm rebleeding	1 (1.4)	2 (1.5)	0.924
Cerebral infarction	6 (8.2)	23 (17.7)	**0.044***
Clinical vasospasm	4 (5.5)	11 (8.5)	0.438
Surgery-related complications			
Patients underwent ventriculostomy	21 (28.8)	37 (28.5)	0.963
No. of ventriculostomies per patient, mean (SD)	2.0 ± 0.9	2.0 ± 1.1	0.924
Ventriculostomy-related hemorrhage**	11/42 (26.2)	7/75 (9.3)	**0.031***
Symptomatic ventriculostomy-related hemorrhage**	1/42 (2.4)	2/75 (2.7)	0.926

Data are presented as numbers (percentages) unless otherwise indicated. *Statistically significant. **Total number of ventriculostomy placements was 42 in the SAC group and 75 in the coiling-only group

SAC, stent-assisted coil embolization; SD, standard deviation

the aneurysmal neck provides mechanical protection against coil protrusion and facilitates easier coil placement into the aneurysmal sac. This consequently allows increased aneurysm packing density, potentially reducing the recanalization rate, as previously reported that recurrence after coil embolization is associated with incomplete occlusion [37]. However, consistent with several prior studies and meta-analysis, the present study showed no significant difference in the immediate aneurysm occlusion degree between SAC and conventional coiling [36, 37, 39, 41]. Presumably, this might be because the stent-assisted technique was typically adopted when the aneurysm morphology was unfavorable with a wide neck or low dome-to-neck ratio, potentially offsetting the mechanical advantage of a stent in increasing the aneurysm packing density.

The angiographic key results of this study align with the results of previous studies, which reported that SAC for treating acutely ruptured aneurysms achieved better complete occlusion at follow-up and lower recanalization than the coiling-only technique [36, 38, 41]. In a previous retrospective analysis conducted on 109 patients with initially incompletely coiled aneurysm, stent use significantly

Table 4 Subgroup analysis of procedure-related complications in patients who did not receive chronic antithrombotic therapy

	SAC ($n=58$)	Coiling-only ($n=107$)	p-value
Intraprocedural complications			
Intraprocedural rupture	2 (3.4)	2 (1.9)	0.532
Intraprocedural thrombosis	2 (3.4)	4 (3.7)	0.925
Postprocedural complications			
Aneurysm rebleeding	1 (1.7)	2 (1.9)	0.947
Cerebral infarction	5 (8.6)	21 (19.6)	**0.042***
Clinical vasospasm	4 (6.9)	11 (10.3)	0.473
Surgery-related complications			
Patients who underwent ventriculostomy	17 (29.3)	29 (27.1)	0.764
No. of ventriculostomies per patient, mean (SD)	2.0 ± 1.0	2.1 ± 1.1	0.754
Ventriculostomy-related hemorrhage**	8/34 (23.5)	4/61 (6.6)	**0.025***
Symptomatic ventriculostomy-related hemorrhage**	1/34 (2.9)	2/61 (3.3)	0.896

Data are presented as numbers (percentages) unless otherwise indicated. *Statistically significant. **Total number of ventriculostomy placements was 34 in the SAC group and 61 in the coiling-only group

SAC, stent-assisted coil embolization; SD, standard deviation

predicted delayed occlusion, with a progressive occlusion rate of approximately 18.5 times higher in the stenting group than in the non-stenting group [20]. A recent meta-analysis reported a significantly lower rate of recanalization rate at follow-up of less than one-third in the SAC group compared to the non- SAC group (4.8% *vs.* 16.6%) [39]. More recently, a retrospective study reported that the recanalization rate decreased by more than half in the SAC group, compared with that in the coiling-only group (10.9% *vs.* 24.8%) [38]. In summary, the angiographic advantage of stent placement was predominant at follow-up angiography rather than immediately. This might be explained by the hemodynamic and biological effects of stenting on coil embolization. Theoretically, placed stents can serve as a scaffold for vascular endothelialization and have a flow diversion effect, reducing intra-aneurysmal flow [20, 28]. Flow diversion can result in stagnant blood, leading to progressive aneurysm thrombosis and aiding in delayed occlusion of the aneurysmal neck [20, 34]. Therefore, the flow remodeling effect may induce delayed occlusion of the coiled aneurysm in patients using a stent-assisted technique, even if incomplete occlusion was initially noted.

Safety evaluation is mandatory when adopting the stent placement as a treatment option for managing acutely ruptured aneurysms. If additional neurosurgical procedures (e.g., EVD) are required, SAC has been widely believed to potentially increase hemorrhagic complications due to the necessity of periprocedural antiplatelet medication [4, 9, 25]. However, it is noteworthy that most hemorrhages were small and asymptomatic. Consistent with the present study, several studies have shown comparable rates of clinically relevant hemorrhagic complications regardless of the endovascular treatment technique [29, 38]. According to a previous large-cohort analysis of 443 patients treated by endovascular treatment and EVD placement for acutely ruptured aneurysms, those who received periprocedural DAPT were at a higher risk of EVD-related hemorrhage, but symptomatic hemorrhage rates were comparable [15]. A recent meta-analysis reported similar results: periprocedural administration of antiplatelet agents in treating ruptured aneurysm increased the risk of ventriculostomy-related hemorrhage, but it was mostly asymptomatic and clinically irrelevant [5].

Stent-related TECs were also a significant concern. Several early studies demonstrated increased TECs in patients using SAC compared with coiling-only [3, 25]. This is generally attributed to the thrombogenicity of a stent, including stent-related endothelial damage and platelet aggregation on the stent surface [28, 40]. However, a recent systemic review reported that stent use does not increase the risk of TECs [4]. Recent retrospective studies have supported the above result, indicating that the stent-assisted coiling technique with proper antiplatelet administration effectively controls TECs [36, 38, 41]. Nevertheless, it should not be disregarded that the incidence of TECs may be affected and vary depending on the methods of antiplatelet administration [32]. The optimal antiplatelet medication for preventing stent-related TECs in acutely ruptured aneurysm remains controversial. A recent study has demonstrated that it occurred more frequently in the antiplatelet premedication-free SAC group in the acute phase of aneurysmal subarachnoid hemorrhage [8]. However, even among the interventional neurosurgeons who agreed to the antiplatelet premedication, the timing and dose were inconsistent [2, 9, 23, 36]. In the present study, the time interval between dual antiplatelet loading (300 mg aspirin and 300 mg clopidogrel) immediately after the decision to perform SAC and stent placement was 110.7 ± 48.0 min. The

time to onset of action of aspirin and clopidogrel was 60 min and 2 h, respectively [1, 27]. Considering these pharmacokinetics, the dual antiplatelet premedication protocol used in the current study might be beneficial to effectively control TECs. Moreover, the type of stents might contribute to the rate of TECs. In our results, using a stent was unrelated to the risk of intraprocedural thrombosis and postprocedural cerebral infarction. This could be because the Neuroform Atlas stent was used in majority of the cases in this study (50/73, 68.5%). The Atlas stent appears to be responsible for a lower rate of TECs than conventional stents, which are characterized by better vessel wall apposition, resulting in less exposure of the metal-covered surfaces to blood flow, thus reducing thrombus formation [11, 38].

Surprisingly, in our results, the SAC group receiving DAPT showed a significantly lower postprocedural cerebral infarction rate than the coiling-only group, suggesting that periprocedural DAPT is potentially efficacious in reducing it. The results from the subgroup analysis in patients who did not receive chronic antithrombotic medications might support this. The safety and effectiveness of antiplatelet use in patients with acutely ruptured aneurysms has been well documented in the literature [12, 21, 26]. This phenomenon might be elucidated by considering the coagulation and inflammation cascade, as previously detailed in the literature [24]. Endothelial disruption due to aneurysm rupture initiates a neuro-inflammatory cascade related to the release of inflammatory cytokines, platelet aggregation, and coagulation cascades, potentially resulting in the occurrence of secondary cerebral infarction [10, 17]. Antiplatelet agents have the potential to alleviate the devastating impacts of postprocedural cerebral infarction through their antiplatelet and anti-inflammatory actions. A previous retrospective study on 161 patients showed that the "SAC with DAPT group" had a significantly lower rate of delayed cerebral ischemia than the "coiling-only without DAPT group" [24]. However, another study reported that routine aspirin administration might decrease the risk of cerebral infarction; however, DAPT showed no additional benefit in reducing it [26]. This issue requires further investigation; there are no established guidelines on antiplatelet management and there is limited consensus regarding the proper timing, duration, and dosage of antiplatelet agents for the treatment of acutely ruptured aneurysms using SAC.

There are other considerations for optimizing the antiplatelets management strategy during SAC of acutely ruptured aneurysms. First, clopidogrel response variability and drug resistance were observed in some patients who adopted conventional DAPT [7]. Modification of the antiplatelet regimen, including adding cilostazol or altering clopidogrel with another thienopyridine (e.g. prasugrel or ticagrelor), have been used to reduce the TECs in clopidogrel non-responders for treating unruptured aneurysm [18, 19]. However, further investigation for tailored antiplatelet medication is warranted because there is a lack of evidence regarding the safety of using alternative antiplatelet agents in the acute phase. Additionally, the single aspirin therapy might be considered in clopidogrel non-responders based on previous studies reported that there is no additional benefit of clopidogrel on the risk of TECs [26, 31]. Second, IV antiplatelet agents enabling immediate and constant antiplatelet action might be a conceivable alternative to traditional DAPT for achieving a balance between TECs and hemorrhagic events [18]. A recent meta-analysis showed that the prophylactic administration of IV tirofiban during SAC of ruptured aneurysms did not increase post-procedural hemorrhage and was associated with lower rates of TECs compared with oral DAPT [35]. Cangrelor, a relatively new antiplatelet agent with immediate platelet inhibition ability, has recently emerged as a potential alternative in acute neurointervention. Its therapeutic efficacy and safety in the acute phase were reported in several retrospective studies [6, 13]. However, further studies are required to delineate the ideal antiplatelet therapy regimen because there is no consensus on optimal dose adjustment for IV antiplatelet agents.

Our results need to be interpreted with caution when generalizing. The major limitation of the present study is its retrospective non-randomized design, potentially inducing selection bias. The SAC group had a wider neck diameter and lower dome-to-neck ratio than the coiling-only group in our cohort. However, no statistically significant differences existed in the patient's clinical status (i.e., Modified Fisher grade, Hunt-Hess grade, and other demographics) between the two groups of our cohort. Moreover, it is inherently challenging to randomize patients to either SAC or coiling-only groups without considering the characteristics of the aneurysms. More meaningful results might be obtained if the randomized study could be conducted in groups with comparable aneurysm features. Additionally, because postprocedural diffusion-weighted MRI was not routinely performed at our institution, clinically silent cerebral infarctions may have been underestimated. Although the clinical significance of these infarctions remains uncertain, it is worth noting that periprocedural antiplatelet medication might reduce their occurrence, thus warranting further investigation. Another limitation is the lack of an antiplatelet medication response test, which has been shown to influence the development of ischemic stroke. Further investigations with a larger sample size are warranted to generalize our results.

Conclusions

The current study suggests that SAC with periprocedural DAPT could be a suitable treatment option for acutely ruptured intracranial aneurysms with comparable

procedure-related complications, improved progressive complete obliteration, and significant lower recanalization rate compared to those of the coiling-only technique. Moreover, the use of periprocedural DAPT might have an unintended protective effect on postprocedural cerebral infarction without an increased risk of symptomatic hemorrhagic complications.

Acknowledgements This study was supported by grants from Korea University Research Fund.

Author contributions In-Hyoung Lee: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing. Sung-Kon Ha: Project administration, Resources, Supervision, Validation. Dong-Jun Lim: Methodology, Resources, Supervision, Validation. Jong-Il Choi: Conceptualization, Data curation, Methodology, Project administration, Supervision, Validation, Writing – review & editing.

Funding This study was supported by grants from Korea University Research Fund.

Data availability The datasets generated during and / or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Competing interests The authors have no conflicts of interest to disclose.

Ethical approval The ethical committee of each participating institution approved the current study (IRB No. 2023AS0308, IRB No. HKS 2021–09-003) and conducted in accordance with the Declaration of Helsinki.

Consent to participate Due to a retrospective nature of it, the written informed consent was waived.

Consent to publish N/A.

References

1. Awtry EH, Loscalzo J (2000) Aspirin. Circulation 101:1206–1218
2. Bechan R, Sprengers M, Majoie C, Peluso J, Sluzewski M, Van Rooij W (2016) Stent-assisted coil embolization of intracranial aneurysms: complications in acutely ruptured versus unruptured aneurysms. Am J Neuroradiol 37:502–507
3. Bodily K, Cloft H, Lanzino G, Fiorella D, White P, Kallmes DF (2011) Stent-assisted coiling in acutely ruptured intracranial aneurysms: a qualitative, systematic review of the literature. Am J Neuroradiol 32:1232–1236
4. Bsat S, Bsat A, Tamim H, Chanbour H, Alomari SO, Houshiemy MNE, Moussalem C, Omeis I (2020) Safety of stent-assisted coiling for the treatment of wide-necked ruptured aneurysm: a systematic literature review and meta-analysis of prevalence. Interv Neuroradiol 26:547–556
5. Cagnazzo F, Di Carlo DT, Petrella G, Perrini P (2020) Ventriculostomy-related hemorrhage in patients on antiplatelet therapy for endovascular treatment of acutely ruptured intracranial aneurysms. A meta-analysis. Neurosurg Rev 43:397–406
6. Cagnazzo F, Radu RA, Derraz I, Lefevre PH, Dargazanli C, Machi P, Morganti R, Gascou G, Fendeleur J, Rapido F, Costalat V (2024) Efficacy and safety of low dose intravenous cangrelor in a consecutive cohort of patients undergoing neuroendovascular procedures. J Neurointerv Surg 16:88–93
7. Camargo L, Lima P, Janot K, Maldonado I (2021) Safety of oral P2Y12 inhibitors in interventional neuroradiology: current status and perspectives. Am J Neuroradiol 42:2119–2126
8. Choi HH, Cho YD, Han MH, Cho W-S, Kim JE, Lee JJ, An SJ, Mun JH, Yoo DH, Kang H-S (2018) Antiplatelet premedication-free stent-assisted coil embolization in acutely ruptured aneurysms. World Neurosurg 114:e1152–e1160
9. Chung J, Lim YC, Suh SH, ShiM YS, Kim YB, Joo J-Y, Kim B-s, Shin YS (2014) Stent-assisted coil embolization of ruptured wide-necked aneurysms in the acute period: incidence of and risk factors for periprocedural complications. J Neurosurg 121:4–11
10. Clarke JV, Suggs JM, Diwan D, Lee JV, Lipsey K, Vellimana AK, Zipfel GJ (2020) Microvascular platelet aggregation and thrombosis after subarachnoid hemorrhage: a review and synthesis. J Cereb Blood Flow Metab 40:1565–1575
11. Dong L, Wang J, Chen X, Zhang L, Zhao Z, Peng Q, Jin Z, Wu J, Lv M, Liu P (2022) Stent-assisted coiling using the Neuroform Atlas stent for treatment of aneurysms that recur after coil embolization. Front Neurol 13:967942
12. Edwards NJ, Jones WH, Sanzgiri A, Corona J, Dannenbaum M, Chen PR (2017) Antiplatelet therapy for the prevention of pericoiling thromboembolism in high-risk patients with ruptured intracranial aneurysms. J Neurosurg 127:1326–1332
13. Entezami P, Dalfino JC, Boulos AS, Yamamoto J, Holden DN, Field NC, Rock AK, Najera E, Paul AR (2023) Use of intravenous cangrelor in the treatment of ruptured and unruptured cerebral aneurysms: an updated single-center analysis and pooled analysis of current studies. J Neurointerv Surg 15:669–673
14. Feng M-t, Wen W-l, Feng Z-z, Fang Y-b, Liu J-m, Huang Q-h (2016) Endovascular embolization of intracranial aneurysms: to use stent (s) or not? Systematic review and meta-analysis. World Neurosurg 93:271–278
15. Hudson JS, Prout BS, Nagahama Y, Nakagawa D, Guerrero WR, Zanaty M, Chalouhi N, Jabbour P, Dandapat S, Allan L (2019) External ventricular drain and hemorrhage in aneurysmal subarachnoid hemorrhage patients on dual antiplatelet therapy: a retrospective cohort study. Neurosurgery 84:479–484
16. Imamura H, Sakai N, Satow T, Iihara K (2020) Factors related to adverse events during endovascular coil embolization for ruptured cerebral aneurysms. J Neurointerv Surg 12:605–609
17. Kanamada AS (2010) Connecting the early brain injury of aneurysmal subarachnoid hemorrhage to clinical practice. Turk Neurosurg 20:159–166
18. Kim KS, Fraser JF, Grupke S, Cook AM (2017) Management of antiplatelet therapy in patients undergoing neuroendovascular procedures. J Neurosurg 129:890–905
19. Koh JS, Hwang G, Park JC, Lee C-Y, Chung J, Lee S-W, Kwon H-J, Kim S-R, Kang D-H, Kwon SC (2023) Tailored antiplatelet therapy in stent assisted coiling for unruptured aneurysms: a nationwide registry study. J Neurointerv Surg 15:1095–1104
20. Lawson MF, Newman WC, Chi Y-Y, Mocco J, Hoh BL (2011) Stent-associated flow remodeling causes further occlusion of incompletely coiled aneurysms. Neurosurgery 69:598–604
21. Mees SD, van den Bergh WM, Algra A, Rinkel GJ (2007) Antiplatelet therapy for aneurysmal subarachnoid haemorrhage. Cochrane Database Syst Rev 4:CD006184
22. Mijiti M, Mijiti P, Axier A, Amuti M, Guohua Z, Xiaojiang C, Kadeer K, Xixian W, Geng D, Maimaitili A (2016) Incidence and predictors of angiographic vasospasm, symptomatic vasospasm and cerebral infarction in Chinese patients with aneurysmal subarachnoid hemorrhage. PLoS ONE 11:e0168657

23. Muto M, Giurazza F, Ambrosanio G, Vassallo P, Briganti F, Tecame M, Schena E, De Nicola M, Sgreccia A, Giannoni M (2017) Stent-assisted coiling in ruptured cerebral aneurysms: multi-center experience in acute phase. Radiol Med 122:43–52
24. Nagahama Y, Allan L, Nakagawa D, Zanaty M, Starke RM, Chalouhi N, Jabbour P, Brown RD, Derdeyn CP, Leira EC (2017) Dual antiplatelet therapy in aneurysmal subarachnoid hemorrhage: association with reduced risk of clinical vasospasm and delayed cerebral ischemia. J Neurosurg 129:702–710
25. Nishido H, Piotin M, Bartolini B, Pistocchi S, Redjem H, Blanc R (2014) Analysis of complications and recurrences of aneurysm coiling with special emphasis on the stent-assisted technique. Am J Neuroradiol 35:339–344
26. Oppong MD, Gembruch O, Pierscianek D, Köhrmann M, Kleinschnitz C, Deuschl C, Mönninghoff C, Kaier K, Forsting M, Sure U (2019) Post-treatment antiplatelet therapy reduces risk for delayed cerebral ischemia due to aneurysmal subarachnoid hemorrhage. Neurosurgery 85:827–833
27. Ospel J, Brouwer P, Dorn F, Arthur A, Jensen M, Nogueira R, Chapot R, Albuquerque F, Majoie C, Jayaraman M (2020) Antiplatelet management for stent-assisted coiling and flow diversion of ruptured intracranial aneurysms: a DELPHI consensus statement. Am J Neuroradiol 41:1856–1862
28. Phan K, Huo YR, Jia F, Phan S, Rao PJ, Mobbs RJ, Mortimer AM (2016) Meta-analysis of stent-assisted coiling versus coiling-only for the treatment of intracranial aneurysms. J Clin Neurosci 31:15–22
29. Roh H, Kim J, Bae H, Chong K, Kim JH, Suh S-i, Kwon T-H, Yoon W (2019) Comparison of stent-assisted and no-stent coil embolization for safety and effectiveness in the treatment of ruptured intracranial aneurysms. J Neurosurg 133:814–820
30. Roy D, Milot G, Raymond J (2001) Endovascular treatment of unruptured aneurysms. Stroke 32:1998–2004
31. Russo R, Bradac GB, Castellan L, Gallesio I, Garbossa D, Iannucci G, Mardighian D, Menozzi R, Pitrone A, Romano G (2021) Neuroform Atlas stent-assisted coiling of ruptured intracranial aneurysms: a multicenter study. J Neuroradiol 48:479–485
32. Ryu C-W, Park S, Shin H, Koh J (2015) Complications in stent-assisted endovascular therapy of ruptured intracranial aneurysms and relevance to antiplatelet administration: a systematic review. Am J Neuroradiol 36:1682–1688
33. Shimamura N, Naraoka M, Matsuda N, Katayama K, Kakuta K, Katagai T, Fujiwara N, Hasegawa S, Ohkuma H (2020) Use of preprocedural, multiple antiplatelet medications for coil embolization of ruptured cerebral aneurysm in the acute stage improved clinical outcome and reduced thromboembolic complications without hemorrhagic complications. World Neurosurg 133:e751–e756
34. Wanke I, Forsting M (2008) Stents for intracranial wide-necked aneurysms: more than mechanical protection. Neuroradiology 50:991–998
35. Xiang Y, Zhao H, Ding C, Chen H, Wang D, Liu A (2021) The Prophylactic Use of Tirofiban versus Oral Antiplatelet Medications in Stent-Assisted Coiling of Intracranial Aneurysms: A Meta-analysis. Am J Neuroradiol 42:713–719
36. Xue G, Zuo Q, Tang H, Zhang X, Duan G, Feng Z, Li Q, Yang P, Fang Y, Zhao K (2020) Comparison of low-profiled visualized intraluminal support stent-assisted coiling and coiling only for acutely ruptured intracranial aneurysms: safety and efficacy based on a propensity score-matched cohort study. Neurosurgery 87:584–591
37. Yang H, Sun Y, Jiang Y, Lv X, Zhao Y, Li Y, Liu A (2015) Comparison of stent-assisted coiling vs coiling alone in 563 intracranial aneurysms: safety and efficacy at a high-volume center. Neurosurgery 77:241–247
38. Yi HJ, Shin D-S, Kim B-T, Lee DH, Sung JH (2023) Comparison of neuroform Atlas stent-assisted coiling and coiling alone in ruptured intracranial aneurysms: a propensity score matching analysis. Neurosurgery 92:607–614
39. Zhang X, Zuo Q, Tang H, Xue G, Yang P, Zhao R, Li Q, Fang Y, Xu Y, Hong B (2019) Stent assisted coiling versus non-stent assisted coiling for the management of ruptured intracranial aneurysms: a meta-analysis and systematic review. J Neurointerv Surg 11:489–496
40. Zhao L, Lin P, Zhang Y, Huang X-Y, Li H-Y, Xia M-K, Huang X, Li Z, Zhou L-X, Tang X-P (2022) Effect of antiplatelet treatment on aneurysmal subarachnoid hemorrhage patients after endovascular treatment: a systematic review with meta-analysis. Neurosurg Rev 45:3523–3536
41. Zuo Q, Yang P, Lv N, Huang Q, Zhou Y, Zhang X, Duan G, Wu Y, Xu Y, Hong B (2018) Safety of coiling with stent placement for the treatment of ruptured wide-necked intracranial aneurysms: a contemporary cohort study in a high-volume center after improvement of skills and strategy. J Neurosurg 131:435–441