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Safety and efficacy of complete versus near-complete coiling in treatment of intracranial aneurysms



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A R T I C L E I N F O	A B S T R A C T
<i>Keywords:</i> Coil embolization Intracranial aneurysm Stent	<i>Objective:</i> This study aimed to evaluate the clinical and angiographic outcomes of aneurysms that were completely or near-completely embolized and ascertain whether complete embolization is important in the stent-assisted coiling (SAC) of intracranial aneurysms. <i>Methods:</i> This retrospective study enrolled 390 patients (417 aneurysms). Among them, complete (100%) or near-complete (>90%) angiographic obliteration of the aneurysms on immediate angiography was accomplished. Baseline characteristics, complications, angiography follow-up results, and clinical outcomes were analyzed. <i>Results:</i> Cumulative adverse events occurred in 30 patients (7.7%), including thromboembolic complications in 17 (4.4%), intraoperative rupture in 10 (2.6%), and others in 3 (0.8%). Statistical analyses revealed an increased intraprocedural rupture rate in the initial completely occluded aneurysms (5.6% compared with 1.0%). The incidence of cumulative adverse events was higher in patients with completely occlude aneurysms (11.1%) than in those with near-completely occluded aneurysms (5.5%). Angiography follow-up was available for 173 aneurysms. Aneurysm occlusion status at follow-up was correlated with stent placement ($p = 0.000$, odds ratio = 5.847), size ($p = 0.000$, odds ratio = 6.446 for tiny aneurysms; and $p = 0.001$, odds ratio = 5.616 for small aneurysms), and initial aneurysm occlusion status ($p = 0.001$, odds ratio = 3.436). Complete occlusion at follow-up was higher in the initial completel occlusion at follow-up was higher in the initial completely occluded aneurysms with SAC (100%) than in the initial completely occluded aneurysms with non-SAC (65.2%). <i>Conclusions</i> : Initial complete treatment may lead to higher complication rates and good clinical outcomes at follow-up.

Introduction

With advances in endovascular techniques, endovascular coil embolization of intracranial aneurysms has become a valid alternative to surgical clipping.^{1–3} Aneurysm recanalization is a major shortcoming of endovascular coiling techniques, as some aneurysms are incompletely embolized. Studies focusing on the outcomes of completely and near-completely coiled intracranial aneurysms are limited. Some scholars described that the use of stent-assisted technology for the treatment of aneurysms facilitates a higher coil packing density and more stable aneurysm neck sealing.^{4–8} Neurointerventionists wonder how densely to pack a stented aneurysm in daily practice. Here we conducted a retrospective single-center analysis of the short- and mid-term clinical and angiographic outcomes of completely or near-completely embolized aneurysms. We also aimed to ascertain whether complete embolization is important in stent-assisted coiling (SAC) of intracranial aneurysms.

Materials and methods

Patient characteristics

The study was approved by the local institutional review board and ethics committee. We retrospectively reviewed 451 patients who underwent endovascular treatment in our institution between July 2004 and June 2015, in whom a total of 481 intracranial aneurysms were intervened. Among them, complete (100%) or near-complete (>90%) angiographic obliteration of the aneurysms on immediate angiography was accomplished in 417 aneurysms (390 patients) (Fig. 1). The

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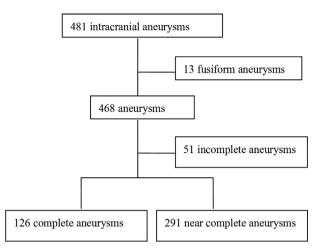


Fig. 1. Flowchart of the study population.

patients' clinical profiles and radiological data were collected and analyzed.

Pharmacologic therapy protocol and endovascular procedures

As to wide-neck aneurysms (neck > 4 mm and/or dome/neck ratio \leq 2), a stent-assisted technique (Enterprise stent, Codman Neurovascular, Raynham, MA, USA; Neuroform stent, Stryker, Kalamazoo, MI, USA; Solitaire stent, eV3, Plymouth, MN, USA) was required. Patients were premedicated with 100 mg of aspirin and a loading dose of 75 mg of clopidogrel for 2–3 days before the stent-assisted embolization. For the stent used without premedication, 300 mg of clopidogrel and 300 mg of aspirin were administered via a naso-orogastric tube.

All of the coil embolization surgeries were performed under general anesthesia. A bolus of 3000 IU of heparin was administered after femoral arterial sheath placement, while intermittent boluses of 1000 IU/h were subsequently administered.

Working projections that provided the best view of the aneurysm neck were selected on the basis of 3-dimensional rotational angiography. Various types of bare platinum coils were used according to physician preference. A stent-assisted technique was required for treating wideneck aneurysms.

Initial and follow-up occlusion status was classified as complete (100%), near-complete (90–99%), or incomplete (<90%). The angiography results were independently assessed by 2 experienced neuro-interventionists. Disagreements were resolved by consensus.

Follow-up data

During the follow-up period, an angiography evaluation with digital subtraction angiography was performed at 3–6 months after endovascular treatment. If no recanalization evidence was observed, the subsequent angiography evaluation was performed at 18 months after treatment.

Clinically, neurological and functional status was evaluated according to the modified Rankin scale (mRS). Good outcomes were defined as an mRS score of 0–2, while poor outcomes were defined as a mRS score of 3–6.

Statistical analyses

SPSS 19.0 software (SPSS Inc., Chicago, IL, USA) was used for the statistical analyses. A Mann-Whitney U test was performed for non-normally distributed continuous variables, while the Pearson χ^2 or Fisher's exact test was used to compare proportions. The univariate analysis cutoff for inclusion in the logistic regression analysis was p < 0.25. Values of p < 0.05 were considered statistically significant.

Results

The patient characteristics and aneurysm features are summarized in Table 1. The cohort consisted of 160 males (41.0%) and 230 females (59.0%) with a median age of 57 years (range, 16–82 years). Of the 417 aneurysms, 259 (62.1%) were ruptured and 158 (37.9%) remained unruptured. The 2 groups were similar in all baseline characteristics.

Initial angiography manifestations

The aneurysm size was up to 3 mm in 78 aneurysms (18.7%), 3–10 mm in 314 aneurysms (75.3%), 11–25 mm in 22 aneurysms (5.3%), and more than 25 mm in 3 aneurysms (0.7%). The aneurysms were located in the internal carotid artery (n = 215), middle cerebral artery (n = 50), anterior communicating artery (n = 104), and other arteries (n = 48).

Stents used in treatment

Among the 417 aneurysms, 197 were treated with SAC using the Enterprise stent in 24, the Solitaire stent in 119, and the Neuroform stent in 54.

Adverse events and mortality

Adverse events are summarized in Table 2. Thromboembolic complications were seen in 17 patients (4.4%). Intraoperative rupture occurred in 10 patients (2.6%). Other adverse events occurred in 3 patients (one case each of gastrointestinal bleeding, coil stretching, and coil migration). Cumulative adverse events occurred in 30 patients (7.7%). Nineteen patients (4.9%) had a permanent disabling neurologic deficit (mRS 3–6). The overall mortality rate was 0.8% (3/390).

The statistical analysis revealed an increased rate of intraprocedural rupture in initial completely occluded aneurysms (5.6% versus 1.0%, p = 0.010). The incidence of cumulative adverse events was higher in patients with completely occluded aneurysms (11.1%) than in those with near-completely occluded aneurysms (5.5%) (p = 0.042).

Follow-up outcomes

Follow-up data were available for 299 patients (Table 3). During a median follow-up period of 30 months (range, 3–124 months), one case

Table 1

Baseline characteristics of cerebral aneurysms treated with endovascular coil embolization.

	Initial aneurysm	P value	
	Complete (n = 126)	Near-complete $(n = 291)$	
Female sex	76 (60.3)	174 (59.8)	0.920 ^a
History			
Hypertension	64 (50.8)	136 (46.7)	0.446 ^a
Smoking	32 (25.4)	62 (21.3)	0.359 ^a
Median age, years	56.5	58	0.066 ^b
Location			0.071 ^a
Internal carotid artery	59 (46.8)	156 (53.6)	
Middle cerebral artery	12 (9.5)	38 (13.1)	
Anterior communicating	42 (33.3)	62 (21.3)	
artery			
Other	13 (10.3)	35 (12.0)	
Size			0.134 ^a
Tiny (<3 mm)	31 (24.6)	47 (16.2)	
Small (3-10 mm)	90 (71.4)	224 (77.0)	
Large (11–25 mm)	4 (3.2)	18 (6.2)	
Giant (>25 mm)	1 (0.8)	2 (0.7)	

Unless indicated otherwise, data are number of cases with percentages in parentheses.

^a χ² test or Fisher's exact test.

^b Mann-Whitney *U* test.

Table 2

Adverse events and clinical outcomes.

	Initial aneu	sysm occlusion status	Total	P value
	Complete (n = 126)	Near-complete $(n = 291)$		
Ischemic events	7 (5.6)	10 (3.4)	17	0.315 ^a
Intraoperative rupture	7 (5.6)	3 (1.0)	10	0.010 ^a
Other adverse events	0 (0)	3 (1.0)	3	0.557 ^a
Cumulative adverse events	14 (11.1)	16 (5.5)	30	0.042 ^a
Permanent disabling neurologic deficit ^b	9 (7.1)	10 (3.4)	19	0.096 ^a
Periprocedural mortality	1 (0.8)	2 (0.7)	3	1.000 ^a

SAH, subarachnoid hemorrhage.

Unless indicated otherwise, data are number of cases with percentages in parentheses.

^a χ^2 test or Fisher's exact test.

^b Because of treatment-related complications, complications of SAH, or unfavorable evolution of SAH.

Table 3

Potential risk factors related to follow-up results.

	I			
	Good outcome (n = 280)	Poor outcome (n = 19)	Total	P value
Median age, years	57	56		0.918 ^a
Sex				0.175 ^b
Female	162 (92.0)	14 (8.0)	176	
Male	118 (95.9)	5 (4.1)	123	
Rupture status				0.343 ^b
Ruptured	176 (92.6)	14 (7.4)	190	
Unruptured	104 (95.4)	5 (4.6)	109	
Location				0.032 ^b
Internal carotid artery	144 (96.6)	5 (3.4)	149	
Middle cerebral artery bifurcation	33 (97.1)	1 (2.9)	34	
Anterior communicating artery	74 (90.2)	8 (9.8)	82	
Other	29 (85.3)	5 (14.7)	34	
Stent placement				0.431 ^b
Yes	144 (94.7)	8 (5.3)	152	
No	136 (92.5)	11 (7.5)	147	
Initial occlusion status				0.238 ^b
Complete	82 (91.1)	8 (8.9)	90	
Near-complete	198 (94.7)	11 (5.3)	209	
Adverse events				0.008 ^b
Yes	17 (77.3)	5 (22.7)	22	
No	263 (94.9)	14 (5.1)	277	

Unless indicated otherwise, data are number of cases with percentages in parentheses.

^a Mann-Whitney U test.

^b χ^2 test or Fisher's exact test.

of rebleeding occurred (initial near-complete occlusion status). The statistical analysis demonstrated that clinical outcomes were correlated with adverse events (p = 0.008) and aneurysm location (p = 0.032).

Angiographic follow-up data were available for 173 aneurysms (163 patients) with a median follow-up period of 6 months (range, 3–14 months) (Table 4). Follow-up angiograms showed complete occlusion in 118 aneurysms (68.2%) and near-complete or incomplete occlusion in 55 aneurysms (31.8%). Follow-up aneurysm occlusion status was correlated with stent placement (p = 0.000, odds ratio = 5.847), size (p = 0.000, odds ratio = 5.616 for small aneurysms) and initial aneurysm occlusion status (p = 0.001, odds ratio = 3.436).

Initial and follow-up angiography outcomes are summarized in Table 5. Complete occlusion at follow-up was seen in 82.6% (38/46) of the initial complete occlusion group versus 63.0% (80/127) of the initial near-complete occlusion group (p = 0.014). In the SAC condition, complete

Table 4

Predictors of aneurysm obliteration at last follow-up.

	Follow-up aneurysm occlusion status		P value	Logistic regression p
	Complete (n = 118)	Near- complete or incomplete (n = 55)		value
Median age, years	57	54	0.211 ^a	
Sex			0.793 ^b	
Female	69 (69.0)	31 (31.0)		
Male	49 (67.1)	24 (32.9)		
Rupture status			0.040 ^b	
Unruptured	56 (76.7)	17 (23.3)		
Ruptured	62 (62.0)	38 (38.0)		
Stent placement			0.000 ^b	
Yes	78 (83.9)	15 (16.1)		0.000 (5.847) [3.054–11.196] ^c
No	40 (50.0)	40 (50.0)		
Size			0.206 ^b	
Tiny	68 (71.6)	27 (28.4)		0.0 (6.446) [2.428–17.117] ^c
Small	45 (67.2)	22 (32.8)		0.001 (5.616) [2.075–15.204] ^c
Large or giant	5 (45.5)	6 (54.5)		
Initial occlusion status			0.014 ^b	
Complete	38 (82.6)	8 (17.4)		0.001 (3.436) [1.610–7.299] ^c
Near-complete	80 (63.0)	47 (37.0)		_

Unless indicated otherwise, data are number of cases with percentages in parentheses.

^a Mann-Whitney U test.

 $^{b}\ \chi^{2}$ test or Fisher's exact test.

^c Numbers in parentheses are odds ratios. Numbers in brackets are 95% confidence intervals. P values were obtained using binary logistic regression.

Table 5

Initial and follow-up angiography outcomes of aneurysms treated with coil embolization.

Initial occlusion status	Follow-up aneurysm occlusion status		
	Complete	Near-complete or incomplete	
Complete treated with non-SAC ($n = 23$)	15 (65.2)	8 (34.8)	
Near-complete treated with non-SAC ($n = 57$)	25 (43.9)	32 (56.1)	
Complete treated with SAC $(n = 23)$	23 (100)	0 (0)	
Near-complete treated with SAC ($n = 70$)	55 (78.6)	15 (21.4)	

SAC, stent-assisted coiling.

Unless indicated otherwise, data are number of cases with percentages in parentheses.

occlusion at follow-up was seen in 100% (23/23) of the initial complete occlusion group versus 78.6% (55/70) of the initial near-complete occlusion group (p = 0.018). In the non-SAC condition, complete occlusion at follow-up was seen in 65.2% (15/23) of the initial complete occlusion group versus 43.9% (25/57) of the initial near-complete occlusion group (p = 0.084). The incidence of complete occlusion at follow-up was higher in the initial near-completely occluded aneurysms treated with SAC (78.6%) than in the initial near-completely occluded aneurysms treated with non-SAC (43.9%) (p = 0.000). The incidence of complete occlusion at follow-up was higher in the initial completely occluded aneurysms treated with SAC (100%) than in the initial completely occluded aneurysms treated with non-SAC (65.2%) (p = 0.004).

In the SAC condition, follow-up angiography data were available for 93 aneurysms; among them, there were 2 cases (2.2%) of severe in-stent stenosis, both of which were asymptomatic.

Discussion

The International Subarachnoid Aneurysm Trial suggested that incompletely coiled aneurysms may be more likely to re-rupture than completely coiled aneurysms, although the overall re-rupture rate after coiling is low.⁹ However, not all aneurysms can be completely occluded in the first treatment. In a systematic review of 8161 coiled aneurysms, initial complete occlusion was reported in 4355 (62.3%), near-complete occlusion in 2065 (29.5%), and incomplete occlusion in 571 (8.2%).¹⁰ At the present time, few studies have compared the outcomes of initial near-completely occluded aneurysms with those of initial completely occluded aneurysms.

In our study, 291 aneurysms (69.8%) had initial near-complete occlusion status. Complete occlusion at follow-up was seen in 82.6% of the initial complete occlusion group versus 63.0% of the initial near-complete occlusion group (p = 0.014). These findings suggest that near-complete initial treatment cannot provide durable closure at follow-up.

The introduction of stent technology has led to a conceptual shift in the management of intracranial aneurysms. Previous clinical studies reported conflicting efficacy results for SAC and non-SAC.^{11,12} Some scholars demonstrated that SAC facilitated a higher coil packing density and more stable aneurysm neck sealing.^{4–8,13} A recent meta-analysis revealed an immediate occlusion rate of SAC of 57.7% (range, 20.2–89.2%) and 48.7% (range, 31.7–89.2%) for coiling only; progressive thrombosis was significantly more likely in SAC (29.9%) than in coiling only (17.5%).¹⁴ However, Hwang et al. noted that stent placement provided no better long-term angiography outcomes for aneurysms with unfavorable configurations for coiling.¹⁵

In the initial near-complete occlusion group, the complete obliteration rate was 78.6% (55/70) in SAC versus 43.9% (25/57) in non-SAC at follow-up (p = 0.000). This finding suggests that stent placement may enhance progressive aneurysm occlusion despite initial unsatisfactory angiography results (Fig. 2).

Embolized aneurysms can develop worse closure despite complete initial occlusion.¹⁶ Choi et al. reported a recanalization rate of 26.4% in a retrospective study of 91 completely coiled aneurysms.¹⁷ Xavier et al. reported a recanalization rate of 24% in a retrospective study of 83 completely coiled aneurysms.¹⁸ Nevertheless, Chalouhi et al. found that overpacking aneurysms with coils when a stent is used does not confer any advantage in obliteration rates.¹⁹ Neurointerventionists wonder how densely to pack a stented aneurysm.

Follow-up angiography demonstrated a significant difference in the incidence of complete occlusion between SAC and non-SAC of initial completely coiled aneurysms (Table 5, Figs. 3 and 4). Among the stented patients, all 23 aneurysms (100%) demonstrated occlusion. In the non-stented patients, 15 of 23 aneurysms (65.2%) were occluded (p = 0.004). These findings suggest that SAC can provide durable closure for initial completely occluded aneurysms (Fig. 4). Complete occlusion is important in SAC of intracranial aneurysms.

In this study, we noted a comparable complication rate (7.7%) to those of previously studies. Pierot et al. reported a total complication rate of 13.5% in a retrospective study of 1088 aneurysms.²⁰ Song et al. reported a total complication rate of 3% in a retrospective study of 606 unruptured aneurysms.²¹

In our study, the statistical analysis revealed an increased rate of intraprocedural rupture in initial completely occluded aneurysms (5.6% versus 1.0%). The incidence of cumulative adverse events was higher in patients with completely occluded aneurysms (11.1%) than in those with near-completely occluded aneurysms (5.5%) (p = 0.042). The clinical outcomes did not significantly differ between the 2 groups at follow-up. Good clinical outcomes (mRS of 0–2) at follow-up were seen in 82 patients (91.1%) with initial completely occluded aneurysms and in 198 patients (94.7%) with initial near-completely occluded aneurysms (p = 0.238). A possible explanation for this is that the majority of patients can survive without severe sequelae if managed appropriately after

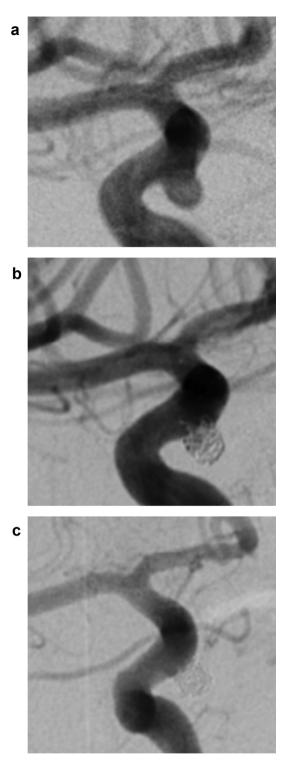
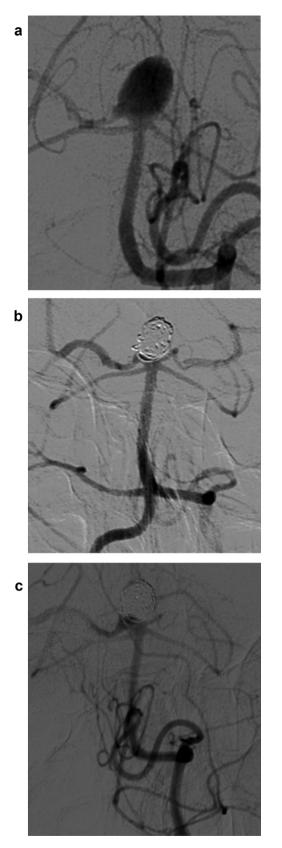


Fig. 2. Coiling of an unruptured aneurysm in a 63-year-old woman. Cerebral angiography showed an aneurysm of the right carotid artery (A). The aneurysm was treated using stent-assisted coiling (Solitaire). Angiography performed immediately after coiling revealed near-complete aneurysm occlusion (B). Angiography performed at 29 months after embolization revealed complete aneurysm occlusion (C).

intraoperative aneurysm rupture.²² These findings suggest that initial complete treatment may lead to higher complication rates and good clinical outcomes at follow-up. The excessive pursuit of an angiographically perfect coil embolization might increase the risk of aneurysm rupture, especially in cases of rupture.^{23,24}



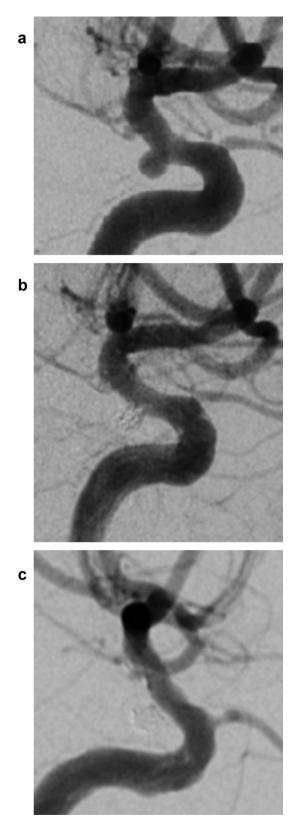


Fig. 3. Coiling of a ruptured aneurysm in a 47-year-old man. Cerebral angiography showed an aneurysm of the basilar artery (A). Angiography performed immediately after coiling revealed complete aneurysm occlusion (B). Angiography performed at 64 months after embolization revealed aneurysm recanalization (C).

Fig. 4. Coiling of an unruptured aneurysm in a 57-year-old woman. Cerebral angiography showed an aneurysm of the left carotid artery (A). The aneurysm was treated with stent-assisted coiling (Solitaire). Angiography performed immediately after coiling revealed complete aneurysm occlusion (B). Angiography performed at 5 months after embolization revealed complete aneurysm occlusion (C).

Limitations

This study has several limitations. First, its retrospective design and single-center setting have inherent demerits. Second, some patients did not undergo long-term follow-up. Third, the morphologies of the enrolled aneurysms were not absolutely the same in the SAC and non-SAC groups. Fourth, other kinds of stents such as the LVIS and Leo stents were not used in this study.

Conclusions

Initial complete treatment may lead to higher complication rates and good clinical outcomes at follow-up. Stent placement may enhance the progressive occlusion of aneurysms despite the initial unsatisfactory angiography results. Our results suggest that initial complete occlusion with SAC can provide durable closure at follow-up.

Patient consent

Witten informed consent was obtained from patients for publication of these case reports and any accompanying images.

Declaration of competing interest

The authors declare that they have no conflicts of interests to this work. We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.

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