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Clinical Article

A Self-expanding Nitinol Stent (Enterprise) for the Treatment of Wide-necked Intracranial Aneurysms: Angiographic and Clinical Results in 40 Aneurysms

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Objective : Self-expanding stents are increasingly used for the treatment of complex intracranial aneurysms. The purpose of this study was to evaluate the usefulness and safety of a self-expanding nitinol stent (Enterprise) in the treatment of wide-necked intracranial aneurysms.

Methods : This was a retrospective study of 39 patients with 40 wide-necked intracranial aneurysms who were enrolled in a single-center registry of patients treated with the Enterprise between June 2009 and December 2011. Thirty patients were asymptomatic, four had cerebrovascular accident sequelae, and five had suffered subarachnoid hemorrhage. One aneurysm had reopened after prior coil embolization, while 39 had not been treated. Clinical charts, procedural data, and angiographic results, including both immediate post-procedural angiograms and follow-up imaging, were reviewed.

Results : The mean neck size of the aneurysms was 5.58 mm (range 3-15.1 mm). Embolization was successful in all patients. There were five procedure-related events. There were no fatalities, but one procedure-related morbidity was noted. The immediate angiographic results included eight complete occlusions (20%), six remnant necks (15%), and 26 remnant sacs (65%). At angiographic follow-up (mean: 11.3 months), out of 18 of the aneurysms treated with stent-assisted coiling, there were 13 (72.2%) complete occlusions, four (22.2%) remnant necks, and one recanalization (5.6%).

Conclusion : Stent-assisted coiling using the Enterprise is effective for the treatment of wide-necked intracranial aneurysms. Further angiographic and clinical follow-up investigation will be needed for evaluation of the long-term outcomes.

Keywords Intracranial aneurysms, Coiling, Stent, Enterprise

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INTRODUCTION

Endovascular treatment of intracranial aneurysms by endovascular coiling has become an alternative treatment to surgical clipping, with lower morbidity and mortality rates in selected cases.[17] However, the possibility of coil migration and long-term angiographic recurrence pose limitations in the treatment of complex

or wide-necked aneurysms.[17)23)] Self-expanding stents allow denser aneurysm packing with increased neck coverage, and may also improve treatment durability through a combination of flow-diversion, parent vessel straightening, and fibroelastic tissue formation along the neck of the aneurysm.[14)23)] Currently, two stents have been approved for stent-assisted coiling in the USA: the Enterprise vascular reconstruction device (Enterprise; Codman Neurovascular/Johnson & Johnson, Raynham, MA, USA) and the Neuroform stent (Neuroform; Boston Scientific/Stryker, Kalamazoo, MI, USA). The Enterprise is a self-expandable nitinol stent with a highly flexible closed-cell design. The stent can be delivered through a standard microcatheter, technically easier than the exchange procedure.[20)23)]

There are many reports of the feasibility and safety of stent-assisted coiling. However, little information is available regarding the follow-up results of the technique. Thus, in this study, we report our initial and follow-up clinical experience with Enterprise stent placement in 39 consecutive patients with 40 wide-neck intracranial aneurysms.

MATERIALS AND METHODS

We reviewed the clinical and radiological records in a single-center registry of all patients who were treated with Enterprise stent-assisted coil embolization during the 30-month period from June 2009 to December 2011. Thirty-nine patients with 40 wide-necked aneurysms were enrolled, including nine men and 30 women with mean age 61.3 years (range 44-85 years). Thirty patients were asymptomatic, four had cerebrovascular accident sequelae, and five had suffered acute subarachnoid hemorrhage. A "wide-necked" aneurysm was defined as having a neck of > 4 mm diameter or an aspect ratio of > 2.0. Twenty-eight aneurysms were located in the anterior and 12 in the posterior circulation (Table 1). Thirty-four aneurysms were found incidentally. Seven were dissecting aneurysms. One aneurysm had reopened after prior coil embolization, while 39 had not been treated. All aneurysms were judged impossible to treat using other techniques.

All patients underwent endovascular treatment under general anesthesia. Clopidogrel 300 mg per day was given in the morning of the procedure in patients with unruptured aneurysms. Because of the risk of rebleeding, no premedication with platelet inhibitors was administered to patients with acutely ruptured aneurysms unless thromboembolic events occurred. Heparin was administered for anticoagulation in a bolus infusion of 4000 IU, followed by 1000 IU/h.

Three neurointerventionalists reviewed the angiographic records. Angiographic results were classified as: complete occlusion (no contrast filling the sac), remnant neck (residual filling of the neck), and remnant sac (residual filling of the sac).[22)]

During follow-up, the aneurysm could change from one class to another or remain unchanged. The clinical and angiographic findings are summarized in Table 1. Follow-up angiography was carried out after more than six months. If conventional angiography was not feasible, 3.0-Tesla magnetic resonance angiography (MRA) was performed.

RESULTS

Initial results and complications

Thirty-nine patients with 40 intracranial aneurysms were evaluated. The mean aneurysm neck size was 5.58 mm (range 3-15.1 mm). The stents were placed at the exact location predicted by the computer simulation. The degree of intracranial aneurysm obliteration was evaluated by angiography. Complete occlusion was achieved in 8/40 (20%) of all stent-assisted cases, while a remnant neck was found in 6/40 (15%) and a remnant sac was observed in 26/40 (65%) (Table 2). There was one technical complication of coil herniation and four thromboembolic events. The coil herniation did not cause any morbidity. In two patients, an embolic infarction was seen on dif-

Table 1. Major findings from 40 aneurysms in 39 patients

No.	Age/Sex	Clinical finding	Location	Maximal size(mm)	Neck size (mm)	Aspect ratio	Embolization results	Periprocedural complication	mRS at discharge	Angiographic follow-up	Retreat-ment
1	M/72	Unruptured	BA	10	6.9	1.13	S	Coil herniation	0		
2	F/69	Unruptured	ICA bifurcation	11.5	7.5	1.53	S	Thromboembolism	3		
3	F/53	Unruptured	ICA, paraclinoid	4.6	4.6	0.72	S		0		
4	F/67	Unruptured	ICA, Pcom	4.7	3.3	1.1	N		0		
5	F/74	Unruptured	ICA, paraclinoid	5.1	4.6	0.65	C		0		
6	F/72	Unruptured	ICA, Pcom	4	4.3	0.84	N	Thromboembolism	1		
7	F/59	Unruptured	ICA, paraclinoid	3.5	3.7	0.62	S		0		
8	F/71	SAH	BA	1.9	3	0.63	C		5		
9	M/66	Unruptured	VA	4.8	6.2	0.77	S		1		
10	F/67	Unruptured	ICA, Pcom	3.7	4.4	0.77	S		0	o	
11	F/58	SAH	ICA, Pcom	8.6	6.6	1.6	S		0		
12	F/78	SAH	VA	4.4	10.2	0.43	S		6		
13	F/65	Unruptured	Acom	8	5.5	1.18	C	Thromboembolism	0		
14	M/62	Unruptured	ICA, paraclinoid	7.3	8.5	0.55	S		3	o	
15	F/67	Unruptured	ICA, Pcom	4	3.7	1.02	S		0	o	
16	F/48	Unruptured	VA	15.1	15.1	0.344	S		0	o	
17	M/50	Unruptured	ICA, paraclinoid	4.6	5.1	0.86	N		0	o	
18	F/68	Unruptured	VA	5.3	5.5	0.56	S		0	o	
19	F/69	Unruptured	ICA, Pcom	9.3	7.8	0.87	C		0		
20	F/60	Unruptured	Right distal ICA	11	8.8	1	S		0		
21	F/44	Unruptured	ICA, paraclinoid	3.9	4.9	0.79	S		0	o	
22	F/66	Unruptured	ICA, paraclinoid	4.7	4.5	0.89	S		0		
23	F/85	SAH	BA	5.1	4.7	0.98	S		5		
24	F/69	Unruptured	ICA, distal	4.2	4.4	0.66	C		0	o	
25	F/47	Unruptured	ICA, paraclinoid	3.2	3.1	0.74	S		0	o	
26	M/54	Unruptured	VA	5	4.4	0.88	S		0	o	
27	F/47	SAH	Right distal ICA	10.7	5.7	1.87	C	Thromboembolism	1		
28	F/74	Unruptured	BA	6.8	4	1.7	S		0	o	
29	M/51	Unruptured	ICA, paraclinoid	4.8	4.8	0.67	S		0		
30	F/58	Unruptured	ICA, dorsal wall	5.2	4.6	0.65	S		0	o	
31	F/59	Unruptured	ICA, paraclinoid	3.9	3.9	0.77	S		0		
32	M/48	Unruptured	VA	4.7	4.5	0.49	S		1		
33	M/45	Unruptured	VA	8.9	8.9	0.51	N		0	o	
34	F/65	Unruptured	ICA, cavernous	15.6	7.2	2.17	N		0	o	o
35	Same above	Unruptured	ICA, paraclinoid	6.5	3.9	1.12	S		0	o	
36	M/59	Unruptured	VA	8.4	8.4	0.83	C		0		
37	F/58	Unruptured	ICA, paraclinoid	4.3	3.8	0.87	N		0		
38	F/53	Unruptured	ICA, paraclinoid	5.4	4	1.1	C		0	o	
39	F/46	Unruptured	ICA, paraclinoid	3.7	3.7	0.68	S		0	o	
40	F/69	Unruptured	ICA, Pcom	4.7	4.7	0.7	S		0	o	

M= male; F= female; SAH= subarachnoid hemorrhage; CVA= cerebrovascular accident; BA= basilar artery; ICA= internal cerebral artery; Pcom= posterior communication artery; VA= vertebral artery; Acom= anterior communicating artery; mRS= modified Rankin scale; C= complete; S= remnant sac; N= remnant neck

Table 2. Immediate angiographic result of embolization

Immediate result of embolization	Aneurysm
Complete	8 (20)
Remnant neck	6 (15)
Remnant sac	26 (65)
Total	40 (%)

Table 3. Angiographic follow-up results

Immediate after embolization	Angiographic follow-up result	Retreatment result
C:2	C:2	
N:3	C:1	
	N:1	
	Recannalized:1	Complete
S:13	N:3	
	C:10	

Total 18, mean follow-up duration (11.3 month)
C= complete; S= remnant sac; N= remnant neck

fusion MR imaging (MRI) that was performed to investigate transient hemiparesis. After several days' observation, the patients were discharged without any symptoms. In one patient, in-stent thrombus was seen on final angiography. Therefore, tirofiban (0.3 mg) was injected through a microcatheter. The next day, the thrombus was not visible on angiography and the patient had no symptoms. In another patient (Pt. 2 in Table 1), acute middle cerebral artery occlusion occurred as a result of in-stent thrombus. Prompt chemical thrombolysis was carried out with abciximab (10 mg) and urokinase (100,000 U), achieving recanalization and a thrombolysis in cerebral infarction (TICI) score of 2b. However, a multiple embolic infarction in the middle cerebral arterial territory was seen on diffusion MRI. Consequently, this patient had morbidity 3 on the modified Rankin scale (mRS).

One thromboembolic event caused procedure-induced morbidity (2.5%). Among the 39 patients, 29 had an mRS at discharge of 0, four patients had a score of 1, two patients had a score of 3, three patients had a score of 5 and one patient had a score of 6. The four patients with mRS 5 or 6 had suffered subarachnoid hemorrhage. Table 1 summarizes the major findings and results for each of the 40 aneurysms in 39 patients.

Follow-up results

Angiographic follow-up was available in 18 of the 40 treated aneurysms and ranged from 6 to 23 months (mean 11.3 months). Two initially occluded aneurysms were still completely occluded. One of three with a remnant neck had progressed to complete occlusion, one remained unchanged and one showed recanalization. Three of the 13 aneurysms with a remnant sac had evolved to remnant neck, while ten were completely occluded. Thus, in 18 aneurysms treated with Enterprise stent-assisted coiling, angiographic follow-up showed 13 complete occlusions (72.2%) and four with a remnant neck (22.2%), while major recanalization to a remnant sac was observed in one aneurysm (5.6%) (Table 3). Additional coiling was performed without complications in the aneurysm that was recanalized. In the patients with angiographic follow-up, no evidence of

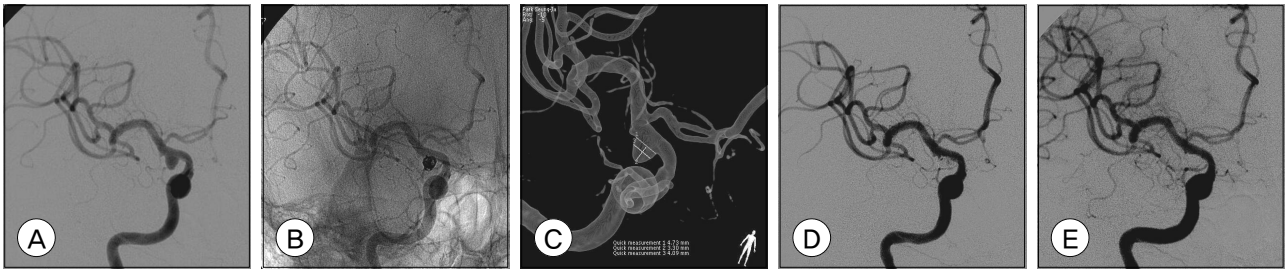

Fig. 1. An internal carotid artery aneurysm (A) originating from a posterior communicating artery, treated with the Enterprise stent system and coils (B). 3D rotational angiography shows the maximum size and neck size of the aneurysm (C). Final angiography shows a remnant sac (D). Angiography at six months reveals complete occlusion of the aneurysm (E).

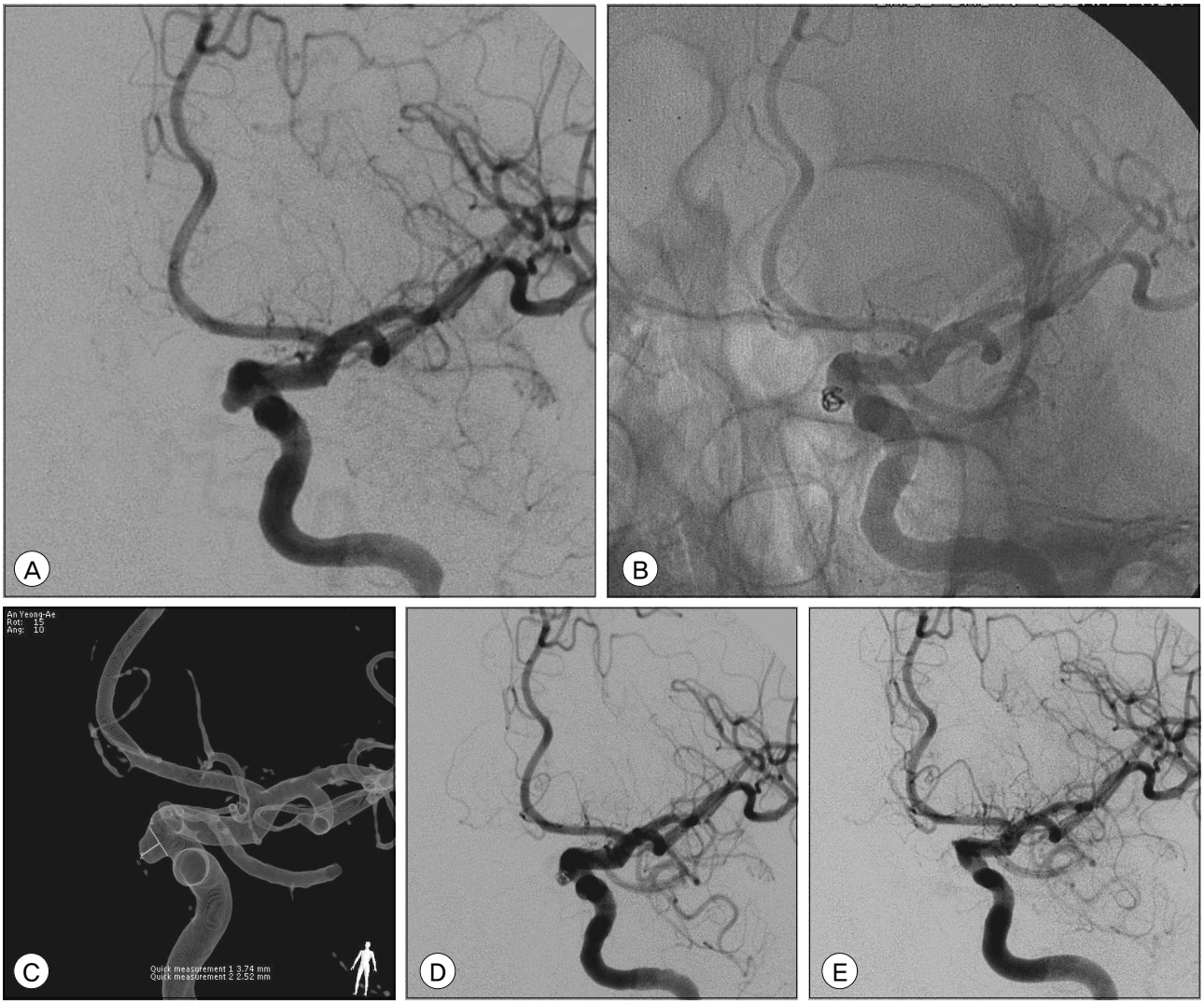

Fig. 2. An internal carotid artery aneurysm (A) in a paraclinoid segment, treated with the Enterprise stent system and coils (B). 3D rotational angiography shows the maximum size and neck size of the aneurysm (C). Final angiography shows a remnant sac (D). Angiography at six months reveals complete occlusion of the aneurysm (E).

stent migration or in-stent thrombosis was observed (Fig. 1, 2).

As an alternative, MRA follow-up was used in five treated aneurysms after 10 to 36 months (median, 12 months). No evidence of recurrence was seen in any of these studies (Table 4).

DISCUSSION

Wide-necked aneurysms are difficult to treat, either surgically or endovascularly, because of their unfavorable geometry, which reduces the possibility of

Table 4. Magnetic resonance angiography (MRA) follow-up results

Case No.	Immediate after embolization	MRA follow-up result (month)
4	N	no recurred (36)
9	S	no recurred (36)
13	C	no recurred (10)
31	S	no recurred (12)
32	S	no recurred (10)

Total 5, median follow-up duration (12 month)
C= complete; S= remnant sac; N= remnant neck

achieving dense packing and elimination of the aneurysm from the circulation. The development of intracranial stents allows treatment of intracerebral aneurysms with unfavorable anatomy. The stent serves as a scaffold in the parent artery to prevent coil migration.[17] Furthermore, stent placement across the aneurysm neck enables additional obliteration by denser and safer packing of the aneurysm lumen and may improve aneurysm occlusion by redirection of flow.[11][12][17]

The Enterprise stent is the first closed-cell stent designed to treat wide-necked intracranial aneurysms. Advantages of the design include the ability of the stent to be partially deployed, recaptured, and redeployed, and it may improve the stability of coils within the aneurysm.[12] Furthermore, the Enterprise stent's delivery system facilitates its navigation and placement. Reported rates for the inability to navigate or deploy the Neuroform stent are as high as 19.8%, compared with only 0-5% for the Enterprise. Despite recent improvements in the delivery system, the failure rate of the Neuroform has remained high.[1][2][6][12][19] However, concerns have been raised in experimental and clinical reports regarding the conformability and apposition of the Enterprise stent's closed-cell design within curved vessels.[4][9] Furthermore, Heller et al. found that incomplete stent apposition, as assessed by 3-Tesla MRA, was more common in Enterprise (55%) versus Neuroform stents (0%).[10] For this reason, problems such as stent migration, in-stent restenosis, and periprocedural thromboembolism can occur frequently. For example, Kadkhodayan et al.[12] reported that the periprocedural rates of transient ischemic attack and periprocedural stroke were higher for the Enterprise (6.1% and 2.6%, respectively) than for the Neuroform (1.4% and 0%, respectively). Cases of stent migration have been reported.[13][15] However, despite the structural weaknesses, numerous other studies reported that periprocedural stroke, in-stent thrombosis, stent migration and clinical outcome did not differ between the Enterprise and the Neuroform.[3][5][7][11][24]

With intracranial atherosclerotic disease, thromboembolic events such as periprocedural stroke and in-stent thrombosis occur frequently.[18] However, stent-assisted coiling is associated with a low rate of thromboembolic events. Exceptionally, in the case of subarachnoid hemorrhage, the risk of hemorrhage or a thromboembolic event is increased.[3]

Chalouhi et al. analyzed 508 patients with 552 aneurysms who were treated with stent-assisted coiling. The risks for procedural complications were subarachnoid hemorrhage and aneurysm location (carotid terminus, middle cerebral artery). The risks for recanalization were age, retreatment, large size, incomplete occlusion, Neuroform stent, and aneurysm location, and for a worse clinical outcome were subarachnoid hemorrhage, age, and procedural complication.[3]

Ease of use may influence periprocedural risk. If a device is difficult to use, the operator may need to make several attempts. As a result, the procedure time will increase and the doctor's concentration may be affected, raising the risk of complications. Thus, ease of use can have a strong effect on the angiographic and clinical outcome.

In our study, the immediate angiographic results were disappointing, showing only 20% cases with complete occlusion, 15% with a remnant neck, and 65% with a remnant sac. However, angiographic follow-up showed an improvement, with 72% complete occlusion, 22% remnant neck, and only 6% recanalizations (Fig. 1, 2). Thromboembolic complications affecting the clinical outcome occurred in only one case (2.5%). These results are consistent with the pattern reported in a recent large study,[8] and agree with other recent reports that stent-assisted coiling has a favorable long-term outcome.[11][12][14][17] However, Enterprise can cause thromboembolic complications.[12] In the patients who had angiographic follow-up, evidence of stent migration or in-stent thrombosis was not observed. Furthermore, in the cases that had only MRA follow-up, there was no evidence of recurrence.

This study showed that stent-assisted coiling is an effective treatment that stabilizes or improves the long-term anatomical results in most cases. However, there is a possibility of thromboembolic events due to the use of the stent.

CONCLUSION

Although this study is limited by its retrospective nature, these results indicate that Enterprise stent-assisted coil embolization is an effective technique in the treatment of wide-necked cerebral aneurysms. Further studies are needed to evaluate the long-term durability of stent-assisted aneurysm occlusion and the rate of thromboembolic events due to stent use.

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