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# Wingspan stent-assisted coiling of intracranial aneurysms with symptomatic parent artery stenosis: Experience in 35 patients with mid-term follow-up results

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### A R T I C L E I N F O

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## ABSTRACT

*Background:* There is a potential risk of aneurysm rupture after parent artery revascularization because of increased blood flow. The purpose of this study is to assess the efficacy and safety of Wingspan stent-assisted coil embolization in the treatment of intracranial aneurysms with symptomatic parent artery stenosis.

*Methods:* Thirty-five consecutive patients (19 men, 16 women; age range, 48–79 years; mean age, 60.4 years) harboring 35 unruptured wide-necked or fusiform intracranial aneurysms (mean size 6.8 mm; range 2.5–18 mm.) with symptomatic parent artery stenosis (mean degree 71.1%; range 50–92%) were treated with the Wingspan stent-assisted coiling. Twenty-four lesions were located in the anterior circulation and eleven in the posterior circulation. Patients were premedicated with antiplatelet therapy consisting of aspirin 300 mg and clopidogrel 75 mg for at least 3 days before the procedure. Following pre-dilatation and stent placement, a coiling microcatheter entered the aneurysm through the interstices of the stent, and then coiling was performed. After the procedure, clopidogrel 75 mg daily was recommended for an additional 30 days, and aspirin 100 mg was recommended throughout follow-up. For all patients, clinical follow-up was conducted by clinic visitation, or telephone interview. Angiographic follow-up (mean time 10.6 months) was obtained in 31 cases (88.6%). The technical feasibility of the procedure, procedure, related complications, angiographic results, clinical outcome and follow-up angiography were evaluated.

*Results:* In every case, technical success was achieved. The degree of stenosis was reduced from 71.1% to 17.4% after balloon angioplasty and stenting. Immediate angiography demonstrated complete occlusion in 25 cases (71.4%), neck remnant in 7 cases (20.0%), and incomplete occlusion in 3 cases (8.6%). Procedure-related morbidity occurred in two patients (5.7%), including thromboembolism (n=1) and occlusion of small penetrating arteries (n=1). At follow-up (mean time 18.3 months), two additional cases of ischemic stroke occurred. The overall frequency of any stroke, intracranial hemorrhage, or death within 30 days or ipsilateral stroke beyond 30 days was 11.4%. No rehemorrhage of treated aneurysm occurred. At angiographic follow-up, four cases demonstrated  $\geq$ 50% in-stent restenosis (12.9%), one of which was symptomatic, and two aneurysms (6.4% of the follow-up angiograms) demonstrated recanalization. *Conclusion:* We found that the Wingspan stent-assisted coil embolization was helpful in the treatment of intracranial aneurysms with parent artery stenosis.

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## 1. Introduction

Intracranial stenosis is a main cause of acute stroke and stroke recurrence [1]. In the recent Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) trial, 25% of patients presenting with 70–99% stenosis experienced a stroke in the ipsilateral vascular territory within 2 years, despite treatment with either warfarin or

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aspirin [2]. The high failure rate of medical therapy has encouraged revascularization strategies such as angioplasty and intracranial stenting. However, one of the most disastrous complications after revascularization is intracranial hemorrhage, especially for patients with intracranial aneurysm arising from the treated segment. Hemodynamic changes, unbalance in the wall sheer stress (WSS) after revascularization may result in the aneurysm rupture. Postprocedural antiplatelet therapy is also a precipitating factor for aneurysm rupture [3].

For several years, we have used Wingspan stent-assisted coil embolization to treat these tandem lesions in the same session. In addition to treating the diseased parent vessel, the Wingspan

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stent can support the aneurysm packing and provide a scaffold for endothelial regrowth [4,5]. We conduct this study to evaluate the technical feasibility, efficacy and safety of this method. Although Wingspan stent-assisted coiling technique is not a new concept, which has been reported by Yavuz et al. in 2008 [6], to our knowledge, this article, for the first time, presents data from a series of patients with tandem lesions in whom Wingspan stent-assisted coiling has been used, including angiographic and clinical follow-up results.

## 2. Patients and methods

## 2.1. Patients

From March 2007 to December 2010, a total of 35 intracranial aneurysms (mean diameter 6.8 mm) with symptomatic parent artery stenosis in 35 patients (19 men, 16 women; age range, 48–79 years; mean age, 60.4 years) were treated with the Wingspan stent-assisted coil embolization at our institution (Table 1). All patients had a history of ischemic events before treatment. None of the aneurysms was in the acute stage of SAH. The average degree of stenosis was 71% (50–92%). The average length of stenosis was 5.5 mm (3–11.2 mm). Twenty-four lesions were located in the anterior circulation and eleven in the posterior circulation.

The inclusion criteria in the series were as follows: fusiform or wide-necked aneurysms; >50% symptomatic parent artery stenosis 10 mm proximal to the aneurysm neck; parent artery with a diameter between 1.5 and 4.5 mm; and provision of written informed consent and review board approval. Exclusion criteria were pregnancy and contraindication to medication (heparin, clopidogrel, aspirin, and radiographic contrast agent).

## 2.2. Endovascular treatment procedures

All procedures were performed under general anesthesia. Patients were premedicated with antiplatelet therapy consisting of aspirin 300 mg and clopidogrel 75 mg for at least 3 days before the procedure. All patients received systemic heparinization to raise the activated clotting time (ACT) at about 300s during the procedure. An angiographic examination of the target vessel was performed to evaluate the aneurysm and the parent artery. The method of stenosis measurement was in accordance with the WASID study [1]. Unifemoral guiding catheter (Johnson & Johnson) was used. A 6F or 8F Envoy guiding catheter (Johnson & Johnson) was then guided into the targeted parent vessel. The Gateway balloon, which is used for pre-dilatation of the lesion prior to inserting the Wingspan stent, was sized to approximate the length of the lesion, and the diameter was estimated at 80% of the normal vessel size. The stent diameter was sized to exceed the diameter of the normal vessel by 0.5 mm. The stent length was estimated to cover the aneurysm neck and the entire diseased segment and to extend at least 3 mm on both of the proximal and distal sides. If necessary, two stents were used. Via the base catheter, a 300-cm exchange microwire (Transend Soft Tip or Transend Floppy, Boston Scientific, Boston, MA, USA) was manipulated across the stenosis. A Gateway balloon was introduced via the microwire to the stenosis lesion. After ascertainment of optimal location by angiography, the balloon was slowly inflated at 6-10 atm for about 10s. The balloon was removed and another angiography was performed. A Wingspan stent was advanced through the exchange microwire, centered across the lesion and deployed to cover the stenosis and the aneurysm neck. After the stent delivery system with the wire was removed, a microcatheter entered the aneurysm through the interstices of the stent and coiling was performed with a variety of commercially available coils.

After sufficient packing of the aneurysm, the microcatheter, guiding catheter and vascular sheath were withdrawn, and homeostasis was achieved by use of an artery closure device. The patient was moved to the neurosurgery intensive care unit for monitoring and received low-molecular weight heparin calcium 4000 IU/12 h for the next 3 days. Clopidogrel 75 mg daily was recommended for an additional 30 days, and aspirin 100 mg was recommended throughout follow-up.

### 2.3. Evaluation of outcomes

The primary endpoint for this study was defined as any stroke or death within 30 days, or stroke in the territory of the treated artery beyond 30 days. Stroke was defined as any hemorrhagic or ischemic event associated with a neurological deficit lasting longer than 24 h. Technical success was defined as performing the balloon angioplasty, placing the stent across the target lesion despite the degree of residual stenosis, and coiling the aneurysm sac. The angiographic results were classified as class 1: complete occlusion (no contrast filling the aneurysmal sac); class 2: neck remnant (residual contrast filling the aneurysmal neck); class 3: residual flow (residual contrast filling the aneurysmal body) [7]. Other procedure-related complications within 24 h and acute stent thrombosis were also evaluated.

During the hospital stays, physicians performed neurological examinations of the patients once each day. After discharge, clinical follow-up data were collected by clinic visitation, or telephone interview. More attention was paid to bleeding of embolized aneurysms, recurrence of ischemic symptoms and occurrence of new stroke.

Angiographic follow-up with DSA was recommended at 6 months and 1 year after the procedure. A follow-up angiographic evaluation was carried out in 31 patients (88.6%). Mean time interval between procedure and last follow-up angiography was 10.6 months. For each patient, the pre- and post-procedural and follow-up (if possible) angiograms were reviewed and compared by two senior endovascular neurosurgeons not involved in the procedure. At follow-up, an aneurysm was considered recanalization if a previously totally occluded aneurysm had a partial recurrence of the neck and/or the sac, or if a subtotally occluded aneurysm had an increasing neck remnant or residual aneurysm. Restenosis was defined as  $\geq$ 50% luminal narrowing.

## 3. Results

## 3.1. Technical and angiographic results

Technical success was achieved in all 35 patients included in the present study. The Wingspan stent was delivered and deployed to the intended location, even when severe vessel tortuousity was present. A microcatheter could easily be navigated through the stent struts into the aneurysm sac. No stent misplacement or dislodgment occurred during the procedure. The degree of stenosis was reduced from 71.1% (50–2%) to 17.4% (0–3%) after stenting. Angiographic results revealed class 1 occlusion in 25 of 35 aneurysms (71.4%), class 2 in 7 (20.0%), and class 3 in 3 (8.6%) (Figs. 1 and 2).

## 3.2. Periprocedural adverse events

Any stroke (ischemic or hemorrhagic) or death occurred in 2 patients within 24 h of the procedure (Table 2). Overall, the procedure-related morbidity and mortality were 5.7% and 0%, respectively. A 68-year-old woman (Patient 11) developed a thrombus in ipsilateral M1 segment at the end of the endosaccular

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Patient	Age (years)/sex	Presentation	Target lesion	Aneurysm size (mm)	Pretreatment stenosis (%)	Stenosis length (mm)	Embolization results	Posttreatment stenosis (%)	Adverse events	Angiographic follow-up
1	55/M	Stroke	ICA (supraclinoid)	5.0	80	7.0	Class 1	30		
2	48/M	Stroke	ICA (supraclinoid)	6.1	74	5.0	Class 1	25		
3	59/M	Recurrent TIAs	ICA (supraclinoid)	5.5	71	7.2	Class 2	15	Stent thrombosis	
4	57/F	Stroke	ICA (siphon)	7.5	50	5.0	Class 1	35		
5	71/F	TIA	V4	3.0	89	4.5	Class 1	0		
6	50/M	TIA	ICA (caverous)	4.5	55	6.1	Class 1	10	Stroke on 21 days	
7	49/M	TIA	V4	5.3	52	4.0	Class 1	20	5	
8	55/F	TIA	ICA (supraclinoid)	4.1	70	3.4	Class 1	0		
9	61/F	Recurrent TIAs	ICA (siphon)	2.5	75	5.1	Class 1	23		
10	63/M	Stroke	ICA (caverous)	12.0	75	6.0	Class 2	11		
11	68/F	Stroke	ICA (terminus)	9.8	60	9.0	Class 1	8	Stroke within 24 h	
12	52/M	Stroke	ICA (terminus)	6.3	81	3.3	Class 2	5		Restenosis
13	65/F	TIA	V4	6.0	66	6.3	Class 1	18		
14	60/F	TIA	V4	5.6	64	4.5	Class 1	20		
15	57/M	Recurrent strokes	ICA (siphon)	15.0	77	5.1	Class 2	15		Recanalization
16	69/F	TIA	ICA (terminus)	2.5	56	10.5	Class 3	10	Coil stretching	NA
17	56/M	Stroke	ICA (siphon)	5.4	55	7.0	Class 1	0	0	
18	49/M	Stroke	ICA (siphon)	8.0	92	3.0	Class 1	40	Stroke at 6 months	Restenosis
19	79/M	Recurrent TIAs	BA	9.2	89	3.0	Class 1	5		NA
20	62//F	TIA	BA	6.0	74	3.8	Class 2	30		
21	66/M	Recurrent strokes	ICA (supraclinoid)	6.0	77	4.5	Class 1	12		
22	53/M	TIA	VB junction	11.0	58	4.0	Class 2	8		
23	53/F	Recurrent strokes	ВА	6.9	52	4.0	Class 1	10	Stroke within 24 h	
24	61/F	Stroke	BA	4.5	90	4.8	Class 3	43	Vasospasm	Restenosis
25	55/F	TIA	ICA (supraclinoid)	3.7	83	6.5	Class 1	30		
26	56/M	Stroke	ICA (supraclinoid)	57	70	59	Class 1	10		
27	74/F	Stroke	ICA (siphon)	10.3	71	35	Class 1	25		NA
28	58/M	TIA	ICA (supraclinoid)	85	60	8.0	Class 1	0		
29	63/F	TIA	ICA (supraclinoid)	18.0	76	3.0	Class 3	30		Recanalization
30	64/M	Stroke	ICA (supraclinoid)	5.6	82	7.0	Class 1	30		Restenosis
31	77/M	TIA	ICA (terminus)	33	70	63	Class 2	22		NA
32	50/F	TIA	BA	2.8	65	3.6	Class 1	14		
33	71/M	TIA	ICA (terminus)	6.5	85	4.5	Class 1	31		
34	66/M	Recurrent TIAs	V4	8.0	64	7.0	Class 1	10		
35	62/F	Recurrent TIAs	ICA (siphon)	7.8	80	11.2	Class 1	14		

## Table 1Summary of relevant clinical and angiographic data in 35 patients.

Note: ICA, internal carotid artery; VA, vertebral artery; BA, basilar artery; VB, vertebrobasilar; TIA, transient ischemic attack.

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**Fig. 1.** Patient 8, a 55-year-old woman. Angiography showed a supraclinoid segment stenosis associated with an aneurysm of the right ICA (A, B). After stent (4 mm × 20 mm) was deployed to cover the lesion and aneurysm neck, a microcatheter entered the aneurysm through the interstices of the stent and coiling was performed (C). Postprocedural (D) and follow-up (E) angiogram revealed complete occlusion of the aneurysm and revascularization of the parent artery.

## Table 2

Periprocedural adverse events.

Complication	No sequela	Morbidity	Mortality	Total	Incidence (%)
Thrombosis	1	1	0	2	5.7
Small penetrating arteries occlusion	0	1	0	1	2.9
Coil stretching	1	0	0	1	2.9
Vasospasm	1	0	0	1	2.9

Note: Results include patients with more than one complication.

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**Fig. 2.** Patient 19, a 79-year-old man. Frontal and lateral angiogram showed a stenosis associated with an aneurysm of the superior basilar artery (A, B). Postprocedural angiogram (C, D) revealed complete occlusion of the aneurysm and revascularization of the parent artery.

coiling procedure. Intra-arterial injection and mechanical disruption were done immediately and partial recanalization was achieved. Angiogram demonstrated that flow into the inferior branch of the middle artery was delayed. After the procedure, the ipsilateral cerebral hemisphere infarction was noted by MRI. Eventually, she suffered from a contralateral hemiparesis at discharge. A 53-year-old woman (Patient 23) developed severe vertigo and nausea about 6 h after the procedure. Diffusion-weighted MRI demonstrated increased signal in the pons. The mechanism was suggested that angioplasty and stenting resulted in occlusion of a small penetrating artery from the basilar artery, though direct evidence was not found by angiography. Eventually, she suffered from an ipsilateral facial sensory disturbance at discharge.

Other procedure-related complications included one case of stent thrombosis that was successfully treated with local administration of urokinase, one case of last coil stretching which was of no clinical consequence and one case of asymptomatic transient vasospasm.

#### 3.3. Primary endpoint during follow-up

Mean time from endovascular procedure to primary endpoint or last clinical follow-up was 18.3 months (range of 1 day to 37 months). One additional ischemic stroke occurred on 15 days, and one additional ischemic stroke in the territory of the treated artery at 6 months. The former was of unknown cause, and the latter was caused by in-stent restenosis. No hemorrhage of treated aneurysm occurred. The event rate of primary endpoint was 11.4%.

## 3.4. Angiographic follow-up

Of the 31 patients who underwent angiographic follow-up, 4 have demonstrated in-stent restenosis (12.9%). Three patients developed an asymptomatic restenosis 6, 9, 14 months after the procedure. The other patient experienced a symptomatic restenosis 6 months after the procedure. In view of the severity of the stenosis and symptoms while on aspirin, balloon angioplasty was performed. Postprocedural control angiography demonstrated substantial improvement in the caliber and the patient recovered fully. In these angiographic followed aneurysms, 2 aneurysms (6.4% of the follow-up angiograms) demonstrated recanalization. The patients' angiogram showed an increasing remnant neck on the 3-month follow-up examination, but the sequent follow-up angiogram showed a stable appearance. Therefore, re-embolization was not a treatment option for them.

## 4. Discussion

The prevalence of intracranial aneurysm in the adult population ranges from 1 to 5%, according to autopsy studies [8]. All aneurysms do not rupture. The International Study of Unruptured Intracranial Aneurysms (ISUIA) demonstrated extremely low rupture rates for small anterior circulation aneurysms measuring <7 mm (0% risk of SAH in 5 years) [9]. However, because of the dismal prognosis for a subarachnoid hemorrhage caused by aneurysm rupture, preventive treatment is increasingly considered necessary. It was presumed that marked stenosis may have protective effect on an

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aneurysm distal to the occlusion [10]. Reduction in the aneurysm size has been documented after intentional partial carotid occlusion [11]. On the contrary, improved cerebral blood flow after stenting may have negative effects. Recently, it has been hypothesized that the rupture mechanism is via the intra-aneurysmal hemodynamic environment created by a particular geometry [12]. Several studies have evaluated the relationship between intraaneurysmal hemodynamic and IA growth and rupture risk [13–15]. Computational fluid dynamics (CFD) studies of intra-aneurysmal hemodynamic have identified certain flow characteristics to be specific to ruptured aneurysms and, therefore, classified as potentially "dangerous", such as intra-aneurysmal pressure, blood flow pattern, and wall shear stress (WSS) [16]. According to Poiseuille's law, the increase in the amount of blood is 4 times the increase in the vessel diameter. Based on these studies, high blood velocity, pressure and WSS environment caused by restoring parent artery after stenting may increase the risk of aneurysm rupture. Post-procedural antiplatelet therapy is disastrous if the aneurysm ruptures. Additionally, some of these aneurysms are probably dissections, the hemorrhagic risk of which is rather high. Therefore, prevention of aneurysm hemorrhage after stenting is a significant objective to be achieved.

This study provides preliminary data on experience with Wingspan stent in combination with endosaccular coiling to treat aneurysm associated with symptomatic parent artery stenosis. In our series, we did not experience any technical difficulty. Not a single one of treated aneurysms experienced rehemorrhage during the follow-up time, despite incomplete occlusion and recanalization. The overall procedure-related morbidity and mortality in this study were 5.7% and 0%, respectively and is similar to periprocedural rates of stroke or death in two other Wingspan series of symptomatic patients with 50–99% stenosis (6.1–6.7%) [17–19]. It seems that the Wingspan-assisted coiling does not increase the risk of procedure.

Though restenosis must be acknowledged as a failure of treatment, prevention of ischemic infarction is another significant objective to be achieved. In our series, the event rate of primary endpoint was 11.4% (mean follow-up time 18.3 months), which is acceptable compared with the rate of stroke in other series [20,21] (8.3-14.0%). At follow-up, four cases of in-stent restenosis (12.9%) were identified, only one of which was symptomatic. The risk of stroke associated with restenosis after stenting of an intracranial artery has not been well studied, however, the risk of stroke associated with restenosis after extracranial carotid stenting appears to be low [22]. This is probably related to the fact that restenosis within the first 6 months of stenting is usually due to neointimal proliferation rather than recurrent atherosclerosis. Neointimal proliferation results in a smooth endothelial surface which is less likely to ulcerate or produce turbulent flow and distal embolization than atherosclerotic stenosis [23]. According to our experience of stent-assisted coiling with other stent (e.g., the Neuroform, Enterprise, Solitaire AB stent), the use of bioactive coils in conjunction with the stent should be avoided. In our series, when asymptomatic in-stent restenosis is identified, patients are maintained on dual antiplatelet therapy and strongly recommended for angiographic follow-up and maximal statin therapy (atorvastatin 60-80 mg daily).

We acknowledge that this study has several limitations: (1) it was not designed as a prospective clinical trial, allowing the results to be confounded by physician's bias on patient selection; (2) because no randomization to other therapeutic approaches including surgical procedure, medical therapy, our data cannot directly address the relative superiority or inferiority of an approach to these lesions and only portray a snapshot of current technique and its associated results; (3) the small number of patients makes the estimation of event rate of primary endpoint imprecise; (4) we do not perform VerifyNow test to measure patients' response to antiplatelet therapy before stenting.

## 5. Conclusion

Our study indicates that Wingspan-sent-assisted coiling of intracranial aneurysm associated with parent artery stenosis is an effective technique with low morbidity and mortality rates. In our hand, this technique does not increase the rate of symptomatic restenosis. Nevertheless, additional, large series with long-term follow-up are necessary to determine the durability of these promising results.

### **Conflict of interest**

None declared.

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