Middle- and Long-term Results of Stent-assisted Coil Embolization for Cerebral Aneurysms: Evaluation of Changes in the Aneurysmal Occlusion and Complications

Masanobu Okauchi, Masahiko Kawanishi, Atsushi Shindo, Kenya Kawakita, and Takashi Tamiya

Objective: Since stenting for assisting cerebral aneurysm embolization was approved, the therapeutic results of coil embolization for cerebral aneurysm have improved. However, various complications due to stent placement, including thromboembolism, have also been reported.

Materials and Methods: In 32 patients who could be followed up after stent-assisted coil embolization of cerebral aneurysms, chronological changes in the aneurysmal occlusion and characteristic complications were evaluated.

Results: The aneurysmal occlusion immediately after the treatment was complete occlusion (CO) in 6 patients (18.8%), neck remnant (NR) in 10 patients (31.1%), and body filling (BF) in 16 patients (50.0%). The aneurysmal occlusion at the follow-up was CO in 17 patients (53.1%), and aneurysmal obliteration was advanced in 14 patients (43.8%) during the follow-up period. As there are complications due to stent placement, occlusion of the parent vessel was noted during the treatment in one patient, and stenosis or kinking of the parent vessel or branches was observed during the follow-up in four patients. Of these four patients, two patients showed in-stent stenosis, one patient showed kinking of the parent vessel associated with linearization of the vessel by stenting, and one patient showed stenosis of a vessel branching from the site of stenting. All were asymptomatic.

Conclusion: Serial improvements in the aneurysmal occlusion were observed after stent-assisted coil embolization. Stenosis due to stretching of the parent vessel as well as in-stent embolization or stenosis may occur as characteristic complications of stenting, and long-term follow-up is necessary.

Keywords ► cerebral aneurysm, stent-assisted coil embolization, outcome, complication

Introduction

Enterprise Vascular Reconstruction Device (VRD; Codman, Miami, FL, USA) and Neuroform EZ (Stryker, Kalamazoo, MI, USA), which are the stents used to assist coil embolization of cerebral aneurysms, were approved in Japan in July 2010 and October 2012, respectively. The therapeutic results

have been improved using these stents even in wide-necked and large aneurysms,^{1,2)} in which the recurrence rate is reported to be high. However, as stent-assisted coil embolization is a procedure involving the placement of a foreign body in a normal part of the blood vessel, attention to various complications, including thromboembolism, is necessary. In this study, we evaluated the middle- and long-term results of stent-assisted coil embolization of cerebral aneurysms and experienced characteristic complications that need particular attention. Our findings are reported with a review of the literature.

Materials and Methods

Between July 2010, when Enterprise VRD was approved, and December 2014, coil embolization was performed in

Department of Neurological Surgery, Kagawa University Faculty of Medicine, Kagawa, Japan

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Corresponding author: Masanobu Okauchi. Department of Neurological Surgery, Kagawa University Faculty of Medicine, 1750-1 Ikenobe, Miki-cho, Kita-gun, Kagawa 761-0793, Japan

Email: okauchi@med.kagawa-u.ac.jp

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245 patients for saccular cerebral aneurysms at our department and affiliated hospitals. Stents were used in patients with a wide-necked aneurysm in whom the parent artery was difficult to preserve by adjunct techniques such as the balloon-assisted and double catheter techniques. Stent-assisted coil embolization was performed in 47 patients (19.2%), and 32 of them who could be followed up were included in this study. The extent of aneurysmal occlusion was evaluated immediately after the procedure and during the follow-up periods. Complications in the peri-procedural and follow-up periods were also evaluated.

According to the protocol of stent-assisted coil embolization at our institution, 100 mg aspirin and 75 mg clopidogrel were administered for at least 1 week before embolization. For patients in whom a more potent antiplatelet effect was desirable, such as those with a parent vessel with a small diameter and those in whom preservation of branches near the aneurysm was necessary, 200 mg cilostazol was added for 1–3 days before the procedure. During the procedure, the activated clotting time (ACT) was maintained twice the pre-procedural level or 250 seconds or longer by intravenous heparin administration, which was tapered off after the procedure. Post-procedurally, argatroban was continuously administered at 5 mg/hour for 48 hours, and MRI and X-ray of the head were performed within a few days. If thrombotic complication was not noted, cilostazol administration was discontinued at discharge. MRI was performed 3–6 months after the procedure, and the number of antiplatelets was reduced to 1 when the results were good. DSA was performed 1 year after the procedure, and antiplatelet therapy was discontinued if the aneurysm was completely occluded, the stent was affixed satisfactorily, and the estimated risk of complications was low. Thereafter, MRI and X-ray of the head were performed annually, and, if there was any change, DSA was performed for checking.

Results

The subjects consisted of 10 males and 22 females with a mean age of 62.3 years (38–86 years). The mean maximum aneurysm diameter was 12.4 mm (4–25 mm), and the mean neck diameter was 6.3 mm (4–10 mm). The sites of the aneurysms are shown in **Table 1**. Coil embolization was performed in five ruptured aneurysms in the acute phase and five ruptured aneurysms in the chronic phase (all had recurred after coil embolization in the acute phase) and 22 unruptured aneurysms (of which three had recurred after coil embolization). As for stents, Enterprise VRD was

Table 1 Aneurysm characteristics

Number of aneurysms	32
Size	
Small	13
Large	18
Giant	1
Location	
Anterior circulation	20
Cavernous internal carotid artery	2
Paraclinoid internal carotid artery	8
Posterior communicating artery	4
Internal carotid artery bifurcation	2
Anterior communicating artery	2
Anterior cerebral artery	2
Posterior circulation	12
Vertebral artery	1
Posterior inferior cerebellar artery	3
Basilar trunk	2
Superior cerebellar artery	4
Basilar tip	2

Aneurysm sizes are classified as small (<10 mm), large (≥10 mm and <25 mm), giant (≥25 mm).

used in 24 patients, Neuroform EZ was used in 5 patients, and multiple stents were used in 3 patients. The mean follow-up period was 31 months (5–53 months).

Extent of aneurysmal occlusion immediately after treatment was complete occlusion (CO) in 6 patients (18.8%), neck remnant (NR) in 10 patients (31.1%), and body filling (BF) in 16 patients (50.0%) (**Fig. 1A**). Peri-procedural complications were observed in four patients (12.5%), and they were parent vessel occlusion, non-aneurysmal subarachnoid hemorrhage, coil unraveling, and stent migration in one patient each. Subarachnoid hemorrhage occurred in a patient of unruptured aneurysm in basilar artery fenestration who underwent stent-assisted coil embolization using an occlusion balloon, and bleeding is considered to have been caused by overdilation of the balloon. In the patient who suffered stent migration, downward migration of the stent was developed during retrieval of unraveled coil during the embolization using a Goose-Neck Snare Catheter (Covidien, Plymouth, MA, USA). Since the stent was covering the aneurysmal neck and most part of the unraveled coil was remained inside the aneurysmal dome, the procedure was terminated at this point. Two patients (6.3%) suffered symptomatic complications, which were parent artery occlusion and subarachnoid hemorrhage that occurred with headache and recurrence without rupture, respectively. The symptoms were resolved in both patients after 90 days. The aneurysmal occlusion at follow-up was CO in 17 patients (53.1%), NR in 8 patients (25.0%), and BF in 7 patients (21.9%) (**Fig. 1A**). The aneurysmal occlusion was advanced during follow-up in

Fig. 1 Aneurysmal occlusion immediately after coiling of cerebral aneurysms and at follow-up (**A**) and its changes during follow-up (**B**).

Fig. 2 Case 1. (**A**) Pre-procedural right vertebral arteriography showed a cerebral aneurysm 7 mm in diameter at the end of the basilar artery. (**B**) Enterprise VRD was placed in the basilar artery via the right posterior cerebral artery. (**C**) Coil embolization was performed with an outcome of NR. (**D**) The outcome improved to CO on DSA after 1 year. CO: complete occlusion; NR: neck remnant; VRD: vascular reconstruction device

14 patients (43.8%), unchanged in 13 patients (40.6%), and exacerbated in 5 patients (15.6%) (**Fig. 1B**). Exacerbation was observed in lesions in the cavernous segment of the internal carotid artery, clinoid segment of the internal carotid artery, at the bifurcation of the internal carotid and posterior communicating arteries, the bifurcation of the internal carotid artery, and in the basilar artery in one patient each. Many of these aneurysms were large with a mean maximum diameter of 18.0 (12–22) mm, and all were treated using Enterprise VRD. None of them needed retreatment. As for complications observed during follow-up, transient cerebral ischemic attacks were noted in one patient (3.1%), stenosis or bending of the parent artery or branches was noted in four patients (12.5%), but all were asymptomatic. Of the four patients who had stenosis, two patients showed in-stent stenosis, one patient showed bending of the parent artery at the distal end of the stent due to straightening of the vessel by stent, and one patient showed stenosis of a branch arising from the site of stent. All these conditions were detected by DSA after 1 year.

Case 1

In Case 1, 66-year-old woman, an unruptured cerebral aneurysm 7 mm in diameter was detected at the tip of the basilar artery by head MRI performed for diabetes screening, and coil embolization was selected as a treatment (**Fig. 2A**). Since the aneurysm was wide necked (5 mm), concomitant stenting was considered necessary. Coil embolization was performed by placing an Enterprise VRD (4.5 × 28 mm) in the basilar artery (diameter: 3.1 mm) via the right posterior cerebral artery (2.2 mm) (**Fig. 2B**). The treatment was completed with the aneurysmal occlusion of NR (**Fig. 2C**), but it improved to CO on DSA performed after 1 year (**Fig. 2D**).

Case 2

In Case 2, 74-year-old woman, cerebral aneurysm was detected in the left anterior cerebral artery by head MRI, which was performed due to headache that had continued for a few days. No subarachnoid hemorrhage was noted, but as no aneurysm was noted on MRI 1 year before, we

Fig. 3 Case 2. (A) Pre-procedural left internal carotid arteriography showed a cerebral aneurysm 11 mm in diameter in the left anterior cerebral artery. (B) Enterprise VRD was placed in the left anterior cerebral artery, and coil embolization was performed with an outcome of CO, but the left anterior cerebral artery was occluded in the stent. (C) Slight recanalization could be achieved by intra-arterial infusion of 120000 units of urokinase and 40 mg of sodium ozagrel (arrow). (D) Post-procedural diffusion-weighted MR imaging of the head showed acute cerebral infarction in the left anterior lobe. CO: complete occlusion; MR: magnetic resonance; VRD: vascular reconstruction device

Fig. 4 Case 3. (A) Pre-procedural right vertebral arteriography showed an aneurysm 8 mm in diameter at the orifice of the right superior cerebellar artery. (B) Enterprise VRD was placed in the basilar artery via the left posterior cerebral artery. (C) Coil embolization was performed, resulting in NR. (D) The aneurysmal occlusion was advanced to CO on DSA after 1 year, but the left posterior cerebral artery was extended and was stenosed due to kinking at the distal end of the stent (arrow). (E) On DSA after 2 years, no marked change was observed in the aneurysmal occlusion of the aneurysm or the vessel bending. CO: complete occlusion; NR: neck remnant; VRD: vascular reconstruction device

assessed that there was a warning sign of bleeding and decided to perform emergency stent-assisted coil embolization. Before the procedure, 300 mg clopidogrel and 300 mg aspirin were administered. On cerebral angiography, an aneurysm of 11 mm in diameter was confirmed in the left anterior cerebral artery, the diameter of which was 2.3 and 1.9 mm on the proximal and distal sides of the aneurysm, respectively (**Fig. 3A**). Coil embolization was performed by placing an Enterprise VRD (4.5 mm × 22 mm) in the left anterior cerebral artery, and the procedure was completed in a condition of CO, but angiography performed after the removal of the microcatheter showed occlusion of the left anterior cerebral artery in the stent (**Fig. 3B**). Although recanalization could be achieved by intra-arterial administration of 120000 units of urokinase and 40 mg of sodium ozagrel (**Fig. 3C**), post-procedural MRI showed cerebral infarction in the left frontal lobe (**Fig. 3D**). Although left-sided paralysis appeared, it was

alleviated to a level not interfering with daily living (mRS1) at discharge after 1 month.

Case 3

In this 70-year-old male, an unruptured aneurysm was detected at the bifurcation of the basilar artery and right superior cerebellar artery during examination for nystagmus, and treatment by coil embolization was selected (**Fig. 4A**). The aneurysm was 8 mm in diameter and was wide necked with a neck diameter of 6 mm. Coil embolization was performed by placing an Enterprise VRD (4.5 × 28 mm) in the basilar artery (diameter: 2.8 mm) via the left posterior cerebral artery (2.0 mm) (**Fig. 4B**). The aneurysmal occlusion at the end of the procedure was slight NR (**Fig. 4C**) but was improved to CO on DSA performed after 1 year. However, the left posterior cerebral artery, in which the stent was placed, was extended and bended and narrowed at the distal end of the stent (**Fig. 4D**). Although

the patient was asymptomatic, he was observed by continuing single-drug antiplatelet therapy. DSA performed after 2 years showed no marked change in the aneurysmal occlusion of the aneurysm or bending of the left posterior cerebral artery, and the patient remained asymptomatic (Fig. 4E).

Discussion

In Western countries, the use of stents to assist embolization of cerebral aneurysms has been started earlier than in Japan, and multiple reports have appeared concerning the long-term results of large-scale studies.³⁻⁷⁾ The CO rate was 28.4%–46.3% immediately after stent-assisted coil embolization and 53.7%–90.8% at follow-up, and the recanalization rate was 1.3%–8.0%. In Japan, PMS Update Vol. 6 Codman Enterprise VRD⁸⁾ was issued in July 2015, reporting a CO rate of 24.4% immediately after the procedure and 50.8% after 3 years, and a recanalization rate during follow-up was 5.1%. In our report, the CO rate immediately after the procedure was 18.8%, but it increased to 53.1% at follow-up, and the results were comparable to those reported previously. In addition, the advancement in the aneurysmal occlusion was noted in 43.8% of the patients at follow-up, that is equivalent to 44% reported by Geyik et al.³⁾ The aneurysmal occlusion was aggravated in five patients (15.6%), all with a large aneurysm (maximum diameter: 12–22 mm). The PMS study also reported that the recanalization rate was significantly higher in aneurysms 10 mm or greater in diameter.⁸⁾ According to the site of aneurysm, exacerbation was observed more frequently in aneurysms of the posterior circulation, such as those at the tip of the basilar artery and in the intracranial vertebral artery, in the PMS study.⁸⁾ In our study, however, four of the five aneurysms that showed exacerbation were located in the internal carotid system.

Since stent-assisted coil embolization is a procedure involving the placement of a foreign body in the parent artery, and since thromboembolic complications occur more frequently than in non-stent-assisted coil embolization,⁴⁾ it is indisputable that the procedure must be performed cautiously. According to our report, thromboembolic complications occurred in two patients (6.3%), who suffered peri-procedural occlusion of the parent artery due to in-stent thrombosis and transient ischemic attacks during follow-up, and their incidence was similar to that in previous large-scale studies (4.2%–6.0%).^{3,4,6)} Bechan

et al.⁹⁾ compared the frequency of complications of stent-assisted coil embolization between ruptured and unruptured cerebral aneurysms and reported that symptomatic complications were observed in 22.2% and 2.2%, respectively, with a significant difference. According to the post marketing surveillance (PMS) study, the incidence of infarct complications within 30 days after the procedure was 5.0%, but it was higher in ruptured cerebral aneurysms (18.8%) and aneurysms with a parent artery less than 2.5 mm in diameter (11.4%).⁸⁾ Our patient who developed in-stent occlusion after stenting of the anterior cerebral artery (Case 2) had the onset with headache predictive of bleeding. Therefore, more careful measures to prevent thrombosis are required particularly when stents are placed in small vessels. Geyik et al.³⁾ reported that thromboembolic complications decreased after the beginning of the use of VerifyNow (Accumetrics, San Diego, CA, USA) and speculated that the increase in thromboembolic complications of stenting can be prevented by administering dual-antiplatelet therapy after confirming the absence of tolerance to drug.

Another characteristic complication of stenting is stenosis or bending of the parent artery or branches. Post-procedural in-stent stenosis was reported to be observed in 0.8%–5.8% of the patients.^{3,5-7,10)} According to the report by Fiorella et al.,¹⁰⁾ in-stent stenosis was observed in nine patients (5.8%) after treatment using Neuroform, and it was symptomatic in two patients. Antiplatelet therapy was continued in all patients, and stenosis was alleviated in four patients but progressed to CO in one patient on a long-term follow-up. Kim et al.¹¹⁾ evaluated in-stent stenosis after stent-assisted coil embolization in 99 patients with aneurysms in the internal carotid artery and reported that the parent artery was narrowed to a mean diameter of 82% after 8 months, that it improved to 91% after 25 months, that stenosis to 40% or less was noted in 7%, but that none of the patients required additional treatment. In our patients, in-stent stenosis was observed in two patients (6.3%), but both have remained asymptomatic with single-drug antiplatelet therapy and are still followed up. We also experienced a patient who developed stenosis of the parent artery due to straightening of the vessel by stenting, and this is also a complication of stent placement that needs attention. Flow diversion is an advantage of stent-assisted treatment that the stent changes the course of the parent vessel and attenuates the momentum of the blood flow into the aneurysm, promoting thrombosis in the aneurysm.¹²⁾ However, when a stent is placed in a tortuous small vessel, attention to the possibility of marked bending

of the vessel at the end of the stent due to stretching of the vessel is necessary.

Conclusion

The middle- and long-term results of stent-assisted coil embolization for cerebral aneurysms were reported, and changes in the aneurysmal occlusion and characteristic complications were evaluated. The aneurysmal occlusion was advanced with time by the concomitant use of stents. Since not only in-stent occlusion or stenosis but also stenosis due to stretching of the parent vessel may occur as complications characteristic of stenting, long-term follow-up is necessary.

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Disclosure Statement

All authors have completed a self-report of conflict of interest (COI) to the Japan Neurosurgical Society. There are no COI to declare in publishing this paper.

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