Efficacy and Safety of Flow-Diverter Therapy for Recurrent Aneurysms after Stent-Assisted Coiling

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ABSTRACT

BACKGROUND AND PURPOSE: Flow-diverter treatment for previously stented aneurysms has been reported to be less effective and prone to complications. In this study, we evaluated the effectiveness and safety of flow diverters for recurrent aneurysms after stent-assisted coiling.

MATERIALS AND METHODS: Patients who underwent flow-diverter placement for recurrent aneurysms after stent-assisted coiling between March 2015 and March 2019 were recruited. Clinical and radiographic characteristics and clinical and angiographic outcomes were retrospectively evaluated.

RESULTS: Among 133 patients who underwent flow-diverter insertion, 17 (male/female ratio = 5:12; mean age, 53.8 years) were treated for recurrent aneurysms after stent placement with (n = 16) or without (n = 1) coiling. Eight patients initially presented with subarachnoid hemorrhage; 7, with headache; and 2, with visual field defects. Angiographic morphology included large/giant saccular in 12 patients, dissecting in 2, fusiform in 1, traumatic pseudoaneurysm in 1, and ruptured blood blister-like aneurysm in 1. The duration between the first treatment and flow-diverter placement ranged from 2 weeks to 15 months (median, 6 months). Flow-diverter placement was successful in all cases without any complications. All patients had favorable outcomes (mRS, 0–2), without any newly appearing symptoms. Aneurysms were followed up with conventional angiography at least once in 6–18 months. Sixteen aneurysms showed complete occlusion, and 1 aneurysm was enlarged.

CONCLUSIONS: Results from this case series investigating flow-diverter placement for recurrent aneurysms after stent-assisted coiling suggested that the procedure is safe and effective. Further study in a larger population may be warranted.

ABBREVIATIONS: LVIS = low-profile visualized intraluminal support; PED = Pipeline Embolization Device; SAC = stent-assisted coiling

Endovascular coil embolization is a standard treatment for intracranial aneurysms. However, its durability and potential for angiographic recurrence are still major shortcomings.1,2 Although stent placement with coil can help enhance durability, the recurrence rate is reported to be approximately up to 14.9%, even after successful stent-assisted coiling (SAC).3 Conversely, retreatment of previously stented aneurysms is challenging for both neurosurgeons and neurointerventionalists due to its questionable efficacy and safety.4,5 Thus, neither conventional clipping nor coil has provided reasonable outcomes as a retreatment technique for recurrent aneurysms after SAC.

Following the introduction of the early version of the Pipeline Embolization Device (PED; Medtronic, Minneapolis, Minnesota),6,7 flow diverters have gained increasing acceptance for aneurysm treatment. In particular, these were useful for the treatment of complex and complicated aneurysms, such as large or giant, dissecting, and blood blister-like aneurysms. Additionally, these types of aneurysms were also susceptible to recurrence.8-11 Thus, flow diverters may be an alternative treatment option for recurrent aneurysms after SAC. Unfortunately, previous studies on flow-diverter treatment for previously stented aneurysms reported some technical issues and unfavorable results.12-16 Nelson et al17 reported that 1 in 4 aneurysms previously treated with another stent was not occluded at

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180 days after PED placement. Fischer et al\textsuperscript{13} reported that the adverse event rate was 13%, and the successful occlusion rate was 65% in 30 cases of PED for recurrent aneurysms after SAC. Daou et al\textsuperscript{15} reported that the complete occlusion rate was 55.6%, with a 14.3% complication rate in PEDs after SAC. However, recent neurointerventional techniques and devices may be helpful in overcoming these technical issues, and more acceptable outcomes are expected.

In the present study, we report on the effectiveness and safety of flow-diverter treatment for recurrent aneurysms after SAC.

**MATERIALS AND METHODS**

The institutional review board of each hospital approved this study and waived the requirement for patient informed consent due to its retrospective design. After the introduction of the PED, patients who underwent flow-diverter placement for the treatment of recurrent aneurysms after SAC in 5 hospitals between March 2015 and March 2019 were recruited.

Planning of flow-diverter treatment was based on consensus by a multidisciplinary team meeting after the careful evaluation of 3D angiograms. Flow-diverter placement was chosen as a retreatment method after agreement that the initial aneurysm was large/giant, ruptured dissecting, or blood blister-like. On the basis of previous results, those types of aneurysms were thought to be prone to re-recurrence, even if retreatment was successful with additional coil insertion.

In cases in which dual-antiplatelet medication was stopped or changed to aspirin monotherapy before the PED retreatment procedure, dual-antiplatelet medication (aspirin, 100 mg, and clopidogrel, 75 mg) was resumed for at least 5 days. Because no patient showed resistance on the antiplatelet resistance test at the initial SAC and no patient had thromboembolic events during follow-up, an additional antiplatelet resistance test before PED placement was not routinely performed. After the completion of treatment, the dual-antiplatelet medication was maintained for at least 6 months, and subsequently, the regimen was changed to aspirin monotherapy, which was continued indefinitely.

All clinical and radiologic data were obtained from the electronic medical records and a prospectively registered aneurysm data base. Data were retrospectively reviewed.

**Flow-Diverter Placement**

All procedures were conducted with the patient under general anesthesia. A 5F intermediate catheter was used in all except 3 cases, combined with a 6F or 7F Shuttle guide sheath (Cook, Bloomington, Indiana) or a 6F Neuron MAX (Penumbra, Alameda, California). The routine procedural details were as follows: 1) After the placement of a 5F intermediate catheter (Sofia; MicroVention, Aliso Viejo, California; Navien, Medtronic, Minneapolis, Minnesota; Revive, Codman Neurovascular, Raynham, Massachusetts) within a 6F or 7F Shuttle or a 6F Neuron MAX catheter, the Markman catheter (Medtronic) was introduced and advanced over a 0.014-inch guidewire into 1 branch of the parent artery beyond the stented segment; 2) the intermediate catheter was advanced over the Markman catheter and microwire as far as possible beyond the stented segment of the parent artery; 3) the size-matched flow diverter was introduced and placed to span the entire stented segment; if required, multiple flow diverters were used to span the entire stented segment; and 4) if an immediate postimplantation angiogram or flat panel CT image showed equivocal apposition of the flow diverter and a previously placed stent in the segment where a metallic artifact due to the coil mass was not prominent, or if the apposition between the PED and the preplaced stent could not be assessed due to the surrounding coil mass (Fig 1), balloon angioplasty was performed for better apposition between the preplaced stent and the flow diverter.

**Clinical and Angiographic Follow-Up**

Routine clinical follow-up was performed at 1, 3, 6, and 18 months. Routine angiographic follow-up was performed at 6 months. If the 6-month angiogram did not show complete occlusion of the aneurysm, further follow-up angiographies were scheduled at 12 months and 18–24 months.

**Outcome Measurements**

Procedural success was defined as the full expansion of the flow diverter spanning the entire stented segment of the parent artery. Clinical outcomes were assessed with the mRS at the latest clinical follow-up. Treatment-related morbidity was defined as the development of any new deficit due to treatment-related complications that were still present at discharge. Treatment-related mortality was defined as death of the patient from treatment-related complications during admission or clinical follow-up. In addition, any treatment-related complication other than neurologic complication was evaluated. Follow-up angiographic outcomes were assessed according to the Raymond class, in which class 1 is defined as complete occlusion; class 2, as neck remnant; and class 3, as sac remnant.\textsuperscript{17}

The procedural success rate, treatment-related morbidity and mortality, and clinical and angiographic follow-up outcomes were retrospectively assessed.

**Statistical Analysis**

Because this study included the results of a single arm of flow-diverter insertion for recurrent aneurysms after SAC, without comparison with other types of treatment, only descriptive statistics are presented. All data are presented as mean and range for continuous variables and number and percentage for categorical variables.

**RESULTS**

Among 133 patients who underwent flow-diverter insertion, 17 (male/female ratio = 5:12; mean age, 53.8 years) were treated for recurrent aneurysms after stent placement with (n = 16) or without (n = 1) coiling. Baseline characteristics of patients and aneurysms and follow-up clinical and angiographic outcomes are shown in the On-line Table.

Eight patients initially presented with subarachnoid hemorrhage; 7, with headache; and 2, with a visual field defect. Except for 1 patient (case 7, Fig 1) who presented with a ruptured ICA fusiform aneurysm and had end-stage renal disease, no patient had an underlying comorbidity. The aneurysm types included large/giant saccular in 12 patients, dissecting in 2, fusiform in 1...
traumatic pseudoaneurysm in 1, and blood blister-like in 1; and the aneurysm locations were the ICA intradural segment in 13 patients, ICA cavernous segment in 1, MCA in 2, and anterior communicating artery in 1 (Fig 2). The types of stents initially used were the Enterprise (Codman Neurovascular) in 11 patients and the Low-Profile Visualized Intraluminal Support (LVIS; MicroVention), Blue, or Jr in 6. Flow-diverter placement was successful in all patients. At retreatment, the mRS was 0 in nine, 1 in four, 2 in 2, and 3 in 2 patients, respectively. The duration between the first treatment and flow-diverter placement ranged from 2 weeks to 15 months (median, 6 months). One patient was retreated 2 weeks after initial treatment. The patient (case 17) had a ruptured blood blister-like aneurysm and showed aneurysm enlargement from 3.5 to 5 mm at 2 weeks’ follow-up angiography after overlapping of 3 LVIS stents as the initial treatment. Due to fear of rehemorrhage, the patient was urgently retreated with 2 PEDs.

A single PED was used in 14; two PEDs, in 2; and 3 PEDs, in 1 patient. Of a total of 21 PEDs, PED Classic and PED Flex were used in 7 and 14, respectively. In every case, the previously stented segment was completely covered by the PED. Balloon angioplasty was performed because incomplete expansion or poor apposition of the PED was suspected in 4 cases, and the apposition between the PED and the preplaced stent could not be assessed due to a surrounding coil mass in the fusiform aneurysm (case 7, Fig 1). There was no difference in the frequency of balloon angioplasty between PED Classic (2 of 7 patients, 28.6%) and PED Flex (3 of 10 patients, 30%). There were no periprocedural neurologic or other complications including vascular injury, access site complication, and contrast material-induced kidney injury.

At the most recent follow-up (mean, 22 months; range, 6–48 months), all patients had favorable outcomes (mRS, 0–2), without any newly appearing neurologic deficits. All aneurysms were followed up with conventional angiography at least once, 6–18 months after PED placement. Sixteen aneurysms (94.1%) showed complete occlusion; however, 1 initially ruptured dissecting MCA aneurysm (case 15) was enlarged. This enlarged dissecting aneurysm underwent a third treatment using an additional flow-diverter placement and has not yet undergone follow-up angiography. Asymptomatic in-stent stenosis (>50%) was observed in 1 case on follow-up angiography.

**DISCUSSION**

In this case series, all aneurysms were successfully retreated using the PED without any complications. Furthermore, although the initial aneurysms (large-/giant-sized, ruptured dissecting, or blood blister-like) were prone to re-recurrence even after successful retreatment with additional coil insertion, 94.1% of the aneurysms retreated using flow diverters had complete occlusion on follow-up angiography.

During the coiling procedure for an intracranial aneurysm, a stent may be used for multiple purposes, such as preservation of a parent or branch artery, prevention of microcatheter kickback, and increased durability. Despite these advantages, SAC has not been widespread until recently due to its technical difficulty and possible complications. However, with the recent development of
low-profile stents, SAC may be an easier and safer procedure than those using previous stents. Currently, SAC has become more common and is used in up to 32.7% of all endovascular coiling. However, because a recurrence after SAC is not uncommon, management after recurrence is an important clinical issue that remains controversial.

Surgical retreatment for previously stented aneurysms is challenging and complicated because direct manipulation of the stented artery or extrusion of the previous coil mass is required, which is associated with a risk of thromboembolism and arterial tearing. Thus, endovascular coil addition with or without a stent has been widely accepted as a retreatment technique for recurrent aneurysms after SAC. However, this conventional endovascular retreatment cannot fully overcome the risk of repeat recurrences because most target aneurysms in this study were vulnerable to recurrence by nature.

Flow diverters are a new treatment strategy for intracranial aneurysms. The flow diverter gradually occludes an aneurysm within an organized thrombus by enhancing an intra-aneurysmal flow diversion and neointima formation. Consequently, flow-diverter treatment has a lower probability of recurrence than conventional coiling, even in lesions vulnerable to recurrence. Therefore, a flow diverter might be a better treatment option for recurrent aneurysms even after SAC. However, in previous studies, flow-diverter treatment after stent placement was reportedly less effective and more complicated, with 40.9%–75.0% occlusion rates and a higher complication rate, up to 16.7%.

These unfavorable results may stem from several technical issues regarding flow-diverter deployment within a previously placed stent. First, the microwire may go through the strut of a previous stent and potentially traverse in an "in-out-in" fashion. This phenomenon results in incomplete opening of the flow diverter. However, in most cases in the present study, this drawback was overcome by advancing the 5F intermediate catheter distally over the Marksman catheter, which promised the inner lumen and the central axis of the previous stent. This method ensures that the intermediate catheter cannot traverse the previous stent in the "in-out-in" fashion, though the microwire and microcatheter may.

Second, the previously placed stent strut or coil interrupts the visibility of the flow diverter, and the entire process of flow-diverter deployment cannot be easily identified using fluoroscopy. Thus, incomplete expansion of the flow diverter may potentially occur despite using a size-matched flow diverter and may be a main cause of thromboembolic complications and less effective flow diversion. In the present study, when a postimplantation angiogram or flat panel CT image showed equivocal apposition of the flow diverter in the segment where a metallic artifact due to coil mass was not prominent or when the wall apposition of the PED could not be assessed due to the surrounding coil mass, balloon angioplasty was performed. Balloon angioplasty was helpful for better apposition of the flow diverter to the previous stent. Third, during the deployment of the flow diverter within the previously stented artery, the usual drag-and-drop technique can cause anchoring of the flow diverter to the previous stent, followed by a stretch of the flow.
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