# Treatment Outcome of Flow Diverter Device for Medium-Sized Cerebral Aneurysms: A Single-Center Report

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**Objective:** Flow diverters (FDs), first introduced in Japan in 2015, were initially limited to wide-necked large cerebral aneurysms, which pose a high treatment risk. However, based on the results of the PREMIER study, the indications have expanded since 2020, and the number of treatment cases is increasing in Japan. At our hospital, FD placement with adjunctive coil embolization has been actively performed for medium-sized cerebral aneurysms, as indicated in the PREMIER study; herein, we report the outcomes of this treatment.

**Methods:** Of the 25 patients with 28 aneurysms who underwent FD placement at our institution between April 2022 and June 2023, 15 with 17 wide-necked unruptured cerebral aneurysms with a maximum diameter of <12 mm in the internal carotid artery (ICA) or vertebral artery (VA) were included. Postoperative complications were investigated in each case, and the aneurysm occlusion status was assessed using ultrashort echo time (UTE)-MRA at 3 months postoperatively and angiography at 6 months postoperatively. Fifteen patients who underwent coiling or stent-assisted coiling (SAC) for the same criteria during the same period were compared. Baseline characteristics and treatment results were compared between FD and coiling/SAC cases.

**Results:** Four males and 11 females with a mean age of  $61.7 \pm 12.8$  years were included, and the median follow-up period was 9 months (6–18 months). There were 14 aneurysms of the ICA and 3 of the VA, and the mean maximum aneurysm diameter was  $7.9 \pm 1.7$  mm. All patients were treated using the Pipeline Flex with Shield Technology (Medtronic, Minneapolis, MN, USA), and 14 aneurysms (82.4%) were treated with adjunctive coil embolization. There were no symptomatic strokes in the perioperative period; only one patient receiving corticosteroid therapy for thyroid eye disease had asymptomatic ICA occlusion at 3 months. Fifteen aneurysms (88.2%) were not visible on UTE-MRA at 3 months postoperatively, and angiography at 6 months showed complete occlusion in 16 (94.1%) aneurysms. The coiling/SAC group had a smaller neck size and higher volume embolization ratio than the FD group; however, complete occlusion was higher in the FD group.

**Conclusion:** FD placement with adjunctive coil embolization for medium-sized cerebral aneurysms is expected to result in good occlusion rates in the early postoperative period.

Keywords flow diverter, unruptured intracranial aneurysm, medium-sized cerebral aneurysm

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# Introduction

The flow diverter (FD), first approved by the Japanese Ministry of Health, Labour and Welfare in 2015, was initially limited to wide-necked large cerebral aneurysms with a high treatment risk. However, based on the results of the PREMIER study,<sup>1,2)</sup> the adaptation was expanded to medium-sized aneurysms by 2020, and the number of treatment cases is increasing in Japan.

In FD placement for large cerebral aneurysms, adjunctive coil embolization can occlude the aneurysm at an early stage and prevent delayed aneurysm rupture. However, there have only been a few reports on the usefulness of adjunctive coil embolization for medium-sized cerebral aneurysms.<sup>3,4)</sup> Therefore, in this study, we report the outcomes of performing FD placement with adjunctive coil embolization for medium-sized cerebral aneurysms, as indicated in the PREMIER study.

## Materials and Methods

#### **Materials**

#### Patient and aneurysm characteristics

A retrospective review was performed of cases in which FD placement was performed at our institution from April 2022 to June 2023. Of the 28 aneurysms in 25 consecutive cases, 17 in 15 cases were first-ever wide-necked unruptured cerebral aneurysms with a maximum diameter of <12 mm in the internal carotid artery (ICA) or vertebral artery (VA), 9 were >12 mm, and 2 recurrent aneurysms were excluded.

Fifteen patients who underwent coiling or stent-assisted coiling (SAC) for the same criteria during the same period were compared. As a rule, coiling/SAC is preferred in cases involving posterior communicating artery (PcomA); for other cases, coiling/SAC was preferred before October 2022, and FD placement was performed thereafter.

This study was approved by the Ethics Review Committee of the National Cerebral and Cardiovascular Center (Approval No. M30-013-3).

#### Methods

#### Endovascular procedure

Dual antiplatelet therapy (DAPT) with aspirin and clopidogrel was administered at least 2 weeks before surgery. Platelet aggregation tests were performed using the P2Y12 assay (VerifyNow; Accumetrics, San Diego, CA, USA) and light transmission aggregometry; if the platelet aggregation test was insufficiently effective, the aspirin dose was increased, and clopidogrel was switched to prasugrel.

Pipeline Flex with Shield Technology (PED Shield; Medtronic, Minneapolis, MN, USA) was used for FD in all FD patients, and adjunctive coil embolization was attempted in all cases of saccular aneurysms in principle. Adjunctive coil embolization was not used in 1 case, in which coil insertion was difficult due to malformation, and in 2 cases, in spindle-shaped VA aneurysms. Adjunctive coil embolization was performed using the jailing technique, with a catheter on a shaft separate from that used for FD implantation. As a rule, the number and size of coils are limited to just enough to cover the aneurysm wall rather than attempting to completely embolize the aneurysm. After FD placement, all patients underwent in-stent balloon inflation, and cone-beam CT with a diluted contrast agent was used to confirm the expansion of the FD and adequate vessel wall apposition.

Neuroform Atlas Stent (Stryker Neurovascular, Fremont, CA, USA) was used for SAC treatment.

DAPT was continued for 6 months after FD placement or coiling/SAC. The clopidogrel or prasugrel dose was then tapered off, and aspirin alone was continued.

#### Image analysis

Ultrashort echo time (UTE)-MRA was performed 3 months postoperatively using MRI (Premier 3T, GE HealthCare, Chicago, IL, USA) and digital subtraction angiography (DSA) at 6 months. In cases treated with FD, UTE-MRA was performed at 6 months postoperatively.

Postoperative complications were investigated retrospectively, and the aneurysm occlusion status on DSA was determined using the O'Kelly–Marotta (OKM) Grading Scale<sup>5)</sup> and Raymond–Roy occlusion classification (RROC).<sup>6)</sup>

UTE-MRA and DSA images were determined by 2 or more neurosurgeons.

#### Statistical analysis

The *t*-test and Fisher's exact test were used to compare baseline characteristics and treatment results between FD and coiling/SAC cases. Statistical analysis was performed using R version 4.3.2 (The R Foundation for Statistical Computing, Vienna, Austria). p Values of <0.05 were considered statistically significant differences.

## Results

The details of FD cases are listed in **Table 1**. The participants were 4 males and 11 females (2 patients had multiple cerebral aneurysms) with a mean age of  $61.7 \pm 12.8$ years and a median follow-up period of 9 months (6–18 months). Fourteen aneurysms were in the ICA and 3 in the VA, and all aneurysms were located intracranially; the ophthalmic artery was incorporated in three cases. The mean neck length of aneurysms was  $5.9 \pm 2.9$  mm, and the mean maximum aneurysm diameter was  $7.9 \pm 1.7$  mm. In 3 cases, the platelet aggregation test was ineffective, the aspirin dose was increased, and clopidogrel was switched to prasugrel.

Table 1 Details of each case (	(FD)	)
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Case	Sex	Age	Aneurysm location	Incorporated branch	Aneurysm neck size	Aneurysm maximum size	Platelet aggregation test	Stent size (Pipeline)	VER (%)	Symptomatic cerebral complication	Post-3 months UTE-MRA	Post-6 months UTE-MRA	Post-6 months DSA ( (OKM)	Post-6 months DSA (RROC)
1	F	48	IC-opth	Opthalmic a.	7.0 mm	10.0 mm	Sufficient	4.0 × 18 mm	12.1	-	ICA occlusion	ICA occlusion	D	Class I
2	Μ	64	ICA(C2)	-	4.0 mm	7.8 mm	Sufficient	4.5 × 16 mm	18.7	-	CO	CO	D	Class I
3	Μ	62	VA	-	16.0 mm	10.0 mm	Sufficient	4.25 × 35 mm, 4.25 × 25 mm	-	-	CO	CO	D	Class I
4	Μ	39	ICA(C2)	-	5.1 mm	5.2 mm	Sufficient	5.0 × 16 mm	27.2	-	CO	CO	D	Class I
5	F	61	ICA(C2)	-	4.8 mm	5.8 mm	Sufficient	3.25 × 18 mm	10.5	-	CO	CO	D	Class I
6	F	67	ICA(C2)	-	4.0 mm	7.3 mm	Sufficient	$3.75 \times 16 \text{ mm}$	8.7	-	CO	CO	D	Class I
7	F	79	ICA(C1-2)	-	7.2 mm	10.9 mm	Sufficient	4.5 × 18 mm	25.7	-	CO	CO	D	Class I
8	F	79	ICA(C2)	-	6.2 mm	7.0 mm	Sufficient	4.0 × 16 mm	18.2	-	CO	CO	D	Class I
9	F	47	ICA(C2)	-	6.2 mm	8.5 mm	Sufficient	4.75 × 16 mm	-	-	ICO	ICO	С	Class II
10	F	39	ICA(C2)	-	3.7 mm	6.6 mm	Sufficient	4.5 × 16 mm	35.5	-	CO	CO	D	Class I
11	F	55	ICA(C2)	-	6.8 mm	8.5 mm	Insufficient	$4.25 \times 16 \text{ mm}$	6.3	-	ICO	CO	D	Class I
12	Μ	69	VA	-	5.2 mm	7.5 mm	Sufficient	$4.25 \times 16 \text{ mm}$	-	-	CO	CO	D	Class I
13	F	73	ICA(C2)	-	3.0 mm	5.8 mm	Sufficient	5.0 × 16 mm	11.4	-	CO	CO	D	Class I
14	F	73	VA	-	5.0 mm	6.4 mm	Sufficient	4.0 × 16 mm	26.5	-	CO	CO	D	Class I
15	F	70	IC-opth	Ophthalmic a.	4.8 mm	9.0 mm	Insufficient	4.5 × 18 mm	17.9	-	CO	CO	D	Class I
16	F	70	IC-opth	Ophthalmic a.	6.6 mm	9.3 mm	Insufficient	4.25 × 16 mm	21.9	-	CO	CO	D	Class I
17	F	53	ICA(C2)	-	4.1 mm	8.9 mm	Sufficient	5.0 × 16 mm	17.0	-	CO	CO	D	Class I

CO, complete occlusion; DSA, digital subtraction angiography; FD, flow diverter; IC-opth, internal carotid artery-ophthalmic artery; ICA, internal carotid artery; ICO, incomplete occlusion; OKM, O'Kelly–Marotta Grading Scale; RROC, Raymond–Roy occlusion classification; UTE-MRA, ultrashort echo time magnetic resonance angiography; VA, vertebral artery; VER, volume embolization ratio

The PED Shield was successfully implanted and fully expanded in all cases, with only one case using 2 PED Shields since the lesion was spindle-shaped and long. Adjunctive coil embolization was used for 14 aneurysms (82.4%), excluding 2 spindle-shaped VA aneurysms and 1 aneurysm that was difficult to embolize owing to its irregular shape. The mean number of coils used was 3 (1–8) with a mean volume embolization rate (VER) of  $18.4\% \pm 8.3\%$ .

No symptomatic strokes were observed, although 3 patients had puncture site complications in the perioperative period. Only one patient who was receiving steroid pulse therapy for thyroid eye disease had asymptomatic ICA occlusion at 3 months postoperatively and no ischemic lesions.

In 15 patients (88.2%), the aneurysm was not visible on UTE-MRA 3 months postoperatively, and in 16 patients (94.1%), complete occlusion of the aneurysm was confirmed on DSA and UTE-MRA at 6 months.

The details of coiling/SAC cases are listed in Table 2. The participants were 1 male and 14 females with a mean age of 57.1  $\pm$  9.5 years and a median follow-up period of 9 months (6-18 months). All aneurysms were in the ICA, while the PcomA and ophthalmic artery were incorporated in 6 cases. The mean neck length of aneurysms was  $4.0 \pm 0.8$  mm, with a mean maximum aneurysm diameter of  $6.8 \pm 1.2$  mm. In 3 cases, the platelet aggregation test was ineffective, the aspirin dose was increased, and clopidogrel was switched to prasugrel. The Neuroform Atlas Stent (Stryker Neurovascular) was implanted in 7 cases. The mean number of coils used was 8 (3-12), with a mean VER of  $27.8\% \pm 5.9\%$ . No symptomatic strokes were observed, although 1 patient had contrastinduced encephalopathy. RROC class I was confirmed in 4 patients (26.7%), and class II was 9 (60.0%) on DSA at 6 months postoperatively.

The coiling/SAC group had a smaller neck size and higher VER than the FD group; however, complete occlusion was higher in the FD group (**Table 3**).

#### **Representative case**

#### Case 1

The patient was a 39-year-old male with an incidentally discovered C2 aneurysm of the right ICA (maximal diameter: 5.2 mm, neck: 5.1 mm). A 6-French ASAHI FUBUKI (ASAHI INTECC, Aichi, Japan) was positioned in the cervical ICA from the left femoral artery, and an SL10 (Stryker Neurovascular) was guided into the aneurysm prior to FD implantation. Then, the PED Shield ( $5.0 \times 16$  mm) (Medtronic) was implanted using 8-French ASAHI FUBUKI (ASAHI INTECC) through the right femoral artery with a 6-French Navien (Medtronic) as coaxial catheter, and Phenom27 (Medtronic) as microcatheter. An AXIUM PRIME Frame (5 mm  $\times$  10 cm) (Medtronic), HydroSoft 3D (4  $\times$  8 mm) (MicroVention Terumo, Aliso Viejo, CA, USA), and Hydro-Soft 3D (3 mm  $\times$  8 cm) (MicroVention Terumo) were implanted using the jailing technique from SL10 (Stryker Neurovascular), which was previously guided into the aneurysm. UTE-MRA at 3 months postoperatively did not reveal an aneurysm, and DSA at 6 months postoperatively confirmed a complete aneurysmal occlusion. One year postoperatively, the patient was treated with a single antiplatelet agent and is, as of the writing of this manuscript, undergoing follow-up (**Fig. 1**).

#### Case 2

The patient was a 47-year-old female with a C2 aneurysm of the right ICA (maximal diameter: 8.5 mm, neck: 6.2 mm, irregular shape) discovered during a headache examination. A PED Shield ( $4.75 \times 16$  mm) (Medtronic) was implanted from the right femoral artery using a 7-French ASAHI FUBUKI (ASAHI INTECC), 5-French Navien (Medtronic), and Phenom 27 (Medtronic). As the irregularity of the aneurysm made coil insertion difficult, an adjunctive coil combination was not performed. UTE-MRA performed 3 months postoperatively revealed an aneurysm neck remnant, and DSA performed 6 months postoperatively showed similar findings. Six months postoperatively, the patient was followed up with a reduced dose of antiplatelet medication (**Fig. 2**).

### Discussion

In the PREMIER study,<sup>1,2)</sup> 76.8% of the 138 patients achieved complete occlusion 1 year postoperatively and 83.3% after 3 years. In the present study, 15 aneurysms (88.2%) were occluded using UTE-MRA at 3 months, and complete occlusion was confirmed in 16 aneurysms (94.1%) using DSA at 6 months, showing a higher and earlier occlusion rate than that in the PREMIER study. The major difference from the PREMIER study was that 82.4% of the patients in our study underwent adjunctive coil embolization, whereas in the PREMIER study, only 3.5% did.

#### The effect of FD placement compared with coiling/SAC

In the present study, RROC class II was more common in the coiling/SAC cases, while complete embolization was

Case	Sex	Age	Aneurysm location	Incorporated branch	Aneurysm neck size	Aneurysm maximum size	Platelet aggregation test	Stent size (Neuroform Atlas)	VER (%)	Symptomatic cerebral complication	Post-3 months UTE-MRA	Post-6 months DSA (RROC)
1	F	42	ICA(C2)	-	3.2 mm	5.7 mm	Sufficient	4.0 × 21 mm	34.7	_	CO	Class I
2	F	44	ICA(C2-3)	-	4.0 mm	8.0 mm	Sufficient	4.0 × 21 mm	25.0	_	ICO	Class IIIb
3	F	68	IC-PC	PcomA	3.5 mm	6.8 mm	Sufficient	_	25.5	_	ICO	Class II
4	F	60	IC-PC	PcomA	5.0 mm	5.2 mm	Insufficient	4.5 × 21 mm	42.3	-	ICO	Class II
5	Μ	51	ICA(C2)	-	2.7 mm	5.2 mm	Sufficient	-	24.1	-	ICO	Class II
6	F	49	IC-opth	Ophthalmic a.	4.2 mm	6.9 mm	Insufficient	-	23.1	-	ICO	Class II
7	F	61	ICA(C3)	-	3.7 mm	6.0 mm	Insufficient	4.5 × 21 mm	22.9	-	ICO	Class II
8	F	69	ICA(C3)	-	4.6 mm	7.7 mm	Sufficient	-	34.7	-	ICO	Class Illa
9	F	68	ICA(C2)	-	5.9 mm	7.4 mm	Sufficient	4.5 × 21 mm	27.0	-	CO	Class I
10	F	54	ICA(C2)	-	3.5 mm	6.5 mm	Sufficient	4.0 × 21 mm	21.6	-	ICO	Class I
11	F	51	IC-PC	PcomA	3.5 mm	5.9 mm	Sufficient	-	28.8	-	ICO	Class II
12	F	74	ICA(C2)	-	4.0 mm	8.9 mm	Sufficient	4.5 × 21 mm	22.9	-	CO	Class I
13	F	52	IC-PC	PcomA	4.5 mm	9.2 mm	Sufficient	-	29.0	-	ICO	Class II
14	F	56	IC-PC	PcomA	4.0 mm	6.4 mm	Sufficient	-	31.7	+	ICO	Class II
15	F	57	ICA(C3)	-	3.7 mm	6.8 mm	Sufficient	_	23.0	-	ICO	Class II

Table 2 Details of each case (coiling and stent-assisted coil embolization)

CO, complete occlusion; DSA, digital subtraction angiography; IC-opth, internal carotid artery-ophthalmic artery; IC-PC, internal carotid artery-posterior communicating artery; ICA, internal carotid artery; ICO, incomplete occlusion; PcomA, posterior communicating artery; RROC, Raymond–Roy occlusion classification; UTE-MRA, ultrashort echo time magnetic resonance angiography; VER, volume embolization ratio

 Table 3
 Comparison between FD and coiling/SAC

	Coil/SAC	FD	p Value
Age	57.1 ± 9.5	61.6 ± 12.8	0.27
Sex Female Male	14 1	13 4	0.34
Incorporated branch Without With	9 6	14 3	0.24
Aneurysm neck size (mm)	$4.0 \pm 0.8$	$5.9 \pm 2.9$	0.02
Aneurysm maximum size (mm)	6.8 ± 1.2	7.9 ± 1.7	0.05
Dome neck ratio	$1.7 \pm 0.3$	$1.5 \pm 0.4$	0.05
Platelet aggregation test Insufficient sufficient	3 12 27 8 + 5 9	3 14 18 4 + 8 3	>0.99
Post-3 months LITE-MBA	27.0 ± 0.5	10.4 ± 0.5	<0.01
Complete occlusion Incomplete occlusion	3 12	15 2	<0.01
Post-6 months DSA (RROC) Class I Class II Class III	4 9 2	16 1	<0.01
01033 111	2	0	

DSA, digital subtraction angiography; FD, flow diverter; RROC, Raymond–Roy occlusion classification; SAC, stentassisted coiling; UTE-MRA, ultrashort echo time magnetic resonance angiography; VER, volume embolization ratio



**Fig. 1** DSA showed an inward aneurysm in the C2 portion of the right ICA (**A**). FD implantation and rough coil embolization were performed (**B**). UTE magnetic resonance angiography at 3 months did not show an aneurysm (**C**). DSA at 6 months confirmed complete occlusion of the aneurysm (**D**). DSA, digital subtraction angiography; FD, flow diverter; ICA, internal carotid artery; UTE, ultrashort echo time

more common in FD cases. RROC classes I and II are sufficient to prevent rebleeding in the acute phase of subarachnoid hemorrhage (SAH); in the treatment of unruptured aneurysms, most class II aneurysms show stable results, although they are more likely to recur than class I.<sup>6</sup>) In small (<10 mm) aneurysms amenable to each technique, FD has a higher occlusion rate than coiling,<sup>7</sup>) suggesting that FD is an aggressive consideration for such aneurysms. At our institution, we plan to continue DAPT for 6 months; however, it should be noted that, after FD implantation, DAPT is generally continued for at least 3 months and antiplatelet agents alone for at least 1 year or indefinitely.<sup>2–4</sup>)

# The effect of FD placement with adjunctive coil embolization

FD placement for medium-sized cerebral aneurysms has a higher rate of complete occlusion and a lower risk of delayed aneurysm rupture than that for large aneurysms.<sup>2)</sup> However, not all patients achieve complete occlusion, and additional treatment options are limited in cases of ineffective FD. In general, the high-density mesh structure of the FD makes it difficult to insert additional coils later. Therefore, additional FD implantation or parent artery occlusion, clipping, and strict follow-up with antiplatelet medication changes are treatment options for FD failure.<sup>8,9)</sup> It is essential to seek ways to obtain high embolization rates during initial FD placement.

Factors related to incomplete occlusion after FD placement include age, aneurysm site, size, and adjunctive coil embolization.<sup>10,11</sup> The PREMIER study<sup>12</sup> of medium-sized cerebral aneurysms reported that non-smoking and side branch involvement were associated with incomplete occlusion. However, since the PREMIER study included only relatively young patients with aneurysms of  $\leq 12$  mm



**Fig. 2** DSA showed an upward irregularly shaped aneurysm in the C2 portion of the right ICA (**A**). Only FD implantation was performed (**B**). UTE magnetic resonance angiography at 3 months showed a neck remnant of the aneurysm (**C**), and DSA at 6 months showed a neck remnant of the aneurysm (**D**). DSA, digital subtraction angiography; FD, flow diverter; ICA, internal carotid artery; UTE, ultrashort echo time

in diameter, and due to the low rate of adjunctive coil embolization, it did not describe the association among age, aneurysm size, adjunctive coil embolization, and incomplete occlusion noted in previous studies for large aneurysms.

Some studies have reported high embolization rates during FD placement with adjunctive coil embolization (**Table 4**). Kitamura et al.<sup>3)</sup> reported that 66.2% of patients with 133 aneurysms were treated with adjunctive coil embolization, and OKM grade D was achieved in 83.2% of patients at 6 months and 88.2% at 1 year postoperatively. They concluded that the size of the aneurysm neck and the use of adjunctive coil embolization were essential factors in achieving a high occlusion ratio. Using various embolization techniques, Bender et al.<sup>13)</sup> also reported the treatment outcomes of FD placement with adjunctive coil embolization in 72 aneurysms, obtaining 85% complete embolization at 6 months and 96% at 1 year postoperatively. Park et al.<sup>14)</sup> reported a lower revision rate in cases of adjunctive coil embolization than with FD placement alone (1.5% vs. 11.8%, p = 0.03). Wang et al.<sup>4)</sup> compared FD placement alone and adjunctive coil embolization groups by aneurysm size and found a higher occlusion rate of adjunctive coil embolization in medium-sized cerebral aneurysms (74.7% vs. 88.8%, p <0.01, mean follow-up period of 9.0  $\pm$  7.5 months). The results of our study also suggest that even when limited to medium-sized cerebral aneurysms, adjunctive coil embolization may facilitate early and complete embolization.

In previous reports, adjunctive coil embolization was not intended for complete embolization of aneurysms; therefore, in principle, the number of coils used was limited to just enough to cover the aneurysm wall<sup>3</sup>) and the packing density of the coils was only 14%-15%.<sup>13</sup>) In our report for mediumsized cerebral aneurysms, the VER was  $18.4\% \pm 8.3\%$ .

	Number of aneurysms	Mean aneurysm size	Adjunctive-coil embolization	Complete occlusion
Present report	17 aneurysms	$7.9 \pm 1.7 \text{ mm}$ (only $\leq 12 \text{ mm}$ is included)	82.4%	94.1% at 6 months
PREMIER study <sup>1,2)</sup>	138 aneurysms	$5.0 \pm 1.9 \text{ mm}$ (only $\leq 12 \text{ mm}$ is included)	3.5%	76.8% at 1 year 83.3% at 3 years
Kitamura et al.3)	133 aneurysms	12.7 ± 4.3 mm	66.2%	83.2% at 6 months 88.2% at 1 year
Bender et al. <sup>13)</sup>	72 aneurysms	11 mm	100%	85% at 6 months 96% at 1 year
Park et al. <sup>14)</sup>	140 aneurysms	<fd alone="" group=""> 10.6 ± 9.2 mm <adjunctive coil="" group=""> 12.8 ± 7.4 mm</adjunctive></fd>	47.9%	<pd alone="" group=""> re-treatment rates 11.8% (follow-up 9.3 ± 5.6 months) <adjunctive coil="" group=""> re-treatment rates 1.5% (follow-up 9.3 ± 5.6 months)</adjunctive></pd>
Wang et al.4)	967 aneurysms	<fd alone="" group=""> 10.0 ± 7.6 mm</fd>	48.7%	<pd alone="" group=""> 77.0% at the last follow-up (follow-up 9.0 ± 7.5 months)</pd>
		<adjunctive coil="" group=""> 15.1 ± 8.1 mm</adjunctive>		<adjunctive coil="" group=""> 86.4% at the last follow-up (follow-up 9.0 ± 7.5 months)</adjunctive>

Table 4 Comparison of previous reports regarding adjunctive coil embolization with FD

FD, flow diverter

In general coil embolization, a VER <20%-25% is prone to recurrence<sup>15,16</sup>; however, a high filling rate was not considered necessary in adjunctive coil embolization in FD placement.

In this study, DSA was used to confirm aneurysm occlusion at 6 months postoperatively; however, UTE-MRA performed at 3 months already showed no aneurysm in 88.2% of cases. As UTE-MRA can significantly reduce the effects of image degradation due to turbulence in aneurysms and metals, its usefulness as a postoperative imaging evaluation in stent-assisted coil embolization and FD implantation has been reported.<sup>17,18</sup>) The present findings suggest that adjunctive coil embolization may provide a high embolization effect as early as 3 months after FD placement in medium-sized cerebral aneurysms. Adjunctive coil embolization is thought to reduce the blood flow velocity and wall shear stress within the aneurysm and promote early endothelialization by stimulating thrombosis within the aneurysm, thereby contributing to a high rate of complete occlusion.<sup>3,19</sup> This effect may occur earlier in smaller than in large cerebral aneurysms.

#### **Complication after FD implantation**

In the PREMIER study,<sup>1,2)</sup> of 138 patients, postoperative stroke was observed in 4 (2.8%) and postoperative aneurysm recurrence in 1 patient; however, no postoperative aneurysm rupture was observed. Adjunctive coil embolization with FD implantation increases the fluoroscopy time, but no increase

in complications has been reported,<sup>3,13</sup> although some reports have shown that ischemic complications are more common in cases with adjunctive coil embolization.<sup>4</sup>

At our institution, there were no symptomatic complications, except for asymptomatic occlusion of the ICA in 1 patient receiving steroid pulse therapy for thyroid eye disease. However, puncture site complications were observed in three patients.

The platelet aggregation test was sufficiently effective in this patient, and the PED Shield (Medtronic) was successfully implanted and fully expanded. ICA occlusion due to in-stent thrombosis is reported to occur in approximately 4% of cases,<sup>20</sup> but is often asymptomatic due to collateral blood flow through the circle of Willis. Assessing the collateral vascular development prior to FD placement may be important.

This report used a bifemoral technique for coil embolization.<sup>13)</sup> The bilateral femoral arteries were punctured using separate catheters for FD implantation and coil embolization, and Perclose ProGlide (Abbott, Chicago, IL, USA) was used for hemostasis. As large catheters are inserted bilaterally into the femoral arteries, more attention should be paid to complications at the puncture site.

#### Limitation

The purpose of conventional FD placement with adjunctive coil embolization is to reduce the incidence of delayed cerebral aneurysm rupture after FD implantation. The details of which patients should undergo adjunctive coil embolization were not clear. This was a retrospective study involving a small number of cases at a single institution; therefore, further investigation remains warranted with a large number of cases.

## Conclusion

Adjunctive coil embolization with FD implantation for medium-sized cerebral aneurysms may result in good occlusion rates during the early postoperative period.

## Disclosure Statement

Hirotoshi Imamura received speakers' bureau/honoraria from MEDTRONIC JAPAN, DAIICHI SANKYO COMPANY, Terumo, Johnson & Johnson, Stryker Japan, and ASAHI INTECC. All the other authors have no conflicts of interest.

# References

- Hanel RA, Kallmes DF, Lopes DK, et al. Prospective study on embolization of intracranial aneurysms with the pipeline device: the PREMIER study 1 year results. *J Neurointerv Surg* 2020; 12: 62–66.
- Hanel RA, Cortez GM, Lopes DK, et al. Prospective study on embolization of intracranial aneurysms with the pipeline device (PREMIER study): 3-year results with the application of a flow diverter specific occlusion classification. *J Neurointery Surg* 2023; 15: 248–254.
- Kitamura T, Fujii T, Yatomi K, et al. Safety and efficacy of pipeline embolization device treatments for intradural internal carotid artery aneurysms in a single center in a Japanese population. *Surg Neurol Int* 2023; 14: 92.
- Wang C, Luo B, Li T, et al. Comparison of the pipeline embolisation device alone or combined with coiling for treatment of different sizes of intracranial aneurysms. *Stroke Vasc Neurol* 2022; 7: 345–352.
- O'kelly CJ, Krings T, Fiorella D, et al. A novel grading scale for the angiographic assessment of intracranial aneurysms treated using flow diverting stents. *Interv Neuroradiol* 2010; 16: 133–137.
- Roy D, Milot G, Raymond J. Endovascular treatment of unruptured aneurysms. *Stroke* 2001; 32: 1998–2004.
- Chalouhi N, Daou B, Barros G, et al. Matched comparison of flow diversion and coiling in small, noncomplex intracranial aneurysms. *Neurosurgery* 2017; 81: 92–97.
- 8) Goertz L, Hesse N, Liebig T, et al. Retreatment strategies for recurrent and residual aneurysms after treatment

with flow-diverter devices. *Neuroradiology* 2020; 62: 1019–1028.

- Young M, Enriquez-Marulanda A, Salih M, et al. Management of intracranial aneurysms that do not occlude on initial follow-up after treatment with the pipeline embolization device. *Neurosurgery* 2024; 94: 271–277.
- Hiramatsu R, Yagi R, Kameda M, et al. Treatment outcomes of 94 cases of pipeline embolization device in a single center: predictive factors of incomplete aneurysm occlusion. *J Neuroendovasc Ther* 2023; 17: 217–223.
- Maragkos GA, Ascanio LC, Salem MM, et al. Predictive factors of incomplete aneurysm occlusion after endovascular treatment with the pipeline embolization device. *J Neurosurg* 2020; 132: 1598–1605.
- 12) Hanel RA, Monteiro A, Nelson PK, et al. Predictors of incomplete aneurysm occlusion after treatment with the pipeline embolization device: PREMIER trial 1 year analysis. J Neurointerv Surg 2022; 14: 1014–1017.
- Bender MT, Jiang B, Campos JK, et al. Single-stage flow diversion with adjunctive coiling for cerebral aneurysm: outcomes and technical considerations in 72 cases. *J Neurointerv Surg* 2018; 10: 843–850.
- 14) Park MS, Nanaszko M, Sanborn MR, et al. Re-treatment rates after treatment with the pipeline embolization device alone versus pipeline and coil embolization of cerebral aneurysms: a single-center experience. *J Neurosurg* 2016; 125: 137–144.
- 15) Yagi K, Satoh K, Satomi J, et al. Evaluation of aneurysm stability after endovascular embolization with Guglielmi detachable coils: correlation between long-term stability and volume embolization ratio. *Neurol Med Chir (Tokyo)* 2005; 45: 561–566; discussion, 565–566.
- 16) Fuga M, Tanaka T, Irie K, et al. Risk factors for recanalization of dense coil packing for unruptured cerebral aneurysms in endovascular coil embolization: analysis of a single center's experience. *J Clin Neurosci* 2022; 98: 175–181.
- 17) Irie R, Suzuki M, Yamamoto M, et al. Assessing blood flow in an intracranial stent: a feasibility study of MR angiography using a Silent Scan after stent-assisted coil embolization for anterior circulation aneurysms. *AJNR Am J Neuroradiol* 2015; 36: 967–970.
- 18) Oishi H, Fujii T, Suzuki M, et al. Usefulness of Silent MR angiography for intracranial aneurysms treated with a flow-diverter device. *AJNR Am J Neuroradiol* 2019; 40: 808–814.
- Jing L, Zhong J, Liu J, et al. Hemodynamic effect of flow diverter and coils in treatment of large and giant intracranial aneurysms. *World Neurosurg* 2016; 89: 199–207.
- 20) Gui S, Chen X, Wei D, et al. Long-term outcomes and dynamic changes of in-stent stenosis after pipeline embolization device treatment of intracranial aneurysms. *J Neurointerv Surg* 2023; 15: 1187–1193.