

Flow diverter devices in ruptured intracranial aneurysms: a single-center experience

Emilio Lozupone, MD,¹ Mariangela Piano, MD,¹ Luca Valvassori, MD,¹ Luca Quilici, MD,¹ Guglielmo Pero, MD,¹ Emiliano Visconti, MD,² and Edoardo Boccardi, MD¹

¹Department of Neuroradiology, ASST Grande Ospedale Metropolitano Niguarda, Milan; and ²Department of Radiology, Policlinico Universitario "Agostino Gemelli," Rome, Italy

OBJECTIVE In this single-center series, the authors retrospectively evaluated the effectiveness, safety, and midterm follow-up results of ruptured aneurysms treated by implantation of a flow diverter device (FDD).

METHODS The records of 17 patients (12 females, 5 males, average World Federation of Neurosurgical Societies score = 2.9) who presented with subarachnoid hemorrhage (SAH) due to the rupture of an intracranial aneurysm treated with an FDD were retrospectively reviewed. Of 17 ruptured aneurysms, 8 were blood blister–like aneurysms and the remaining 9 were dissecting aneurysms. The mean delay between SAH and treatment was 4.2 days. Intraprocedural and periprocedural morbidity and mortality were recorded. Clinical and angiographic follow-up evaluations were conducted between 6 and 12 months after the procedure.

RESULTS None of the ruptured aneurysms re-bleed after endovascular treatment. The overall mortality rate was 12% (2/17), involving 2 patients who died after a few days because of complications of SAH. The overall morbidity rate was 12%: 1 patient experienced intraparenchymal bleeding during the repositioning of external ventricular drainage, and 1 patient with a posterior inferior cerebellar artery aneurysm developed paraplegia due to a spinal cord infarction after 2 weeks. The angiographic follow-up evaluations showed a complete occlusion of the aneurysm in 12 of 15 surviving patients; of the 3 remaining cases, 1 patient showed a remnant of the aneurysm, 1 patient was retreated due to an enlargement of the aneurysm, and 1 patient was lost at the angiographic follow-up.

CONCLUSIONS FDDs can be used in patients with ruptured aneurysms, where conventional neurosurgical or endovascular treatments can be challenging.

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KEY WORDS flow diverter device; ruptured aneurysm; blood blister–like aneurysm; subarachnoid hemorrhage; dissecting fusiform aneurysm; interventional neurosurgery; vascular disorders

THE main objective of the treatment of ruptured aneurysms is to avoid rebleeding. This objective can be achieved either by endovascular techniques or by open neurosurgery. However, in certain cases of ruptured aneurysms, such as blood blister–like aneurysms (BBAs) or dissecting aneurysms, surgery can be technically challenging.¹

In the last few years, the flow diverter device (FDD) has become an important tool in the management of unruptured aneurysms, especially in wide-neck, dissecting, or fusiform aneurysms.^{1,6,11,16} Many papers report the fea-

sibility, safety, and effectiveness of FDDs in the treatment of unruptured aneurysms; conversely, few investigators reported their experience with the FDD in the treatment of ruptured aneurysms.^{3,4,10}

The FDD disrupts and modifies the flow inside the aneurysm, consequently leading to intrasaccular thrombosis and aneurysmal shrinkage.⁸ However, the “occlusion process” of the aneurysm can require weeks or months, and the risk of bleeding is not conceptually excluded until the occlusion of the aneurysm is achieved.⁶ In addition, the FDD requires dual antiplatelet therapy both before and for

ABBREVIATIONS ACA = anterior cerebral artery; ASA = acetylsalicylic acid; BBA = blood blister–like aneurysm; DSA = digital subtraction angiography; EVD = external ventricular drainage; FDD = flow diverter device; ICA = internal carotid artery; MCA = middle cerebral artery; mRS = modified Rankin Scale; PCA = posterior cerebral artery; PED = Pipeline Embolization Device; PICA = posterior inferior cerebellar artery; SAH = subarachnoid hemorrhage; WFNS = World Federation of Neurological Societies.

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TABLE 1. Demographic, clinical, and aneurysm characteristics as well as features of the endovascular procedure

Case No.	Age (yrs), Sex	WFNS Score	Location	Aneurysm Type	Aneurysm Size	Time to Treat (days)	Stent	Adjunctive Coils
1	58, F	5	ICA	BBA	Small	0	2 PEDs	No
2	19, F	5	ICA-MCA	Dissecting	Small	1	1 Silk	No
3	12, F	3	MCA	Dissecting	Large	3	1 PED	No
4	29, F	2	ICA	BBA	Small	1	2 PEDs	No
5	24, M	2	MCA	BBA	Small	13	1 PED	No
6	6, M	3	MCA	Dissecting	Small	0	1 PED	Yes
7	62, F	5	ICA	BBA	Small	1	1 PED	No
8	72, F	5	ICA	BBA	Small	1	2 PEDs	No
9	67, F	2	PCA	BBA	Small	20	1 Silk	No
10	59, M	4	MCA	Dissecting	Giant	0	2 PEDs	Yes
11	60, F	2	Basilar	BBA	Small	10	1 PED	No
12	48, F	1	Vertebral	Dissecting	Small	0	1 PED	No
13	52, F	1	ACA	Dissecting	Small	3	1 Surpass	No
14	72, M	1	Vertebral	Dissecting	Small	1	1 PED	No
15	55, F	5	Basilar	BBA	Small	2	1 PED	No
16	39, M	1	Vertebral	Dissecting	Small	14	1 PED Flex	No
17	58, F	3	PICA	Dissecting	Small	1	1 PED Flex	No

many months after the deployment; this can represent a problem in patients who may undergo additional intracranial procedures, such as extraventricular drain placement or craniotomy for decompression or hematoma evacuation.^{3,12}

In this study, we report our single-center experience of ruptured aneurysms—as BBAs or dissecting aneurysms—managed by implantation of an FDD. Our purpose was to evaluate the safety, effectiveness, and midterm follow-up results of the treatment with the FDD in ruptured aneurysms.

Methods

We retrospectively reviewed the database of our neurointerventional department at ASST Grande Ospedale Metropolitano Niguarda to identify patients with ruptured intracranial aneurysms treated acutely via implantation of an FDD.

Study Population

Seventeen patients treated at our hospital between January 2009 and February 2015 were included in our retrospective review. The group included 12 females and 5 males, ranging in age from 6 to 72 years (average age 46 years). Three patients were included in a previously published paper.¹⁵ Fifteen patients presented with subarachnoid hemorrhage (SAH) detected at unenhanced CT due to a ruptured intracranial aneurysm; 1 patient presented with SAH and an acute ischemic lesion in the left basal ganglia; and 1 patient presented with acute occipital headache with evidence of previous bleeding at lumbar puncture. World Federation of Neurological Societies (WFNS) scores ranged from 1 to 5 (average 2.9). Before the endovascular treatment 4 patients had undergone unsuccessful surgical exploration. The mean delay between the SAH and the endovascular procedure was 4.2 days (range 0–20 days).

Aneurysm Types

All 17 ruptured aneurysms were treated with an FDD (Table 1). Eight aneurysms were BBAs and the remaining 9 were dissecting aneurysms. Ten were in the anterior circulation and 7 in the posterior circulation. Six aneurysms were located on small arteries distal to the circle of Willis (anterior cerebral artery [ACA], middle cerebral artery [MCA], and posterior cerebral artery [PCA]). The average size of all aneurysms was 5.1 mm; if BBAs were excluded, the mean aneurysm size for the dissecting aneurysms was 8 mm.

Endovascular Treatment

All endovascular procedures were performed under general anesthesia and via a right femoral artery approach, using a 6-Fr femoral artery short sheath and a 6-Fr guiding catheter (Envoy, Cordis). The Pipeline Embolization Device (PED, and PED Flex; ev3) was used in the treatment of 14 ruptured aneurysms, a Silk flow diverter (Balt Extrusion) in 2 aneurysms, and a Surpass Streamline flow diverter (Stryker) in 1.

A total of 21 FDDs (16 PEDs, 2 PED Flex, 2 Silk, and 1 Surpass) were used in the 17 aneurysms treated. In 4 patients (Cases 1, 4, 8, and 10), 2 FDDs were implanted to increase the mesh density. In 2 patients (Cases 6 and 10) platinum coils were concomitantly deployed into the aneurysmal sac (Table 1). At the end of all endovascular procedures a CT scan was performed to exclude any intraprocedural bleeding.

Antiplatelet and Other Drug Therapies

Abciximab was administered in 15 patients immediately following the deployment of the FDD: a bolus dose of 0.25 mg/kg followed by a 12-hour infusion of 0.125 ng/kg/min. Dual antiplatelet therapy (acetylsalicylic acid [ASA] 100 mg/day and ticlopidine 250 mg twice a day)

TABLE 2. Adverse events

Case No.	Complications	
	Intraprocedural	Periprocedural*
1	None	Death
2	Small amount of SAH due to wire perforation	Death
3	None	None
4	None	None
5	None	None
6	None	None
7	None	None
8	None	None
9	PCA occlusion resolved after administration of ASA & abciximab	None
10	None	None
11	None	Intraparenchymal hematoma after EVD
12	None	None
13	Migration of distal tip of microcatheter	None
14	None	None
15	None	None
16	None	None
17	None	Spinal cord ischemia

None of the patients experienced rebleeding of the aneurysm after treatment. There were no delayed adverse events (6–9 months after treatment).

* Defined as 1 day to 1 month.

was started approximately 2 hours after the endovascular procedure. The ticlopidine was suspended 1 month after the procedure while the ASA was continued for another 3 months. Two patients at the time of the SAH were already receiving dual antiplatelet therapy for comorbidities; in such cases the inhibitor of the IIb/IIIa receptor was not administered during the endovascular procedure.

Follow-Up

A clinical evaluation was conducted between 6 and 12 months after endovascular treatment and whenever patients returned for follow-up imaging. The patients' clinical conditions at follow-up evaluations were scored using the modified Rankin Scale (mRS). Imaging follow-up evaluations were performed according to the following scheme. Between 1 and 3 months after treatment, CT angiography (or MR angiography if coils were present) was performed. A digital subtraction angiography (DSA) follow-up control study was obtained between 6 and 12 months after treatment, with or without CT or MRI. Patency of the parent artery, presence and degree of in-stent stenosis, residual filling of the aneurysm, and shrinking of the aneurysmal sac were evaluated.

Results

Endovascular Procedure and Adverse Events

In all 17 patients the FDD deployment was technically successful. None of the aneurysms re-bleed after the implantation of the FDD (Table 2). No procedural- or

TABLE 3. Clinical and angiographic follow-up results

Case No.	Angiographic Midterm Follow-Up (6–12 mos)	mRS Score (6–12 mos)
1	Not available	6
2	Not available	6
3	Exclusion	0
4	Exclusion	0
5	Exclusion	0
6	Exclusion	0
7	Exclusion	0
8	Not available	5
9	Exclusion	0
10	Enlarged	1
11	Exclusion	3
12	Exclusion	0
13	Reduction	0
14	Exclusion	0
15	Exclusion	0
16	Exclusion	0
17	Exclusion	4

device-related deaths were recorded. Two patients died a few days after the endovascular treatment because of complications of the SAH itself. Case 1 had 3 episodes of SAH before the treatment and died 3 days after the procedure; Case 2 with severe anorexia died 8 days later as complication of her massive SAH. No delayed deaths were recorded.

Intraprocedural or periprocedural (defined as 1 day to 1 month after the procedure) morbidity was 12% (2 of 17). In Case 11 a significant intraparenchymal hematoma occurred 5 days after the endovascular procedure during a surgical repositioning of external ventricular drainage (EVD); the patient showed a left hemiplegia with an mRS score of 5 at discharge. In Case 17 with a posterior inferior cerebellar artery (PICA) aneurysm, a PED Flex FDD was deployed in the vertebral artery without covering the origin of the spinal artery. Two weeks after the procedure, this patient presented with acute paraplegia after an episode of bronchospasm followed by severe hypotension; MRI showed an acute lower spinal cord infarction while DSA showed the patency of the vertebral artery previously treated with FDD. No delayed (defined as 1–12 months after the procedure) morbidity was recorded.

Adverse intraprocedural events occurred in 3 procedures, with no clinical sequelae. There was 1 intrastent thrombosis, 1 minor subarachnoid bleeding, and 1 migration of the distal tip of the microcatheter. In Case 2 with a dissecting aneurysm of the terminal segment of the internal carotid artery (ICA) extending to the M₁ segment of the MCA, during the superselective microcatheterization of the MCA, the microwire perforated the vessel wall and caused a small amount of SAH. In Case 9 with a dissecting aneurysm of a PCA perforator, an intrastent thrombosis occurred after the positioning of the Silk FDD; after administration of 500 mg of ASA and 4 mg of abciximab, the occlusion resolved without any clinical sequelae. In Case 13

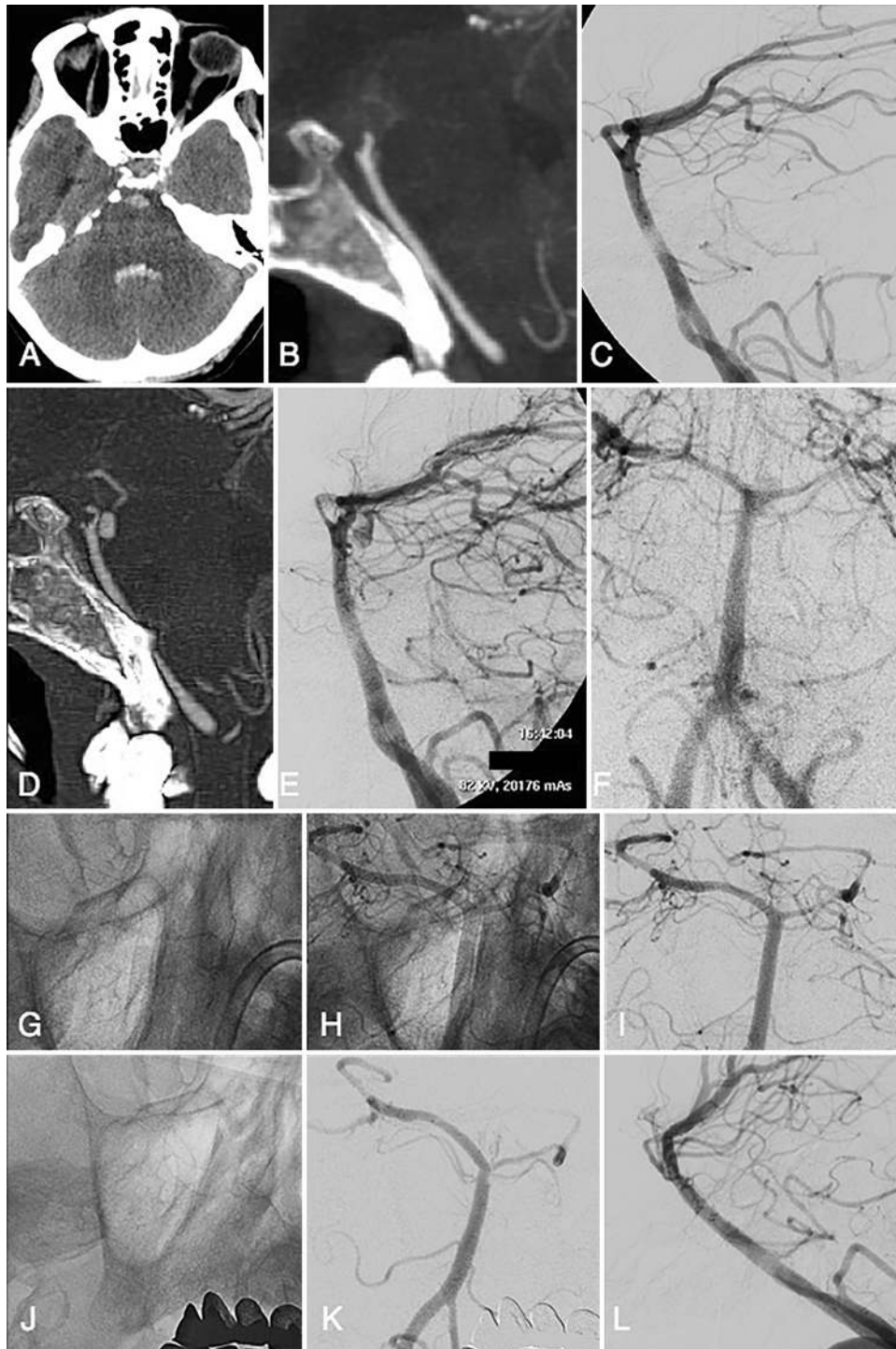


FIG. 1. Case 11. Images obtained in a 60-year-old woman with sudden onset of headache and confusion. An unenhanced axial CT scan (A) showed SAH in the prepontine cisterns, basal cisterns, and fourth ventricle. No source of bleeding was detected on CT angiography (B) and DSA (C). A CT angiogram (D) acquired 10 days later showed a small aneurysm located on the posterior aspect of the basilar apex. Lateral and frontal angiograms (E and F) confirmed the presence of a small pseudoaneurysm of a perforator of the basilar artery that was subsequently treated via implantation of a PED from the right PCA to the mid-third of the basilar artery. Postprocedure frontal angiograms (G–I) showed good positioning of the PED with a reduction of flow inside the pseudoaneurysm. Six-month DSA follow-up (J–L) showed the disappearance of the pseudoaneurysm.

with a dissecting aneurysm of the A₂ segment, during the delivery of the Surpass Streamline FDD the distal tip of the pusher microcatheter detached and migrated into a

small distal left parietal branch of the MCA; no clinical sequelae were recorded. No delayed adverse events occurred in any patient.

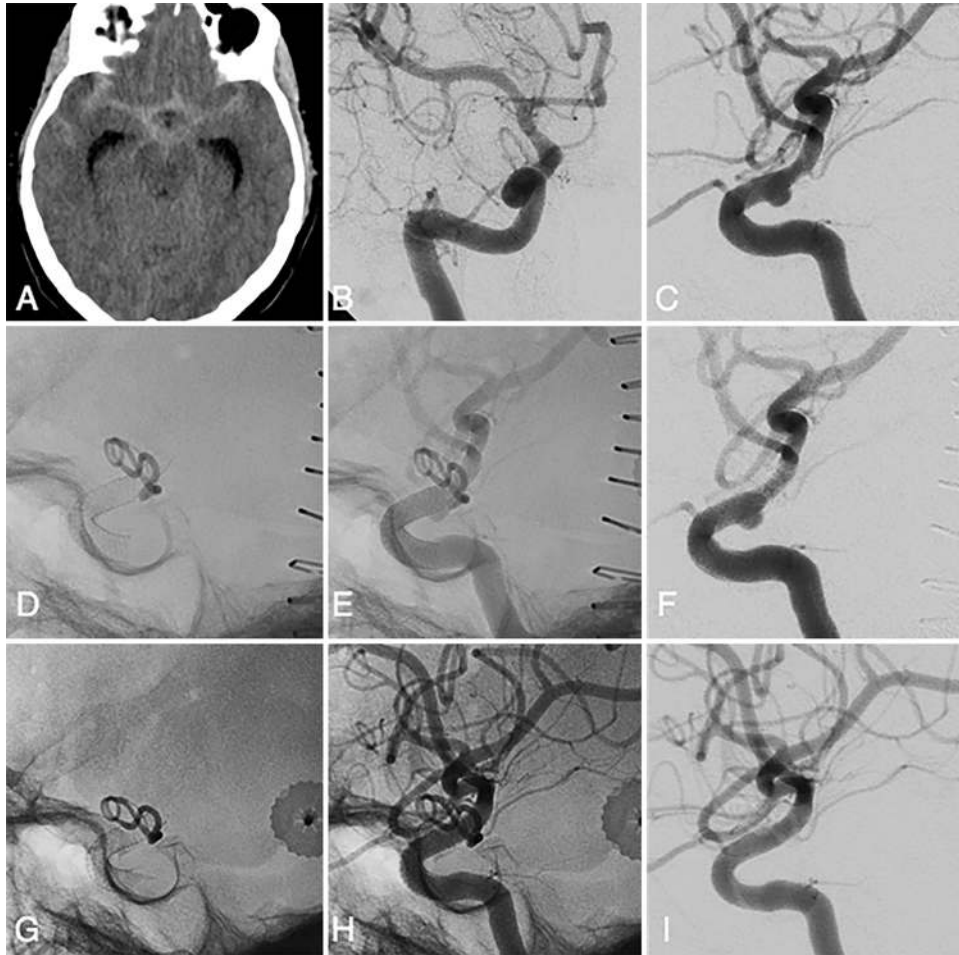


FIG. 2. Case 7. Images from a 62-year-old woman who presented in a coma. Unenhanced axial CT (A) demonstrated a huge SAH in the basal and sylvian cisterns due to a ruptured BBA of the right ICA as shown in frontal and lateral angiograms (B and C). The patient underwent surgical exploration to clip the aneurysm. Clipping was unsuccessful and the patient was transferred to the angiography suite. Unsubtracted and subtracted lateral angiograms (D–F) after deployment of a PED in the right ICA show the correct position of the device and the surgical clip. Six-month angiographic follow-up (G–I) show the complete exclusion of the aneurysm.

Follow-Up Evaluations

A clinical evaluation was conducted between 6 and 12 months after the endovascular treatment (Table 3). One patient had an mRS score of 5 (Case 8), 1 patient had an mRS score of 4 (Case 17), 1 patient had an mRS score of 3 (Case 11), 1 patient had an mRS score of 1 (Case 10), and the remaining 11 patients presented with an mRS score of 0.

Angiographic follow-up evaluations were available in 14 (93%) of 15 surviving patients; the only patient who could not be examined was the patient with an mRS score of 5 (Case 8). In 12 patients (86%) complete exclusion of the aneurysm was achieved (Figs. 1–3). In Case 10 the aneurysm was not excluded due to displacement of the 2 FDDs previously implanted, and MRI showed an enlargement of the aneurysm. This patient underwent a subsequent endovascular procedure with deployment of 2 more FDDs; the angiographic follow-up performed 6 months after the retreatment showed complete exclusion of the aneurysm. In Case 13 a small remnant of the aneurysm was present at the 6 and 12 months angiographic follow-up. No

significant stenosis or intrastent thrombosis was observed at follow-up imaging.

Discussion

In this study we report our experience in the treatment of ruptured aneurysms with FDD. None of the aneurysms re-bled after the endovascular procedure and none of the clinical complications recorded were directly correlated to the FDD implant. The overall mortality rate was 12% (2/17), and, in those 2 patients, the bad outcome was due to the SAH itself. The overall morbidity rate was 12%. In 1 case, the patient had a huge intraparenchymal bleeding during a repositioning of EVD a few days after the endovascular procedure; in the other case, 2 weeks after the endovascular procedure, the patient with a PICA aneurysm experienced a lower spinal cord ischemia.

In recent years, the advent of FDD has introduced a major improvement in the treatment of unruptured wide-neck, dissecting, or fusiform aneurysms.^{6,11,15,16} The disruption of flow into the aneurysm induces intrasaccular thrombosis and aneurysmal shrinkage.⁸ However, this

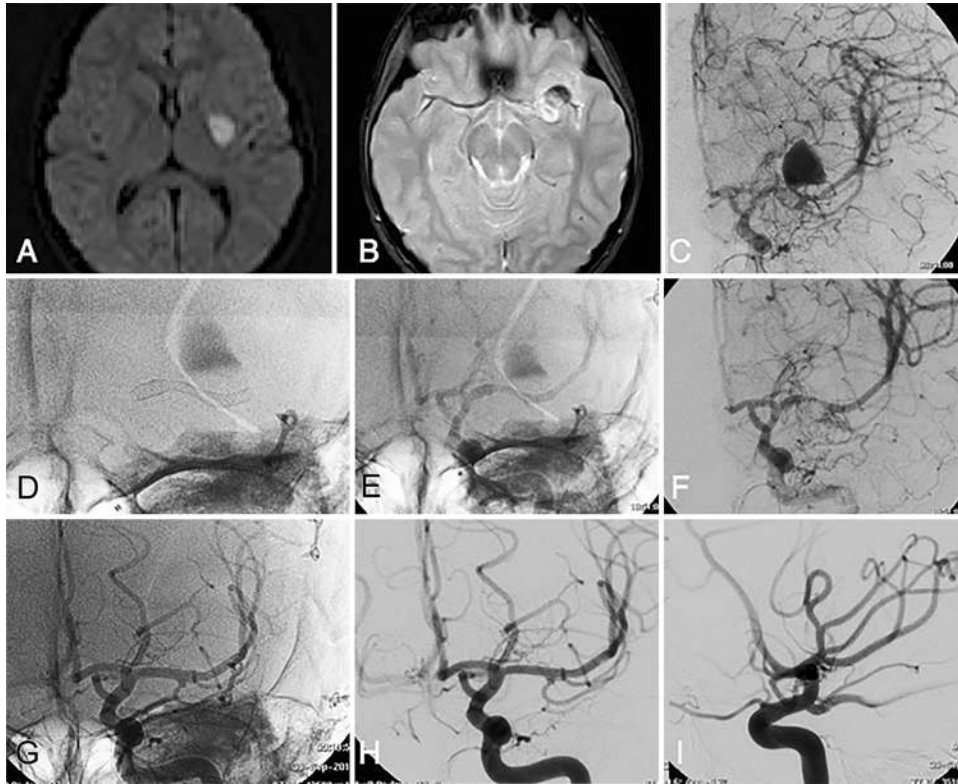


FIG. 3. Case 3. Images obtained in a 12-year-old with acute onset of right hemiplegia and headache. Diffusion-weighted imaging (A) and axial T2-weighted images (B) showed a small ischemic lesion in the left internal capsule/striatum due to a large ruptured dissecting aneurysm of the left MCA better viewed on the frontal angiogram (C). The patient underwent a surgical exploration of the aneurysm and was then transferred to our hospital. A Pipeline FDD was deployed in the M₁ and M₂ segments of the left MCA. Unsubtracted and subtracted frontal angiograms (D–F) show the correct deployment of the FDD across the aneurysm with initial stagnation of flow inside the aneurismal sac. Six-month angiographic follow-up (G–I) shows the complete exclusion of the aneurysm with optimal reconstruction of the MCA.

process requires some time and during this period there may exist a risk of re-rupture. In addition, the use of dual antiplatelet therapy may increase the risk of a major bleeding in cases involving neurosurgical procedures that are sometimes required in patients with SAH.^{3,12}

Despite these limits, our data support the idea that the risk of rebleeding of a ruptured aneurysm, treated using an FDD, is low, even in those aneurysms such as BBAs known to have a higher risk of rebleeding compared with others.¹³ Similar findings have been reported in other publications.^{3,4,10}

Aydin et al., in his series of 11 patients, did not report any re-bleeds with an overall morbidity and mortality rate of 9%, respectively.³ Correspondingly, Lin et al., in his multicenter series of 26 patients, reported a similar rate of periprocedural/delayed complications (12%), including 1 case of rebleeding of a saccular aneurysm treated with a PED 1 day before.¹⁰

In BBAs and ruptured dissecting aneurysms, conventional endovascular and/or surgical strategies can be technically difficult, nondefinitive, or even impossible.^{1,5,7,9,13,14} In such cases, implantation of an FDD could represent a reasonable choice as supported by our data. Moreover, we report an 86% occlusion rate at midterm follow-up. This rate is substantially comparable with the occlusion rate of unruptured aneurysms treated with FDDs in other series.^{6,11,15,16}

The treatment of an unruptured aneurysm with an FDD requires dual antiplatelet therapy (P2Y₁₂ receptor antagonists and ASA) that should be started at least a few days before the procedure to reach an optimal level of platelet inhibition.¹⁵ Unfortunately, in the setting of SAH due to a ruptured aneurysm, to introduce the conventional antiplatelet therapy would delay the endovascular treatment³ and would expose the patient to the risk of re-rupture of the aneurysm (especially BBAs); in addition, the rebleeding of the aneurysm during antiplatelet therapy would result in a massive SAH. Conversely, the inhibitors of IIb/IIIa glycoproteins have a very potent inhibitory effect on platelets, and a rapid onset of action, but are available only for intravenous use and can be used just for short periods of time.²

We addressed the problem of the antiplatelet therapy in acute procedures by administering the inhibitors of IIb/IIIa glycoproteins immediately after the deployment of the FDD and by the introduction of dual antiplatelet therapy in the following hours. In our series, we report only 1 case of acute intrastent thrombosis, which rapidly resolved after an adjunctive intravenous bolus of abciximab and ASA.

The limitations of this work are that it is a retrospective observational study conducted on a small population. These limitations may affect the low rate of complications, especially regarding the rebleeding rate of the aneurysm treated by FDD implantation.

Conclusions

Parent artery reconstruction with FDDs in ruptured aneurysms appears to be safe and can be a valid alternative treatment when conventional endovascular or surgical techniques are challenging.

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Disclosures

Dr. Valvassori has served as a consultant to Medtronic, Stryker, Microvention, Phenox, Balt Extrusion, and ABMedica. Dr. Boccardi has served as a consultant to Medtronic, Microvention, and Balt Extrusion.

Author Contributions

Conception and design: Lozupone, Piano, Valvassori, Boccardi. Acquisition of data: Lozupone, Piano. Analysis and interpretation of data: Lozupone, Piano, Valvassori, Visconti, Boccardi. Drafting the article: Lozupone. Critically revising the article: Piano, Quilici, Pero, Boccardi. Reviewed submitted version of manuscript: Boccardi. Approved the final version of the manuscript on behalf of all authors: Lozupone. Statistical analysis: Quilici, Pero. Administrative/technical/material support: Valvassori. Study supervision: Valvassori, Boccardi.

Correspondence

Emilio Lozupone, Department of Neuroradiology, ASST Grande Ospedale Metropolitano Niguarda, Via Roccaporena 51, Rome 00191, Italy. email: emilio.lozupone@live.it.