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Pipeline embolization of ruptured, previously coiled cerebral aneurysms: Case series and considerations for management

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Abstract:

PURPOSE: Aneurysmal recurrence represents a significant drawback of endovascular coiling, particularly in aneurysms that have previously ruptured. Given the high recurrence rate of coiled aneurysms and particularly the risk of posttreatment rupture in previously ruptured aneurysms that have been treated by coiling, the question of how best to treat ruptured aneurysms that recur postcoiling remains.

MATERIALS AND METHODS: We conducted a retrospective analysis of twenty patients who underwent pipeline embolization of previously ruptured, coiled cerebral aneurysms.

RESULTS: Pipeline embolization device (PED) treatment resulted in complete aneurysmal occlusion in 10 patients (62.5%) at first angiographic follow-up, and 11 patients (68.75%) at last follow-up. No PED-related complications were encountered and there were no peri-procedural or postprocedural hemorrhages, or symptomatic ischemic events following flow diversion.

CONCLUSIONS: PED as a second-line treatment is a safe and effective modality for achieving aneurysmal occlusion in recurrent, previously ruptured, primarily coiled aneurysms. Additionally, a staged coil-to-PED approach may be considered for the management of acutely ruptured aneurysms to achieve aneurysmal obliteration in an effort to mitigate recurrence, and reduce the amount of postprocedural studies.

Keywords:

Aneurysm, endovascular, flow diversion, hemorrhage, pipeline, subarachnoid

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Introduction

With the development of new medical technologies, the treatment of intracranial aneurysms has increasingly been favoring endovascular modalities, including coiling, stenting, stent-assisted coiling, and flow diversion, that are less invasive and often less morbid than microsurgical clipping.^[1] Coil embolization is one of the most commonly utilized procedures for management of cerebral

aneurysms and has been shown to result in greater likelihood of independent survival in comparison to microsurgical clipping.^[2] A significant drawback of this technique, however, is the high aneurysmal recurrence and retreatment rates, with 13%–48% recurrence, and approximately 10%–13% retreatment.^[1-5]

Aneurysm size, width of aneurysm neck, treatment type and outcome during acute phase after rupture, and length of follow-up are associated with increased risk of aneurysmal recurrence.^[6-8] The

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difficulty in managing patients with aneurysmal recurrences lies in distinguishing unstable aneurysm residuals, potentially prone to hemorrhage, from benign nonprogressing neck remnants, and thus to identify those patients who will need further treatment. Dorfer *et al.* found that the angiomorphology of aneurysmal recurrences after initial endovascular treatment is an important parameter to distinguish unstable aneurysm residuals, potentially prone to hemorrhage, from benign nonprogressing lesions.^[6] Neck remnants have been reported in 20%–60% of aneurysms treated endovascularly. In a 2018 study by Munich *et al.*, assessing 626 recurrent aneurysms (all of which were Raymond Roy Class II and III) that had been initially treated with coiling or stent-assisted coiling, it was found that unruptured aneurysms with residual necks had low risk of rupture (0.6%). Ruptured aneurysms with residual neck remnants, however, had a posttreatment rupture rate of 3.4%, suggesting that rupture at presentation is a statistically significant predictor of posttreatment re-rupture, and that these aneurysms require more aggressive treatment to obtain complete occlusion.^[9]

Given the high recurrence rate of coiled aneurysms and particularly the risk of posttreatment rupture in previously ruptured aneurysms that have been treated by coiling, the question of how best to treat ruptured aneurysms that recur postcoiling remains. Recoiling of previously coiled aneurysms has been reported to have variable rates of near-complete to complete occlusion (46.8%–76%) and high incidence of recurrence (11%–50%).^[11] In addition, 13.2%–19.5% of previously coiled aneurysms require multiple retreatments to achieve occlusion.^[1,10–12] Recent studies have pointed to the efficacy and safety of using pipeline embolization devices (PED) in treating recurrent previously coiled intracranial aneurysms. A PED is a flexible, low-porosity endoluminal stent that promotes thrombosis of the aneurysmal sac by reducing blood flow between the patent artery and the aneurysmal sac.^[13] The strength of PEDs lies in their long-term endoluminal reconstruction. Because a PED does not directly interact with the aneurysm itself, PED deployment is not affected by the previously deployed coils in the aneurysm.^[11]

Few studies have specifically evaluated the safety and efficacy of PED treatment following recurrence of previously coiled aneurysms. Placement of a PED as a secondary treatment following failure of endovascular coiling has a reported efficacy of 69%–100%, however most of these studies pooled initial patient presentations, including both previously ruptured and unruptured aneurysms, into a single cohort for evaluation.^[1,5,14] In this paper, we assess the efficacy and safety of using PED to treat ruptured aneurysms that were treated by primary coiling, with significant residual or recurrence.

Materials and Methods

Patients

Patients with cerebral aneurysms treated with PED between January 2016 and January 2019 at a single institution, by a single practitioner, were reviewed. PED treatment was offered for recurrent complex, wide-neck aneurysms, partially thrombosed aneurysms, and aneurysms with multiple recurrences treated unsuccessfully by other means. Twenty patients with previously ruptured, coiled cerebral aneurysms, re-treated with the pipeline embolization device were identified. Two patients were excluded as they were previously retreated with flow diversion [Figure 1]. Baseline patient characteristics, aneurysm characteristics, and procedural characteristics were recorded. All study procedures were performed in accordance with the ethical standards of the hospital and college institutional review boards (Protocol #: 12883) and with the Helsinki Declaration of 1975, as revised in 2000. For this type of study, formal consent is not required.

Pipeline embolization device procedure

At least 7 days prior to intervention, the patients were started on 75-mg clopidogrel and 325-mg aspirin daily. Baseline aspirin and clopidogrel function assays were obtained prior to intervention. During the procedure, an initial bolus of heparin was administered after sheath placement, and the activated clotting time was maintained at a level at or above 250 s. An

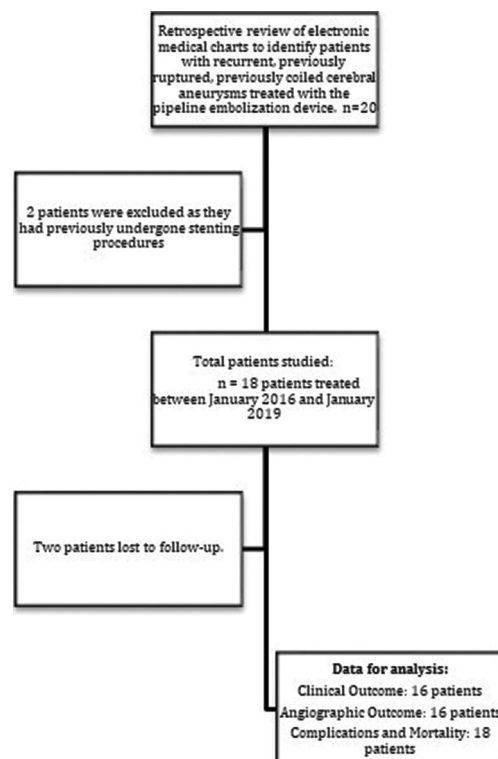


Figure 1: Flow diagram showing patient selection

angiographic evaluation was performed to assess aneurysm dimensions. Treatment with the PED was performed with the patient under general anesthesia. The number of stents was left to the operator's discretion. After embolization, another angiogram was obtained. After deployment of the pipeline embolization device, a cone beam computed tomography (CT) scan was obtained. For patients treated by PED following coil embolization in the acute setting after rupture, a CT of the head was obtained to assess for hemorrhage stability and presence of developing hydrocephalus prior to treatment. Patients were evaluated in the hospital after treatment for any complications. After discharge, patients were scheduled for clinical and angiographic follow-up. Patients continued taking both aspirin and clopidogrel for approximately 6 months after the procedure. Follow-up catheter angiography was performed at 6 months to assess for residual or recurrent aneurysm. At this point, a decision was made regarding continuation of clopidogrel. Repeat catheter angiography or noninvasive vascular imaging was performed at 1 year, based on the degree of aneurysmal occlusion at initial follow-up.

Outcomes

Patients underwent follow-up angiography at approximately 6 months, with some having subsequent angiography as well. All procedural and postprocedural complications were documented. The outcomes of interest in this study were the following: (1) the efficacy of the PED in the management of previously coiled, ruptured cerebral aneurysms, (2) peri-procedural complication rate, (3) re-rupture rate after secondary treatment, and (4) recurrence and retreatment rates after PED placement. Aneurysmal occlusion at follow-up was evaluated by the treating neurosurgeon and was categorized as occluded, nearly occluded, or incomplete occlusion.

Results

Patient and aneurysm characteristics

Twenty patients with previously ruptured, coiled, cerebral aneurysms who later underwent PED placement for aneurysm recurrence were retrospectively identified. Two patients were excluded as they had previously been treated, or retreated with flow diversion prior to arrival at our institution. In the 18 cases, the mean patient age was 56.94 years. 12 patients (66.7%) were female. Demographic data are found in Table 1. Recurrent aneurysms were identified in the internal carotid artery (ICA, 5.6%), posterior communicating artery (PCOM, 72.2%), anterior choroidal artery (11.1%), middle cerebral artery (5.6%), and posterior inferior communicating artery (PICA, 5.6%) [Table 1]. All aneurysms were saccular. The average aneurysm size

prior to treatment was initially 7.33 mm, with 15 small aneurysms (78.9%) and 3 large aneurysms (15.8%).

Treatment

In patients who had prior treatment, the mean number of interventions before PED placement was 1.1. Seventeen aneurysms were initially treated by unassisted coiling (94.4%), and 1 aneurysm was treated by balloon-assisted coiling (5.6%). The mean time from primary treatment to PED placement was 28 months (range: 22–2971 days). Indications for retreatment included residual aneurysm (55.6%), aneurysm recanalization (22.2%), and coil compaction (22.2%). The mean number of PEDs placed was 1.83, ranging from 1 to 5. Two patients required more than two devices because of the need for extensive parent vessel reconstruction. Over time and experience, the number of pipeline devices required to accomplish successful flow diversion has reduced, typically to a single device. The above data are represented in Table 1.

Efficacy of pipeline embolization devices treatment of previously coiled aneurysms

Two patients did not have a follow-up angiographic evaluation either because of loss to follow-up. Of the 16 patients who had follow-up angiograms, PED treatment resulted in complete aneurysm occlusion in 10 patients (62.5%) at first angiographic follow-up, and 11 patients at last follow-up (68.75%). Two patients underwent retreatment with pipeline embolization following initial angiographic follow-up. All incompletely occluded aneurysms had significant stasis within the residual, and were considered well protected. The mean angiographic follow-up time from PED placement to first angiogram was 7.6 months (range: 84–331 days). The above data are represented in Table 2.

Complications

Four patients suffered from adverse events following primary coiling and in the setting of acute subarachnoid hemorrhage, two deep-venous thrombi, one ischemic stroke, one pneumonia, and two unfavorable discharges. Only the ischemic stroke, however, was considered a procedure-related complication. There were no repeat hemorrhages between primary and secondary treatments. No PED-related complications were encountered. There were no peri-procedural or postprocedural hemorrhages or symptomatic ischemic events following flow diversion. Patients tolerated aspirin and clopidogrel treatment well, without any known complication.

Discussion

The introduction of the PED revolutionized intracranial aneurysm management, particularly for large,

Table 1: Patient characteristics and indications for treatment

Case number	Hunt-Hess/ Fisher	Aneurysmal location	Maximum diameter (mm)	Primary treatment	Raymond- Roy	Time from initial Tx (months)	Indication for re- treatment	Number of devices
1	5/4	PCOM	15	Coil	3	31	Residual aneurysm	4
2	3/4	PCOM	9	Coil	2	12	Coil compaction	1
3	2/3	PCOM	8	Coil	3	8	Residual aneurysm	1
4	5/4	PICA	3	Coil	3	3	Coil compaction	5
5	3/4	PCOM	7	Stent-coil	3	10	Residual aneurysm	2
6	2/3	PCOM	7	Coil	1	41	Residual aneurysm	1
7	2/2	AChor	4	Coil	1	66	Residual aneurysm	1
8	5/4	ICA	15	Coil	2	9	Residual aneurysm	3
9	3/3	PCOM	6	Coil	3	1	Residual aneurysm	1
10	N/A	PCOM	13	Coil	3	97	Residual aneurysm	1
11	3/4	PCOM	5	Coil	2	2	Aneurysm recanalization	2
12	3/4	PCOM	6	Coil	3	80	Coil compaction	2
13	2/3	MCA	8	Coil	2	6	Residual aneurysm	1
14	2/4	PCOM	5	Coil	2	2	Residual aneurysm	1
15	N/A	PCOM	5	Coil	2	97	Aneurysm recanalization	2
16	1/4	AChor	3	Coil	1	7	Aneurysm recanalization	1
17	3/4	PCOM	9	Coil	2	8	Aneurysm recanalization	2
18*	N/A	PCOM	4	Coil	N/A	Unknown	Coil compaction	2

*Patient initially treated at an outside hospital. PCOM: Posterior communicating artery, PICA: Posterior inferior cerebellar artery, AChor: Anterior choroidal artery, ICA: Internal carotid artery, MCA: Middle cerebral artery, N/A: Not available

Table 2: Angiographic follow-up and outcomes postpipeline embolization devices

Case number	Initial angiographic result (months)	Latest angiographic result (months)
1†	N/A	N/A
2	Incomplete occlusion (7)	Nearly occluded (16)
3	Occluded (8)	-
4	Incomplete occlusion (11)	Occluded (23)*
5	Occluded (7)	-
6	Occluded (7)	-
7	Occluded (9)	-
8	Occluded (9)	-
9	Nearly occluded (8)	-
10†	N/A	N/A
11	Nearly occluded (8)	-
12	Occluded (7)	-
13	Nearly occluded (3)	-
14	Occluded (7)	-
15	Occluded (11)	-
16	Incomplete occlusion (6)	Incomplete occlusion (12)
17	Occluded (6)	-
18	Occluded (7)	-

*Patient was retreated with PED after initial retreatment, †Patient lost to follow-up. PED: Pipeline embolization devices, N/A: Not available

wide-necked aneurysms of the ICA.^[13] The significant recurrence rate in previously treated aneurysms has prompted an increased use of PED in these aneurysms as a second-line treatment. While prior treatment failure certainly places the patient at risk for further recurrence, PED provides a distinct advantage in restoring physiological cerebral flow dynamics and providing a scaffold for endothelialization. To the best of our knowledge, this is the first study to look specifically at the efficacy and safety of the PED in the

management of recurrent ruptured, previously coiled, cerebral aneurysms.

Of the 16 patients in our study who had follow-up angiograms, complete occlusion at last follow-up was found in 11/16 patients (68.75%). Two patients underwent retreatment with pipeline embolization following initial angiographic follow-up. Five aneurysms were incompletely, though nearly, occluded at last angiographic follow-up [Table 3]. Three out of five (60%) of incompletely occluded aneurysms were of the PCOM artery. All the five aneurysms were treated by pipeline embolization within 1 year of initial treatment. Microsurgical clip ligation was not pursued in these patients either because of morphological concerns of the aneurysm or because of patient and/or practitioner preference, as well as the perceived reduced morbidity with endovascular techniques. Importantly, all incompletely occluded aneurysms had significant stasis within the residual, and were considered well protected. These findings are similar to those previously reported for all-comer recurrent aneurysms re-treated by PED. Interestingly, one of these aneurysms was of the anterior communicating artery aneurysm, which exhibited residual filling from the contralateral anterior cerebral artery. For this reason, a second device was placed in the contralateral anterior cerebral artery in an effort to “jail” the anterior communicating artery aneurysm. He has not reached appropriate time for follow-up angiogram following second device placement.

Several studies have specifically evaluated the safety and efficacy of PED treatment following recurrence of previously coiled aneurysms [Table 4] and revealed

Table 3. Summary of Patients with Incomplete Aneurysmal Occlusion

Patient	2	9*	11*	13†	16
HTN	Yes	No	No	Yes	No
DM	No	No	No	No	No
Tobacco use	Yes	No	No	Yes	No
Family History	Yes	No	Yes	Yes	Yes
Hunt-Hess/Fisher	3/4	3/3	3/4	2/3	1/4
Aneurysm Location	PCOM	PCOM	PCOM	MCA	ACOM
Initial Aneurysm Size (mm)	9	6	5	8	3
Aneurysm Shape	Multilobulated	Windsock	Saccular	Saccular	Saccular
Raymond-Roy After Initial Coiling	2	3	2	2	3
Time from initial Tx (mo)	12	1	2	6	7
No. Treatments Prior to PED	1	1	1	1	1
No. PEDs used	1	1	2	1	1
Retreatments after PED	None	None	None	None	PED
Complications	None	None	None	None	None
Time to Last Follow-up (mo)	16	8	8	3	12
Result of Last Angiogram	Subtle residual	Significant stasis	Significant stasis	Significant stasis	Incomplete occlusion

* Aneurysm intentionally underpacked with the intent of returning to place PED. † Aneurysm intentionally underpacked to preserve the origin of a branch vessel

Table 4: Comparison to previous literature

Authors	Prior treatment	Number of patients	Number of previously ruptured aneurysms, n (%)	Complete occlusion rate (%)	Clinical outcome
Daou <i>et al.</i> , 2015 ^[1]	Primary coiling	32	17/32 (53)	76.7	3% IPH
Benaissa <i>et al.</i> , 2015 ^[23]	Primary coiling +/- stent	29	24/29 (83)	60.7	6.9% permanent morbidity
Kühn <i>et al.</i> , 2017 ^[14]	Primary coiling	18/24	11/18 (61)	69.2	12.5% IPH; no long-term sequelae
Dornbos <i>et al.</i> , 2017 ^[5]	Primary coiling	7/13	4/7 (57)	100	No long-term sequelae
Akgul <i>et al.</i> , 2021 ^[24]	Primary coiling +/- stent or balloon	86	Unknown	87.4	4.6% overall complications

*Results reflect outcomes of the entire cohort. IPH: Idiopathic pulmonary hemosiderosis

complete obliteration rates of 69%–100%. When combined with those demonstrating near-complete occlusion (>90%), occlusion rates increased to >85%, consistent with radiographic outcomes for PED placement in untreated aneurysms and with those seen in microsurgical clipping of recurrent aneurysms.^[15-17,23,24] These studies, however, present results of heterogeneous populations including both ruptured and unruptured aneurysms.

Daou *et al.* conducted a study in which patients underwent PED placement following coiling in recurrent aneurysms and discovered complete aneurysm occlusion in 76.7% of patients and near-complete aneurysm occlusion in 90% of patients, for a total rate of complete and near-complete aneurysm occlusion of 86.7%. They also found that 97% of patients had a favorable clinical outcome based on modified Rankin scores of 0 or 1.^[1] Of the 32 patients included in their study, 17 initially presented in the setting of rupture, however the results for these patients were not included in separate analysis. In a 2017 study, Dornbos *et al.* evaluated seven patients that underwent PED retreatment of previously coiled aneurysms.^[5] Of these, four initially presented as a rupture. Five of the seven

patients were available for angiographic follow-up, including all four initially ruptured aneurysms. They found that of patients who underwent PED placement following failed primary coiling, 80% achieved complete occlusion at 6 months, and 100% were found to display complete occlusion at 1 year. Kühn *et al.* performed an assessment of PED placement for management of recurrent intracranial aneurysms in a sample of 24 patients.^[14] They presented 6-month follow-up data for 11 patients with previously treated ruptured aneurysms. Nine patients showed complete occlusion following PED placement (81.8%), and two showed near-complete occlusion (18.2%). Twelve-month follow-up was available for nine patients, eight of which showed complete occlusion (88.9%) and one showed a near-complete occlusion (11.1%). Progression from near-complete occlusion at 6 months to complete occlusion at 12 months was seen in one case. After flow diverter placement, previously ruptured aneurysms showed a higher occlusion rate than previously unruptured aneurysms.

Posterior communicating artery aneurysms

Of the 18 aneurysms secondarily treated by PED in our series, 13 (72.2%) were of the PCOM. Of the patients who

underwent angiographic follow-up, 8/11 (72.2%) were completely occluded following flow diversion. PCOM aneurysms are one of the most commonly encountered aneurysms, representing about 25% of all aneurysms and 50% of all internal carotid aneurysms.^[18] PCOM aneurysms in particular have the second highest rate of recurrence after coiling at 37.2%, as reported by Raymond *et al.*, with several other studies also finding PCOM aneurysms to have significantly higher risks of recurrence and need for retreatment.^[4] A study by Yu *et al.* in 2018 found that recurrent aneurysms of the PCOM were more likely to be type III–V (formation of a new aneurysm neck or aneurysm sac), which they also found was associated with a greater likelihood of re-rupture.^[17] As per Munich's findings, previously ruptured PCOM aneurysms that have been treated with coiling are even more prominently at risk for re-rupture and need for secondary treatment.^[9]

Staged procedure

Several of our patients underwent a staged procedure involving initial coil protection of the aneurysm in the setting of acute rupture, followed by short-term treatment with the pipeline embolization device [Figure 2]. A staged procedure was defined as occurring within 3 months of the initial coiling treatment. To our knowledge, this has only been described once previously in the literature, in the form of a case report by Haider *et al.*, who described a patient who suffered from aneurysmal subarachnoid hemorrhage secondary to a multilobulated left PCOM aneurysm.^[19] The aneurysm was initially treated by endovascular coiling, however was unable to be completely coiled due to its configuration and herniation of the coils into the parent vessel. The patient was intentionally left undercoiled with the plan to return in 2 weeks for definitive flow diversion.

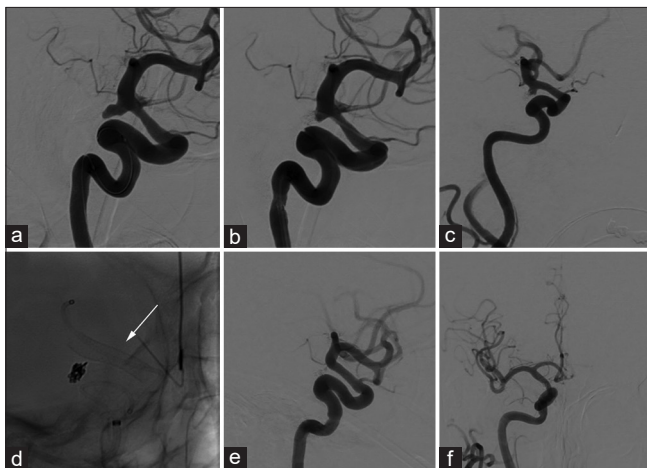


Figure 2: Angiographic course of a patient who underwent a staged coil-to-pipeline embolization device treatment over 1 month. Initial diagnostic internal carotid injection revealing a broad-based, irregular, posterior communicating artery aneurysm (a), which was primarily coiled (b and c). Unsubtracted views showing the pipeline construct, placed in a staged fashion (d). Follow-up angiography revealing obliteration of the previously treated aneurysm (e and f)

Six-month angiography revealed complete occlusion of the aneurysm with no residual or recurrence. Similarly, our cases demonstrate how an anatomically complex ruptured intracranial aneurysm may initially be treated with staged endovascular coiling in the acute phase until dual antiplatelet therapy use and treatment with PED is no longer contraindicated. The treatment paradigm allows the aneurysmal rupture site to be secured in the short term and the patient to undergo potentially invasive procedures in the acute phase that may not have been possible while on dual antiplatelet therapy. We believe that early PED provides a scaffold for neointimal formation and vessel reconstruction, generating a more durable result. This will likely result in less postprocedural imaging studies, and fewer number of endovascular interventions necessary to manage recurrent aneurysms.

Complications

In our study, we observed no procedure-related complications, no peri-procedural ischemic stroke, or intracranial hemorrhage. Importantly, no postprocedural hemorrhage or aneurysmal recurrence was observed in our follow-up period. For patients who underwent pipeline embolization for retreatment of previously coiled aneurysms, complication rates of 0%–12.5% have been reported.^[1,5,14] Both ischemic and hemorrhagic complications have been observed after the placement of pipeline embolization device. Intracerebral hemorrhage is a well-known complication of PED treatment.^[15,20–22] This phenomenon is believed to be the result of hemorrhagic conversion of embolic infarcts aggravated in the setting of dual antiplatelet therapy. Interestingly, Kühn *et al.* observed three cases of intracranial hemorrhage in their study population, however all three were seen only in patients with previously ruptured aneurysms, suggesting that previously ruptured aneurysms are potentially more prone to develop intracranial hemorrhage during the healing process after flow diverter placement.^[14] In our patient population, however, this was not encountered.

Limitations

The major limitations of this study include its retrospective, single-center, single-practitioner nature, which may not always reflect the results of other institutions. Additionally, this study includes only a modest sample size of patients with recurrent, ruptured, previously coiled aneurysms who underwent treatment with the PED.

Conclusion

PED as a second-line treatment is a safe and effective modality for achieving aneurysmal occlusion in recurrent, previously ruptured, primarily coiled aneurysms. Similar occlusion rates were achieved in comparison to recurrent unruptured aneurysms treated by PED as

well as previously untreated aneurysms treated with PED. No further aneurysmal recurrence or clinical symptomatology was encountered at most recent follow-up. We propose that a staged coil-to-PED approach be considered for management of ruptured aneurysms to achieve aneurysmal obliteration. This may result in fewer postprocedure imaging studies as well as fewer number of endovascular interventions necessary to manage recurrent aneurysms.

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Conflicts of interest

There are no conflicts of interest.

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