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Original Article

Immediate and follow-up results for 44 consecutive cases of small (<10 mm) internal carotid artery aneurysms treated with the pipeline embolization device

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Abstract

Background: The pipeline embolization device (PED) provides effective, durable and safe endovascular reconstruction of large and giant intracranial aneurysms. However, 80% of all cerebral aneurysms found in the general population are less than 10 mm in size. Treatment of small aneurysms (<10 mm) with flow diverters may be advantageous over endosaccular modalities that carry risks of procedural rupture during aneurysm access or coil placement.

Methods: We retrospectively reviewed a prospective, single-center aneurysm database to identify all patients with small (<10 mm) internal carotid artery (ICA) aneurysms who underwent endovascular treatment using the PED. Patient demographics, aneurysm characteristics, procedural details, complications, and technical and clinical outcomes were analyzed.

Results: Forty-four cases were performed in 41 patients (age range 31-78 years). PED was successfully implanted in 42 cases. A single PED was used in 37/42 (88%) cases. Mean postprocedure hospital stay was 1.7 ± 0.3 days and 98% of patients were discharged home. Major complication occurred in one patient (2.3%), who died of early subarachnoid hemorrhage. Transient neurological deficit, delayed intracerebral hemorrhage (asymptomatic), and delayed groin infection occurred in one patient each. Follow-up rate was 91.8% (45 aneurysms in 35 patients) with a mean follow-up of 4.0 ± 1.9 months. By 6 months post-PED implantation, angiographic success (complete or near complete aneurysm occlusion) was observed in 80%. Mild (<50%), asymptomatic, nonflow limiting in-stent stenosis was observed in 5.4% (2/37 cases). All the 35 patients with follow-up remained at preprocedure neurological baseline.

Conclusion: Small (<10 mm) ICA aneurysm treatment with PED implantation is safe and carries a high rate of early angiographic success.

Key Words: Cerebral aneurysms, flow diverter, pipeline embolization device

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INTRODUCTION

Since its inception in 2007, flow-diverting technology has revolutionized the treatment approach of large and giant cerebral aneurysms from an endosaccular to an endoluminal focus. This innovative strategy has enabled successful endovascular treatment of intracranial aneurysms previously considered difficult to treat with the conventional modalities of clipping and coiling with or without adjunctive devices (i.e., large, giant, wide-necked, or with diffuse circumferential involvement of the parent artery).[6,11,18,19,21,30] The Pipeline embolization device (PED; Covidien Vascular Therapies, Mansfield, MA) is currently the only Food and Drug Administration (FDA)-approved flow diverter available in the United States. Its on-label usage as dictated by the FDA is limited to the treatment of large or giant (≥10 mm) wide-necked intracranial aneurysms from the petrous to the superior hypophyseal segments of the internal carotid artery (ICA).[32] Clinical experience worldwide with PED has demonstrated the effectiveness, durability, safety, and cost-effectiveness of endovascular reconstruction primarily in large and giant aneurysms [5,8,19,30] Rates of occlusion at 6 months following PED treatment of such aneurysms have been impressive, ranging from 81.8% to 94.4%.[18,21,30,33]

Nevertheless, large and giant intracranial aneurysms only encompass a small fraction of all intracranial aneurysms. In contrast, over 80% of all cerebral aneurysms found in the general population are less than 10 mm in size.[31,35] There is considerable documentation in the literature that the majority of ruptured aneurysms are smaller than 10 mm.[13,14,26,34] Treatment of small aneurysms (<10 mm) with flow diverters may be advantageous over endosaccular modalities, which inherently carry a risk of procedural rupture during access of the aneurysm sac or coil placement.[2,20,22,29] Specific data regarding the procedural, angiographic, and clinical outcomes of PED treatment in small aneurysms is limited in the literature and commonly reported in conjunction with series on large and giant aneurysms.[12,18,27,30]

In this report, we present periprocedural outcomes and 2- to 6-month angiographic follow-up results for a series of 44 cases with ICA aneurysms less than 10 mm in size that were treated with the PED at a single-center by a single-operator.

MATERIALS AND METHODS

Patient selection

We retrospectively reviewed a prospective, single-center aneurysm database to identify all patients with small (<10 mm) ICA aneurysms who underwent endovascular treatment using the PED. Data with respect to the following variables were prospectively collected: patient demographics, anatomic characteristics of the aneurysm, details of the interventional procedure, procedural and periprocedural complications, and technical and clinical outcomes. Patients presenting with severe headache and clinical suspicion for subarachnoid hemorrhage (SAH) were screened with a computed tomography (CT) scan of the head and, if necessary, lumbar puncture to rule out a hemorrhage event.

Endovascular procedure

Embolization procedures were performed as previously published.[6] In brief, all patients were treated preoperatively with a dual antiplatelet regimen consisting of aspirin 325 mg daily and clopidogrel 75 mg daily for 7 days prior to the intervention. The degree of P2Y12 receptor inhibition was not routinely tested. All procedures were performed with systemic anticoagulation using heparin with a 5000-unit bolus at the start of each case followed by an intraprocedure rebolus of 1000 units at each additional hour. The goal of each procedure was complete coverage of the aneurysm neck or fusiform/diseased vessel segment with the PED and maximum vessel wall apposition along the length of the PED. A triaxial system was used through femoral access. This consisted of a 6 French Flexor Shuttle sheath (Cook Medical, Bloomington, IN), a 5 French Navien distal intracranial catheter (formerly ReFlex Distal Intracranial Catheter) (Covidien Vascular Therapies, Mansfield, MA) serving as the guide catheter[7] and a Marksman microcatheter (Covidien Vascular Therapies, Mansfield, MA). The distal PED was opened in the ipsilateral supraclinoid ICA or, more commonly, in the ipsilateral M1 segment. Proper device expansion and deployment was assessed with native fluoroscopy. If a partially deployed PED did not open properly secondary to device failure or was malpositioned, the device was corked and removed.[5] Control digital subtraction angiography (DSA) was performed immediately after deployment and at 5 and/or 10 minutes after deployment to confirm patency of the parent vessels and to rule out intraluminal thrombus. At the end of the procedure, a Dyna CT scan without contrast was performed to assess PED morphology and to evaluate for intracranial hemorrhage. Groin closure and hemostasis was achieved with manual compression after allowing several hours for the PTT to normalize postprocedure.

Procedural assessment and follow-up

Procedural outcomes evaluated include the removal of incompletely deployed PED, the number of cases successfully completed, length of postprocedure hospital stay, number of patients discharged home, and immediate angiographic results. Immediate angiographic results were graded based on contrast stasis within the aneurysm using our previously described scale of mild, moderate or pronounced stasis and complete occlusion.[6] Procedural and periprocedural complications were also recorded

and evaluated. These categories included mortality, transient neurological deficit, major and minor stroke, intracerebral hemorrhage (ICH), SAH, cranial nerve palsy, PED thrombosis, vessel dissection, and groin complications. Major stroke was defined as stroke present after 7 days that increased the NIH stroke scale by ≥4 points, and minor stroke was defined as a stroke that resolved completely within 7 days or increased the NIH stroke scale by ≤3 points. Groin complications included groin infection or significant groin hematoma, defined as a hematoma requiring prolonged hospital stay or preventing ambulation.

Follow-up angiographies were performed at 2-3 or 6-month post-PED implantation. Standard projections and the original working projections for PED deployment were used to assess any residual flow within the aneurysms. Aneurysm occlusion was classified as complete occlusion, near-complete occlusion (with trace residual aneurysm filling), or persistent filling. In-stent stenosis was calculated on the basis of the minimal lumen diameter, and was graded as none (0% to <25%), mild (25% to <50%), moderate (50% to <75%), or severe (75-100%). Dual antiplatelet therapy consisting of aspirin 325 mg daily and clopidogrel 75 mg daily was continued for 6 months postprocedure. After 6 months, patients were instructed to discontinue clopidogrel and continued daily aspirin 325mg until their 1-year follow-up angiography.

Data are presented as counts, percentages and means. When means are presented, the standard error of the mean (SEM) is used to assess sample distribution.

RESULTS

Patient and aneurysm characteristics

Between September 2011 and July 2012, 41 consecutive patients with a total of 53 unruptured small ICA aneurysms less than 10 mm were treated with the PED. The mean age of the patients was 54.9 years (range 31-78). Table 1 presents the patient demographics and aneurysm characteristics. Of the 41 patients, 38 (92.7%) were women and 3 (7.3%) were men. Twenty-eight (68.3%) of the patients were White, 11 (26.8%) were Black, 1 (2.4%) was Asian, and 1 (2.4%) was Hispanic.

Of the 53 ICA aneurysms treated, the majority was paraophthalmic/clinoidal (34/53, 64.1%). Cavernous, ophthalmic, supraclinoid, and petrous locations accounted for 12 (22.6%), 5 (9.4%), 1 (1.9%), and 1 (1.9%), respectively. Seven of the cavernous aneurysms treated were in patients who had adjacent primary paraophthalmic aneurysm and the petrous aneurysm treated was a posttraumatic dissecting aneurysm. The mean size of the aneurysms treated was 5.34 ± 0.3 mm. Of the 53 treated aneurysms, 35 (66%) were saccular, 17 (32.1%) were fusiform and 1 (1.9%) was dissecting. Fusiform aneurysms were defined as involving >25% of the parent artery circumference. None of the patients treated presented with SAH and none had preexisting indwelling endoluminal devices.

Table 1: Patient demographics and aneurysm characteristics

	n or mean±SEM
Total patients, *n*	41 (100%)
Age (years), mean	54.9±1.6
Sex, *n* (%)	
Men	3 (7.3)
Women	38 (92.7)
Race, *n* (%)	
White	28 (68.3)
Black	11 (26.8)
Asian	1 (2.4)
Hispanic	1 (2.4)
Total aneurysms treated, *n*	53 (100%)
Aneurysm size (mm), mean	5.34±0.3
Aneurysm location, *n* (%)	
Petrous	1 (1.9)
Cavernous	12 (22.6)
Ophthalmic	5 (9.4)
Paraophthalmic	34 (64.1)
Supraclinoid	1 (1.9)
Aneurysm type, *n* (%)	
Saccular	35 (66)
Fusiform	17 (32.1)
Dissecting	1 (1.9)

SEM: Standard error of mean

PED treatment characteristics

Altogether, 44 treatments were performed in 41 patients with a total of 53 aneurysms. The details from these procedures are shown in Table 2. Three patients had bilateral paraophthalmic ICA aneurysms and these were treated on separate dates. Six patients had multiple aneurysms that were treated during a single procedure. For each of these six patients, the additional aneurysms were ipsilateral and adjacent to the primary aneurysm. Of the 44 cases, 2 cases (with 3 aneurysms) were unsuccessful PED implantations secondary to significant tortuosity of the distal ICA. Of the 42 cases with successful PED implantation, a total of 50 aneurysms were treated. Thirty-seven of these cases (88.1%) required only a single PED while five cases (11.9%) required two PEDs. Removal of incompletely deployed PED ("corking") occurred in 6 of the 42 cases (14.3%). A total of 54 PEDs were used and 47 (87%) were successfully implanted. PEDs were removed either secondary to technical failure of the device to open or secondary to device malposition. None of the cases required additional balloon angioplasty after PED implantation. This was a function of using the

technique whereby the distal PED end was first properly positioned and well apposed to the parent vessel wall prior to completing final PED deployment. Adjunctive coils were placed immediately prior to device deployment in two cases (4.8%). The duration of fluoroscopy and amount of systemic heparin administered were used as an estimate of procedure length. The mean fluoroscopy time and mean intravenous heparin dose were 34.8 ± 2.9 minutes and 5,300 ± 100 units, respectively.

Immediate angiographic and clinical outcomes

Immediate angiographic results at the end of the procedure are presented in Table 3. Immediate complete angiographic occlusion was observed in one patient (2.4%) with a 6 mm fusiform cavernous aneurysm. Pronounced, moderate, and mild contrast stasis was observed in 21 (50%), 11 (26.2%), and 7 (16.7%) patients, respectively. Two patients (4.8%) had no contrast stasis within the aneurysm sac upon conclusion of the procedure. Both these patients had fusiform paraopthalmic artery aneurysms, 3 and 7 mm in size.

The mean postprocedure length of hospital stay for all patients was 1.7 ± 0.3 days. Two patients had total hospital stays of >5 days secondary to periprocedural complications compounded by baseline medical comorbidities as detailed below. In total, 40 of 41 patients (98%) were discharged home following treatment.

Periprocedural complications

Periprocedural complications are presented in Table 4. Of the 44 cases, major clinical periprocedural complication was encountered in one patient (2.3%), which has been described in detail in a prior publication.[6] In summary, the patient had emerged from anesthesia neurologically intact after successful PED implantation for a 3 mm wide-necked left-sided paraophthalmic artery aneurysm. Five hours after, she developed a change in mental status secondary to interval new acute SAH. Immediate post-SAH angiography demonstrated no change in the aneurysm morphology and no contrast extravasation. The timing of the hemorrhage is most consistent with a wire perforation during the initial procedure. Despite maximal medical and surgical interventions, the patient died from complications from the SAH.

Transient neurological deficit occurred in one patient (2.3%). This patient with uncontrolled hypertension and a prior left-sided middle cerebral artery stroke had transient mild speech and vision changes in the setting of elevated systolic blood pressure following PED treatment of tandem left paraophthalmic and cavernous aneurysms. None of the patients treated had a major or a minor ischemic stroke. However, one patient (2.3%) had delayed ICH in the right occipital lobe 3 days after a technically uncomplicated PED treatment for a 4 mm right-sided paraopthalmic artery aneurysm. This patient was receiving systemic anticoagulation for a recent deep vein thrombosis, and the hemorrhage occurred during the heparin to warfarin transition. This patient was ultimately discharged to home in good condition on postprocedure day 11.

None of the patients treated experienced new or exacerbation of cranial nerve palsy, *in situ* PED thrombosis, iatrogenic vessel dissection, or significant groin hematoma. Delayed groin infection was observed in one patient (2.3%), which was treated with oral antibiotics without further complication.

Table 2: PED treatment details

	n or mean±SEM
Total cases, *n*	44
Successful PED deployment	42 (95.5%)
Unsuccessful PED deployment	2 (4.5%)
Total aneurysms successfully treated with PED	50 (94.3%)
Total PEDs implanted, *n*	47
Number of PEDs implanted per case, mean	1.1±0.05
Number of PEDs implanted per case, *n*	
1	37 (88.1%)
2	5 (11.9%)
Mean fluoroscopy time (combined AP, lateral) per case, min	34.8±2.9
Mean intravenous heparin used per case (rounded to nearest 100), units	5300±100
Cases with adjunctive coils placed	2 (4.5%)
Cases requiring removal of incompletely deployed PED	6 (14.3%)

PED: Pipeline embolization device, SEM: Standard error of mean, AP: Anteroposterior

Table 3: Immediate angiographic results following PED deployment

Degree of contrast stasis	No. of cases (%)
None	2 (4.8)
Mild	7 (16.7)
Moderate	11 (26.2)
Pronounced	21 (50)
Complete occlusion	1 (2.4)

PED: Pipeline embolization device

Table 4: Periprocedural complications

	n (%)
Mortality*	1 (2.3)
Stroke	0 (0)
Hemorrhage	
ICH	1 (2.3)
SAH*	1 (2.3)
Transient neurological deficit	1 (2.3)
Groin complication	1 (2.3)

*SAH and mortality were complications in the same patient. ICH: Intracranial hemorrhage, SAH: Subarachnoid hemorrhage

Follow-up angiographic and clinical outcomes

Of the 38 surviving patients successfully treated with PED implantation there were a total of 49 aneurysms treated. Follow-up angiography has been done for 45/49 (91.8%) aneurysms, with a mean follow-up of 4.0 ± 1.9 months. Table 5 details the aneurysm characteristics and the angiographic outcomes of the aneurysms with follow-up. Of the 45 aneurysms with angiographic follow-up, 24 aneurysms had early follow-up at 2-3 months postprocedure, and 21 aneurysms at 6 months. Table 6 summarizes the observed angiographic occlusion rates at follow-up. Angiographic success, defined as having complete angiographic occlusion or near complete occlusion, was observed in 18/24 (75%) aneurysms at 2-3 month follow-up and 18/21 (85.7%) aneurysms at 6-month follow-up. Figures 1 and 2 show aneurysms with angiographic success at 2-3 months after PED treatment. Six aneurysms had persistent filling on 2-3 month follow-up angiography and have the following angioarchitecture: one fusiform, one medial cavernous, one medial paraophthalmic, one lateral paraophthalmic, and two ophthalmic. Of the 37 vessels with angiographic follow-up, 2 (5.4%) showed nonflow limiting mild (25% to <50%) in-stent stenosis. Both of these cases were asymptomatic and, thus, neither was treated. Additionally, there were no instances of PED migration on follow-up angiography. Of the 35 patients with follow-up, all remained at preprocedure neurological baseline.

DISCUSSION

We present in this report a dedicated series investigating the safety and efficacy of the PED for treatment of small ICA aneurysms less than 10 mm in size. The PED was successfully implanted in 39 patients with 50 aneurysms. A single PED was used in 88.1% of the cases. Ninety-eight percent of patients were discharged home following the embolization procedure. Of the 44 cases in this series, a major periprocedural complication of death secondary to SAH occurred in 1 patient (2.3%). Transient neurological deficit, delayed ICH, and delayed groin infection occurred in one patient each (2.3% each).

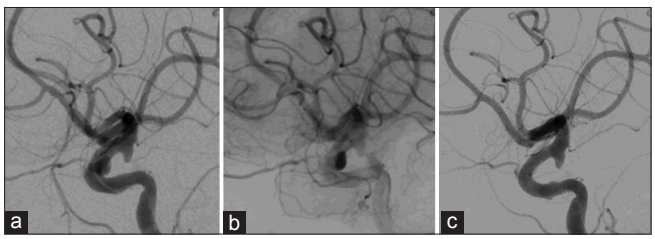

Figure 1: PED treatment of a 6 mm paraophthalmic aneurysm with angiographic success at 2 months (Case 1). (a) Preembolization DSA. (b) Immediately after implantation there is pronounced contrast stagnation within the aneurysm persisting into the venous phase. (c) Two-month follow-up DSA demonstrates complete angiographic occlusion

Of the 49 surviving aneurysms successfully treated, the follow-up rate was 91.8%. By 6 months following PED implantation, angiographic success was observed in 80%. Mild, nonflow limiting, in-stenosis was observed at a rate of 5.4% (2/37 cases). Of the 35 patients with follow-up, all remained at their neurological baseline.

Parent vessel reconstruction with PED implantation is gradually becoming the endovascular modality of choice for large and giant, fusiform or wide-necked aneurysms. Several series have reproducibly demonstrated that the high technical success rate and durability of PED treatment in these aneurysms can be achieved with a low incidence of complications.[6,18,27] The safety profile of PED treatment has been partially attributed to avoidance of direct catheterization of the saccular component of aneurysms, a process that is associated with a risk of procedural rupture.[18] This risk is particularly high for endosaccular coiling of small aneurysms.[18,19,21] For this reason, an endoluminal approach may also be applicable in the treatment of small aneurysms. Few reports have been published thus far on PED use in small aneurysms.[18,21,27] The majority of these experiences are described in combination with those of the large and giant aneurysms, making it difficult to directly compare outcomes. In Lylyk's report on the initial Buenos Aires Experience with PED implantation in 63 intracranial aneurysms, 33 aneurysms were small (<10 mm), however, this was not further stratified into the number of these aneurysms located along the anterior versus posterior circulation.[18] Similarly, although Saatci *et al*. provided long-term outcomes on 239 aneurysms treated with the PED of which 136 aneurysms were less than 10 mm in size, detail on the distribution of these small aneurysms along the cerebrovasculature was lacking.[27] This heterogeneity in the literature on PED use complicates the direct comparison of results reported in these studies. Our current series fills this void in the literature by providing the outcomes and follow-up data specific for small ICA aneurysms treated with the PED.

A few publications on PED use do stratify results by anatomical size and location but are limited by a small

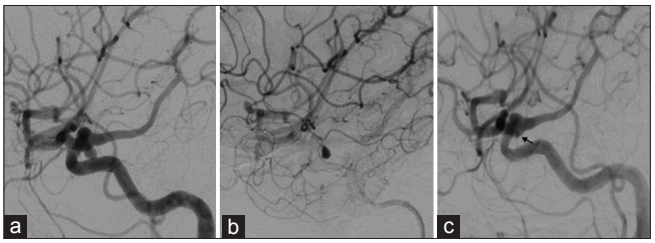

Figure 2: PED treatment of a 6 mm paraophthalmic aneurysm with angiographic success at 2 months (Case 11). (a) Preembolization DSA. (b) Immediately after implantation there is pronounced contrast stagnation within the aneurysm persisting into the venous phase. (c) Two-month follow-up DSA demonstrates near complete angiographic occlusion with only trace filling of the aneurysm (arrow)

Table 5: Immediate and follow-up anatomic outcome in 35 cases (33 patients) with 42 treated aneurysms

Case #	Aneurysm size (mm)	Aneurysm location	Aneurysm type	PED dimensions (mm)	Immediate angiographic aneurysm stasis	Aneurysm flow/ occlusion at 2 months
1	6	Paraophthalmic	Saccular	4.25×14	Pronounced	Complete
2	6	Paraophthalmic	Saccular	4.5×18*	Pronounced	Complete
3	3	Paraophthalmic	Saccular	3.75×16, 3.75×14	Moderate	Complete
4	8	Paraophthalmic	Saccular	4.5×14	Pronounced	Complete
5	5	Paraophthalmic	Saccular	4×14	Pronounced	Complete
6	5	Paraophthalmic	Saccular	4.25×10	Moderate	Complete
7	4	Paraophthalmic	Saccular	3.5×12	Pronounced	Complete
8	4	Paraophthalmic	Saccular	4.5×14	Moderate	Complete
9	9	Cavernous	Fusiform	5×16	Pronounced	Complete
10	3	Paraophthalmic	Saccular	4.25×10, 4.75×12	Mild	Complete
11	6	Paraophthalmic	Saccular	3.25×14	Pronounced	Trace residual
12	5	Ophthalmic	Fusiform	4×12	Pronounced	Trace residual
13	9	Supraclinoid	Fusiform	4×20	Pronounced	Residual filling
14	4	Ophthalmic	Saccular	4×12	Moderate	Residual filling
15	4	Cavernous	Saccular	3.75×14	Moderate	Residual filling
16	4	Ophthalmic	Saccular	4×12	Pronounced	Residual filling
17	8	Paraophthalmic	Saccular	3.75×12	Mild	Residual filling
Case #	**Aneurysm size (mm)**	**Aneurysm location**	**Aneurysm type**	**PED dimensions (mm)**	**Immediate angiographic aneurysm stasis**	**Aneurysm flow/ occlusion at 3 months**
18	8	Petrous	Dissecting	4.25×20, 4.5×20	Pronounced	Complete
19	7	Paraophthalmic	Fusiform	4×20	Moderate	Complete
20	5	Paraophthalmic	Saccular	4.25×14	Mild	Complete
21	4	Paraophthalmic	Saccular	4.25×16	Pronounced	Trace residual
22	3	Paraophthalmic	Saccular	4.75×10	Mild	Trace residual
23	8	Paraophthalmic	Saccular	3.75×14	Moderate	Trace residual
24	6	Paraophthalmic	Saccular	4×12	Pronounced	Residual filling
Case #	**Aneurysm size (mm)**	**Aneurysm location**	**Aneurysm type**	**PED dimensions (mm)**	**Immediate angiographic aneurysm stasis**	**Aneurysm flow/ occlusion at 6 months**
25	1	Paraophthalmic	Saccular	4.5×20	Pronounced	Complete
	2	Cavernous	Saccular		Pronounced	Complete
	3	Cavernous	Saccular		Pronounced	Complete
	5	Cavernous	Saccular		Pronounced	Complete
	8	Cavernous	Saccular		Pronounced	Trace residual
26	5	Paraophthalmic	Fusiform	3.75×18	Pronounced	Complete
	5	Cavernous	Fusiform		Pronounced	Residual filling
27	6	Cavernous	Fusiform	4.25×16, 4.25×20	Occluded	Complete
28	6	Paraophthalmic	Fusiform	4×20	Moderate	Complete
29	5	Paraophthalmic	Saccular	4×14	Mild	Complete
30	2	Ophthalmic	Saccular	4×18	Pronounced	Complete
	8	Paraophthalmic	Saccular		Pronounced	Trace residual
31	7	Paraophthalmic	Saccular	4.5×14	Moderate	Residual filling
32	6	Paraophthalmic	Fusiform	4.25×16	Pronounced	Residual filling
33	3	Cavernous	Saccular	3.5×14	Pronounced	Complete
34	7	Paraophthalmic	Fusiform	4.5×16	None	Trace residual
35	7	Ophthalmic	Saccular	4.5×12*	Pronounced	Complete
	2	Paraophthalmic	Saccular		Pronounced	Complete
36	3	Petrocavernous	Fusiform	4.5×20, 4.5×14	Moderate	Trace residual
	2	Paraophthalmic	Fusiform		Moderate	Complete
37	7	Cavernous	Saccular	4.75×14	Moderate	Complete

*Denotes use of adjunctive coils, PED: Pipeline embolization device

Table 6: Follow-up angiographic occlusion rate

	2-3 month f/u: Outcome rate (%)	6 month f/u: Outcome rate (%)
Complete occlusion	13/24 (54.2)	14/21 (66.7)
Near complete occlusion	5/24 (20.8)	4/21 (19)
Residual filling	6/24 (25)	3/21 (14.3)
Angiographic success*	18/24 (75)	18/21 (85.7)
	N=24	*N*=21

*Angiographic success defined as complete occlusion or near complete occlusion

sample size of aneurysms measuring less than 10 mm along the ICA.[3,10,17,30] In Szikora's initial Budapest experience with the PED, only 5 of the 19 aneurysms treated were along the ICA and less than 10 mm.[30] It is unclear from the report whether periprocedural complications were encountered in PED treatment of these 5 small ICA aneurysms. From the remaining publications, the periprocedural complication rate associated with PED treatment for small ICA aneurysms may be inferred from detailed analysis of the published results. In the Hong Kong PED experience, Chan *et al*., treated six patients with 10 small ICA aneurysms with 0% major morbidity and mortality rate.[3] In contrast, in Lubicz's PED experience in 20 patients with 27 aneurysms, 9 of these patients had 13 aneurysms less than 10 mm along the ICA.[17] Of these nine patients, one died (11%) as a result of probable PED thrombosis after discontinuation of dual antiplatelet therapy (only clopidogrel daily) in the setting of an ICH that developed 17 hours after PED implantation.[17] This patient had a 3 mm wide-necked ophthalmic artery aneurysm and a 3 mm wide-necked ICA bifurcation aneurysm treated with two PED in a single session. Recently Deutschmann *et al*. reported results of 12 patients with 12 wide-necked aneurysms treated with PED; 8 of these were ICA aneurysms less than 10 mm.[10] Of their 12 cases, transient mild aphasia was observed in 1 patient and amaurosis fugax was observed in another. Whether either of these two patients (16.6%) had small ICA aneurysms is unclear from the presented data.

Our experience with PED treatment for small ICA aneurysms is comparable to the few published reports on this experience. The 2.3% mortality in our series of 44 cases is closer to the bottom of the range of 0% observed by Chan *et al*., and 11% observed by Lubicz *et al*. Compared with the PED experience for large and giant aneurysms with reported mortality rates up to 5.5%,[17,18,21,27,30,32] we reported a mortality rate that is less than half. We did not observe any major morbidity in our series. In contrast, treatment of large and giant aneurysms with PED has been associated with a major morbidity of 1-5.5%.[27,30]

Three of our patients did experience minor complications as follows: transient neurological deficit (n = 1), delayed ICH (n = 1), and delayed groin infection (n = 1). The delayed ICH occurred 3 days after a technically uncomplicated PED treatment for a 4 mm right-sided paraopthalmic artery aneurysm. This patient was receiving systemic anticoagulation for a recent deep vein thrombosis, and the hemorrhage (right occipital ICH) occurred during the heparin to warfarin transition. The patient remained in good neurological condition and was discharged home on postprocedure day 11. The 6.9% rate of minor complications in this report is lower than the minor complication rate reported for PED treatment of large and giant aneurysms, which has been observed as high as 9.4%[18,21,23,30,31] and included occurrences of transient neurological deficits, delayed ICH, exacerbation of cranial neuropathies, delayed groin complications, carotid cavernous fistulas, and device migration.

Our results in this series were achieved without significant ischemic complications. We attribute this to our technique of PED deployment. Prior to fully deploying a PED, we ensured that the distal PED end was fully open and well apposed to the parent vessel wall. In this series, 6 of the 42 cases (14.3%) required removal of an incompletely deployed PED. With this method, none of the cases in this series required additional balloon angioplasty after PED implantation or any other postprocessing maneuvers that would subsequently increase the risk profile of the procedure. Our experience with this technique supports the belief that the primary concern with PED implantation is not ischemic complications but rather hemorrhagic.[15,36] Periprocedural ischemic complications can be managed with intraarterial thrombolytics, whereas hemorrhagic complications are typically associated with major morbidity and mortality in the setting of dual antiplatelet therapy.[28,15,36] As such, we do not routinely test for P2Y12 receptor inhibition. Additionally, the VerifyNow (Accumetrics, San Diego, CA) assay used to measure the degree of P2Y12 receptor inhibition has been demonstrated unreliable with fluctuations observed in serial testing of the same patient.[9] The results also vary from institution to institution and are not associated with a standardized threshold of desired P2Y12 receptor inhibition. Several centers have demonstrated acute titration of clopidogrel dose or replacement with prasugrel (Effient) for "hyporesponders" was associated with increased hemorrhagic complications in PED procedures.[1,9] For these reasons, the utility of P2Y12 testing in PED procedures remains to be validated. Until then, we maintain the safety profile of our PED procedures by following the protocol set by the Pipeline for Uncoilable or Failed Aneurysms (PUFS) trial where P2Y12 testing was not performed and dual antiplatelet regimen consisted of oral aspirin 325 mg and clopidogrel 75 mg daily for 6 months.[32]

Mild in-stent stenosis (25% to <50%) was observed in 2 of the 37 cases (5.4%) with follow-up angiography. Both cases were asymptomatic and required no additional intervention. This rate is less than half the rate (1/7)

reported by Chan *et al*.,[3] and falls within the 3.5-10% range observed in large and giant aneurysms treated by the PED.[18,19,21,30]

Follow-up data in this series demonstrates that complete aneurysm occlusion can be achieved as early as 2 months following PED treatment for small ICA aneurysms. Of the 17 treated aneurysms that had angiographic follow-up at 2 months, almost 60% were completely occluded. At 2-3 months after PED implantation, angiographic success was achieved in 75% demonstrating either complete or near complete occlusion. By 6 months follow-up, this rate increased to 80%. All ICA aneurysms (100%) located along the posterior/ventral surface of the vessel wall achieved angiographic success at all follow-up time points [Figures 1 and 2]. Our results are approximately in line with the obliteration rates observed in other experiences on PED use in small ICA aneurysms. Of the five small ICA aneurysms treated with PED in the report by Szikora *et al*., all five were completely occluded at 6-month follow-up,[30] while Chan *et al*., reported an occlusion rate of 70% (7/10) at 2-6 months,[30] and Deutschmann *et al*., reported a 50% rate at 5-6 months.[10] Lastly, 11 of the 12 small ICA aneurysms treated with PED by Lubicz *et al*., achieved angiographic success at 3-6 months.[17]

Our occlusion rates are also comparable to those observed for PED treatment of large and giant aneurysms. Complete occlusion rates for large and giant aneurysms are over 80%, however, the majority of follow-up in these studies were performed at 6- or 12-month intervals and also confounded by adjunctive coil use as well as a higher number of PEDs implanted.[18,19,21,27,31] In contrast, Lylyk and colleagues found only a 47% 3-month obliteration rate for large and giant aneurysms. As such, results from our series demonstrating a 75% angiographic success for PED treatment of small ICA aneurysms at 2-3 months follow-up support the hypothesis proposed by several groups that small aneurysms may achieve occlusion faster than large and giant aneurysms.[8,18,27] In addition, our high angiographic success rate is achieved with an average of 1.1 ± 0.05 PEDs implanted per case. This is in contrast to the average of 3.1 PEDs used per case in the PUFS trial demonstrating over 80% occlusion at 6 months.[32] The ability to achieve early angiographic success with only a single PED for the majority (>80%) of the cases in this report illustrates the elegance and good economy of the endoluminal approach via flow diversion with PED for the treatment of small ICA aneurysms.

In this series, we have demonstrated the safety and efficacy of PED implantation for the treatment of small ICA aneurysms. Compared with the literature on PED treatment of large and giant aneurysms,[8,18,21,23,30,31] we report a lower complication rate and demonstrate high early angiographic success in the PED treatment of small ICA aneurysms. Additionally, compared with traditional endovascular modalities of coiling with or without adjunctive devices, PED use for small ICA aneurysms has several potential advantages. Unlike coiling, aneurysm occlusion with PED is a progressive biologic process. As such, a PED treated aneurysm with a small residual on initial follow-up imaging will typically progress to complete angiographic occlusion over time. In contrast, a small neck remnant of a coiled aneurysm either persists or enlarges and subsequently requires additional treatment. A significant advantage of the endoluminal approach is avoidance of the most feared risk of intraprocedural aneurysm rupture during access or coil placement inherent to endosaccular techniques.[2,20,22,29] For unruptured aneurysms, this intraprocedural rupture risk ranges from 1.2% to 4%[16,24,29] and is associated with high rates of morbidity and mortality. The combined risk of permanent neurologic disability and death associated with intraprocedural rupture is as high as 29% for unruptured aneurysms.[4] Small aneurysm size is a known risk factor for intraprocedural rupture and well documented in the literature.[2,20,22,24] For aneurysms 6 mm or smaller, this risk approaches 5%[2,20,22,24] with an estimated mortality ranging from 1% to 16.7%[20,24,29] and major morbidity of 27.8%.[24] Considering this risk profile for treating small aneurysms with endosaccular techniques, the 2.3% major morbidity and mortality reported in this series of PED treatment for small ICA aneurysms supports an endoluminal approach as a valid alternative. The durability of PED treatment is another advantage of using this modality for small ICA aneurysms. The recurrence rate of aneurysms less than 10 mm treated with coiling has been reported as high as 21% with approximately half requiring retreatment.[25]

At present in the United States, the FDA has limited the on-label indication of PED use to large and giant ICA aneurysms. Large and giant intracranial aneurysms only encompass a small fraction of the cerebral aneurysms observed in population studies.[31,33,35] The International Study of Unruptured Intracranial Aneurysms (ISUIA) reported that 73.9% of the observed 1449 cerebral aneurysms were characterized as small, less than 10 mm.[31] In a meta-analysis of the literature on the prevalence of unruptured intracranial aneurysms, Vlak *et al*. found that 83% of the aneurysms were small.[33] Most recently, the Japanese have published the largest prospective cohort on the natural history of unruptured cerebral aneurysms. Of the 6679 aneurysms observed, aneurysms less than 10 mm accounted for 89.6%.[33] What's more, several reports indicate that the majority of ruptured aneurysms are smaller than 10 mm.[13,14,26,34] Given these findings, PED implantation has the potential to further revolutionize the endovascular approach for intracranial aneurysm treatment. Internationally, several series on PED experience include data on treatment of small aneurysms.[5,17,30] We present the largest series to

date on PED treatment of small ICA aneurysms. Our results show that these aneurysm types can be safely treated with PED implantation. Furthermore, high angiographic success in these aneurysms can be reached as early as 2 months posttreatment. Early angiographic success represents the potential for complete parent vessel reconstruction sooner than 6 months as previously suggested and as such, a decrease in the rupture risk of an aneurysm with a shorter waiting period. Such information can be reassuring for patients by decreasing the stress and anxiety associated with waiting for aneurysm occlusion.

CONCLUSION

Parent vessel reconstruction via flow diversion with the PED is a valid and safe treatment alternative for small ICA aneurysms. This endoluminal approach avoids endosaccular access and as such, theoretically reduces the intraprocedural aneurysm rupture risk associated with coiling. Compared with PED implantation for large and giant aneurysms, use in small ICA aneurysms may be achieved with a lower complication rate and earlier angiographic success. As our series continues to grow and additional follow-up data is available, we continue to provide further insight on PED applications for such aneurysms. Furthermore, earlier angiographic occlusion may allow for shortened duration of dual-antiplatelet regimens, although this would require further study.

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