Tiny Pipes: 67 Cases of Flow Diversion for Aneurysms in Distal Vessels Measuring Less Than 2.0 mm

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■ BACKGROUND: **Flow diversion is increasingly used for off-label treatments of distal circulation aneurysms. Reports of use in sub-2.0-mm vessels are scant.**

■ METHODS: **A prospectively collected, institutional review board–approved cerebral aneurysm database was reviewed to identify patients who underwent flow diversion with a 2.5-mm diameter Pipeline embolization device.**

■ RESULTS: **Sixty-seven aneurysms were treated in 67 procedures (66 [99%] successful, 64 [96%] single device, 2 [3%] with 2 devices) in 57 patients. Average age was 56 years and 60% were female. Aneurysm location was 51 (76%) anterior cerebral artery, 14 (21%) middle cerebral artery, and 2 (3%) posterior cerebral artery. Aneurysm size was 4.1 ± 3.0 mm (1–20 mm). Safety outcomes included 3 major strokes (4.5%) resulting in permanent neurologic deficit (modified Rankin Scale score 6,4,4), including 1 mortality (1.5%). Acute stent thrombosis was observed intraprocedurally or within 24 hours of each stroke. There were 2 small-volume (<10 cm^3, 40 cm^3) dependent intracerebral hemorrhage (3.0%) that resolved without permanent neurologic deficit. For effectiveness, 71% of patients underwent follow-up angiography. Complete occlusion was achieved by 88% at 6 months, 86% at 12 months, and 89% at last follow-up. A slight vessel diameter reduction was apparent on average 6.9 months after the procedure, which was statistically significant at the proximal ($P = 0.001$) but not distal ($P = 0.317$) device end. Preoperative average parent vessel diameter was 1.9 mm proximally (range, 1.1–2.6 mm) and 1.7 mm distally (range, 1.0–2.3 mm) of the Pipeline embolization device. Follow-up average vessel diameter was 1.7 mm proximally (range, 0.7–2.4 mm) and 1.6 mm distally (range, 0.6–2.1 mm). Flow delay associated with vessel diameter reduction occurred once. There were no cases of asymptomatic vessel occlusion.**

■ CONCLUSIONS: **Flow diversion can be safe and effective for aneurysms originating from vessels <2.0 mm in diameter. Heightened vigilance for the prevention and management of acute stent and vessel thrombosis is warranted in these cases.**

INTRODUCTION

Since its approval for the treatment of large proximal carotid aneurysms, the Pipeline embolization device (PED) (Medtronic Neurovascular, Irvine, California, USA) has increasingly been used for off-label applications on small aneurysms,[1-3] distal anterior circulation aneurysms,[4,5] and posterior circulation aneurysms.[6] With a minimum nominal diameter of 2.5 mm, which can be expanded to 2.75 mm, there is controversy about the lower threshold of vessel caliber in which a PED may safely be deployed, with potential concerns being vessel injury, acute stent thrombosis, and delayed vessel occlusion. Previous series reporting PED for vessels <3.0 mm are limited to ≤12

Key words
- Distal circulation aneurysms
- Flow diversion
- Pipeline embolization device
- Sub-2.0 mm vessels

Abbreviations and Acronyms
ACA: Anterior cerebral artery
ACoA: Anterior communicating artery
DSA: Digital subtraction angiography
ICA: Internal carotid artery
MCA: Middle cerebral artery
PCA: Posterior cerebral artery
PED: Pipeline embolization device
SAH: Subarachnoid hemorrhage

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patients.[7-10] We performed a large single-institution retrospective study of safety and efficacy of the 2.5-mm PED deployed in vessels with a cross-sectional diameter <2.0 mm.

METHODS

A prospectively maintained institutional review board–approved database of patients with cerebral aneurysm undergoing routine care at our institution was reviewed to identify patients treated with PED from August 2011 to January 2018 who received a 2.5-mm-diameter PED of any length. Although patients were identified based on receiving a 2.5-mm-diameter PED, all except 1 had a preoperative proximal or distal vessel caliber measurement of 2.0 mm or smaller. Dual antiplatelet therapy consisting of aspirin 325 mg daily and clopidogrel 75 mg daily was initiated at least 7 days before all embolization procedures. Antiplatelet therapy testing was used on a case-by-case basis as described in previous reports.[11,12] The first-generation PED Classic was used before January 2015, after which the PED Flex was used in all cases. All procedures were performed by dual-trained endovascular neurosurgeons. The treatment decision was based on age, comorbidities, aneurysm size, location, irregularity, and growth, among other factors. Surgical and alternative endovascular treatments were considered before the decision to use PED in an off-label fashion.

Catheter access was triaxial[4,13] and adjunctive coiling was performed as previously described.[14] Control angiography was performed at 10-minute and 20-minute intervals after PED deployment to observe for platelet aggregation within the stent, which was treated with intra-arterial abciximab according to protocol.[15] Patients were typically discharged 1 day after the procedure.

Demographic information, aneurysm characteristics, procedural details, and outcomes were collected for each patient. Follow-up angiography was conducted 6, 12, and 24 months after embolization. Clopidogrel was typically discontinued 6 months after embolization and aspirin was reduced to 81 mg daily 12 months after embolization. Preoperative, embolization, and postoperative angiograms were consulted for parent vessel measurement at the proximal and distal ends of the stent. Follow-up angiography was analyzed for in-stent stenosis. Major stroke was defined as a >4-point increase in National Institutes of Health stroke score persisting for >7 days.

Statistics

The Levine test for homoscedasticity was used to compare sample variances and the corresponding 2-sample t tests were performed to evaluate the temporal variability of proximal and distal vessel diameters.

RESULTS

A total of 788 PED procedures were performed from August 2011 to January 2018. A 2.5-mm device was chosen for use in 67 procedures (66 [99%] of which were successful) performed on 57 patients. One device was implanted in 64 cases (96%), 2 devices in 2 procedures (3%), and 0 devices in 1 procedure (1%). Demographic details were average age 56 years (range, 33–78), 60% female. Anatomic details were average maximum diameter of the aneurysm fundus 4.1 mm (±3.0 mm; range, 1–20 mm) with 65 (97%) small and 2 (3%) large aneurysms. Aneurysm location was 51 (76%) anterior cerebral artery (ACA), 14 (21%) middle cerebral artery (MCA), and 2 (3%) posterior cerebral artery (PCA) (Table 1). Cervical tortuosity, defined as a hairpin loop in the cervical internal carotid artery (ICA), was navigated in 16 anterior circulation cases (25%), and high-grade (III or IV) cavernous ICA anatomy, defined as previously described,[16] was encountered in 22 anterior circulation cases (34%). Previously treated patients included 21 coilings (31%), 7 aneurysm clippings (10%), and 2 flow diversions (3%). Most aneurysms were unruptured (61%), whereas 37% had previously ruptured and 1% had acutely caused subarachnoid hemorrhage (SAH).

Technical nuances included the use of adjunctive coiling and postdeployment balloon angioplasty in 5 (7%) and 4 cases (6%), respectively. The average fluoroscopy time was 38.2 ± 23.3 minutes, and average radiation exposure was 2133 ± 1153 mGy. Vasospasm

Table 1. Demographics and Anatomy

	Number (N = 67)	Standard Deviation (%)
Age (years)	55.8	10.8
Female sex	40	60
Previously treated	30	45
Clip	7	10
Coil	21	31
Flow diversion	2	3
Unruptured	41	61
Acute subarachnoid hemorrhage	1	1
Previously ruptured	25	37
Size (average)	4.1	3.0
Small (<10 mm)	65	97
Large (10–25 mm)	2	3
Aneurysm location		
Anterior circulation	65	97
Anterior cerebral	51	76
A1	2	3
A1-2/anterior communicating artery	38	57
A2-3	9	13
Distal	2	3
Middle cerebral	14	21
M1	3	4
M2	4	6
Bifurcation	6	9
Distal	1	1
Posterior circulation	2	3
P1	2	3

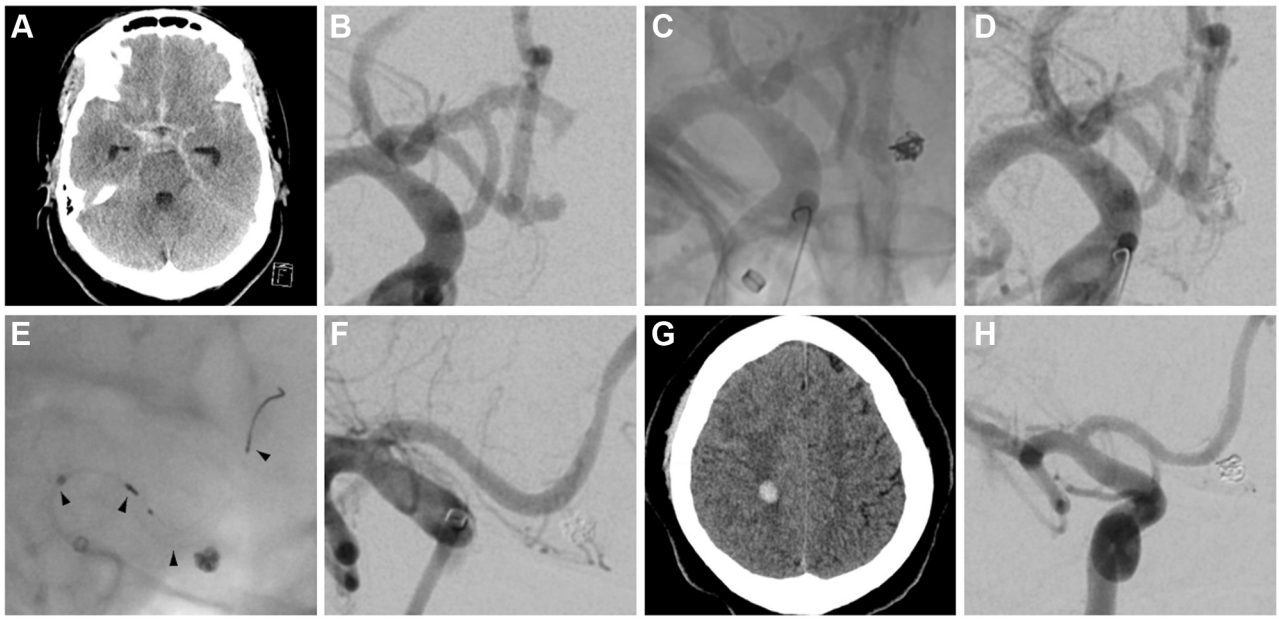

Figure 1. Tricenarian patient who presented with (**A**) Hunt-Hess grade 2, Fisher grade 3 subarachnoid hemorrhage (**B**) from a ruptured, broad-based 3 mm right A1-A2 aneurysm (**C**) treated with coil embolization (**D**) resulting in neck residual that (**E**) subsequently underwent 2.5 × 12 mm PED placement (*arrowheads*, left to right, microcatheter tip, resheathing pad, PED stent, tip coil). (**F**) Immediate postdeployment digital subtraction angiography showing aneurysm occlusion. (**G**) Small <10 mm cortical intracerebral hemorrhage discovered during workup of 4/5 left lower extremity weakness on postembolization day 2. (**H**) 6-month follow-up digital subtraction angiography showing complete aneurysm occlusion and parent vessel preservation.

prophylaxis or treatment with intra-arterial verapamil was performed in 26 cases (39%). There were 5 instances (7%) of platelet aggregation observed intraprocedurally along the stent and 5 (7%) concomitant intraprocedural administrations of abciximab.

Clinical follow-up was 19 months ± 10 months on average (range, 3–41 months). Three strokes resulted in permanent neurologic deficits (modified Rankin Scale score 6, 4, and 4) and accounted for a major complication rate of 4.5% and 1 mortality (1.5%). One stroke occurred while treating a previously ruptured recurrent morphologically irregular ACA aneurysm with a minimum ACA diameter of 1.2 mm. The stent was successfully placed but the patient awoke with lower extremity weakness. Digital subtraction angiography (DSA) showed stent thrombosis, which did not open with escalating abciximab or stentriever thrombectomy; salvage balloon angioplasty ruptured the vessel and led to the patient's death. The second major stroke occurred during treatment of an unruptured 9 mm MCA aneurysm treated with Pipeline and adjunctive coiling. The minimum MCA diameter was 1.2 mm in this case. The final major stroke occurred in a patient with a previously ruptured and coiled recurrent A2-A3 aneurysm with a minimum parent vessel diameter of 1.3 mm. Acute stent occlusion was observed intraprocedurally or within 24 hours in all 3 cases. Two (3%) small-volume (<10 cm^3 and 40 cm^3) dependent intracerebral hemorrhage (Figure 1) were considered minor complications because they resolved without permanent neurologic deficit (Table 2).

At preoperative angiography, the average proximal and distal vessel diameters were 1.93 and 1.70 mm, respectively. At embolization, the average proximal and distal vessel diameters were 2.10 and 1.96 mm, respectively. Parent vessel measurements were collected at follow-up angiography on average 6.9 months after the procedure; the average proximal and distal vessel diameters at follow-up were 1.72 and 1.63 mm, respectively. The reduction in proximal vessel diameter from preoperative to postoperative was statistically significant ($P = 0.001$), but the observed distal vessel diameter reduction was not ($P = 0.317$). Among cases with both preoperative and follow-up DSA available, 4 (7.3%) showed >25%–50% vessel diameter reduction, and 2 cases (3.6%) showed >50% reduction on the proximal end of the device. Distally, 1 (1.8%) case showed >25%–50% vessel diameter reduction, and there were no cases of reduction >50%. A single instance of flow delay associated with vessel diameter reduction occurred (Table 3).

Follow-up angiography was available for 71% of the procedures. Complete occlusion was achieved in 88% of aneurysms at 6 months and 86% at 12 months. The slight decline in percent complete occlusion at 12 months can be attributed to a slightly different subset of patients presenting for 12-month DSA than for 6-month DSA. At last follow-up, which occurred on average 10 months after the procedure, 89% of aneurysms were completely occluded, 2% showed trace filling, 2% showed an entry remnant, and 6% showed continued aneurysm filling (Table 2).

Table 2. Clinical Outcomes

	Number	%
Major stroke	3	4.5
Mortality	1	1.5
Subarachnoid hemorrhage	1	1.5
Minor complication	7	10.4
Minor stroke	0	0
Intracerebral hemorrhage	2	3
Transient ischemic attack	1	1.5
Dissection	2	3
Cranial nerve palsy	1	1.5
Groin hematoma	1	1.5

Occlusion Outcomes

	6 Months, n (%)	12 Months, n (%)	24 Months, n (%)	Last Follow/Up, n (%)
Complete occlusion	36 (88)	18 (86)	3 (100)	42 (89)
Trace filling	2 (5)	0	0	1 (2)
Entry remnant	0	1 (5)	0	1 (2)
Aneurysm filling	3 (7)	2 (10)	0	3 (6)
No imaging	25 (38)	45 (68)	63 (95)	19 (29)
Cases with digital subtraction angiography	41 (62)	21 (32)	3 (5)	47 (71)

Table 3. Vessel Diameters at Stent Landing Zone

	Proximal			Distal		
	Average (mm)	Standard Deviation (mm)	n	Average (mm)	Standard Deviation (mm)	n
Preoperative vessel diameter	1.93	0.33	64	1.70	0.28	64
Embolization vessel diameter	2.10	0.32	67	1.96	0.31	67
Postoperative vessel diameter	1.72	0.34	58	1.63	0.30	58
Two-sample *t* test *P* value (preoperative vs. follow-up)	0.001			0.317		
Cases with >25% —50% vessel diameter reduction, n (%)	4 (7.3)			1 (1.8)		
Cases with >50% vessel diameter reduction, n (%)	2 (3.6)			0		

DISCUSSION

This was a retrospective study of 57 patients who underwent a total of 67 PED procedures in parent vessels measuring <2.0 mm diameter. This is a fundamentally different use of flow diversion of which previous reports are limited to series of ≤12 patients, compared with its on-label indication for large predominantly sidewall proximal ICA aneurysms. Occlusion outcomes were excellent (88% at 6 months, 89% at last follow-up), and safety outcomes (4.5% stroke leading to major neurologic change) were acceptable. The risks and benefits associated with this application of flow diversion are unique and warrant further investigation in this and future reports.

Safety outcomes in this series were comparable with both on-label PED series and small aneurysm series. The PUFS (Pipeline for Uncoilable or Failed Aneurysms) clinical trial reported a 5.6% major complication rate, and 1.9% mortality for large proximal ICA aneurysms.[17] The ASPIRe (Aneurysm Study of Pipeline in an Observational Registry) meta-analysis compounded 29 PED series and reported similar outcomes, with a major morbidity of 6.8% and mortality of 1.6% across on-label PED treatments.[18] The major morbidity of 4.5% and mortality of 1.5% observed in this series are lower than these on-label PED series outcomes. Small aneurysms constitute most aneurysms treated in this cohort (n = 65, 97%). Overall, the observed outcomes in the present series are comparable with other series of small intracranial aneurysms. A multicenter retrospective study of PED by Kallmes et al.[19] included 294 small (<10 mm) aneurysms and reported a major neurologic morbidity of 4.5%, and neurologic mortality of 1.4%. Griessenauer et al.[1] reported a thromboembolic complication rate of 8.7% and 1 mortality (0.9%) unrelated to the implanted PED across 149 sub-7 mm aneurysms.

Small aneurysms account for most SAH,[20] and distally located small aneurysms, such as anterior communicating artery (ACoA) region aneurysms, which accounted for most of the lesions treated in this series (Table 1), are overrepresented in SAH series.[21] Other small aneurysm PED series have reported similar morbidity for small paraclinoid and paraophthalmic ICA aneurysms,[1-3] which are underrepresented in SAH.

Previous reports of flow diversion in very-small-caliber vessels are limited to small case series. Puri et al.[9] reported no complications in a series of 7 patients with anterior circulation aneurysm with average vessel diameters of 2.0/1.9 mm (proximal/distal). Similarly, Mazaris et al.[8] treated 4 distal PCA aneurysms with PED, with adjunctive coiling in 1 case. Average vessel diameters of 2.0/1.9 mm (proximal/distal) were reported with no new neurologic deficits and 50% of patients developing mild in-stent stenosis. Nossek et al.[7] reported a series of 5 patients with distal ACA aneurysm with average 2.0/1.8 mm (proximal/distal) vessel diameters and no symptomatic complications. Martin et al.[10] treated 12 distal circulation aneurysms, 6 in anterior and 6 in posterior circulation, with sub-3.0-mm-diameter PEDs. One symptomatic posterior inferior cerebellar artery stroke (8%) and 1 asymptomatic frontopolar stroke occurred. The present series included ACoA region (Figure 1), distal ACA (Figure 2), MCA, and PCA (Figure 3)

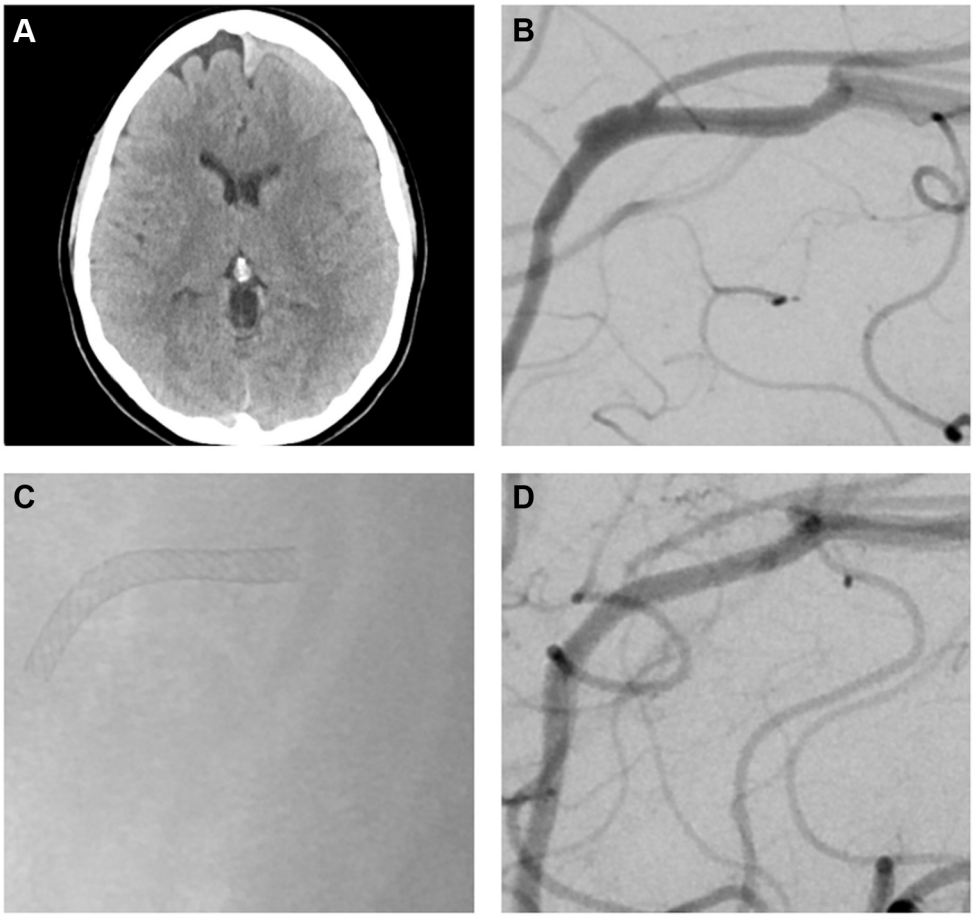

Figure 2. Middle-aged patient presented with headaches and (**A**) parafalcine and convexity acute subdural hematoma from (**B**) dissecting A2-3 aneurysm with parent vessel measurement of 1.5 mm proximally and 1.8 mm distally underwent (**C**) Pipeline embolization with a single 2.5 × 14 mm device (**D**) with aneurysm occlusion and stable parent vessel diameters on 6-month follow-up digital subtraction angiography.

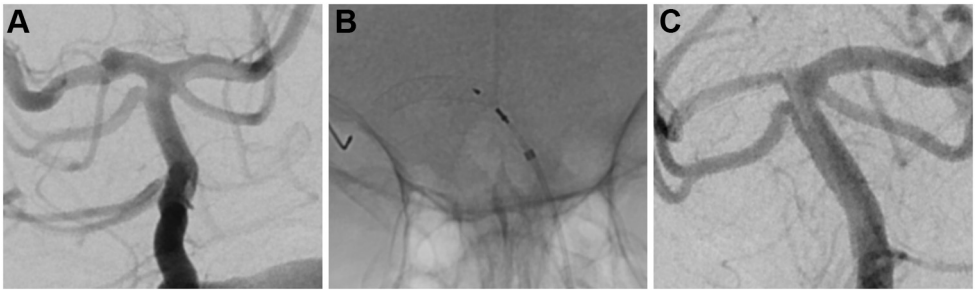

Figure 3. Quaternarian with incidentally discovered (**A**) 3-mm right P1-P2 junction aneurysm (**B**) underwent treatment with 2.5 × 10 mm PED. (**C**) 6-month follow-up digital subtraction angiography showing 25%–50% stenosis at proximal margin of the stent without associated flow limitation that remained stable on 12-month follow-up digital subtraction angiography.

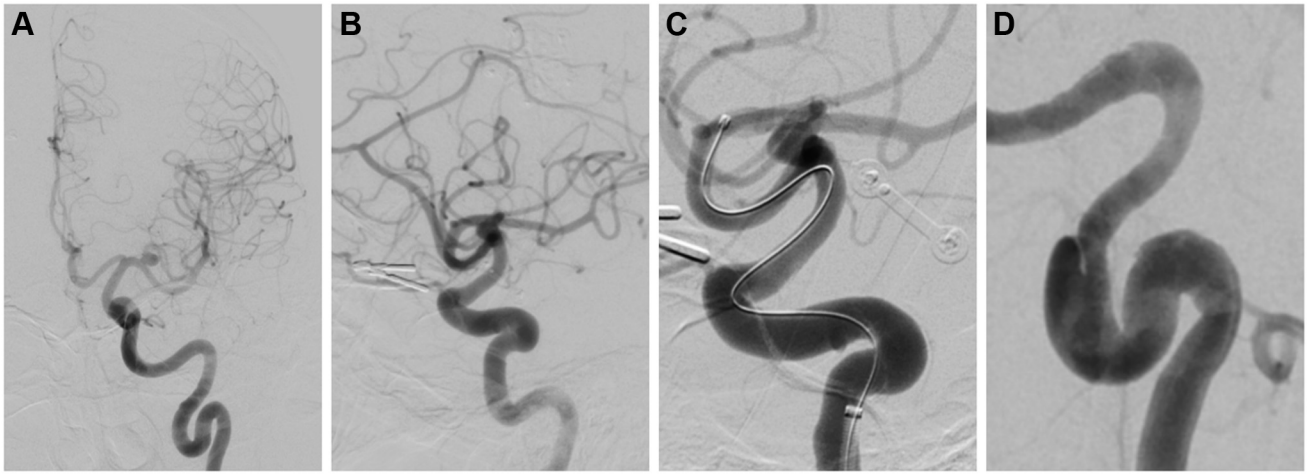

Figure 4. Quinquagenarian with a history of subarachnoid hemorrhage from a ruptured right middle cerebral artery (MCA) aneurysm who refused microsurgical clipping and underwent attempted Pipeline embolization of an unruptured 4-mm saccular left MCA aneurysm. Tortuosity including (**A**) hairpin loop of the cervical internal carotid artery (ICA) apparent on anteroposterior digital subtraction angiography and (**B**) type III cavernous internal carotid artery anatomy apparent on lateral digital subtraction angiography (**C**) prevented bringing the Pipeline embolization device (PED) to the level of the aneurysm despite advancement of the microcatheter into the distal MCA. The support and forces used in attempting to bring the PED up resulted in a dissection flap (**D**) within the cervical ICA without symptomatic consequence over 7 months of clinical follow-up.

aneurysms. The average preoperative proximal and distal vessel diameters in the present series of 1.93 mm and 1.70 mm, respectively, are smaller than the proximal and distal measurements of any of the aforementioned small-vessel series.

Safety concerns regarding flow diversion within small vessels can be grouped into 3 general categories: vessel trauma, acute stent thrombosis, and delayed in-stent stenosis. The concern for vessel injury arises from the need for distal access and robust support to deliver and open the PED in the distal circulation, often in the presence of significant tortuosity. A vessel dissection during the only aborted case (1%) in this series occurred in a patient with a history of SAH from a ruptured right MCA aneurysm who refused microsurgical clipping and underwent attempted PED of an unruptured 4-mm saccular left MCA aneurysm. In this case, although the Marksman (Medtronic Neurovascular) was navigated into the distal MCA, the 058 Navien (Medtronic Neurovascular) intermediate catheter would not track beyond the vertical segment of a type III posteriorly displaced cavernous ICA and the PED could not be advanced to the level of the aneurysm. After removal of the intermediate and microcatheters, a non–flow-limiting dissection flap along a hairpin loop within the cervical ICA was noted, which was asymptomatic over 7 months of clinical follow-up (Figure 4).

A series of technological improvements over time have made events such as this uncommon. In our current triaxial setup, the added support of the AXS Infinity (Stryker Neurovascular, Freemont, California, USA) guide sheath, which has multiple durometers with variable stiffness,[22] facilitates tracking the rest of our catheters through regions of tortuosity (25% in the cervical ICA, 34% type III or IV cavernous ICA, and frequent recurved ACA takeoffs). With distal PED deployments, we commonly give 10 mg of prophylactic verapamil (39% of cases) once the guide is tracked to the carotid bifurcation and consequently did not experience significant issues with vasospasm. Puri et al.[9] used a similar technique of prophylaxis by administering 10 mg verapamil routinely in their small-vessel PED series. The enhanced flexibility and atraumatic tips of more contemporary intermediate catheters[23,24] enable tracking into the supraclinoid ICA and V4 segment with relative ease and even into the M1 or A1 in exceptional cases. In their small-vessel PED series, Martin et al.[10] noted that they often used a larger microwire or buddy wire technique to navigate tortuosity and acknowledged that this increased the risk of vessel injury. In cases of extreme tortuosity, we sometimes use a pentaxial system of 4 telescoping catheters inside an 8-F short sheath to enhance support and minimize catheter step-off, thereby reducing the risk of vessel trauma or vasospasm.

In addition, the introduction of a hypotube delivery pusher enabled greater push with the second-generation PED Flex, and its angled tip-coil reduced the risk of vessel perforation,[13] which was not observed in this series. Complication rates did not differ significantly by device generation in this series. We converted to using the Via (Sequent Medical/MicroVention; Terumo, Tustin, California, USA) microcatheter midway through this series, finding that its increased column strength and stiffness facilitated bringing the PED through regions of vessel tortuosity and deploying it predictably without the accordion effect of the Marksman in distal locations.[25] The Via was used in 35 cases after using the Marksman in the first 32 and the minor complication (16% vs. 6%) and major stroke rates (6% vs. 3%) were both decreased in cases using the Via27. We also came to learn, as did Puri et al., that a different technique is required for PED deployment in these ultradistal locations. This technique relies on the greater intrinsic opening strength of a 48-strand small-diameter device to allow them to be deployed by more

unsheathing rather than typical pushing with larger-diameter PED devices. We believe that this strategy minimizes the force buildup during deployment and mitigates the possibility of translating push force into wire perforation.[9] Each of these marginal technological improvements compounded each other and resulted in an overall low rate of vessel injury, despite the obvious reason for concern, in this series.

Our experience suggests that heightened concern for acute stent thrombosis associated with PED deployments in small-caliber vessels is justified. There were 5 cases (7.5%) in this series in which platelet aggregation along the stent was observed intraprocedurally, higher than in our overall experience with anterior circulation PED (4%).[13] We have been successful in treating these patients with escalating doses of intra-arterial abciximab according to a protocol described previously,[15] although we recognize that some institutions prefer alternative glycoprotein IIb/IIIa inhibitors such as eptifibatide or tirofiban because of their shorter half-lives.[26] The present experience also suggests that platelet plugging may be more difficult to reverse in small-caliber vessels. In our overall PED series of 30 patients treated with intra-arterial abciximab, only 4 (13%) went on to experience symptomatic ischemic infarcts. In the present series, 2 of 5 patients (40%) had major strokes. One of these was a sexagenarian with a 9-mm right MCA aneurysm treated with PED with adjunctive coiling through a single-intermediate jailed approach.[14] A lack of opacification of the covered MCA branch was recognized intraprocedurally, treated, and angiographically resolved but the patient still developed hemiparesis. Salvage maneuvers to open an acutely thrombosed stent may result in further injury, as occurred in a patient with ACoA aneurysm treated with ACA PED in whom escalating abciximab and stentriever thrombectomy failed to reverse thrombosis and balloon angioplasty ruptured the vessel, leading to the patient's death.

Our experience suggests that heightened concern for symptomatic delayed stent thrombosis secondary to hyperendothelialization with PED in sub-2.0-mm vessels is not justified. Mazaris et al.[8] observed asymptomatic in-stent stenosis with mild associated flow limitation in 2 of 4 patients treated for PCA aneurysms with PED. Martin et al.[10] speculated that a small decrease in the caliber of sub-2.0-mm vessels would be more restrictive of flow than in larger vessels and more likely to progress to complete occlusion. Neither flow restriction nor occlusion was observed in their series of 12 patients treated with PED ≤3.0 mm in diameter. Even in a recent report from our group involving the use of PED in the MCA of a 9-month old infant, the PED was placed successfully in a 1.1-mm vessel with long-term vessel patency.[27]

In the present series, there was a statistically significant reduction in parent vessel caliber at the proximal end of the stent but not the distal end of the stent. We believe that this is a consequence of device design: although PED is designed to adopt different diameters and take the shape of the vessel in which it is placed, it has been our observation that smaller diameter devices are not so contourable. If there is a tendency for the device to adopt a similar diameter across its length, this is restricted by the smaller (typically distal) vessel diameter and results in a greater reduction in the larger (typically proximal) diameter. In addition, the ability to retrack the 027 delivery catheter through the construct and achieve a proximal bump that aids in compression and expansion of the device is commonly not possible because of the distal location and vessel tortuosity of these cases. Overall, the percentage of patients showing reduced vessel diameter was small: 7.3% with >25%–50% reduction, 3.6% with >50% reduction (proximal), and 1.8% with >25%–50% reduction, and no cases with >50% reduction (distal). Only 1 patient in this series experienced flow delay associated with reduced vessel diameter. This particular patient presented with a morphologically irregular 7-mm saccular aneurysm originating from A2-3. Anteroposterior DSA at 6 months follow-up showed development of in-stent stenosis (>50%) near the proximal end of the device. This patient was asymptomatic. Plavix was continued and stenosis had improved at 12 months follow-up angiography. An example of an asymptomatic in-stent stenosis is shown in **Figure 3**.

Occlusion outcomes of the present study compared favorably with small aneurysm series and were similar to the aforementioned small-caliber vessel series. Griessenauer et al.[1] reported 87% complete occlusion across 149 sub-7-mm in 117 patients, with DSA available for 82.6% of aneurysms. Chalouhi et al.[2] reported 72% complete occlusion at last follow-up, with DSA available for 75% of cases on average 6.3 months after procedure in their study of 100 small intracranial aneurysms. Among the series of PED in small vessels, Martin et al.[10] reported 75% complete occlusion and 92% achieving at least near occlusion in 12 patients treated with PED. Mazaris et al.'s series of 4 PCA aneurysms observed 75% occlusion and 25% residual filling at 12 months.[8] Nossek et al.[7] reported 100% occlusion across 5 patients with ACA aneurysm at on average 11 months after embolization. Puri et al.[9] reported 100% occlusion with 86% availability in follow-up. In the present series, complete occlusion was observed in 42 (89%) cases of this cohort at on average 10 months after embolization.

Antiplatelet therapy decisions to balance thromboembolic and hemorrhagic risk are always challenging, perhaps more so when treating aneurysms arising from small vessels. We do not test P2Y12 routinely for all patients undergoing PED and do not typically adjust antiplatelet regimens based on its results, given our observation that repeat P2Y12 response unit (PRU) measurements within 24 hours produce a different category of therapeutic response for 24% of patients.[12] P2Y12 testing was performed for 41 of 67 cases (61%) in this series, including 4 of 5 cases with acute platelet aggregation, of which 3 were therapeutic (P2Y12, 40–200) and 1 was hypotherapeutic. We separately reported the largest series of clopidogrel hyporesponders (P2Y12 >200) to undergo PED, in which we observed rates of ischemic complications on a par with the overall PED literature (2/52 cases, 4%).[11] Given the increased risks of acute stent thrombosis, this population may be appropriate for clopidogrel alternatives, such as prasugrel and ticagrelor, with more predictable pharmacodynamics.

When hemorrhagic complications occur after PED, antiplatelet agents must be managed in a nuanced case-by-case fashion. Both intracerebral hemorrhages in the present series were in a dependent distribution after ACA PED. P2Y12 testing showed that one patient had become hyperresponsive to plavix, whereas the other was hyporesponsive. In the former case, clopidogrel was held and the patient was discharged on aspirin monotherapy, whereas in the latter case, plavix was resumed after stable head CT. Both patients returned to clinical baseline and aneurysms were

completely occluded with parent vessel preservation on follow-up DSA.

PED is an important tool in our management of distal aneurysms arising from small vessels. It is particularly effective for broad-based, dissecting, and fusiform aneurysms, which can be difficult to reconstruct with clipping as well as for residual or recanalizing aneurysms after coiling. We have used PED successfully in a variety of configurations for ACoA region aneurysms (**Figure 1**), which was the most common location in this series.[4] Its safety and efficacy for aneurysms located at branch points where the covered division supplies a terminal circulation are not clear. In these locations, adjunctive coiling can be used to augment occlusion outcomes,[14,28] although this seems to increase the risk of acute stent occlusion. When using coil assistance with small-vessel PED, we have more recently moved to using assured higher-potency antiplatelet agents such as ticagrelor.

There are several limitations to this study, including those inherent in retrospective observational series. Follow-up was incomplete: follow-up DSA occurred at an average interval of 6.9 months and was available in 71% of patients, which is lower than our overall PED population.[28] However, clinical follow-up extended for 19 months on average and is likely to have captured most symptomatic complications. Comparison was performed with preoperative angiography rather than intraoperative angiography because of the vasodilatory effects of anesthesia and in some cases verapamil. Aneurysms treated in this study averaged 4 mm fundus diameter, which is small. The decision to treat was multifactorial, based on location, irregularity, and clinical history, including comorbidities such as smoking or a history of aneurysm rupture, and rooted in our observation that small aneurysms account for an increasing percentage of SAH.[20]

CONCLUSIONS

PED for distal circulation cerebral aneurysms arising from vessels with diameter <2.0 mm represents a safe and effective application of flow diversion technology. The small-vessel PED deployment technique differs in its emphasis on an unsheathing rather than pushing device. Heightened vigilance for the prevention and management of acute stent and vessel thrombosis is warranted in these cases. Despite the distal location, issues related to vessel trauma and delayed occlusion secondary to hyperendothelialization are uncommon and should not limit use of this technique.

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Conflict of interest statement: A.L.C. is a proctor for the Woven Endobridge (WEB) device (Sequent Medical, Aliso Viejo, California, USA), a proctor for the Surpass device (Stryker Neurovascular, Fremont, California, USA), a consultant for Stryker Neurovascular, a proctor for the Pipeline embolization device (Medtronic Neurovascular, Irvine, California, USA), a consultant for Medtronic, a proctor for the FRED device (MicroVention, Tustin, California, USA), and consultant for MicroVention-Terumo and InNeuroCo. G.P.C. is a consultant for both Medtronic and MicroVention-Terumo, and participates in clinical trials for Medtronic and Stryker. L.M.L. is a proctor for the Pipeline embolization device (Medtronic Neurovascular), a consultant for MicroVention-Terumo, and participates in clinical trials for Stryker. The other authors have no conflict of interest to disclose. No author received financial support for the generation of this submission.

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