The Pipeline Embolization Device for the treatment of posterior circulation fusiform aneurysms: lessons learned at a single institution

Clinical article

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Object. Vertebrobasilar fusiform aneurysms (VFAs) are rare lesions characterized by abnormal dilation and tortuosity of the vertebral and/or basilar arteries. Untreated, these aneurysms have a tendency to progress, often resulting in neurological symptoms or rupture leading to subarachnoid hemorrhage. The microsurgical treatment of these lesions can be difficult due to their location and the circumferential involvement of the arteries. These features make microsurgical treatment prone to high morbidity. The Pipeline Embolization Device (PED) has gained popularity for the treatment of aneurysms of the internal carotid artery. Its use in the posterior circulation has been limited, likely due to a fear of perforating artery occlusion.

Methods. The authors retrospectively reviewed their database of patients treated with the PED and identified 12 patients who had VFAs. The clinical features, complications, and outcomes of these patients were analyzed.

Results. At an average follow-up of 11 months, the mean modified Rankin Scale score was 1.9. Complete aneurysm occlusion was seen in 90% of the patients with radiographic follow-up. Three patients suffered new neurological deficits postoperatively. One of these patients died, while the remaining 2 demonstrated significant clinical improvement at follow-up.

Conclusions. With attention to the anatomy of perforating arteries, staged contralateral vertebral artery sacrifice, and adequate platelet inhibition, PED may be an effective treatment option—alone or in a hybrid construct with stents of less coverage for VFAs—with an acceptable complication rate.

Key Words • basilar artery • cerebral aneurysm • Pipeline • stent • vertebral artery • vascular disorders

Vertebrobasilar fusiform aneurysms are uncommon entities characterized by abnormal dilation, elongation, and tortuosity of the vertebral and/or basilar arteries. VFAs most commonly manifest as posterior circulation ischemic strokes, but they may also cause cranial nerve palsies, brainstem compression, obstructive hydrocephalus, and intraparenchymal or subarachnoid hemorrhage (SAH).VFAs have an ominous natural history with a reported mortality up to 30%. Passero and Rossi reported that 43% of patients without treatment experienced anatomical progression and 60% experienced new symptoms. Untreated VFAs are a significant cause of morbidity, yet reliable treatment remains elusive for neurosurgeons. Microsurgical options are hindered by the location of the pathology and the circumferential involvement of the parent artery. Therefore, endovascular options may provide a more reliable and effective treatment.

The use of flow-diverting stents has recently gained tremendous popularity in treating complex saccular and fusiform intracranial aneurysms. The higher metal surface area provided by these stents facilitates an initial flow diversion and subsequent endothelialization with intraluminal reconstruction of the diseased vessel. Consequently, aneurysm thrombosis occurs due to the stagnation of blood flow within the aneurysm, which happens in a delayed fashion, with variable occlusion rates reported in the literature, including one study reporting up to 95% occlusion at 1 year.

The Pipeline Embolization Device (PED, ev3/Co-
vidien) was approved by the FDA in 2011 for the treatment of large or wide-necked aneurysms of the internal carotid artery from the petrous segment to the hypophyseal segment. It is a tightly braided, self-expanding, cobalt, chromium, and platinum stent with 30%–35% metal surface area coverage designed to promote flow diversion away from the aneurysm, while at the same time allowing blood flow to perforating branches. There are several reports demonstrating the use of PEDs in treating posterior circulation aneurysms.6–9,17,23,27 Some of these early series reported significant morbidity and mortality associated with PED use in the posterior circulation.6,7,26 Furthermore, few of these studies have addressed the use of multiple PEDs, which is often necessary in treatment of VFAs in particular. Here, we describe our experience with using the PED for treating VFAs in 12 patients.

**Methods**

We retrospectively reviewed our database of patients treated with the Pipeline Embolization Device (between April 2011 and April 2013) to identify those suffering from VFAs. Twelve consecutive patients with VFAs who underwent treatment with a PED were identified. No patients with VFAs treated with the PED were excluded from this analysis. The decision to use the PED was made by the neuroendovascular surgeon following review of each patient’s case and radiological studies.

Prior to the procedure, each patient was given dual antiplatelet therapy. When possible, this consisted of clopidogrel 75 mg and aspirin 325 mg for 5 days. In the acute setting, patients were routinely given a loading dose of clopidogrel 600 mg and aspirin 325 mg the night before surgery. We measured antiplatelet activity using point-of-care aspirin and P2Y12 assays (VerifyNow, Accutronics). When antiplatelet treatment was not therapeutic (i.e., aspirin reaction unit above 550 or P2Y12 reaction unit [PRU] below 230 or less than 30% inhibition), an intraarterial loading dose of 0.25 mg/kg abciximab (0.25 mg/kg) typically was given at the time of PED placement, followed by a 12-hour infusion (0.125 μg/kg/min or 10 μg/min).

Immediate posttreatment digital subtraction angiography (DSA) was reviewed to confirm the patency of the parent vessel and jailed branches. Magnetic resonance imaging and MR angiography (MRA) typically (in all but 3 patients) were performed prior to discharge to assess for any ischemic injury. Follow-up DSA and MRI/MRA typically were performed at 6 months, followed by MRI and MRA yearly thereafter. Interpretation of follow-up DSA was performed by the physician performing the procedure, while assessment of aneurysm occlusion by MRI/MRA was performed by an attending neuroradiologist at our institution. DSA was performed earlier than 6 months if the patient’s symptoms got worse or did not improve. Additional DSA after 6 months was considered if the patient became symptomatic or MRI/MRA demonstrated unfavorable changes.

All procedure-related complications are reported, regardless of their clinical manifestations. Patients were considered to have procedure-related ischemic injury if they demonstrated restricted diffusion in any vascular distribution covered by PEDs. These ischemic injuries are reported, regardless of their clinical manifestation. Patients with evidence of punctate areas of restricted diffusion, consistent with microemboli, are also reported. Clinical outcome was assessed according to the modified Rankin Scale (mRS) score. This was obtained via recent follow-up in our clinic or by a validated telephone questionnaire.7 If patients were unable to participate in this questionnaire themselves, their primary caregiver was asked to participate.

**Results**

The clinical data obtained for 12 consecutive patients undergoing placement of the PED for treatment of their VFAs are presented in Table 1. The most common presenting symptom was progressive headaches, present in 5 patients (41.7%). Two patients (16.7%) presented with cranial nerve palsies, and 2 patients (16.7%) presented with acute SAH. One patient (8.3%) presented with syncope. One patient presented with left lower-extremity weakness in the setting of an acute multiple sclerosis exacerbation, but workup revealed an incidental VFA. Another patient, who had a history of malignancy, presented with unilateral neck swelling; workup for this swelling revealed this patient’s VFA. The mean preoperative mRS was 1.0 ± 1.2 (± SD). Two patients presented with hydrocephalus requiring external ventricular drain placement.

The mean postoperative mRS score was 1.9 ± 2.2. The average follow-up duration was 11.0 ± 7.4 months (range 3–24 months). Ten patients underwent follow-up DSA and all but 1 (90%) demonstrated complete occlusion of the VFA. The mean time to follow-up DSA was 4.9 ± 1.8 months (range 1.75–6 months). One patient had residual aneurysm filling and an endoleak requiring additional treatment. In 1 case, follow-up DSA revealed stenosis proximal to the stent construct. This required balloon angioplasty, which resulted in radiographic improvement. In another case, incidental in-stent stenosis was noted on follow-up DSA; distal blood flow was not compromised and this did not require endovascular intervention. Neither patient was symptomatic from these angiographic findings. The reasons for 2 patients not having follow-up DSA were death in one patient and loss to follow-up in the other.

Procedure-related complications occurred in 3 patients (25%). Two patients developed new hemiparesis and 1 developed new nystagmus and dizziness that resolved at the 6-month follow-up evaluation. Both patients with hemiparesis required discharge to skilled nursing facilities and one of these patients ultimately died of pulmonary complications. The other patient was ambulating with a walker 2 months after her surgery. We are not aware of any additional complications occurring in this cohort of patients during the follow-up period.

Large infarcts noted on postoperative images were present in 2 patients (16.7%). One had a left cerebellar hemisphere infarct but was not symptomatic (Fig. 1A and B). The other patient, who awoke with new hemiparesis, had right temporoparietal and bilateral cerebellar hemisphere infarcts (Fig. 1C and D). This patient was noted to have extensive atherosclerosis and these infarcts likely
were related to emboli that were dislodged during the procedure. Three patients (25%) had postoperative MR images with punctate areas of restricted diffusion, consistent with microembolic phenomenon; no clinical deficits were observed in these 3 patients.

**Illustrative Cases**

**Case 7.** This 46-year-old man presented with a history of chronic headaches. During workup for his headaches, he was found to have a left VFA (Fig. 2A and B). Interestingly, 30 years prior to presentation he suffered a gunshot wound to the left neck requiring iatrogenic sacral füge of his left internal carotid artery. Anticoagulation with heparin was maintained during the procedure with an activated clotting time of 260 seconds. The PRU was 204, indicating adequate platelet inhibition. The patient was treated with 4 PEDs (three $4 \times 25$ mm; and one $4 \times 30$ mm). The procedure was uneventful and the patient remained neurologically well. On follow-up DSA 3 months later, adequate vessel remodeling was noted with complete occlusion of the aneurysm. However, the patient was found to have stenosis proximal to the stent construct (Fig. 2C and D). Angioplasty was performed, with resultant improvement in vessel caliber.
area with more clinically relevant perforators and a sidewall aneurysm at the right AICA take off. The patient awoke from the procedure with a mild left hemiparesis (motor examination Grade 3/5) and was found to have multiple infarcts in the right posterior cerebral artery territory that were due to atherosclerotic emboli during the procedure (Fig. 1C and D). We also chose not to sacrifice the contralateral vertebral artery to avoid abrupt thrombosis of the large aneurysm sac. The patient returned 2 months after this procedure for the addition of coils into the sidewall aneurysm. At that time, we found the vertebrobasilar aneurysm to be completely occluded (Fig. 3E and F) despite patency of the contralateral vertebral artery. The patient was discharged home from this procedure with an mRS score of 3.

Discussion

Vertebrobasilar fusiform aneurysms are among the most formidable entities encountered by neurosurgeons. They have an ominous natural history with a reported mortality up to 30%. Their location and involvement of the vessel circumference make effective treatment particularly challenging. Traditional surgical and endovascular treatment options have included parent vessel occlusion with surgical ligation or coil occlusion, surgical trapping with or without bypass, clip reconstruction, and stenting with or without coiling. With recent advancements in neuroendovascular technology, flow-diverting stents, such as the Pipeline Embolization Device, provide a new therapeutic option for total intraluminal reconstruction for the treatment of VFAs. The PED provides 30%–35% metal surface area coverage, as opposed to the roughly 10% provided by the conventional open cell stents. The decrease in porosity causes stagnation of blood flow within the aneurysm, thereby promoting its thrombosis while maintaining patency of nearby perforating vessels. The stent scaffold eventually leads to endothelialization of the PED and, therefore, complete intraluminal reconstruction of the diseased vessel. Since its approval by the FDA for use in the internal carotid artery in 2011, the PED has gained tremendous popularity, with an increasing safety profile in treating complex aneurysms in the anterior circulation. However, due to the increased number of perforating vessels in the posterior circulation and the vital brainstem structures supplied by these perforators, neuroendovascular surgeons have been cautious in their application of the PED in the posterior circulation, including in the treatment of VFAs.

Siddiqui et al. recently reported their experience using flow-diverting stents in the treatment of 7 patients with VFAs. Six patients were treated with PEDs and 1 patient was treated with a Silk stent. Patients were treated with dual antiplatelet therapy. In each case, multiple stents were used in a telescoping fashion to cover the diseased vessel segment (range 3–9 stents). At the time of follow-up, 4 of the 7 patients (57.1%) died (mRS Score 6), 1 patient (14.3%) had severe disability (mRS Score 5), and the remaining 2 patients had good outcomes (mRS Scores 1 and 0). The authors concluded that there was significant

Fig. 2. Case 7. Anteroposterior (A) and oblique (B) DSA projections demonstrating left VFA. Lateral (C) and oblique (D) DS angiograms obtained 3 months following the initial procedure showing stenosis proximal to the stent construct (C).
mortality and morbidity associated with treating VFAs with flow-diverting stents. Similarly, Raphaeli et al. report that one of their 4 patients (25%) with VFAs treated with flow-diverting stents had died.²⁴ Although dual antiplatelet therapy was used in this series, the degree of platelet inhibition immediately before the endovascular procedures was not reported.

Chalouhi et al. recently reported favorable outcomes in their series of 7 patients with posterior circulation aneurysms treated with the PED; this series included 3 patients with VFAs.² A single PED was used to treat 3 patients with VFAs, while the remaining patient with a VFA was treated with 3 PEDs deployed in a telescoping fashion. There was no reported perforator infarct or new neurological deficit. The authors attributed their favorable outcomes to several factors, including avoidance of overlapping PEDs in the basilar artery, avoidance of PED use in bifurcation aneurysms, and strict anticoagulation (initial heparin bolus of 100 U/kg followed by maintenance of activated clotting time of 2 times the patient’s baseline) and antiplatelet protocols (platelet inhibition > 30%). The authors concluded that, with the aforementioned caveats, the application of the PED in the posterior circulation can be performed safely.

In this report, we describe our experience using the PED to treat 12 patients with VFAs. The mean postoperative mRS score was 1.9. Although 3 patients experienced new postoperative neurological deficits, 2 of these patients had significantly improved at the time of their follow-up. We experienced 1 death in this series. This patient developed acute respiratory distress syndrome while intubated after his procedure, requiring tracheostomy. He ultimately died of pneumonia after discharge from the hospital.

Our population was heterogeneous in terms of presentation, which represents the patient population one may encounter in clinical practice. Most patients presented electively with headaches. However, 2 patients (16.7%) presented with acute SAH. Both of these patients had a 2-point increase in their mRS score compared with their preoperative mRS score. Although the factors contributing to their decline in functional status may be multifactorial, the presence of SAH may have played a significant role as opposed to procedure-related complications, especially given that neither of these patients demonstrated postoperative infarcts on MRI.

The fact that the majority of patients in this series did not present with SAH may be one reason for the
comparatively good outcomes observed in our cohort. In contrast to the study by Siddiqui et al., most of our patients presented with headache, rather than cranial nerve palsies or symptoms from mass effect. The presence of these symptoms may indicate a larger or more tortuous lesion, and therefore one that is more difficult to treat. This may be one reason for the disparity in outcomes between the 2 studies. An additional reason may be the exclusive use of the PED in the study by Siddiqui et al. In their illustrative cases, they describe placement of the PED as far proximally at the posterior cerebral artery ostia. Although further experience is needed to draw any definitive conclusions, our use of the PED only proximal to the AICA may be “perforator protective” and have influenced our outcomes. Additionally, while Siddiqui et al. describe their use of dual antiplatelet therapy, their therapeutic thresholds were not defined. It is possible that a different threshold was used, and, therefore, a different degree of platelet inhibition was experienced.

As described above, we adhered to a strict antiplatelet regimen pre- and postoperatively. When these values were not observed, additional antiplatelet therapy was administered. In the 2 patients who presented with acute SAH (Cases 4 and 5), aspirin and clopidogrel were administered prior to their procedure and were continued postoperatively. Although the use of antiplatelet therapy in the acute setting following SAH remains controversial, we did not experience any hemorrhagic complications using this management strategy. However, the small number of patients in our study prevents conclusions regarding the safety of antiplatelet therapy in the setting of acute SAH.

We did not observe any instances of acute in-stent thrombosis in our series. One patient was found to have in-stent stenosis on follow-up DSA but was asymptomatic; the stenosis was mild and did not require intervention. An additional patient had stenosis proximal to the stent construct and required angioplasty. Furthermore, only 2 patients had postoperative infarcts noted on radiological studies, both of which appeared in distributions suggestive of embolic phenomena rather than vessel thrombosis.

In contrast to the vessels of the anterior circulation, the basilar and rostral vertebral arteries are rich with perforating arteries serving vital brainstem structures and whose occlusion may cause devastating neurological deficits. Protection and maintenance of blood flow through the ostia of these arteries is of paramount importance during neuroendovascular procedures in the posterior circulation. This becomes even more important when using flow-diverting stents with high metal surface area coverage, as blood may be diverted away from the perforating artery and remain within the parent vessel.

One consideration aimed at protecting essential vertebrobasilar perforating arteries is the location of PED placement within the parent vessel. Anatomical studies have demonstrated a particularly high density of perforating vessels in the rostral basilar artery. Furthermore, the perforating arteries of this location may supply more critical structures (e.g., the pons and midbrain) than those located caudally. Of particular importance, many of these vessels are too small to be seen on DSA. With this in mind, we have adopted a policy of only using the PED caudal to the AICA. When stent coverage is required rostral to the AICA, we opt for a stent with 6% metal surface area coverage, in an effort to preserve flow through the ostia and within perforating arteries (see Case 12 in Illustrative Cases). For this reason, we use a hybrid stent construct, consisting of PEDs caudal to the AICA origin and stents with less metal surface area coverage rostral to it. When using this method, we typically deploy the PEDs first. We then cross the PED construct to deploy the stent with less metal surface area coverage, anchoring it on the PED construct. We have not experienced any significant perforating artery occlusions using this technique.

In all cases in this series, we preserved the patency of the contralateral vertebral artery during the patients’ initial treatment with PEDs. The patient in Case 11, the only patient requiring multiple procedures, ultimately required sacrifice of the vertebral artery in a delayed fashion due to persistent symptoms and the presence of an endoleak. Using this strategy, successful aneurysm occlusion was obtained (Fig. 4), and this patient remained without evidence of significant infarction or perforator injury. Although our experience is only preliminary and occurred in the setting of a failed initial treatment strategy, we believe that sacrifice of the vertebral artery in a delayed fashion may allow for a more controlled aneurysm thrombosis, with preservation of perforating arteries.

As more recent reports reveal, prevention of devastating perforating artery thrombosis may be affected by strict adherence to peri- and postoperative dual antiplatelet therapy and intraoperative anticoagulation. For patients treated electively, we typically administer aspirin 325 mg and clopidogrel 75 mg daily for 5 days prior to the procedure; for patients treated acutely, we routinely give a loading dose of aspirin 325 mg and clopidogrel 600 mg the night before the procedure. In all cases, we confirmed platelet inhibition prior to beginning the procedure. We believe that confirmation of adequate platelet inhibition is critical since the FDA estimates that up to 14% of patients in the United States possess low levels of the hepatic enzyme CYP2C19, which is essential to the pharmacological activity of clopidogrel. A more re-

![Fig. 4. Case 11. Anteroposterior (left) and oblique lateral (right) DSA projections demonstrating complete occlusion of the right vertebral artery by a combination of coiling and Onyx 32. This resulted in cessation of residual aneurysm filling and the endoleak involving the previous stent construct.](image-url)
The posterior circulation, namely VFAs. Traditional treat-
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our experience and the lessons we have learned using the
strategies. However, in this report, we aimed to describe
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geneity of the patients reported here, we are cautious in
of selection bias. Given the small number and hetero-
study were identified from a database of patients treated
with rare disease entities. The patients presented in this
series, all patients but one were treated using multiple
PEDs. We routinely placed multiple PEDs in a telescop-
ing fashion, typically with 50% overlap. Contrary to pre-
vious reports, we did not find the use of multiple PEDs
causal to the origin of AICA to predict clinical or radio-
graphic complications. In our series, the need for multiple
devices to treat extensive vertebrobasilar dolichoectasia
was not prohibitive against use of the PED in the poste-
rior circulation.

Our study suffers from the inherent limitations of
a retrospective review and small sample size associated
with rare disease entities. The patients presented in this
study were identified from a database of patients treated
with the PED and, therefore, we recognize the influence of
selection bias. Given the small number and hetero-
genecity of the patients reported here, we are cautious in
drawing definitive conclusions regarding these treatment
strategies. However, in this report, we aimed to describe
our experience and the lessons we have learned using the
PED for the treatment of a formidable vascular lesion of
the posterior circulation, namely VFAs. Traditional treat-
ments of these lesions involved extensive open surgery
or endovascular sacrifice of the vessel with considerable
mortality and morbidity. Here, we demonstrate that use of
the PED may be effective to secure these lesions.

We believe that the PED may provide an effective al-
ternative to microsurgical reconstruction in the treatment
of VFAs with acceptable complication rates compared
with traditional treatment options. Three patients (25%)
experienced procedure-related complications. While this
rate may be considered high for a surgical procedure, it
may represent an improvement compared with earlier re-
ports describing this technique. This improvement may
be simply due, at least in part, to more technical experi-
ence with the device. However, we believe that attention
to antiplatelet therapy and to perforating artery anatomy
(i.e., using a hybrid construct when necessary to stent
rostral to the AICA), and selective sacrifice of the con-
tralateral vertebral artery also played a part. Meticulous
attention to these details may permit effective utilization
of the PED for the treatment of VFAs. Further experience
with these techniques is needed to determine their effect
on long-term outcome.

Conclusions

The microsurgical treatment of VFAs can be diffi-
cult and associated with high morbidity and mortality.
Treatment with the Pipeline Embolization Device, a flow-
diverting stent, may provide an effective and less invasive
alternative to microsurgical intervention with an accep-
table complication rate. Cautious introduction of the PED,
with particular attention to perforating artery anatomy,
selective contralateral vertebral artery sacrifice, and ade-
quate platelet inhibition, is crucial for the successful
treatment of VFAs with the PED.

Disclosure

Dr. Lopes is a consultant for Covidien, Stryker, Codman, and
Penumbra. Dr. Moftakhar is a consultant for Covidien and Penum-
bra.

Author contributions to the study and manuscript prepa-
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submitted version of manuscript: all authors. Approved the final ver-
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