Patency of the ophthalmic artery after flow diversion treatment of paraclinoid aneurysms

Clinical article

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Object. In this study the authors determined the patency rate of the ophthalmic artery (OphA) after placement of 1 or more flow diversion devices across the arterial inlet for treatment of proximal internal carotid artery (ICA) aneurysms, and correlated possible risk factors for OphA occlusion.

Methods. Nineteen consecutive patients were identified (mean age 53.9 years, range 23–74 years, all female) who were treated for 20 ICA aneurysms. In all patients a Pipeline Embolization Device (PED) was placed across the ostium of the OphA while treating the target aneurysm. Flow through the OphA after PED placement was determined by immediate angiography as well as follow-up angiograms (mean 8.7 months), compared with the baseline study. Potential risk factors for OphA occlusion, including age, immediate angiographic flow through the ophthalmic branch, status of flow within the aneurysm after placement of PEDs, whether the ophthalmic branch originated from the aneurysm dome, and number of PEDs placed across the ophthalmic branch inlet were correlated with patency rate.

Results. Patients were treated with 1–3 PEDs (3 aneurysms treated with placement of 1 PED, 12 with 2 PEDs, and 5 with 3 PEDs). In 17 (85%) of 20 treated aneurysms, no changes in the OphA flow were noted immediately after placement of the device. Two (10%) of 20 patients had delayed antegrade filling immediately following PED placement and 1 patient (5%) had retrograde flow from collaterals to the OphA immediately after placement of the device. One patient (5%) experienced delayed asymptomatic ICA occlusion; this patient was excluded from analysis at follow-up. At follow-up the OphA remained patent with normal antegrade flow in 13 (68%) of 19 patients, patent but with slow antegrade flow in 2 patients (11%), and was occluded in 4 patients (21%). No visual changes or clinical symptoms developed in patients with OphA flow compromise. The mean number of PEDs in the patients with occluded OphAs or change in flow at angiographic follow-up was 2.4 (SEM 0.2) compared with 1.9 (SEM 0.18) in the patients with no change in OphA flow (p = 0.09). There was no significant difference between the patients with occluded OphAs compared with nonoccluded branches based on patient age, immediate angiographic flow through the ophthalmic branch, status of flow through the aneurysm after placement of PEDs, whether the ophthalmic branch originated from the aneurysm dome, or number of PEDs placed across the ophthalmic branch inlet.

Conclusions. Approximately one-quarter of OphAs will undergo proximal thrombosis when covered with flow diversion devices. Even though these events were well-tolerated clinically, our findings suggest that coverage of branch arteries that have adequate collateral circulation may lead to spontaneous occlusion of those branches.

Key Words • flow diverter • ophthalmic artery • patency • intracranial • aneurysm • Pipeline Embolization Device • vascular disorders • interventional neurosurgery

Flow-diversion devices have been approved by the FDA for treatment of complex intracranial aneurysms of the ICA proximal to the origin of the posterior communicating artery. These devices are supposed to maintain normal blood flow through parent and branch vessels while disrupting flow into the aneurysm sac, causing thrombosis, and eventually sealing of the aneurysm ostium through neointimal proliferation across the device struts. These changes in blood flow dynamics have been studied in experimental and in vitro models. Early clinical series have suggested that the rate of complete aneurysm obliteration with the PED (ev3) and similar devices is very high. However, concerns exist regarding the fate of side branches and perforating vessels in clinical cases after placement of these devices.

The PED underwent evaluation under an Investigational Device Exemption in a prospective study targeting ICA aneurysms not amenable to conventional endovascular techniques, many of which were in the region of the OphA. As such, angiographic findings in these patients

Abbreviations used in this paper: DS = digital subtraction; ICA = internal carotid artery; OphA = ophthalmic artery; PED = Pipeline Embolization Device; PUFS = Pipeline for Uncoilable or Failed Aneurysm Study.
specifically focused on patency of the OphA may provide insight into the impact on branch vessels of single or multiple PED implantations. In this study we assessed the fate of the OphA and any change in angiographic flow in the artery immediately after placement of a flow-diverting stent and at angiographic follow-up in a consecutive series of 19 patients with 20 paraclinoid aneurysms.

Methods

The study was approved by the Institutional Review Board of the Mayo Clinic. Patients included in this study were treated as part of ongoing multicenter studies on the PED such as the Pipeline for Uncoilable or Failed Aneurysm Study (PUFS) or treated under compassionate use. Full inclusion criteria and details of the PUFS continued access cohort (PUFS CA) trial can be viewed at the FDA website (http://www.accessdata.fda.gov/cdrh_docs/pdf10/P100018b.pdf). All of the patients undergoing treatment were premedicated with aspirin and clopidogrel and full anticoagulation was maintained during the procedure (target activated clotting time between 250 and 300 seconds). Following the procedure, patients were maintained on dual antiplatelet therapy for 3 months. After 3 months, clopidogrel was discontinued and aspirin was continued indefinitely. This antiplatelet regimen was the same in all patients. No patient underwent testing for clopidogrel response. All of the procedures were performed with the patient under general endotracheal anesthesia. A bi- or triaxial access technique and, in all of the cases, a Marksman (ev3) microcatheter, were used to obtain distal access past the segment of the vessel harboring the target aneurysm. Pipeline Embolization Devices were sized to match the maximum diameter of the target vessel. One or multiple devices were used at the discretion of the operators to maximize the chance of complete aneurysm occlusion and/or to ensure adequate coverage of the aneurysm neck and of a segment of parent artery proximal and distal to it (usually at least 5 mm). Digital subtraction angiography was performed at 2 frames per second prior to and following placement of the PED.

In this study we identified 19 patients treated for 20 aneurysms. In each patient a PED was placed across the ostium of the OphA while treating the target aneurysm. Determination of OphA patency was made for each patient immediately after the original procedure and at the follow-up angiogram obtained furthest from the initial procedure by 1 of the authors (D.F.K.). A note was also made of any subjectively determined change in flow patterns (“slowing” of angiographic flow after PED deployment and/or at follow-up). Every patient underwent a detailed clinical examination before the procedure, immediately after the procedure, the following day, 1 month afterward, and at each corresponding follow-up angiogram. In the initial part of the series a total of 5 patients underwent detailed examination by a neuroophthalmologist before the original procedure and 1 month afterward. Potential risk factors for OphA occlusion, including patient age, immediate angiographic flow through the ophthalmic branch, status of flow through the aneurysm after placement of PEDs, whether the ophthalmic branch originated from the aneurysm dome, and number of PEDs placed across the ophthalmic branch inlet were correlated with patency rate using the Student t-test. We identified probability values < 0.05 to be statistically significant.

Results

Aneurysms included in this study are summarized in Table 1. The series includes 19 female patients (mean age 53.9 years, range 23–74 years) with 20 ICA aneurysms. Flow through the OphA after device placement was determined by immediate angiography as well as follow-up angiograms at 3 months (1 patient), 6 months (9 patients), 8 months (1 patient), and 12 months (9 patients). The average length of angiographic follow-up for this cohort was 8.7 months ± 3.2 months. No patients were lost to follow-up. Patients were treated with 1–3 PEDs (3 aneurysms were treated with placement of 1 PED, 12 with 2 PEDs, and 5 with 3 PEDs). In 17 (85%) of 20 patients no changes in the OphA flow were noted immediately after placement of the device. One patient (Case 3) experienced immediate slowing of antegrade filling after PED placement (Fig. 1), 1 patient (Case 7) had retrograde flow through the ophthalmic branch from external carotid collaterals initially (Fig. 2), and 1 patient (Case 19) experienced slow flow noted immediately after placement of the device. One patient (5%) experienced asymptomatic ICA occlusion diagnosed on a routine 6-month follow-up study; this patient was excluded from analysis at follow-up.

At follow-up angiography, the OphA remained patent with normal flow in 13 (68%) of 19 eligible aneurysms, patent but with slow antegrade flow in 2 (11%), and was occluded in 4 (21%). In the patients with an occluded proximal OphA, retrograde filling through collateral external carotid branches was clearly visualized on follow-up angiograms in 2 patients, and was indeterminate in the other 2 patients based on unsatisfactory visualization; however, no transient or permanent visual disturbances were noted clinically in any of the patients with occluded OphAs. In the patients with angiographically visible collateral circulation, the OphA was reconstituted by ethmoidal vessels in 1 patient and, interestingly, by vessels originating from the inferolateral trunk in the other patient (Fig. 3).

The mean number of PEDs in the patients with occluded OphA or change in flow at angiographic follow-up was 2.4 ± 0.2 (SEM) compared with 1.9 ± 0.18 (SEM) in the patients with no change in OphA flow, but this finding was not significant (p = 0.09). One of the patients (Case 3) had delayed antegrade flow through the ophthalmic branch immediately after the procedure and was found to have an occluded OphA at 6 months. Another patient (Case 7) had retrograde flow through the OphA immediately after the procedure but was found to have a fully patent ophthalmic branch at 1-year follow-up. Thus, it appears that flow pattern immediately after device placement may not be a predictor of long-term OphA patency. There was no significant difference between the cohort with occluded branches compared with nonoccluded branches based on patient age (p = 0.85), immediate angiographic flow through the ophthalmic branch (p
Discussion

In the current study we demonstrated that approximately one-quarter of OphAs covered with a flow diverter will undergo occlusion over time. These cases of OphA occlusion were well tolerated clinically, as no patient experienced visual loss. There was no significant difference between the occluded and nonoccluded ophthalmic branches when patient age, immediate angiographic follow-up, number of PEDs placed, aneurysm flow status immediately postprocedure, or the presence of an ophthalmic branch originating from the aneurysm sac were compared. Thus, we are unable to identify specific risk factors that might increase the risk of ophthalmic branch artery occlusion.

These findings are important because they demonstrate that placement of even a single flow diverter may lead to branch occlusion. However, in our study we avoided placement of devices across other intracranial branches, such as the anterior choroidal artery. As such, using our current data we cannot assess the impact of flow diversion devices on intracranial arteries other than the OphA, and the observations from our study cannot be extrapolated to other side branches, especially those with terminal flow. The OphA has rich, distal collateral supply from external carotid branches. These collateral vessels
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might increase the tendency for proximal occlusion, if a flow diverter caused some diminution in inflow and the distal bed takes over supply to downstream branches. In contradistinction to the OphA, other side branches such as the anterior choroidal or perforating vessels such as the lenticulostriate arteries are end arteries and may likely stay open after placement of a flow diverter because of the pressure gradient ensuring flow through the vessel partially covered by the flow diverter. As such, it remains possible that occlusion rates will differ among these vessels.

Previous preclinical studies using both computational techniques as well as animal models have focused on the propensity for branch artery occlusion following flow diversion implantation. Appanaboyina et al. used computational fluid dynamics modeling to show that after placement of a flow diverter that covers up to 90% of the perforating vessel ostium, flow through the inlet is reduced by less than 10% of baseline. Implantation of up to 3 overlapping flow diversion devices in the rabbit aorta was well tolerated, given that small lumbar branch vessels (which by diameter can be approximated to human perforating vessels) remained patent in every case. These studies are promising, but they were performed in extracranial vessels in rabbits and there may be significant differences in these vessels compared with human intracranial aneurysms. Skizora et al. reported the treatment of intracranial aneurysms with PEDs and found that of 28 branch arteries covered by 1 or more flow diverters, the OphA showed no flow in 1 case immediately and occlusion at the 6-month follow-up in 2 other cases. To date, there exists only a single published case report of a perforating artery occlusion following flow diversion implantation, suggesting that coverage of branch arteries is also typically well tolerated.

Our study was limited by the relatively small number of treated aneurysms, which diminishes our power to detect meaningful differences among groups. Ours is an angiographic study, and lack of angiographic opacification may not necessarily mean complete absence of flow through the vessel, which may explain the absence of clinical correlates in the 2 patients with lack of angiographic visualization of the OphA through the ICA or external carotid collaterals. Furthermore, our longest

Fig. 1. Case 3. A: Lateral DS angiogram of the right ICA in a 60-year-old woman demonstrating a complex, multilobed aneurysm (arrows) with a patent OphA (arrowhead). B: Digital subtraction angiogram immediately after placement of 3 PEDs (located between arrows) demonstrating absence of flow (arrowhead) through the OphA. C: Digital subtraction angiogram from the same sequence showing location of PEDs (between arrows) and delayed, antegrade flow (arrowheads) through the OphA. D: Six-month follow-up angiogram in the same patient demonstrating resolution of aneurysm and proximal occlusion of the OphA.

Fig. 2. Case 7. A: Lateral DS angiogram of the left ICA in a 56-year-old woman demonstrating a complex, irregular paraclinoid aneurysm (arrow) and patent OphA (arrowheads). B: Digital subtraction angiogram immediately following placement of 2 PEDs (between arrows) demonstrating no flow (arrowhead) through the OphA. C: Images from the same digital subtraction angiography session immediately following placement of 2 PEDs (between arrows) demonstrating retrograde flow (arrowheads) through the OphA. D: Follow-up angiogram of the left ICA 1 year after PED placement in the same patient demonstrating patency of the OphA (arrows).
angiographic follow-up was 12 months after device placement, and this may not be long enough to determine the true long-term patency of the OphA in these patients.

Conclusions

We have demonstrated that approximately one-quarter of OphAs covered with flow diversion devices will undergo angiographic occlusion. Even though these events were well tolerated clinically, our findings suggest that coverage of branch arteries that have adequate collateral circulation may lead to spontaneous occlusion. Our data do not apply to arterial branches without significant collateral vessels, which may be less likely to occlude, but more clinically dangerous to cover with a flow-diversion device.

Disclosure

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