

The Advent of Flow Diversion and Its Implications for Cerebral Aneurysm Treatment

A discussion of the principles of flow diversion and current use of flow diversion devices by location and type of aneurysm.

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Within the past 20 years, there has been a veritable paradigm shift in the treatment of cerebral aneurysms. During this time, our understanding of the pathophysiology and clinical risk profile of these lesions in combination with technologic progress has led to a more nuanced approach to aneurysms. Previously, treatment was directed toward immediate physical and radiographic obliteration of an aneurysm via microsurgical clipping in order to minimize the risk and mortality associated with aneurysmal rupture or rerupture. With the advent of the Guglielmi detachable coil (Boston Scientific Corporation), an endovascular means to accomplish these goals arose. The ISAT 1 and 2 and BRAT trials affirmed clinical equipoise and, in some cases, superiority of endovascular embolization to open surgical clipping in the treatment of ruptured cerebral aneurysms.¹⁻⁶ Combined with further natural history data on the rupture risks of untreated aneurysms, these data provide the background for an informed risk-benefit discussion regarding the treatment of cerebral aneurysms.^{7,8}

Despite these advances, large-necked, giant, and fusiform aneurysms remained a vexing problem. Giant aneurysms represented a challenge surgically, especially in regions where surgical access is associated with unac-

ceptable morbidity (eg, the cavernous segment), and coil embolization presents a technical challenge.^{1,8} Frequently, coiling alone results in insufficient embolization of the lesion, and coil compaction leads to very high recurrence rates. Adjunctive measures such as balloon- and stent-assisted coiling were necessary to achieve occlusion. However, even with these measures, there was a high risk of recurrence in these large, broad-based lesions. Unlike smaller lesions, the inability to achieve the necessary coil packing for cure leads to their recurrence, growth, and rupture in some instances.

Beyond saccular lesions, fusiform aneurysms of both the anterior and posterior circulation present an even greater challenge. Open surgery relies on vessel clip reconstruction or vessel sacrifice with or without bypass. These strategies are rife with risk that in many instances can equal the risk of the lesion itself. With previously available devices, endovascular options were largely limited to vessel sacrifice. Multiple stents, which were used as an adjunctive measure for coil support, were occasionally placed successively to attempt endovascular luminal interruption of flow to the lesion.⁹ This presented a challenge because multiple devices were needed, increasing the thromboembolic and procedural risk of treatment.

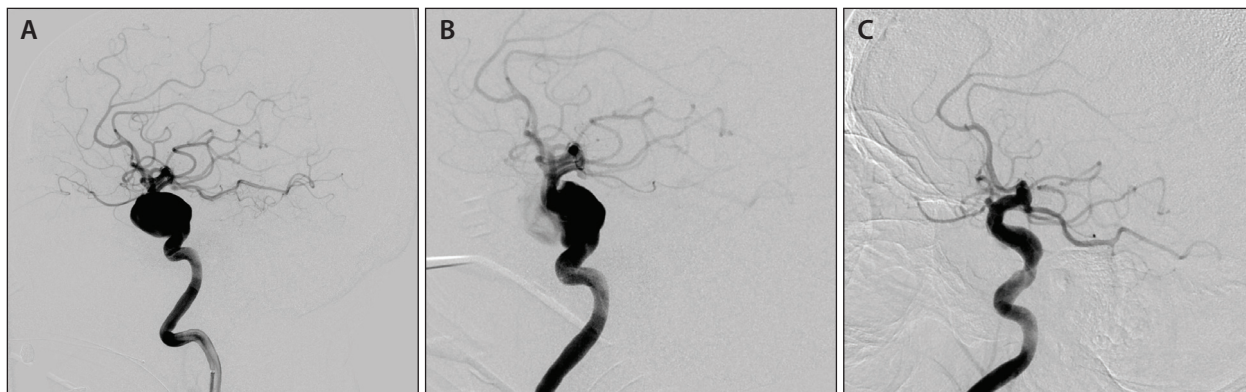


Figure 1. A 77-year-old woman presented with left eye ophthalmoplegia and orbital pain and was found to have a giant 25- X 20-mm cavernous ICA aneurysm (A). Two telescoping PEDs were placed through the lesion with immediate evidence of stasis within the aneurysm (B). Six-month follow-up imaging shows remodeling of the vessel with near-resolution of the lesion (C).

PRINCIPLES OF FLOW DIVERSION

Flow diversion arose as a concept for the treatment of aneurysms using endoluminal methods, and flow diversion devices were developed with the hope that vessel reconstruction may present an alternative to the clip/coil paradigm. Flow diversion relies on reestablishing normal flow through the parent vessel and reducing flow through the aneurysmal lesion, which leads to progressive occlusion of the aneurysm and endothelialization along the device.^{10,11} These devices are low-porosity stents that rely on the flow differential maintained between the parent and daughter vessels versus the pathologic flow into an aneurysmal lesion.

Unlike in microsurgical clipping and coil embolization, where the aneurysm is immediately obliterated, flow diversion relies on changes in the flow dynamics within aneurysms to cause aneurysmal thrombosis over time and allow for neointimal proliferation to eventually seal off an aneurysm.¹¹⁻¹³ As an intraluminal device, flow diverters themselves possess thrombotic risk prior to endothelialization. Therefore, dual antiplatelet loading is needed before device implantation and should be continued 3 to 6 months after deployment, which creates an additional nuance.^{14,15} The need for dual antiplatelet therapy should be further considered for potential hemorrhagic complications (eg, subarachnoid hemorrhage, distal intraparenchymal hemorrhage). Fortunately, aneurysmal rupture remains a small concern with these devices and is seen in only 2% to 4% of cases. Distal hemorrhage related to the placement of the device remains a concern, as these complications were observed in 5% to 10% of treated patients with giant aneurysms.^{11-13,16-19}

Current controversy exists as to the ideal regimen, choice of regimen, and timing of discontinuation of dual antiplatelet therapy.¹⁴ Beyond the risk of throm-

boembolism, the risk of in-device occlusion or delayed stenosis and occlusion of side branches are also concerns. Fortunately, animal models and retrospective studies have repeatedly demonstrated the safety of these devices over larger daughter vessels when the device is in the internal carotid artery and covers the ophthalmic artery, a daughter vessel; studies in rabbits have demonstrated that the ophthalmic artery does not occlude. Studies examining the patency and durability of flow through the ophthalmic, posterior communicating, and anterior choroidal arteries have demonstrated the clinical safety of these devices. Vessel occlusion occurred in fewer than 5% of patients, and of those with occluded vessels, none demonstrated clinical deficit as a result.²⁰⁻²⁵

INITIAL INDICATIONS AND EXPANDED HORIZONS

Initially, clinical indications for the application of flow diversion devices focused on previously untreatable or poorly treatable lesions and large/giant wide-necked aneurysms of the anterior circulation. Several feasibility trials across multiple international centers demonstrated an almost 99% deployment success rate and a 75% occlusion rate in the treatment of giant lesions proximal to the internal carotid artery bifurcation and recurrent lesions.^{12,16,26,27} The success of these studies led to the US Food and Drug Administration (FDA) approval of the Pipeline embolization device (PED; Medtronic) for use in anterior circulation aneurysms. Presently, PED and its second generation, the Pipeline Flex, are the only flow diverters available in the United States. Internationally, the Silk device (Balt Extrusion), p64 flow modulation device (phenox GmbH), Flow Re-direction Endoluminal Device (FRED; MicroVention Terumo), and Surpass device (Stryker) are available.²⁸

PROXIMAL ANTERIOR CIRCULATION

In concert with the FDA approval, flow diverters are mainly used to treat lesions of the anterior circulation proximal to the internal carotid artery (ICA) bifurcation. Figure 1 demonstrates an on-label use of the PED for the treatment of a large irregular cavernous artery aneurysm. “Telescoped” devices are used to span the large neck of a fusiform giant aneurysm. The immediate reduction in aneurysm filling and size and ultimate vessel remodeling with flow diversion is apparent, demonstrating the ability of these devices to treat previously untreatable lesions. Flow diversion is successful in reducing the initial flow into an aneurysm and further leading to complete thrombosis.^{11,18,29,30} Figure 1 demonstrates the effectiveness of these devices in treating these lesions, which previously were either difficult to treat or completely eradicated.

With time and familiarity, flow diversion devices are increasingly being used for smaller, broad-based lesions that would otherwise be difficult to approach endovascularly. Flow diversion presents a solution to recurrent and remnant aneurysms after attempted coil embolization or microsurgical clipping. Previously, the principle driving force for treatment of an aneurysm (ruptured or unruptured) was to achieve complete occlusion of the lesion or a Raymond–Roy classification 1 or 2 result.^{31–34} The use of Guglielmi detachable coils alone within narrow-necked saccular lesions effectively achieves this goal.

However, for broad-necked lesions, the ability to achieve sufficient coil packing within the lesion is often compromised.^{1,4–6,35} Adjunctive measures such as balloon-assisted coiling and stent coiling can often support the addition of more coils, yet recurrence and coil compaction remains a significant problem.^{36–38} Flow diversion provides an alternative mechanism to thrombose an aneurysm and to reconstruct a vessel lumen. Case-controlled studies have explored the use of flow diversion versus coil embolization for anterior circulation lesions and found a greater rate of occlusion for lesions treated with PED compared to coiling (94% vs 71%) with an equivalent safety profile.³⁹ The concept of promoting lesional thrombosis and providing a scaffolding to reconstruct the native vessel may demonstrate the increased utility of these devices. On the other hand, recent randomized trials, specifically the FIAT trial, demonstrated less than favorable outcomes in patients randomized to flow diversion, with approximately 10% mortality.⁴⁰ This

information needs to be taken in context of previous clinical experience but serves to show that flow diversion does not totally replace the need for other endovascular or surgical techniques.

INCOMPLETE TREATMENT AND RECURRENCE

Incomplete treatment and recurrence of aneurysms despite initial treatment due to either aneurysmal growth or coil compaction is a topic well described within the endovascular literature. Initial coil embolization or stent-coil embolization do not preclude other mechanisms of further treatment. More coils, stents, or flow diversion remain options. However, after placement of a flow diverter, additional coil embolization is not feasible because the decreased porosity of these devices does not allow access to the aneurysms with a microcatheter.^{15,24,41,42} As such, when a remnant or residual lesion is encountered, the only available treatment is placement of an additional flow diverter, which carries further risk to perforators and side branches depending on the parent vessel. Figure 2 illustrates the utility of flow diversion in treating recurrent and broad-based lesions.

For lesions in which there is concern for flow diversion to completely occlude the aneurysm, adjunctive coil embolization should be considered. As previously mentioned, coil embolization is performed through separate catheterization and jailing of the coil microcatheter underneath the flow diverter. Adjunctive coils are placed to promote thrombosis to optimize aneurysm treatment.^{39,43} Figure 3 demonstrates a ophthalmic segment lesion with concerning features that was successfully treated by flow diversion with adjuvant coiling to promote thrombosis.

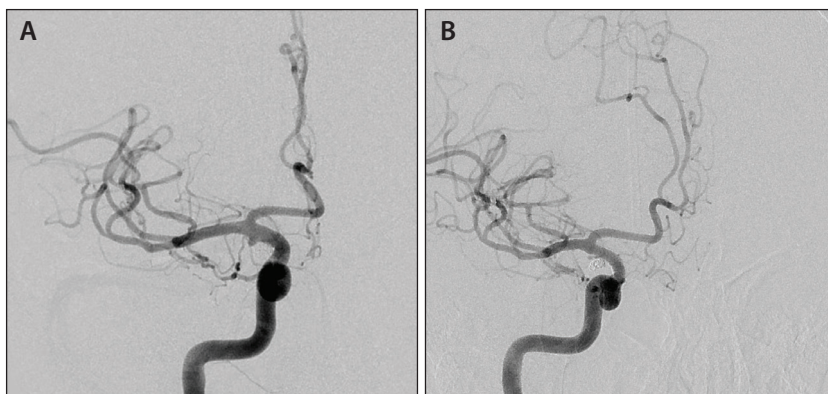


Figure 2. A 62-year-old woman with a prior subarachnoid hemorrhage secondary to a posterior communicating artery aneurysm presented with an ipsilateral 4-mm anterior choroidal lesion and coil compaction of the posterior communicating lesion (A). A single PED was placed, and 6-month follow-up demonstrated complete occlusion of both lesions (B).

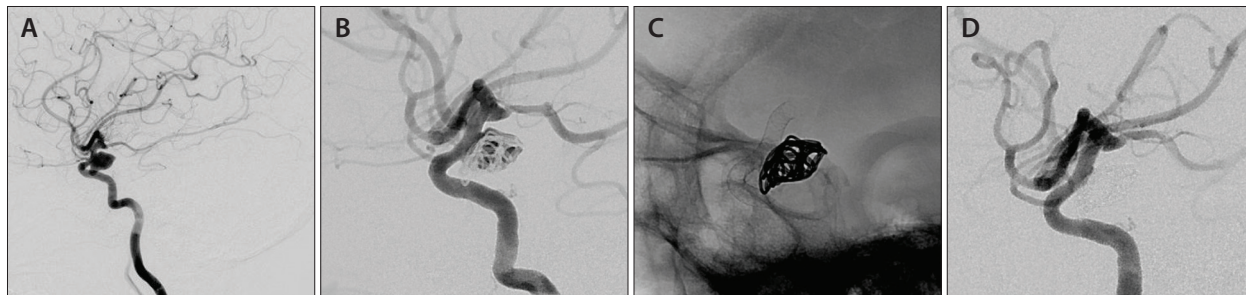


Figure 3. A 55-year-old woman who was incidentally found to have a 12- X 7-mm right ophthalmic segment ICA aneurysm with several blebs and irregular dome (A). This was managed with a combination of flow diversion and adjuvant coil embolization due to the concerning features of the lesion (B, C). Six-month follow-up demonstrated complete resolution of the lesion (D).

CRANIAL NERVE COMPRESSION

Cranial nerve palsies secondary to mass effect from a cerebral aneurysm present a challenge specifically to the endovascular surgeon. Open surgical obliteration relieves aneurysmal mass effect, which leads to rapid amelioration of the cranial nerve compression in most cases.⁴⁴ Unfortunately, previous endovascular methods often led to continued compression rather than treatment of aneurysmal mass effect. Recent case studies have demonstrated the efficacy of flow diversion in treating the aneurysm and relieving cranial nerve deficits, owing to the remodeling effect of these devices over time.^{45,46} This allows for endovascular treatment of lesions previously requiring open surgery.

DISTAL LESIONS

Fusiform, broad-based, and complex lesions are not limited to the proximal ICA. Within the initial experience with flow diversion, use within the distal anterior circulation was limited. Yet, with broader experience with the device, several case reports have demonstrated the feasibility and efficacy of flow diversion devices within the anterior and middle cerebral artery.^{41,47-49} Flow diversion is a treatment option in these complex lesions, but broader recommendations are pending further clinical experience.

POSTERIOR CIRCULATION

Despite its success within the anterior circulation, there remains trepidation to use flow diversion in the treatment of lesions of the vertebrobasilar system. As an intraluminal device with decreased porosity, there is a risk of causing side vessel (ie, perforator vessel) occlusion, which may have devastating consequences in the posterior circulation. Although the use of flow diversion was initially limited within the posterior circulation, there were significant complications.^{25,50-52} In a series of 101 patients by Fischer et al, three of five major complications occurred in the posterior circulation, including in-device thrombosis and associated hemorrhage.⁵³ Further, a perforator infarc-

tion rate of 14% has been observed even in more recent studies. However, as previously discussed in the anterior circulation, many lesions in the posterior circulation are insufficiently treated or incapable of treatment by open surgical techniques or coiling alone. In recent case series, acceptable treatment results demonstrating a near 90% occlusion rate have been reported.⁵⁴

RUPTURED ANEURYSMS

The use of intraluminal devices in the setting of aneurysmal rupture presents a unique challenge. Ruptured aneurysms represent inherently unstable vascular lesions and are frequently accompanied by intraventricular hemorrhage and hydrocephalus, necessitating cerebrospinal fluid diversion. Typically, endovascular and open surgical treatments immediately secure the lesion without requiring anticoagulation or antiplatelet treatment. Some vascular lesions are suboptimally treated with either open surgery or coiling alone, and flow diversion presents an additional option in these exceptional circumstances. However, hemorrhagic and thromboembolic risks need to be balanced and considered when using these novel devices.^{15,18,55-57}

BLISTER ANEURYSMS

Blister lesions are rare but notoriously difficult to treat via previously available open or endovascular techniques. Blister aneurysms are small lesions (< 2 mm) and are thought to be the manifestation of an overall diseased vessel leading to subarachnoid hemorrhage.⁵⁸⁻⁶⁰ Due to their small size and possible false wall structure, coiling and or stent coiling is challenging and often does not fully secure the lesion or prevent further aneurysmal rupture. Further, open surgery with either clipping or muslin/muscle wrapping can have poor results. Flow diversion as a principle presents an ideal alternative to treat these lesions because it allows for vessel remodeling over time (Figure 4). Retrospective studies have demonstrated early success in treating these difficult lesions.^{61,62}

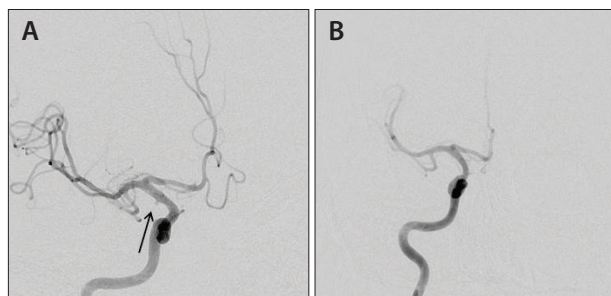


Figure 4. A 39-year-old man presented with a “worst headache of life.” CTA was negative for subarachnoid hemorrhage, but angiography later revealed a blister ICA communicating segment aneurysm (A). The patient was given aspirin 325 mg and prasugrel 30 mg, and two overlapping PEDs were placed. Follow-up at 6 months demonstrated slight vessel narrowing but obliteration of the lesion (B).

COMPLICATIONS OF FLOW DIVERSION

As with all open and endovascular interventions, flow diversion is not without its own risks. Beyond the ischemic risks, there is a small but real risk of hemorrhage associated with the device. These are related to mechanical complications, aneurysmal rupture, and cryptogenic hemorrhage. Mechanical complications are the most modifiable of these risks. With increased experience with flow diversion and newer-generation devices, an improved safety profile and improved overall outcomes have been demonstrated.^{27,42,52,55,63-66}

Aneurysmal rupture is thought to be due to a transient increase in aneurysmal flow as a result of device placement.^{13,18,19} Although the risk is small, some centers use adjunctive coiling to promote thrombosis and mitigate this risk (Figure 2). Finally, cryptogenic hemorrhage or distal parenchymal hemorrhage associated with device placement is a rare complication observed with use of these devices.⁶⁷ Presently, these complications are thought to be a result of the hemorrhagic conversion of embolic stroke associated with dual-antiplatelet therapy required for device placement or associated hyperperfusion. With approximately 100 cases reported in the literature, there appears to be an increased association when multiple devices are required to treat giant aneurysms.⁶⁸⁻⁷⁰

CONCLUSION

The addition of flow diversion to the endovascular armamentarium not only allows for a new means of treatment, but also a change in the thought process of aneurysm treatment. These devices have expanded the horizons of the endovascular neurosurgeon and improved the treatment of previously difficult-to-treat

lesions. Further study is needed to understand the expanded indications of flow diversion devices and their long-term durability. ■

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