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Flow diverters (FDs) are being used with increasing frequency, especially to target large and complex aneurysms not amenable to treatment with conventional endovascular methods.[8,10,11,26] The Pipeline embolization device (PED) is the first FD approved by the FDA following the results of the PUFS trial for the management of large or giant wide-necked intracranial aneurysms in the internal carotid artery from the petrous to the superior hypophyseal segments. Although initially indicated for a limited type of aneurysms, the use of the PED is being extended for the management of a variety of aneurysms in different settings.[5-7,9] The main factors that are considered in deciding if an aneurysm is suitable for treatment with the PED include aneurysm size, location, geometry and shape and rupture status.[16] Studies have shown a high technical success rate, a high rate of aneurysm occlusion accompanied by low recurrence and re-treatment rates.[10,12,20] Current evidence also supports the PED as a safe device associated with low morbidity and mortality.[10,21,23,27] Although treatment failure with flow diversion has been reported, the characteristics of these aneurysms with persistent filling have not been well established. Furthermore, the course of these aneurysms remains a topic of uncertainty. The initial thrombosis caused by FDs does not result in immediate cure of the aneurysm rather FDs act as a scaffold for endothelial overgrowth at the aneurysm neck resulting intra-aneurysmal flow stasis and thrombosis while promoting remodeling of the parent vessel and parent vessel reconstruction which results in gradual occlusion of the aneurysm.[22]

Prior literature on the efficacy of PED have shown a high complete aneurysm occlusion rate, with most studies reporting occlusion rates > 80%[3,13] and this compares favorably to endovascular coil embolization, where the reported complete occlusion rate is 66%(ISAT).[4] Recurrence after successful PED treatment has not been reported with the available short- and medium-term data. This is in contrast to high recurrence rates with coiling (9-34% at 12 months) that increases with large, giant, wide-necked, and nonsaccular aneurysms that are the target for PED treatment.[1] The retreatment rate is much lower with PED treatment as compared to coiling in ISAT (17.4%).[4] Flow diverters seem to be more effective than the conventional endovascular techniques in select cases.

Aneurysm location in the distal anterior circulation (PCOM artery, anterior choroidal artery and MCA) is a significant predictor of persistent aneurysm. Parent vessels for such aneurysms are usually small, and aneurysms often arise at major branch points. In addition, the A1 segment of the ACA and M1 segment of the MCA are rich in lenticulo-striate perforators, and covering these areas with PEDs could theoretically increase the risk of perforator strokes with neurological deficits. These factors render PED delivery and deployment more difficult. Also, PEDs (with available sizes from 2.5 to 5 mm) are in general designed for parent vessels that are larger than the caliber of distal anterior circulation vessels. In a small vessel, the device may be elongated and the stent pores may become larger which may impair the flow diversion effect and lower the chances of aneurysm thrombosis. This may affect the reliability of PED deployment in smaller distal vessels. However, there are some distal anterior circulation aneurysms that are morphologically challenging for either traditional microsurgical or endovascular approaches, and the use of PEDs may have an advantage in these cases. In these cases, placing a single, long flow diverter stent and avoiding telescoping of multiple devices along perforator-rich segments can reduce the risk of perforator occlusion.

The PED was originally approved for the treatment of aneurysms proximal to the PCOM artery.[14] PCOMA aneurysms are among the most frequently encountered cerebral aneurysms. A fetal PCOM artery is an end vessel with no distal collaterals. Since fetal PCOM arteries represent the only supply to the PCA, care should be taken when treating PCOM aneurysms incorporating a fetal variant.[19] In fact, fetal PCOM artery aneurysms are often treated surgically since endovascular therapy is thought to cause a higher treatment risk.[19] Several reports have suggested that flow diversion for fetal PCOM aneurysms is ineffective and does not lead to aneurysm occlusion and has high potential for serious complications.[17,19] Aneurysms arising from a fetal PCOM are less likely to be occluded even after placement of a flow diverter due to the high flow and the high physiological demand for this artery which maintains pressure gradient across the ostium.[14] PCOM aneurysms with a fetal PCA are better to be treated with microsurgical clipping.[18] Attempting flow diversion may add procedural risks and make surgical clipping even more technically complex.

MCA aneurysms represent the third most common cause of subarachnoid hemorrhage and almost 1/5 of unruptured aneurysms.[24] The majority of MCA aneurysms arise at the level of the bifurcation tend to be wide-necked, incorporate one

or more side branch vessels and tend to have an unfavorable anatomical configuration.[15] Wide-necked MCA bifurcation lesions have been classically treated with microsurgery with excellent results. Traditional endovascular approaches can sometimes be challenging with a risk of occluding branch vessels as well as the risk of coil herniation. Flow diversion for MCA aneurysms should be considered when other surgical or endovascular approaches are not an option or do not offer superior outcomes and for lesions that persist after previous surgery or endovascular treatment.[26] Clinical data should demonstrate better or similar results than clipping to challenge surgical intervention, with current occlusion rates from clipping reported to be >90% in most studies.[25]

Stent placement negatively affects the safety and efficacy of the PED in the management of recurrent aneurysms. The rate of complete aneurysm occlusion is lower in previously stented aneurysms (50-65%) with potential for a higher complication rate (14.3%) and technical failure rate.[28] If a stent was placed initially, recurrence would be less eligible for PED treatment and might require surgical clipping to achieve aneurysm occlusion. The presence of a previous stent may: reduce the hemodynamic effect of the PED, disrupt the process of wall apposition of the PED to the parent vessel, preventing the endothelialization process inhibiting complete aneurysm occlusion, complicate the navigation of the delivery catheter into position and the actual deployment of the PED and because the PED should be deployed distal to the stent, the distal end of the PED may "catch" on the previously placed stent, which may cause anchoring and stretching of the device, leading to less effective results. It is important to note that patients of advanced age can have a weaker neo-intimal response and therefore may have higher odds of incomplete aneurysm occlusion.

The majority of cases require the placement of only one PED, and a single PED should be usually placed as there was no difference in aneurysm occlusion when more than 1 device were deployed.[29] Coiling and flow diversion have been shown to be complementary, rather than competitive modalities for intracranial aneurysm treatment.[3] Using coils along with the PED in select cases can be more effective with a higher occlusion rate and lower retreatment rate, by promoting endosaccular thrombosis and providing a mechanical scaffold.

The PED is indicated for large and giant aneurysms.[4] However, large and giant aneurysms represent a small fraction of all cerebral aneurysms with the majority of aneurysms in the general population being <10 mm in size. Traditional endovascular strategies including coiling and stent-assisted coiling are usually used for small aneurysms (≤ 7 mm). Some retrospective studies have demonstrated high occlusion rates (75-90%) and low complication rates (<5%) with treating these small aneurysms.[10] In experienced centers the PED is demonstrating a better efficacy profile and a similar safety profile to coiling of smaller aneurysms.[10] With the increasing use of the PED for the treatment of small, simple aneurysms, the question arises as to whether the use of this device routinely, or even as a first line treatment for these aneurysms is as safe and effective as the current standard endovascular techniques. This needs to be further studied

Good clinical outcomes have been reported with flow diversion of saccular or non-symptomatic fusiform posterior circulation aneurysms.[3] Treatment with the PED may be a preferable alternative to open surgical treatment for these aneurysms. Because of the large number of perforating vessels in the posterior circulation that supply vital brainstem structures, complex aneurysm anatomy, and aneurysm location, flow diversion should be used with caution. Aneurysm morphology and presentation are critical factors to consider when selecting posterior circulation aneurysms for treatment with the PED.[30]

Device deployment is successful in 95% to 100% of cases (99% in PUFS).[2] Selection of the appropriate diameter and length of the device is essential to ensure proper device function and to minimize the chance for unanticipated stent shortening or migration. *(FDA-Summary of Safety and Effectiveness of Data, PED, P100018)* The delivery catheter must recross the PED over the delivery wire to recapture the distal coil tip after complete stent deployment. Up to 50% foreshortening is expected when fully deployed compared with 1.5% -7.1% and 1.8%-5.4% foreshortening in Wingspan® and Neuroform® 3 stents. *(Bench testing conducted by Boston Scientific)*

There is a potential risk of an endoleak-like phenomenon with implantation of an undersized device, which results in poor wall apposition. Similarly, implantation of an oversized device may result in poor coverage of the lesion because of an incomplete compaction of the strands.[31] When a branch vessel is incorporated into the target aneurysm, its runoff can potentially contribute to persistent filling of the aneurysm by the very same physiological processes theoretically responsible for the preservation of jailed branch vessels and perforators arising from normal segments. One may expect that final closure of such aneurysms would require concomitant occlusion of the associated branch.

While the PED can allow for treatment of large, wide-necked aneurysms with high efficacy, aneurysm location, previous treatment, patient age and the use of concomitant coiling may influence treatment outcomes.

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