Flow Diversion

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Endovascular treatment of aneurysms can be accomplished either by endosaccular occlusion using coils or liquid embolics or by parent vessel reconstruction using stents, alone or with coils. Although good for small, narrow-necked aneurysms, endosaccular occlusion with coils produces a low level of complete occlusion in giant (8.3%), large (21.1%), and small, wide-necked aneurysms (43.1%) [Fiorella et al. BNI-CCF Neuroform Database]. One study reported an overall recanalization rate of 20.9% that was related to the size of the dome and neck of the aneurysm [Murayama Y et al. *J Neurosurg* 2003]. The best evidence for the importance of achieving complete occlusion comes from the Cerebral Aneurysm Rerupture After Treatment (CARAT) study, which reported that the degree of aneurysm occlusion after treatment was strongly associated with risk of rerupture (ie, a 17.6% risk of rerupture when the rate of occlusion was <70%) [Johnston SC et al. *Stroke* 2008].

The Next Aneurysm Innovation of the Future

Michael E. Kelly, MD, PhD, University of Saskatchewan, Saskatoon, Canada, discussed the newest therapeutic option for aneurysm treatment: flow diversion. Dr. Kelly discussed the device with which he is most familiar, the Pipeline embolization device (PED), a unique endovascular construct designed to achieve definitive aneurysm occlusion through reconstruction of the parent vessel. The PED is a flexible microstent that is delivered through a microcatheter. During deployment, the stent can be packed to achieve maximal metal surface area coverage. One Pipeline stent produces higher flow reduction compared with three overlapping Neuroform stents. These stents work by disrupting the inflow/outflow zone leading to thrombosis of the aneurysm. The stent acts as a lattice to promote endothelialization and thrombus resorption without affecting side branches and perforators.

Although clinical evidence for flow diversion devices is limited, the Pipeline Embolization Device for the Intracranial Treatment of Aneurysms (PITA) trial reported a very high rate (93%) of complete angiographic occlusion at 6 months in patients with internal carotid aneurysms, including some with wide neck aneurysms [Nelson PK et al. *Am J Neuroradiol* 2011]. Similar rates of occlusion have been reported in smaller trials [Lylyk P et al. *Neurosurgery* 2009; Szikora I et al. *Am J Neuroradiol* 2010] and by Dr. Kelly's team, which reported angiographic cure in 11 of 14 patients after a mean follow-up of 11.2 months (range 3 to 18 months).

Flow diversion is recommended for aneurysms that are not amenable to any other endovascular or neurosurgical techniques but require treatment. Flow diversion is not recommended for most subarachnoid hemorrhage cases. Implant complications, such as thrombosis, vessel injury, and trapping of outflow zone, and delayed complications, such as ipsilateral intracerebral hemorrhage, in-stent stenosis, and failure of aneurysms to occlude, have been reported.

No Need to Abandon Established Therapy

Taking the opposite position, William Thorell, MD, University of Nebraska Medical Center, Omaha, Nebraska, maintained that coil embolization represents the endovascular "state-of-the-art" for treatment of brain aneurysms and should not be abandoned in favor of standalone flow diversion therapies. "Flow diversion should be viewed primarily as an adjunct, while additional tools should be developed to improve endosaccular therapy of intracranial aneurysms," he stated.

A large percentage of brain aneurysms can be treated effectively with coil embolization with and without adjuncts. The intraprocedural and postprocedural complication rates are low, and the retreatment rate is modest and decreasing. Importantly, coiling can be performed without antiplatelet medications, improving the safety of hydrocephalus management. Coil embolization has a 42% to 86% complete occlusion rate, an aneurysm recurrence rate of 15% to 33%, a rebleeding rate of 0.02% to 1% per year, and a retreatment rate of 6% to 19% with death or dependent rates of 9.8% to 25% per year [Molyneux AJ et al. *Lancet* 2005; Wiebers DO et al. *Lancet* 2003; Raymond J et al. *Stroke* 2003; Cloft HJ et al. *Am J Neuroradiol*; Gunnarson T et al. *Am J Neuroradiol*; Pierot L et al. *Am J Neuroradiol*; Johnston SC et al. *Stroke* 2008].

Because flow diversion is so new Dr. Thorell said, "there is an element of flow diversion that we don't understand." Although postprocedural bleeding is rare, the process is

not completely understood. Other weaknesses include: the need for antiplatelet therapy; flow cessation in the aneurysm may not occur immediately; it is not a good choice for bifurcated aneurysms; and the deployment of flow diversion precludes further endovascular therapies.

Coil embolization of brain aneurysms can be used very effectively with relatively low morbidity and mortality rates. For the aneurysms with high procedural risk and those that require surgery or have a high rate of treatment failure, standalone flow diversion may be more appropriate.

Do We Need to Pause and Catch Our Breath?

New endovascular strategies for the treatment of cerebral aneurysms have emerged, providing direct anatomical reconstruction of the parent vessel wall deficiency. Typically, these strategies incorporate the use of low-porosity (high coverage) endoluminal sleeves, such as PED, to provide definitive and durable anatomical closure of complex (and simple) cerebral aneurysms. With increasing acceptance, it is likely that these devices will extend the subset of aneurysms that is suited for endovascular management. Peter Nelson, MD, NYU Langone Medical Center, New York, New York, cautioned however, that additional experience will be required to fully understand the indications for these new devices, their limitations, and the optimal treatment strategies for their use.

In defense of direct endoluminal reconstruction, two international trials have demonstrated the effectiveness of this technique. The PITA trial [Nelson PK et al. *Am J Neuroradiol* 2011], a European/South American multicenter, prospective, single-arm study (n=31) in patients with wide-necked or recurrent coiled aneurysms, reported that 93% of patients had complete aneurysm occlusion at 6 months, as determined by angiography. There were no deaths; however, 6.5% of patients experienced perioperative stroke. The Pipeline for Uncoilable or Failed Aneurysms (PUFS) trial, a US/European/Middle Eastern multicenter, prospective, single-arm study (n=108) in patients with wide-necked large and giant aneurysms that were unsuitable for treatment with coils, reported that 74% of patients met the effectiveness endpoint of complete aneurysm occlusion without stenosis at 6 months, as determined by angiography; 5.6% had died or experienced a stroke within the first 180 days.

Moreover, the initial commercialized experience through May 2010 similarly was characterized by a low incidence of significant complications, with a reported neurological morbidity of 2.02% and mortality of 2.44% (Table 1) and a prevalence of device-related morbidity that was not dissimilar from that reported with other endovascular techniques.

Table 1. Pipeline Morbidity and Mortality as of May 8, 2010 Commercial PED Cases (n=941; Europe, Australia, and Canada).

Event	Number	Percentage
Neurological morbidity	19	2.02
Perforator occlusion	3	0.32
Delayed ipsilateral parenchymal hemorrhage	9	0.96
Parent vessel occlusion (in-stent thrombosis)	4	0.43
PED-related thromboembolic event	1	0.11
Worsening symptomatic mass effect	2	0.21
Mortality	23	2.44
Aneurysm rehemorrhage (acutely ruptured aneurysm)	2	0.32
Delayed aneurysm rupture (previously unruptured)	9	0.96
Delayed ipsilateral parenchymal hemorrhage	2	0.21
Worsening hydrocephalus/CVA	3	0.32
Parent vessel occlusion (device malfunction)	1	0.11
Fatal drug reaction (postprocedure)	1	0.11
Unknown etiology	3	0.32
Total morbidity and mortality	42	4.46

PED=Pipeline Embolization Device; Data assembled by Keith Gill, Kathleen McConnell, James Lago et al. U*npublished data.*

Untoward sequelae that were reported in these studies included anticipated complications that were shared with other endovascular approaches: perforator occlusion, delayed ipsilateral parenchymal hemorrhage, in-stent thrombosis, thromboembolic events, and worsening symptomatic mass effect. While the low frequency of these familiar complications is encouraging, especially considering the complexity of the aneurysms that were treated, according to Dr. Nelson, the etiologies of other infrequent complications are unique and poorly understood at this time. One disconcerting issue relates to the phenomenon of delayed aneurysm rupture after treatment of previously unruptured aneurysms (0.96%). Although this phenomenon appears to be restricted to larger aneurysms, no unifying explanation for this complication has been accepted.