Flow Diverters for Intracerebral Aneurysms: The Past, Present, and Future

The continued evolution of flow diversion for intracranial aneurysm treatment has helped neurointerventionalists achieve high aneurysm occlusion rates with low hemorrhagic and ischemic complications, and there are promising technologic advancements to come.

By Kareem El Naamani, MD, and Stavropoula I. Tjoumakaris, MD, FAANS, FAHA

The neurointerventional field witnessed its first technologic revolution in the early 1990s when Guido Guglielmi introduced the concept of detachable coils.[1] With the addition of adjunctive devices such as intracranial stents and balloons, endovascular therapy for ruptured and unruptured intracranial aneurysms became a viable option. In the next decade and a half, there was an abundance of studies and trials in the neurointerventional literature showing the efficacy and safety profile of endovascular therapy.[2,3] However, to improve rates of complete aneurysm obliteration and decrease recurrence, especially in larger, wide neck aneurysms, expanding therapeutic alternatives was inevitable.[4] In 2011, based on the PUFS safety and efficacy trial, the FDA approved the Pipeline embolization device (PED, Medtronic) as the first flow-diverting stent for the treatment of aneurysms in the internal carotid artery (ICA).[5] This introduction of flow diversion produced a significant paradigm shift in endovascular therapy where treatment of intracranial aneurysms shifted from endosaccular treatment to parent artery endothelial reconstruction and para-aneurysmal perforator preservation.[6]

THE PAST

The mechanism of action of flow diverters (FDs) is divided into the hemodynamic stage, thrombus formation, and endothelialization, which take place progressively over time. In the hemodynamic stage, which occurs immediately after FD deployment, blood is disrupted from flowing into and out of the aneurysm from the parent artery.[7] Next, thrombus formation takes place where a stable thrombus forms during the following days to weeks.[8] Lastly, the endothelialization stage may last for months to years, whereby the aforementioned thrombus transforms to its final collagen stage.[8]

Based on years of benchmark work, several companies started manufacturing FDs for clinical use. The three main first-generation FDs approved for use in the United States are the PED, the Surpass Streamline (Stryker), and the Flow-Redirection Endoluminal Device (FRED, MicroVention Terumo). Although these FDs differ in metal composition, all share the main goal of aneurysm obliteration through blood diversion, thrombus induction, and parent artery endothelialization. Given the metallic properties of FDs, dual antiplatelet therapy is required to prevent thromboembolic complications.

This limited the use of first-generation FDs in ruptured aneurysms where a balance between the risk of hemorrhagic rerupture due to blood thinner use and the risk of thromboembolic complications due to FD deployment was difficult to achieve. Taking into consideration the high rate of morbidity associated with the

first-generation FDs, which ranged from 8.3% to 25.8%, manufacturing companies focused on the production of new-generation FDs with surface modification technologies to attempt to decrease the thrombogenicity of FDs.[9-13]

THE PRESENT

A closer analysis of these surface modifications led to modified successors of the three main first-generation FDs used in the United States. The PED was the first FDA-approved FD for ICA aneurysm treatment. Although the PED showed high morbidity rates specifically in treating giant ICA aneurysms, the second-generation Pipeline Flex embolization device (Medtronic), which was FDA approved in 2014, did not differ in terms of surface modification.[14] The two modifications with protective sleeves and resheathing pads only decreased the rate of technical complications and malpositioning.[14]

Ultimately, the Pipeline Flex with Shield technology (Pipeline Shield, Medtronic) was developed and CE Mark approved in 2015. This newest generation of PEDs was equipped with a synthetic layer of phosphorylcholine coating on the metallic strands to reduce thrombogenicity. In 2018, the Surpass Streamline FD was FDA approved for the treatment of intracranial aneurysms.[15] Similar to the Pipeline Flex, the second-generation Surpass Evolve (Stryker) did not provide further surface modification versus the first-generation device. The two main modifications of the Surpass Evolve were a reduced wire count and the dispensing of a preloaded system, which provided better flexibility and wall apposition, decreasing the morbidity rate from 8.3% to 4%.[8]

The most recent first-generation FDs to be approved were the FRED and FRED Jr devices for the treatment of intracranial aneurysms and aneurysms distal to the circle of Willis, respectively.[16,17] Subsequently, the next-generation FRED device with X technology, the FRED X (MicroVention Terumo) was recently developed and FDA approved. In this surface modification technique, the entire surface of the FRED was enhanced with the X technology, which is formed with covalent bonds that create a protective hydration layer around the stent to reduce platelet adhesion and allow for endothelialization.

THE FUTURE

The lingering concern for thrombotic events and the hemorrhagic risk imposed by dual antiplatelet therapy have redirected the focus of current research to the idea of bioresorbable flow diverters (BRFDs). A handful of in vitro studies have provided results on the use of bio- and hemocompatible coating technologies.[18-21] The idea behind BRFDs is aneurysm occlusion, healing the parent artery, and harmless resorption of the device by the body. Potential advantages of BRFDs include reducing the risk of chronic device-induced thrombogenesis, minimizing the chronic inflammation that leads to in-stent stenosis via neointimal hyperplasia, reducing the risk of late side-branch occlusion, restoring physiologic vasomotion, diminishing imaging artifacts, and abating interference with pediatric vasculature due to their temporary nature.[22-27]

Technologic advancements in FDs expand in the modes of deployment with robotic-assisted intracranial aneurysm embolization. Although not approved for use in the United States, robotic systems are being used in Canada and Europe to assist in aneurysm embolization. Cancelliere et al presented a case series of six patients with ruptured and unruptured intracranial aneurysms.[28] Neck bridging stents and FDs were successfully deployed in all the patients using the CorPath GRX robotic system (Siemens Healthineers Endovascular Robotics). In addition to providing precision and limiting the operator's radiation exposure, these robotic systems allow for cross-continental treatment of intracranial aneurysms.

CONCLUSION

The neurointerventional field has been a milieu for technologic advancements that are continuously evolving. Flow diversion has revolutionized aneurysm treatment, and its evolution will continue to assist neurointerventionalists in achieving high aneurysm occlusion rates with low hemorrhagic and ischemic complications. ■

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Kareem El Naamani, MD
Department of Neurological Surgery
Thomas Jefferson University Hospital
Philadelphia, Pennsylvania
Disclosures: None.

Stavropoula I. Tjoumakaris, MD, FAANS, FAHA
Professor of Neurological Surgery
Chair, University Faculty Affairs Department of Neurosurgery
Director, Endovascular Surgery & Cerebrovascular Neurosurgery Fellowship
Director, Neurosurgery Clerkship
Thomas Jefferson University Hospital at Sidney Kimmel Medical College
Philadelphia, Pennsylvania
stavropoula.tjoumakaris@jefferson.edu
Disclosures: National Principal Investigator, FRED X postapproval study.