Application of New Techniques and Technologies: Stenting for Cerebral Aneurysm

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Given previous success [1] and technological limitations of endovascular devices, the "gold standard" for the treatment of wide-necked cerebral aneurysms has been surgical repair. Several issues with the morphology of these lesions have limited the application of previous endovascular technology to their successful treatment.

Parent artery preservation, coil herniation and migration, arterial branch occlusion, and higher rates of recanalization have all plagued safe and effective exclusion of wide-necked aneurysms via endovascular means (*Fig. 11.1*). The balloon-remodeling and dual-catheter techniques, and the development of three-dimensional and complex-shaped coils have attempted to address these difficulties.

We are currently in the midst of an explosion of endovascular technology. The neuroendovascular field has benefited by continued improvement in devices used in other organ systems as well as an interest by individuals and device companies in products specifically designed for use in the neurovasculature. The brain aneurysm stent is one such device, with one currently available for clinical use and others soon to be released, pending approval.

The original proposed indications for endovascular stents were to prevent vessel collapse from elastic recoil, to prevent propagation of dissection after angioplasty, and to force asymmetrical plaques into a cylindrical shape within the vessel lumen.[30] Although animal studies began longer than 35 years ago, widespread clinical use of endovascular stents has been adopted much more recently, and remains an area of considerable controversy. In 1969, Charles Dotter placed a spiral coil into a dog popliteal artery and long-term patency was demonstrated.[4] In 1983, Dotter et al.[5] reported endovascular placement of nitinol stents into canine arteries. In 1985, Julio Palmaz developed the balloon expandable stent delivery system, and Schatz and Palmaz et al. published their experience with the device in dogs.[27] In 1986, Jaques Puel (Toulouse, France) implanted the first stent (Wallstent) into a human coronary artery, and in 1987, Puel and Ulrich Sigwart (Switzerland) reported the first clinical experience with 24 self-expanding stents in coronary arteries of 19 patients.[30] This was the beginning of a revolutionary treatment for coronary stenosis replacing the need for bypass surgery in many patients.

Investigators quickly learned that stent use was not without risk, and the two main categories of problems with these devices were occlusive and hemorrhagic events (*Fig. 11.2*). The largest early randomized trial of balloon-expandable-stent implantation with balloon angioplasty (PTCA) alone in patients with coronary artery disease delineated the advantages and disadvantages.[29] The Benestent Study Group demonstrated that restenosis at 6 months was 22% for the stent group versus 32% for PTCA alone.[29] Acute and subacute vascular occlusion was 2.7% in patients with stents versus 3.5% for PTCA patients.[29] A concerning statistic was the rate of bleeding complications between the groups, 13.5% in the stent group and 3.1% for PTCA.[29]

CEREBRAL ANEURYSM STENT HISTORY: PRE-FDA APPROVAL

In November 1995, an animal model evaluated the combination of an endovascular stent and coils for an experimental fusiform aneurysm in swine.[20] The first clinical case was reported in 1997, and involved the use of a balloon-expandable cardiac stent combined with Guglielmi detachable coils for a fusiform vertebrobasilar junction aneurysm.[13]

The use of stents for salvage after coil herniation for wide-necked aneurysm embolization was published in 2000.[6,18] The Buffalo group used an AVE coronary stent in the management of a paraclinoid aneurysm with a Guglielmi detachable coil, and shortly thereafter reported treatment of cavernous internal carotid artery (ICA), superior hypophyseal, vertebral, and midbasilar aneurysms with stents and coils.[6,16,17,21] The first significant series of cases was reported in December of 2002, with 111 balloon-expandable cardiac stents used for the treatment of cerebral aneurysms and intracranial atherosclerotic disease.[19]

## CEREBRAL ANEURYSM STENT: HISTORY: POST-FDA APPROVAL

Only one stent is currently approved for use in the United States. The Food and Drug Administration (FDA)

FIGURE 11.1. Ill-advised attempt at coiling a very wide-necked ruptured PCOM aneurysm without adjuvant use of a balloon-remodeling or endovascular stent. This attempt resulted in coil herniation into the ICA and PCA with PCA perforator occlusion and contralateral hemiparesis.

approval is restricted as a humanitarian device exemption (HDE). The Neuroform stent is indicated for use with embolic coils for the treatment of wide neck (≥4 mm or a dome-to-neck ratio 2) intracranial, saccular aneurysms that are not amenable to treatment with surgical clipping. FDA HDE approval was granted September 11, 2002. Device use requires Institutional Review Board approval. A HDE is intended to benefit patients in fewer than 4000 individuals in the United States per year. Despite the limited FDA indica-

tions, limited surgical options for certain vascular pathologies have led some investigators to apply the technology to lesions outside the approved guidelines. Although the approval is for wide-necked saccular aneurysms, numerous centers have used the device as a flow-diversion tool to treat fusiform and blister-like aneurysms (7–10, 28) (personal communication, D. Fiorella). These represent particularly challenging lesions because surgical options are limited for safe, effective treatment (*Fig. 11.3*). The efficacy of wrapping is currently
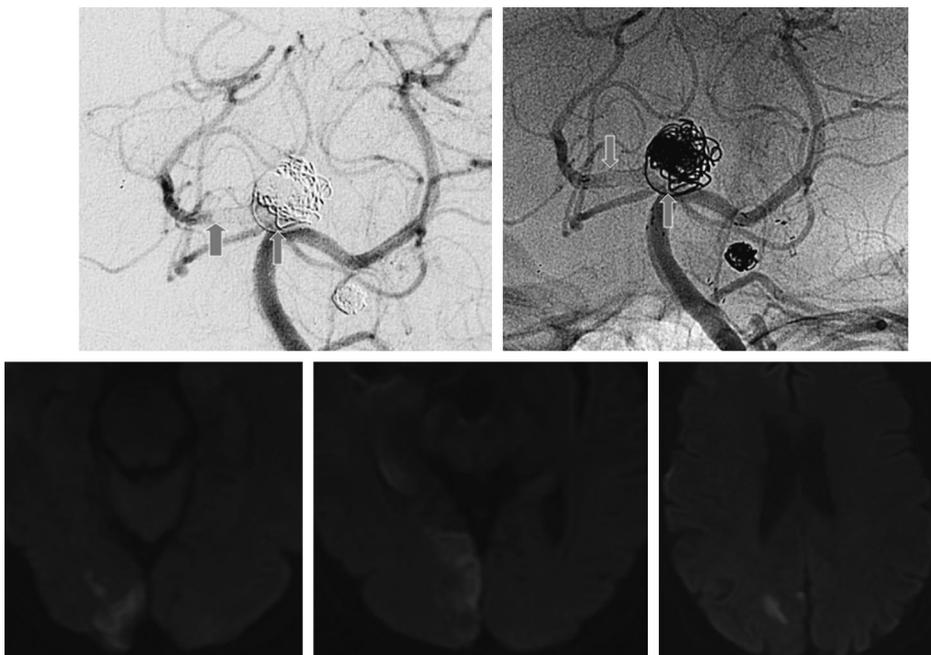
FIGURE 11.2. Delayed stent thrombosis 2 weeks after second stent deployment for "Y" configuration coiling of recurrent basilar tip aneurysm. The patient self-discontinued Plavix because of gum bleeding with tooth brushing. Diffusion-weighted magnetic resonance scanning shows an embolic infarction from a nearly complete PCA occlusion. *Arrows* delineate the thrombus margins.
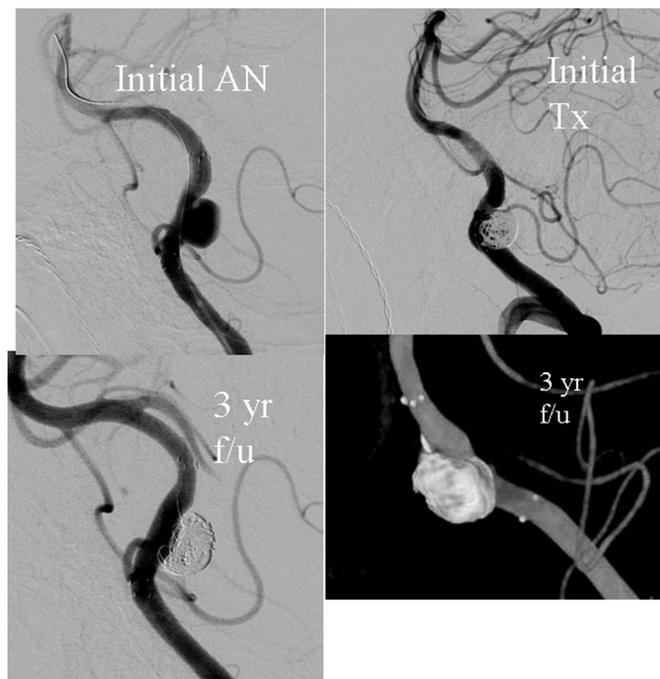
FIGURE 11.3. Stent coiling of fusiform vertebral posteroinferior cerebellar artery region aneurysm. Stable occlusion at delayed 3-year follow-up. AN, aneurysm; Tx, treatment; f/u, follow-up.

unknown. Deconstructive vascular procedures with or without bypass are often the only treatment option for these aneurysms. Therefore, in an attempt to preserve parent arteries, stent deployment with or without coil deposition may provide an attractive and effective alternative to previous surgical options in certain nonsaccular aneurysms; however, use in these situations is outside approved indications.

Endovascular stents required dual antiplatelet agents to prevent hyperacute, subacute, and delayed thrombosis. The typical medications used are aspirin and Plavix (clopidogrel) 3 to 5 days before deployment, 6 weeks of dual-therapy after the procedure, and aspirin for life. Special caution is recommended in patients with subarachnoid hemorrhage (SAH). Danger exists in the immediate procedure in the situations of vascular perforation or aneurysm rupture and in access site complications. Significant danger also exists for potential adjuvant surgical and invasive procedures, including but not limited to craniotomy, ventricular drain or shunt, lumbar puncture, central line placement, tracheostomy, feeding tube placement, and angioplasty for vasospasm.

To our knowledge, no randomized controlled trial has been performed to date in the United States to evaluate the efficacy and complication rates of the Neuroform stent. Multiple small single and combined institution self-adjudicated clinical series have been reported. In January 2004, the preliminary experience with the device in 19 patients at the

Barrow Neurological Institute was published.[9] Nineteen patients with 22 aneurysms were treated, 5 were treated after SAH. Difficulty in stent delivery was encountered in 7 (32%) of 22 patients, with 1 deployment failure. Two significant thromboembolic events occurred, one resulting in death. No delayed follow-up was reported.

In June 2004, The Thomas Jefferson Group published their series of 48 patients (16 SAH), in whom only 41 stents were successfully deployed.[1] They reported an 8.9% death rate, with 1 procedure-related death (2%). Seven percent of patients suffered thromboembolic events. This was a periprocedural evaluation only, with no delayed clinical or angiographic follow-up. They reported a 10.7% overall complication rate, with neurological complication accounting for 8.8% of this amount. The delivery device was rapidly changed by the company.

In June of 2005, the combined experience of the Barrow Neurological Institute and the Cleveland Clinic was reported.[7] Eighty-six stents were placed in 64 patients for broad aneurysm neck (n = 51 stents; average neck, 5.1 mm; aneurysm size, 8.2 mm), fusiform/dissecting morphology (n = 17), salvage/bailout for coils prolapsed into the parent vessel (n = 7), and giant aneurysm (n = 11). Sixteen patients (25%) were treated in the context of SAH (8 acute, 7 subacute, and 1 remote). Follow-up angiographic (n = 43) or magnetic resonance angiographic (n = 5) data (average follow-up, 4.6 mo; median, 4 mo; range, 1.5–13 mo) for 48 aneurysms (46 patients) after stent-coil embolization demonstrated progressive thrombosis in 25 patients (52%), recanalization in 11 patients (23%) (8 of whom were retreated; 16%), and no change in 12 patients (25%). Five patients were treated for dissecting aneurysms with stents alone. Follow-up angiography in this group demonstrated interval vascular remodeling with decreased aneurysm size in all patients. Delayed, severe, in-stent stenosis was observed in three patients, one of whom was symptomatic and eventually required angioplasty and bypass surgery.

The combined data from the Cleveland Clinic and the Barrow Neurological Institute has recently been updated (personal communication, D. Fiorella). Data rom the 3.5-year follow-up have been reviewed. A total of 284 patients with 302 aneurysms were treated during a 42-month period, with an average radiographic follow-up period of 12.9 months. Twenty-one of the patients were treated after acute SAH, and one-third of these had nonsaccular aneurysms. One hundred sixty-six patients with delayed angiographic follow-up were retrospectively reviewed. Eighty (48.2%) of 166 cases demonstrated progressive aneurysm thrombosis, 40 (24.1%) of 166 cases showed unchanged occlusion status, 46 (27.7%) of 166 cases exhibited recanalization, 25 (15.1%) of 166 cases required retreatment. Small aneurysms had a 9.3% recanalization rate, 3.1% were retreated. Most retreatments were in large or giant aneurysms.

Twenty-five patients (8%) suffered ischemic stroke (5.3% of these were significant, and two cases were delayed). Eight patients (2.8%) experienced neurovascular death, four patients in delayed fashion. Access site complications were observed in 2.1% of patients. In-stent stenosis was seen in 10 (5.6%) of 177 patients with radiographic follow-up (*Fig. 11.4*). Three of these were symptomatic (1.7%), two had strokes, one had transient ischemic attacks, and one had a treatment complication. Partial or complete resolution of in-stent stenosis was seen in five of six patients with additional radiographic imaging.

As with many novel endovascular devices, reports of unique and innovative technical applications appeared shortly after the release of the device. A "Y" configuration basilar to bilateral posterior cerebral artery (PCA) dual stent technique for the coil embolization of wide-necked basilar tip aneurysms was one of the first of these innovations.[22,31] This has also been performed in middle cerebral artery (MCA) aneurysms, the so-called "YMCA" technique.[26]

Balloon-remodeling catheters have been used inside deployed stents to define the lumen of the parent arteries within fusiform aneurysms.[10] Stents have been placed across the anterior communicating artery (ACOM) for wide-neck ACOM aneurysms and through the posterior communicating artery (PCOM) across the basilar apex for wide-necked basilar aneurysms, the so-called "Cross-over" technique.[2] Stent use as monotherapy for blister-like unclippable pseudoaneurysms, both as primary therapy and rescue therapy for aneurysm regrowth after previous clip ligation, has also been reported.[8] The so-called "waffle-cone" technique has been used by a few centers, placing the distal end of a stent directly into the apex of a termination aneurysm and coiling through the sidewall of the stent, such as the case treated by the authors in *Figure 11.5*.[14]

Many endovascular therapists prefer to stage the stent deployment and coil embolization with procedures separated by several weeks to allow for stent stability improvement, presumably by endothelial growth in the stented artery. Others "trap" the coil deployment catheter in the aneurysm before stent placement to avoid problems accessing the aneurysm through the stent. Neither of these techniques has been formally evaluated, and they are used simply as a matter of preference.

CEREBRAL ANEURYSM STENT: NON-FDA-APPROVED DEVICES

Outside the United States, and in clinical trials within the United States, other stents are available, some intended specifically for aneurysms and others for other body regions with different target pathologies. A closed-cell retrievable nitinol stent, the Leo stent, has been evaluated with small pilot studies.[15,24] Stents covered with various synthetic materials have been used as monotherapy for aneurysms such as giant MCA aneurysms.[23]

The Cordis Corporation has completed a study of the Enterprise self-expanding closed-cell design stent and is currently awaiting FDA approval. Preliminary experience with the device has been published, and this stent also has the
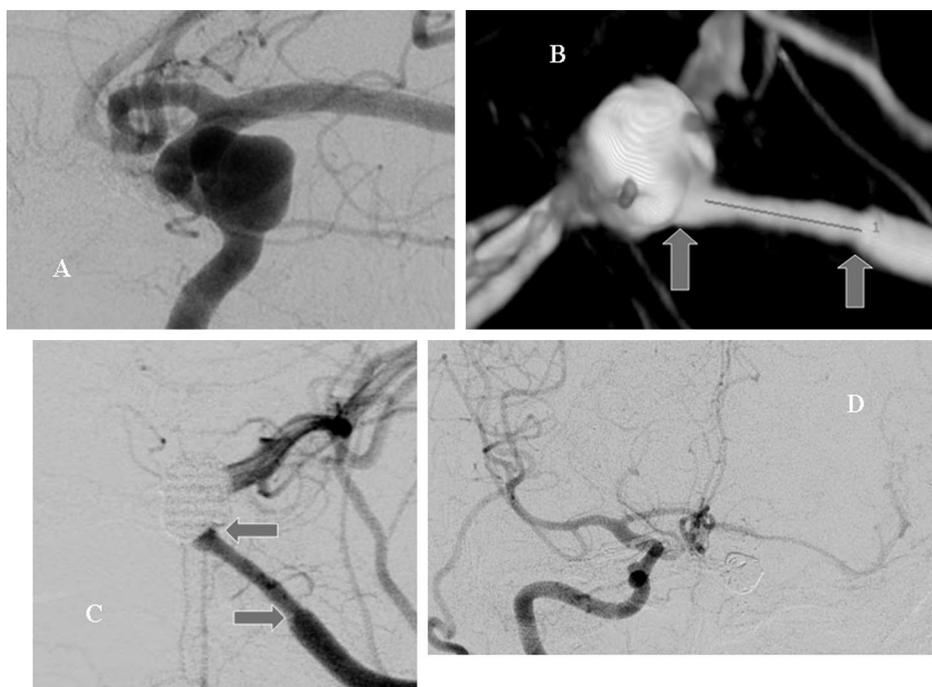
FIGURE 11.4. Delayed in-stent stenosis. *A*, original aneurysm with excellent caliber of ICA. *B*, angiographic follow-up showing significant in-stent stenosis with excellent occlusion of the aneurysm. *C*, three-dimensional angiographic reconstruction of stenosis. *D*, hemodynamic significance of stenosis with spontaneous ACOM cross-fill to the side of the stenosis. *Arrows* delineate the proximal extent of the ICA stenosis.

FIGURE 11.5. "Waffle-cone" technique. Giant basilar apex aneurysm recurrent after clip ligation treated with distal-end stent deployment near the apex of the aneurysm and coiling through the sidewall of the aneurysm. *Arrows* delineate stent margins.

improved feature that it can be recaptured after as much as 70% of the device has been deployed.[12]

ANEURYSM STENT CONCLUSIONS

The aneurysm stent definitely broadens the category of aneurysms that can now be treated endovascularly. Wide-necked aneurysms once not even considered for endovascular repair are now routinely treated with stent-assisted coiling. These devices also give an endoluminal option for patients with fusiform and blister-like aneurysms that previously had no true repair. Early data suggest that aneurysms treated with stents in addition to coils may have improved durability of repair. Flow models indicate multiple stents or different stent design may provide adequate flow diversion to protect aneurysms from rupture.[3,11,25] Significant evaluation will be necessary to validate this possibility.

Stent use is not without cost to the patient. Ischemic stroke rates seem to be in the 5 to 10% range, and delayed stenosis or thrombosis occurs in approximately 6% of patients. However, only approximately 2% of the stenosis patients are symptomatic, and the narrowing often resolves spontaneously. Stent use requires strong platelet inhibition and extreme caution is indicated in SAH patients. Compli-

ance with aspirin and Plavix treatment is extremely important and must be emphasized.

How can we reduce complication rates with the current technology? Device changes have already occurred with the presently available products, and new stents will soon be approved for use. Antiplatelet needs are being refined. Delivery and coiling techniques are constantly evolving and are shared by endovascular therapists.

Are stents the endovascular tool that will replace clip ligation? Should every coiled aneurysm also be stented? Should aneurysms be stented and not coiled? How will technological advancement change the safety and effectiveness if these devices? The answers to these questions are not currently available, but stents or a variation of this technology will likely permanently alter the future of cerebral aneurysm treatment. At this point in time, open surgery still plays a significant role in the treatment of all cerebral aneurysms, particularly those with wide-necked morphology.

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