

Endovascular Treatment of Aneurysmal Subarachnoid Hemorrhage

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KEYWORDS

- Aneurysm • Intracranial • Subarachnoid hemorrhage
- Endovascular treatment

Intracranial aneurysms are common entities whose natural history and definitive management remain controversial. Their prevalence varies according to study design but is estimated at approximately 2.3% in the general population.^{1,2} The most dreaded complication related to intracranial aneurysms is rupture leading to subarachnoid hemorrhage (SAH), a devastating condition still associated with a 30-day mortality rate of 30% to 40%,^{3–5} despite a consistent decline over the past 3 decades.^{6,7} The annual risk of rupture is 1.3%.⁸ Only one-third of patients surviving an aneurysmal SAH remain functionally independent.^{7,9} The primary goal in managing patients presenting with aneurysmal SAH is to prevent a new rupture of the aneurysm, which is associated with an even higher mortality rate. Surgical and endovascular methods are available to achieve this goal. This article reviews endovascular management of ruptured intracranial aneurysms.

Surgical clipping has been the gold standard of treatment for more than 70 years, since Walter Dandy first applied a silver clip to the neck of an unruptured internal carotid artery aneurysm at the The Johns Hopkins Hospital in 1937.¹⁰ The surgical approach to intracranial aneurysms was then refined by the adaptation of microsurgical techniques to the neurosurgical field by Yasargil.

The concept of endovascular treatment of intracranial aneurysms, drawing on work performed by Serbinenko¹¹ in the 1970s, was initially based on the use of balloons inflated within the aneurysmal cavity. In 1991, Guglielmi and coworkers published the first description of the endovascular application of detachable platinum coils (the Guglielmi Detachable Coil) to induce thrombosis and obliteration of intracranial aneurysms in humans. After Food and Drug Administration approval was granted in 1995,¹² the use of endovascular coiling has steadily increased and has been adopted as an alternative technique for the treatment of ruptured and unruptured intracranial aneurysms. Only two randomized, prospective studies comparing endovascular coiling and surgical clipping have been reported. The first one is a single-center study published in 1999, which found no significant difference in the obliteration rates at 12 months in 109 patients with SAH randomly assigned to surgical clipping or endovascular coiling.¹³ The second, the International Subarachnoid Aneurysm Trial (ISAT), compared clipping versus coiling in 2143 patients with ruptured intracranial aneurysms. Patients treated endovascularly were at a lower risk of death or dependence at 1 year compared with the surgical group, with an absolute risk reduction of 7.4%, which was maintained for up to 7 years.¹⁴ The

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risk of rehemorrhage was low but more common after coiling than clipping. The neurosurgical community found these results controversial, pointing to possible selection biases detrimental to the surgical group and to the level of expertise of the neurosurgeons performing the surgical treatments (general vs vascular neurosurgeons). Questions concerning the durability and long-term efficacy of coil embolization and protection against rerupture were also raised. Despite these drawbacks, the ISAT did support the notion that endovascular therapy is a valid alternative to surgical clipping.

ENDOVASCULAR TECHNIQUES

Endovascular techniques for the treatment of intracranial aneurysms with conservation of the parent artery, also known as constructive therapies, include standard coil embolization, coil embolization with balloon remodeling or stent assistance, and balloon-assisted liquid polymer embolization (Fig. 1A, B, and C). The use of covered stents (or stent grafts) has been proposed as an option for large, fusiform, or wide-necked aneurysms, primarily located in the carotid and vertebral arteries, where the risk of occluding functionally important side branches is relatively low (see Fig. 1D). The long-term patency of stent grafts placed in relatively small vessels, such as the internal carotid artery, is another potential drawback of this approach and remains currently unknown.¹⁵ Stents with a tight mesh or stents covered with semipermeable membranes (collectively known as flow diverters) may represent an improvement over conventional stent grafts in terms of parent artery and side branches patency. These stents may expand the indications of stent grafting to intracranial lesions, although their use in ruptured aneurysms needs to be carefully evaluated. Parent artery occlusion, also referred to as deconstructive therapy, remains a valid alternative option for nonsurgical candidates whose aneurysms are not amenable to constructive treatment methods.

The clinical condition of patients, the aneurysm location and morphology (in particular the diameter of the neck and its relation to the parent artery), and the presence of branches arising from the sac or the neck are important considerations when choosing the most appropriate treatment plan. The aneurysm neck, in particular its size and relation to the parent artery and potential side branches, is the key feature in determining if coil embolization is an appropriate treatment option. Standard coil embolization is considered feasible for aneurysms with a small neck (<4 mm), a dome-to-neck ratio

equal or greater than two, and in the absence of important branches arising from the sac or the neck.¹⁶ Coil embolization is achieved primarily with platinum coils. Although a careful analysis of the aneurysm morphology is essential to planning efficient therapy, aneurysms with a seemingly unfavorable configuration can occasionally respond well to simple coiling (Fig. 2). Advances made in platinum coil technology have tried to address incomplete aneurysm occlusion, which increases the risk of coil compaction and aneurysm recanalization. Reported rates of recanalization are approximately 21% to 28.6% but can be as high as 60% for giant aneurysms.^{17–19} Recently developed hybrid, or biologically active, coils are chemically pretreated to enhance their thrombogenicity²⁰ in an effort to try decreasing the recanalization rate.²¹ Currently available modified coils include polyglycolic acid/lactide copolymer-coated coils (Matrix, Boston Scientific, Natick, MA, USA; Cerecyte, Micrus, Sunnyvale, CA, USA; and Nexus, Micro Therapeutics, Irvine, CA, USA) and hydrogel-coated coils (HydroCoil, MicroVention, Aliso Viejo, CA, USA).²² Other types of coated or active devices, such as coils with radioactive components or coils coated with biologic material, such as collagen or cells, are in experimental phases. Matrix coils comprise an inner core of platinum covered with a biodegradable polymer (polyglycolide/polylactide) designed to accelerate aneurysm fibrosis, neointima formation, and inflammation.²¹ The safety of these coils for aneurysm treatment is similar to that of bare platinum coils.^{23,24} Higher rates of recanalization (32%, from 26.1% for small aneurysms with small necks to 75% for large aneurysms)^{21,25} and thromboembolic events (up to 20% vs 2.5%–11%),^{26,27} however, are reported with Matrix coils versus bare platinum coils. Progressive resorption of the polymer coat leading to loss of volume and instability is a possible explanation for the high recurrence rates associated with these coils.²⁸ A recently published study of 152 patients with ruptured and unruptured aneurysms treated exclusively with Matrix coils showed similar results with no better recanalization rates than those previously reported for bare platinum coils (recanalization rates: 31.1% for aneurysms <10 mm and 56% for aneurysms >10 mm, with more frequent recanalization in ruptured aneurysms).²⁹ HydroCoils are standard platinum coils coated with an expandable hydrogel material that results in delayed progressive coil expansion on contact with blood.³⁰ These coils are supposed to provide superior aneurysm volume filling to bare platinum coils³¹ and to promote healing and endothelialization at the aneurysm neck.^{31,32} Despite these features,

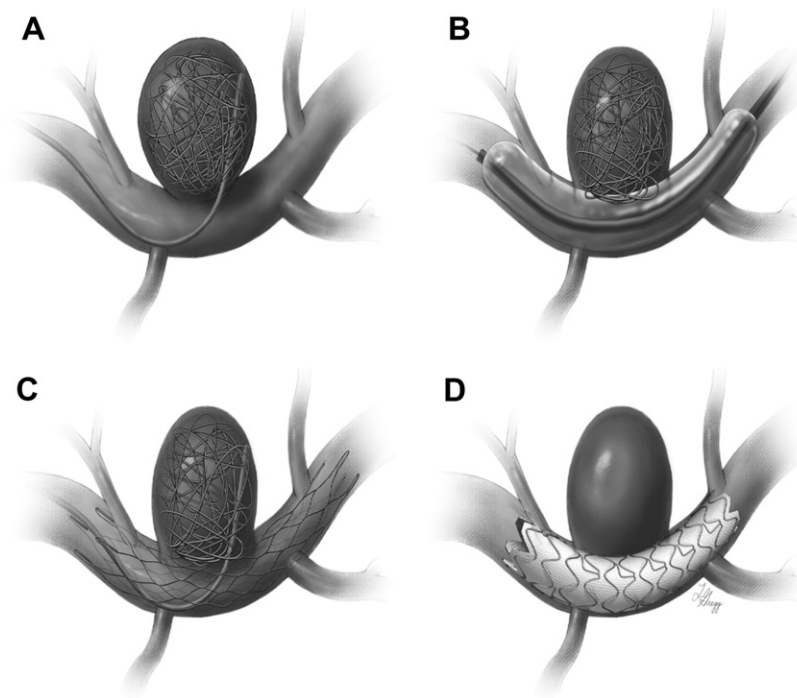


Fig. 1. Endovascular treatment of intracranial aneurysms: constructive techniques. (A) Coil embolization: the microcatheter was placed within the aneurysmal cavity, which was progressively filled (packed) with detachable microcoils of various diameters, length, and geometric configurations (helical, 2-D, 3-D, etc). Dense packing resulting in exclusion of the aneurysm from the circulation was obtained with a volume of coil material not exceeding 40% of the total aneurysm volume, the residual space being filled with thrombus. Standard coil embolization requires a favorable aneurysm geometry, particularly in regard to the sac-to-neck ratio. A low ratio (ie, a wide neck aneurysm) does not hold the coils within the aneurysmal cavity, jeopardizing the patency of the parent artery. (B) Balloon remodeling: inflation of a compliant microballoon across the aneurysm neck concomitantly to coil deployment allows treating lesions with unfavorable sac-to-neck ratio. The balloon was sequentially inflated and deflated in order to assist the placement of each coil. (C) Stent-assisted coiling: the deployment of a stent prior to aneurysm catheterization and coiling offers assistance for wide neck aneurysms without the need for iterative parent artery obliteration but leaves a permanent intravascular device that requires antiplatelet therapy and carries a still uncharacterized risk of delayed flow impairment (acute or subacute in-stent thrombosis, chronic in-stent stenosis from endothelial hyperplasia). Stent and balloon remodeling assistance can be combined for the treatment of dysplastic or fusiform aneurysms. (D) Stent graft/flow diverters: stent grafts can potentially interrupt the flow within the aneurysmal cavity without placement of intra-aneurysmal material. Such an approach is rapid (low radiation exposure) and solves the mass effect issues sometimes associated with dense packing of aneurysms located in the immediate vicinity of fragile structures, such as the optic nerve. Drawbacks of currently available stent grafts include poor trackability, unknown long-term patency of the parent artery, and, more importantly for neurovascular applications, the risk of side branches occlusion. Some of these issues may be addressed by the new generations of devices (flow diverters) with a semipermeable architecture currently under development or in early clinical evaluation. (Fig. 1A data from Piotin M, Mandai S, Murphy KJ, et al. Dense packing of cerebral aneurysms: an in vitro study with detachable platinum coils. *AJNR Am J Neuroradiol* 2000;21(4):757-60.)

recanalization rates remain high, up to 27% for large aneurysms.³³ More concerning, however, are reported cases of aseptic meningitis and delayed hydrocephalus,^{22,33,34} which seem specific to the HydroCoil as no cases have so far been described with polyglycolic acid/lactide copolymer-coated coils alone,²³ although some have occurred when Matrix coils were used in

combination with HydroCoils.³⁵ Delayed perianeurysmal inflammation with dramatic neurologic dysfunction (bilateral visual loss) has been reported after embolization with HydroCoils.³⁶ Perianeurysmal inflammation leading to visual loss has also been described in cases of paraclinoid aneurysms treated with standard platinum or coated coils.³⁷ The factors leading to these various coil-related

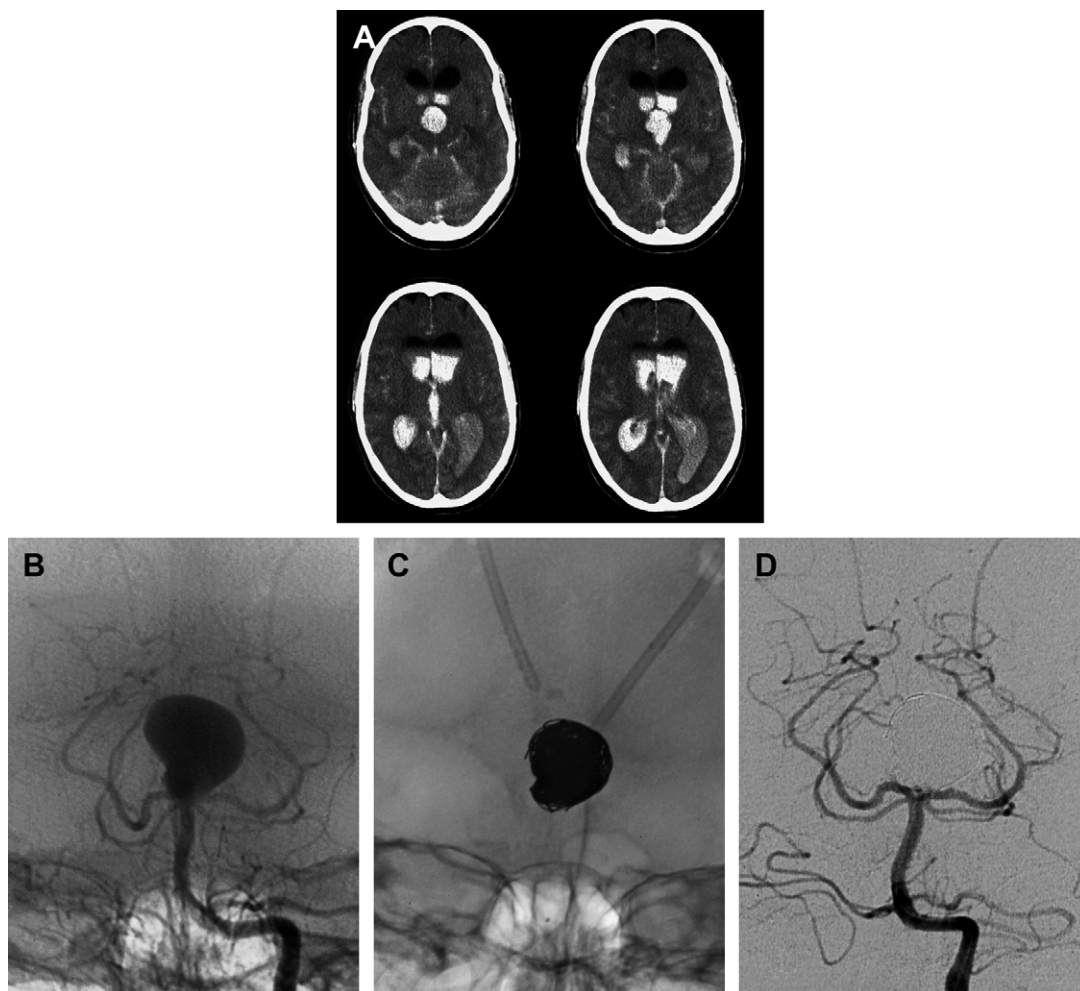


Fig. 2. A 45-year-old comatose patient with SAH and IVH. (A) Head CT documenting diffuse SAH and IVH. The patient was transferred to the authors' institution for further management. (B) DSA, transfacial view, showing a large basilar tip aneurysm. (C) Nonsubtracted image of the pack of microcoils (bare platinum coils). (D) DSA, transfacial view after treatment. Mild irregularity is observed at the neck, but there is no residual opacification of the aneurysmal cavity. At the 2-year follow-up visit, her neurologic examination was notable only for memory and cognitive changes.

events have not yet been elucidated, and more information is needed regarding the role of coils, clot burden, aneurysm size, and inflammatory mediators in the development of these complications.

Recent advances in stent technology have led to the development of flexible self-expanding nitinol stents (or reconstruction devices) (Neuroform, Boston Scientific Neurovascular, Natick, MA, USA; Enterprise, Cordis Neurovascular, Miami Lakes, FL, USA; and LEO, Balt, Montmorency, France) dedicated to intracranial aneurysm therapy, specifically for the treatment of complex and wide-necked aneurysms. Advantages of these self-expanding intracranial stents over the balloon expandable stents previously used for

assisted coiling include improved trackability, which helps navigate tortuous intracranial vasculature (although this is true only for the latest generation of self-expanding stents); improved deliverability; and decreased vessel injury during deployment.³⁸ Variations in stent design include open-cell (Neuroform)³⁹ versus closed-cell design (Enterprise and LEO),^{40,41} low radial force (Neuroform)³⁹ versus high radial force (LEO)⁴⁰ versus low radial force/high compression resistance (Enterprise), and stent recoverability after partial deployment (a characteristic inherent to the closed-cell design, with up to 70% of stent length for the Enterprise³⁸ and up to 90% of the stent length for the LEO).⁴⁰ Despite several technical differences in stent design, these devices have been

safe and effective in assisting the treatment of cerebral aneurysms.^{40–42} The major argument against the use of these devices for the management of patients with aneurysmal SAH is linked to the need for concurrent antiplatelet therapy. A recent series of patients treated with stent-assisted coiling had a higher rate of hemorrhagic complications in the group presenting with SAH: two patients had a fatal outcome believed related to antiplatelet therapy, one from a massive intraventricular hemorrhage (IVH) secondary to an external ventricular drain change, the other from a parenchymal hemorrhage of unknown origin. The risk of parenchymal hemorrhage in patients taking antiplatelet therapy, however, may be independent of their having suffered a SAH. In the authors' experience, one patient with a nonruptured clinoid segment aneurysm was successfully treated with stent-assisted coiling, having suffered a nonfatal contralateral occipital lobe hemorrhage 2 days after the procedure. The goal of antiplatelet therapy is to reduce the risk of thromboembolic complications related to the stent placement itself and to the subsequent presence of an intraluminal foreign body, at least until the stent structure is covered by a layer of endothelial cells. Although protocols may slightly vary according to institutional and operator preferences, patients scheduled for elective therapy are typically placed under a combination of oral antiplatelet agents

several days prior to the procedure. In the authors' practice, patients are asked to take clopidogrel (75 mg) and aspirin (325 mg) daily starting 5 days before stent placement. Patients already taking these medications for other purposes are given an additional loading dose of clopidogrel (300 mg) the day preceding treatment. Such a drug regimen is not possible in patients presenting with aneurysmal SAH. There is no clear consensus about antiplatelet therapy in patients with SAH. As an example, the approach adopted at the authors' institution for ruptured wide-necked aneurysms that benefit from stent-assisted coiling is described. These aneurysms are divided into lesions that likely can be secured initially with partial coiling only but require a follow-up procedure for complete treatment and lesions unlikely to be secured with coiling only. This evaluation is based on the morphology of the aneurysm as depicted with 3-D digital subtraction angiography (DSA). In aneurysms that can be secured initially with partial coiling, the immediate goal is to ensure that the risk of re-rupture is eliminated (ie, that no residual flow is left within the aneurysmal cavity, in particular at its dome). This initial treatment may be helped by the use of the balloon remodeling technique and may even achieve definitive therapy (**Fig. 3**). The residual component, if any, is then addressed at a later date with the assistance of a stent, using

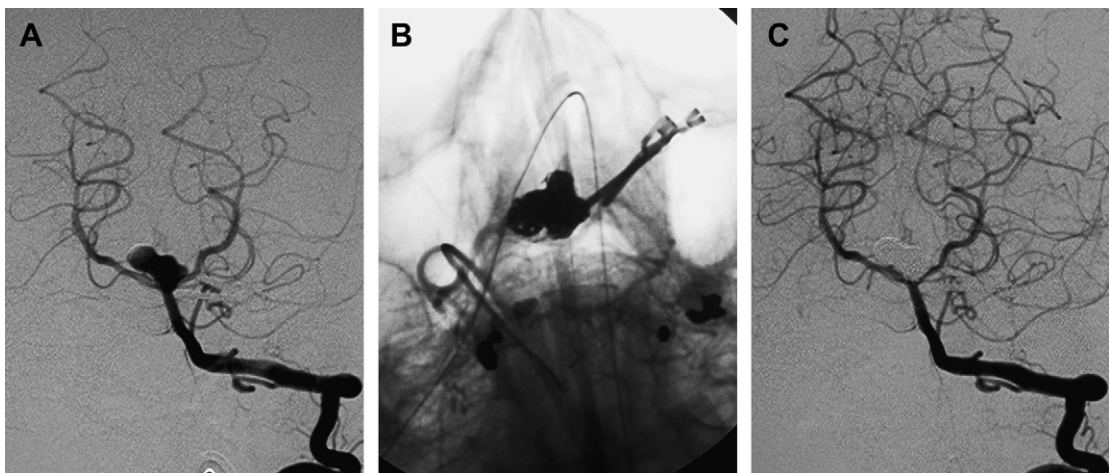


Fig. 3. A 49-year-old woman with a history of ruptured, surgically treated posterior communicating aneurysm, presenting with a new aneurysmal SAH. (A) DSA, left vertebral injection, anteroposterior view, showing an irregular, wide-necked aneurysm of the basilar tip. Coiling alone was attempted first. After successful deployment of several coils, coils loops starts protruding into the basilar artery and right P12 segment. A microballoon (Hyper-Form [4 mm × 7 mm], ev3 [ev3 Neurovascular, Irvine, CA, USA]) was advanced into the distal basilar artery, and the coiling was completed (using a remodeling technique described by Moret and colleagues⁴³). (B) Nonsubtracted image of the pack of microcoils (bare platinum coils). (C) DSA, left vertebral injection, anteroposterior view, confirming the absence of residual flow within the aneurysm. Follow-up angiography at 8 months was unchanged, and the patient was neurologically intact.

standard antiplatelet preparation. Even when this first approach has been elected, a stent may be deployed if it becomes obvious that adequate treatment will not be achieved with coiling alone (**Fig. 4**). In situations where it seems likely that adequate treatment will not be achieved by coiling alone, a stent may be used as first intention

therapy. In such instances, a microcatheter is placed within the aneurysmal cavity first, in order to secure access for subsequent coiling (jailing technique). The use of the jailing technique in this instance principally prevents the unlikely but potentially catastrophic situation in which a stent is deployed but the aneurysm cannot be

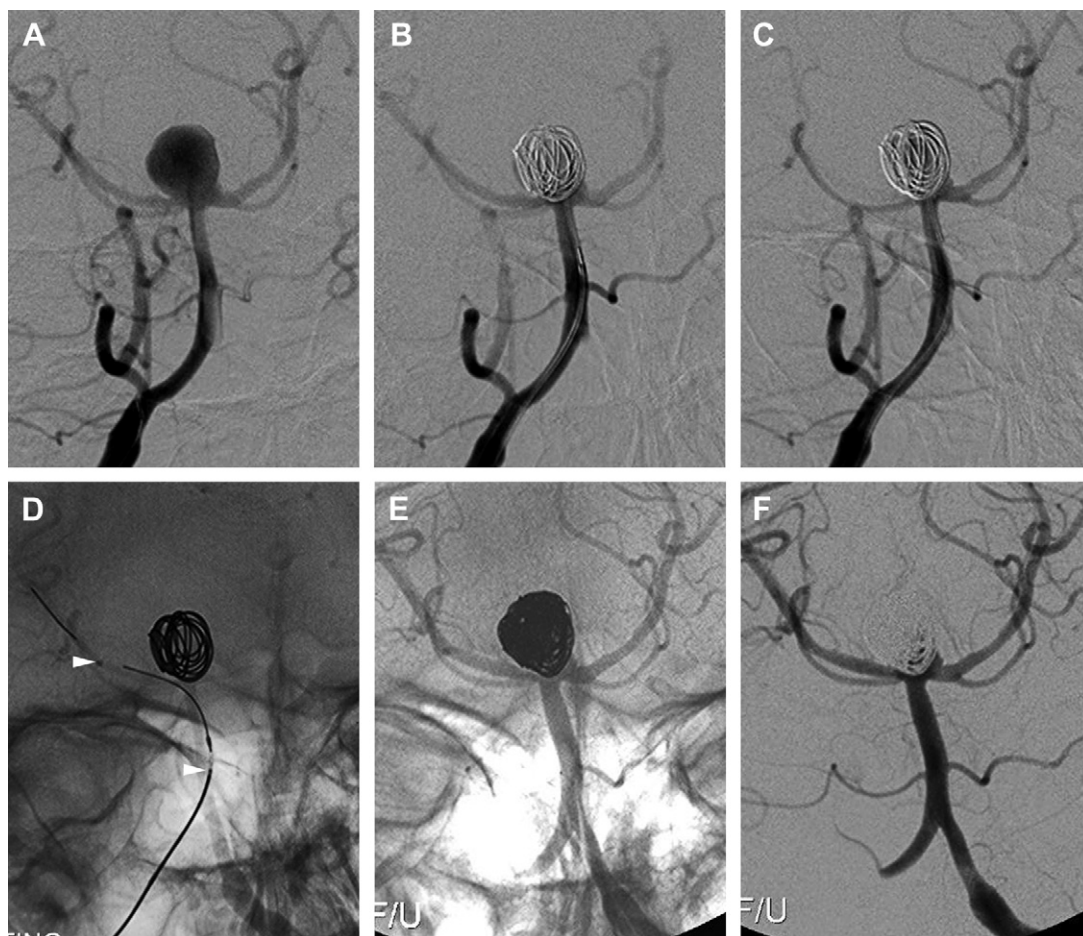


Fig. 4. A 54-year-old lethargic patient with diffuse SAH and IVH. After transfer to the authors' institution, a ventricular shunt was placed and angiography obtained. (A) DSA, right vertebral injection, transfacial view, documenting a basilar tip aneurysm. The angiographic projections and the 3-D reconstructions showed that the left posterior cerebral artery (PCA) was arising from the base of the aneurysm itself, with no detectable posterior communicating artery on that side. (B) DSA, right vertebral injection, transfacial view, after placement but before detachment of the first microcoil (Guglielmi Detachable Coil 18, Boston Scientific, Natick, Massachusetts). Both PCAs are patent. (C) DSA, right vertebral injection, transfacial view. After detachment of the first coil, the configuration of the coil pack was slightly different and the right PCA no longer patent. The decision was made to deploy a stent across the neck of the aneurysm into the right PCA. (D) DSA, left vertebral injection, transfacial view. A second microcatheter has been advanced into the right PCA. The proximal and distal markers of the stent (Enterprise, Cordis Neurovascular, Miami Lakes, FL, USA) are visible on this nonsubtracted image (white arrowheads). (E) DSA, left vertebral injection, nonsubtracted transfacial view, showing the pack of coils at the end of the procedure. The left aspect of the aneurysm base was not packed in order to preserve the patency of the left PCA. (F) DSA, left vertebral injection, transfacial view. This final angiographic control confirms the patency of both PCAs. It also shows residual aneurysmal neck, from which the left PCA takes origin. It was believed that the aneurysm was at this point secured and, further, would be performed at a later date, if needed, possibly with the assistance of a second stent. The patient was discharged home on day 16 neurologically intact.

subsequently catheterized. The stent is then advanced and deployed using a standard technique (Fig. 5). In the authors' practice, antiplatelet therapy is administered only when the stent has been successfully deployed. In the absence of injectable aspirin (eg, as in the United States), the authors' regimen consists aspirin (600 mg) administered rectally and clopidogrel (450 mg)

delivered via a nasogastric tube. Intravenous heparin (initial dose 5000 IU intravenous bolus, monitored and adjusted using activated clotting time) is added after detachment of the first micro-coil within the aneurysmal cavity. A concern with this approach lies in the potential need for subsequent placement of a ventricular shunt under antiplatelet therapy. In order to avoid, as much as

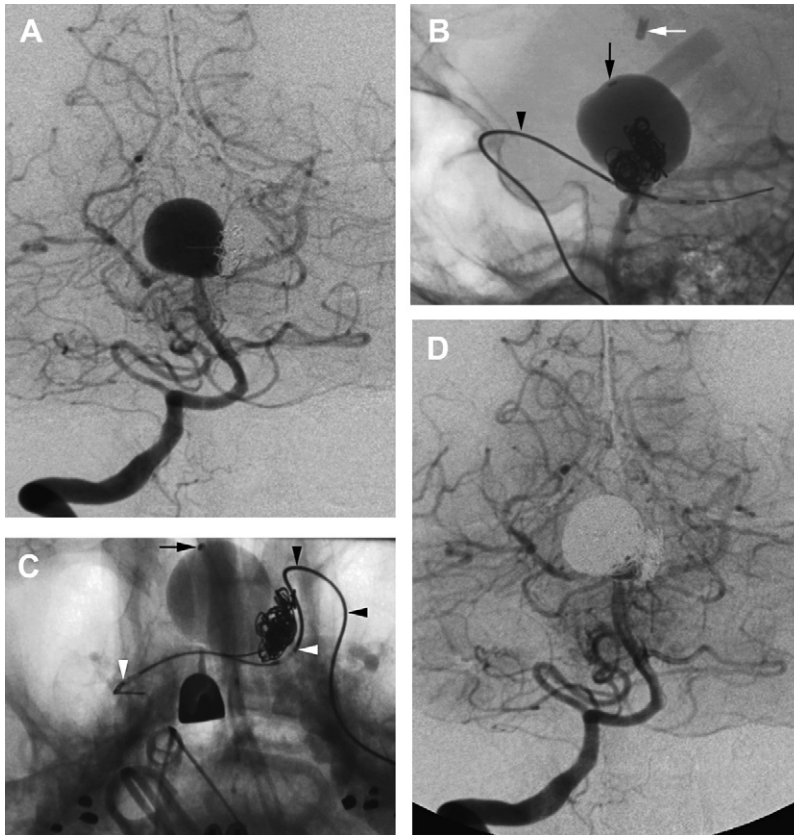


Fig. 5. A 58-year-old man with a history of ruptured basilar tip aneurysm treated 16 years earlier by endovascular coiling. The patient was transferred to the authors' institution for management of a new SAH. At admission, he was in acute respiratory failure and cardiac distress (ejection fraction of 15%). He underwent angiography once his vital functions were believed stable enough for transport. (A) DSA, right vertebral injection, transfacial view, documenting a basilar tip aneurysm. The 3-D reconstructions showed that both PCAs were originating from the base of the aneurysm. The compacted coil pack from the initial treatment can be seen along the left lateral aspect of the aneurysmal sac. The decision was made to proceed with stent-assisted coiling as first intention therapy. (B) DSA, right vertebral injection, lateral view. A microcatheter has first been placed within the aneurysmal cavity (black arrow). A second microcatheter has then been advanced across the neck of the aneurysm into the right PCA via the left internal carotid and posterior communicating arteries (black arrowhead). Note presence of a ventricular shunt (white arrow). (C) DSA, right vertebral injection, transfacial view, showing the microcatheter within the aneurysm cavity (black arrow), the second microcatheter through the left posterior communicating artery (black arrowheads), passing across the neck of the aneurysm. The proximal and distal markers of the stent (Enterprise, Cordis Neurovascular, Miami Lakes, FL, USA) are visible on this nonsubtracted view. Note also the compacted coil pack from the initial treatment performed 14 years before. (D) DSA, right vertebral injection, transfacial view, final angiographic control showing some residual neck at the base of the aneurysm, from which the left PCA takes origin. Both PCAs are patent. It was believed that the aneurysm was secured at this point and that the residual base could be addressed, if needed, at a later date. Unfortunately, the patient subsequently developed severe hemodynamic instability and metabolic imbalance with diffuse bilateral cerebral edema resistant to medical management, including barbiturate coma. He died 3 days after treatment from a cardiac arrest.

possible, such a situation, a CT scan is obtained immediately prior to the procedure and a shunt placed if ventricular enlargement is observed.

Several flow-diverting devices are in development or in early clinical evaluation phases. These new devices clearly carry promises for the endovascular management of intracranial aneurysms. It is, however, too early to define with certainty their exact role, in particular in regard to the treatment of aneurysmal SAH. As discussed previously, the use of antiplatelet therapy in the setting of SAH remains controversial, an issue possibly more significant for flow diverters, which might carry higher thromboembolic risks due to their intrinsic physical characteristics. Among the potential drawbacks or still unresolved features of these new devices in the setting of SAH are the delay between device deployment and aneurysm obliteration/thrombosis, the absence of structural elements reinforcing the aneurysm wall (no coils), the potential difficulty of subsequent access when primary occlusion fails, the preserved patency of important surrounding small arteries, and the durability of the achieved therapy. These points are illustrated in two recent publications concerning one of these emerging flow-diverting devices (Pipeline, Chestnut Medical Technologies, Menlo Park, CA, USA), a device made of a braided mesh cylinder composed of platinum and cobalt chromium microfilaments offering, after deployment, an approximately 30% to 35% surface coverage. This coverage is supposed to create significant flow disruption while remaining porous enough to maintain patency of the parent artery and adjacent branch vessels covered by the stent. One of these publications describes passage of contrast into the cavity of a midbasilar artery aneurysm that can still be observed by angiography 48 hours after the placement of seven more partially overlapping devices.⁴⁴ In the other publication, two patients with fusiform aneurysms were each treated with three devices, resulting in aneurysm obliteration in one case and in flow reduction in the other, for which treatment was completed by adjunct coiling.⁴⁵ Although encouraging, these results raise questions about the preserved patency of perforating branches when several devices have to be used in a concentric manner and the risk of rebleeding during the latency period between deployment and actual aneurysm thrombosis, if the devices were used for the treatment of aneurysmal SAH.

SUMMARY

Endovascular therapy is now a well-accepted alternative to surgical clipping for ruptured and nonruptured intracranial aneurysms. The current

state-of-the-art endovascular techniques for the treatment of aneurysmal SAH include coiling alone and coiling assisted by the balloon remodeling technique. The use of newly developed self-expandable stents seems tempting, as their safety and efficacy have been demonstrated for the treatment of nonruptured aneurysms. The important role played by antiplatelet therapy, prior and after stent deployment, however, renders their use for the treatment of ruptured aneurysms controversial. Although a recent publication warns about this specific application as carrying a higher risk of hemorrhagic complication, the size of the reported series does not allow drawing significant conclusions at this time.

New flow-diverting devices currently in development or early clinical evaluation carry great promise for the treatment of nonruptured aneurysms. As is the case with stent-assisted coiling, the role that these new devices will play in the management of aneurysmal SAH remains unclear at this time.

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