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Endovascular Treatment of Intracranial Aneurysms and Vasospasm After Aneurysmal Subarachnoid Hemorrhage

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Over the past decade, dramatic advances have occurred in endovascular technology and techniques for the treatment of intracranial aneurysms. The introduction of the Guglielmi detachable coil (GDC; Boston Scientific Target, Fremont, California) in 1991 for endosaccular aneurysm occlusion [1] has revolutionized the field. Subsequent development of soft and three-dimensional (3D) coil technology has expanded the application of the basic coil occlusion technique. Although endosaccular coiling seems to work best for small to medium-sized aneurysms with narrow necks, successful endovascular treatment of aneurysms with wide necks is now possible because of the addition of balloons and stents to the endovascular armamentarium. In this article, we review the evidence to support endovascular approaches for the treatment of intracranial aneurysms, basic treatment techniques, and complication avoidance and management from the perspective of surgeons who use endovascular and surgical approaches. The importance of adequate management of vasospasm in the overall outcome of patients with ruptured cerebral aneurysms and aneurysmal subarachnoid hemorrhage (SAH) is discussed.

Patient selection for endovascular treatment of intracranial aneurysms

Proper selection of patients for endovascular treatment of intracranial aneurysms requires a careful assessment of the factors influencing the risks of the various therapeutic options. The assessment of risks and benefits ultimately affects the decision whether to proceed with endovascular embolization, craniotomy, and arterial reconstruction by direct clipping, proximal artery occlusion, or a conservative management approach. Until recently, endovascular coil embolization was reserved for patients with SAH who were in poor condition and those for whom craniotomy with aneurysm clipping was considered to present a high risk. With the continuing evolution of technology and techniques, the safety and efficacy of endovascular treatment have improved to the extent that coil embolization has been projected to surpass craniotomy and clipping for aneurysms in terms of the number of aneurysms treated per year in the United States for the year 2004 (Boston Scientific Target, unpublished data, 2004). The operator should be mindful of existing therapeutic options to determine which provides the greatest benefit for the individual patient. Not infrequently, we encounter a case in which a given aneurysm cannot be safely secured by one therapeutic modality and where it is wiser to abort the

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procedure and entertain other treatment options rather than to assume the risk of a potentially devastating complication.

A description of the clinical and anatomic considerations guiding the authors' decision-making process in the treatment of cerebral aneurysms follows.

Clinical considerations

One of the most evident advantages of endovascular approaches to cerebral aneurysm treatment is the lower cardiovascular stress (ie, shorter procedure, less tissue manipulation) placed on the patient and the possible avoidance of general anesthesia altogether in patients who are poor surgical candidates. In addition, endovascular approaches may be preferable for the subset of patients who are high-risk candidates for craniotomy because of their age [2] and medical comorbidities. By eliminating the necessity for brain tissue manipulation, especially in a brain that is swollen as the result of SAH, endovascular embolization can result in improved short-term functional outcomes when compared with craniotomy [3].

Conversely, surgical clipping is the mainstay for other patient subgroups. For example, patients with large intraparenchymal hemorrhages in addition to SAH are typically better treated by craniotomy, during which the mass effect of the lesion can be addressed while the aneurysm is being secured.

Anatomic considerations

Each aneurysm responds uniquely to embolic devices, but there are common anatomic characteristics that can help in the selection of the optimal therapeutic modality. Knowledge of the anatomic features of the aneurysm can guide the selection of devices and the subsequent embolization techniques that can yield the optimal result.

A comprehensive four-vessel diagnostic cerebral angiogram should be performed with careful attention paid to access routes to the aneurysm (access anatomy) as well as to the definition of the aneurysm neck from the aneurysm dome and parent vessel. Clear resolution of the neck, dome, and parent vessel of some aneurysm locations and configurations is not possible with conventional digital subtraction angiography. In such cases, the acquisition of a 3D rotational angiogram or a 3D CT angiogram can be extremely helpful in therapeutic planning. Measurement of the aneurysm dimensions and neck size in multiple projections allows selection of the appropriate types and sizes of coils and adjunctive devices (eg, stents, balloons). The dome-to-neck ratio (aspect ratio [ie, the maximum dimension of the aneurysm dome/the width of the aneurysm neck]) and neck size are parameters that can significantly affect the treatment approach decision and, in the case of an endovascular approach, aid in the selection of types and sizes of coils and adjunctive devices that may be necessary. Calcification of the neck region is another angiographic feature that should be evaluated, because this can indicate problems for aneurysm clipping. In such cases, we favor endovascular approaches over microsurgical approaches. In addition, the presence of intraaneurysmal thrombus should be noted, because this can result in a delay in coil settling and an increase in the chance of aneurysm recanalization.

Aneurysm location

The location of an aneurysm may favor endovascular embolization or surgical clipping. The degree of difficulty encountered with microsurgical and endovascular approaches is altered by variations in individual anatomy. Consideration of exactly which features or characteristics should guide treatment approach decisions has sparked ongoing debate between cerebrovascular neurosurgeons and neuroendovascular surgeons.

The following summary is derived from the authors' experience with surgical and endovascular methods for the treatment of various types of intracranial aneurysms plus the interpretation of available evidence to support such decisions. The decision to treat each lesion should be individualized for each patient according to the configuration of the aneurysm, comorbidities of the patient, and experience of the operator. Ultimately, the operator should assist the patient to make an informed decision regarding the best treatment modality for his or her condition.

Many basilar apex aneurysms have ideal configurations for endovascular placement of coils and adjunctive devices. In such cases, the parent artery points directly into the aneurysm. Such a configuration facilitates access with the microcatheter and increases the likelihood of the coil mass remaining stable within the aneurysm. Although adjunctive devices may be required to obtain a successful result, endovascular treatment of these aneurysms presents less morbidity and mortality [4–8] and is less invasive than craniotomy [9–11]. Some basilar apex aneurysms have

favorable anatomy for clipping (anteriorly pointing, located above the posterior clinoid process), but even in carefully selected surgical series, the risks of morbidity and mortality are higher with craniotomy [4–13].

Aneurysms of the superior cerebellar artery are more straightforward to treat surgically than are basilar apex aneurysms. Endovascular treatment of these lesions often requires stent or balloon assistance to obtain ideal occlusion of the aneurysm with preservation of the parent vessel [14].

Proximal posterior inferior cerebellar artery (PICA) aneurysms are often easily accessible by endovascular means but generally require a far lateral craniotomy approach for clipping. Endovascular treatment in this setting represents a less invasive solution to these aneurysms [15], but the choice in this case is more dependent on the configuration of the particular aneurysm and the comfort level of the surgeon with the skull base approach.

Although distal PICA aneurysms are readily accessible to surgical treatment with minimal brain retraction via a suboccipital approach, the endovascular approach is also an option [16]. Even though these lesions are difficult to treat with endovascular embolization without sacrificing the parent vessel, PICA occlusion distal to the tonsillomedullary segment of the PICA is often well tolerated by patients [17].

Treatment of cavernous aneurysms of the internal carotid artery (ICA) should be limited to symptomatic lesions or those at risk for rupture (eg, lesions with carotid-cavernous fistula, thromboembolism, mass effect, subarachnoid extension beyond the dural ring) [2]. Treatment of such lesions depends on whether the artery can be reconstructed or would require sacrifice after successful balloon test occlusion (BTO). The treatment of these aneurysms is almost exclusively endovascular because of the morbidity associated with surgical approaches to the cavernous ICA region.

Treatment of paraclinoid aneurysms of the ICA varies, depending on the symptomatology and configuration of the aneurysm as well as on the access anatomy. For patients presenting with progressive visual loss caused by mass effect, surgical aneurysm clipping with decompression or parent vessel occlusion results in an increased likelihood of improved visual function when compared with coil embolization [18]. For patients presenting with a progressive increase in aneurysm size or SAH and for some asymptomatic patients, treatment patterns are trending toward endovascular coiling because of the less invasive nature of that approach compared with craniotomy [19]. Paraclinoid aneurysms may require stent or balloon assistance for coil embolization, and this is a common site for use of these devices. Craniotomy can involve drilling of the clinoid process and surgical exposure of the cervical ICA.

Aneurysms located on the posterior communicating artery are lesions for which surgical and endovascular treatment approaches are considered to have clinical equipoise. Features like a fetal configuration of the posterior cerebral artery or complex access anatomy tend to favor surgical exploration in these cases. From an endovascular perspective, these are often straightforward aneurysms to treat if the configuration of the carotid siphon is amenable to catheterization [20].

The configuration of an ICA bifurcation aneurysm is similar to that of a basilar apex aneurysm with respect to the orientation of the artery and the aneurysm, but surgical approaches are safer in this region than in the basilar apex region. The decision between coiling and clipping is often based on operator experience, aneurysm anatomy, and patient comorbidities.

Aneurysms of the anterior communicating artery territory can be difficult lesions to treat by surgical or endovascular approaches because of the complexity of the regional anatomy. More than 50% of the aneurysms in patients enrolled in the International Subarachnoid Aneurysm Trial (ISAT) were located in the anterior communicating artery territory, and patients in the endovascular arm had better short-term outcomes than those in the surgical arm [3]. These results may have been a result of the degree of brain retraction or resection that is necessary for an operative approach. For those anterior communicating artery aneurysms in which the neck is undefined and stent-assisted coiling might be appropriate, surgical clipping may be preferable, however, because the A1 segment is usually too small to allow for the intravascular placement of a stent [21].

Pericallosal artery aneurysms and other aneurysms located on distal segments of the anterior cerebral artery are less technically complex to treat surgically than are aneurysms in the territory of the anterior communicating artery. The ability to perform endovascular coil embolization of these aneurysms is heavily influenced by intracranial vessel tortuosity and the aneurysm configuration and cause (traumatic versus infectious) [22].

Aneurysms of the middle cerebral artery (MCA) tend to possess a complex anatomy at the neck region, with the aneurysm typically occurring at a bifurcation or trifurcation of the M1 segment. The aneurysm neck often involves the origin of one or more vessels, making the treatment of such lesions challenging for endovascular approaches. In most cases, the neck anatomy precludes complete coil embolization of the inflow zone, which may lead to aneurysm regrowth [23,24]. Because of the proximity of the artery to the cortical surface, these aneurysms are often best treated with craniotomy and clipping. Some patients with more proximal M1 segment aneurysms may benefit from endovascular embolization.

Dome-to-neck ratio

The anatomy of aneurysms with an aspect ratio of greater than 2 is favorable for conventional endovascular coiling; moreover, such aneurysms seem to present a greater risk for rupture [25]. For aneurysms with an aspect ratio of less than 2 or with a neck size greater than 4 mm, primary coiling may result in herniation of coils into the parent artery or inability to pack the neck region tightly [4,26,27]. This leads to a higher incidence of partially treated aneurysms and a higher risk for recanalization or growth of the aneurysm. For aneurysms with unfavorable aspect ratios or neck size, adjunctive balloon or stent assistance may be necessary. Preprocedural management with antiplatelet medication is necessary if stent- or balloon-assisted coiling is planned. This is not ideal for nonsecured ruptured aneurysms, given the potential risk of rebleeding when administrating such agents.

Fusiform aneurysms

A comprehensive description of the selection of appropriate therapy for fusiform aneurysms is beyond the scope of this article. In general, these lesions have a poor natural history, and the treatment is high risk. Patients with fusiform aneurysms can manifest with a variety of symptoms as the result of SAH, aneurysmal growth with direct compression of neural structures, distal embolization of intraluminal thrombus, or progressive occlusion of the ostia of small perforating arteries along the length of the aneurysm.

Therapy must address the symptomatology, because the risk of treating these aneurysms can approach or exceed the natural history of the disease. As opposed to saccular aneurysms, in which the goal is to exclude the aneurysm from the circulation, complete exclusion is often not possible with fusiform aneurysms, despite adequate collateralization, because of the presence of vital perforating end arteries. For patients presenting with thromboembolic events, anticoagulation can be considered, but this therapy must be weighed against the likelihood of fatal SAH in the event of aneurysm rupture. Compression-related symptoms can be treated by occlusion of one or more feeding arteries, which may lead to hemodynamic changes within the aneurysm and may result in the alleviation of symptoms caused by mass effect and, in some cases, complete aneurysm thrombosis. Surgical bypass procedures may or may not be necessary in these cases. If permanent vessel occlusion is required, it is performed only after BTO. An appealing option for the treatment of such lesions is the placement of intravascular stents (one or more) to reconstruct the parent vessel. The use of stents in this situation can change the hemodynamic environment within the aneurysm, potentially leading to thrombosis. The deployment of two or more stents in the same location can provide a lower porosity mesh, favoring the flow changes within the lesion.

Covered and partially covered stents should soon be available and surely have a place in the treatment of fusiform aneurysms. The issue of perforators and branch patency remains to be studied and defined.

Summary

Although attempts at treatment of most aneurysms by endovascular methods may be possible, a wise practitioner recognizes the limitations that apply in each particular case. As with any specialty, sound judgment is as important as operative skills to avoid procedural complications and provide good patient care. All practitioners, whether cerebrovascular neurosurgeons or neurointerventionists, need to possess an understanding of the available treatment options for their patients. The continued evolution of endovascular technology and techniques will undoubtedly expand the application of this approach to a broader patient population.

Devices and agents for endovascular treatment of aneurysms

Detachable balloons and alternatives to permanent vessel occlusion

Permanent vessel occlusion may be a viable endovascular therapeutic option for patients

tolerating BTO in whom treatment of the aneurysm with preservation of the parent vessel cannot be safely achieved. The goals of endovascular treatment by parent artery occlusion are to induce intra-aneurysmal thrombosis through alterations in the local hemodynamics and subsequent shrinkage of the aneurysm and to maintain collateral blood flow. Clot organization and fibrosis as well as elimination of hemodynamic factors responsible for aneurysm growth can lead to a reduction in the size of the aneurysm, thereby relieving the symptoms caused by neural compression. Aneurysm involution can take a long time, especially if the walls are thick and calcified [28]. Pressure-related signs and symptoms usually improve soon after parent artery occlusion or flow reversal within the parent artery, because the pulsation of the sac is diminished and small reductions in aneurysm size occur. Transient swelling can occur acutely after thrombosis of the aneurysm, however, and can exacerbate symptoms like cranial nerve palsies [29] or hydrocephalus.

The traditional endovascular approach to parent vessel sacrifice involves the use of detachable silicone balloons. In this technique, the balloon is prepared and advanced through a guide catheter to the appropriate location. Balloon placement for permanent occlusion is dependent on aneurysm location and test occlusion findings relative to the presence or absence of aneurysm reperfusion from collateral flow. Ideally, the aneurysm should be excluded from the circulation, with a first balloon being placed distal to the aneurysm neck and a second balloon placed proximal to it. This approach can be used in the treatment of cavernous carotid aneurysms.

For the more common anatomic configuration in which the perforating arteries originate distal to the aneurysm, two balloons are placed in a tandem fashion proximal to the aneurysm to occlude the parent vessel. The second balloon is added to prevent migration of the first balloon. Both detachable balloons are delivered through a single guide catheter. After the more distal of the two balloons has been positioned and inflated, the other balloon is partially inflated to arrest the flow in the proximal portion of the vessel. Before detachment of the balloons, additional angiograms should be obtained and may indicate the risk of aneurysm reperfusion via collaterals. In the event of massive aneurysm reperfusion, balloon repositioning or reassessment of the effectiveness of this treatment may be necessary. If the position of the balloons is judged to be optimal, the distal balloon is detached; the proximal balloon is then fully inflated and detached as well. Changes in hemodynamics within the aneurysm induce thrombosis of the sac.

In cases of carotid ophthalmic aneurysms, the balloons can be positioned (1) over the aneurysm neck, between the aneurysm and the ophthalmic artery, if there is more than a 5-mm segment in which to deposit the balloon; (2) in front of the orifice of the ophthalmic artery if there is a functional anastomosis with the external carotid artery; or (3) below the ophthalmic artery if there is no reperfusion of the aneurysm by collateral circulation [7]. The recent withdrawal of the only US Food and Drug Administration (FDA)–approved detachable silicone balloon from the United States market has led to the development of other strategies for permanent parent vessel occlusion. One such strategy involves the combination of temporary proximal flow arrest with a nondetachable balloon with permanent parent vessel occlusion with coils [30].

In cases of vertebrobasilar system aneurysms, striving to attain the dual goals of inducing thrombosis of the aneurysm lumen and maintaining collateral blood presents somewhat of a dilemma. Although thrombosis is best achieved by placing the occluding balloon as close as possible to the aneurysm, the presence of vital perforators just proximal to the aneurysm precludes the placement of the balloon in this position. Placement of the balloon in a more proximal position leads to preservation of adequate collateral flow through or past the aneurysm orifice. In most cases, unilateral occlusion of the dominant vertebral artery is sufficient to induce thrombosis within the aneurysm. Otherwise, occlusion of the contralateral vertebral artery can be performed 3 or 4 weeks later, after repeat test occlusion of this artery to verify adequate retrograde flow from the posterior communicating artery [7]. When bilateral vertebral artery occlusion is indicated for the treatment of a basilar aneurysm, the authors perform occlusion distal to the origin of the PICA on one side and proximal to the PICA origin contralaterally.

The indications for endovascular permanent vessel occlusion are becoming rarer with the advent of newer techniques, such as stent-assisted coiling, and the development of new technology, such as specifically designed devices for the intracranial circulation.

Results of permanent vessel occlusion

The likelihood of aneurysm thrombosis after proximal endovascular parent artery occlusion is

related to the magnitude of persistent flow from collaterals [29]. Higashida et al [31] reported stable complete thrombosis in 68 (100%) cavernous aneurysms in their series after endovascular parent artery sacrifice. Symptoms of local compression caused by giant aneurysms improved, despite the lack of evidence of a reduction in aneurysm size on follow-up CT scans. The effectiveness of this procedure decreases in the anterior circulation when it is performed for aneurysms distal to the ophthalmic artery. Fox et al [29] reported that although all cavernous-carotid aneurysms in their series were completely thrombosed after proximal parent vessel occlusion, only 10 (48%) of 21 aneurysms located above the ophthalmic artery origin became thrombosed without an additional aneurysm trapping procedure. Similarly, vertebral artery occlusion for proximal aneurysms, such as those arising from the intracranial vertebral artery, is quite effective, with results being progressively less successful for aneurysms of the vertebrobasilar junction, basilar artery, superior cerebellar artery, and basilar bifurcation [32].

Despite a negative preoperative test occlusion, neurologic deficits can occur after parent artery sacrifice. The rate of permanent postprocedural neurologic deficits in patients with a negative BTO after endovascular sacrifice of the ICA varies from 0% to 10% [29,31,32]. When the neurologic deterioration is related to hemodynamic factors, the collateral flow can be augmented with aggressive hyperdynamic therapy, which may lead to reversal of the deficit. An emergency arterial bypass procedure might also be considered in this setting.

The long-term changes in intracranial circulation hemodynamics occurring after elective parent artery sacrifice are not completely understood. The major concern is that by increasing blood flow in collateral vessels, parent artery sacrifice may lead to the formation of de novo aneurysms [33]. In a review of the literature, Dyste and Beck [34] reported the presence of symptomatic aneurysm formation or enlargement after carotid occlusion in 4% to 10% of cases after therapeutic carotid occlusion. In their series, Timperman et al [35] found de novo aneurysms in 2 (3%) of 58 cases of therapeutic carotid occlusion. Both patients in these cases presented with ruptured anterior communicating artery aneurysms. Whether these de novo aneurysms are related to the same pathologic process that caused the original aneurysm or result from increased blood flow in the intact carotid artery remains to be proved.

Era of aneurysm coiling

The major paradigm shift in intracranial aneurysm treatment was initiated by the introduction of electrolytically detachable coils by Guido Guglielmi. The persistence and creativity of this Italian neurosurgeon led to the major advancement represented by the invention of the GDC system, thus beginning a new era in the endovascular treatment of aneurysms. In the early 1980s, while applying current to a stainless steel electrode introduced into an experimental aneurysm to promote electrothrombosis, Guglielmi observed accidental electrolytic detachment of the electrode tip. Several years later, Guglielmi and engineer Ivan Sepetka worked to combine the processes of endovascular electrolysis and electrothrombosis, an undertaking that eventually led to the development of the GDC system [1,36]. Theoretically, with the GDC system, an aneurysm could be excluded from the intracranial circulation while the patency of the parent vessel was preserved. Different types of coils have been used successfully for endovascular occlusion of intracranial aneurysms. At present, FDA-approved coils are available from the following six device manufacturing companies: Boston Scientific Target, Micrus, Cordis (Miami Lakes, Florida), MicroVention (Aliso Viejo, California), MicroTherapeutics (Irvine, California), and Cook (Bloomington, Indiana). Undeniably, the evolution of detachable coil technology has revolutionized the overall approach to the management of intracranial aneurysms. The recent development of bioactive coils has strengthened the role of coils even more in the treatment of intracranial aneurysms.

Aneurysm coiling technology: basic treatment concepts

The concept of aneurysm coiling is based on the ability to fill the sac with a soft compliant platinum agent that can be retrieved in the event of an improper fit. Controlled delivery is the primary advantage of the detachable systems, with the coil being detached only when the correct position is documented by angiography. A further advantage is the flexibility and softness of the coils, which varies from one system to another; this enables filling of the aneurysm sac and minimizes the risk of rupture during deployment.

Most coil systems consist of a thin, spiral-woven, platinum wire formed in the shape of a helix and soldered to a stainless steel delivery wire. When positioned within a microcatheter, the coil assumes a straight shape and can easily be

advanced into the aneurysm. The coils have a circular memory that is expressed when the coil is pushed out of the microcatheter and deployed within the aneurysm. Coil softness refers to the ease with which a coil can compress and expand and is influenced primarily by the diameter of the platinum wire. Soft coils are made of a thinner platinum wire than are standard ones. Soft and standard coils are available in a range of sizes and lengths so that aneurysms can be packed piecemeal with appropriately sized coils. Changes in coil design have made the coils resistant to stretching. More elaborate designs have become available, including two-diameter coils in which the helix of the initial coil segment defines a smaller diameter than the remaining helices. With two-diameter coils, the leading coil loop tends to remain inside the aneurysm sac while avoiding contact between the advancing coil tip and the aneurysm wall because of the smaller loop diameter. This design also reduces the predisposition of the first coil to herniate from the aneurysm during deployment. In an attempt to decrease the incidence and degree of coil compaction [37], 3D coils were developed. These coils spontaneously form a complex 3D configuration during delivery and have been used successfully to occlude aneurysms with an unfavorable geometry for conventional coil embolization. In fibered coils, the thrombogenicity of the platinum coil is enhanced by the attachment of Dacron fibers.

The GDC detachment system is described here because it was the first aneurysm coiling system developed and served as the basis for the development of other coil systems. The stainless steel delivery wire is insulated, except for the most distal part, the detachment zone. A radiopaque marker is incorporated in the delivery wire 3 cm proximal to the detachment zone. During detachment, this marker aligns with the proximal marker on the microcatheter (the microcatheter contains two markers; the distal one goes inside the aneurysm and the proximal one gives the operator the ability to check the advancement and alignment of the coil before detachment). By checking the position of the proximal markers on the delivery wire and microcatheter, the operator can ensure that the coil has advanced outside the microcatheter tip (even though the distal marker on the catheter tip may be obscured by overlying previously placed coils) and avoid advancing the stiff delivery wire into aneurysm sac. When the coil has been placed in a satisfactory position, a positive, low-voltage, direct current is applied to the delivery wire. The current induces electrolysis at the solder junction between the coil and delivery wire, and the coil is gradually detached. This technique allows delivery of the coil without displacement from its location. Ideally, the aneurysm is progressively filled with coils until angiographic obliteration of the sac and preservation of the parent artery are achieved.

The coil systems have general characteristics in common but vary in their size, shape, and detachment system. Methods of detachment currently available include electricity-based (Boston Scientific Target, Micrus, MicroTherapeutics) and hydraulic (Cordis, MicroVention, Cook) approaches. Nuances for each system exist, but the details are not within the scope of this article.

The most recent innovation in the coil systems is the addition of bioactive agents to the classic platinum coil. The theoretic advantage is to promote the organization of thrombus within the aneurysm and thus to reduce the incidence of aneurysm recanalization. The Matrix coil (Boston Scientific Target) was the first bioactive coil introduced in the United States. These coils are made of platinum covered with a bioabsorbable polymeric material (polyglycolic acid [PGA]/lactide) [38]. The advantage of the Matrix system over conventional platinum coil systems has been shown in animal studies [38,39], but its effectiveness in preventing aneurysm recanalization in human beings remains to be seen. The Cerecyte coil (Micrus) is another example of a PGA-modified platinum coil.

Another bioactive coil, the Hydrogel coil (MicroVention), uses a different concept. Rather than facilitating thrombus organization, this device has been designed to improve filling within the aneurysm sac, with complete or near-complete exclusion of thrombus. The device consists of a carrier platinum coil coupled to an expandable hydrogel material, which undergoes a three- to nine-fold increase in volume when placed in a physiologic environment (acid pH–induced swelling occurs within 20 minutes). The presence of the hydrogel within the coil mass leads to a greater filling of the aneurysm sac, potentially serving as a base for a more elaborate healing response. Unlike thrombus, the hydrogel material is stable and unaffected by natural thrombolytic processes and thus may diminish observed rates of aneurysm recanalization [40]. This benefit has been shown in animals [40]; again, the long-term benefits and limitations of clinical application remain to be seen.

Basic technique of coil embolization

The basic technique described here assumes that intensive medical decision making has been performed with consideration of the indications for the procedure, individual characteristics of the patient and his or her aneurysm, and goals for the coiling procedure (complete occlusion whenever safe and feasible or partial coiling when protecting the dome of a ruptured aneurysm unsuitable for primary coiling or clipping).

Anesthesia

At most centers, aneurysm coil embolization is performed with the patient in a state of general anesthesia. This approach does not allow direct intraprocedural assessment of the patient's neurologic status. Although some advocate that intraprocedural monitoring can be performed using motor or somatosensory evoked potentials and electroencephalography, the risks associated with general anesthesia and mechanical ventilation would still be present. As reported by Henkes et al [41] in cases performed under general anesthesia, most ischemic complications cause symptoms immediately after the procedure. At the authors' institutions, GDC embolization of intracranial aneurysms is performed in awake patients after the administration of sedative and analgesic agents (midazolam, fentanyl, morphine, or hydromorphone) [42]. The potential advantages of this approach, including decreased cardiopulmonary morbidity rates, a shorter hospital stay, and lower hospital costs, still require confirmation by a direct comparison with other anesthetic procedures [42]. Qureshi et al [42] pointed out that thromboembolic complications can be promptly recognized and treated in awake patients.

Preprocedural medications

For patients with unruptured and nonacutely ruptured aneurysms scheduled for primary coiling, we routinely administer aspirin (81–325 mg daily) for at least 4 days before the procedure. If balloon- or stent-assisted coiling is anticipated, clopidogrel (75 mg daily for 4 days before the procedure or a loading dose of 450 mg 4 hours before the procedure) is added to the regimen. Intravenous heparin (50–70 U/kg) is given just after placement of the introducer sheath, with the aim of obtaining an activated coagulation time in the range of 250 to 300 seconds. For patients with ruptured aneurysms, we routinely proceed without administering heparin and antiplatelet agents. If balloon or stent assistance is necessary, we may opt for partially coiling the aneurysm, completing the treatment during the same admission but after the acute phase of rupture has passed (ie, when the patient has recovered neurologically).

Procedure

After a femoral sheath has been placed (6 or 7 French) in the right groin, a diagnostic angiogram is obtained. Appreciation of the aneurysm neck and its relation to adjacent perforating and major arteries is a prerequisite to the embolization procedure. It is particularly important to isolate the aneurysm neck from the parent vessel angiographically so that any coil prolapse into the parent vessel can easily be detected. This often requires the acquisition of multiple oblique views. Once a "working projection" is identified, it is recorded for use during the embolization procedure. In some cases, the complex 3D geometry of the aneurysm and surrounding vessels or the overlapping of different structures prevents the acquisition of an adequate view for safe embolization of the aneurysm.

Once the diagnostic angiogram has been obtained, a guide catheter is placed in the target vessel as distal as is safely possible. Such positioning of the guide catheter provides a stable platform to carry out the steps of the coiling procedure.

A coaxial system consisting of a microcatheter and microwire is used to catheterize the aneurysm. The coaxial system and guide catheter are flushed continuously with a solution of saline and heparin (1000 IU of heparin per 1000 mL of saline) to prevent thrombus formation between the two catheters or while the coils are being advanced through the microcatheter.

Access to the aneurysm is obtained via the micro-guide wire, followed by microcatheter placement. Road mapping is helpful during this part of the procedure. Care is taken to avoid touching the aneurysm wall with the tip of the wire or microcatheter. An appropriately sized coil is chosen by matching the helix radius of the coil to the estimated diameter of the aneurysm. The best choice for the first coil is one that bridges the aneurysm neck and allows dense homogeneous packing of the aneurysm. In principle, the longest coil available to fill as much of the aneurysm sac as possible should be used. The first and second coils are critical for achieving complete occlusion. The first coil should be placed in a basket-like configuration within the aneurysm. The placement of a second basket coil within the first may provide

a more stable configuration for the deposition of subsequent coils.

After placement and before detachment of each coil, a control angiogram is obtained with injection of contrast material through the guide catheter to confirm proper placement of the coil as well as to demonstrate patency of the adjacent arteries. After placement of the initial basket coil or coils, the remaining cavity is filled with smaller diameter coils, which are placed within the loops of the basket to prevent bulging into the parent artery. Coils are deposited until dense packing is achieved or when the aneurysm accepts no more coils (resistance is encountered with risk of herniation into the parent vessel). Although some authors suggest packing the aneurysm as much as possible and stopping the procedure only when the last coil cannot be introduced inside the sac (thus, the last coil is always wasted), we prefer to individualize the degree of packing to the aneurysm morphology and the procedural goals.

Balloon remodeling technique

The balloon remodeling technique was the initial alternative to surmount the problem presented by coil embolization of wide-necked aneurysms [43]. In this technique, a soft semicompliant or conformable balloon is positioned across the neck of an aneurysm and inflated during coiling. The balloon works as a mechanical barrier that allows tighter packing of the aneurysm while preventing coil herniation into the parent artery during coil delivery. Also, the balloon stabilizes the microcatheter during coil delivery and forces the coils to conform to the 3D shape of the aneurysm. This technique is most suitable and less technically challenging for proximal aneurysms of the ICA or the vertebrobasilar system. To avoid undesired movements of the microcatheter within the aneurysm when the remodeling technique is used, the balloon must be placed first in the parent vessel in front of the aneurysm neck. Selective microcatheterization of the aneurysm is then performed. Inflation of the balloon in front of the aneurysm neck temporarily occludes the neck and the parent vessel. Under balloon protection, coils are then deposited into the aneurysm. After placement of each coil into the aneurysm but before detachment, the balloon is deflated to test the stability of the coil. If no displacement of the coil is observed, the coil is detached. If movement is detected after balloon deflation, the coil is considered unstable and repositioned or removed.

In experienced hands, application of the remodeling technique has been associated with complete angiographic occlusion in 77% to 83% of aneurysms immediately after treatment [43,44]. The technique has several drawbacks, however. The procedure is technically demanding, and the operator is required to use two microcatheters simultaneously. The dangers of local thrombus formation and distal embolization are increased by temporary interruption of blood flow in the parent vessel, and thromboembolic complications have been observed in 5% to 8% of patients treated [43,44]. The need to inflate and deflate the balloon repeatedly risks intimal damage. There is also concern that an increase in intra-aneurysmal pressure during balloon inflation across the aneurysm neck [45], coupled with forceful placement of coils in a closed space [44], may increase the risk of bleeding, especially during treatment of acutely ruptured aneurysms. The incidence of intraprocedural rupture with the remodeling technique can be as high as 5%, which is a rate twice that encountered with conventional coil embolization [44]. In the event of rupture, however, the balloon can be inflated immediately to stop the hemorrhage and allow placement of additional coils to occlude the aneurysm. In this way, bleeding is rapidly managed, and clinical consequences can be minimized. Despite these limitations, this technique is a valid part of the armamentarium of endovascular surgeons and has been used by experienced teams to treat between 1.4% and 20% of the aneurysms embolized at their centers [41,43,44]. Although the long-term effectiveness of this technique in promoting stable occlusion of wide-necked aneurysms is unknown, short-term outcomes are promising. In their series of 56 patients, Moret et al [43] reported that 20 of 21 completely occluded aneurysms remained completely occluded at follow-up angiography 3 to 6 months later.

Stent-assisted coiling technique

Although the balloon remodeling technique constitutes an important method for the endovascular treatment of intracranial aneurysms, the adjunctive use of stents seems to offer an appealing alternative. Incentive for the use of a stent in conjunction with coils includes the potential for a lower risk of dissection or vessel rupture [41]. In the authors' experience, the implantation of a stent across the neck area serves as a buttress to the coil mass and contributes to changing the

hemodynamic parameters locally by redirecting the flow and providing a substrate for endothelialization in that area [46,47].

Several concerns have been raised about the safety of stents in the treatment of intracranial aneurysms [48]; however, preliminary clinical experience suggests that some of these concerns are unjustified. For example, stents are known to induce intimal hyperplasia, and it has been argued that excessive neointimal proliferation after stent placement can result in hemodynamically significant stenosis, especially of the smaller intracranial branches. The occurrence of neointimal hyperplasia is usually evident in the first few months after treatment as a consequence of the vessel reacting to the presence of a foreign body. In the authors' series of stent-assisted coiling (with coronary stents) for the treatment of 12 ophthalmic segment aneurysms in 11 patients, no case of in-stent stenosis was found over the course of angiographic follow-up (mean of 26.5 months; range: 5–55 months) [49].

Concerns also exist that occlusion of the ostia of small side branches and perforating arteries by stent placement may result in ischemia or infarction in the territory of these vessels. The authors' experience with stenting in the basilar artery in a canine model did not reveal any effect of the stents struts on the perforators, however [50]. These experimental results were mirrored by our clinical observations. Lopes et al [51] examined the postprocedural cerebral angiograms of 10 patients (7 had aneurysms and 3 had intracranial stenosis) in which the stent was placed across a normal major branch artery. Over the course of a mean follow-up interval of 10 months, all major branches remained patent, no infarctions were associated with the territory of the major branch arteries crossed by the stents, and no patient experienced a related episode of clinical ischemia. It is also possible that in patients with fusiform aneurysms of the basilar trunk and other critical segments, the involved perforating vessels have become "nonfunctional," thus explaining the absence of permanent neurologic sequelae after stent placement with or without secondary coil placement. Because of the high porosity of the stents used, lateral branches, such as the ophthalmic artery and the anterior inferior cerebellar artery, remain patent after a stent is placed across their origins.

Self-expandable intracranial stents

Some potential pitfalls associated with the use of balloon-mounted stents in the intracranial circulation have prevented widespread application of stent implantation. Intended for use in the coronary circulation, balloon-mounted stents lack the suppleness necessary to navigate the tortuousities inherent to the intracranial circulation to reach lesions beyond the carotid siphon. They are ideal for side wall aneurysms on straight vessels, but because most intracranial aneurysms arise at branch points, the efficacy of coronary stents in the treatment of these lesions is greatly reduced. Also, the balloon inflation needed to deploy the stent can be associated with a small risk of vessel dissection or rupture [52,53] and theoretically could lead to delayed stenosis [54,55]. In an attempt to minimize these risks, a push was made to develop a self-expanding stent pliable enough to navigate the turns of intracranial vessels and effectively span the neck of a branch point aneurysm yet with enough radial force to contain an intra-aneurysmal coil mass. The first available such stent was the Neuroform stent (Boston Scientific Target).

The Neuroform stent is constructed of nitinol (a nickel-titanium alloy), which possesses a high degree of elasticity and deformability. This self-expanding stent has an ultrathin open-cell mesh design and exerts a lower amount of radial force than stents used in the treatment of atherosclerotic disease. Instead of being mounted on a balloon, the stent comes preloaded in a coaxial, over-the-wire, 3-French microcatheter delivery system. The delivery catheter has a braided shaft with a hydrophilic coating to facilitate vascular access. Because the stent is fully enclosed within the microcatheter, it can be passed through vessels without abrading the vessel wall. The ultrathin property of the stent struts makes the stent essentially radiolucent, and this feature is offset by four radiopaque platinum marker bands at each end. The entire system consists of the 3-French micro-delivery catheter with the stent preloaded and a second 2-French stabilizer catheter. Usually, the delivery system for the stent is advanced over the exchange wire to the point that it spans the neck of the aneurysm. At this point, the stent is deployed by holding the stabilizer in position and pulling back the delivery catheter.

Use of the Neuroform stent was associated with the pitfalls common to a first-generation device. Howington et al [56] described difficulties with navigation and delivery of this stent in tortuous vessels and thromboembolic complications, especially in acutely ruptured aneurysms. As is the case with any stent implantation,

patients receiving this self-expanding stent require dual antiplatelet therapy (aspirin plus clopidogrel or ticlopidine). Unfortunately, the aspirin-clopidogrel regimen is contraindicated in patients with an acutely ruptured aneurysm who might benefit from stent-assisted coiling. Although it is possible to administer the loading dose of clopidogrel in these patients and then deploy the stent, such an approach could be complicated by recurrent hemorrhage. Moreover, if thrombus forms during the procedure, the use of intra-arterial thrombolysis would increase the risk of repeat hemorrhage significantly. Howington et al [56] suggested that the ideal aneurysm for the Neuroform stent is one that has not ruptured and is treated in an elective fashion after appropriate antiplatelet therapy has been initiated.

Reports of the experience with the first-generation Neuroform stent at two centers are available. Fiorella et al [20] reported the results obtained with attempted implantation of this device in 19 patients with 22 aneurysms during a 5-month period. A total of 25 stents were deployed, with 5 patients having multiple stents placed. Fourteen patients had unruptured aneurysms at the time of treatment. The indications for use of the device in their series were broad-necked aneurysms in 13 patients, fusiform or dissecting aneurysms in 3, salvage or bailout in 1, and giant aneurysms in 2. Technical problems included difficulty in deploying the stent in six cases; stent displacement in two cases; and inability to deploy the stent, inadvertent stent deployment, and coil stretching, respectively, in one case each. Twenty-one of the 22 aneurysms were treated with the Neuroform stent: 4 with the stent alone and 17 with stent-assisted coiling. Among the coiled aneurysms, complete or nearly complete (more than 95%) occlusion was achieved in 6 aneurysms and partial occlusion was achieved in 11. Clinically significant adverse events included two periprocedural thromboembolic complications. One of the patients died after thrombolysis was attempted. The other patient made an excellent functional recovery after undergoing successful thrombolysis of a thrombosed basilar artery stent. In the series reported by Benitez et al [57], 56 patients were identified as having wide-necked intracranial aneurysms suitable for stent-assisted coiling. A total of 49 aneurysms in 48 patients were treated with the Neuroform stent associated or not associated with coils. Stent deployment failed in eight cases (14%). Six aneurysms were stented only; 1 aneurysm was initially coiled, followed by stent placement; and 41 aneurysms were initially stented, followed by coil placement. There were five (8.9%) deaths, one (1.8%) of which occurred secondary to a stroke after the procedure. Four (7%) patients experienced thromboembolic events, of which three (5.3%) events were related to the procedure. In addition, there were two femoral pseudoaneurysms. The overall complication rate was 10.7%.The combination of two Neuroform stents implanted in a "Y-shaped" configuration to treat wide-necked basilar apex aneurysms has been suggested [58]. The overall impact of this technique application remains to be seen.

Unquestionably, the introduction of the Neuroform stent represented an important advance in the endovascular treatment of aneurysms with a low dome-to-neck ratio, which otherwise would be difficult to treat with coils. Second and third-generation Neuroform stents are now available, and in our personal experience, their performance is improved in comparison with the original device.

Many other specifically designed intracranial stents are being developed and should become available in the near future. Design modifications are expected to include asymmetric and covered stents and should enhance the results of endovascular approaches for the treatment of intracranial aneurysms.

Liquid embolic agents

Given the significant number of recurrences after coiling, especially in large and giant aneurysms with wide necks [26,59,60], other avenues of endovascular treatment were sought. The use of a liquid agent that would be able to obliterate the aneurysm sac completely and seal the neck has significant attractions and has been examined for several years [61–63]. The liquid nonadhesive embolic agent proposed for this purpose is Onyx (MicroTherapeutics). Specifically designed for endovascular use, Onyx is an ethylene vinyl alcohol copolymer dissolved in an organic solvent, dimethyl sulfoxide (DMSO). When this liquid embolic agent comes into contact with an aqueous solution, it precipitates and initially forms an outer soft and spongy polymer cast, with a semi-liquid center. As further material is injected into the cast, it fills the space into which it is injected, and additional material then breaks out through the outer layer of the existing cast [64]. Experimental studies in different animal models have

demonstrated the feasibility and safety of endovascular treatment of aneurysms by the use of this method [65,66].

The technique of Onyx embolization begins with the placement of a highly compliant DMSO-compatible occlusion balloon (Equinox or Hyperglide; MicroTherapeutics) within the parent vessel over the aneurysm neck. The balloon is left deflated while a DMSO-compatible microcatheter (Rebar; MicroTherapeutics) is placed within the aneurysm. A slow test injection of contrast material through the microcatheter is made with the balloon inflated to ensure that the neck is "controlled," and a satisfactory seal is achieved with stasis of contrast material within the aneurysm. The microcatheter is then purged with saline to clear any contrast residue and primed with DMSO with a volume to match the dead space within the catheter. Onyx (HD 500) is then introduced into the microcatheter. After a volume of approximately 0.2 mL has been injected, the Onyx approaches the end of the microcatheter and the balloon is inflated to the predetermined volume (measured when creating the seal between the aneurysm neck and parent vessel, as mentioned previously). The balloon maintains the patency of the parent vessel during the procedure while the aneurysm is filled with the Onyx, which forms a cast that seals the aneurysm off from the circulation and, in effect, reconstructs the parent vessel wall (Fig. 1).

The disadvantage of Onyx embolization is that it increases the technical complexity of the procedure [64]. The agent is injected at a rate of approximately 0.1 mL/min by using the specifically designed Cadence Precision Injector syringe (MicroTherapeutics), which operates by means of a screw thread. Because Onyx is a viscous material, it accumulates around the microcatheter tip and gradually enlarges to form a kernel that remains attached to the end of the microcatheter. After each injection, the balloon is left inflated for another 3 minutes and is then deflated to allow cerebral reperfusion for at least 2 minutes, and the cycle is repeated. With each injection, new portions of the aneurysm fill; eventually, the material flows down to the margins of the balloon and occludes the aneurysm neck. When the material comes into contact with the balloon, the injection is slowed or stopped with brief 15- to 30-second pauses to minimize the risk of leakage into the parent artery and beyond the balloon. It is important to ensure that material covers the aneurysm neck to achieve complete and durable occlusion and reduce the risk of aneurysm regrowth. The microcatheter position is not adjusted once the injection has begun. After angiographic confirmation of complete or satisfactory occlusion of the aneurysm, the catheter syringe is decompressed by aspiration of 0.2 mL of the material and a 10-minute pause is taken to allow complete solidification of the polymer with the balloon deflated. The balloon is then reinflated, and the microcatheter is removed by gentle traction [64].

Mawad et al [67] described their experience with stent-assisted Onyx embolization for the treatment of giant aneurysms in 11 patients. In their series, all aneurysms were excluded from the circulation, with preservation of the parent artery. Six-month follow-up angiographic images documented no recanalization of the aneurysm in 9 patients and minimal recanalization in 1 patient. The complications in this series included one death (vessel dissection, resulting in fatal intracranial hemorrhage) and one case of transient hemiparesis caused by watershed ischemia (prolonged balloon inflation occluding the ICA). Some concerns regarding the safety of the clinical use of DMSO are mentioned in the literature, especially with respect to the risks of parent vessel occlusion and DMSO-induced angionecrosis [64–67].

Two clinical trials, one European and one American, were designed to investigate the safety and efficacy of the Onyx embolic system in selected patients with intracranial aneurysms. The American trial, comparing Onyx versus coil embolization, was recently halted, and the results are not yet available. The results of the Cerebral Aneurysm Multicenter European Onyx trial were recently published [64]. This prospective single-arm observational study was conducted at 20 European centers, enrolling a consecutive series of 119 patients with 123 aneurysms judged suitable for Onyx treatment. The definition of a suitable aneurysm was one that was likely to be difficult to treat or presented a high risk for conventional coil techniques or neurosurgical clip placement, had recurred after coil embolization, or had failed to respond to surgical or endovascular treatment. Their results comprised data obtained for 97 of 119 patients with 100 of 123 aneurysms; 87% of patients harbored unruptured aneurysms, and 81% of aneurysms were large or giant. Angiographic images obtained at the 12-month follow-up examination were available for 71 of 97 patients. Of these, aneurysm

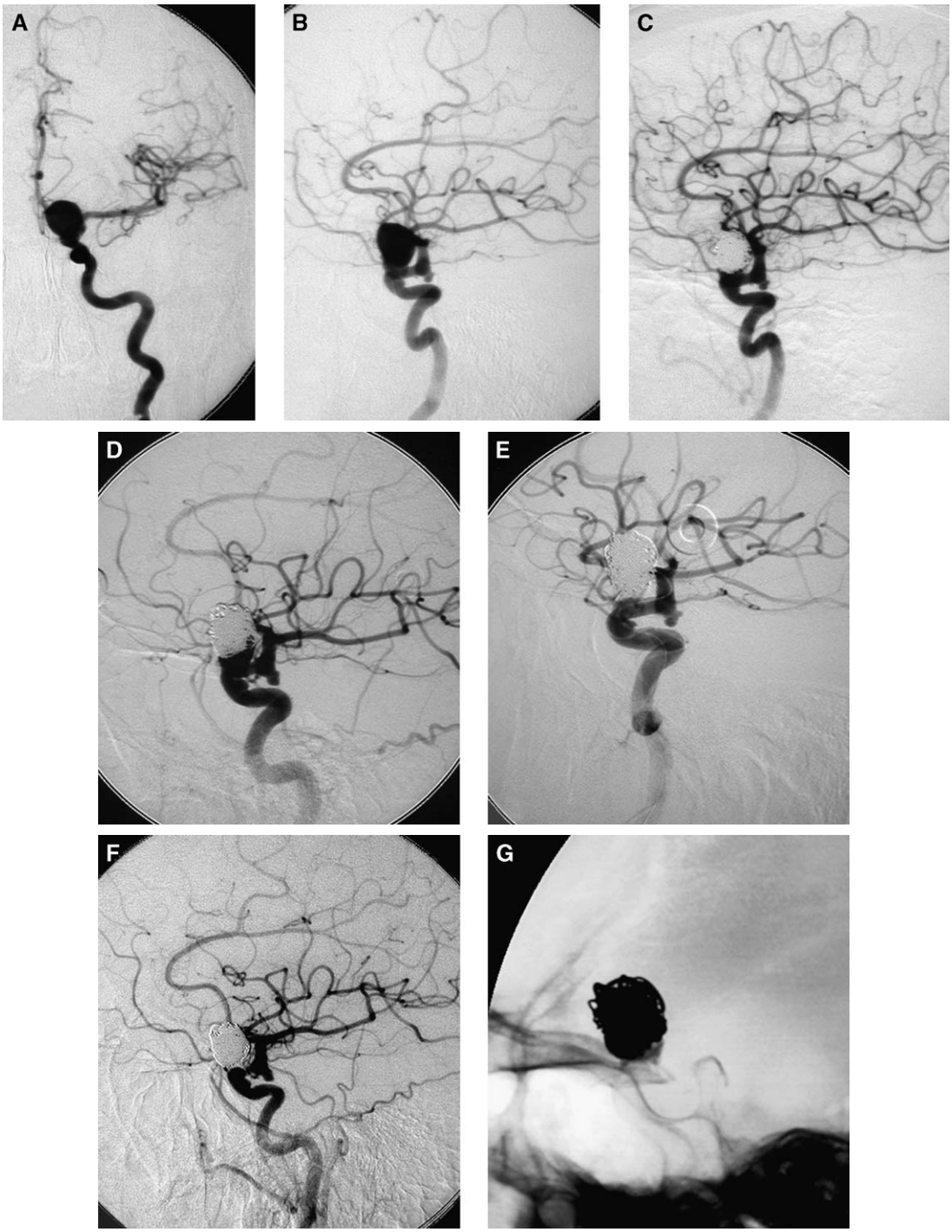


Fig. 1. Case illustration. This 64-year-old woman presented with an unruptured left internal carotid artery aneurysm (*A*, anteroposterior view; *B*, lateral view). (*C*) The patient initially underwent primary coiling of her aneurysm with partial occlusion of the sac. Three months after the procedure, the aneurysm remnant was found to be larger. (*D*) A further increase in size was noticed at 9 months. (*E*) At this point, the patient received retreatment with Onyx, which resulted in complete occlusion of the aneurysm. (*F*) No aneurysm regrowth was observed on the follow-up angiogram obtained 28 months after the second treatment. (*G*) Note that the Onyx conforms to the coil mass.

occlusion was complete in 79% of patients, subtotal in 13%, and incomplete in 8%. Permanent neurologic morbidity related to the procedure was present in 8.2% of patients, including monocular blindness caused by leakage of the agent into the ophthalmic artery (two cases), ipsilateral infarctions (two cases), SAH caused by dissection (two cases), and worsening of cranial nerve palsy (one case). An additional 8.2% of patients had transient neurologic complications. During the study period, 7.2% of the patients died: two deaths were related to the procedure, one was related to SAH (pulmonary complications), and four were of unrelated causes. The two procedure-related deaths were associated with femoral access site complications. The functional status of 75 of the 82 patients alive and with follow-up at 12 months was Rankin Scale grade 2 or better. Delayed occlusion of the parent vessel occurred in 9 patients; delayed occlusion was asymptomatic in 5 patients and resulted in permanent neurologic deficit in 2. Retreatment was required for recurrence of 10 (10%) aneurysms between 3 and 12 months after initial treatment, which seemed to be dependent on the aneurysm size (5%, 13%, and 5% of small, large, and giant aneurysms, respectively) [64].

Outcomes of coiling for intracranial aneurysm treatment

The immediate clinical and angiographic results after GDC embolization of ruptured intracranial aneurysms were assessed by Vinuela et al [60]. These authors reported 403 patients treated at eight United States centers participating in the FDA study between December 1990 and July 1995, which led to device approval in September 1995. All aneurysms were treated within 15 days of rupture. The most common reasons for selecting endovascular treatment in this series included high surgical risk because of aneurysm size and location (69%), failed surgical exploration (12.7%), and poor neurologic (12.2%) or medical (4.7%) status. Because of this preselection, most (57%) aneurysms were in the posterior circulation. Immediate angiographic results varied, primarily according to the size of the aneurysm neck and sac. Complete aneurysm occlusion at the conclusion of the embolization procedure was observed in 70.8% of small aneurysms (4 to 10 mm in largest diameter) with small necks (<4 mm). In this subgroup, technical failures (inability to place coils because of technical difficulties, such as vessel tortuosity or wide neck) were uncommon (occurring in only 3.6% of cases). In contrast, complete occlusion was achieved in only 31% of small aneurysms with wide necks and technical failure occurred in 16.9%. Despite the high-risk preselected population, overall rates of morbidity (8.9%) and mortality (6.2%) were low and were not significantly influenced by aneurysm location when anterior and posterior circulation aneurysms were compared (morbidity: 8.1% versus 9.6%, mortality: 6.4% versus 6.1%, respectively). In critically assessing these results, it must be remembered that the aneurysms treated represented the early experience at the participating centers. As more experience has been accumulated, several centers have reported their results after coiling of intracranial aneurysms [68–71]. Current success rates can be expected to be higher because of improved selection criteria and treatment strategies, along with the availability of a greater range of coil sizes and types.

Murayama et al [26] reported their 11-year experience (beginning in December 1990) with GDC embolization at the University of California at Los Angeles Medical Center. For comparative purposes, the patients were divided into two groups: group A included their initial 5 years' experience with 230 patients harboring 251 aneurysms, and group B included the later 6 years' experience with 588 patients harboring 665 aneurysms. Overall, angiographically demonstrated complete occlusion was achieved in 55% of aneurysms and a neck remnant was displayed in 35.4% of lesions. Coil occlusion was incomplete in 3.5% of aneurysms and attempted unsuccessfully in 5%. A comparison between the two groups revealed a higher rate of complete embolization in group B than in group A (56.8 versus 50.2%, respectively). The overall morbidity/mortality rate was 9.4%. Follow-up angiograms were obtained in 53.4% of cases of aneurysms, and recanalization was exhibited in 26.1% of aneurysms in group A and 17.2% of those in group B. The overall recanalization rate was 20.9%. Aneurysm recanalization was related primarily to neck remnants and larger size. The overall incidence of delayed aneurysm rupture was 1.6%, a rate that improved in the more recent 5 years to 0.5%. Ten of 12 delayed ruptures occurred in large or giant aneurysms.

The addition of improved 3D coils and softer stretch-resistant coils to allow more complete packing at the region of the aneurysm neck seems

to have resulted in an improvement in the overall results of treatment. Niemann et al [72] reported a series of 133 patients with 141 aneurysms treated by a single neurointerventionist with ACT microcoils (Micrus), a new generation of spherically shaped 3D coils. Of the aneurysms treated, 110 were ruptured and 31 were unruptured. Complete angiographic occlusion was achieved in 74% of aneurysms, 24% had subtotal (≥95%) occlusion, and 2% had incomplete (<95%) occlusion.

As mentioned, the long-term stability (efficacy) of aneurysm occlusion with coils is still unknown, because some aneurysms recanalize [73] and even rupture [74,75] despite initial satisfactory treatment (complete angiographic occlusion). Raftopoulos et al [76] analyzed a prospective series of 103 patients with 132 aneurysms treated with coiling considered the first therapeutic option. In this study, clipping was performed only for cases in which endovascular embolization was deemed unlikely because of aneurysm characteristics or for those cases in which embolization had failed. Three groups were defined: group A comprised 64 aneurysms treated by endovascular embolization (these aneurysms had a neck-to-sac ratio of <1:3), group B comprised 63 aneurysms that were not considered suitable for endovascular treatment and were surgically clipped, and group C comprised 12 aneurysms that were not satisfactorily (>95%) embolized and were subsequently clipped. The frequency of residual aneurysms was 31.2% in group A, 1.6% in group B, and 0% in group C. Poor outcomes (defined as Glasgow Outcome Scale score of 1–3) at 2 to 6 months after treatment in patients with good clinical status before treatment occurred in 10.7% of the patients in group A, 0% in group B, and 8.3% in group C.

More recent reports have concentrated on the results and importance of follow-up angiography. Cognard et al [77] reported their observations in 169 aneurysms (ruptured and unruptured) in which at least one follow-up angiogram was obtained a minimum of 3 months after treatment. At the end of the initial procedure, occlusion was judged to be total in 95 (56%) cases, subtotal in 66 (39%), and incomplete in 8 (5%). Because of initial subtotal or incomplete occlusion, a second procedure was performed in 18 patients, with subsequent total occlusion achieved in 14. The first follow-up angiogram confirmed total occlusion in an additional 39 aneurysms that initially had been considered subtotally occluded. Overall, total occlusion was obtained in 148 (88%) aneurysms. This study underscores the importance of long-term follow-up angiographic studies. Recurrence was observed in 5% of the totally occluded aneurysms at 3 months of follow-up and in 9% of 99 aneurysms that were totally occluded on the first follow-up angiogram and were assessed with a second follow-up study a mean of 18 months later. Of 39 aneurysms totally occluded on the second follow-up angiogram, 3 (8%) had recurred when a third angiogram was obtained an average of 38 months later. Recurrence was more frequent in ruptured aneurysms than in unruptured aneurysms (17% versus 7%) as well as in large aneurysms compared with small aneurysms, but there was no difference in the frequency of recurrence relative to aneurysm location.

Byrne and colleagues [78] reviewed the 5-year experience at Oxford University with GDC treatment of ruptured intracranial aneurysms. Surviving patients were followed up for a median of 22 months. Angiographic occlusion was assessed in 259 aneurysms in 250 patients. After treatment, 64% of the aneurysms were completely occluded. At angiographic follow-up, usually obtained between 6 and 12 months later, the degree of occlusion observed at the conclusion of the embolization procedure remained stable in 86.4% of small aneurysms and in 85.2% of large aneurysms. In 38 aneurysms (14.7%), a remnant had enlarged to some degree. In 8.5% of cases, improvement of the initial degree of occlusion was observed at follow-up angiography as a result of thrombosis that occurred subsequent to the completion of packing.

Raymond et al [59] retrospectively reviewed the angiograms of 466 patients with 501 aneurysms, of which 54.1% were ruptured and 45.9% were unruptured. The mean size of the aneurysms was 9.67 mm, with a mean neck size of 4.31 mm. The most frequent aneurysm sites were the basilar bifurcation (27.7%) and the carotid ophthalmic artery (18.0%). Recurrences were subjectively divided into minor and major (suitable for retreatment) categories. In their series, short-term (≤1 year) follow-up angiograms were available in 70.5% of cases and long-term (>1 year) follow-up angiograms were available in 55%, for a total of 76.5% cases followed up. Recurrences were found in 33.6% of treated aneurysms that were followed up for a mean duration of 12.31 months after treatment. Major recurrence was present in 20.7% at a mean of 16.49 months. Aneurysm hemorrhage occurred in 3 (0.8%) patients during a mean clinical follow-up period of 31 months. Predictors of aneurysm recurrence included an

aneurysm size of 10 mm or greater, treatment during the acute phase of rupture, incomplete initial occlusion, and longer duration of follow-up. Aneurysms completely occluded in the initial treatment were found to have recurred even after 37 months of follow-up. The aforementioned series have confirmed the overall safety of this technique; however, concerns remain because of the lack of long-term follow-up data regarding efficacy (procedural durability).

No agreement exists as to the timing and duration of angiographic follow-up after coil embolization of intracranial aneurysms. In general, we obtain an initial follow-up angiogram at 3 to 6 months in patients with aneurysms that are totally occluded or those having a minimal residual neck. In patients with residual aneurysm filling that extends beyond the neck, an earlier study (usually at 1–3 months after coiling) is indicated to assess the stability and size of the remnant and the possible need for additional treatment. The necessity and timing of additional follow-up studies are determined on an individual basis; however, all patients, even those with stable occlusion on the first follow-up angiogram, should undergo a 1-year follow-up study. The need for repeat angiographic follow-up, which exposes patients to the low but definite risk of an invasive procedure, is one of the current limitations of endovascular treatment of aneurysms. The results obtained with magnetic resonance angiography suggest that this imaging technology has the potential to replace angiography for assessing aneurysm occlusion after coiling [79]. Transcranial color Doppler imaging has been described as a useful tool to assess aneurysm occlusion after coiling [80].

Several factors are directly related to the possibility of achieving complete and stable angiographic occlusion of aneurysms, especially aneurysm and neck size and dome-to-neck ratio. Fernandez Zubillaga et al [81] reported complete aneurysm occlusion in 85% of small-necked (4 mm or smaller) aneurysms and in only 15% of aneurysms with necks exceeding 4 mm. The importance of the ratio between maximal sac diameter and neck diameter (dome-to-neck ratio) has been debated [77,82]. It has been suggested that when this ratio is less than 2, the aneurysm has a so-called "wide neck" and that optimal results are obtained when this ratio is at least 2 [82]. When aneurysms are selected for endovascular treatment on the basis of this favorable anatomic-geometric consideration, complete angiographic occlusion can be achieved in 72% of acutely ruptured aneurysms and in 80% of unruptured ones [82]. Small-sized aneurysms with wide necks present the greatest technical challenge [60].

The recent addition of bioactive coils is expected to improve the overall results obtained with bare platinum coils. Vinuela et al [83] reported a 19% recanalization rate for aneurysms with a neck remnant treated with Matrix coils compared with 50% for those treated with GDCs after 18 months of follow-up. Chaloupka et al [84] reported a 15.3% rate of retreatment with Matrix coils compared with a rate of 29.6% with GDCs. Alexander et al [85] reported a 3.9% rate of retreatment in 51 of 101 patients treated with Matrix coils who had a 6-month follow-up, with no information available about the remaining 50 patients.

The preliminary results for the Acceleration of Connective Tissue Formation in Endovascular Aneurysm Repair study, a company-sponsored (Boston Scientific Target) registry evaluating patients treated with Matrix coils, were recently presented [86]. The primary end point for the study was the rate of angiographic recanalization at 3 months; secondary end points were angiographic recanalization rates at 12 months and the occurrence of adverse events and clinical outcomes. Patients with de novo aneurysms of less than 25 mm in diameter and Hunt and Hess (HH) grade 0 to 3 at admission were included in the study. Ninety-nine aneurysms were treated in 96 patients at 11 centers in the United States and Europe. The median age of these patients was 53 years (range: 20–82 years), and 72% were women. Median aneurysm size was 8 mm (range: 1.3–19.6 mm); 27% of the aneurysms were considered large and the remaining 73% were considered small. Regarding neck size, 79% of the aneurysms were considered to have wide necks (neck >4 mm or <2:1 dome-to-neck ratio). Seventy-seven percent of the aneurysms were in the anterior circulation. Forty-five percent of patients presented with SAH with the following HH grade distribution: I, 46%; II, 27%; and III, 27%. Angiographic images analyzed at 3 months for 74 (75%) of the 99 aneurysms treated demonstrated a 12% recanalization rate, with 5% considered minor (no treatment required) and 7% major, and there was a 15% total recanalization rate at 12 months (results available for 62% of aneurysms treated).

A company-sponsored (MicroVention) multicenter prospective study to evaluate the results of aneurysm treatment with a bioactive coil

(HydroCoil Embolic System; MicroVention), HydroCoil for Aneurysm Occlusion, is being conducted [87]. This hybrid hydrogel-platinum coil was used for the endovascular treatment of 186 patients with 191 aneurysms enrolled between October 2002 and February 2004 at 15 sites worldwide. The primary end points for the study are adverse events at the time of the treatment and at 3 to 6 months and 12 to 18 months thereafter plus angiographic recurrence of the aneurysm at 3 to 6 months and 12 to 18 months after treatment. Among the study patients, 71 (37%) of 191 aneurysms had ruptured. The mean aneurysm size was 8 mm, the mean neck size was 4.4 mm, and the mean dome-to-neck ratio was 1.7. The immediate angiographic results demonstrated rates of complete occlusion, near-complete occlusion, and incomplete occlusion of 49.4%, 42.4%, and 8.2%, respectively. These rates are equivalent to those obtained with bare platinum coils. Angiographic images analyzed at 3 months for 101 of the 186 treated patients demonstrated a 15.9% recanalization rate for aneurysms smaller than 10 mm and a 36.4% recanalization rate for those equal to or larger than 10 mm. The major criticism of this study was that any combination of HydroCoil and bare platinum coils could be used, and the percentage of HydroCoils used relative to all coils used varied from 5% to 100% [87].

The need for improvement in the long-term durability of coiling is still an open issue. The addition of bioactive coils, intracranial stents, and the upcoming new technology is likely to lead to a dramatic improvement in technical achievement of complete aneurysm obliteration, but the effect of the addition of new technology on the durability of the results remains to be proved.

Randomized trials of coiling versus clipping

Vanninen et al [88] reported the results of a single center, prospective, randomized study of GDC embolization versus surgery for the treatment of recently (<72 hours) ruptured intracranial aneurysms suitable for either treatment approach. Fifty-two patients were assigned to the endovascular treatment group and 57 to the surgical treatment group. The two groups were demographically well matched. Despite the relatively broad inclusion criteria, 70 other patients treated during the same period were not randomized because of the following reasons: endovascular treatment was not anatomically feasible (33 patients), presence of a large hematoma requiring evacuation (35 patients), or presence of cranial nerve compression (2 patients). There were no differences in 3-month clinical outcomes, as determined by the Glasgow Outcome Scale [9], in the two treatment groups: 81% of the patients initially assigned to endovascular treatment and 79% of the patients assigned to surgery had a good or moderate recovery. No differences were observed between the two groups when neuropsychologic outcome was assessed at 12 months, and the scores were significantly improved in both groups 3 to 12 months after treatment. According to the study protocol, MRI of the brain was performed at 12 months. Patients in the surgical group had more ischemic lesions in the parent artery territory of the ruptured aneurysm, in addition to signs of brain retraction injury. Although this trial showed equivalent outcomes with current endovascular embolization techniques and with surgery, it did not answer questions about long-term durability of the treatment.

The ISAT [3] was designed as a randomized multicenter trial to compare the safety and efficacy of endovascular coiling with that of standard neurosurgical clipping of aneurysms judged suitable for both treatments. During the study period, 9559 patients with SAH were identified: 2737 had primary coil embolization (coiling was preferred in elderly patients, patients with poor clinical grades, and patients with posterior circulation aneurysms), 3615 had clipping (chosen in young patients, patients with MCA aneurysms, and patients with larger aneurysms), and 1064 had unknown treatment. Of those 9559 patients, 2143 with ruptured intracranial aneurysms were randomly assigned to receive neurosurgical clipping (n = 1070) or endovascular treatment by detachable platinum coils (n = 1073). Among the randomized cases, 88% of patients were World Federation of Neurosurgical Societies (WFNS) grade 1 to 3, 93% of the aneurysms were 10 mm or smaller, and 97% of the aneurysms were located in the anterior circulation (50.5% anterior communicating and 27% posterior communicating or anterior choroidal).

Clinical outcomes were assessed at 2 months and at 1 year with planned interim ascertainment of recurrent hemorrhages and death. The primary objective was to determine whether endovascular coiling, compared with neurosurgical clipping, reduced the proportion of patients with a modified Rankin Scale score of 3 to 6 (dependency or death) at 1 year by 25%. Trial recruitment was stopped by the steering committee after the interim analysis

on the basis of the following results: 190 (23.7%) of 801 patients allocated endovascular treatment were dependent or dead at 1 year compared with 243 (30.6%) of 793 patients allocated neurosurgical treatment. The relative and absolute risk reductions in dependency or death after allocation to endovascular versus neurosurgical treatment were 22.6% (95% confidence interval [CI], 8.9–34.2) and 6.9% (95% CI, 2.5–11.3), respectively. The risk of rebleeding from the ruptured aneurysm after 1 year was 2 per 1276 patient-years and 0 per 1081 patient-years for the groups allocated endovascular and neurosurgical treatment, respectively. The study conclusion was that in patients with ruptured intracranial aneurysms for which endovascular coiling and neurosurgical clipping are therapeutic options, the outcome in terms of survival free of disability at 1 year was significantly better with endovascular coiling. Furthermore, the most recent data available from this study suggested that the long-term risks of further bleeding from the treated aneurysm were low with either therapy, although somewhat more frequent with endovascular coiling. The cumulative risk of rebleeding at 1 year was 0.15% for coiling versus 0.07% for clipping [89].

As with any study of this magnitude, the ISAT evoked criticisms regarding the design, number of patients randomized, definition of an aneurysm suitable for both approaches, whether state-of-the-art aneurysm surgery was well represented, and other issues. Unquestionably, the ISAT has provided the only level I evidence available so far comparing endovascular coiling and surgical clipping of intracranial aneurysms. Moreover, in the hands of the ISAT investigators, endovascular coiling was a safer treatment option for patients with good WFNS grades and small anterior circulation aneurysms. The looming question regarding durability of aneurysm coiling is still open and much longer follow-ups are needed to assess this issue.

Complications: avoidance and management

Ischemic complications

The frequency of ischemic complications occurring during endovascular aneurysm embolization is reported to range from 2.5% to 24% [90,91]. The incidence of asymptomatic embolic events may be even greater [92]. Rordorf et al [92] used diffusion-weighted MRI performed within 48 hours in 14 consecutive elective GDC procedures to evaluate the incidence of silent ischemic events during aneurysm treatment. All embolizations were performed under systemic heparinization, and all flush solutions were heparinized; in addition, the guiding catheters and microcatheters were placed for continuous heparinized infusions. Small areas of restricted diffusion, presumed to represent procedure-related embolic infarctions, were found on the images of 8 of 14 patients. All except one of the areas were located ipsilateral to the catheterization. Six patients had evidence of multiple infarctions. Most lesions were small (<2 mm); 1 patient with coil stretch and herniation into the parent vessel had numerous infarctions, with a dominant posterior frontal infarction. Pre- and postprocedure National Institutes of Health Stroke Scale scores were unchanged for 13 of 14 patients. Overall, the rate of asymptomatic emboli was 61% (8 of 13 treatments) in uncomplicated procedures. These investigators concluded that silent thromboembolic events related to the use of the GDC system are a common occurrence, despite meticulous technique and systemic anticoagulation. Although clinical consequences are rare, the high occurrence rate suggests that alterations in technique, such as the addition of antiplatelet agents, should be considered [92].

Prevention of thromboembolic complications is fundamental. The authors routinely administer antiplatelet agents (eg, aspirin) before performing coiling procedures for nonacutely ruptured or unruptured aneurysms. This practice seems to be safe not only in the event of intraprocedural rupture but in terms of lowering the risk of thromboembolic complications in these patients. In the authors' opinion, antiplatelet agent therapy is even more important when bioactive coils are used. The rate of thromboembolic events when using such devices seems to be higher and justifies the use of such agents [86,87]. The addition of clopidogrel to the antiplatelet regimen is recommended for those patients in whom stent-assisted coiling is anticipated. Heparin is administered intravenously to achieve an activated coagulation time in the range of 250 to 300 seconds for nonacutely ruptured or unruptured aneurysms, because subtherapeutic levels of anticoagulation during the procedure may also lead to thromboembolic phenomena. The fact that heparin actually stimulates platelet aggregation should be kept in mind, especially with the advent of new direct thrombin inhibitors, such as bivalirudin [93].

Different stages of the procedure can trigger thrombus formation with or without consequent

distal embolization. Meticulous attention to detail and extreme caution are recommended when trying to manipulate the guide catheter into a stable position. This portion of the procedure can be the most challenging and time-consuming, especially in elderly patients with tortuous atherosclerotic proximal vessels. During coil placement, thromboembolic complications can be a consequence of thrombus dislodged from within the aneurysm (particularly in partially thrombosed aneurysms) or thrombus formation around the coil mass during or even after the procedure. This risk is especially high in cases of coil herniation through the neck into the parent vessel or into distal branches arising near the aneurysm neck.

When coils herniate, several options are available, depending on the situation. The herniation of one or even several coils into the parent vessel is not necessarily associated with thromboembolic complications. As long as the herniation is well tolerated clinically, observation alone is a valid option. That is usually the case when a single loop of the coil herniates into the parent vessel. In this situation, the authors prefer to start or keep patients on a dual antiplatelet regimen (usually aspirin and clopidogrel) for 6 to 8 weeks. If the errant coil is noticed to be moving within the parent vessel, however, it should be considered a potential cause of secondary thromboembolism. In these cases, coil removal or trapping is a viable option, depending on the situation. Many devices are available for coil removal. For coil trapping or fixation, a stent can be deployed to force the herniated coil against the parent vessel wall, which may promote secondary endothelialization. As a maneuver of last resort in the setting of ischemia caused by the occluding effects of the migrated coil or coils, an emergency craniotomy with coil and thrombus extraction can be performed to reestablish flow and attempt to reverse the ongoing ischemia [94].

When distal embolism is suspected or documented, superselective thrombolytic therapy can restore patency and potentially reverse disabling neurologic deficits. Many agents have been reported for this application, including hyperheparinization, urokinase [95], alteplase [91], abciximab [96], eptifibatide [91], or a combination of these drugs [96]. Fiorella et al [96] reported their experience with the treatment of intraprocedural thromboembolic complications in 13 patients (10 aneurysm cases) with abciximab, alone or in combination with tissue plasminogen activator. After identification of the complication, patients received intra-arterial (n = 5) or intravenous (n = 8) abciximab. Complete (n = 7) or partial (n = 6) resolution of thrombus was observed in all cases. Five patients had small infarctions in the distribution of the thromboembolic complication. In the authors' experience, the results obtained with intra-arterial or intravenous injection of glycoprotein IIb or IIIa inhibitors, such as eptifibatide and abciximab, have been satisfactory, with a high rate of recanalization or thrombus degradation and a low rate of hemorrhagic complications.

To prevent or minimize the risk of aneurysm rerupture and catastrophic consequences, Cronqvist et al [95] suggest that fibrinolysis for thromboemboli that occur during coiling should be considered only if the aneurysm has been sufficiently embolized. In such cases, rapid completion of coiling should be performed, followed by thrombolysis. Prompt fibrinolysis is not always successful [95], and its success depends on clot composition. An embolus consisting of fresh thrombus that develops during the procedure is much more likely to be dissolved by thrombolysis than is an embolus consisting of an atherosclerotic plaque fragment dislodged during catheterization of the proximal vessels.

Intraprocedural rupture

Intraprocedural aneurysm rupture is reported to occur in 2% to 8% of patients during aneurysm coiling (Fig. 2) [60,68,97]. Rupture seems to be more common in the treatment of small aneurysms, especially in the acute phase immediately after SAH [60,68]. Operator experience is also an important factor, with intraoperative rupture being most common in the early phase of the learning curve. In 75 patients treated during the acute phase after SAH, Raymond and Roy [68] experienced five ruptures in the first 25 patients, one in the next 25 patients, and none in the last 25 patients treated.

Aneurysm rupture can occur during several phases of the embolization procedure, ranging from diagnostic angiography injection to coil insertion. Doerfler et al [98] reported five patients with intraprocedural aneurysmal rupture. In one patient, rupture was caused by guide wire perforation of the aneurysm wall. In two patients, the microcatheter itself perforated the aneurysm. In another two patients, rupture occurred during placement of the first coil. In this series,

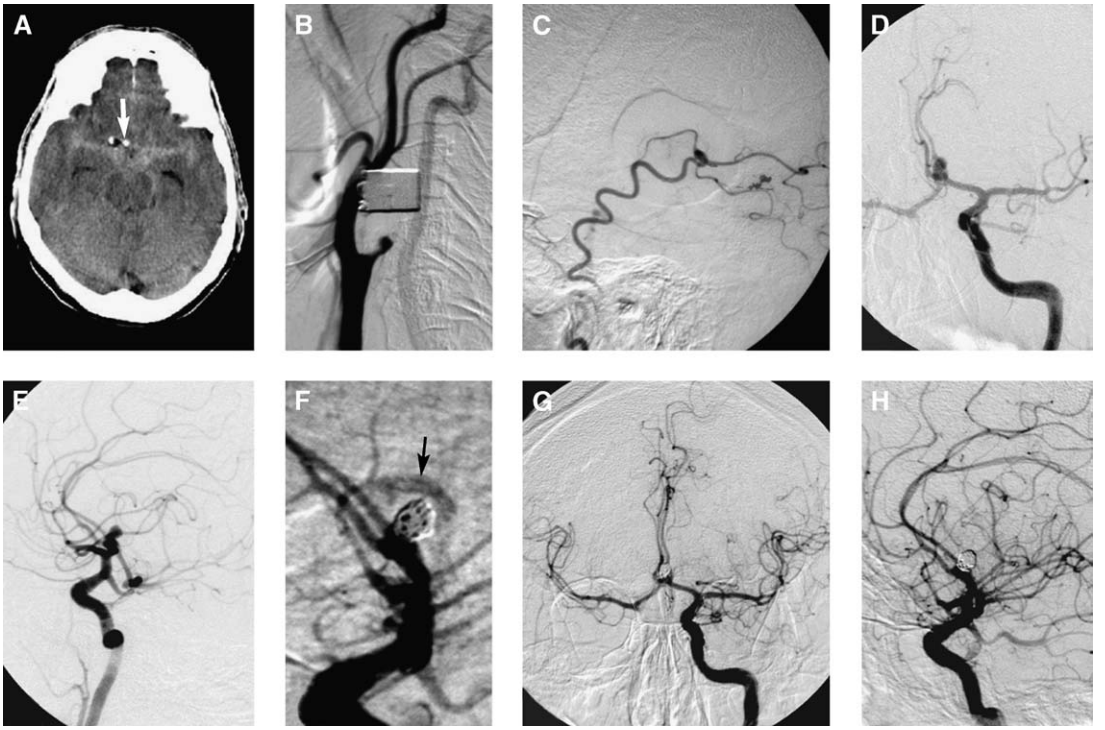


Fig. 2. Case illustration. This 59-year-old man presented with subarachnoid hemorrhage (*A*, CT scan), with Hunt and Hess grade 2 and Fisher grade 3. Twenty years previously, the patient underwent occlusion of the right internal carotid artery (ICA) (note the presence of calcification in the paraclinoid area on the right side [*white arrow*]) with a Selverstone clamp (*B*, angiogram) preceded by a superficial temporal artery–to–middle cerebral artery bypass (*C*, angiogram). A cerebral angiogram performed at the time of the present admission demonstrated an anterior communicating artery aneurysm filling from the left ICA (*D*, anteroposterior [AP] view; *E*, lateral view). The patient was brought to the angiography suite for aneurysm coiling. (*F*) After placement and detachment of the third coil within the aneurysm, contrast extravasation was noticed. Rapid completion of the coiling procedure with the placement of two additional coils resulted in cessation of contrast extravasation. The final angiographic result documents complete aneurysm occlusion with parent vessel preservation (*G*, AP view; *H*, lateral view). The patient had a good outcome (modified Rankin Scale score of 1 at 30 days).

intraprocedural rupture occurred in 3% of 164 patients with ruptured aneurysms and was associated with a mortality rate of 20%.

Levy et al [97] reported intraprocedural rupture in 6 (2%) of 274 patients with intracranial aneurysms treated with coil embolization. The rupture resulted from detachment of the last coil in 3 patients, detachment of the third coil (of four) in 1 patient, and insertion of the first coil in another patient.

Microwire-related perforations can be minimized by selecting the appropriate wire, with preference given to soft-tipped wires, particularly in the setting of acute rupture. Microcatheter-related ruptures occur while attempts are made to catheterize the aneurysm and obtain stable and optimal placement of the microcatheter within the aneurysm. During this maneuver, it is important to avoid excessive slack in the microcatheter, which can cause it to move forward suddenly and perforate the aneurysm [99]. When catheterizing the aneurysm, the guide wire precedes the entry of the microcatheter into the aneurysm. Using road mapping techniques, the microcatheter is slowly advanced and placed at the center of the aneurysm. Undesirable forward movements are avoided when positioning the microcatheter by relieving any forward tension that might remain within the microcatheter guide wire system before withdrawing the guide wire. Slack from the microcatheter is removed by making several passes with the guide wire. After ensuring that

no residual forward tension is present, the guide wire is slowly withdrawn under direct fluoroscopic control. While the first coil is delivered, excessive stress against the aneurysm wall is avoided. This maneuver is greatly enhanced by the availability of 3D coils with a small inner loop. In acutely ruptured aneurysms, the hemorrhage site can be identified sometimes as a daughter sac on the aneurysm fundus. When possible, the first coil should be delivered away from these sites. Rupture occurs less often during delivery or after detachment of subsequent coils [100].

The clinical manifestations of intraprocedural rupture are variable. Although minimal extravasation of blood may not produce symptoms in some cases, awake patients tend to have headaches of varying severity. Neurologic focal deficits and impairment of the level of consciousness may follow, depending on the severity of the hemorrhage [42]. When an intraprocedural rupture occurs in anesthetized patients, hemodynamic monitoring reveals an otherwise unexplained increase in systemic blood pressure and heart rate [100]. Prompt management of the rupture is of utmost importance to minimize its consequences. Intraprocedural heparinization is promptly reversed by the administration of intravenous protamine. The authors routinely keep protamine (30 mg) on the back table in the angiography suite ready for infusion. This practice can save precious minutes in the case of an unexpected intraprocedural rupture. It is critical to avoid withdrawing the device responsible for the rupture (micro-guide wire, microcatheter, or coil). The device may tamponade the rupture site and limit the size of hemorrhage. When the microcatheter is responsible for the rupture, a coil can be delivered within the subarachnoid space as the microcatheter is slowly brought back to the sac in an attempt to seal the leak. Similarly, if a coil is responsible for the rupture, it is important to continue to deliver the coil. In general, once a rupture has occurred, the remaining aneurysm sac is packed with coils as quickly as possible. In refractory situations, temporary or permanent balloon occlusion of the parent artery can be performed [100]. The outcome of an intraprocedural rupture can be variable and is related primarily to the severity of the bleed. In the event of a severe rupture, monitoring and treating increased intracranial pressure are mandatory. Immediate placement of an external ventricular drain in the angiography suite can be a life-saving maneuver; thus, the operator should be familiar with this procedure.

Infection

Although infection is a concern after the placement of any endovascular implant, it is extremely rare after aneurysm coiling. Al-Okaili and Patel [101] reported a single case of perianeurysmal brain abscess formation after coil embolization of a giant unruptured right posterior communicating artery aneurysm. The possibility of infection should be considered especially when coils are placed in an aneurysm extending into or adjacent to a potentially contaminated space, such as the sphenoid sinus, or when they are used in the treatment of mycotic aneurysms. Periprocedural administration of antibiotic therapy for prophylaxis has been suggested in such cases [101]. Some authors recommend that all patients with endovascular implants receive appropriate prophylactic coverage during any invasive procedure in case of bacteremia, but no consensus exists regarding this practice [101].

Shunt-dependent hydrocephalus and vasospasm

Preliminary clinical evidence suggests that shunt-dependent hydrocephalus occurs less frequently in patients undergoing endovascular coiling than in those treated with surgical clipping. In the previously mentioned Finnish randomized trial reported by Vanninen et al [88], shunt insertion was required significantly more often in the surgical group. Similarly, in a retrospective series, Gruber et al [102] observed that shunt-dependent hydrocephalus developed in 23.2% of patients undergoing surgery and in 17.7% of patients undergoing early endovascular treatment. The reasons for these differences are unknown.

One potential limitation of the endovascular approach in patients treated acutely after aneurysm rupture is the inability to remove cisternal clot, with a theoretic risk of increasing the likelihood of vasospasm. Early series, however, suggested that the risk of delayed cerebral ischemia after endovascular treatment of acutely ruptured intracranial aneurysms is no higher than that encountered after surgical clipping [88,103]. Some authors maintain that the incidence of spasm after coiling may be even lower, because mechanical injury is decreased by endovascular treatment [104,105]. Murayama et al [103] reported that symptomatic vasospasm occurred in 23% of 69 HH grade I, II, or III patients who underwent GDC occlusion of intracranial aneurysms within 72 hours of rupture, resulting in an overall combined morbidity and mortality rate of

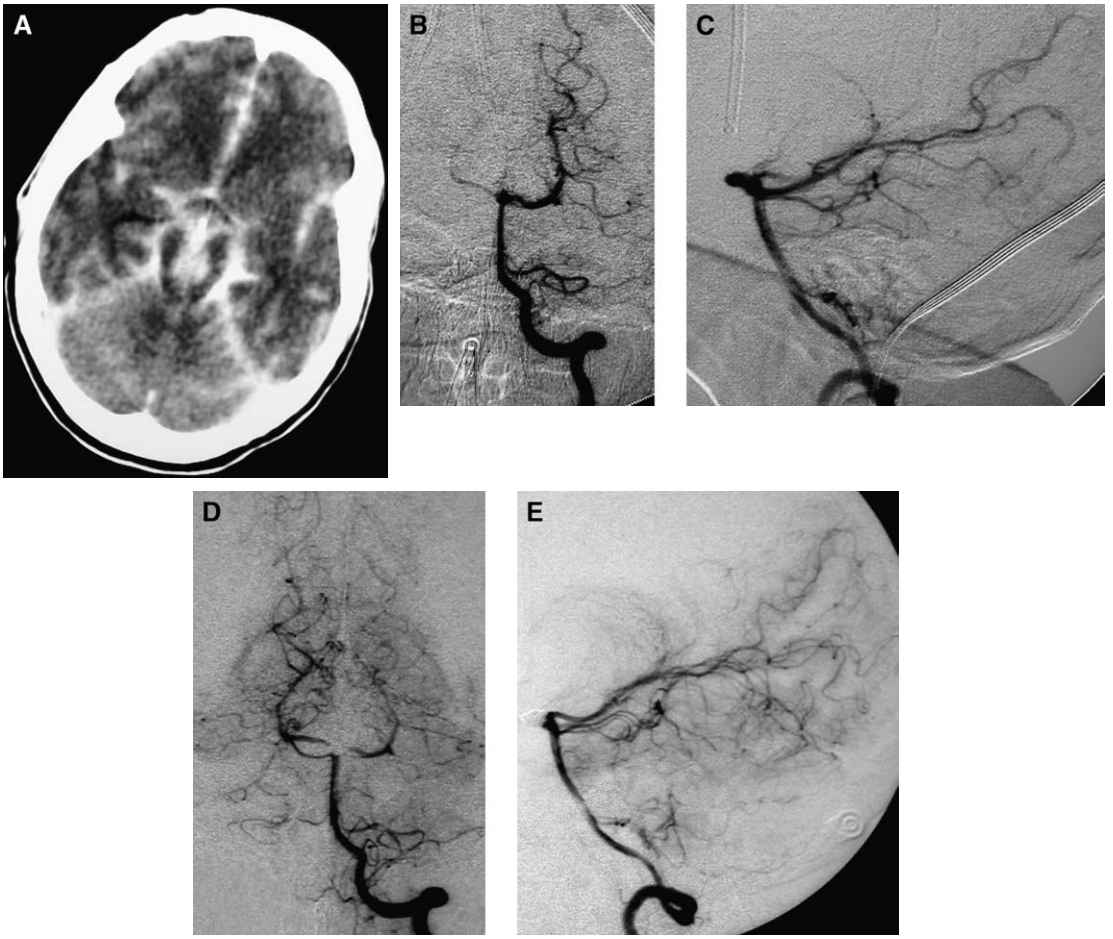


Fig. 3. Case illustration. This 59-year-old woman presented with severe headache. (*A*) An axial CT scan revealed diffuse subarachnoid hemorrhage. By digital subtraction angiography (DSA), anteroposterior (AP) (*B*) and lateral (*C*) views demonstrated a basilar tip aneurysm projecting anteriorly. (*D*, *E*) Aneurysm coiling was successfully performed with near-complete occlusion of the aneurysm after treatment. Daily serial transcranial Doppler (TCD) imaging demonstrated diffuse increased velocities 4 days after the initial aneurysm rupture. By DSA, AP (*F*) and lateral (*G*) projections revealed severe vasospasm of the basilar artery and its branches. (*H*) It also demonstrated severe vasospasm of the M1 segment of the right middle cerebral artery (MCA). (*I*) Note the resolution of vasospasm after the performance of balloon angioplasty. The same study also demonstrated severe diffuse vasospasm in the distribution of left MCA and anterior cerebral artery (*J*), which showed improvement after intra-arterial papaverine infusion (*K*). Two days later, increased left internal carotid artery (ICA) territory velocities were recorded. (*L*) DSA obtained at this time demonstrated severe vasospasm, which was more marked in the supraclinoid segment of the ICA. (*M*) Note the position of the angioplasty balloon over the wire on this unsubtracted image. (*N*) The vasospasm resolved after angioplasty. (*O*, *P*) Forty-eight hours later, TCD velocities were increased once again and DSA demonstrated severe diffuse vasospasm bilaterally in the distribution of the MCA and anterior cerebral artery. (*Q*, *R*) Note the improvement after intra-arterial papaverine infusion. After a 25-day admission, the patient was transferred to a rehabilitation unit (with a modified Rankin Scale score of 1). Six-month follow-up angiographic AP (*S*) and lateral (*T*) views show near-complete occlusion of the aneurysm, with some residual filling at the neck area.

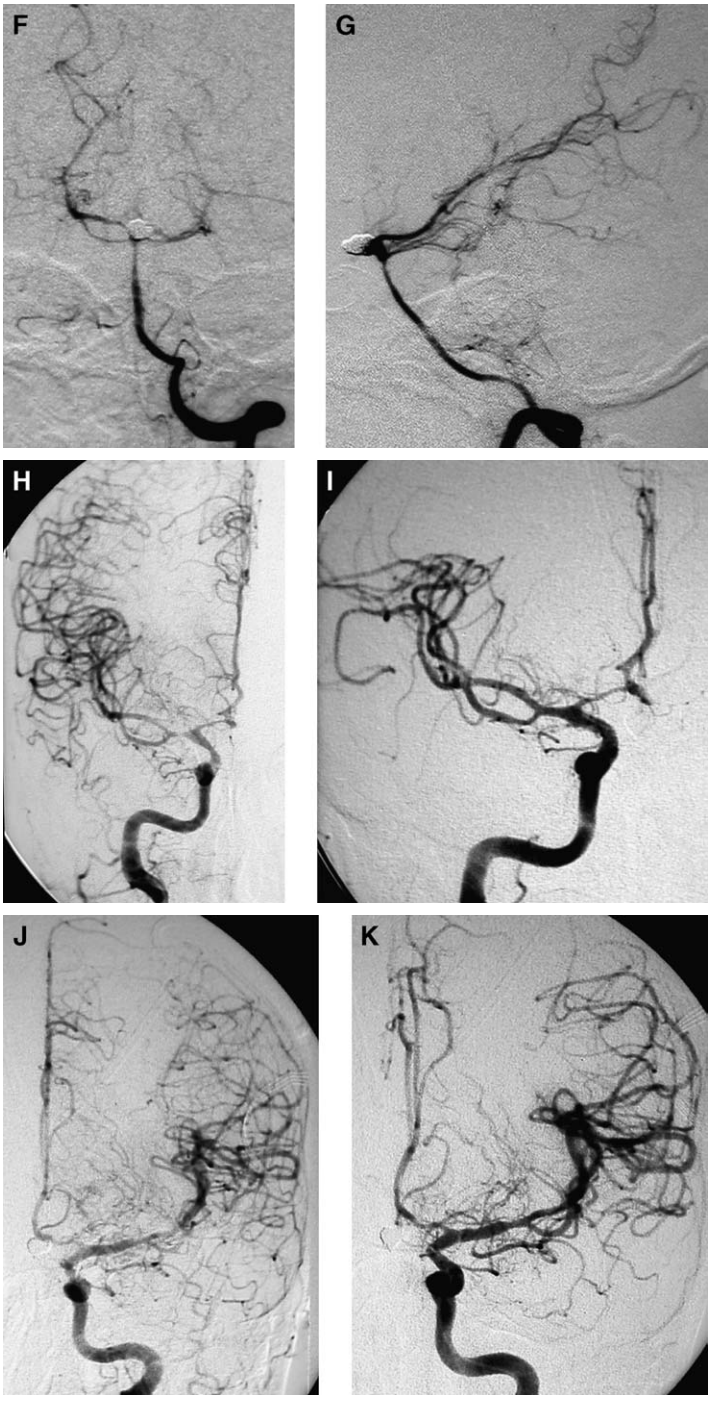
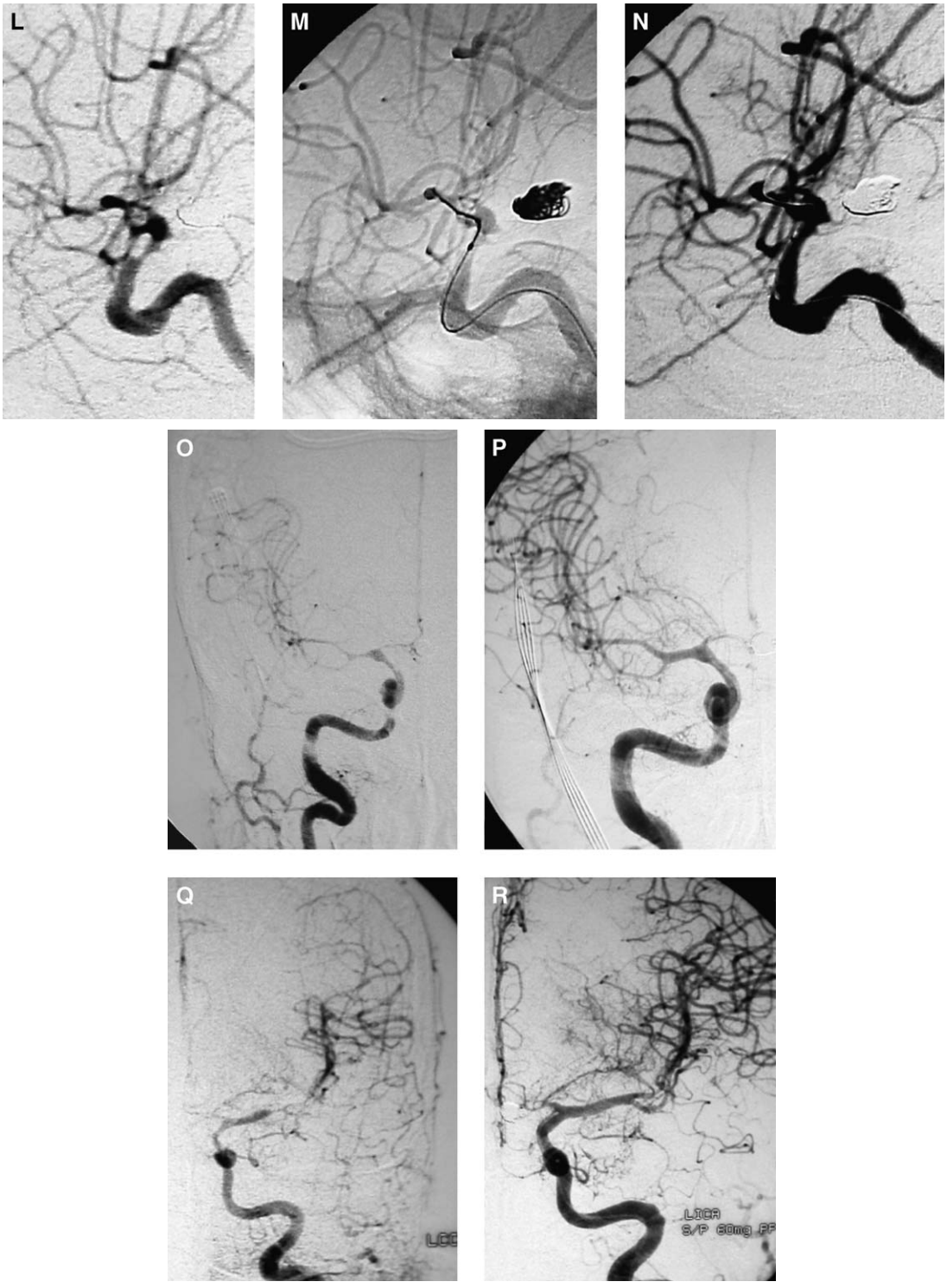


Fig. 3 (*continued*)



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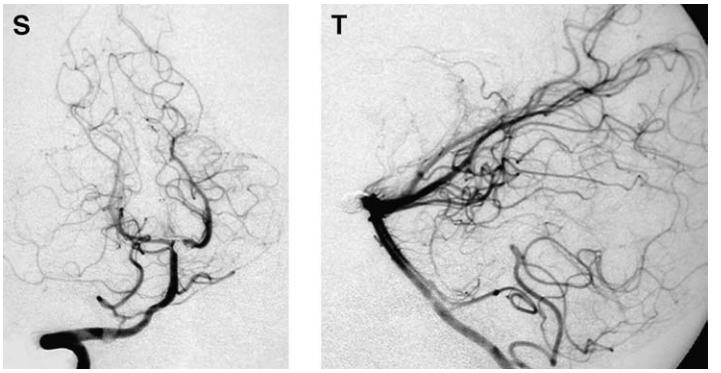

Fig. 3 (*continued*)

5.6% at 6 months. A negligible difference in the occurrence rate of clinically symptomatic vasospasm was observed in the Finnish randomized trial that compared surgery with GDC embolization for the treatment of acutely ruptured intracranial aneurysms [88]. No difference was found in the incidence of vasospasm in clipped and coiled aneurysms in two more recent studies [106,107].

Prevention and treatment of cerebral vasospasm

Given the importance of adequate management of vasospasm treatment in the overall outcome of patients with ruptured intracranial aneurysms and SAH, a discussion of the prevention and treatment of cerebral vasospasm is provided below.

Cerebral vasospasm is the delayed narrowing of the luminal diameter of the arteries at the base of the brain that occurs after SAH; it is often associated with radiographic or clinical evidence of diminished cerebral perfusion in the distal territory of the affected artery. Ischemic injury caused by vasospasm continues to be the leading cause of morbidity and mortality in patients with aneurysmal SAH [108]. In 1987, the Cooperative Aneurysm Study investigators reported an incidence of angiographic vasospasm exceeding 50%, with ischemic symptoms in 32% of these cases [109]. Despite extensive research regarding the prevention and treatment of this condition, these rates remain valid today [110–113]. Angiographic vasospasm is usually observed 3 to 5 days after the hemorrhage, with a peak at 5 to 14 days and resolution over the course of 2 to 4 weeks [114]. Approximately 50% of patients present with a clinical manifestation of delayed ischemic neurologic deficit (DIND). Among those with DIND, 15% to 20% experience permanent neurologic deficits or die from vasospasm, despite maximal medical therapy [115,116]. The DIND associated with symptomatic vasospasm usually appears shortly after the onset of angiographic vasospasm, with the acute or subacute development of focal or generalized symptoms and signs [114,117]. Cerebral angiography remains the "gold standard" for the evaluation and radiographic diagnosis of cerebral vasospasm. Transcranial Doppler ultrasound and newer modalities, such as CT perfusion [118], brain tissue oxygen content monitoring [119], microdialysis [120,121], and diffusion or perfusion magnetic resonance techniques [122,123], are helpful adjuncts in the early diagnosis and follow-up of this entity, however.

Awareness of the risk factors that predispose patients to developing vasospasm (location and volume of subarachnoid blood, younger age, and positive smoking history) [124–126] and early recognition of symptoms and clinical signs are essential for the optimal management of this condition. After early aneurysm clipping or embolization, the maintenance of a normovolemic state, as demonstrated by Lennihan et al [127], should be the aim (central venous pressure [CVP] >5 mm Hg, pulmonary artery diastolic pressure [PADP] >7 mm Hg) considering that prophylactic hypervolemic therapy (CVP >8 mm Hg, PADP >14 mm Hg) has failed to prove effectiveness in preventing vasospasm. Hypervolemic therapy should remain the initial treatment of choice when vasospasm exists, however. Pharmacologic treatment with calcium channel blockers, with nimodipine being the mainstay agent, has been

Table 1
Case series of balloon angioplasty in the treatment of cerebral vasospasm

Authors	No. patients and characteristics	Timing of angioplasty	Angiographic improvement (%)	Clinical improvement (%)	Recurrence (%)	Complications
Zubkov et al [145]	89 All grades with vasospasm	51 patients before surgery 16 patients after surgery	100	72	0 (at 5–7 days)	3 arterial ruptures, 1 TIA, 1 patient in worse condition
Eskridge et al [146]	48 No response to HV and HTN	<18 h of DIND	100	66	0	2 arterial ruptures, 2 rebleeds from unclipped aneurysms, 1 thrombosis (6 weeks after angioplasty)
Higashida et al [116]	13 No response to HV and HTN	No evidence of infarction on CT	100	69	0	1 hemorrhagic infarction
Coyne et al [137]	13 No response to HV and HTN	<48 h of DIND	100	31	—	None
Takahashi et al [162]	20 No response to HV and HTN	No evidence of infarction on CT	100	70	0	1 aneurysm rupture
Firlik et al [155]	14 No response to HV and HTN	Days 6–12	100	92 (12 of 13 patients) improved, 58% complete resolution	0	—
Nemoto [163]	10 No response to HV and HTN	—	60	40	—	—

Elliot et al [164]	Comparison between angioplasty and IA papaverine: 39 patients angioplasty, 13 patients papaverine No response to HV and HTN	—		(results measured by TCD imaging)	GOS score favorable in 67% of angioplasty cases	1	—
Polin and Kassell [165]	Comparison between 38 patients treated by balloon angioplasty and matched controls (North American Tirilazad Trial)	—		(angiogram)	Logistic regression: no difference in outcome between groups	—	—

Abbreviations: DIND, delayed ischemic neurologic deficit; GOS, Glasgow Outcome Scale; HTN, hypertension; HV, hypervolemia; IA, intra-arterial; TCD, transcranial Doppler; TIA, transient ischemic attack; —, not mentioned.

Modified from Newell DW, Eskridge J, Mayberg M, et al. Endovascular treatment of intracranial aneurysms and cerebral vasospasm. Clin Neurosurg 1992;39:348–60.

shown to improve the final outcome [128]. Nimodipine has been shown to improve the overall outcome in SAH cases in spite of not changing the absolute incidence of radiographic vasospasm [129]. The mechanisms by which nimodipine exerts its beneficial effect after aneurysmal SAH remain uncertain. There is no evidence that nicardipine and AT877 improve overall outcome. Mixed results have been associated with U74006F (tirilazad mesylate) [130,131].

Therapy with intravenous magnesium sulfate infusion has been suggested [132,133]. By acting as a calcium antagonist (calcium and magnesium have opposing effects on vascular tone), this agent might exert a neuroprotective effect, leading to a reduction in the incidence of clinical vasospasm as well as to an improvement in outcome for patients with symptomatic vasospasm [134]. Also, magnesium sulfate may compete with calcium for intracellular sites or limit the influx of calcium from damaged cellular membranes [134], producing beneficial effects by antagonizing the damaging actions of increased intracellular calcium concentration induced by cerebral ischemia [133].

Recently, lumbar drainage has been proposed as an effective way to reduce the risk of developing clinical vasospasm through removal of spasmogenic factors in the cerebrospinal fluid (CSF). In a retrospective study, Klimo et al [135] showed that CSF lumbar drainage performed after SAH was associated with a marked reduction in the risk of clinically evident vasospasm and its sequelae, shortened hospital stay, and improved outcome.

Endovascular treatment of cerebral vasospasm

Endovascular treatment with angioplasty and intra-arterially delivered drugs is often reserved for patients who fail to improve with the use of maximal medical therapy. In these cases, early endovascular intervention could play an important role (Fig. 3).

First described by Zubkov in 1984 [136], endovascular treatment of vasospasm using balloon angioplasty has been performed with increasing frequency in selected patients by mechanical dilation of the stenotic arteries through a microballoon catheter under fluoroscopic guidance. The results from initial clinical trials of angioplasty showed no recurrence of vasospasm within 7 days of treatment, with some rare cases of vessel dissection or rupture [116,137–140].

Angioplasty is effective in reversing vessel constriction and may lead to significant and sustained neurologic improvement, which is seen in many cases. Recurrent vasospasm at the angioplasty site is rare, although it may occur in vessel segments just proximal and distal to the site. After balloon dilation of arteries, transient alteration in myocyte structure [141], resulting in a degree of functional impairment of vascular smooth muscle cells persisting for at least 7 days, has been noticed. The long-lasting effect of balloon dilation is caused by disruption of the normal architecture of the collagen matrix in the arterial wall [142]. Hypothesizing that normal smooth muscle function is required for the development of vasospasm, preventive balloon angioplasty has been suggested by some authors [143]. In animal models of SAH, early angioplasty was shown to prevent the development of vasospasm [143]. On the basis of these findings, Muizelaar et al [144] conducted a phase I study in which 13 patients with Fisher grade 3 SAH underwent multivessel angioplasty within 3 days of SAH. None of these patients developed clinical vasospasm, but 1 of them had a vessel rupture during the procedure.

Table 1 [166] summarizes several case series in which balloon angioplasty was evaluated for the treatment of cerebral vasospasm. Despite successful dilation of vasospastic arteries, clinical outcome may not improve in one third of patients, however. Maximum benefits with angioplasty may be seen in patients with good clinical status at admission who experience subsequent acute deterioration because of vasospasm unresponsive to intensive medical therapy. Zubkov et al [145] found that improvement was most prominent in patients who presented with HH grade I or II and subsequently deteriorated; all such 13 patients in their series experienced neurologic improvement after angioplasty. Among the SAH patients with HH grade III at presentation, 85% improved with angioplasty compared with a 40% improvement in patients with HH grades IV and V. Angioplasty for patients with cerebral infarction does not seem to cause hemorrhagic transformation. Nevertheless, the clinical benefit seems to be limited [137]. Eskridge et al [146] found that angioplasty was most successful if performed within 12 hours of symptom onset. Other studies indicate that a shorter 2-hour window may exist to improve patient outcome before irreversible ischemic damage occurs [147]. Comparing two groups of patients undergoing endovascular treatment for symptomatic cerebral vasospasm (one group within 2 hours of symptom onset and the other 2 hours or more thereafter), Rosenwasser et al [147] found

Table 2
Case series involving intra-arterial injection of papaverine in the treatment of cerebral vasospasm

Authors	No. and characteristics of patients	Dosage and timing of papaverine	Angiogram improvement (%)	Clinical improvement (%)/results	Recurrence (%)	Comments
Kassell et al [157]	12	100–300-mg infusion	66	33	17	1 patient transient deterioration of mental status and hemiparesis
Kaku et al [156]	14 No response to HV and HTN, no evidence of infarction on CT	6–20 mg in repeated doses with angioplasty and IA nicardipine	92	80	0	Tachycardia
Clouston et al [153]	10 No response to HV and HTN	150–600-mg manual injection <48 hours after DIND	93	50	21	1 patient permanent monocular blindness, 1 patient arterial rupture without neurologic decline
Numaguchi et al [159]	Analysis of repeat IA papaverine in 24 patients (12 with no improvement)		100	50 after second infusion, 33 after third infusion	100	
Milburn et al [158]	34 patients, 81 arterial territories	300-mg infusion over 15 to 60 minutes, day 3 to day 19 after SAH	100	Not mentioned	100	
Fandino et al [154]	10 patients/23 vascular territories, no response to HV and HTN	360 mg/120 ml, infusion rate of 0.1 mL/s, days 4 to 16 after SAH	100	Good recovery 70%, moderate disability 30%	Not mentioned	Improvement of cerebral oxygenation
Firlik et al [155]	15 patients, 32 arteries		78	26	40% (6 of 15 patients)	4 complications: 1 brain stem depression, 1 systemic hypotension, 1 seizure, 1 symptom aggravation
Polin et al [167]	Comparison between 31 patients treated by balloon angioplasty and matched controls (North American Tirilazad Trial)	Not mentioned	13 (immediate)	Logistic regression: no difference in outcome between groups	Not mentioned	Not mentioned

Abbreviations: DIND, delayed ischemic neurologic deficit; HTN, hypertension; HV, hypervolemia; IA, intra-arterial; SAH, subarachnoid hemorrhage; TIA, transient ischemic attack.

Modified from Qureshi AI, Dawson R, Frankel MR, et al. Recent advances in the management of vasospasm in patients with subarachnoid hemorrhage. The Neurologist 1996;2:53–65.

Table 3
Advantages and disadvantages of balloon angioplasty and intra-arterial injection of papaverine for the treatment of cerebral vasospasm

Modality	Advantages	Disadvantages
Papaverine injection	Low risk of vessel injury	High incidence of spasm recurrence
	Possibility of treating branches distal to A1, M2, and P1	Can cause an increase in intracranial pressure
		Can cause seizures
Balloon angioplasty	Low incidence of spasm recurrence	Risky to treat branches distal to A1, M2, and P1
	Re-establishes vessel lumen diameter	Risk of vessel dissection by microwires
	May be useful as prophylactic maneuver	Risk of vessel rupture during balloon inflation
		May be limited by tortuous anatomy and severe spasm distal to the target vessel

similar good angiographic resolution of spasm in both groups (approximately 90% in each group) but distinct differences in sustained clinical improvement (70% in the early treatment group versus 40% in the delayed treatment group).

Despite continuous advances in catheter technology, vessel rupture and dissection remain the primary complications of angioplasty [138,146,148]. The performance of an angioplasty at a site proximal to an unclipped aneurysm may present a risk for rupture of the aneurysm [146]. Therefore, treatment of the aneurysm before angioplasty has been recommended for patients with unsecured ruptured aneurysms [138,149]. Murayama et al [150] reported their experience with combined endovascular treatment for cerebral aneurysm occlusion and vasospasm in a single session. They concluded that this combination is safe and feasible. In some cases, this is not possible and the severity of spasm precludes aneurysm catheterization. In such cases, dilation of the vessel with intra-arterial infusion of papaverine (30-mg dose) can facilitate microcatheter navigation.

Papaverine is an opium alkaloid that causes vasodilation of cerebral vessels through direct action on smooth muscle cells. It also prevents the constriction of smooth muscle secondary to a wide variety of stimuli [151]. It is essential that papaverine be infused just proximal to the spastic arterial segments to maximize the therapeutic effect of the drug [152].

Intra-arterial injection of papaverine for the treatment of cerebral vasospasm has been reported in several series (Table 2) [153–159]. The results of these studies suggest that the vasodilating effect of intra-arterial papaverine may be long lasting and even more apparent more than 10 days after the onset of SAH. The benefit was most prominent in patients who underwent angioplasty along with intra-arterial papaverine administration for symptomatic vasospasm in vascular territories not accessible to angioplasty [156]. Evaluation of various dosages indicated that using papaverine at a rate of 300 mg in 100-mL saline was adequate and safe in most cases [157]. Delayed responses (up to 30 minutes) have been described in some patients. Recurrence rates of up to 20% were seen in patients who received only intra-arterial papaverine. Vasospasm recurrence, probably caused by the short duration of action of the drug [152], has been described after papaverine administration [157] but seems to respond to a second infusion. Notable adverse effects of papaverine administration include increased intracranial pressure, seizures, and hemodynamic compromise [160,161]. A summary of the advantages and disadvantages of intra-arterial papaverine injection and balloon angioplasty for the treatment of cerebral vasospasm is provided in Table 3.

New horizons

Forthcoming additions to the current armamentarium of aneurysm treatment are likely to influence this field in the near future. A better understanding of aneurysm population genetics is likely to enhance the selection of candidates for treatment. The development of new devices, such as asymmetric stents, covered stents, coiling adjuncts, and improved bioactive agents, should allow for improvements in the effectiveness and durability of intracranial aneurysm treatment. Controlled studies to assess the impact of each addition to the endovascular armamentarium should be performed in an attempt to quantify the impact of any given new device or therapy on the outcomes of this condition. A better understanding of intra-aneurysm hemodynamics and the possibility of simulating aneurysm flow before treatment might make it possible to assess the

magnitude of different therapeutic options on the specific aneurysm harbored by a particular patient. In the future, it might be possible to use computer modeling of a patient's radiographic data to predict the changes caused by the placement of a coil or a stent.

Technologic advances are likely to continue to affect the treatment of intracranial aneurysms. The swing of the pendulum toward less invasive modalities seems to be irreversible, for the betterment of the patients.

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