

Multimodal treatment of Intracranial Aneurysm

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Abstract

Aneurysmal subarachnoid hemorrhage (SAH), despite improvements in imagistic and medical treatment, is still a serious disease with high rates of case mortality and morbidity (40%). Technical planning and therapy options of patients with aneurysmal SAH have changed during the angioCT and 3D angiography era, and long-term outcome has significantly improved during the past few decades. However, the outcome is still determined mainly by specialist experience and severity of initial bleeding or early rebleeding.

Keywords: aneurysm, surgical clipping, stent, coil, embolization

Introduction

Intracerebral aneurysms are of variable pathogenesis and usually the largest group is represented by saccular aneurysms formed at proximal cerebral vessel bifurcations. Likely based on a focal vessel wall weakness, fragile out-pouchings typically develop in areas of high shear stress and at areas of the vessel tree where there is higher intravascular pressure (along the proximal intracranial branching of the internal carotid artery and less frequently of the vertebro-basilar system). Initiation, growth and rupture of an aneurysm are

likely driven by a combination of several factors, each contributing to a variable degree in each of the evolutionary steps of an aneurysm's history.

Current treatment modalities include for open surgical treatment various techniques to reconstruct the artery (clips) or to reinforce the aneurysm wall (wrapping) or to bypass circulation of the vessel carrying an aneurysm (aneurysm trapping and bypass surgery). Endovascular treatment is less invasive techniques that have been developed on the principles of aneurysm filling with coils or polymers or vessel occlusion (aneurysm trapping).

More recently, vessel reconstruction with stents rather than aneurysm filling has been advocated as treatment. Both coils and stent techniques aim to induce slowing of blood flow and initiation of thrombosis within the aneurysm. Secondary vessel wall repair with scar tissue occurs within weeks. With small vessel wall defects, coil implantation seems to allow successful repair under this principle, provided that the lumen of the aneurysm pouch is suitable for coil introduction. With larger vessel wall defects in proportion to the vessel diameter (segmental defects), either the vessel must be occluded if tolerated by the patient, or the vessel is reconstructed with the use of stent implants.

Surgical techniques

The goal of surgical treatment is usually to place a clip across the neck of the aneurysm to exclude the aneurysm from the circulation without occluding normal vessels. When the aneurysm cannot be clipped because of the nature of the aneurysm or poor medical condition of the patient, the following alternatives may be considered:

1. Wrapping: Although this should never be the goal of surgery, situations may arise in which little else is possible (eg, fusiform basilar trunk aneurysms). Three situations can be described:

- to reinforce a residual or additional ectasia next to the clipped aneurysm, usually proximal to the clip;
- to treat an arterial ectasia, so called preaneurysmal ectasia, which proved not clippable at surgery;
- and -to protect a nervous or vascular neighbouring structure which was compressed by the clip grip.

Several agents for wrapping techniques can be used. The agents include cotton, muscle, silastic sheet, gauze, Teflon, adhesives (Biobond, fibrin glue, and polyglactin 910 fibrin sealant), collagen-impregnated Dacron fabric (Dupont, Wilmington, DE) or other polymer. Plastic resins may be slightly better than muscle or gauze for this purpose (Figure 1A,B). Some studies demonstrate benefit with plastic or other polymer, but others show no difference from natural course. In one study with long-term follow-up, the protection from rebleeding during the first month was unchanged, but, thereafter, the risk was slightly lower than for the natural history.

2. Trapping/Bypass: Effective treatment requires both distal and proximal arterial interruption with direct surgery (ligation or occlusion with a clip). Treatment may also

incorporate extracranial-intracranial (EC-IC) bypass to maintain flow distal to the trapped segment.

The balloon occlusion test (BTO) represents the main criteria for choosing an appropriate bypass conduit.

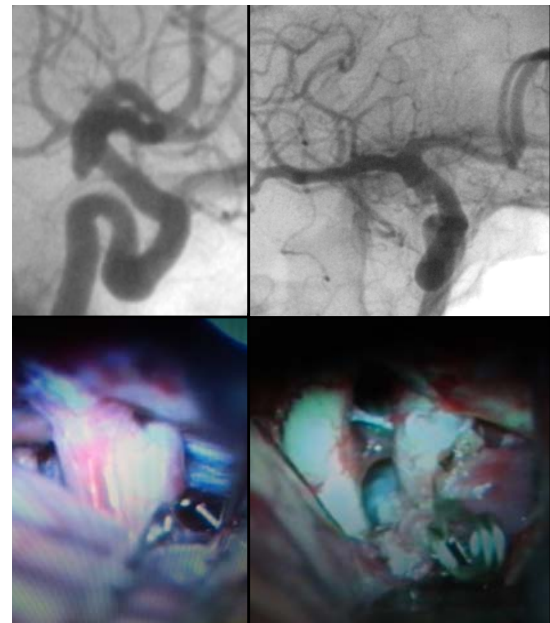


Figure 1 **A** Angiography images of a PCoA infundibular aneurysm; **B** – intraoperative images of infundibulum and wrapping with muscle

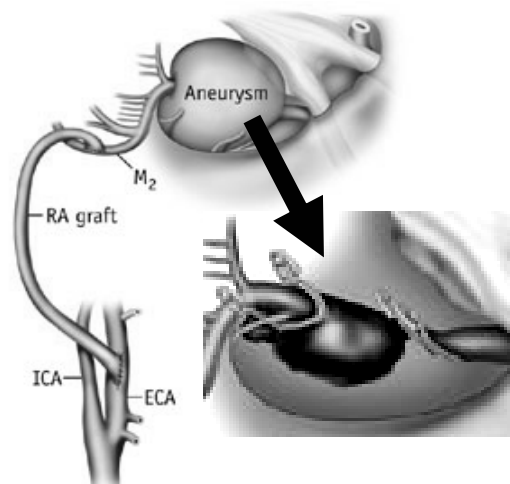


Figure 2 High flow bypass - external carotid artery-radial artery graft-middle cerebral artery (ECA-RAG-MCA) with aneurysm trapping

During the study, three different conditions were evaluated: -good clinical tolerance during the occlusion test, no sign of hypoperfusion at Diamox single positron emission computed tomography (SPECT); -good clinical tolerance, appearance of hypoperfusion at SPECT; -poor clinical tolerance. The ICA can easily be occluded without bypass in the first condition.

It is a routine to perform STA-MCA bypass with low flow in the second condition. It is general to perform saphenous vein graft (ECA-SVG-M2) or radial artery graft (ECA-RAG-M2) is generally performed in the third condition (Figure 2). Bypass surgery included low flow bypass such as superficial temporal artery to middle cerebral artery (STA-MCA) direct anastomosis and high flow bypass such as external carotid artery-radial artery graft-middle cerebral artery (ECA-RAG-MCA) bypass grafting and external carotid artery-saphenous vein graft-middle cerebral artery (ECA-SVG-MCA) bypass grafting. The Bypass surgery for posterior circulation aneurysms includes occipital artery-posterior inferior cerebellar artery (OA-PICA) and STA-P2 anastomosis.

3. Proximal (hunterian) ligation: Proximal ligation has been used with some success for giant aneurysms, particularly of the vertebrobasilar circulation. Advanced endovascular techniques, however, now offer better alternatives for such lesions.

4. Microsurgical clipping: After performing a craniotomy, use microsurgical techniques with the operative microscope to dissect the aneurysm neck free from the feeding vessels without rupturing the aneurysm. Final treatment involves the placement of a surgical aneurysm clip around the neck of the aneurysm, thereby obliterating the flow into the aneurysm. The goal at surgery is to obliterate the aneurysm from the normal circulation without compromising any of the adjacent

vessels or small perforating branches of these vessels (Figure 3A,B). The clips are manufactured in various types, shapes, sizes, and lengths and are currently manufactured to be MRI compatible.

Intraoperative angiography is now frequently used as an adjunct to clipping and permits confirmation of aneurysm occlusion and patency of nearby vessels. The frequency of its use varies widely; however, many vascular neurosurgeons choose to use this technique selectively for difficult aneurysms.

Recently, a new technique called near-infrared indocyanine green videoangiography (ICGA) has become popular as a novel less invasive way to assess aneurysm and blood-vessel patency during aneurysm surgery. After intravenous injection of the indocyanine green dye, an operating microscope equipped with appropriate software can within minutes detect blood flow within the vasculature using near infrared technology. The technique is less invasive than intraoperative angiography, but one disadvantage is that only vessels that can be seen by the operating microscope can be evaluated.

The operative morbidity and mortality associated with clipping depends on whether the aneurysm has ruptured; ruptured aneurysms are more treacherous to operate on and morbidity is higher. The risk of surgery for unruptured aneurysms is estimated to be 4-10.9% morbidity and 1-3% mortality. Many factors affect the morbidity rates, with larger aneurysms in certain locations and in older, less medically healthy patients faring less well. Surgeon experience likely plays a role, with high-volume surgeons working in high-volume institutions likely having lower morbidity; the definition of high-volume, however, is a matter of controversy.

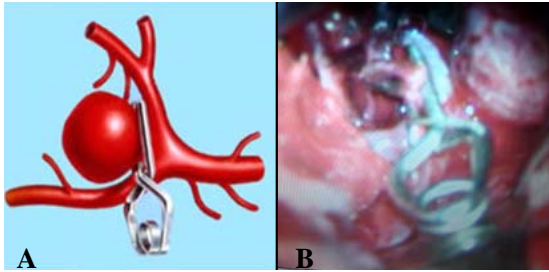


Figure 3A, B Schematic and intraoperative images of MCA bifurcation aneurysm clipped

Coiling technique

The use of detachable coils is a safe and effective alternative to surgical clipping of intracranial aneurysms. At present there is a wide range of coils, but their basic principles are similar to that of bare GDCs and include 3D and 2D coils. Variable degrees of stiffness are available, including standard, soft, and ultrasoft coils. Many investigations are currently evaluating new coils, including biologically active coils, radioactive coils, and coated coils with a swelling hydrogel. The aim of these innovations is to promote intra-aneurysmal clot organization and fibrosis or to increase packing density, which is associated with a higher long-term occlusion rate.

All endovascular procedures were performed under general anesthesia and systemic heparinization. A bolus infusion of heparin (30–40 IU/kg body weight) was followed by a continuous drip (1000–1500 IU/h), with the purpose of doubling the baseline activated clotting time. No patient was placed on of aneurysm – pattern vessel. Special attention should be considered in aneurysm sac catheterization, because there is a risk of aneurysm perforation by the top of the microcatheter or microguidewire in time of manipulation. The first coils selected to use should be the coil which enables to obtain the widest 3D configuration when is detached. This will provide the basic skeleton for anchoring the

following coils. Aneurysm packing, by the use of an Excelsior 10 microcatheter (Target Therapeutics), is obtained by forming a basket with one or more 3D coils that were subsequently filled with smaller 2D coils. In all cases, it's recommended to pack the aneurysm with the same type of coils. Soft, ultrasoft, or both soft and ultrasoft coils are used at the end of the procedure to complete aneurysm obliteration. In case of Matrix coils, to avoid friction inside the microcatheter, the coils are placed in a saline solution for at least 60 seconds to hydrate the polymer completely. When packing difficulties (high frictions between coils, compartmentalization) with Matrix coils were encountered because of their stiffness. In case of a coil helix migration into the parent vessel during coil positioning or due to an improper configuration for the next coil introduction, withdrawal of the coil and providing a new optimal configuration before deployment is recommended. With the successive introduction of the coils may become difficult to angiographical image the position of new coils introduced. However placement should be continued until the alignment of radio-opacity markers is obtained (on the metal guide on the delivery microcatheter) thus ensuring a safe detachment.

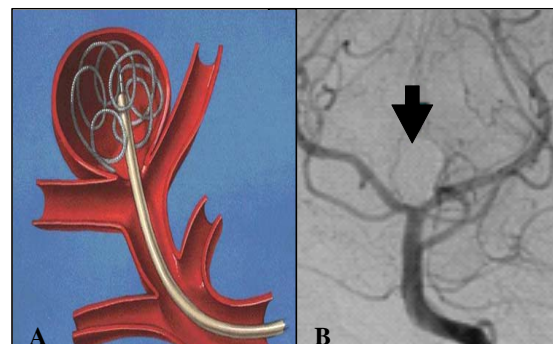


Figure 4A, B Schematic and angiographic images of basilar tip aneurysm coiled

Using fluoroscopy with digital subtraction, detachment of each coils can be traced in real time. After the desired position for the coils is achieved, the detachment device is connected to the proximal end of coils delivery guidewire, and the disconnection it tocks place within a 2-60sec depending on the type of disconnection mechanism (Figure 4 A, B).

After detachment, the delivery guidewire is withdrawn, and if necessary a new coils is added into the aneurysm until a dense packing of coil configuration is achieved. The coils mass so obtained will lead to a stagnation of blood flow in the aneurysm sac, a thrombosis triggering antiplatelet medication before treatment.

Technique of endosaccular coil placement procedure begins with a classic angiographic images acquisition. After obtaining the best working position, a road-map image of the pattern vessel is performed and the aneurysm sac is selectively catheterized with a microcatheter with two radio-opaque coaxial markers. The catheter tip may be manually curved to fit the complex anatomical configuration phenomenon and aneurysm isolation from blood circulation through the formation of neo-endothelium over its neck.

Balloon-assisted technique

The neck remodeling or balloon-assisted embolization technique originally described by Moret et al has been used in the endovascular treatment of wide-necked aneurysms or in aneurysms with an unfavorable neck-to-fundus ratio in which a standard coil placement technique may be unsuccessful.

The procedures begin with 7F and 6F femoral sheaths insertion into both femoral

arteries, and a digital subtraction angiography is performed. The parent vessel is catheterized with a microcatheter (Excel 14, Excelsior 10–18, Target/Boston Scientific, Fremont, CA; Rapid Transit 18; Cordis, Miami Lakes, FL) placed near the aneurysmal neck. The calibers of the parent arteries and the size of the aneurysmal neck were approximately calculated, and a microballoon size is chosen on the basis of these calculations. A nondetachable balloon (Sentry 10–15 mm, Target/Boston Scientific, or Hyperglide, Micro Therapeutics Corp, Irvine, CA) will be then advanced through the contra-lateral femoral sheath to the neck of the aneurysm. The microcatheter is advanced into the aneurysm dome, while the balloon is uninflated. Finally, the balloon is carefully inflated to occlude the aneurysmal neck, while the tip of the microcatheter is in a location in the body of the aneurysm that is suitable for coil deposition. Coils of appropriate diameter, length, and stiffness were deposited in the aneurysm dome and detached electrolytically. For balloon inflation, a 1-mL precision injector with threaded plunger syringe (MicroTherapeutics) is used (Figure 5A,B).

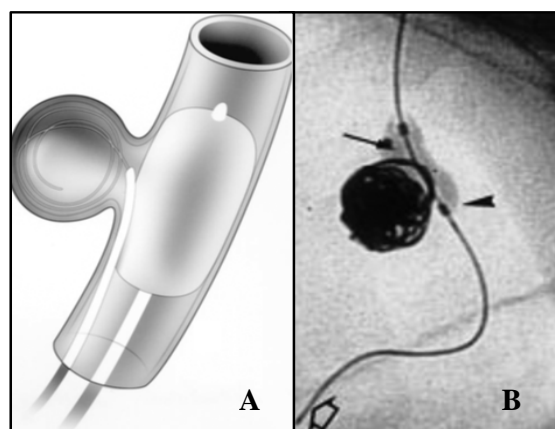


Figure 5 A, B Schematic and angiographic images of ICA aneurysm coiled by balloon-assisted technique

The microballoon will never be inflated more than its nominal volume. The initial framing coil is deployed through the intraaneurysmal microcatheter, after which the balloon was deflated and 1 to 2 minutes were permitted to elapse before the coil is electrolytically detached so that stability (did not herniate out of the aneurysm sac into the parent artery) of its placement could be ascertained. If no coil movement was noted, the coil is detached and the balloon reinflated before deployment of the next coil. This process is repeated until the aneurysm is embolized as completely as possible. By the time the balloon was inflated at the end of the procedure, the microcatheter had always been withdrawn.

Stent and stent-assisted coil techniques

Surgical or endovascular occlusion of small aneurysm is difficult because of tearing or narrowing the parent vessel during clipping and insufficient saccular space to deploy coil. Fusiform aneurysm is another difficult and dangerous type of vascular lesion due to its fragile wall and indistinct neck. Initially the “deconstructive” methods, described as proximal occlusion or trapping, had been treatment of choice for fusiform aneurysm. Begin with the development of stent material and technique, the new concept has been evolved recently into “endovascular bypass” or “endovascular reconstruction” which is enabled to preserve affected parent artery and perforators, and occlude aneurysm safely. Compared with the deconstructive methods, the reconstructive ones may be more definitive and optimal treatment physiologically.

The use of stents in intracerebral aneurysms treatment has two principles

technique: sole stenting technique and stent-assisted coiling.

Sole stenting technique (stent placement across the neck of an aneurysm causes) is one of reconstructive methods based on hemodynamic flow diversion principle that can, on occasion, cause aneurysmal occlusion/thrombosis without the need to introduce coils (Figure 6). Stent-assisted coiling technique is a technique of using an intravascular stent to create a bridging scaffold followed by endovascular placement of coils through the interstices of the stent into a wide-necked or fusiform aneurysm.

The most used stents specifically designed for intracranial treatment are Neuroform stent (Boston Scientific), Leo stent (Balt), self-expanding Nitinol stent (Cordis Enterprise), and electrolytically detachable SOLO stents. Leo and Cordis Enterprise stents are of closed-cell design and Neuroform stents are of open-cell design. The closed-cell design allows all coils to be placed within the aneurysm and outside the flow of the parent artery with stent-assisted coiling.



Figure 6 Angiographic image of anterior choroidal artery aneurysm treated by sole stenting technique

Neuroform stents have the disadvantage of being non-retrievable and strut prolapse can occur in curved vasculature due to its open-cell design. Both Leo and Enterprise stents can be retrieved or repositioned even after 90% of deployment; this allows safer and more precise deployment.

A new stent with a more tightly constructed mesh, Pipeline Chestnut Medical, designed to cause increased hemodynamic diversion relative to the Neuroform or Enterprise, is undergoing experimental investigation and has already been used effectively in several patients. Before choosing the endovascular device to use, we had to resolve 2 technical issues: sharply define the required diameter of the device, and precisely determine whether a balloon-expandable stent (BES) or sirolimus-eluting stent (SES) was to be deployed. To solve the first issue, we chose a device with a diameter closest to the size of the diameter of the vessel to receive a stent. A BES is indicated if we hoped to modify the angle of the vessel and an SES when a modification of the laminar flow was deemed to promote aneurysm thrombosis.

Technique of Stent Deployment and Endosaccular Coiling

By using magnified fluoroscopy and digital biplane road mapping, the microcatheter was navigated into the cerebral vessel, distally from the neck of the aneurysm which was passed with the aid of a 0.010- or 0.014-inch guide wire (Fas-Dasher; Boston Scientific/Target or Silver Speed, Medtronic MIS, Sunnyvale, CA).

The stent is preloaded in a 3F delivery microcatheter. A separately packaged stabilizer is inserted through the hub of the stent delivery microcatheter until its tip abuts the stent.

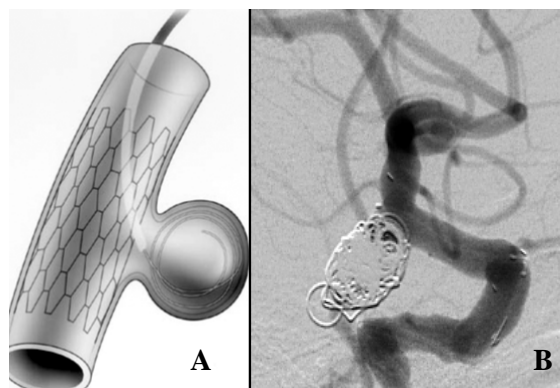


Figure 7 A, B Schematic and angiographic images of posterior communicating artery aneurysms coiled by stent-assisted technique

The stabilizer is essentially a 2F microcatheter that can be placed inside the 3F stent delivery microcatheter over a 0.014-inch wire. The delivery microcatheter is placed coaxially through a 6-F guide catheter (Envoy, Cordis Neurovascular; or Guider, Boston Scientific/Target). The microcatheter is exchanged over a long micro guide wire which is used to introduce the stent system. When using BESs, we inflated the devices to their nominal pressure (8 atm in most cases). In case of SES system, the stent delivery microcatheter and stabilizer are advanced over an exchange wire as a unit and positioned until the aneurysm neck is centered between the ends of the stent. The stent is deployed by gently retracting the microcatheter while holding the position of the stent fixed with the stabilizer. This unsheathes the stent and allows expansion within the vessel. As the stent deploys, the four marker bands on each end define the endoluminal surface. After deployment of the stent, the stent system with the exchange wire is removed, and a microcatheter with a preshaped soft microguidewire (Transend-14; Boston Scientific, Fremont, CA) can be used to

enter the aneurysm through the interstices of the stent. Finally, detachable coils are introduced into the aneurysm and detached as usual until occlusion is achieved. After sufficient packing of the aneurysm, the microcatheter is pulled back.

Once the stent and coils were placed, DS angiography sequences were performed to assess the deployment of the stent (Figure 7A,B); the patency of the parent vessel and of the perforating or adjacent vessels; the modification of the flow within the aneurysm; and the distal arterial tree.

Liquid embolic occlusion technique

Onyx (Micro Therapeutics, Inc., Irvine, CA) is a liquid embolic material designed for endovascular use. It is an ethylene vinyl alcohol copolymer dissolved in the organic solvent dimethyl sulfoxide (DMSO). The mechanism of action consist in embolic material precipitation when it comes into contact with an aqueous solution with formation of a soft spongy polymer cast, initially with an outer layer, remaining semi-liquid centrally. As further material is injected into the cast, it fills the space into which it is injected, and then additional material breaks out through the outer layer of the existing cast.

In the treatment of intracranial aneurysms, the material, as currently used, is constrained by the placement of a balloon over the neck of the aneurysm. The material solidifies completely over a period of about 10 minutes with diffusion of the solvent DMSO.

As part of the evaluation for the use of Onyx during the procedure, a seal test was performed to determine whether the neck of the aneurysm could be satisfactorily occluded by the balloon. A gentle injection of contrast material was made into the

aneurysm via the microcatheter with the balloon inflated; stasis of contrast material was seen when the aneurysm neck could be controlled without significant leakage. This also ensured that no adjacent side branches filled. If adequate control of the aneurysm neck could not be obtained with the balloon, the Onyx treatment is not recommended.

20- and 30-mm braided-shaft balloons (Hyperglide; Micro Therapeutics, Inc.) were available, and most recently the highly compliant Hyperform balloon (Micro Therapeutics, Inc.), designed to occlude bifurcation aneurysms, became available. These new devices have improved the range of aneurysms in which the neck could be satisfactorily occluded.

Procedural Technique

The technique begins with the placement of a highly compliant DMSO-compatible occlusion balloon (Equinox or Hyperglide) in the parent vessel over the neck of the aneurysm. The balloon is left deflated while a DMSO-compatible microcatheter (Rebar, Micro Therapeutics, Inc.) is placed within the aneurysm. A slow test injection 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 residue of contrast material, and primed with DMSO with a volume to match the catheter dead space. Onyx (HD 500) is then introduced into the microcatheter. Once sufficient volume (usually 0.2 mL) of the material has been injected, Onyx approaches the end of the microcatheter, and the balloon is inflated to the predetermined volume. Onyx is

injected at a rate of about 0.1 mL per minute by using the specifically designed Cadence Precision Injector syringe (Micro Therapeutics, Inc.), which operates by a screw thread. Because of the viscosity of Onyx, it accumulates around the tip of the microcatheter and gradually enlarges to form a kernel that stays attached to the end of the microcatheter. After each injection, the balloon is left inflated for another 3 minutes and then deflated to allow cerebral reperfusion for at least 2 minutes; then the cycle is repeated. With each injection, new portions of the aneurysm fill, and eventually the material flows down to the margins of the balloon and occludes the neck of the aneurysm (Figure 8 A, B). When the material is in contact with the balloon, injection is slowed or stopped with brief 15–30-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 that is sometimes observed with wide-neck large and giant aneurysms. The microcatheter position is not adjusted at all once injection has started.

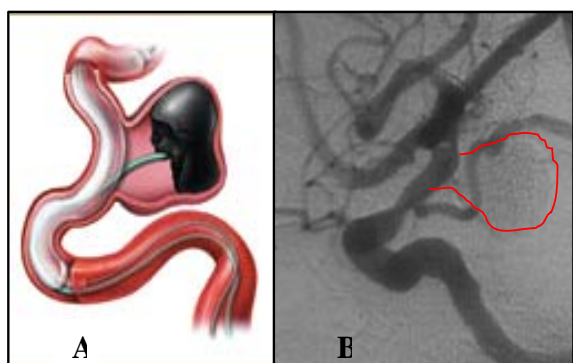


Figure 8 A, B Schematic and angiographic images of posterior communicating artery aneurysms occluded with onyx (red contour is the limit of aneurysm filled by onyx)

Following angiographic confirmation of the complete or satisfactory occlusion of the aneurysm, the catheter syringe is decompressed by aspiration of 0.2 mL 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.

Conclusions

Most of the literature studies show that both deconstructivtion and reconstructive (microsurgical clipping and endovascular therapies) treatment techniques are highly effective at preventing acute rebleeding from ruptured aneurysms. It is increasingly clear that excellent results can be achieved with clipping and coiling, and that outcomes are better in centers with experience and expertise in both techniques. Also, specific treatment strategies must be particularized, taking into consideration the patient's age, neurological status, and medical comorbidities, as well as angioarchitectural aspects such as aneurysm location, size, geometry, neck to dome ratio, and intraluminal presence of thrombosis or calcification.

It was already demonstrated that, even a densely packed aneurysms have a propensity to coil compaction and subsequent recurrence, necessitating longterm follow-up and possibly further treatment, even years after the initial procedure. Recurrence after complete aneurysm clipping is extremely unlikely, and late invasive imagistic investigation is probably not necessary. However, if there is incomplete clipping or multiple aneurysm situation, continued surveillance is warranted.

A multidisciplinary approach emphasizing honest and valid assessment of local expertise and unbiased collaboration between surgeons and interventionalists is critical to decision making and will lead to improved outcomes.

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