STROKE (HP ADAMS JR, SECTION EDITOR)

Endovascular Treatment of Ruptured Intracranial Aneurysms

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Abstract Aneurysmal subarachnoid hemorrhage (SAH) is a catastrophic neurologic event. Early triage of patients with SAH should include cardiopulmonary stabilization, neurologic assessment, and imaging. Conventional angiography with 3dimensional rendering is necessary to accurately assess aneurysm morphology and location, so that treatment can be planned appropriately. Current evidence suggests that coil embolization can be beneficial for aneurysms amenable to endovascular treatment. The use of remodeling techniques has expanded the range of aneurysms treatable by endovascular means. Balloon remodeling can be a powerful technique for treating ruptured aneurysms with unfavorable morphology. However, stent-assisted technique is associated with significantly higher complication rates in ruptured aneurysms and requires dual antiplatelet agents, and should therefore be considered with great caution for ruptured aneurysms. Complications of ruptured aneurysm embolization include aneurysm perforation, which should be addressed with immediate occlusion of the aneurysm, and thromboembolism, which can be managed most effectively with glycoprotein IIb/IIIa inhibitors.

Keywords Aneurysm · Coil embolization · Subarachnoid hemorrhage · 3-dimensional angiography · Balloon-assisted coiling · Stent-assisted coiling

Introduction

Treatment of ruptured aneurysms has evolved tremendously since Walter Dandy first described surgical clipping of an intracranial aneurysm [1]. The concept of endovascular

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approaches to aneurysm treatment became recognized in 1974 when Serbinenko described the use of detachable balloons for aneurysm embolization [2]. The modern era of endovascular aneurysm treatment began in 1991 when Guglielmi and Vinuela performed the first endovascular treatment of an intracranial aneurysm with detachable coils [3]. The FDA subsequently approved the use of such coils for treatment of aneurysms in 1995. Since then, the proportion of aneurysms treated by endovascular means has been steadily growing relative to open craniotomy and surgical clipping.

One reason for the increasing preference for endovascular treatment is the results of the International Subarachnoid Aneurysm Trial (ISAT), which compared surgical clipping with endovascular coil embolization in patients with ruptured aneurysms thought to be equally amenable to either [4, 5]. In that randomized study of 2143 patients, endovascular treatment conferred an absolute risk reduction of death or disability of 7.4 % (23.5 % for endovascular, 30.9 % for clipping; P=0.0019) at 1 year. These results and others provide the evidence to support current SAH management guidelines, which state "endovascular coiling can be beneficial" for patients with ruptured aneurysms that are amenable to either clipping or coiling [6••].

Endovascular treatment of ruptured aneurysms has now firmly become a part of the management of patients with SAH. There are many aspects to endovascular aneurysm treatment, including treatment planning, imaging, operative techniques, anesthesia, and management of complications, which can all effect patient outcomes. Special attention must be paid to all of these facets of treatment in order to achieve success.

Triage and Pre-Operative Imaging

Patients with aneurysmal SAH are very ill. Initial triage must focus on stabilization of airway, gas exchange, and hemodynamics. Thereafter, noncontrast CT typically

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provides the diagnosis of SAH. Initial assessment should include the use of a SAH grading system—the World Federation of Neurological Surgeons and the Hunt and Hess scales are the most widely recognized—for prognostic purposes [7]. Patients with poor grade or with hydrocephalus typically will require an external ventricular drain (EVD). It is usually most appropriate to have the EVD placed in advance of endovascular treatment. This allows for additional monitoring of intracranial pressure during the endovascular operation, and avoids potential complications related to placement of an EVD after the intra-operative administration of heparin or other antithrombotics. Once the patient has been diagnosed and stabilized, definitive aneurysm imaging is necessary.

Precise characterization of aneurysm morphology is necessary to choose optimum treatment modality. Aneurysms with a narrow neck-the junction between the aneurysm and the parent vessel-are typically regarded as endovascular candidates because the coils are likely to stay within the aneurysm sac. Embolization is usually possible with neck size of <4 mm or a dome-to-neck ratio of greater than 2, although newer techniques allow endovascular treatment of aneurysms with wider necks. Aneurysms that incorporate branches into their neck or dome may be more appropriate for microsurgical clipping, because these branches can be preserved or reconstructed with open neurosurgical techniques. Aneurysm location also plays an important role in choosing treatment modality. Because of difficulty with surgical access, many aneurysms arising from the basilar artery or its branches are often regarded as best treated by endovascular means. There are many nuances of aneurysm location and morphology that factor into treatment decisions, and current guidelines recommend referral to centers that have both experienced cerebrovascular surgeons and endovascular specialists [6..] to allow for multidisciplinary assessment.

The ability of initial imaging to define aneurysm location and morphology is thus very important. MRA, CTA, and conventional angiography have all been used for the initial detection of aneurysms with varying degrees of sensitivity, specificity, and spatial resolution. The sensitivity of MRA in detecting intracranial aneurysms is size-dependent; aneurysms>5 mm are very likely to be detected with MRA, but sensitivity drops off precipitously for aneurysms below 5 mm [8]. Even with modern improvements in MRA technology and increased sensitivity [9], MRA can be timeconsuming and therefore more cumbersome in the setting of acute SAH. In contrast, CTA can be performed quickly and reliably at high-volume centers and may offer an advantage in terms of sensitivity, which has been reported to be as high as 100 % compared with conventional angiography [10].

While the ability to detect aneurysms with non-invasive imaging approaches that of conventional angiography, there remains a significant difference in terms of spatial resolution and definition of morphology. Conventional angiography continues to provide additional information above and bevond what can be gathered by CTA or MRA, which often has important therapeutic implications [11•]. In particular, 3dimensional (3D) angiography allows the operator to manipulate a computerized rendering of the aneurysm, which supports a better understanding of aneurysm morphology (Fig. 1). Modern 3D angiography also allows the operator to take accurate measurements and to identify a best working projection prior to embolization, all without exposing the patient to additional radiation or contrast load [12]. Furthermore, diagnostic angiography creates the basic platform for continuing with endovascular therapy, which offers an obvious logistical advantage. Thus, for multiple reasons conventional angiography remains the standard of care for the evaluation of patients with SAH [6••].

Technical Considerations

3D Angiography

As mentioned above, 3D angiography provides important anatomic information. Thus, any endovascular approach to aneurysm treatment should begin with 3D angiography. After image acquisition, manipulation of the 3D rendering by the interventionalist is necessary. This is because the 3D rendering is subject to nuances of windowing, which can



Fig. 1 Dimensional rotational angiography provides the ability to understand aneurysm morphology and relationship to neighboring branches. This example shows a flame-shaped aneurysm of the left middle cerebral artery bifurcation, involving both branches

hide small branches that may arise near the aneurysm. In addition, the manual manipulation of the 3D image leads to a much better spatial understanding of the aneurysm [13], which supports more appropriate and directed treatment. The 3D rendering also allows for clear definition of the aneurysm neck (Fig. 1). Once the neck is defined, manipulation of the 3D rendering supports the identification of the best working projection, which is the best viewing angle to differentiate the aneurysm neck from parent vessel and to identify any neighboring arteries. Frequently, 2 different views can be very helpful in simultaneously visualizing the aneurysm and its relationship with the parent vessel or neighboring vessels. At other times, it is helpful to visualize the aneurysm with the working projection, and to visualize the guide catheter within the parent vessel in another projection. Both situations illustrate the utility of biplane angiography, which is a typical feature of modern neuro angiography suites [14].

Once the aneurysm morphology is clearly understood, a treatment plan can be developed. The goal for endovascular treatment of an acutely ruptured aneurysm should be to completely occlude the aneurysm and thus protect it from re-rupture. Sometimes however, aneurysm shape may preclude complete occlusion with primary coil embolization alone. In such cases there are several options—partial embolization, balloon-assisted coil embolization, or stent-assisted coil embolization.

Aneurysm Catheterization and Coil Embolization

Endosaccular embolization of an aneurysm begins with appropriate proximal arterial access. Typically, a 6 French guide catheter is navigated into a safe position in the cervical vasculature. This may provide adequate proximal support but sometimes more distal support is needed, particularly in the case of more distal aneurysms, significant tortuosity, or small aneurysms. In such cases, a distal access catheter (approximately 4 French) can be navigated more distally and offer more support to the microcatheter [15]. Regardless of whether a distal catheter is used, a microcatheter must then be navigated into the aneurysm itself. This is done using roadmapping technique, wherein a subtracted image of the arterial anatomy is superimposed on real-time fluoroscopy, and can be based on 2D or 3D imaging [16]. The microcatheter, typically approximately 1.7 to 1.9 French, is navigated over a soft-tip microguidewire, typically 0.010 to 0.014 in. in diameter. Once the catheter is safely in a stable position, detachable coils are used to occlude the sac of the aneurysm.

The first coil—the framing coil—creates a basket across the neck of the aneurysm, which contains the subsequent coils. Thus, the first coil deployed is the largest, should be sized to match the diameter of the aneurysm, and is typically a spherical shape. Subsequent coils are smaller and softer, may be spherical or helical, and act as filling. Coils can be bare platinum or coated with a bioactive material designed to increase the volume of the coil mass [17] or to promote thrombosis and fibrosis [18]. However, there has been no evidence that these bioactive coils improve rates of aneurysm occlusion [19, 20], and there have been several reports that suggest some bioactive coils may have higher recanalization rates [21] or retreatment rates [22•]. Though there is currently no evidence to support the use of coated or bioactive coils over bare platinum coils, individual interventionalists may prefer particular coil types for specific aneurysm configurations.

Whichever coil type is used, interval control angiograms are performed periodically to assess for aneurysm occlusion. When to stop the procedure depends on progressive angiographic occlusion, resistance to coil deployment, and possibility of herniation into the parent artery [23]. After the microcatheter is removed, a final post-embolization angiogram is typically done to confirm that there is no evidence for thromboembolic complications and to assess for completeness of aneurysm occlusion.

Remodeling Techniques

Not infrequently, the morphology of the aneurysm neck will not support primary coil embolization. Specifically, attempting coil embolization of aneurysms with a wide neck may result in herniation of the coil into the parent vessel. In such cases, a balloon may be used to achieve temporary remodeling of the neck to support the creation of a cohesive coil mass [24]. In this technique a compliant, non-detachable balloon is temporarily inflated in the parent vessel across the neck of the aneurysm while a coil is deployed into the aneurysm sac. Before the coil is detached, the balloon is deflated and the coil mass is assessed for signs of movement. Once it is confirmed that the coil mass remains in the aneurysm, it may be detached. The process can then be repeated for subsequent coils. This technique enables the embolization of wide neck aneurysms that may not have otherwise been treated by endovascular means, and thus is an important option for patients with subarachnoid hemorrhage. Some studies have suggested that there is a higher rate of complications with balloon-assisted coiling, including thromboembolism and aneurysm rupture [25]. However, subsequent prospective studies have shown similar rates of intra-operative aneurysm rupture and thromboembolic events, with overall complication rates of 17.4 % for primary coil embolization and 16.9 % for balloon-assisted coiling of ruptured aneurysms [22•, 26•, 27•]. With appropriate technique, balloon remodeling provides a powerful approach the treatment of ruptured aneurysms, especially because no hardware is left behind in the parent artery.

Aside from balloon remodeling, stents can also be used to remodel the parent vessel at the neck to achieve coil embolization of wide neck aneurysms [28]. Stent-assisted coil embolization entails the placement of either an Enterprise (Codman & Shurtleff Inc., Raynham MA) or NeuroForm (Stryker Neurovascular, Fremont CA) stent across the neck before proceeding with coil embolization of the aneurysm. The microcatheter may be navigated through the struts of the stent and into the aneurysm (mesh technique) or be placed in the aneurysm before the stent is deployed (jailing technique) [29]. Regardless of the approach used, a stent provides the obvious advantage of preventing coil prolapse out of the aneurysm and into the parent artery. It has also been postulated that a stent may provide additional hemodynamic benefit by diverting flow through the stent, and by acting as a scaffold for endothelialization across the neck, thereby reducing the likelihood of aneurysm recurrence [30•]. Stent-assisted coiling is generally associated with low rates of morbidity in the treatment of unruptured aneurysms, though complications appear to be approximately10fold more frequent in patients with SAH [31, 32]. Amenta et al. reported a major complication rate of 15.4 % in a series of 65 SAH patients treated with stent-assisted coiling [33], and Golshani et al. reported a 17 % complication rate in 36 patients [34]. Most complications were thromboembolic.

A stent represents a permanent implant in the normal artery and requires the use of dual antiplatelet therapy with aspirin and clopidogrel. In elective stent-assisted coil embolization of unruptured aneurysms, most practitioners will start these medications 3-7 days prior to the procedure to ensure adequate platelet inhibition prior to stent implantation. However in the case of SAH, most physicians are rightly hesitant to use these medications before the aneurysm is secure. Furthermore, many SAH patients require ventriculostomy, which can be complicated by the use of dual antiplatelets. For these reasons, many centers don't initiate aspirin and clopidogrel until after stent placement and/or coil placement. This, combined with the fact that patients with SAH are also in a prothrombotic state [35], likely accounts for the dramatically higher rate of thromboembolic events with stent-assisted coiling for acutely ruptured aneurysms. In fact, most thromboembolic events occurred in patients that were not pre-treated with antiplatelets [34], and lower rates of thromboembolism (9 %) have been reported with use of these medications prior to stent placement [36]. But as mentioned above, this may increase the risk of ventriculostomy-related hemorrhage. In a retrospective study, Kung et al. found 3.4 times more hemorrhage in SAH patients treated with stent assisted coiling compared with primary coil embolization (32 % and 14.7 %, respectively) [37]. Given the high rates of thromboembolic and hemorrhagic complications, stent-assisted coiling should probably be avoided in acutely ruptured aneurysms, and only considered in highly-selected cases that are unlikely to require ventriculostomy.

One of the newest endovascular treatments for intracranial aneurysms is the use of flow-diverting stents, such as the Pipeline Embolization Device (Covidien / ev3 Neurovascular, Irvine CA). These devices disrupt flow into the aneurysm and allow progressive thrombosis within the aneurysm, without the need for endosaccular embolization [38]. Clinical results have been very encouraging for unruptured large and wide neck aneurysms [39, 40]. However, given the delayed nature of aneurysm thrombosis with flow diversion and the need for dual antiplatelet therapy, this treatment should not be considered for acutely ruptured aneurysms [41].

Intra-operative Management and Anesthesia

Blood Pressure

There is no consensus as to the optimum blood pressure to prevent rebleeding in patients with SAH prior to aneurysm treatment. However, there have been some reports of an association between hypertension and rebleeding rates [42]. Thus, current guidelines suggest that blood pressure be monitored and controlled to balance the risk of aneurysmal re-rupture and cerebral hypoperfusion [6..]. The most effective antihypertensives for this purpose are probably intravenous nicardipine or labetalol. To minimize the risk of cerebral hypoperfusion, it is probably reasonable to allow modest blood pressure elevation (MAP<110, SBP<160), which does not appear to increase the risk of rebleeding [43...]. Sudden increases in blood pressure, such as at the time of endotracheal intubation, should also be avoided [44]. Once the aneurysm has been secured higher blood pressure can be tolerated, particularly in the setting of delayed cerebral ischemia due to vasospasm.

Anesthesia

In general, most practitioners utilize general anesthesia with endotracheal intubation during embolization of ruptured aneurysms. However, some centers perform these procedures with conscious sedation, which allows neurologic assessment throughout the procedure [45]. Potential disadvantages of this practice include patient motion that could interfere with the procedure, patient discomfort, increased risk of intraoperative re-rupture of the aneurysm, and the need for emergent intubation in patients with abrupt changes in mental status. Given the limited advantages of conscious sedation for the endovascular treatment of ruptured aneurysms and the risk of severe complications, general anesthesia with careful monitoring is recommended for endovascular treatment of patients with ruptured aneurysms [23, 46].

Antithrombotics

Thromboembolic events are some of the most common complications of neuro interventional procedures. Therefore, most centers have a protocol for anticoagulation during cerebrovascular interventions-a typical protocol might call for a systemic heparin bolus to achieve an activated coagulation time of 250–300 s [47]. Other centers premedicate patients with antiplatelets, even when the use of a stent is not planned [23]. Of course, this should be avoided in patients with SAH as it could significantly increase the risk of rebleeding. There may also be risk associated with intraoperative systemic heparin administration prior to embolization of the aneurysm. While there have been no reports of early heparin administration resulting in rebleeding, there are numerous accounts of aneurysm rupture related to microcatheter placement or coil deployment [48]. In such cases, the prior administration of heparin would certainly complicate the situation. The risk of such intraoperative aneurysmal rupture must be balanced against the known risk of thromboembolic events, which leads to the common practice of administering heparin after the framing coil has been placed. Unfortunately, no trials have addressed this issue, and there is no evidence to guide current clinical practice.

Managing Complications

Aneurysm Perforation

While less common than other intraprocedural complications, intraoperative re-rupture of cerebral aneurysms is typically more catastrophic. The incidence of perforation has been reported to be 1.4&-4.1 % for treatment of ruptured aneurysms [48, 49], and is much lower for unruptured aneurysms. Risk factors for intraoperative rupture include small diameter (<3 mm), atherosclerosis, worse Fisher grade, and the presence of vasospasm [50]. Of these, small aneurysm size is the most significant. Reports of outcome after intraoperative rupture vary widely, with mortality ranging from 0 % to 33 % and morbidity of 17 %-50 % [49, 50]. When intraoperative rupture occurs, better outcomes have been consistently observed with rapid control of bleeding [49, 51]. Therefore, while intraoperative rupture cannot be predicted in any individual case, adequate preparation before its occurrence can lead to quicker treatment and better outcomes. Of course, the overriding goal in the case of acute re-rupture is hemostasis, and management should typically proceed in the following steps. First, perforation must be diagnosed. The microwire, microcatheter, or coil may be seen to breach the wall of the aneurysm on roadmap fluoroscopy, and angiography confirms the diagnosis when contrast extravasation is seen. Microwire perforations may have the least clinical sequelae, probably because the rent is smaller than with coil or catheter perforations [48]. Once perforation is recognized, the interventionalist must avoid immediate retraction or withdrawal of the device. Particularly in the case of microcatheter perforations, the catheter itself will partly occlude the rent, and bleeding becomes more severe if it is removed. Furthermore, removing the catheter will result in loss of access to the aneurysm. Sometimes temporary tamponade may be achieved with a balloon across the neck, and therefore one should be prepared by an assistant while the interventionalist works to complete embolization. Simultaneously, heparin should be reversed with protamine, typically at a dose of 1-1.5 mg per 100 U heparin given, with a maximum dose of 50 mg. The blood pressure should be reduced, with a systolic goal of <120 or MAP of <80 mmHg. Intracranial pressure should be monitored and relieved; an EVD should be placed immediately after the aneurysm is secured if one is not already in place. As these and many other steps involve multiple personnel and must happen rapidly, the use of checklists has been advocated [52, 53•]. These checklists for emergency procedures should be reviewed with staff periodically to ensure timely and appropriate actions when they are needed the most.

Thromboembolism

Thromboembolic events have been observed radiographically in 51 % [54] and clinically in 5 % of patients with ruptured aneurysms [55]. As with aneurysm perforation, thromboembolic complications are much more likely during the treatment of ruptured aneurysms compared with unruptured aneurysms [56]. The causes of thrombosis during these procedures are multifactorial, but may include hypercoagulability in the setting of SAH [35], slow flow related to guide catheter positioning or vasospasm [53•], and platelet adhesion on the coil mass or prolapsed coil loops [57]. Thromboembolism may be recognized angiographically as a filling-defect on or around the coil mass, or with distal branch occlusion or emboli. The operator should assess for such changes with interval control angiography and careful post-intervention angiography. When detected, prompt treatment can lead to reperfusion and avoidance of significant neurologic disability. Given the importance of preparation and team cooperation, checklists have also been proposed for the emergency treatment of intraoperative thromboembolic events [53•]. For treatment of the thrombus itself, many neuro interventionists utilize glycoprotein IIb/IIIa inhibitors, delivered locally or systemically. Abciximab can be given as

an intravenous bolus at 0.25 mg/kg, or can be delivered intraarterially in smaller doses, usually around 10 mg [58]. Use of tirofiban and eptifibatide have also been reported [59, 60], and we typically use intravenous or local tirofiban at our institution. Thrombolysis with tPA for the acute management of thrombotic events has also been reported, but often fails to achieve recanalization (44 % success) and has been associated with significant morbidity and mortality [61]. Furthermore, local thrombolysis with tPA would certainly pose a high hemorrhage risk in the setting of recently ruptured aneurysms. Therefore, use of local or systemic tPA in the management of thromboembolic complications is not recommended. Besides pharmacologic therapy, some have reported the use of mechanical thrombectomy for thrombotic events [62], which may be most useful for larger thrombi.

Conclusion

Endovascular treatment of ruptured aneurysms has become increasingly sophisticated. As technology has advanced to provide more effective devices, our techniques have become more refined to allow for the successful treatment of a wider range of aneurysms with lower rates of complications. In the future, we can only expect the role of endovascular treatment modalities for aneurysms and other cerebrovascular disease to continue to expand.

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