ASK THE EXPERTS

What Are the Greatest Needs in Cerebral Aneurysm Care?

Experts discuss the need for advances in technology for complex aneurysms, the importance of maintaining surgical expertise in the endovascular era, and the potential of biomarkers to guide decision-making for aneurysm treatment.

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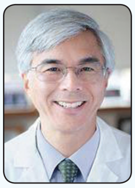

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Endosaccular coil occlusion of a cerebral aneurysm in a human was first reported in 1941[1]; yet, the technology did not exist to readily perform this procedure in routine clinical practice. Fast forward 50 years to developments in computer-aided image guidance and catheter technologies, including the introduction of the Guglielmi detachable coil (GDC; Boston Scientific Corporation) in 1991,[2] which led to a transformation in the treatment of cerebral aneurysms. Initially a treatment for nonsurgical aneurysms, publication of the ISAT study in 2002 provided randomized controlled data that proved the superiority of GDC occlusion of ruptured cerebral aneurysms compared with surgical clipping in selected patients.[3] Today, endovascular treatment of cerebral aneurysms has become de facto standard of care for treating ruptured cerebral aneurysms and for many unruptured aneurysms as well. Which unruptured aneurysms require treatment is still not well defined.

Despite new methods of treatment, aneurysmal subarachnoid hemorrhage remains a devastating disease. Approximately 40% of subarachnoid hemorrhage patients succumb to the disease. Although aneurysmal subarachnoid hemorrhage is a small fraction of acute strokes overall, it results in 25% of life-years lost because of the stroke severity and young patient population affected.[4,5] Aneurysm occlusion to prevent recurrent hemorrhage is the initial important step, and endosaccular occlusion has become the first line of prevention for many patients. Heading off aneurysmal subarachnoid hemorrhage is an important goal for cerebrovascular specialists.

Identification of patients at risk for aneurysmal subarachnoid hemorrhage is challenging, and cerebrovascular specialists rely on their experience and clinical acumen. Asymptomatic cerebral aneurysms are being identified at a greater rate than ever before, and an increasing array of endovascular technologies are available to treat these patients.[6] Some aneurysms will grow and rupture, but prospectively, we don't know which ones. The ISUIA study tells us that small aneurysms (≤ 7 mm in diameter) rarely rupture,[7] but in practice, we see that many ruptured aneurysms are ≤ 7 mm at presentation. The Japanese UCAS cohort study helps to explain some deficiencies in the ISUIA data set, showing that irregular aneurysms and those at anterior and posterior communicating arteries are at a greater risk for rupture.[8] More concerning still, a longitudinal study from aneurysm diagnosis to rupture or death in Scandinavia demonstrated that the mean size of ruptured aneurysms was 5.6 mm and that 25% of small aneurysms went on to rupture during surveillance.[9] A recent meta-analysis of 26 studies by Malhotra et al suggests that annual risk of rupture for small aneurysms can be stratified further still: ≤ 3 mm, nearly 0% rupture risk per year; 3 to 5 mm, ≤ 0.5% risk; and 5 to 7 mm, 1% risk.[10] Medical management of risk factors such as smoking and hypertension is central to preventing aneurysm rupture,[5] but reliable methods to determine each individual's risk of rupture would be a welcome guide to treatment.

Historically, we have focused on location and aneurysm morphology to determine the risk of aneurysm rupture. More recent studies suggest that a variety of physiologic parameters may be useful to better delineate the risk of hemorrhage. Using computational fluid dynamics, Xiang et al hypothesized that wall shear stress drives destructive cell-mediated inflammation, causing aneurysm growth and hemorrhage.[11] Additionally, inflammation appears to have a central role in cerebral aneurysm formation and subsequent rupture.[12-14] Components of the inflammatory cascade in the wall of a cerebral aneurysm may be evaluated with cross-sectional imaging techniques such as MRI and gadolinium chelate or other novel contrast agents such as ferumoxytol.[15,16] In the future, these noninvasive tests, or other tests like them, may help us to better select patients for treatment and allay the fears of those who do not require intervention.

Over the past decade, there has been a profusion of new technologies to treat cerebral aneurysms. Coupled with high-resolution biplane angiography systems, these devices make procedures in the cerebral circulation accessible to a broad range of operators. Technologic advancement is always a worthy process. It is the power behind modern medicine, and it creates hope for aneurysm patients, some of whom were previously untreatable.

With growing political conviction and governmental will to institute efficient and cost-effective health care in the United States, there is every reason to believe that endovascular treatment of unruptured cerebral aneurysms will remain relevant. Time and effort now to prove our techniques in randomized controlled trials, still the gold standard in modern medical investigation, is worthwhile. Although we are still in a relatively favorable economic health care environment, we need to plan for the future of our specialty and gather data to prove that treatment of unruptured cerebral aneurysms prevents stroke due to aneurysmal subarachnoid hemorrhage and increases quality of life.

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Over the past 20 years, remarkable changes have occurred in how we treat cerebral aneurysms. These changes have mostly arisen from advances in two categories: aneurysm detection and endovascular aneurysm treatment. Due to the increased availability of cross-sectional imaging, we are now able to detect unruptured incidental aneurysms at a higher frequency. Once these aneurysms have been detected, they are now easier to treat and can be treated at more centers because of tremendous advances in neuroendovascular technology. Both devices and intraprocedural imaging have improved, making these procedures easier to perform by a larger pool of practitioners.

Of course, there are downsides to these developments. I worry that cerebral aneurysms are being overtreated, now more than ever. The majority of unruptured aneurysms will never threaten the patients who harbor them; however, the few that do rupture often cause devastating strokes. Given the low risk of rupture and an aging population, most unruptured aneurysms are best treated with reassurance. We need to ensure that neuroendovascular practitioners remain trained and motivated to accurately counsel patients about the differential risks of aneurysm rupture and those of treatment.

As neuroendovascular techniques have allowed the treatment of more aneurysms, training and expertise in open aneurysm surgery have become more difficult to acquire. In some cases, open surgery is helpful and necessary, and thus, we must ensure that open neurovascular surgical expertise is not lost. There are efforts to propagate laboratory training courses that can address this in part. Regionalization of aneurysm care to maintain case volume at some centers would help as well, but it is not clear how this can best be achieved. We must also understand how providing mechanical embolectomy for patients with emergent large vessel occlusion strokes will affect cerebral aneurysm treatment. It is probable that endovascular aneurysm treatment, like most other procedures, is safer when performed at high-volume centers. However, it is not clear that this volume will be maintained for endovascular procedures as the landscape of stroke treatment changes.

From a technical perspective, the wish list would certainly include the development of devices that would enable us to treat complex, wide-necked, and fusiform aneurysms without the need for anticoagulation and antiplatelet medications. We have seen tremendous technical innovation in the field of aneurysm devices, but many of these involve leaving metallic implants in the parent vessel. These mandate that patients take medications that can be expensive and elevate the risk of hemorrhagic complications.

Aneurysm treatment devices have evolved so quickly over recent years that I am not sure that the biggest bugbear of endovascular treatment is adequately being addressed. Aneurysm recurrence after endovascular treatment increases the need for surveillance and the potential that additional treatments will be required. I think recurrence and, more importantly, aneurysm rupture after endovascular treatment is probably becoming less common, but this needs to be closely studied.

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The reported prevalence of intracranial aneurysms is high (3.2%), but only a limited number of these aneurysms will rupture.[1] Rupture of intradural aneurysms leads to intracranial bleeding, with frequently devastating consequences including neurologic sequelae and death. In cases of ruptured aneurysms, emergency treatment is indicated to prevent rebleeding and vasospasm. For unruptured aneurysms, treatment indications remain debatable and need to take into account several factors such as patient age, aneurysm size, and aneurysm morphology (regular or irregular). Currently, determining which unruptured aneurysms have the highest risk of rupture is difficult. Therefore, identifying biomarkers that could point to those at high risk of rupture would facilitate clinical decision-making in the management of unruptured aneurysms. Recent studies suggest that aneurysms with wall enhancement are unsteady and thus present an increased risk of bleeding.[2] Further studies are required to evaluate the predictive value of this imaging factor as well as identify other biomarkers.

Intracranial aneurysms should be managed in highly experienced centers with multidisciplinary teams involving neurosurgeons, neurointerventionalists, neuroanesthesiologists, and neurologists. After the ISAT study, intracranial aneurysm management is now primarily based on endovascular techniques. However, coiling continues to have limitations including difficulty in treating wide-necked aneurysms as well as recanalization, which frequently occurs in large and giant aneurysms. Alternative (or adjunctive) techniques to coiling have been developed, such as balloon-assisted coiling (remodeling technique), stent-assisted coiling, flow diversion, and flow disruption.[3] For some of these techniques (ie, stent-assisted coiling, flow diversion), the patient must be treated with dual antiplatelet therapy (DAPT), which is a limiting factor for the treatment of ruptured aneurysms. Development of surface-modified flow diverters (or stents) that eliminate the need for DAPT or use single antiplatelet treatment is an important step to make these therapies feasible for ruptured aneurysms.

Flow diverters have been proven to be highly efficacious in treating large and giant aneurysms; yet, flow diverters carry a relatively high rate of complications, leading to morbidity and mortality.[4] Even so, the high efficacy of flow diverters has allowed treatment options for progressively enlarged to smaller aneurysms, aneurysms located on distal vessels (singularly with the appearance of small-diameter flow diverters), and bifurcation aneurysms (even if these indications are still controversial). Further developments of small and bifurcated flow diverters are needed to increase treatment options for aneurysms located on distal vessels or bifurcations. Optimization of radial force, deployment, and metal coverage are also key focus areas to reduce the rate of complications and the delay in aneurysm cure, which is relatively long for flow diversion.

Flow disruption is the most recent technique in the field of intracranial aneurysm treatment and has been extensively evaluated in several prospective studies.[5] Aneurysm treatment with the Woven EndoBridge (WEB) device (Terumo Interventional Systems) is at least as safe as standard coiling. One-year follow-up results show good treatment efficacy; however, long-term results are required to confirm early efficacy. Looking at both flow disruption and flow diversion, the goal of aneurysm treatment is to close the neck or disrupt flow at the level of the neck to induce intra-aneurysmal thrombosis. It will likely be important to develop a device that closes the neck without occupying space in the aneurysm sac and introduces limited metal into the parent artery.

Above and beyond these technical developments, a more detailed understanding of the pathophysiology and genesis of intracranial aneurysms is needed to finely tune future intracranial aneurysm treatment (ruptured and unruptured). Finally, development of new techniques in the surgical field (eg, bypass techniques) is also important for the treatment of very complex aneurysms that are untreatable by endovascular means.

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We live in historic times for the treatment of stroke and cerebral aneurysms. In particular, the endovascular approach has completely revolutionized the treatment of these deadly lesions, moving from invasive open surgery to a minimally invasive endovascular approach. Thanks to the improvement in device technology over the past decade, the scientific and clinical evidence showing the superiority of the endovascular approach is overwhelming. However, there are areas of study that still need to be addressed. Flow diversion is a major advancement in the treatment of cerebral aneurysms. The challenge for the future is to evaluate if the second- and third-generation flow diversion devices can be used in ruptured aneurysms and smaller vessels. Surface modifications to decrease the amount and strength of DAPT will perhaps be the answer to flow diversion in the context of an aneurysmal subarachnoid hemorrhage. Smaller delivery systems and flow diversion that can be released from smaller delivery catheters may be able to meet the challenges of cerebral aneurysm treatment in small arteries.

Another challenge is the endovascular treatment of wide-necked bifurcation aneurysms. Intrasaccular devices and complex stents that can assist in coil embolization are attempting to address this challenge. There are some minor issues with the devices currently used to treat wide-necked bifurcation aneurysms; however, improvements in device technology over the next few years will likely make this approach even more feasible and effective.

State-of-the-art technology and advancement in any medical or surgical field unfortunately comes with a price tag. In fact, another major need is to bring endovascular technology to developing countries. This is a complex and multifaceted issue that is related to device costs, availability of high-definition angiography suites, personnel training, and systems of care. Hopefully, these issues will be resolved in the near future so that patients with cerebral aneurysms in developing countries can reap the full benefits of such amazing technology. ■