Neuroendovascular surgery

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Neuroendovascular surgery and interventional neuroradiology both describe the catheter-based (most often) endovascular diagnosis and treatment of vascular lesions affecting the brain and spinal cord. This article traces the evolution of these techniques and their current role as the dominant and frequently standard approach for many of these conditions. The article also discusses the important changes that have been brought to bear on open cerebrovascular neurosurgery by neuroendovascular surgery and their effects on resident and fellow training and describes new concepts for clinical care.

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NEUROENDOVASCULAR surgery is now the most commonly practiced therapeutic approach for most vascular conditions affecting the brain and spinal cord. It is used more frequently than open neurovascular surgery for the management of complex vascular conditions, with high rates of safety and efficacy. The expansion of endovascular techniques into the treatment of stroke, the third highest cause of death in the United States, has provided meaningful benefit to large numbers of patients worldwide.^{11,62} When combined with the use of neuroendovascular techniques to treat chronic subdural hematoma (cSDH), a condition predicted to become one of the most common neurosurgical conditions of the future, neuroendovascular surgery is poised to become one of the most necessary and important treatment modalities within our entire specialty.⁷ As a result of this ever-increasing patient demand, clinicians, community hospitals, academic centers, and industry are all directing tremendous resources into the field. This has led to great interest in device design using new technologies. At the same time, the shift away from open surgical approaches has had far-reaching implications for how we train neurosurgical residents and fellows and how we certify these individuals once their training is completed.⁶⁴ Indeed, care and training implica-

tions involve radiologists, neurologists, vascular surgeons, and cardiologists.

Background

The Portuguese neurologist Egas Moniz invented angiography sometime over the period between 1926 and 1927.⁶ This invention ushered in the age of diagnostic and therapeutic angiography. The role of cerebral angiography grew concurrently with the young specialty of neurosurgery. Cushing, Dandy, and others were all busy defining neurosurgery as a specialty distinct from surgery; in this, cerebral angiography had a prominent role. At that time, imaging modalities included plain radiography, myelography, pneumoencephalography, and angiography. Angiography generated radiopaque images of the cerebral vasculature and could be used to identify vessel occlusions and eventually identify vascular lesions. Distortion and displacement of the vascular anatomy could also be used for tumor localization. Over the last 75 years, there has been an ongoing evolution of the surgical aspects of neurosurgery but simultaneously in diagnostic imaging and imaging-based therapies as well. Propelled forward by the introduction of computed tomography (CT) and magnetic resonance

ABBREVIATIONS AI = artificial intelligence; AVF = arteriovenous fistula; AVM = arteriovenous malformation; cSDH = chronic subdural hematoma; CT = computed tomography; MRI = magnetic resonance imaging.

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imaging (MRI), neuroimaging and neurosurgery have become inseparable and, in many ways, indistinguishable. At the same time, angiography also has continued to be refined and developed, first as a diagnostic tool but then very quickly as a discrete therapeutic modality. To those who performed diagnostic cerebral angiography, the potential for intervening in vascular pathology was immediately apparent, but the tools—the catheters and wires—needed to achieve distal catheterization were not initially available. The eventual introduction of braided catheters and hydrophilic wires, which allowed quick and safe catheterizations, set the foundation for intervention. It would be an oversimplification to suggest that several specific breakthroughs or leaps in catheter-based technologies were responsible for this. There has been a steady introduction of new devices and techniques, some novel to the neurological space and some borrowed from other subdisciplines, such as interventional cardiology and vascular interventional radiology, all of which played a role. Several key introductions stand out, including flexible catheters, steerable wires, detachable balloons, detachable coils, intracranial stents, flow diverters, intrasaccular devices, and most recently, stent retrievers and aspiration catheters; these have all been introduced at some point over the last quarter century. Overall, there has been a continuous stream of new devices and concepts as more disease processes become amenable to neuroendovascular therapies.

Technical Aspects of Angiography

The initial requirement for cerebral angiography is X-ray imaging. X-ray exposure plus contrast combined with mask subtraction allows images of high resolution of the vasculature to be generated. Early systems used cut film and film cassettes, requiring a technologist to exchange multiple cassettes while series or angiography “runs” were obtained. Modern systems consist of an image intensifier and digital subtraction flat panel detectors that utilize a fraction of the radiation dosage for the acquisition of images of the finest detail. The ability to rotate the image intensifier around the patient—in our case, around the patient’s head—allowed the development of 3D rotational images. Rotation combined with appropriate software similarly allows the generation of CT or Dyna CT images by the same equipment, reintroducing CT back into the procedure room. CT in the angiography suite allows, in addition to standard CT imaging, CT angiography and CT perfusion. Experimental units are now exploring real-time MRI as a possible way to perform cardiovascular and neurovascular interventions. Once again, this will require an entirely new set of devices and tools, in the form of catheters, wires, coils, stents, flow diverters, and stent retrievers, all of which must be MRI visible and compatible.

Cerebral Aneurysms

The treatment of aneurysms has fascinated clinicians over the centuries. John Hunter performed direct suture ligation of popliteal aneurysms in 18th-century London.²¹ With similar ingenuity, cerebral aneurysm surgery was performed by some of the earliest practitioners of our specialty. Dandy was the first to apply a silver clip to the

neck of an aneurysm in 1937.³⁴ Microsurgical clipping of aneurysms, popularized by Yaşargil and refined by many, including Drake, Malis, Spetzler, Samson, Flamm, and others, helped define a generation of vascular surgeons.^{35,73} Interestingly, neuroendovascular treatment of aneurysms also had its start in neurosurgery. In 1962, Gallagher introduced horse hair directly into the domes of surgically exposed aneurysms foreshadowing filling aneurysm domes with detachable coils.²⁶ Serbinenko fashioned detachable balloons to treat aneurysms, which he would float up into the dome and, once in position, detach from the delivery catheter.^{66,67} Detachable balloons for the treatment of cerebral aneurysms ultimately were shown to have limited efficacy, and after a period of initial excitement, they ultimately faded from use. At most centers, the treatment of cerebral aneurysms remained open clip reconstruction until 1991. At that same year, Guido Guglielmi described controlled placement of detachable coils and electrothrombosis for the treatment of aneurysms.²⁸

The development of detachable coils led to an explosion in the endovascular treatment of cerebral aneurysms. Coils of different sizes, 3D configurations, and lengths all helped the initial technology to become widespread (Fig. 1). Complete occlusion rates were high but not as high as those achieved with direct surgical clipping, particularly for select groups of aneurysms. Wide-necked and more complex lesions still remained problematic and demonstrated high rates of recurrence. Balloon remodeling, introduced by Moret and colleagues in 1997, allowed dense packing of wide-necked aneurysms, but the technique required a degree of technical expertise acquired over a learning curve, and an increase in complication rates was initially appreciated and noted in the literature.⁵¹ At the same time, neurosurgeons and neurointerventional radiologists at several centers had been borrowing stents from the interventional cardiology suite and publishing case reports about treating wide-necked aneurysms with a combination of stents and coils. These devices, designed specifically for cardiac usage, were stiffer and more difficult to use in the tortuous neurovascular anatomy, but when positioned correctly, they could be used with detachable coils to obliterate complex lesions. Borrowing cardiac stents soon became unnecessary with the introduction of stents specifically designed for intracranial use (Neuroform stent, Boston Scientific Target).³² The use of stents required that patients be on a regimen of antiplatelet medication for extended periods of time, adding to the risk of the procedure itself as well as risks associated with the recovery period. These risks, however, were quickly accommodated by interventionalists, and overall risk profiles dropped dramatically as improved overall occlusion rates were demonstrated. Stent-coil constructs decreased the coil packing and aneurysm recurrence. Prior to the introduction of stents, coil packing had been managed by dense packing techniques with or without balloon remodeling. Some manufacturers explored bioactive coils to promote thrombus formation and endothelialization, but these modified coils were shown to have limited efficacy and to have no clear advantage over pure platinum coils when used alone.^{46,63} Still others explored the use of polymers to treat cerebral aneurysms, but again, increased risk and pa-

FIG. 1. Complete occlusion of a ruptured saccular aneurysm with coiling. **A and B:** Digital subtraction angiogram and 3D reconstruction showing a basilar tip aneurysm measuring 7.6 mm. **C:** Final postembolization angiogram showing solid packing of the aneurysm. **D:** Late follow-up angiogram (3D reconstruction) showing a Raymond-Roy class I occlusion. Figure is available in color online only.

tient morbidity temporarily derailed this strategy and prevented widespread acceptance of the technique.⁴³ A European trial confirmed the difficulty and the technique was held up clinically but has remained an active area for industry research.⁴⁹ Interest in this technique continues, and it is very likely that neuroendovascular surgeons will see some type of liquid embolic material for use in conjunction with an appropriate assist device in the near future.

With the introduction of detachable coils and then intracranial stents, greater and greater numbers of aneurysm patients were being treated worldwide.⁷² This trend was first examined by the International Subarachnoid Aneurysm Trial (ISAT), which found an overall decreased risk of death and morbidity in the endovascular group treated with detachable coils when compared to those treated with open surgery.^{48,50} A higher re-bleed rate was noted in the endovascular group (2 patients) compared to no re-bleeds in the surgical group.⁵⁰ However, with this firm evidence, the worldwide treatment of both ruptured and unruptured aneurysms by detachable coils quickly surpassed open surgery as the primary treatment modality. An exponential increase in publications related to aneurysm coiling marked the technique as a standard of care.⁶⁵ In some countries (Finland, the United States, and Japan, for example), however, significant numbers of patients continued to be treated with open surgery. But even in those countries, more recent data suggest that neuroendovascular management now approaches 60%–70%. Improved noninvasive imaging increased the detection of unruptured and in many cases smaller aneurysms. This, when

combined with reduced treatment morbidity, contributed to a growing number of patients that could be considered candidates for treatment. Industry reacted by continuing to direct significant resources into research and development of new endovascular technologies.

Flow Diversion

The concept of flow diversion was initially explored by Wakhloo years prior, but Nelson and colleagues developed the first commercially available flow diverter.^{1,8,10,24,54} Flow diversion introduced the concept of a more physiological therapy for aneurysms, focusing on treating the parent vessel without the requirement of entering the aneurysm dome. With data that indicated complete occlusion rates that approached 90% at 1-year follow-up (Pipeline for Uncoiled or Failed Aneurysms Study [PUFS]) another radical shift occurred in the way we make treatment recommendations for selected intracranial aneurysms.⁹

Thus, cerebral aneurysms, both ruptured and unruptured, can be treated with a wide variety of endovascular tools, including detachable coils, intracranial stents, flow diverters, and most recently intrasaccular devices.^{5,68,71} Research into surface modification of devices to mitigate or negate the need for anticoagulation or antiplatelet medications is actively being pursued. Some such devices are already under clinical investigation.⁴² The number of aneurysms that cannot be resolved by an endovascular solution continues to decrease (Figs. 2 and 3). Multiple clinical studies have even demonstrated the safety of using stents and flow diverters in the setting of acute and subacute subarachnoid hemorrhage.⁵³ Even giant aneurysms, in the past managed with balloon test occlusion and vessel sacrifice or complex bypasses, can now be managed with flow diversion and an overnight hospital stay.^{8,17,18,29,30,66} Giant aneurysms are now routinely treated with flow diversion with great efficacy and considerably lower morbidity than in the past.⁴³ Moreover, the indications for flow diversion have been extended to smaller aneurysms that are usually treated with coiling, stent-coiling, or clipping.¹³

Research continues into the areas of surface modification, delivery mechanisms, and miniaturization of devices to reach even the most distal abnormalities. As a consequence, the training of endovascular neurosurgeons, interventional neurologists, and interventional neuroradiologists has allowed for complex endovascular services to be provided at community hospitals, when these services were once the purview of academic and specialty practices. This has slowed the referral of patients to more experienced centers, which has resulted in an increase in the number patients being treated endovascularly in the community and fewer patients being treated with open surgery. Due to the increasing complexity of some problems, some patients may require either retreatment or more complex second-stage strategies to achieve obliteration.

Induced Endovascular Bypass/Ischemic Preconditioning/Ischemic Collateralization

The introduction of flow diversion devices has had a dramatic effect on the management of cerebral aneu-

FIG. 2. The use of flow diversion revolutionized the management of giant aneurysms of the internal carotid artery (ICA). **A and B:** Digital subtraction angiogram and 3D reconstruction showing a giant aneurysm of the left ICA. **C:** Postembolization unsubtracted image depicting the treatment of the aneurysm with multiple flow diverters as well as good apposition proximally and distally. **D:** Immediate control angiogram in lateral projection showing significant flow stagnation inside the giant aneurysm. **E:** Late follow-up shows complete occlusion of the aneurysm. Figure is available in color online only.

rysms. It has also indirectly advanced our understanding of cerebrovascular reserve, ischemic collateralization, and the concept of ischemic preconditioning. It became apparent that intracranial stents, initially designed to treat wide-necked aneurysms, when telescoped or overlapped, created a critical density/porosity across the aneurysm neck that promoted aneurysm thrombosis and endothelialization. Soon, specifically designed devices (Pipeline/Silk/Surpass) were studied in clinical trials and demonstrated occlusion rates that approached 100%.⁸ Historically, the aneurysm had been the focus of treatment. Now, with flow diversion, the focus of treatment was shifted away from the aneurysm and toward the diseased parent vessel. A

significant improvement over detachable coils alone, balloon remodeling, and stent-coil constructs, flow diversion provided a more physiological treatment of intracranial aneurysms by focusing the treatment on the parent vessel rather than the aneurysm itself. The underlying principle is that the parent vessel is diseased, not only the aneurysm. Devices, once implanted and deployed against the vessel wall, promoted endothelial proliferation and remodeling of the diseased parent vessel. Initially approved for the treatment of aneurysms of the skull base (cavernous and ophthalmic segments of the internal carotid artery), their use soon expanded to aneurysms along straight segments beyond the supraclinoid carotid.⁸ Experience soon

FIG. 3. The treatment of intracranial aneurysms with flow diverters provided higher occlusion rates and low complication rates for smaller aneurysms as well. **A:** Digital subtraction angiogram showing an unruptured right carotid terminus aneurysm. **B:** Unsubtracted image showing the delivery of a Pipeline Flex embolization device (Medtronic) after adjunctive partial coiling. **C:** Late follow-up angiogram in posteroanterior projection showing complete occlusion of the aneurysm.

expanded to include aneurysms incorporating the origin of branching vessels (ophthalmic artery, posterior communicating artery, and anterior choroidal artery) and aneurysms occurring in specific anatomical locations such as the middle cerebral artery bifurcation, anterior communicating artery, and basilar artery bifurcations. The high occlusion rates achieved with flow diversion, particularly for large/giant aneurysms, further decreased the need for open bypass procedures, allowing direct remodeling of vasculature that previously required test occlusion, vessel sacrifice, or complex bypass. A major insight occurred from the direct observation of the covering of large branching vessels. Branches that, if compromised at open surgery, would result in acute stroke could be covered with a flow diverter and *slowly* allowed to close while leptomeningeal collaterals developed. This critical observation and byproduct of flow diversion effectively created an induced endovascular bypass and could be exploited to treat the most complex aneurysms in a variety of locations, including aneurysms that remained incompletely occluded after failed coiling or clipping procedures.

This seems to involve robust collateral development from watershed territories, which are very different from the friable ischemic neovascularity seen in pathological conditions such as moyamoya disease. Ischemic neovascularity by its very nature is tenuous and prone to hemorrhage. The development of such fine neovascularity is a process that depends on local angiogenic factors. Large leptomeningeal collateralization, on the other hand, involves extension or shifting of large watershed regions between major vascular territories, a consequence of which is the ability to tolerate the coverage of large branched vessels with dense flow diversion device constructs without stroke or local angiogenic ischemic stimulus. The process of flow diversion induction or induced bypass occurs over months (3–6 months) concurrent with the endothelialization process. If the shifting watershed is inadequate, then the jailed branch will not be covered with endothelium and will remain patent. The immediate implication of this is that large branching vessels may be covered to promote aneurysm occlusion while exploiting a form of plasticity of the cerebrovasculature. What is less understood is what implication this has for future treatments of stroke and large-vessel occlusion. Stroke patients have significant difficulties when large-vessel occlusions occur in territories with limited collaterals or in situations in which there is not enough time to stimulate collateral revascularization. Patients with extensive collateral networks have been shown to do better neurologically and to tolerate longer times to treatment and intervention.⁶¹ All of this suggests that more research is needed. Clearly, utilization of the great potential of the remodeling of the collateral network may be upon us.

Arteriovenous Malformations, Dural Fistulas, and Vein of Galen Malformations

The treatment of arteriovenous malformations (AVMs) and dural arteriovenous fistulas (AVFs) has been associated with neuroendovascular surgery since its inception. Angiography, being the primary way to characterize a

vascular lesion and understand its angio-architecture, lends itself to intervention. Early practitioners treated AVMs using embolic beads, which—not unlike detachable balloons—could be introduced into a malformation to block arteriovenous shunting. This was imprecise, and large shunts would allow the passage of the embolic beads into the venous side, potentially leading to morbidity and death. The introduction of liquid embolic agents, initially in the form of n-BCA, an acrylic adhesive, catapulted endovascular management of complex vascular malformations to the level of open surgery and stereotactic radiosurgery.^{39,59} Advances in microcatheter and microwire design facilitated the distal catheterization of vascular malformations so that embolic agents could be injected directly to close arteriovenous shunts, decrease nidus size, and in some cases cure malformations.⁵² Experienced interventionalists would perform multistage embolizations with the goal of decreasing overall lesion size and in accordance with the hypothesis that this practice would reduce hemorrhage risk. Berenstein, Lasjaunias, TerBrugge, and others pioneered embolization of vascular malformations.^{2,44,56} Their techniques, built on a solid foundation of the understanding of neurovascular anatomy, propelled the young specialty forward. Ultimately, it was shown that incomplete embolization, unless target-directed to a specific angio-architectural abnormality, did not reduce the overall hemorrhage rate.⁶⁰ As we have seen with the evolution and advancement of the treatment of other vascular lesions, improved catheter, microwire, and embolic materials all contributed to improved AVM endovascular management. Lesions with low Spetzler-Martin grades could be managed solely with surgery or a combination of embolization and surgery. Early on, more complex lesions were often referred for endovascular management alone when deemed ineligible for other treatments. Grade IV and V lesions might be managed with embolization or partial embolization. Distal catheterization and multistage embolization were not considered unusual at the time. High-grade lesions presenting with hemorrhage would be characterized angiographically and nidus defects identified. Partial or incomplete embolization was successful in decreasing lesion size and excluding these angio-architectural abnormalities, but an effect on natural history was not observed.⁴⁴ The development of embolic agents progressed rapidly from Silastic spheres and particles to acrylic-based glues and polymer adhesives. The introduction of polymer adhesives allowed deep and extensive nidus penetration without the need for repeat distal catheterization and could be performed over long embolization procedure time periods.^{39,59} A variety of strategies emerged, including multiple pedicle embolizations of the nidus. This was used by Cekirge and others to “embolize for cure” both grade IV and grade V lesions.⁶⁴ Theoretically discussed and considered in the past, transvenous embolization is now being extensively explored. Initial reports documented higher post-procedure hemorrhage rates,¹⁴ but growing practitioner familiarity with the technique appears to be rapidly improving on this initial experience. The issue of which lesions to treat, particularly with respect to asymptomatic lesions, had been and remains an area of intense debate.

FIG. 4. The endovascular management of AVMs can be curative for small AVMs or an adjunct for posterior microsurgical resection and/or radiosurgery for larger lesions. **A–E:** Angiograms showing left occipital Spetzler-Martin grade I AVM treated with transarterial Onyx injection and assistance of a Scepter balloon. Follow-up showed complete obliteration.

ARUBA (A Randomized Trial of Unruptured Brain Arteriovenous Malformations) sought to add some clarity to the discussion.⁴⁷ Unfortunately, the trial failed on multiple levels, including the small number of patients who were ultimately recruited and randomized, the small number placed into each treatment arm, the wide variety of AVM types, and in not following patients long enough to elucidate the natural history of the lesions.²³ The negative initial effect of the study was a reduction in patient referrals for treatment consideration. Multiple publications in the post-ARUBA period demonstrated improved outcomes over the ARUBA results.^{31,55} Many centers outside the United States continue to offer extensive embolization for a goal of obliteration for all grades of lesions. Multipedicle polymer injections and transvenous approaches are all utilized with widespread practitioner support. In the United States, embolization as a current stand-alone treatment is less frequently performed. Embolization is often performed before surgery or before or after radiosurgery.²⁰ Some centers prefer to perform radiosurgery upfront to improve nidal exposure and then perform selective embolization of concerning features. Endovascular management as a solitary treatment is, however, slowly gaining in popularity (Fig. 4). It is likely that transvenous embolization will continue to increase as neurointerventionalists become more comfortable with the technique and complications related to the technique decrease. AVMs will remain complex lesions that clearly are best managed with a multimodality overlap of microsurgery, embolization, and radiosurgery.

Vein of Galen malformations are extremely rare and unusual lesions, occurring in one out of a million live

births.^{12,34} They are treated almost exclusively with endovascular techniques. In the newborn presenting with heart failure or diagnosed in utero, the lesions are amenable to endovascular intervention.¹² An initial treatment stage is often performed and followed later by additional staged intervention when the child is large enough to undergo more extensive embolization and lesion control. These complex lesions must be differentiated from aneurysmal dilation of the vein of Galen secondary to venous sinus stenosis or atresia and thalamic AVMs. Embolization strategies include closing the individual arteriovenous shunts that form the basis of the malformation.

Arteriovenous Fistulas

Dural AVFs represent a specific class of vascular lesion that incorporates the dural supply of the brain or spinal cord, allowing direct arterial shunting toward venous structures. When this occurs intracranially, venous hypertension can lead to cortical dysfunction, venous hypertension, and hemorrhage.¹⁵ In the spine, dilation of venous structures along the spinal cord can lead to myelopathy from tissue engorgement and venous hypertension as well as physical compression. The complex anatomy and points of arteriovenous shunting can add a degree of complexity to their management. While some neurovascular surgeons still discuss and offer open surgical solutions to these complex lesions, glue embolization has become a standard for even the most complex of lesions. Polymer-based embolization materials have been particularly useful in the obliteration of these lesions. When these materials are combined with balloon injection catheters, deep penetration to the point of fistulization can be achieved.⁵⁸ Transvenous

approaches are also routinely employed and are highly successful when direct arterial access to the fistula cannot be achieved.

Spinal Vascular Malformations and Fistulas

Similar to cranial AVMs, a wide variety of spinal vascular lesions can be effectively categorized, controlled, and in some instances, cured with endovascular techniques. Even the more complex metamer type of lesions, which are unlikely to be cured, may be partially embolized and decreased in size, with control of abnormal features.²⁵ Less complex lesions are often well controlled with embolization. Type 1 spinal dural AVFs can effectively be embolized, negating the need for open surgical disconnection in many situations. More complex spinal AVMs may not be amenable to complete endovascular treatment. In some cases, success in treating these lesions has more to do with the nature of the vascular supply (anterior spinal artery) and access to the lesion for safe embolization.

Venous Sinus Stenting

Transvenous approaches have become quite useful in the treatment of AVMs and dural AVFs. Real success, however, has been in the management of dural sinus stenosis, often associated with a diverticulum of the sinus. With venous sinus stenting, promising results have been achieved in treating intracranial hypertension and venous stenosis-related pulsatile tinnitus.^{14,52} Venography is performed to characterize the venous sinus anatomy. Areas of stenosis and outflow obstruction can often be identified, even when not clearly visible on noninvasive imaging, and intraprocedural pressure measurements can be obtained, confirming pressure gradient and the likelihood of a positive response to sinus stenting. Immediate improvement can be appreciated when the procedure is performed under the correct circumstances.

Carotid-Cavernous Fistulas

The treatment of carotid-cavernous fistulas also has had an extensive neuroendovascular evolution. Though early on these lesions were often treated with balloon test occlusion and vessel sacrifice, carotid-cavernous fistulas are now almost exclusively treated by an endovascular strategy or radiosurgery. Early interventionalists noted that the site of the fistula can be entered and closed, often by packing the cavernous sinus. Treatment has evolved over time from the use of detachable balloons to the current use of detachable coils and, in some rare clinical presentations, flow diverter placement.²² For less directly accessible lesions, superior orbital vein access with direct puncture and catheterization as an alternative approach to the cavernous sinus as well as transvenous routes can all be exploited. These options obviate the need for a deconstructive procedure such as parent vessel sacrifice.

Carotid Artery Stenting

Extracranial carotid occlusive disease remains a major cause of death and disability because of its association

with stroke.¹¹ Because of this, carotid endarterectomy was extensively studied and became one of the most frequently performed operations in the United States.³⁶ Superiority over the medical management of the time was proven in several large prospective trials. A challenge to open endarterectomy came in the form of carotid artery stenting with embolic protection. The Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) proved equipoise between carotid artery stenting combined with embolic protection and open endarterectomy.⁴¹ The composite outcome was the same, but patients undergoing carotid endarterectomy had more myocardial infarctions and patients undergoing carotid stenting had more ischemic stroke. Younger patients in general benefited more from stenting, and older patients benefited more from carotid endarterectomy. Newer stents and protection systems became easier to use and deploy. Some of these devices and techniques utilize flow reversal to decrease distal embolization risk. With improved medical management with statin medications, tighter risk factor control, and next-generation antiplatelet medications, there is again a need to revisit medical management in the asymptomatic population. CREST II seeks to examine this and determine which patients will ultimately benefit from intervention.

Mechanical Thrombectomy

More than any other application for interventional and endovascular therapies, even more so than cerebral aneurysm treatment, mechanical thrombectomy has transformed our field, leading to an explosion in intervention for large-vessel occlusion.^{27,62} Earlier attempts by desperate practitioners—including intra-arterial thrombolysis and the use of balloons and stents—eventually led to the development of specifically designed devices that met with only limited success. As with many seemingly beneficial devices, a second generation of devices, including stent retrievers and aspiration catheters, demonstrated a significantly improved safety profile but more importantly, impressive improvement in revascularization, which immediately translated into improved patient outcome.^{3,4} Outcomes improved so significantly that the improvement caused a re-examination of the criteria for intervention, including time limit and physiological preconditions.^{19,33,57,61} This gave way to expanded windows for intervention. Not only were time limits extended, but also discussions on the ability to preserve additional tissue at risk, even in the setting of an established stroke, have made stroke intervention a significant part of the foundation of endovascular practice (Fig. 5).

Systems similar to STEMI (ST-elevation myocardial infarction)/cardiac catheterization quickly developed, and mechanisms to designate centers that could promote stroke intervention were established. “Stroke center,” “mechanical thrombectomy ready,” and “comprehensive stroke center” designations have all been applied with oversight by the Joint Commission and other certifying bodies. This rapid expansion of services has strained the existing endovascular workforce, pressured our training programs, and triggered a critical examination of our certifying processes in order to adequately provide appropriate training for

FIG. 5. Mechanical thrombectomy of the right middle cerebral artery in 2 passes using a stentriever and aspiration. **A:** Digital subtraction angiogram in posteror anterior projection showing complete occlusion of the right M₁ segment. **B:** After one pass, it is possible to see recanalization of the M₁, but an occluded M₂ segment. **C:** Control angiogram depicting reperfusion.

the individuals who will eventually be needed to serve the population at risk. Some data suggest that approximately 50,000 patients underwent mechanical thrombectomy in the United States last year.⁶² It is additionally estimated that the actual number of patients who could benefit from these interventions might be 10 times that number—or 500,000 patients annually in North America alone. Endovascular neurosurgeons have therefore had to become experts in the treatment and management of acute stroke in addition to managing the more traditional neurovascular conditions encountered in clinical practice, such as aneurysms (with or without subarachnoid hemorrhage), AVMs, dural AVFs, and carotid disease. Research into the development of neuroprotective agents that could be administered in the field to allow the transportation of patients to the most appropriate centers for intervention remains active. At the same time, we are just beginning to understand the role of collateral circulation in limiting the extent of stroke and potentially improving recovery. As stated earlier, flow diversion, which slowly allows robust collateralization, has given an early insight into the plasticity of the collateral watershed, which we may be able to someday exploit in patients with large territories at risk.

Tumor Embolization and Intra-Arterial Chemotherapy

The ability of the cerebrovascular tree to provide direct vascular access to tumors both benign and malignant has been exploited since the 1970s. With improved catheterization techniques, the vascular supply of most tumors can be readily accessed. In some clinical situations—for example, in the treatment of meningiomas—preoperative embolization can facilitate resection and decrease intraoperative blood loss. As with all endovascular strategies, keen understanding of the vascular anatomy is required so that normal structures and territories are not put at unnecessary risk.

Intra-arterial chemotherapy for more malignant tumors, such as gliomas, has had a resurgence over the last few years. Initially coupled with blood-brain barrier disruption, chemotherapeutic agents can be directly infused into glial tumors, decreasing systemic side effects of medications while achieving higher local doses.³⁹ This

can all be done with similar outcomes when compared to other more accepted delivery mechanisms. The blood-brain barrier has remained a significant limitation, and blood-brain barrier disruption is most likely required to allow some large therapeutic molecules to reach their targets. Additionally, the selection of available pharmaceutical agents that are effective remains limited, although the technique itself remains sound and primed for the appropriate therapy.

Multiple trials coupling intra-arterial chemotherapy with the use of focused ultrasound to open the blood-brain barrier to facilitate specific drug delivery are currently under investigation.⁴⁰ Several centers, additionally, have looked at utilizing combined agent therapy for intra-arterial infusion for recurrent disease. Again, the results of these investigations have been mixed, and more investigation is needed. What remains clear is that the vascular route for drug delivery remains promising and by definition provides direct access to any territory of the brain. Optimistically speaking, eventually the right neuro-pharmaceutical/chemotherapy/immunotherapy drugs will be developed and potentially could be delivered intra-arterially.

Subdural Hematoma Embolization

An aging population and the regular use of antiplatelet and anticoagulation medications may make the occurrence of chronic subdural collections one of the most common neurological conditions requiring treatment in the future. The treatment of conditions in the aging population has come to the forefront of neuroendovascular surgery in the form of the treatment and management of stroke/large-vessel occlusions and of chronic subdural hematomas (cSDHs). For generations, chronic subdural collections have been managed with craniotomy and/or drainage both operatively and at the bedside. Originally described by Korean and Japanese interventionists almost 20 years ago, embolization of the middle meningeal artery supply to the dura and subdural membranes has recently generated renewed interest, and clinical studies have demonstrated very promising results.^{37,69,70} Endovascular surgeons have reported success with both particle and liquid embolic agents to achieve devascularization of the involved dura and subdural membranes. The technique can be employed

FIG. 6. The endovascular treatment of cSDHs is once again pushing boundaries in the field. **A:** Noncontrast CT image of the head showing bilateral cSDHs, larger in the left side. **B:** Superselective catheterization of the left middle meningeal artery (MMA) is performed. **C:** Control angiogram of the left MMA demonstrating occlusion of the anterior branch after injection of polyvinyl alcohol particles. **D:** Immediate postoperative Dyna-CT image showing penetration of contrast beyond the membranes of the hematoma. **E:** Three-month follow-up CT image showing significant decrease in the left hematoma. **F:** Seven-month follow-up CT image showing complete resolution of the hematoma.

as a rescue technique in individuals who have undergone previous craniotomy as well as a primary upfront treatment particularly in patients with significant comorbidities (Fig. 6). Mechanistically thought to alter the hydrodynamic balance between the dura, the CSF, and the subdural collection, embolization of the dura has demonstrated direct connection to subdural membranes and capillaries, which are thought to play a role in re-hemorrhage.³⁸ The presence of these subdural membranes and associated capillaries is also thought to play a role in preventing resorption of the chronic collections and contribute to their persistence and progression. Particle embolization and liquid embolic agents have demonstrated excellent results in a recent flurry of publications. These encouraging results have suggested the need for a large prospective randomized trial to investigate the true role of middle meningeal artery embolization as a stand-alone treatment for cSDH, the planning of which is currently underway.

Resident/Fellow Education and Training

The unprecedented expansion of endovascular techniques has led to a need to educate neurosurgical residents in the application of endovascular therapies, but more importantly, a need to train them in the basic skill sets needed, just as they would learn newer techniques in spine or tumor neurosurgery. The Neurosurgery Residency Review Committee and American Board of Neurological Surgeons (ABNS) have correctly made repeated and regular adjustments in the area of endovascular case

minimums for neurosurgery residents not only to include diagnostic angiography, but now also to include more complex intervention experience, such as aneurysm coiling.⁶⁴ The ability to effectively apply or perform endovascular techniques in neurosurgical practice requires formal fellowship training. This was initially addressed by the Committee on Advanced Surgical Training (CAST) of the Society of Neurological Surgeons. CAST took input from organized neurosurgery, neurology, and radiology to form the Neuro-Endovascular Surgery Advisory Committee (NESAC).¹⁶ NESAC initially certified training programs as well as practitioners. Further input from the ABNS, the American Board of Psychiatry and Neurology (ABPN), and the American Board of Radiology (ABR) has now led to the formation of the Credentialing Endovascular Surgery Advisory Committee (CESAC), which will facilitate the process of individual certification and make recommendations to specific respective boards, leading to focused practice certification for practitioners. NESAC, in its current state, will continue to review and certify endovascular training programs. Both NESAC and CESAC are composed of designated representatives from the ABNS, ABPN, and ABR.

The scope of practice of neurovascular endovascular surgery has become complex, requiring training in specific skill sets and techniques. It is expected that the required skill set will only increase as more vascular pathologic processes can be addressed by endovascular means. The future of neuroendovascular surgery is therefore inseparable from the future of vascular neurosurgery. In fact, they

are one and the same. Residents interested in the vascular disease processes that affect the central nervous system must understand the application of neuroendovascular techniques and if they want to treat these pathologies must be adequately trained in their implementation.

The Future

It is certain that neuroendovascular surgery will continue to be one of the primary methods of treating neurovascular diseases of the brain and spinal cord in the future. The experimental growth of acute stroke interventions alone could make endovascular treatments some of the most important for the population at large. Great forces are being brought upon healthcare delivery and in particular where and when patients are treated. Artificial intelligence (AI) and robotics, seemingly still in their infancy, will undoubtedly play a factor. Robotic systems have already been approved for cardiac and peripheral interventional radiology applications.⁴⁵ With these systems, the operator sits apart from the patient in a shielded area and controls the robot using a customized user interface. AI-type systems can analyze the operator/interventionist's movements and force application and mimic them. These systems can then "learn" and improve upon the operator's skills and techniques. Such systems have already demonstrated the ability to perform remote endovascular procedures from miles away. It is inevitable that such systems will become available and utilized to treat our patients.

It remains an exciting time to be part of neuroendovascular surgery. Complex vascular disease can be treated with disease-centered emerging technology, safely and effectively. At the same time, the scope of the diseases that can be treated and the indications for treatment continue to expand. When AI and robotics are added to the picture, the future seems ripe with opportunity and discovery.

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Disclosures

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