The description of cerebral aneurysms dates back to antiquity. Little was known, however, about the pathological mechanisms of aneurysm formation and treatment options for this disease until 200 years ago. The modern era of aneurysm treatment began with the hunterian ligation of the proximal artery, followed by clip and coil occlusion. In this article, the authors describe the transition from conservative therapy to internal carotid artery (ICA) ligation and gradual occlusion of the ICA to the direct placement of clips on aneurysms. The driving forces and rationale behind each major advancement are summarized, and the authors attempt to predict what these innovations mean for the future of intracranial aneurysm management.

The transition from hunterian ligation to intracranial aneurysm clips: a historical perspective

NIKA V. POLEVAYA, B.S., M. YASHAR S. KALANI, PH.D., GARY K. STEINBERG, M.D., PH.D., AND VICTOR C. K. TSE, M.D., PH.D.

Departments of Neurosurgery and Developmental Biology, Stanford University School of Medicine, Stanford, California; and Howard Hughes Medical Institute, Chevy Chase, Maryland

✓ The description of cerebral aneurysms dates back to antiquity. Little was known, however, about the pathological mechanisms of aneurysm formation and treatment options for this disease until 200 years ago. The modern era of aneurysm treatment began with the hunterian ligation of the proximal artery, followed by clip and coil occlusion. In this article, the authors describe the transition from conservative therapy to internal carotid artery (ICA) ligation and gradual occlusion of the ICA to the direct placement of clips on aneurysms. The driving forces and rationale behind each major advancement are summarized, and the authors attempt to predict what these innovations mean for the future of intracranial aneurysm management.

KEY WORDS • intracranial aneurysm • clip occlusion • history of neurosurgery

Ancient Times

The first description of an arterial aneurysm, attributed to Imhotep, can be found in the Ebers Papyrus. Records of attempts to treat these lesions date back to 2725 BC, when an Egyptian physician used a fire-glazed instrument to treat a bulging aneurysm. Although treatment of arterial dilation dates back to antiquity, the notion and underlying causes of the vascular changes predisposing patients to such aneurysms remained largely unknown. In 117 BC, Flænien Rufus, an Ephesian physician trained in Alexandria, Egypt, provided the first insight into the underlying causes of this class of vascular lesions by suggesting that their origins might lie in trauma. Progress in treatments for the disease and coining of the term “aneurysm” did not occur until Galen described the entity in AD 200. The next 1500 years saw an expansion of our knowledge about aneurysms, mostly due to the work of Islamic physicians. The definition of the term “aneurysm” in its modern sense as a dilation of a weakened artery was made by Lancisis, who defined the concept in 1728. To treat these lesions, several approaches were used with various degrees of success, and the history of the evolution of surgical intervention is described herein. The gradual progression from suture ligation of the proximal artery, to surgical clip placement, to endovascular coil occlusion, and the more modern combination endovascular techniques, has made it possible to treat these now mostly curable lesions.

Abbreviations used in this paper: CA = carotid artery; ICA = internal carotid artery; MR = magnetic resonance.

Proximal Artery Ligation Era

The rapid progress in aneurysm surgery started with the advent of proximal artery ligation. In a work published posthumously in the 1760s, Jean-Louis Petit reported his discovery that there is no significant effect on the brain even if one of the carotid arteries is thrombosed. His patient had an aneurysm at the bifurcation of the right common carotid artery that was cured spontaneously. Seven years later, an autopsy performed in that patient showed the lumen of the vessel to be completely occluded by an organized thrombus. Arterial ligation was popularized in the 1800s by John Hunter, who demonstrated safe and reproducible means of ligating certain peripheral arteries. Hunterian ligation, named in his honor, was adopted by many surgeons for the treatment of aneurysms of the ICA. Operating in 1885 on a patient thought to suffer from a tumor of the middle fossa, Victor Horsley (Fig. 1) pioneered ligation of the ICA for intracranial aneurysm treatment. The patient was described by Keen to be “in extremely good health” 5 years after that operation. Many surgeons after Horsley have ligated the ICA on encountering an intracranial aneurysm during an operation. It was not until 1928, however, that the first planned ICA ligation was performed for the sole purpose of treating a nontraumatic saccular aneurysm. The early, scattered cases of ICA ligation for aneurysms encountered during a craniotomy for a suspected brain tumor were not all as successful as Horsley’s case. These ligations were quite frequently followed by cerebral infarction. Many surgeons of the time, including Harvey Cushing, were rather pessimistic about the surgical treat-
treatment of nontraumatic saccular aneurysms, with morbidity and mortality rates of 13% each. In 1969, a larger series of 461 patients with CA ligation was published by Sahs and Locksley, in which they reported a 20.7% mortality rate and a 30% stroke rate. After the advent of microsurgery and microtechniques, the formerly widespread use of proximal artery ligation was abandoned for surgical clip placement to treat ordinary, smaller aneurysms. Nevertheless, CA occlusion continues to play an important role for certain giant aneurysms in these vessels. The danger of cerebral ischemia and infarction after CA occlusion has been greatly reduced by decreasing the risk of thromboembolism and by preoperative studies to determine the potential for collateral flow, which, if inadequate, can be supplemented by a surgically created arterial bypass.

The Transition Period

The outcomes of proximal artery ligation for aneurysm treatment so frustrated many surgeons, including Norman Dott of Edinburgh (Fig. 2), that he decided to take the risk of tackling an aneurysm directly. In 1931, with no angiographic assistance, he performed a frontal craniotomy in a 53-year-old patient, discovering a 3-mm aneurysm of the ICA, at which point he wrapped it with muscle from the patient’s leg. Many other surgeons, including Harvey Cushing, also tried to strengthen the weakened walls of intracranial aneurysms in an attempt to stabilize the flow and prevent further expansion of the lesion. However, in the sporadic cases of such treatment, surgeons reported quite variable degrees of success. These operations mainly occurred as a consequence of a craniotomy being performed for some other purpose, such as to treat a suspected tumor, and were not planned initially for aneurysm obliteration. Recently, Sadasivan, et al., revisited the wrapping approach by using an experimental venous pouch aneurysm model in rats to test different wrapping materials’ potential to strengthen the aneurysm wall. These authors found that cotton was the most suitable material for wrapping aneurysms, whereas traditional wrapping materials such as muscle and bovine collagen were absorbed shortly after application.

The advent of the Selverstone clamp in the 1950s influenced aneurysm surgery profoundly. The clamp was placed around the ICA to reduce the blood pressure within the lesion, allowing the walls to thicken and clotting to occur within the aneurysm sac. The Selverstone clamp provided surgeons with the ability to vary the degree of occlusion postoperatively, because the tools used to tighten the device extended from the clamp to the surface of the skin. This device could thus be reopened at the first sign of insufficient collateral circulation. Nornes demonstrated that graded occlusion of the ICA with the Selverstone clamp provides superior outcomes to those experienced with full occlusion. Silvani, et al., showed that complete clamp closure is likely to cause ischemic side effects.

The capacity for collateral circulation of the circle of Willis proved to be a major concern for both traditional proximal artery ligation and graded occlusion of the ICA by using the Selverstone clamp. As a consequence, neurosurgeons in the 1960s and 1970s devised various methods

![Fig. 1. Portrait of Victor Horsley. (Obtained at http://www.neurosurgery.org/cybermuseum/portraithall/leaders/leaders.html.) Reproduced with permission from the American Association of Neurological Surgeons, 5550 Meadowbrook Dr., Rolling Meadows, IL 60008.](image)
Technological advancements such as extracranial–intracranial arterial bypass attempted to solve the problem of diminished collateral circulation resulting from the ICA occlusion. Silvani, et al., suggested that extracranial–intracranial bypass minimized ischemic complications during gradual occlusion of the ICA; however, unfortunately it did not eliminate them completely.

Although the Selverstone clamp provided a tempting alternative to direct ICA ligation, several studies showed that it might not be the ideal aneurysm treatment. Mount investigated the outcomes in a large patient series, indicating a mortality rate of 13.8% and a morbidity rate of 40%. The outcome of gradual occlusion depended largely on the aneurysm location and its overall size as well as site accessibility for clamp placement. Also, several surgeons have shown that Selverstone clamp application may puncture the artery and induce thrombosis within the arterial lumen, causing complete occlusion and possibly death due to ischemia.

The advent of MR imaging imposed a new constraint on the implantable metallic devices used for aneurysm treatment, along with improved accuracy for surgical planning and postoperative monitoring. Devices such as the Selverstone clamp now were subject to MR compatibility scrutiny. Dujovny, et al., conducted a series of prominent studies in which they tested a wide range of neurosurgical devices used for aneurysm treatment. They investigated the mechanical and metallurgical properties of a series of arterial clamps, including Crutchfield, Selverstone, Salibi, and Kindt clamps, with respect to their composition, surface cleanliness, magnetic properties, and corrosion resistance. Crutchfield and Selverstone clamps were found to be nonferromagnetic. The Selverstone clamp, however, turned out to be much more corrosion-prone than other devices, suggesting that it would not be an adequate long-term solution for patients.

Norman Dott introduced another method of direct aneurysm attack when, in 1933, he attempted to ligate the neck of an aneurysm with surgical sutures. This approach was popular among the surgeons of that time. It demanded agility and confidence from the operator. Direct suture ligation is an extremely technical exercise; it requires the surgeon to dissect out the aneurysm neck and thread a suture around it. However, as reported by Sundt, the surgical clip soon displaced this method. The clip provided greater closing pressure and easier application to the many potential aneurysm sites for which surgical access was difficult. Several other surgeons, including Campbell and Burklund in 1953, and Drake and Amacher in 1969, attempted to combine the suture ligation with excision of aneurysms; however, these methods failed to gain widespread popularity and were abandoned for surgical clip placement.

**The Clip**

A major revolution in the treatment of this class of vascular lesions occurred serendipitously, much like many other phenomena in science and medicine. In 1911, in his quest to develop tools for tumor resections, Harvey Cushing (Fig. 3) produced what was to become the first vascular clip. Known as “the silver clip” or the Cushing clip, the tool was used in tumor surgeries for “placement on inaccessible vessels, which, though within reach of a clamp, are either too delicate or in a position too awkward for safe ligature.” Cushing, however, never used his invention for obliteration of intracranial aneurysms. McKenzie modified the Cushing clip and, somewhat ironically, in 1937, Cushing’s competitor Walter Dandy (Fig. 4) became the first neurosurgeon to use this device to clip an aneurysm. The new clip allowed surgeons to exclude an aneurysm selectively from the parent circulation, a concept that marked the beginning of the modern era of aneurysm surgery.

The clip that Dandy used in his 1937 procedure evolved significantly over the next several decades. It is noteworthy that in his writing in 1938 and in his textbook on brain surgery in 1945, Dandy addressed the issue of collateral circulation and the application of both ligation of the ICA in the patient’s neck and intracranially with a silver clip placed on the artery to “trap” the aneurysm. The simple V-shaped Dandy clip (the silver clip modified by McKenzie) was subsequently modified by Oliviercrona, who added winged blades to allow reopening of the device (the original Dandy clip could not be reopened). Schwartz introduced a miniature spring forceps clip to aid the reopening and to avoid shearing and tearing of the aneurysm. Mayfield modified Schwartz’s clip in 1952 because the earlier

---

**Fig. 2. Portrait of Norman Dott. (Obtained at http://www.st-andrews.ac.uk/~sshm/dott.html.)**
device was too large and its application into the small spaces of the cranium was quite awkward. Mayfield also attempted to reduce the risk of slippage by adding serrations to the clip, and designed an applicator that had tweezer-like dexterity and a drop lock. The evolution beyond the Mayfield clip resulted in a series of devices with significantly greater closing pressures to avoid incomplete occlusion of the aneurysm neck. Further development of aneurysm clips has been driven by balancing crucial factors such as size (to reduce the visual obstruction of the operating field), risk of slippage, potential damage to the aneurysm neck and the surrounding vasculature, and last but not least, the clip’s biosafety on MR imaging. Sugita and Spetzler clips are beautiful examples of the current solution to finding such a balance.

The development of aneurysm clips was greatly influenced by two revolutionary inventions: cerebral angiography and the operating microscope. Angiography was the brainchild of Egas Moniz, and produced in 1927. During the following decade, many surgeons added this diagnostic tool to their arsenal for combating aneurysms. Surgeons were no longer limited to addressing aneurysms of the ICA proper, and by the mid-1950s, many had extended such treatment to aneurysms on the branches of ICA. These advances paved the way for the development of surgical techniques for posterior circulation aneurysms. Kurze was the first neurosurgeon to use the operating microscope in surgery for intracranial aneurysms (in 1957, in Los Angeles). Nevertheless, the microscope was not reported as an adjunct to aneurysm surgery until 1966, after which Yaşargil is widely credited with popularizing this approach. The advent of microneurosurgery placed extra emphasis on clip development, demanding ever more slender clips that would allow the approach to narrow spaces of the cranial anatomy.

Even as late as the 1960s, many neurosurgeons doubted the effectiveness of aneurysm surgery. To a significant extent, this skeptical outlook was based on some of the less successful outcomes reported in series of aneurysm patients. In several small series, mortality rates as high as 86% were reported, although a mean mortality rate of 28.7% for aneurysm treatment with intracranial clip placement was reported by 1956. As detailed by Stein, Dandy himself had considered clipping and ligature of aneurysms on branches of the ICA “hopeless.” In 1963, Merritt advised surgery only for the purpose of resolving large associated hematomas. Alvord and Thorn concluded in 1977 that “no great difference in the number of survivors (the inverse of mortality) could be detected in previously reported series of cases regardless of the method of treatment, site or number of aneurysms, or any other factor
which could then be analyzed.” By 1970, however, with advances in microneurosurgery, clip occlusion of intracranial aneurysms was shown to have significantly better outcomes than CA ligation.32 The main factors influencing the success of the outcome appeared to be dome size, aneurysm location, and the patient’s age.

The invention of MR imaging has influenced modern clip development as well as the development of arterial clamps. Dujovny and colleagues17,18 performed a detailed analysis of the ferromagnetic properties of the Yaşargil, Sugita, and Perneczky clips and discovered great variability in these properties among different clips (even between clips of the same type) in response to MR imaging, suggesting that clips be tested before their application. Several intracranial clip fractures due to long-term corrosion have been reported, motivating meticulous investigation of stress corrosion properties of the various modern clips.26 The availability of modern metallurgical analysis tools has enabled this group of investigators to assess the microstructures, hardness, chemical composition, and susceptibility to stress corrosion failure of various clips,20 providing a rationale for the improvement of clip design, materials used, and individual testing of clips before application.

Unfortunately, clip occlusion continues to pose several major limitations. Not all aneurysms are amenable to clip placement. Aneurysms in which the dome-to-neck ratio is too small are much more difficult to clip, with fusiform and dissecting aneurysms being extreme examples. Also, any clip placement procedure poses the risk of incomplete occlusion, which may predispose the aneurysm to regrowth or rebleeding. Another risk that patients face during cerebral aneurysm surgery is that of an intraoperative aneurysm rupture due to clip placement. Perhaps in the future, malleable clips that conform to the angioarchitecture of a particular patient may help to circumvent some of these problems.

Conclusions

With the advancement of neurosurgical technology, the limitations of conservative management of aneurysms became increasingly apparent. Nonsurgical treatment groups in various studies tended to demonstrate significantly higher overall morbidity and mortality rates, with many patients dying of fatal subarachnoid hemorrhage and vasospasm.4,11,22,30 In cases of higher-grade aneurysms, mortality rates reached 80 to 90% for conservatively treated patients, even with modern treatments to lower blood pressure.11 The prognosis for conservative therapy for intracranial aneurysms was worse in comparison with both ICA ligation treatment and direct clip placement, both of which showed much higher patient improvement rates (70–80%).11,30 Because of these grim outcomes, most surgeons now argue for early and urgent surgical treatment for intracranial aneurysms, especially in the case of high-grade lesions, ones that have ruptured, or apparent increase from the original aneurysm size.4,11,23

Historically, the poor outcome associated with conservative therapy prompted the neurosurgical pioneers to use hunterian ligation; complete ligation at first, then followed by the transitional practice of gradual occlusion. Although occasionally used to this day for cases of giant, fusiform, and complex lesions,16,46 hunterian ligation did not prove to be the optimal treatment for intracranial aneurysms due to its ischemic and embolic complications in many patients, prompting continuation of the search for better treatments (Fig. 5). Aneurysm clips had initially compet-

**Fig. 5.** Timeline of major events in aneurysm treatment history.
ned with the practice of graded ICA ligation; however, technological improvements to the clip, the advent of the operating microscope, cerebral angiography, and MR imaging resulted in significantly more consistent and better outcomes for clip occlusion of aneurysms.

Currently, patients undergoing aneurysm surgery have a much lower risk of death or gross neurological morbidity. Hence, the concept of a “good outcome” is now subject to revision, because it requires a more subtle analysis of the neuropsychiatric state of the patient. Through the persistence, curiosity, and courage of the many neurosurgical pioneers, the clip has become a relatively safe and effective tool for aneurysm treatment and provides minimal obstruction of the operating field, optimal closing pressure, and small probability of slippage and tissue damage. These surgeons and their ingenious tools have transformed the natural history of aneurysm progression from a once discouraging and lethal vascular pathological entity into a mostly curable neurosurgical lesion.

References

33. Moniz E: L’encephalographie arterielle, son importance dans la localisation des tumeurs cerebrales. Rev Neurol (Paris) 2:72, 1927
History of intracranial aneurysm treatment methods


Manuscript received March 16, 2006. Accepted in final form May 11, 2006.

Address reprint requests to: Victor C. K. Tse, M.D., Ph.D., Department of Neurosurgery, Stanford University School of Medicine, MSLS Room P310, Stanford, California 94305-5327. email: vkt@stanford.edu.