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The Treatment of Acutely Ruptured Cerebral Aneurysms: Endovascular Therapy versus Surgery

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In 1937, Dandy performed the first successful, planned clipping of an aneurysm using a vascular clip designed by Harvey Cushing (1). Since that time, advancements in neurosurgical technique (including the use of the operating microscope, microsurgical instruments, better anesthesia, and improved perioperative management of complications of hemorrhage, such as hydrocephalus and vasospasm) have allowed the neurosurgeon to approach and clip successfully the majority of cerebral aneurysms.

The endovascular treatment of cerebral aneurysms dates from the mid-1970s with the introduction of parent vessel occlusion with balloons by Serbinenko (2). This treatment was successful in appropriate cases, but limited in applicability. The direct endosaccular balloon embolization of cerebral aneurysms was less successful owing to the complications of aneurysmal rupture and balloon deflation (3–5). Endovascular therapy became much more appealing with the development and subsequent approval by the Food and Drug Administration (FDA) (in 1995) of the Guglielmi detachable coils (GDCs) (Target Therapeutics, Fremont, Calif) (6, 7). These coils are made of a soft platinum helix that can be introduced into an aneurysm through a microcatheter. Detachment of the coil is effected by the application of a small positive current to the pusher device (to which the coil is attached by a small solder joint). This feature allows coil repositioning or resizing before final deployment. Improvements in the newer endovascular tools, such as the GDCs, and the resultant less invasive nature of endovascular techniques, have forced a reassessment of the standard management of aneurysms.

Initial controversy related to GDC technology was the global question of use versus nonuse. The controversy has been resolved in favor of use. This conclusion is based on current clinical practice, numerous publications documenting the successful application of GDCs, and FDA approval (6–13) (Target Therapeutics, supplied historical data, June 1997). Indeed, the GDC method has been used in more than 15 000 patients worldwide. Despite the documented acceptance of this treatment, controversies related to its use persist. Why? Parochial issues, like “turf,” cloud the response; but the basic dilemma is that we don’t know precisely when or where to use GDCs. This results from a lack of controlled comparisons between surgical clipping and endovascular GDC therapy upon which to base scientific decisions.

It is clear that the GDC technique, like traditional neurosurgical clipping, is not an end-all or be-all method of treatment. Despite the many advances made in the treatment of aneurysms over the last two decades, the overall outcomes from subarachnoid hemorrhage (SAH) and from aneurysmal rupture have changed little. Patients with SAH face a mortality rate of between 35% and 50%, and an associated morbidity of from 18% to 25% (14–16). In other words, only about 30% of SAH patients will have a good outcome, meaning return to premorbid functionality (17). While there is abundant evidence that the endovascular treatment of aneurysms can be beneficial to selected patients, there is little evidence that this, or any other treatment on the horizon, will dramatically alter the above figures. Rather, it is likely that progress in reducing cerebral aneurysm morbidity and mortality will proceed in incremental steps, with the GDC approach playing an important role, but not rendering surgical clipping obsolete. The evolving role of endovascular treatment of cerebral aneurysms is the focus of this discussion.

Natural Course without Treatment

Long-term follow-up of patients with unruptured intracranial aneurysms has revealed an average annual rupture rate of approximately 2% to 3% (2.3%), with a cumulative rate of hemorrhage of 20% at 10 years and 35% at 15 years, apparently independent of aneurysmal site (18). An important corollary is that the cumulative probability of rupture is significantly higher for multiple aneurysms. Untreated ruptured aneurysms have an even higher rate of rehemorrhage, approximately 20% during the first 2 weeks after initial hemorrhage (19).

Given the high morbidity and mortality associated with aneurysmal rupture, nontreatment of cerebral aneurysms leaves the patient at great risk and cannot be generally recommended.

Surgical Treatment

In assessing management outcome of intracranial cerebral aneurysms, it is important to take into consideration the expertise of the surgeon. When assessing neurosurgical methodology on the basis of published data, this important variable is usually optimized, because the litera-

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ture typically reflects the best neurosurgical experience. Additionally, evaluations of SAH that are population based, not biased by the experience of a particular neurosurgeon or institution, may best characterize the clinical course and the outcome of a group of patients with SAH. In one such study, performed in King County, Wash, 166 of 171 patients experiencing SAH were hospitalized. Of the 102 who underwent aneurysmal surgery, 40 had acute hydrocephalus, 32 had symptomatic vasospasm, and 30 rehemorrhaged. Sixty-eight percent survived to 1 month and 62% to 1 year (20). This once again underscores the high morbidity and mortality associated with SAH, even with modern neurosurgical management.

The available information on the outcome of neurosurgical management of aneurysmal SAHs and unruptured aneurysms points to several important factors that influence the surgical risk. To tailor the surgical management to each patient's needs, the following factors should be taken into consideration.

Clinical Grading.—In spite of the controversy surrounding which grading system is actually better at predicting eventual outcome, there is a general consensus that a poor initial grade predicts poor outcome. A recent prospective study, based on a consecutive series of 765 patients, confirmed a correlation between initial grade and outcome. In patients with an initial Glasgow Coma Scale score of 15, 84% had a good outcome, 8% had moderate disability, and 8% had a poor outcome; conversely, in patients with an initial score of 3, no patient had a good outcome, 12.5% had moderate disability, and 87.5% had a poor outcome (21). However, admission criteria alone as prognosticators of outcome can be misleading, as elegantly demonstrated in an important review by Winn and Mayberg (22). These authors point out that, when using an aggressive management strategy, clinical admission criteria may be insufficient to reliably predict outcome. Outcome, in their experience, seems to be determined largely by the extent of initial hemorrhage and subsequent development of intracranial hypertension. A prospective study from Sweden of an unselected series of 275 patients also confirms that the overwhelming cause of morbidity and mortality was the initial hemorrhage (23%), while delayed ischemic deterioration due to vasospasm accounted for an unfavorable outcome in about 5% of cases. Initial clinical condition and amount of extravasated blood correlated very strongly with outcome (23).

Location and Size of Aneurysm.—In a population-based study performed in Rochester, Minn, survival rates for posterior circulation aneurysms were considerably lower than comparable rates for anterior circulation aneurysms (24). Size also is an important determinant of successful surgical treatment, with larger aneurysms associated with poorer outcomes. With the notable exception of giant basilar tip aneurysms, size (not location) was found to be the key predictor of risk for surgical morbidity in a series reported by Solomon et al (25). The results of surgery of unruptured intracranial aneurysms were excellent or good in 100% of aneurysms less than 10 mm in diameter, 95%

with aneurysms 11 to 25 mm in diameter, and 79% in aneurysms greater than 25 mm.

Multiple Intracranial Aneurysms.—Twenty percent of patients harbor multiple intracranial aneurysms. These patients seem to fare less well than patients with single aneurysms. Overall, treatment mortality in a series of 302 patients with multiple intracranial aneurysms was higher (24%) than that in a series of 1314 patients with single cerebral aneurysms (20%). Increased manipulation of cerebral arteries during surgery for multiple aneurysms seems a plausible explanation for this difference (26).

Timing of Surgery.—The effect of timing of surgery on outcome remains controversial, though early treatment is increasingly recommended. While early surgery decreases the risk of rehemorrhage, delayed surgery, according to some authors, favorably affects the management mortality of those patients admitted with a grade of 4 or 5 on the Hunt and Hess scale (27). However, a larger population-based study from Finland performed to assess the effects of neurosurgical treatment on survival and functional outcome of SAH showed that the functional outcome at 4 years was significantly better in the group in whom surgery was performed early, even though survival was only marginally improved (28).

Medical Condition of the Patient.—Management morbidity and mortality are affected by complicating medical conditions. Cardiac complications may be responsible for much of the initial prehospitalization mortality. The frequency of electrocardiographic abnormalities is statistically greater for patients who have an increased amount of intracranial blood or intracerebral clot (29).

Age of the Patient.—Although prior studies have suggested that advanced age is associated with poor outcome following SAH, age does not seem to be associated with adverse outcome when patients are stratified according to clinical grade at admission (30). Furthermore, quality-of-life scores in the older age group appear acceptable for those who survive (31).

Finally, it is becoming increasingly clear that less obvious morbid conditions, which may be missed without such techniques as neuropsychological testing and neuroimaging, occur in an even larger population of surgical patients, including relatively low-risk patients. In one group of patients with a grade of 0 on the Hunt and Hess scale who had surgery for anterior circulation aneurysms, 26% had a moderate neuropsychological deficit when tested 6 months after surgery (personal communication, L. Grattan, June 1997). After aneurysmal rupture and clipping, patients as a group show impairment in executive functions and in some aspects of memory in comparison with normative data. In one study, 65% of the patients were impaired in at least one cognitive domain, with 19% showing executive impairment alone, 14% showing memory impairment alone, and 32% showing deficits in both domains (32). In a series of 155 survivors of surgical aneurysmal repair, 26% had postoperative ischemic lesions at neuroimaging, many of which were not apparent at routine neurologic examination (G. H. Zoarski, L. Grattan, M. I.

Rothman, D. Greenberg, E. F. Aldrich, J. M. Mathis, "Incidence of Postoperative Ischemic Brain Lesions Demonstrated by CT following Surgery for Ruptured Saccular Intracranial Aneurysms and the Implications for Functional Outcome," presented at the annual meeting of the American Society of Neuroradiology, Seattle, Wash, June 1996).

Endovascular Therapy

The US experience with GDC embolization of cerebral aneurysms has been encouraging. In the initial case series of 735 aneurysms treated with GDCs presented for FDA evaluation, the procedure was successful in approximately 75% of cases, with a greater than 90% occlusion of the lumen (13). Seventy-three percent of the treated patients had good outcomes, with a Glasgow Outcome Scale score of 1. Nevertheless, the overall major morbidity/mortality rate was 14%, a figure greater than that often reported in surgical series. However, this initial series is believed to have been strongly influenced by patient selection. The patients were required to be poor surgical candidates, with a poor clinical grade after SAH or with an aneurysm in an anatomic location or of a configuration associated with high surgical risk; 38% of the aneurysms were in the posterior circulation (while the natural occurrence of aneurysms in this location is only 8% to 12%); and 12% of the patients had undergone a failed surgical attempt at aneurysmal clipping. These factors adversely affected the outcome results of GDC therapy, but to an unknown extent (as there is no comparable surgical series).

More recent reports on the GDC treatment of aneurysms suggest that ruptured aneurysms may be successfully treated with similar or better clinical outcomes but lower complication rates. Several series report successful treatment of ruptured aneurysms in up to 80% of cases, with technical complications associated with major morbidity/mortality in 5% to 10% (11, 13) (G. M. Debrun, V. A. Aletich, P. Kehrl, et al, unpublished data). For unruptured aneurysms, cure has again been reported in up to 80% of cases, with major morbidity/mortality rates of 5%. These figures are approaching, but are not yet equal to, those cited in many reports of surgical clipping. Since endovascular treatment of cerebral aneurysms is still relatively new, operator experience continues to play an unknown role in outcome. Debrun et al reported a 50% to 80% increase in the success of endovascular treatment, while major morbidity/mortality decreased from over 10% to less than 5% as they accrued experience with the GDCs (Debrun et al, unpublished data).

The same factors that affect patient outcome with surgery apply to endovascular therapy. While definitive outcome analysis is not available, we predict that clinical grade at the time of admission will continue to be a major factor in patient mortality and morbidity after SAH. Additionally, the size and configuration of an aneurysm are already known to impact our ability to successfully achieve aneurysmal occlusion. Other factors, such as the patient's age and preexisting medical problems, the aneurysm's location, and the interval between SAH and inter-

vention, will undoubtedly have importance, but they are likely to be less significant than with surgical clipping.

Other management risk factors are peculiar to endovascular treatment of aneurysms. A few attempts at coiling (5% to 10%) will be aborted without coil deployment as a result of technical problems encountered during the procedure (eg, inability to contain coils in an aneurysm with a wide neck, or threatened parent vessel occlusion). In these cases, however, there is a low risk of complication, as the coil/delivery system is removed, leaving the possibility of subsequent surgical intervention. Another factor unique to GDC therapy is the 10% to 20% probability that a small residual portion of the aneurysm will be untreated (11, 13) (Debrun et al, unpublished data). The eventual outcome of these incompletely treated aneurysms remains a critical factor in determining the long-term success of GDC treatment. It is not known what percentage of these remnants will result in subsequent thrombosis, regrowth, and/or rupture, but anecdotal reports of all these outcomes have been recounted.

Early results suggest that GDC treatment does reduce the rehemorrhage rate, even in aneurysms that are not totally occluded by coiling (33). The less invasive nature of endovascular therapy relative to surgery and its applicability beyond 48 hours after SAH without exacerbating vasospasm make it a useful adjunct to surgery, even when total aneurysmal occlusion cannot be immediately achieved. Indeed, investigation should be directed at determining the usefulness of initially treating all patients with higher grade SAHs with GDCs and then following with surgery as needed after the period of risk for vasospasm has passed.

Interdisciplinary Treatment

Currently, conservative selection criteria for endovascular treatment of aneurysms include anatomically propitious vascular configurations and aneurysmal location for coiling, as well as poor clinical grade after SAH. At our institution, the majority of patients with ruptured aneurysms undergo emergency surgical procedures. However, a patient with a poor clinical grade and without a mass lesion is considered primarily for endovascular therapy. The management of unruptured cerebral aneurysms is discussed by a neurovascular team made up of members from neurosurgery, neuroradiology, neuroophthalmology, neurology, and neurointensive care that meets in a formal session and reviews prospective cases to determine a consensus for "most appropriate therapy" and to analyze outcomes. This routine has allowed us to develop several general guidelines in our own practice: 1) surgery remains the standard of reference for therapy and is undertaken when surgical risks are low or deemed equivalent to endovascular treatment (eg, typical middle cerebral and posterior communicating artery aneurysms); 2) endovascular treatment is indicated primarily when there are obvious advantages over surgery (eg, cavernous sinus and many basilar tip aneurysms); and 3) a combined approach is selected when circumstances indicate a less than optimum

situation for either approach alone (eg, poor clinical grade after SAH but an aneurysm that most likely cannot be completely occluded by endovascular therapy).

The Future

The continuous refinement of our tools and the better understanding of the pathophysiology of the disease, associated with ever-improving outcome information, will force an ongoing reassessment of our therapeutic recommendations. It is predictable that some of the questions we face will be answered by randomized, controlled studies. Until that occurs, management recommendations will rest on less stringent criteria, including the training, skill, and judgment of the local operators; availability of therapeutic alternatives; and economic considerations.

The ultimate choice of any medical therapy depends on the analysis of its risk/benefit ratio, as compared with the natural course of the disease and alternative therapies. By and large, simpler treatments supersede more complicated ones, given a comparable efficacy, because they tend to be less costly. Endovascular treatment of appropriately selected aneurysms is simpler than craniotomy and surgical clipping. Endovascular therapy currently requires a shorter period of operator training, is generally faster to perform, and is associated with more rapid patient recovery.

While GDC treatment represents the most promising technology to date for endovascular therapy of cerebral aneurysms, it must be remembered that it is only one step in the evolving process of this rapidly developing area. Even now, one could argue that all small, easily accessible, narrow-necked aneurysms should undergo an initial attempt at GDC coiling. The future promises materials that are not only safer but better able to occlude a wider anatomic variety of aneurysms. It is likely that with these technical improvements, endovascular techniques will play an increasing role in the overall management of cerebral aneurysms.

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