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Indications for Treatment of Cerebral Aneurysms from an Endovascular Perspective: The Creation of an Evidence Base for Interventional Techniques

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Since the first use of the Guglielmi detachable platinum coil (GDC) to treat an intracranial aneurysm in 1990 by the University of California at Los Angeles group [1], the treatment of intracranial aneurysm disease has been revolutionized. The GDC device opened the prospect of a completely new approach to the treatment of cerebral aneurysms. No longer is the treatment of cerebral aneurysms exclusively the province of a neurosurgeon by a direct approach at craniotomy. The endovascular techniques that have been developed in the last 14 years and are described in this issue have fundamentally changed the treatment approach and are likely to continue to do so.

The results of the International Subarachnoid Aneurysm Trial (ISAT) [2] have shown that for that group of patients with ruptured cerebral aneurysms suitable for endovascular coil treatment, there is a 7.4% (95% confidence interval [CI], 3.6–11.1) absolute reduction in the risk of death or dependency at 1 year and a 24% (95% CI, 12–33) relative risk reduction (modified Rankin score of 3–6, 23.5% after endovascular allocation and 30.9% after neurosurgical allocation) at 1 year [3]. Thus, short-term safety and efficacy of the technique have been proven to a grade 1 evidence level. This has been done within less than 10 years of the first use of the device in Europe and only 7 years after approval of the device by the US Food and Drug Administration (FDA). The speed of obtaining such grade 1 evidence for the use of a new technique has probably never been achieved before. Challenges remain for the endovascular community and device manufacturers in two areas, however: improving the long-term angiographic results and widening the range of aneurysms that can be dealt with by endovascular techniques.

An endovascular approach to cerebral aneurysms will always be potentially more elegant than an exovascular approach by craniotomy provided that it can be achieved as safely or more safely and with a similar degree of efficacy. The definition of efficacy is ultimately clinical, namely, survival free of symptoms from the aneurysm. In most cases, this means prevention of rupture or rerupture from the aneurysm. To establish this will take many years of complete and systematic follow-up of substantial cohorts of patients. The short- and medium-term results of angiographic occlusion are regarded as a reasonable surrogate marker; however, they should be recognized as such, and it remains to be confirmed in large patient cohorts what the significance of angiographic findings are relative to this clinical outcome. The present challenge for the community is how and in what manner to assess the existing and new devices that are becoming available. It is essential that new devices be introduced in a systematic and responsible manner and that they undergo systematic assessment. We need to ensure that increasing procedural complexity does not introduce an

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unacceptable increased risk to patients in exchange for no proven additional benefit.

Indications for detachable platinum coil treatment

What the International Subarachnoid Aneurysm Trial says and what it does not say

Much has been written by specialist societies [4–6], and there have been many discussions at meetings after the first publication of the initial ISAT results. It is important to understand the applicability of the results. First and foremost, the trial tested the technology and clinical experience available during the period of recruitment (1994–2002). During that time, endovascular techniques and experience evolved considerably, and neurosurgical techniques probably did not change much. Second, it is important to recognize that in any large clinical trial of a technique(s), there will be some differences between specialists in the patterns of enrollment and patient eligibility. Not every surgeon or interventionist necessarily regards the same patients as suitable for both treatments. Certainly, some endovascular operators are more comfortable treating aneurysms in different locations and with different anatomic configurations just as neurosurgeons are more comfortable clipping certain aneurysms, and individual skill varies. Thus, the exact suitability of any individual patient will and must remain the balanced judgment of the neurosurgeon and neurointerventionist, bearing in mind all the factors for that patient. These include the anatomy of the aneurysm, the clinical state and age of the patient, the skill and experience of the neurosurgeon and interventionist, the facilities available to them, and the timeliness with which treatment can be performed. Therefore, inevitably and quite correctly, there will be variations in the proportions of patients treated by the two techniques between neurosurgical centers. Nevertheless, for most patients with ruptured aneurysms, endovascular treatment will be anatomically feasible for the average trained interventionist and will be the safer treatment recommendation for the patient.

Application of newer techniques

Balloon-assisted coil treatment

This technique has been increasingly used by experienced practitioners and undoubtedly widens the anatomic range of aneurysms suitable for coiling. Its use was included in the ISAT. An operator needs to be familiar with the use of balloons, and their use undoubtedly carries a risk of vessel damage; however, the technique allows a wider anatomic range of aneurysms to be treated and widens the proportion of aneurysms treatable by endovascular techniques.

Use of intracranial stents

The approval by the FDA of the Neuroform Microdelivery Stent System (Boston Scientific, Natick, Massachusetts) has been greeted with enthusiasm by many practitioners. The availability of a self-expanding stent that can now be placed with reasonable ease in the intracranial vessels is a major advance, and there is no doubt that other similar devices will become available [7]. This device was not available or used during the ISAT. The main application of this device is improving angiographic outcomes in broad-necked aneurysms in combination with coils. Many practitioners use it as an alternative to balloon assistance. Nevertheless, one must sound a note of caution; particularly with the use of this device in the acute situation, the thromboembolic risk is increased with the use of stents, and the use of powerful antiplatelet drugs is usually required with the device. In the acute situation after subarachnoid hemorrhage (SAH), this presents its own risks. When standard platinum coils and balloon assistance can achieve good short-term results in prevention of rerupture, then, in my view, their use should be predominantly in the nonacute situation. It may be safer to confine them to retreatment, when necessary, of broad-necked internal carotid or basilar aneurysms, which is likely to be their most appropriate application. There is always a danger of overenthusiasm with such a device; that is, "when you have a hammer, everything looks like a nail."

Use of bioactive and coated coils

Animal studies indicate that the reaction to implanted suture material, such as polyglycolic acid/lactide incorporated into or on a platinum coil, induces significantly more tissue response than bare platinum in experimental aneurysms with a thickened tissue layer at the neck [8]. On this basis, there is the hope that this will improve angiographic outcomes in patients, ultimately, with a lower risk of rebleeding. The latter will be impossible to prove, because the frequency of late

rerupture after treatment with bare platinum coils is extremely low and any systematic study to demonstrate a significant difference would need to be so large and take so long as to be impossible to perform. It may be possible to demonstrate a difference in angiographic outcome provided that systematic and preferably randomized studies are performed (anecdotal case reports will not suffice). Such data will not be forthcoming without proper systematic studies, as in the field of cardiology, where the introduction of new stent technology (eg, drug-eluting stents) is routinely accompanied by data from systematic and usually randomized studies. This should certainly be the case if there is increased cost or any change to the safety profile of the device. Such studies should be demanded by the clinical community in the neurointerventional field.

Hydrogel-coated coils

Expanding hydrogel coatings on detachable platinum coils (Microvention, Aliso Viejo, California) [9] have been introduced into clinical use and have some attractions. They provide more complete filling of the aneurysm with a biocompatible material, which not only allows greater volume filling of the aneurysm but has two potential advantages: provision of a better scaffold at the aneurysm neck to allow endothelialization and reduction of the number of coils required to occlude an aneurysm, thus potentially reducing cost or at least not increasing it.

Onyx liquid embolic system

The Onyx system, which is composed of the liquid embolic agent ethylene vinyl alcohol copolymer dissolved in dimethyl sulfoxide, all of which seems to induce a vascular response, is starting to be used to treat intracranial aneurysms with the object of producing a healing reaction in the arterial wall. There have been many skeptical reactions to the use of this material, and it use is still limited to a fairly small number of physicians. The publication of the results of the multicenter European study showed some encouraging results in highly selected cases, however [10]. Recent experience has suggested that occlusion rates in the treatment of large and giant aneurysms are significantly better than those achieved with coil techniques, particularly when Onyx is used in association with stents. It may have a role to play in the management of large and giant aneurysms and recurrences after coiling, where the alternative treatment strategies are limited [11].

Summary

An approved device for endovascular treatment of intracranial aneurysms has only been available in the United States for less than 10 years. In that time, a revolution in the treatment of cerebral aneurysms has started and continues. The elegance and attraction of an endovascular approach for patients and physicians, if it matches open surgery in its safety and efficacy, cannot be argued. We now have grade 1 evidence for superior safety and efficacy at 1 year, and data are starting to accumulate of follow-up over 5- to 8-year time scales, which are reassuring that this benefit continues. Presently, in some experienced centers with access to a full range of devices, in excess of 90% of all intracranial aneurysms presented for treatment are being treated by endovascular techniques; however, a proportion of 75% to 80% is realistically achievable. What is beyond doubt and widely agreed is that patients should be managed in centers where both techniques are available. In this way, patients will receive the best possible care. It is thus difficult to argue with the conclusion of the American Society of Neuroradiology and American Society of Interventional and Therapeutic Neuroradiology position statement published in 2003 that "The study data allow us to conclude that patients with SAH and aneurysm anatomy indicating a high likelihood of success by endovascular techniques should be offered that option. This conclusion must be tempered by the limited data for long-term durability beyond 1 year" [6]. We hope that this latter statement will be addressed, at least in part, by the data that will shortly emerge from the medium-term follow-up to 5 years in the ISAT cohort.

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