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COMMENTARY

The Treatment of Unruptured Cerebral Aneurysms: Cause for Concern?

In this issue of the *American Journal of Neuroradiology* are 2 articles examining the risks associated with the treatment of unruptured intracranial aneurysms (UIAs).[1,2]

These articles used the National Inpatient Sample (NIS) data base. This samples one-third of all nonfederal hospital discharges in the United States and is a very powerful tool for examining clinical outcomes; it provides a very large sample size. It enables the study of a wide variety of conditions and their treatment, with the ability to examine differences with time that reflect what is happening in the real world of day-to-day clinical care.

The studies examined the effect of hospital and physician volume and the effect of clipping and coiling on the morbidity, complications, and mortality following treatment of an UIA. The studies used a surrogate end point for adverse outcome, namely non-home discharge (ie, discharge to a long-term or rehabilitation facility or in-hospital death). The study of Johnston et al showed that this correlates well with the clinical complications and adverse outcomes when applied to the treatment of UIAs.[3]

There may be a small proportion of patients in this cohort that had large symptomatic aneurysms that cause mass effect on cranial nerves with either optic nerve or third nerve compression; however, it is probable that the large proportion of patients were treated for small incidental aneurysms of <10 mm. When a patient is independent and walks into a hospital well and neurologically intact, any clinical outcome other than being in the same condition on discharge, able to return home and resume normal activities and work after a short interval, is a potential disaster for both the patient and the family. The data from these studies show that the probability of their non-home discharge and the need to be discharged to a rehabilitation facility after treatment by surgical clipping were 1 in 7 (approximately 14%), and for the patients treated by coiling, about 1 in 20 (approximately 5%). These figures should give cause for serious concern.

Many physicians, neurosurgeons, and interventionists might observe that these data do not accord with either the literature—be they case series, registries, or meta-analyses—or their own clinical outcomes. The literature, however, has the inevitable biases, particularly publication and center-selection biases. Published studies frequently come from high-volume and academic centers, which tend to publish their own case series and participate in multicenter studies. Case series with poor results are seldom published. The NIS data base provides a realistic picture across a broader health care environment from a wide range of hospitals because it reflects day-to-day practice in the United States.

When the International Study of Unruptured Intracranial Aaneurysms (ISUIA) published the clinical outcomes of clipping and coiling in the *Lancet* in 2003,[4] the results came as a surprise to many neurosurgeons. Those data came from many large international academic medical centers, and the 1-year clinical outcomes were substantially worse than expected. It showed that 12% of patients who were prospectively enrolled and underwent clipping were dependent or had a poor cognitive status following surgical treatment of an unruptured aneurysm.

The dramatic shift to coiling during the period of these studies between 2002 and 2008, from 19% to 63% of cases, has reduced the nationwide morbidity and mortality for UIA treatment from almost 15% to 7.6%. The time trends provide strong evidence that complications, morbidity, and mortality decline in direct proportion to increased coiling rates in almost all the measured fields.

Nevertheless, there is no reason to be complacent about the outcomes of coiling. The results of coiling in the published studies are better than those of clipping, with most articles and meta-analysis data suggesting morbidity rates of approximately 5%,[5] in line with these articles suggesting approximately 5% discharge rate to continuing care facilities or rehabilitation. Caution should be exercised in directly comparing the clipping and coiling data from these studies. The populations in the 2 groups are likely to differ and are thus not necessarily wholly comparable; however, most interesting, the surgical population had a mean age 3 years younger than that of the coiling population, and it would also be reasonable to assume that most of the high surgical risk posterior circulation aneurysms were treated by coiling.

The effect of volume, both physician and hospital, is also clearly evident from these data—higher volume strongly correlating with improved outcomes. This supports the need to centralize care in larger regional and academic centers to obtain optimum results when treatment decisions are made. Such regionalization often can present challenges even in the publicly organized health care systems and may be even more difficult in private health care systems.

The treatment risks observed in these studies must be balanced against the natural history risk of an UIA. It is likely that most of the patients having treatment had small- or medium-sized anterior circulation aneurysms, though the nature and size of the aneurysms are not available. This immediately raises the question as to whether these risks are too high to justify treatment on any reasonably balanced risk assessment. Even if one takes the upper end of the estimates for the annual rupture risk of a small anterior circulation aneurysm of <7 mm at 1% (and ISUIA suggested much less than this), then a surgical clipping treatment is exposing the patient to approximately 14 years of natural history on the day of surgery; for coiling, the figure would be approximately 5 years. If the annual rupture risks are as low as 0.5% or 0.1%, then the treatment risks appear unacceptably high.

The argument frequently used for surgical preference compared with coiling is that the former is the "definitive cure" (whatever that means), without the need for further follow-up. In the context of an incidental UIA, in which the risk of rupture is likely to be low without treatment, then a reduction of future risk from perhaps 1 in 100 or 1 in 500 per year to 1 in 5000 or 10,000 is irrelevant relative to procedural risks of 1 in 20 or 1 in 7. These figures reinforce the fact that when one undertakes treatment of UIAs, the overriding priority is to

minimize adverse events and clinical complications. Striving for angiographic perfection at the expense of a clinical event may not be a good idea when we have no idea how much such angiographic perfection changes the long-term rupture risk (and this is something we will never be able to measure after coil treatment).

Patients in general and the public at large are often poor at assessing relative risks in everyday life. Considerable anxiety is created by the fear of events with major impact but very low probability (such as an aneurysm rupture or radiation contamination in the current context).

Sadly, answering the question "Should an UIA be treated?" remains a major dilemma for the neuroscience community and is likely to remain so for the foreseeable future. The major effort made by Raymond et al[6] to address these questions in a systematic and scientific way with a randomized trial, the Trial of Endovascular Aneurysm Management, failed for a variety of reasons, which were well-addressed in a recent article in *Trials*.[7]

The authors are to be congratulated on succinct and powerful reminders of what we should all bear in mind, "First do no harm," and the need to put the relative risks of treatment and rupture risk in proper context. This should be at the back of the minds of all physicians advising and treating patients with unruptured aneurysms, be they neurosurgeons, neuroradiologists, or neurologists.

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