Patients With Small, Asymptomatic, Unruptured Intracranial Aneurysms and No History of Subarachnoid Hemorrhage Should Be Treated Conservatively

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It is well known that cerebral aneurysms are surprisingly prevalent in normal individuals and is estimated to be between 3.6% to 6.0% of the population. The essential paradox appears to be the dichotomy between the epidemiological data and surgical experience. Wiebers' study suggests that patients with unruptured cerebral aneurysms <7 mm in diameter have a benign natural history, but this contrasts with the experience of neurosurgeons, such as Weir, who are confronted by a substantial proportion of their patients with subarachnoid hemorrhage because of small ruptured aneurysms.

How could this paradox be explained? It seems to us that we still have a very incomplete picture of the prevalence, size, distribution, and natural history of unruptured aneurysms over longer time epochs. Furthermore, it is quite possible that aneurysms may form quickly, as suggested by Weir, and rupture early during their expansion phase, although still quite small in diameter. The duration of this growth period to rupture is uncertain. There does seem to be reasonable evidence that aneurysms of ≤7 mm, once detected (at an uncertain time after their development) have a fairly low rate of rupture over a 5-year period. Both clinicians and their patients, however, are concerned about lifetime risk, and long-term data are still lacking.

In assessing the risks and benefits of intervention in a patient who is found to have an unruptured aneurysm, the treatment decision is also influenced by the current evolution in therapeutic strategies. In ruptured cerebral aneurysms, endovascular coiling was shown to be superior to surgery in a single randomized controlled trial with a relatively short follow-up of 12 months. It seems likely that these technologies will continue to improve, which will further alter the risk/benefit ratio of intervention in individual patients.

For these reasons, we still believe that there is an enormous amount of work to do in terms of understanding the genesis, factors influencing rupture rates, and lifetime risk before we can be too rigorous about treatment algorithms for unruptured aneurysms. Fortunately, both protagonists are of our view that the decision about surgery needs to be individualized with numerous factors coming into play, including the general health of the patient, the patient’s age, the risks of the interventional treatment and, of course, the patient’s own wishes. Given the immediate risk of an intervention designed to modify outcome, the risk-tolerance of individual patients becomes an issue. Clearly, size isn’t everything!

References


KEY WORDS: aneurysm subarachnoid hemorrhage surgery
The management of patients with unruptured intracranial aneurysms depends on the natural history of these lesions and on morbidity and mortality rates associated with their repair. Epidemiological evidence from multiple vantage points suggests that a large majority of intracranial aneurysms do not rupture. It is therefore desirable to identify which unruptured aneurysms are at greatest risk of rupture and least risk for repair when considering which ones to treat.

Over the years, some have called attention to patients with small ruptured aneurysms diagnosed following subarachnoid hemorrhage (SAH), inferring that small unruptured aneurysms among patients with no history of SAH may have substantial subsequent rupture rates. Others have tried to extrapolate the natural history of UIAs by considering incidence rates of SAH to infer prevalences of UIAs in the population. The findings of the International Study of Unruptured Intracranial Aneurysms (ISUIA)\textsuperscript{1,2} and other natural history studies emphasize that the natural history of UIAs cannot be extrapolated from considering series of patients with ruptured aneurysms. Considerable confusion has arisen from not recognizing the substantial difference between the following questions: (1) what is the probability of a ruptured aneurysm being a certain size, and (2) what is the probability of future rupture of a given-sized aneurysm discovered before rupture? The second of these questions is relevant to clinical management of patients with UIAs. Available information suggests that most aneurysms that are going to rupture do so at the time of or soon after they form, and that the critical size for rupture is lower for those aneurysms that rupture early. The critical point is that one learns nothing about the natural history of UIAs by studying series of patients with ruptured aneurysms (and no UIAs). This applies not only to aneurysmal size but also to aneurysmal location.

A report in 1998\textsuperscript{3} by the ISUIA Investigators, based on 2621 patients with UIAs from Phase I of this study, included retrospective natural history data and prospective surgical morbidity and mortality data. Based on those data and other available information regarding unruptured intracranial aneurysms, the conclusion that one could not generally advocate repair of small UIAs in patients without prior SAH (Group I) was unavoidable. The magnitude of the difference between the best available natural history data concerning these patients and the morbidity and mortality associated with repair was such that one would be taking more than a normal lifetime of risk in 1 day to surgically repair such a lesion.

Following publication of the ISUIA data, others came to the same conclusion regarding conservative management of this group of patients.\textsuperscript{3–6} An expert panel convened by the American Heart Association with major neurosurgical representation concluded that “in consideration of the apparent low risk of hemorrhage from incidental small (<10 mm) aneurysms in patients without previous SAH, treatment rather than observation cannot be generally advocated.”\textsuperscript{4} Johnston et al\textsuperscript{5} in an extensive cost utility analysis regarding UIAs concluded that “treatment of small, asymptomatic, unruptured cerebral aneurysms in patients without a history of SAH worsens clinical outcomes and thus is neither effective nor cost-effective.”

More recent data from ISUIA\textsuperscript{2} include prospective natural history information regarding unruptured intracranial aneurysms and generally support the conclusions noted. Credible evidence to the contrary is lacking. It is unlikely that selection bias is relevant in the outcomes of this prospective cohort of largely asymptomatic patients whose aneurysmal characteristics were well represented across the entire gamut of aneurysmal sizes, locations, and patient ages and closely resembled those for the entire group of UIA patients and the treated UIA group. Analysis of censoring patterns also confirmed the above regarding potential treatment selection bias. Prospective ISUIA natural history data confirm retrospective results that aneurysm size (particularly in Group I patients) and location play a significant role in determining the risk of future rupture and provide more detailed rupture risk according to aneurysm size, location, and patient group. Compared with rupture rates in the retrospective cohort, however, there was an increased rupture rate among Group I prospective patients who had unruptured aneurysms at least 7 mm in diameter.

Operative morbidity and mortality associated with prospective repair of unruptured intracranial aneurysms involving 1917 UIA patients undergoing surgical repair and 451 undergoing endovascular repair revealed overall morbidity and mortality at 1 year of 12.2% and 9.5%, respectively. The
groups differed substantially in that higher risk patients were selected for endovascular repair. Age was a strong predictor of surgical outcome, and aneurysm size and location predicted surgical and endovascular outcomes.

The new ISUIA data allow one to go beyond aneurysmal size alone to identify subgroups of patients with UIAs who may be more or less likely to benefit from UIA repair (based on size/location/group specific natural history and age/size/location specific treatment morbidity and mortality rates). Although the question for the current discussion was centered around small Group I unruptured aneurysms, it is important to recognize the need to compare natural history and treatment morbidity and mortality rates for all sizes and sites of Group I and Group II UIAs, because more risky UIAs with respect to natural history often are more risky to repair. One must be particularly thoughtful regarding surgical repair of UIAs in patients ≥50 years of age and endovascular repair in patients ≥70 years of age.

Although it is always prudent to consider many medical components in a patient’s history regarding the advisability of surgery, the likelihood of improving on the observed natural history risk in the current group of patients (particularly those with anterior circulation UIAs <7 mm in diameter) is so low that it does not seem reasonable to invoke other common patient characteristics that would warrant repair. Some potential exceptions may warrant different consideration, such as the rare patient with a small Group I UIA causing symptoms other than rupture, particularly if these symptoms are acute or progressive. Other complex factors which are often taken into account include a positive family history of intracranial aneurysm or SAH and the presence of daughter sacs, multiple lobes, or other unusual hemodynamic or morphological aneurysmal characteristics. Such factors could confer greater risk with regard to natural history, but this cannot be substantiated by the available natural history data. It is, of course, also very important to consider the patient’s perspective regarding his or her desire to have the aneurysm treated even with the low risk of rupture but only with full recognition of the physician’s substantial capacity and responsibility to influence a patient’s peace of mind by the physician’s own perspective and counsel.

Endovascular treatment of intracranial aneurysms is an evolving technology which may offer benefits of definitive management without the risks of a craniotomy. Long-term efficacy of endovascular techniques is not yet known, and it is premature to make definitive comparisons of these techniques to open surgery for UIAs with current information. Although one meta-analysis involving both ruptured and unruptured aneurysms has suggested surgical morbidity and mortality was significantly higher than endovascular morbidity and mortality, morbidity was assessed at hospital discharge only and the studies involved are not standardized for entry criteria or end points. A recent randomized trial provided short-term comparative data regarding surgical and endovascular treatment of ruptured intracranial aneurysms. A randomized trial for those patients with UIAs appropriate for aneurysmal treatment comparing endovascular techniques with open surgery would be required to optimally compare these techniques.

References

Key Words: endovascular therapy ■ intracranial aneurysm ■ interventional radiography ■ patient care management ■ surgery
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Against

Bryce Weir, MD

It is foolhardy to remove from consideration of treatment any aneurysm solely because its maximal size is <10 mm or 7 mm. Annually, ≥15,000 American patients have subarachnoid hemorrhage (SAH) from aneurysms with a maximum diameter <7 mm and consequently experience irreparable morbidity and severe mortality. The majority of their aneurysms were, of course, unruptured, single, asymptomatic, and even smaller at some point before rupture.

If the rupture rates for <10-mm aneurysms in International Study of Unruptured Intracranial Aneurysm (ISUIA) I or <7 mm in ISUIA II are used with the known number of ruptured aneurysms of these sizes admitted each year to calculate the prevalence of such small aneurysms in American adults, there is an unbelievably high result: in the range of 7% to 14%. Previous best estimates of prevalence on the basis of retrospective and prospective, radiological and pathologic data have been ≈2% for all sizes of aneurysms and for those <10 mm, less than 1%. In autopsy studies, unruptured aneurysms have not outnumbered ruptured ones; the reverse is the case. Between ISUIA I and ISUIA II, the rupture rate has gone from <0.05% per year for <10 mm (no previous SAH), to 0.1% per year for <7 mm (no previous SAH), or more than doubled despite the fact that the size has moved in the direction of a lower rupture rate and follow-up for cumulative rates fell from 7.5 to 5 years. Also of note is the fact that this rate can now be contrasted with a morbidity and mortality of ≈5% for anterior circulation aneurysms ≤12 mm in patients <50 years, whereas in ISUIA I, only the global rate of 15.7% at 1 year for patients without previous SAH was given for all sizes and sites of aneurysms and all ages of patients.

The 5-year rupture rate of 0% for <7 mm aneurysms of the internal carotid, anterior communicating, or middle cerebral artery sites was compared with 2.5% for posterior communicating/posterior circulation aneurysms. The removal of posterior communicating aneurysms from the anterior circulation had no physiological justification. The remarkable difference in tendency to rupture between single and multiple small aneurysms suggested in ISUIA I (1 of 424 versus 17 of 641 at <10 mm) was probably not replicated. In ISUIA II, for single aneurysms, 2 ruptures in 535 at risk occurred in <7 mm, but there were 5 in the 7- to 9-mm range. In the multiple aneurysm cases, 7 ruptures in 439 at risk occurred at <7 mm but only 1 between 7 and 9 mm (the denominators are not given for the 7- to 9-mm sizes in the article). However, as in the first report, larger single aneurysms had a higher rupture rate than larger multiple aneurysms. Importantly, if there is not a highly significantly greater tendency for small multiple aneurysms to rupture, one cannot dismiss as irrelevant the longest follow-up data on unruptured aneurysms (almost entirely multiple-aneurysm cases), which found that after 20 years, 18% of 2- to 6-mm aneurysms had ruptured, as had 53% of 7- to 9-mm aneurysms. Also, in another large study, there was no difference in the sizes at rupture between single and multiple aneurysms.

Possible unintended selection bias may be inferred, for instance, from the following. Anterior communicating/anterior cerebral aneurysm cases made up only 10.3% of the 1692 untreated ones in ISUIA II. The 5-year rupture rates for <7-mm aneurysms was 0% for some anterior circulation aneurysms including this site. This suggests that these are uniquely safe lesions. However, in ruptured aneurysm clinical series, these aneurysms make up 35% to 50% of cases. They make up an even higher percentage of the smaller ruptured aneurysms in these series, and they rupture at the smallest average size. In pathologic series, the ratio of ruptured to unruptured aneurysms is high at this location, and the proportion of unruptured aneurysms at this site is lowest in elderly people. Aneurysms at this site are the most common exceptions to the rule that in multiple aneurysm cases, it is the larger and more proximal aneurysms that rupture.

ISUIA II was a prospective study, but it was not randomized. Not only were cases selected for no treatment, but there was a large crossover during the study from no treatment to treatment, which resulted in the censoring of such cases. The majority of them were followed for a relatively short time, so only 35 patients were assessed at 6 years after entry in the “without previous SAH” group of aneurysms <7 mm. The conclusions do not constitute class I evidence, and of course it is only 1 study. What cannot be known with certainty is whether the patients that were never treated were truly representative of the universe of unruptured aneurysm cases.
The risk of surgery is taken “up front,” whereas the risk of rupture does not diminish with time. A 40-year-old now has an anticipated life expectancy of >37 years; even the 60-year-old has >20 years.\(^3\) A policy based on repeated observation to watch for growth to a dangerous size has limitations because some aneurysms rupture without growing, and growth rates are unpredictable.\(^3\) The decision to recommend treatment for small, asymptomatic aneurysms should depend on the patient’s psychological makeup, their ability to understand relative risks in the absence of definitive data, their wishes, life expectancy, comorbidities, aneurysm number, site and morphology, arterial anatomy and anomalies, observed changes in the aneurysm between repeat visualizations, family history, underlying vascular diseases, smoking history, and the experience of the treating physician and hospital (and the size but not just the size).

References

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