Management of unruptured intracranial aneurysms (UIAs) has been controversial, and over recent decades, practice of neurologists and neurosurgeons has been governed more by bias than by scientific evidence. Given the high morbidity and mortality of aneurysmal subarachnoid hemorrhage (SAH), there is a consensus that prevention of hemorrhage is a desirable strategy, but it remains unproven and highly unlikely that a policy of treating all unruptured aneurysms will be effective in reducing overall morbidity and mortality in the affected population. The dilemma is well-summarized in a statement of prestigious aneurysm surgeon, Dr Bryce Weir: “It is essential that we preemptively treat patients deemed to be at high risk for aneurysm rupture to avoid both the horrendous risks of morbidity and mortality associated with SAH but also to prevent the delivery of an iatrogenic insult to patients destined to coexist peacefully with their unruptured aneurysms before dying of some other cause.”

The International Study of Unruptured Intracranial Aneurysms (ISUIA) has clearly demonstrated that risk of rupture is related to aneurysm size and also location of the aneurysm in the posterior circulation or at the internal carotid/posterior communicating artery sites (ICA/P-Com). A recent meta-analysis by Wermer et al also has substantiated risk factors of larger aneurysm size and location, as well as female sex and Japanese or Finnish descent.

Symptomatic aneurysms also are likely associated with increased risk of rupture, undoubtedly a reflection of the relationship to aneurysm size and instability. There seems general agreement that symptomatic aneurysms, even if small, should be considered for early treatment. Symptomatic aneurysms are, therefore, not included in this discussion. There remains, however, considerable uncertainty regarding the management of small (<7 mm diameter) incidental intracranial aneurysms and hard evidence to guide management (ie, clinical trial data comparing treatment over observation) are lacking.

### Epidemiology

Epidemiological studies of SAH and the natural history of UIAs have demonstrated differences among certain populations, leading to strong management recommendations by aneurysm specialists, especially in Finland and Japan. Noteworthy are the studies of Juvela et al using a Finnish population with UIAs, largely patients with previous aneurysmal SAH from another treated aneurysm and other existing aneurysms. In this cohort of 142 patients with 2575 person-years of follow-up, the overall annual risks of SAH were 1.3% and 1% for small (<7 mm) aneurysms at baseline. Notably, all verified aneurysms that later ruptured had increased in size and formation of de novo aneurysms was estimated at 2% per year. This ongoing long-term hemorrhage risk led the authors to recommend operative treatment, specifically craniotomy and clipping of all UIAs regardless of size or location.

### Table. Unruptured Intracranial Aneurysm Natural History

<table>
<thead>
<tr>
<th>Aneurysm Location</th>
<th>&lt;7 mm, Group 1*</th>
<th>&lt;7 mm, Group 2†</th>
<th>7–12 mm</th>
<th>13–24 mm</th>
<th>≥25 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cavernous (n=210)</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>3.0%</td>
<td>6.4%</td>
</tr>
<tr>
<td>AC/MC/IC (n=1037)</td>
<td>0%</td>
<td>1.5%</td>
<td>2.6%</td>
<td>14.5%</td>
<td>40%</td>
</tr>
<tr>
<td>Post-P comm (n=445)</td>
<td>2.5%</td>
<td>3.4%</td>
<td>14.5%</td>
<td>18.4%</td>
<td>50%</td>
</tr>
</tbody>
</table>

Hemorrhage rates by aneurysm size and location. Five-year cumulative rupture rates of unruptured aneurysms in the International Study of Unruptured Intracranial Aneurysms Prospective Cohort, according to size and location. AC indicates anterior communicating or anterior cerebral artery; cavernous, cavernous carotid artery; IC, internal carotid artery (not cavernous carotid artery); MC, middle cerebral artery; and post-P comm, vertebobasilar, posterior cerebral arterial system, or the posterior communicating artery.

*Patients in group 1 had no history of subarachnoid hemorrhage.
†Patients in group 2 had a history of subarachnoid hemorrhage from a separate aneurysm.

Adapted from Lancet. 2003;362:103–110.

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Controversy: Clipping of Asymptomatic Intracranial Aneurysm That is <7 mm

No

David G. Piepgras, MD

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of size if technically feasible and patient age and medical risk factors are not inordinate. Important also is their finding that among the studied population, mortality caused by SAH from a previously verified UIA was one-third that of death caused by unrelated causes.

A recent study of unruptured cerebral aneurysms in a Japanese population with largely incidental aneurysms and no prior history of SAH reported an overall annual rupture rate of ≈1%. A risk of rupture increased with increasing size of the aneurysm, whereas aneurysms with 7 mm or larger diameter (exclusive of giant aneurysms) had an annualized rupture risk of ≈3%, aneurysms <7 mm in diameter had a rupture risk of ≈0.4% per year. Aneurysm location at the anterior communicating and posterior communicating sites also had a higher risk of SAH. Those aneurysms with a daughter sac also were at increased risk for hemorrhage. Management recommendations based on these findings were not specifically stated; however, other Japanese authors have recommended treatment of small UIAs, especially in those patients with multiple small aneurysms.

The ISUIA involved predominantly North American and Northern European subjects, of whom 1692 constituted a prospective cohort. The ISUIA has clearly documented a higher rupture risk with increasing aneurysm size and also aneurysm location in the posterior circulation and ICA/P-Com sites. Rupture rates for small aneurysms (<7 mm) in the anterior circulation and exclusive of the ICA/P-Com site, however, were extremely low (<0.1% per year). In comparison, small aneurysms at the ICA/P-Com and vertebral basilar sites had an annualized rupture rate of ≈0.5% (Table), similar to that of the aforementioned Japanese study. In the ISUIA study, however, small aneurysms at the anterior communicating site were not associated with a higher hemorrhage risk.

Importantly, in the ISUIA prospective cohort, both treated and untreated, there was an annualized death rate of ≈2%, with the leading causes of death being unrelated to the intracranial aneurysm.

Management
Management strategy for any patient with UIA must consider the reality that treatment of UIA, whether craniotomy/clipping or endosaccular coiling, has a finite risk of major morbidity or mortality. For craniotomy and clipping, those risks, although low for the smaller anterior circulation aneurysms (≈3% in the ISUIA prospective cohort; Figure), increase significantly for patients >50 years of age, as well as for aneurysms in the verteobasilar circulation. This combination of factors (a very low rupture rate for incidental UIAs <7 mm in diameter, adverse survival natural history for persons with an UIA compared with the normal population, and inherent operative risks) make craniotomy and clipping for all small incidental UIAs an unsound management strategy. Exceptions may exist for those few patients without medical risk factors who are young in age and have special characteristics, such as a previous history of SAH from another (treated) aneurysm, aneurysms at the ICA/P-com or basilar caput locations, or a compelling family history of aneurysmal SAH. Under such circumstances, if treatment of a small aneurysm is to be recommended, then consideration should first be given to endosaccular coiling, which, provided suitable anatomy, has a lower procedural risk than aneurysm clipping and a good likelihood of aneurysm obliteration.

For most of the populace encountered in a routine neurological and neurosurgical practice, however, small (<7 mm) asymptomatic UIAs are best-managed with risk factor modification stressing cessation of smoking and management of hypertension.

Follow-up of the UIA with MR angiography or computed tomography angiogram is recommended in most situations with the expectation that the aneurysm will remain stable. A minority of aneurysms, even smaller aneurysms, may eventually develop a significant change in size or configuration. These aneurysms may be appropriately regarded as unstable and having an adverse natural history, such that treatment should be considered.

Disclosures
The author was a member of the Steering Committee of the International Study of Unruptured Intracranial Aneurysms (ISUIA), which was supported by a grant (RO1-NS-28492) from the National Institute of Neurological Disorders in Stroke (NINDS).

References


Key Words: aneurysm, subarachnoid hemorrhage, unruptured intracranial aneurysm
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Stroke. 2013;44:S100-S102
doi: 10.1161/STROKEAHA.111.000689

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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