Risk of Subarachnoid Hemorrhage After Surgical Treatment of Unruptured Cerebral Aneurysms

K. Tsutsumi, MD; K. Ueki, MD; M. Usui, MD; S. Kwak, MD; T. Kirino, MD

Background and Purpose—Recent progress in noninvasive imaging techniques has resulted in increased detection of unruptured aneurysms. Although many neurosurgeons advocate surgical intervention for such unruptured aneurysms, the long-term results of surgery for unruptured aneurysms have not been carefully investigated.

Methods—We analyzed 173 consecutive patients who had unruptured intracranial saccular aneurysm(s) detected by angiography that was performed for reasons other than subarachnoid hemorrhage (SAH). Of those, 115 cases were surgically treated and studied. All patients were followed up for either SAH, repeat treatment of aneurysms, or death. The median follow-up period was 8.8 years.

Results—Four of the 115 patients suffered SAH either from a de novo aneurysm (2) or from regrowth of clipped aneurysm (1), or from regrowth after wrapping (1). Additionally, 1 patient also suffered SAH from an unstudied basilar aneurysm. One patient was incidentally found to have de novo aneurysm and underwent reoperation 14 years after the first operation. The cumulative risk for SAH for the 114 cases excluding the basilar aneurysm case was 1.4% in 10 years and 12.4% in 20 years.

Conclusions—Although this study confirmed the long-term efficacy of clipping unruptured aneurysms, the risk of SAH was high compared with that in the general population, even after treatment. Considering the high mortality rate of SAH, long-term follow-up by angiography may be warranted for patients with surgically treated unruptured aneurysms. (Stroke. 1999;30:1181-1184.)

Key Words: cerebral aneurysm ■ cerebral angiography ■ subarachnoid hemorrhage

Noninvasive imaging techniques to visualize cerebral vessels, such as MR angiography and 3-dimensional CT, have shown rapid progress over the past decade in both quality and availability. Such progress has increased the chance of finding incidental asymptomatic cerebral aneurysms. When unruptured aneurysms are encountered, most neurosurgeons recommend surgical treatment, especially for aneurysms larger than 5 to 7 mm in diameter.1,2 The decision of whether to operate on patients with asymptomatic cerebral aneurysms should be based on an appropriate evaluation of surgical risk and benefit. Several studies estimating the surgical risks and natural risks for unruptured aneurysms have been published,3–7 including a recent report by the International Study of Unruptured Intracranial Aneurysms (ISUIA), sponsored by NIH/NINDS.8 However, the effect of surgical treatment of unruptured aneurysms on the prevention of future subarachnoid hemorrhage (SAH) is unclear. The simplest schema is that surgical obliteration of aneurysms eliminates the risk of SAH. Contradicting this notion, we recently showed that patients with completely obliterated ruptured aneurysms still carry a high risk for SAH because of formation of new aneurysms or regrowth of the original aneurysms.9–11 We hypothesized that such a risk may reflect an underlying predisposition of patients to aneurysm formation and that patients with unruptured aneurysms may be at a similar risk even after obliteration of the aneurysms. To verify this, we conducted a long-term follow-up study on 115 patients with surgically treated unruptured cerebral aneurysms.

Subjects and Methods

From 1976 to 1994 in Aizu Chuou Hospital, Aizuwakamatsu, Fukushima, Japan, 173 patients were found to have cerebral aneurysms through use of cerebral angiography performed for reasons other than SAH. Of those, 115 patients underwent surgery after a fully informed consent was obtained. The remaining 58 patients chose not to receive surgery after being informed. In-hospital medical records of these patients were reviewed, and the follow-up information was obtained either by interviews at the clinic, by telephone calls, or by letters to identify causes of death or incidents suggestive of SAH. SAH was diagnosed by CT scan in all cases. The causes of death were determined on the basis of information obtained from doctors who took care of the patient at their deaths. The end point of the follow-up was set on January 1998. The Kaplan-Meier method was used to calculate the risk of SAH. Patients who died during the period of causes other than SAH, were
### Cases of SAH After Treatment of Unruptured Aneurysms

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, y</th>
<th>Sex</th>
<th>Reason for Angiogram</th>
<th>Original Site</th>
<th>Type of Surgery</th>
<th>Aneurysm Site</th>
<th>Type of New Aneurysm</th>
<th>Time to SAH, y</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>F</td>
<td>Infarction</td>
<td>L MCA</td>
<td>Clipping</td>
<td>LMCA</td>
<td>Regrowth</td>
<td>11</td>
<td>Death</td>
</tr>
<tr>
<td>2</td>
<td>40</td>
<td>F</td>
<td>Infarction</td>
<td>R MCA, L ICA</td>
<td>Clipping</td>
<td>R ICA</td>
<td>De novo</td>
<td>12</td>
<td>Death</td>
</tr>
<tr>
<td>3</td>
<td>59</td>
<td>F</td>
<td>Infarction</td>
<td>ACoA, L ICA</td>
<td>Clipping</td>
<td>LMCA</td>
<td>De novo</td>
<td>16</td>
<td>Poor</td>
</tr>
<tr>
<td>4</td>
<td>67</td>
<td>F</td>
<td>Infarction</td>
<td>R MCA</td>
<td>Wrapping</td>
<td>RMCA</td>
<td>Regrowth</td>
<td>7</td>
<td>Death</td>
</tr>
</tbody>
</table>

ICA indicates internal carotid artery; ACoA, anterior communicating artery; and MCA, middle cerebral artery.

lost to follow-up, or underwent retreatment of aneurysms were treated as censored data at that time point.

### Results

In the 115 patients studied, angiography was performed for ischemic events in 39, intracerebral hemorrhages in 26, vertigo in 10, brain tumors in 8, head injuries in 7, chronic subdural hematomas in 7, headache in 6, oculomotor nerve palsies in 5, and for other reasons in 7. The mean age of the patients was 57.6 years (range, 20 to 79 years). There were 55 men and 60 women. The preoperative cerebral angiography included 4-vessel study in 8 patients, 3-vessel study in 84, 2-vessel study in 20, and 1-vessel study in 3. Multiple aneurysms were found in 29 patients: 2 aneurysms were treated by clipping in 20 patients, wrapped in 4, and untreated in 5 because of the small size.

The follow-up period ranged from 1 to 21 years, with the median follow-up period being 8.8 years. Only 1 patient was lost to follow-up, at 5 years after the treatment. During the follow-up period, 30 patients died of causes other than SAH: 10 of cardiovascular disease, 4 of pneumonia, 3 of stroke other than SAH, 3 of surgical complications, and 6 of other known causes. One of the 3 surgical deaths occurred in the first month after the surgery, and 2 occurred within 6 months. Four patients suffered permanent neurological deficit caused by surgery: hemiparesis in 3 and dementia in 1. Therefore, surgical mortality and morbidity in this series were 2.6% (3/115) and 3.5% (4/115), respectively. The remainder of the 108 cases were unchanged after surgery. The cause of death could not be determined in 4 cases; 2 of these were cases of sudden death in which the patients were suspected of having had acute myocardial infarction.

Five of 115 patients had SAH that was confirmed by CT. In all 5 cases, cerebral angiography was performed to identify the bleeding site. Bleeding was from a newly formed (de novo) aneurysm (ie, not found at the initial angiography) in 2 cases, from regrowth of clipped aneurysm in 1 case, from growth of wrapped aneurysm in 1 case, and from a basilar artery aneurysm that was not covered by the initial bilateral carotid angiography in 1 case. As the ruptured aneurysm in the last case was not originally screened, we excluded this case from further analyses. For the remaining 4 cases, the mean interval between the original treatment and SAH was 11.5 years (range, 7 to 16 years). In the regrowth case postoperative angiography was not obtained, but the surgical record, including intraoperative photographs, indicated that the clipping was complete and no residual neck was observed at surgery. Of these 4 patients, 3 died and 1 recovered with major morbidity. During the follow-up period, 1 patient was incidentally found to have developed a de novo aneurysm and underwent reoperation 14 years after the first operation. The details of the 4 cases of SAH from a regrowth or de novo aneurysm are summarized in the Table, and a representative case of a de novo aneurysm causing SAH, case 2 in the Table [bc+], is shown in Figure 1. The cumulative risk for developing SAH, based on 114 cases and calculated by the Kaplan-Meier method, was 1.4% in 10 years and 12.4% in 20 years. These data were compared with the cumulative risk of recurrent SAH in 220 patients with completely obliterated ruptured cerebral aneurysms previously analyzed by the same method at our institution (Figure 2). The risks for those 2 groups were not significantly different ($P=0.522$, log-rank test).

### Discussion

Several studies have shown that the natural risk of SAH from unruptured aneurysms is 1% to 2% per year, and the risk of SAH in the normal population is 0.01% to 0.05% per year.6,7,12–14 The International Study of Unruptured Intracranial Aneurysms (ISUIA) recently reported surprisingly low rates of SAH from unruptured aneurysms, posting <0.05% per year for aneurysms <10 mm in diameter and approximately 1.0% for those >10 to 25 mm in diameter. However, the patients enrolled in that study apparently consisted of a specific group selected for nonsurgical treatment and may not represent the actual risk in nonselected unruptured aneurysms.

An optimistic assumption is that appropriate surgical treatment of aneurysms would eliminate the risk or at least reduce it to the level of normal population. However, the patients in our series still had a significantly higher risk of SAH even after surgery (1.4% in 10 years and 12.4% in 20 years) compared with the normal population. In fact, the risk was similar to that of patients with surgically treated ruptured aneurysms. In a study of 220 cases, we have shown that patients with completely obliterated ruptured aneurysms...
carry a higher risk for recurrent SAH: 2.2% in 10 years and 9.0% in 20 years. The risk in the current series was similar to that in patients with obliterated ruptured aneurysms (Figure 2). Given that surgery does not change the underlying vascular condition that contributed to aneurysm formation, it is reasonable to assume that the higher risk of SAH from de novo aneurysms or regrowth of aneurysms was similar between ruptured and unruptured aneurysms.

The notion that systemic factors could influence the formation of cerebral aneurysms is not new. Over the past 30 years, many authors have reported the studies of numerous families carrying a high risk of cerebral aneurysm and subsequent SAH, strongly suggesting that inheritable systemic conditions contributed to aneurysm formation. In addition, some diseases with known genetic alterations, such as autosomal dominant polycystic kidney diseases, Ehlers-Danlos syndrome type IV, Marfan’s syndrome, and neurofibromatosis type 1, show predisposition to cerebral aneurysms. Our data may suggest that nonfamilial, sporadic cerebral aneurysm patients could also harbor similar systemic conditions.

During operation on asymptomatic aneurysms, the priority of the procedure is safety, which often forces surgeons to compromise by performing imperfect clipping or wrapping of aneurysms to avoid the kinking or occlusion of normal vessels. The risk of regrowth and subsequent bleeding from such aneurysms may well be higher for completely obliterated ruptured aneurysms. Although the number was too small for individual statistical analysis, SAH occurred in 1 of 10 wrapped unruptured aneurysms (10%) in our series compared with 1 of 105 clipped aneurysms (1%). Thus, the unique situation of unruptured aneurysms that could diminish the benefit of surgery also has to be recognized before the decision of whether to operate is made.

In summary, our data indicate that surgery for unruptured aneurysms decreases but does not eliminate the risk of SAH and that patients are at significantly higher risk for SAH in a long-term period. Bleeding can be either from de novo aneurysms or from regrowth of treated aneurysms, and such risk may be inherent in patients with cerebral aneurysms. Surgical intervention is therefore justified if performed at a sufficiently low risk, but such patients must be recognized as carrying a higher risk for new aneurysm formation even after surgery and may benefit from cautious follow-up for a long period. Continuous improvement of noninvasive imaging techniques will contribute to make such an approach safer and more reliable.

References


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Stroke. 1999;30:1181-1184
doi: 10.1161/01.STR.30.6.1181

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/30/6/1181

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