Risk of Recurrent Subarachnoid Hemorrhage After Complete Obliteration of Cerebral Aneurysms

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

Background and Purpose—The neck clipping of cerebral aneurysms is a well-established treatment for subarachnoid hemorrhage (SAH) caused by aneurysmal rupture. However, it is still unclear how great a risk of recurrence patients with a successfully treated aneurysm carry over a long-term period.

Methods—Of 425 patients with SAH surgically treated in Aizu Chuou Hospital from 1976 to 1994, 220 cases meeting the following criteria were studied: (1) all aneurysms detected by 3- or 4-vessel cerebral angiography were clipped, (2) complete obliteration of aneurysm(s) was confirmed by postoperative angiography, and (3) the patient survived >3 years. All patients were traced until January 1998 for recurrent SAH or death. The mean follow-up period was 9.9 (range, 3 to 21) years.

Results—Six patients (2.7%) had recurrent SAH, each with an interval ranging from 3 to 17 years (mean, 11 years) since the original treatment. In addition, 2 patients were found to have regrowth of the originally operated aneurysms. The cumulative recurrence rate of SAH, calculated using the Kaplan-Meier method, was 2.2% at 10 years and 9.0% at 20 years after the original treatment.

Conclusions—The recurrence rate was considerably higher than the previously reported risk of SAH in the normal population, and the rate increased with time. These data indicate that patients with ruptured cerebral aneurysms still carry higher risks for SAH in a long-term period, even after complete obliteration of the aneurysm, and that periodic examination to detect recurrent aneurysms may be indicated for such patients. (Stroke. 1998;29:2511-2513.)

Key Words: cerebral aneurysm ■ cerebral angiography ■ subarachnoid hemorrhage

Treatment of ruptured cerebral saccular aneurysms is one of the most important achievements of modern neurosurgery. The safety of the surgical procedure in obliterating aneurysms has improved dramatically with the introduction of the surgical microscope, and the invention of various microsurgical tools, including reliable aneurysmal clips, has also contributed to reduce perisurgical morbidity and mortality to a level that was inconceivable in the 1950s.1,2 Furthermore, refinement of surgical skills enables early intervention, which has further improved the results by eliminating the risk of rebleeding during the acute, unstable period.3,4 As such, surgical aneurysmal clipping is a standardized procedure, and patients often return to their previous activity if they survive the acute phase of the disease. However, the degree of risk that patients with successfully treated aneurysms carry in a long-term period is still unclear, as is the optimal follow-up strategy for these patients.5–7 Although repeating angiography may be advocated for those with multiple aneurysms or with an incompletely obliterated aneurysm, it is not a common practice if the clipping is considered “perfect.”8–10 To address this issue, we conducted a long-term follow-up study on 220 patients treated at our hospital for ruptured cerebral aneurysms since 1976, in whom the complete obliteration was confirmed by postoperative angiography. The community-based practice of our institution in a relatively closed region allowed us a nearly complete follow-up for a large series of patients for as long as 21 years.

Subjects and Methods
From 1976 to 1994, 696 patients were admitted to our hospital for subarachnoid hemorrhage (SAH) confirmed by CT scans, and 425 patients underwent surgery to obliterate ruptured cerebral aneurysms by aneurysm clipping. Of those, 220 cases that met the following criteria were studied: (1) all the aneurysms detected at the preoperative 3- or 4-vessel cerebral angiography were treated; (2) complete obliteration of aneurysm(s) was confirmed by postoperative angiography; and (3) the patients survived for >3 years. The 3-year cutoff was chosen to focus on the long-term results for fully recovered patients. In addition, there were no recurrent SAHs during the first 3 years after the operation among the patients fulfilling criteria (1) and (2). In-hospital medical records were carefully reviewed, and follow-up information was obtained by interviews at the clinic, by telephone calls, or by letters to identify the cause of death or incidents suggestive of recurrent SAH. In all cases, SAH was diagnosed by CT scans. Causes of death were determined on the basis of information obtained from doctors who took care of the patients at their deaths.
The Kaplan-Meier method was used to calculate the risk of recurrence of SAH. If a patient died during the period of causes other than SAH, was lost to follow-up, or underwent retreatment of aneurysms, it was treated as censored data at that point.

### Results

The mean age of the analyzed patients was 55.8 years (range, 24 to 79 years). There were 104 men and 116 women. The types of clips used were the Sugita in 203 cases, Yasargil in 11, Heifetz in 3, and Sundt-Kiss in 1. Multiple aneurysms were found in 31 patients, and the total number of clipped aneurysms was 260. The location of the aneurysm was anterior communicating artery in 89, anterior cerebral artery in 16, middle cerebral artery in 83, internal carotid artery in 53, and vertebrobasilar artery in 19 aneurysms.

The follow-up period ranged from 3 to 21 years, with a mean follow-up period of 9.9 years. Only 1 patient was lost to follow-up, at 7 years after surgery. During the follow-up period, 28 patients died of the causes other than SAH: malignant neoplasm (6), cardiovascular disease (6), stroke other than SAH (3), pneumonia (8), renal failure (3), and cirrhosis (1). The cause of death could not be determined in 1 case.

Recurrence of SAH was observed in 6 cases. Only 1 of the 6 cases originally involved multiple aneurysms. The mean interval between the original treatment and the recurrence was 11.0 years (range, 3 to 17 years). Of these, 1 patient suffered severe SAH and died before treatment. In the remaining 5 cases, cerebral angiography was performed to identify the bleeding site, which was confirmed at the surgery. Bleeding was from a de novo aneurysm at a different location from the original site in 2 cases and from an aneurysm regrowth at the original location in 3 cases. Sugita clips were used in the 3 regrowth cases. Prognosis was good in 3 cases and poor in 1; in 2 cases the patient died. There also were 2 patients who showed regrowth of the original aneurysm on angiography performed as a study for transient ischemia attacks at 12 and 18 years, respectively, after the first operation. A Sugita clip was used in one and a Yasargil clip in the other; both underwent surgery. The surgery in the 5 regrowth, (3 ruptured and 2 nonruptured) confirmed that the previously applied clip obliterated a part of the aneurysm that was of a size equivalent to the original aneurysmal size, indicating that the slippage of the clip was not the likely to be the cause. These results are summarized in the Table.

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<th>Case/Age/Sex</th>
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<td>R MCA</td>
<td>Regrowth</td>
<td>10</td>
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</tbody>
</table>
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ICA indicates internal carotid artery; ACom, anterior communicating artery; and MCA, middle cerebral artery.

Kaplan-Meier analysis showed the cumulative risk for the recurrence of SAH to be 0.5%, 2.2%, 5.5%, and 9.0% at 5, 10, 15, and 20 years postoperatively, respectively (see the Figure).

### Discussion

Our study showed that patients with ruptured aneurysms still carry a higher risk of SAH even after complete obliteration of the original aneurysms. The incidence of SAH in the general population is estimated to be 0.0% to 0.03% per year in multiple studies, and the recurrence rate for SAH in our series was >10 times higher. Although the mean age of the patients in our series was 55.8 years, which was relatively high, the risk was still higher than the age-specific incidence in the population aged >60 years in those studies, which was 0.03% to 0.06% per year. Interestingly, the risk seems to increase with time, most likely reflecting the time required for the formation of new aneurysms. This is not surprising, considering that neck clipping is to eliminate the immediate cause of bleeding but not to correct the underlying cause of aneurysm formation. Our data thus indicate that a patient with a perfectly applied aneurysm clip is not as free from disease as the normal population.

Of the 6 cases with recurrent SAH, 5 originally had a single aneurysm, and only 1 had multiple aneurysms. Given that the ratio of single-aneurysm cases versus multiple-aneurysm cases in the whole series was 6.1 (189 versus 31), there seems to be no
difference in the risk of recurrent SAH between single-aneurysm cases and multiple-aneurysm cases in this series.

Once aneurysmal SAH occurs, 30-day contemporary mortality rates reach 40%.\textsuperscript{13,14} Therefore, an adequately designed follow-up strategy might further improve the prognosis of patients with SAH. Given the mean interval-to-recurrence of 11 years shown by our study and the fact that 5 of 6 recurrences occurred >9 years after the first surgery, one possible strategy would be to repeat an imaging study to visualize cerebral vessels every 9 to 10 years. Unfortunately, MR angiography or 3-D CT for cerebral arteries are not presently reliable in patients with intracranial aneurysm clips. However, recent introduction of titanium aneurysmal clips that are compatible with MR angiography will increase the opportunity for screening with MR angiography in the future.\textsuperscript{15} Otherwise, digital subtraction angiography seems to be the most appropriate test to detect de novo aneurysms or regrowth of original aneurysms, although whether the risk of digital subtraction angiography, estimated to be 0.1% to 0.5% for permanent neurological deficit,\textsuperscript{16,17} is acceptable for its use in such follow-up studies may be controversial.

These data also serve as a baseline for endovascular surgery when it is to be evaluated for long-term efficacy in the prevention of SAH.

References
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*Stroke*. 1998;29:2511-2513
doi: 10.1161/01.STR.29.12.2511

*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:
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