The Natural History of Intracerebral Aneurysms

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The International Study of Unruptured Intracranial Aneurysms enrolled 4060 patients from 61 centers in the United States, Canada and Europe. Forty-two percent were observed without planned surgery at time of entry, while 58% underwent surgery or endovascular procedure at time of entry. The morbidity and mortality in these groups were determined and correlated with size, location and other comorbidities.

STUDY METHODOLOGY

This study was a prospective study of eligible patients with an unruptured cerebral artery aneurysm diagnosed between 1991 and 1998 at one of 61 participating neurosurgical centers. Study subjects had at least one unruptured aneurysm. Some had a past history of a successfully treated ruptured aneurysm at a different site. Subjects had to have no disability or minimal disability to be included. Approximately 40% of all subjects had hypertension.

Exclusion criteria included: mycotic and traumatic aneurysms, diameter less than 2 mm, a history of intracranial hemorrhage or subarachnoid bleed from an undetermined source, and malignant brain tumor.

Patients were assigned to either an operated or an unoperated cohort on the basis of clinical decision. All aneurysms were defined by arteriography. Unoperated patients were followed-up annually. Operated patients were assessed at 7 and 30 days post-procedure and then annually. Morbidity included assessment of both functional and cognitive status. The assessment instruments included an annual questionnaire assessment, review of medical care, and the telephone interview for cognitive status when needed.

Detailed information was obtained for all end points and assessed centrally at the Mayo Clinic. Analyzed data included CT and MRI scans, cerebrospinal fluid, intra-operative findings, and autopsy reports.

Statistical analysis included chi-squared test for categorical variables and t test for continuous variables. Predictors of hemorrhage were ascertained from a proportional hazards regression model.

RESULTS

Unoperated Cohort

There were 1692 patients in the observed cohort, mean age of 55, 75% women and 92%
HEIDENREICH—INTRACEREBRAL ANEURYSMS

Table 1. 5-year Cumulative Rupture Rate According to Size and Location for Unoperated Aneurysms

<table>
<thead>
<tr>
<th>Prior History of Subarachnoid Bleed Unrelated to Index Aneurysm</th>
<th>No Prior History of Subarachnoid Bleed</th>
<th>7–12 mm</th>
<th>13–24 mm</th>
<th>≥25 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cavernous carotid artery (n = 210)</td>
<td>0</td>
<td>0</td>
<td>3.0%</td>
<td>6.4%</td>
</tr>
<tr>
<td>Anterior/middle/internal carotid artery (n = 1037)</td>
<td>1.5%</td>
<td>0</td>
<td>2.6%</td>
<td>14.5%</td>
</tr>
<tr>
<td>Posterior cerebral/vertebrobasilar system (n = 445)</td>
<td>3.4%</td>
<td>2.5%</td>
<td>14.5%</td>
<td>18.4%</td>
</tr>
</tbody>
</table>

White. Only 4 were lost to follow-up, and 727 were censored due to surgical or endovascular treatment or death. The mean follow-up was 4.2 years.

Three percent in the unoperated cohort had an aneurysm rupture during follow-up, 96% occurring within 5 years.

Significant predictors of hemorrhage by relative risk (RR) with internal carotid aneurysms as reference were: size of 7–12 mm diameter RR = 3.3 [95% CI 1.3–8.2], 12 mm diameter RR = 17 [8.0–36.1], and 3 locations of basilar artery RR = 2.3 [1.1–4.2], cavernous artery RR = 0.15 [0.04–0.64], and posterior communicating artery with carotid RR = 2.1 [1.1–4.2]. Ninety percent of all observed unruptured aneurysms were in the anterior circulation. Age was not a significant factor.

The 5-year mortality rate was 12.7% with rupture of aneurysms accounting for 17% of the deaths. Sixty-five percent of all ruptured aneurysm resulted in death. In small aneurysms of less than 7 mm diameter without any previous history of subarachnoid bleed, the rupture rate was 0.1% per year.

Predictors of poor surgical outcome included size greater than 12 mm, location in the posterior circulation/basilar artery, previous history of stroke, and aneurysmal symptoms of headache.

In the surgical group the overall mortality at 30 days was 1.5%, and at 1 year was 2.3%. Morbidity at 30 days was 11%, and at 1 year was 10%.

The endovascular group was older than the surgery group (53.7 vs 51.5), and the mean size of the aneurysms was larger with more located in the cavernous sinus or basilar artery than the surgical cohort. Procedure-related mortality at 1 year was 4.8% with morbidity of 6.4%.

**DISCUSSION**

An unruptured cerebral aneurysm is often found on routine MRI or CT scanning for indications other than symptoms associated with aneurysm. Two percent of some autopsy series reveal unruptured cerebral aneurysms. This study has a large number of subjects and is prospective. It provides detailed discrimination of the natural history of cerebral aneurysms.

This study population was symptomatic with nearly 50% presenting with headache, undefined spells, cranial nerve defects, or transient ischemic attacks. Nearly 40% had hypertension, and approximately 20% had a family history of aneurysm. The cohort that

Operated Cohort

1917 patients underwent surgical repair, and 451 had endovascular repair. Mean follow-up was 4.0 years. Baseline characteristics were significant for younger age for surgical repair (51.5), and endovascular repair (53.7) compared to the unoperated cohort (55.2).
went unoperated and observed was older than the other cohorts. The cohort that had endovascular obliteration had a significantly higher number of aneurysms that were large (>12 mm) and in the posterior/basilar circulation compared to the unoperated and surgical groups. These differences are consistent with a clinical decision for observing older patients and attempting less invasive procedures when the aneurysm is larger and nearer the brainstem. Given this selection, one cannot directly compare the morbidity and mortality findings of the unoperated, surgical and endovascular procedures.

Clearly with the associated co-morbid conditions, the mortality and morbidity of a cerebral aneurysm is significant regardless of treatment option. The observed unoperated cohort had a 5-year cause specific mortality rate for cerebral aneurysm of 2.2%. The risk for fatal rupture is much less for small aneurysms of <7 mm that are located in the anterior circulation and in the cavernous sinus. The rupture rate given from this study was approximately 0.1% per year.

This study gives details on the natural history of cerebral aneurysms with details on high and low risk lesions. It is this detail that allows better risk stratification for both clinical and insurance medicine decisions.