Prognosis for patients with nonsurgically-treated aneurysms

Analysis of the Cooperative Study of Intracranial Aneurysms and Subarachnoid Hemorrhage

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The clinical review of this large series of patients with aneurysmal subarachnoid hemorrhage has revealed that the prognosis, with surgical or nonsurgical treatment, is related to several factors, but most significantly to the condition of the patient 1 day after hemorrhage. Autopsy study indicates that the prognosis for patients with unsuspected or "incidental" unruptured aneurysms is better than could be expected with surgical treatment.

KEY WORDS  intracranial aneurysm  conservative vs surgical treatment

This analysis is based on statistics drawn from the Cooperative Study for Subarachnoid Hemorrhage and Intracranial Aneurysm which will hereinafter be referred to as the Study. In the present context, "nonsurgical" means treatment by bedrest alone.

The natural history of aneurysms is related to their nonsurgical treatment; although similar, the terms "natural" and "nonsurgical" are not synonymous. The natural history of this disease concerns the fate of all those who have aneurysms since it follows the development of an aneurysm through life to death. The evaluation of nonsurgical treatment, on the other hand, concerns only a segment of the total aneurysm population. In fact, some patients with aneurysmal subarachnoid hemorrhage (SAH) might die before reaching a hospital, and thus their course is part of "natural history" but not of "nonsurgical treatment." Given a patient with a ruptured aneurysm, if it has been decided that at some time treatment is to be surgical, the "treatment" rendered before operation is obviously conservative. The course during the period before operation is also part of the natural history and is synonymous with nonsurgical treatment.

Having defined nonsurgical treatment to mean bedrest only, an evaluation of this treatment can be made on a part of the aneurysm population, but the reasons for choosing that part must be precisely defined. Nonsurgical treatment can be compared to surgical treatment only if the criteria for each are the same. The surgical patient who is not operated on until 2 or 3 weeks after subarachnoid hemorrhage must be compared to a nonsurgical patient who has been in the same condition for a similar 2- or 3-week period. One cannot, for example, compare
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nonsurgical treatment of elderly patients in poor condition with surgical treatment of young patients in good condition.

Analysis

Fate of Patients with Non-surgically Treated Ruptured Aneurysms

In a series of 830 patients treated conservatively following a single aneurysmal hemorrhage, 562 had died in 3 years. The mortality rate rose sharply during the first 21 days following the hemorrhage; 36% died in the first 3 days and more than 50% in the first 14 days (Fig. 1). Of the 562 deaths, 498 (88%) were due to a second subarachnoid hemorrhage and its complications. The remaining 64 (12%) were due to unrelated or unknown causes.

It is important that the surgeon knows the day-by-day risk of death from a second hemorrhage. On the first day, 80 of 830 patients died (10%); on the second day, 34 (5%) died; by the end of the seventh day, 222 patients were dead, a total mortality of 27% in the first week of conservative therapy. The mortality dropped progressively from 15% in the 8- to 14-day interval, to 7% in the 22- to 28-day interval. There was an unexplained rise to 16% in the 2nd month. The risk then dropped off sharply to 1% or 2% for the third to the twelfth months. The rise in the second month may mean that at this time greater physical activity is assumed and the chance of rebleeding increases.

The risk of intracranial operation must be evaluated in terms of a specific aneurysm at a specific site, and at a specific posthemorrhage time. The specific surgeon’s technical ability and experience are also important factors. Thus, the risk factor cannot be made a function of time only. However, we have seen that the first 4 weeks are the critical ones, after which the incidence of rebleeding drops off precipitously.

It is evident from Table 31 of the Study that the longer the time interval elapsed from SAH, the greater is the chance of long-term survival. If the patient survives 3 weeks, the chance of surviving 6 weeks is 83%. For patients who survive 6 weeks, the chance of surviving 1 year is about 82%. It should be pointed out that these data represent "an average of a large sampling of patients of all ages, conditions, and sites of lesions." 

The risk of rebleeding has been determined to vary from 0.5% to 4% on any single day, being highest for aneurysms of the anterior communicating artery, next for those of the internal carotid artery, and least for those of the middle cerebral artery. The risk of rebleeding is greatest from the 7th to the 10th day, falling off gradually between the 14th and 21st day, and then drops sharply at 28 days.

Since prevention of a second hemorrhage is the goal of surgical therapy, the mortality rate associated with second hemorrhages is noteworthy. Rebleeding does not necessarily mean death. Of 1243 patients with a single anterior circle aneurysm 290 had had a second hemorrhage by the end of 28 days. Including those patients who died before admission to hospital, the mortality rate in the first day was about 22%, rising to 27% at the end of the seventh day. For the second hemorrhage, however, the mortality rate was 43% for aneurysms of the anterior circle, 46% for those of the internal carotid, 42% for those of the anterior communicating, and 41% for those of the middle cerebral artery.

Fate of Patients with Untreated Unruptured Aneurysms

In the Study there were 320 aneurysms (9.6%) which had not ruptured. Excluding cavernous sinus aneurysms, 165 were symptomatic and potentially capable of producing SAH. Of these, 131 were treated surgically, leaving 34 untreated cases in which the natural course could be studied. Nineteen of
TABLE 1

Age of patients with ruptured intracranial aneurysms in an autopsy series of 2000 patients*

<table>
<thead>
<tr>
<th>Age Group (yrs)</th>
<th>Patients with Aneurysms</th>
<th>Patients with Ruptured Aneurysms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Cases</td>
<td>Total Autopsies</td>
</tr>
<tr>
<td>1-9</td>
<td>0</td>
<td>125</td>
</tr>
<tr>
<td>10-19</td>
<td>0</td>
<td>99</td>
</tr>
<tr>
<td>20-29</td>
<td>4</td>
<td>90</td>
</tr>
<tr>
<td>30-39</td>
<td>9</td>
<td>82</td>
</tr>
<tr>
<td>40-49</td>
<td>22</td>
<td>182</td>
</tr>
<tr>
<td>50-59</td>
<td>31</td>
<td>306</td>
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<td>60-69</td>
<td>33</td>
<td>361</td>
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<td>70-79</td>
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<td>210</td>
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<tr>
<td>80-89</td>
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<td>100</td>
</tr>
<tr>
<td>90+</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>122</td>
<td>1563</td>
</tr>
</tbody>
</table>

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these 34 patients were followed for 20 months to 12 years. Nine (26%) subsequently died of SAH.

McCormick at the University of Iowa found 122 patients with aneurysms among 2000 consecutive autopsies. In 72 (59%), the aneurysms were unruptured. Since in the Study only 9.6% were unruptured and 2.6% of these were incidental, McCormick’s figures suggest that the natural history of aneurysms may be more benign than is ordinarily considered. It should be remembered that this was an autopsy series and that the University of Iowa is the main referral hospital for the study and treatment of SAH for the state of Iowa and large parts of surrounding states. There is thus a bias toward the ruptured aneurysm. It is of further interest that, although aneurysms in the McCormick series were found with almost equal frequency in the decennial age groups in which aneurysms occur (Table 1), there is an unexplained higher frequency of ruptured aneurysms in the 20- to 49-year-old age group. This point is important because it raises the question of the relation of the patient’s age to the prognosis for aneurysms that are present but unrecognized.

Incidental Aneurysms. The prognosis for the patient with an incidental aneurysm has always posed a particularly difficult problem. In the Study, many were discovered only at autopsy. Fifty-two patients who had other serious disease were found in the course of their workup to have unsuspected (incidental) aneurysms. Only two of these 52 patients bled and died during the 5 years after the diagnosis was made. This suggests a good prognosis, in contrast to the previously described 34 patients with symptomatic but unruptured aneurysms, nine of which subsequently bled and died.

Prognostic Value of Gross Survival Data

The fact that the 1-year survival rate for patients with single aneurysmal SAH treated by bedrest alone was quite low points up the seriousness of the problem (Fig. 2). The Study showed that although the nonsurgically treated population was “adversely distorted by a tendency to select more favorable cases for operation, this selection was mitigated to some degree by the fact that nearly one-half of the nonsurgical cases were from a clinical trial designed to avoid selection” (McKissock, et al.3). A high percentage of patients who would otherwise have been considered favorable candidates for operation were therefore delegated to a nonsurgical treatment group. It is evident that this somewhat selected group of patients favorably influenced the prognosis of the total nonsurgical group, and that the differences in survival were related to selection phenomena rather than to differences in the natural mortality of bleeding aneurysms at specific
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sites. From a complicated analysis in which the patient’s age, condition, severity of the hemorrhage, and aneurysm site were considered and related to various treatment categories (carotid ligation, intracranial operation, and bedrest), it became obvious that a larger fraction of patients treated nonsurgically were seriously ill on the first day after SAH or were in the older age groups.

Therefore, average gross survival figures for all patients with single ruptured aneurysms at any site studied in this large series indicated a much worse outlook than did those of a pure, unselected population which would have a higher percentage of younger, good-condition patients whose prognosis proved to be better. Second, because a high proportion of patients selected for operation were younger and in good condition, it was evident that gross survival data in such a surgical group were no indication of the results that might have been obtained by operation in an “unselected” population with bleeding aneurysms; a greater number of patients in this “unselected” group would have been in poor condition for surgery. Third, it is clear that comparisons of gross survival data are valid only if the factors that determine delegation of patients to either a surgical or nonsurgical category are precisely defined. Finally, because of the wide range of variables bearing on the problem (patients’ condition, age, severity of hemorrhage, etc.), gross survival figures are of no prognostic value to the individual patient, and can be only roughly applied to a large number of cases.

With regard to the prognosis for 1-year survival from a single aneurysmal SAH treated by bedrest only, it may be said: 1) patients with vertebrobasilar or middle cerebral aneurysms have a better chance for survival than do those with internal carotid or anterior communicating artery aneurysms; 2) the survival rate for patients with anterior communicating artery aneurysms is greater in men (41%) than in women (30%), probably a reflection of the greater incidence of this lesion in men; 3) the condition of the patient 1 day after SAH materially affects survival. Comparison of the extremes of condition in patients with internal carotid artery aneurysms shows that survival varied from 47% for those in good condition to 8% for those seriously ill; for patients with middle cerebral artery aneurysms, from 53% for those in good condition to 12% for those in poor condition; and for those with anterior communicating artery aneurysms, from 54% to 7% respectively.

Results of Nonsurgical Treatment of Aneurysms

Selection of Patients. The Study reveals that a considerable number of patients were automatically delegated to a nonsurgical treatment category because of their poor condition, peculiarities of the circle of Willis, or because the aneurysm was considered inoperable. Those patients in the McKissock group who were considered likely to die from the immediate effects of the hemorrhage or who were unable to tolerate digital carotid occlusion were excluded from randomization and assigned to conservative treatment. I believe the inclusion of these selected patients whose fate is predictable is biased and invalid for evaluating nonsurgical treatment since the nonsurgical treatment is compared to surgical treatment conducted under different circumstances.

Before assessing the results of nonsurgical treatment, we should know why a patient was not operated on, since the Study indicated that surgery was generally the preferred mode of treatment. Referring to Table
86 in the Study, Nishioka defined eight conditions that could allocate a patient to non-surgical status. Three of these conditions were in patients who could also have been considered good candidates for surgery: refusal of surgery, recommendation of conservative therapy by the physician, and allocation to conservative management by randomization. The other conditions precluding surgery were the poor state of the patient, death before operation, inoperability of the aneurysm, multiple aneurysms, and by and large, the group treated nonsurgically contained a preponderance of patients in poor condition. Therefore, only patients in the first three groups, who would also have been good surgical candidates, can be considered suitable for comparison of the merits of non-surgical and surgical treatment. The analysis makes it clear that surgical orientation can control mortality by assigning candidates to nonsurgical treatment who are in poor condition for operation, while delegating to surgery those in good condition. Moreover, patients who improved from a poor to an acceptably good condition for operation are successively added to the latter group. By such manipulation, the mortality rate of this nonsurgical group of patients could be “calculated at 100% regardless of the patient’s condition at the time of admission to hospital or at the time of the initial neurosurgical evaluation!”

The influence of the mode of selection of patients is further emphasized when considering the 34 patients in the nonsurgical category (Table 86 of the Study) who refused operation. Of these, four died, and 28 were followed for 6 years, a survival rate of 82%. Moreover, 26 (93%) were working. An analysis of all nonsurgical patients would give an unusually high mortality rate because it would include a large number of poor risk patients rejected for operation.

**Survival**

The duration of survival in a series of patients who eventually died after one SAH is shown in Fig. 3 (cumulative percentages). Of these 140 patients, 114 (81%) died within the first 3 months after the initial hemorrhage. Of the total deaths, 44% were due to rebleeding and 25% to progressive deterioration. Among the small number of late repeat hemorrhages after 1 year, fatal rebleeding occurred at 17 months in one patient, and at 2 years in two patients. The longest interval between SAH and death was 7 years.

**Mortality Related to Condition.** It is apparent (Table 94 in the Study) that mortality is related directly to the severity of illness at any time in the first 2 weeks after SAH, but especially during the first week. The presence of intracerebral hematoma has been considered an indication for early operation as a life-saving measure. Hemispheric deficits are related to a higher mortality, but a hemispheric deficit is expected with intracerebral hematoma. In 133 of 304 patients allocated to conservative treatment because they were “too ill for surgery,” 63 (47%) had hemispheric deficits.

**Week-to-Week Risk of Fatal Recurrent Hemorrhage.** Sixty patients in a series of 240 who had nonsurgical treatment because of random allocation, refusal of surgery, or because it was considered preferred treatment, died because of a recurrent hemorrhage during the first 3 months after the initial SAH. The total risk during this time therefore was 25%. During the first week, 15 of 240 patients (6.2%) rebled and died, leaving 225 patients at risk on the eighth day. By the end of the second week 14 patients had died, a risk of 5.8%, while by the end of 3 months the risk was 2.2%.

**Hypotensive and Hypothermic Treatment of Intracranial Aneurysm.** Of 109 patients in the Study treated with induced hypotension, 59 (54%) were selected for this treatment because they were considered poor surgical risks or because the aneurysms were considered inoperable. Mortality increased relative to the severity of the illness. The over-all survival rate of 52% varied with the
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patient’s condition, falling from 87% in Grade II to 22% in Grade V patients. Patients with hypertension fared poorly. Of the survivors, 44 (40%) had minimal disability. In general, then, there was no indication that hypotensive therapy had any appreciable effect on recovery. Slosberg \(^5\) however reported an unusually high survival in a carefully controlled series of 15 patients.

In a group of 62 patients with single aneurysmal hemorrhage treated by hypothermia, there were only five survivors, all of whom were severely disabled. Selection of this form of treatment was determined by a moribund condition in 48 patients, and in 10 the aneurysm was inoperable. In the remaining four, the aneurysm was not demonstrated by angiography.

All 14 patients who had combined hypothermic and hypotensive treatment died, 12 were seriously ill or moribund when treatment was begun.

Conclusions

The results obtained in a representative segment of an “unselected” group of 86 patients with nonsurgically treated aneurysms (34 who refused surgery and 52 in whom “incidental” or unsuspected aneurysms were found) are challenging. In the former group of 34 patients, 19 (26%) died of recurrent hemorrhage while in the latter group of 52 patients, only two (3.8%) died in the 5 years after the diagnosis of aneurysm was made. Statistics, however, being what they are, can be made to mean many things depending upon who makes them, what the reader is trying to learn, and what the writer is trying to say. Analyses of treatments of intracranial aneurysms have usually been of little value because they have lacked the absolute objectivity necessary for a proper comparative evaluation.

Summary

The early (72-hour) mortality for subarachnoid hemorrhage (SAH) from a single aneurysm is about 36%. This is associated frequently with a destructive hematoma especially from middle and distal anterior cerebral artery aneurysms. The initial mortality from a first aneurysmal SAH is about 15% but probably closer to 20%. The tendency for rebleeding rises steadily to a peak at 7 days, then begins to taper off at 3 weeks, falling sharply after 28 days. The risk of rebleeding varies from 0.5% to 4% on any single day, being highest for the anterior communicating artery and lowest for the middle cerebral artery aneurysms. If a patient survives 3 weeks after aneurysmal SAH from one of the three major sites, the chance of surviving for 6 weeks is 83%; if he survives 6 weeks, the chance of surviving 1 year is 82%. Recurrent hemorrhage from an aneurysm is rare after 1 and especially after 2 years. The discovery of an “incidental” aneurysm at the time of angiography does not necessarily indicate a dire prognosis. The most important factors influencing survival were the patient’s age and his condition 1 day after SAH; the younger the patient and the better his condition, the better was the chance of survival.

References


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