Original Contributions

Has There Been a Decline in Subarachnoid Hemorrhage Mortality?

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We studied subarachnoid hemorrhage in the population of Rochester, Minnesota, for the 40-year period from 1945 through 1984. The average annual incidence rate of subarachnoid hemorrhage in Rochester has remained constant at approximately 11 per 100,000 population. Age-specific incidence rates increased with age. However, the average annual mortality rate for subarachnoid hemorrhage in Rochester has shown a decreasing trend, from 6.8 per 100,000 population in 1955-1964 to 4.3 in 1975-1984. It is likely that this is due to a decrease in case-fatality rates from 57% in 1945-1974 to 42% in 1975-1984 (p=0.10). This decreasing trend was also evident in annual mortality rates from subarachnoid hemorrhage for US white men and women. The reason for the improved case-fatality rate is unclear, but it may be related to changes in management. The interval from onset of subarachnoid hemorrhage to surgery decreased from a median of 12 days in 1975-1979 to 2 days in 1980-1984, and of those who survived to receive medical attention, more patients received some form of medical treatment in 1980-1984. Whether either or both of these changes have led to the decrease in the case-fatality rate is uncertain. (Stroke 1989;20:718-724)

Despite major improvements in surgical techniques for aneurysmal subarachnoid hemorrhage (SAH), 30-day mortality from SAH has been shown to have changed very little from what it was 40 years ago. Population studies have shown that there is a 50–60% 30-day mortality rate, which is similar for SAH due to aneurysm or presumed aneurysm and for SAH from all causes. It has been suggested that early surgery for aneurysmal SAH decreases the total management mortality rate. The characteristics of SAH in the population of Rochester, Minnesota, from 1945 through 1974 have been reported. In this study we extended those observations to include the period from 1975 through 1984 to assess whether changes in management may have had an effect on survival after SAH.

Subjects and Methods

The population of Rochester lends itself well to epidemiologic studies because medical care is provided primarily by the Mayo Clinic and one smaller group practice and because diagnoses for Rochester residents by all of the providers are entered into a central computer file. This index made it possible to identify all Rochester residents who had a first episode of primary SAH during the 40-year period from 1945 through 1984. During the first 30 years, only a few patients had computed tomographic (CT) scans confirming the SAH. Verification was obtained by various combinations of clinical history, lumbar puncture, and angiography. For the 10-year period between January 1, 1975, and December 1, 1984, each medical record had to include evidence of SAH on CT scan of the head or bloody cerebrospinal fluid (CSF) obtained from a nontraumatic lumbar puncture. These findings were required in addition to a clinical picture of an acute neurologic illness, which was usually accompanied by severe headache and meningismus. Patients who were found dead without other history were not included unless SAH was confirmed by autopsy.

We excluded patients in whom trauma was the likely cause of hemorrhage and patients in whom pathologic evidence indicated that a primary intracerebral hemorrhage had a secondary communication with the CSF.

On the basis of the attending physician’s description, the condition was graded 1 through 5 in order of increasing severity of symptoms at the time of first medical attention, according to the criteria of Hunt and Hess. The level of consciousness was
TABLE 1. Neurologic Status 30 Days After First SAH for 49 Patients in Rochester, Minnesota

<table>
<thead>
<tr>
<th>Code</th>
<th>Definition</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Dead</td>
<td>21</td>
</tr>
<tr>
<td>2</td>
<td>Normal</td>
<td>13</td>
</tr>
<tr>
<td>3</td>
<td>Neurologic deficit, resumed normal activities</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>Neurologic deficit, unable to resume normal activities</td>
<td>7</td>
</tr>
<tr>
<td>5</td>
<td>Memory deficit</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>Memory deficit+code 3</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>Memory deficit+code 4</td>
<td>2</td>
</tr>
<tr>
<td>8</td>
<td>Neurologic deficit unrelated to SAH</td>
<td>0</td>
</tr>
</tbody>
</table>

SAH, subarachnoid hemorrhage; normal activities, patients were able to undertake all tasks they were capable of doing before SAH; memory deficit had to be diagnosed by a neurologist.

graded as 0, normal level of consciousness; 1, somnolent but could be awakened and responded to command; 2, unconscious and not responding to command but responding purposefully to pain; and 3, coma with no purposeful response to pain. The type of treatment given, including surgery, was recorded, and the outcome was analyzed in terms of morbidity and mortality. On the basis of CT head scan or autopsy, a judgment was made in each case as to the presence or absence of an intracerebral hematoma.

Rebleeding was diagnosed only if there was evidence of new blood on the CT scan or in the CSF or if documented at autopsy. Vasospasm as a cause of clinical deterioration was diagnosed only if proven by angiogram after deterioration occurred. If a patient deteriorated and had ischemic changes on CT scan but no angiogram was performed, then a diagnosis of ischemia of uncertain cause was made. These strict definitions mean that the rebleeding rates and cerebral vasospasm rates were minimal rates.

Focal neurologic deficit (FND) was defined as the development of a lateralizing neurologic deficit. "Minor" indicated a mild motor, sensory, or speech change occurring in isolation or in combination. "Major" indicated moderate to severe hemiparesis or severe dysphasia, or both. An isolated cranial nerve palsy alone or altered level of consciousness alone, in the absence of other focal neurologic signs, was not included. Time of onset was coded as 1, occurring before first medical assessment; 2, occurring after first medical assessment but before surgery; 3, postoperative immediate (i.e., FND present within 4 hours of awakening from anesthesia); and 4, postoperative delayed (i.e., FND first observed >4 hours after awakening from anesthesia).

The neurologic status at 30 days after onset was determined for all patients. The neurologic status codes are defined in Table 1.

Average annual incidence rates for aneurysmal SAH and SAH due to all causes were calculated for each of the four 10-year periods from 1945 through 1984. The person-years that were used in the denominators of these calculations were interpolated from decennial census data. The average annual incidence rates for the decades 1945–1954, 1955–1964, and 1965–1974, previously published, used the US census data at the midpoint of each 10-year period as the denominator. Consequently, they differ slightly from the corresponding rates in our study. The overall incidence and age- and sex-specific incidence rates for the 40 years from 1945 through 1984 were calculated by using the cumulative person-years for this period. All rates were age-adjusted, and the rates for the entire 40 years were age- and sex-adjusted to the 1960 US white population.

Average annual mortality rates for death due to SAH from all causes were calculated by using the same denominators as described above. These rates were calculated for each of the 10-year periods 1945–1954, 1955–1964, 1965–1974, and 1975–1984. The average annual mortality rates for the 3 decades from 1945 through 1974 differed slightly from previously published data for the same reason that the incidence rates differed for the period (see above). Annual mortality rates for SAH for US white males and females were obtained from Vital Statistics of the United States, US Department of Health and Human Services. The average annual mortality rates for Rochester were age- and sex-adjusted, and the US white male and female mortality rates were age-adjusted to the 1960 US white population.

Analyses for survival, rebleeding, and focal neurologic deficit were performed only on those patients with aneurysmal or presumed aneurysmal SAH. The probability of surviving for 30 days after the incident SAH was estimated by the Kaplan-Meier method for the 4 decades from 1945 through 1984 and for the 30-year period from 1945 through 1974. The log-rank test was used to compare differences in survival between the 4 decades and between the 2 periods from 1945 through 1974 and from 1975 through 1984.

The probabilities of surviving free of a second SAH and free of FND for 30 days after the incident SAH were estimated with the Kaplan-Meier method. For rebleeding, the first episode of rebleeding was considered as an end point, and the analyses were performed for the 2 periods 1945–1974 and 1975–1984. For FND, the first FND occurring preoperatively or postoperatively was considered as an end point; the analysis was performed only for the decade 1975–1984 because no information was available for the period from 1945 through 1974. Patients who died before reaching the hospital or who had a clinical grade of 4 or 5 at first medical assessment were excluded from the rebleeding and FND outcome analyses. Patients who died from a cause other than rebleeding or FND were censored at death.

Proportional hazards analysis was performed only on data from patients with aneurysmal or presumed...
aneurysmal SAH who survived to receive medical attention. Cox proportional-hazards analysis was used to identify variables that predicted 30-day survival for patients in the decade 1975–1984. The variables assessed were age, sex, clinical grade on admission, level of consciousness on admission, FND present on admission, systolic and diastolic blood pressure on admission, year in which the SAH occurred, evidence of intracerebral or ventricular hemorrhage, history of hypertension, and time between onset of SAH and first medical attention. The use and duration of medical treatment and time from onset of treatment to surgery were not analyzed because the medical treatment was not uniform enough to use a time-dependent covariate analysis.

Intracerebral and ventricular hemorrhage were diagnosed if present on the admission CT scan or at autopsy if the patient died within 24 hours of first medical attention and no CT scan had been performed. Patients were classified as having a history of hypertension if they were receiving antihypertensive medication or if there were two or more readings in the Mayo Clinic record, within the 2 years preceding the SAH, of systolic blood pressure \(\geq 160\) mm Hg or diastolic blood pressure \(\geq 95\) mm Hg, or both. Each variable was assessed individually, and those judged to be significant \((p<0.05)\) were used for further analysis. Logical interaction terms among the variables noted were also assessed.

Relative risk of death within 30 days was determined for various clinical grades and for levels of consciousness. A relative risk of 1 was set for clinical grade 1 patients and separately for patients who were alert.

Results

During the 10-year period 1975–1984, there were 52 incident cases of first SAH. One patient had an arteriovenous malformation, one patient had a central nervous system vasculitis, and one patient had amyloid angiopathy with rupture of a leptomeningeal artery. The remaining 49 patients had SAH from rupture or presumed rupture of an intracranial aneurysm. There were 39 women and 10 men, and their ages ranged from 17 to 84 (median 51) years.

In 47 of the 49 patients, angiography, autopsy, or CT was performed; aneurysm was confirmed in 38. The nine unproved cases had such a typical clinical presentation and course that they were included in the aneurysm group even though five had a negative angiogram. CT scans were performed on 31 patients, and 27 (87%) had evidence of subarachnoid blood, 14 (45%) had a parenchymal hematoma, and 6 (19%) had ventricular hemorrhage. Information on history of hypertension before SAH was available in 31 of the 49 patients (63%); 16 patients had a history of hypertension, and 15 did not. No patients were receiving anticoagulant therapy, none had diseases known to be associated with aneurysms (e.g., polycystic kidney disease), and none of the women were pregnant. Six of the 49 patients (12%) died before receiving medical attention. Of the 43 patients who received medical attention, 35 (81%) were seen within 8 hours of onset, and 39 (91%) were seen within the first 48 hours after onset; 24 (56%) were clinical grade 1 or 2, five (12%) were grade 3, and 14 (32%) were grade 4 or 5. Among the 43 patients, the level of consciousness was normal in 23 (53%); six (14%) were somnolent, six (14%) were unconscious but responded purposefully to pain, and eight (19%) were in deep coma. Among these 43, an FND developed in 16 patients (37%), and 12 (28%) were clinical grade 1, 2, or 3 at first assessment; six patients had the FND at first medical attention, and 10 had an FND subsequent to their first medical attention but before surgery.

The average annual incidence rates for each of the 4 decades and for the entire 40-year period are shown in Table 2. The age-adjusted average annual incidence rate per 100,000 population for SAH due to aneurysm or presumed aneurysm for the 40-year period was 12.2 for women and 7.2 for men. The age-specific average annual incidence rate increased with age, although no further increase was noted in the group aged 70 years or older (Figure 1).

The average annual mortality rates for the total Rochester population and the annual mortality rates for US white males and US white females are shown in Figure 2. The age-adjusted average annual mortality rates per 100,000 population were 6.3 (95% confidence interval, 3.3–9.3) for 1945–1954; 6.8 (4.1–9.5) for 1955–1964; 6.6 (4.2–9.0) for 1965–1974; and 4.3 (2.6–6.1) for 1975–1984.

The probability of surviving to 30 days was 58% for 1975–1984 and 43% for 1945–1974 \((p=0.10)\) (Figure 3).

The probability of surviving for 30 days free of a second SAH for those whose condition was clinical grade 1, 2, or 3 at first medical attention was 78% for 1975–1984 and 76% for 1945–1974 (Figure 4). For 1975–1984 there were 29 patients whose condition was grade 1, 2, or 3 at first medical attention, and there were five rebleeding episodes within 30 days of the first SAH. For 1945–1974, there were 79

### Table 2. Average Annual Incidence of SAH in Rochester, Minnesota, 1945–1984

<table>
<thead>
<tr>
<th>Period</th>
<th>All SAH</th>
<th>SAH (aneurysm)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Rate</td>
</tr>
<tr>
<td>1945–1954</td>
<td>29</td>
<td>9.5</td>
</tr>
<tr>
<td>1955–1964</td>
<td>41</td>
<td>12.0</td>
</tr>
<tr>
<td>1965–1974</td>
<td>59</td>
<td>12.2</td>
</tr>
<tr>
<td>1975–1984</td>
<td>52</td>
<td>10.1</td>
</tr>
<tr>
<td>(total period)</td>
<td>181</td>
<td>11.1 (10.7)</td>
</tr>
</tbody>
</table>

SAH, subarachnoid hemorrhage; rate, incidence per 100,000 persons, age-adjusted to 1960 US white population. Rates within parentheses are age- and sex-adjusted to 1960 US white population.*SAH due to aneurysm or presumed aneurysm.
patients whose condition was grade 1, 2, or 3 at first medical attention, and there were 16 rebleeding episodes within 30 days of the first SAH.

The probability of surviving for 30 days free of FND for the 29 patients who were clinical grade 1, 2, or 3 at first medical attention for 1975–1984 was 57% (Figure 5). Among these, 14 patients had an FND either preoperatively (12) or postoperatively (two) within 30 days of the SAH. Six of these patients had the FND at the time of first medical attention.

No details on specific medical therapies are provided because medical management varied considerably. Surgery was performed in 25 patients (58% of the 43 who received medical attention); all 25 had some form of aneurysm repair. In addition, 11 of these 25 patients had either a parenchymal hematoma or subdural blood collection removed, and five patients had placement of an atrioventricular shunt. Surgery was performed more often in 1980–1984, with 81% (13 of 16 patients) who survived until medical attention having surgery compared with 44% (12 of 27 patients) in 1975–1979. In 1980–1984, the median time from the onset of SAH until surgery was 2 days, and all patients except one were operated on within 6 days of SAH. For 1975–1979, the median time from the onset of SAH until surgery was 12 days, and all patients were operated on >6 days after the SAH. Surgical outcome was classified as normal in nine patients (36%), disability not due to surgery in 11 patients (44%), disability secondary to surgery in three patients (12%), and two patients (8%) died in the hospital. Rebleeding occurred in seven patients, five of whose conditions were grade 1, 2, or 3 at first medical assessment.

The neurologic status 30 days after the SAH for all 49 patients is shown in Table 1. Of the 28 people who survived 30 days, 18 (64%) were either neurologically normal or had a mild deficit and were capable of resuming normal activities. Six-month follow-up was available for 44 patients, and their neurologic status was unchanged from their 30-day
Figure 5. Probability of survival free of focal neurologic deficit (FND) after first subarachnoid hemorrhage (SAH) due to aneurysm or presumed aneurysm among patients whose condition was clinical grade 1, 2, or 3 at first medical attention in Rochester, Minnesota, 1975–1984. Curve starts at 79% because six patients had FND coincident with onset of SAH.

status. The 30-day case-fatality rate for 1974–1984 was 42%, compared with a 57% rate for 1945–1974.

In the decade 1975–1984, 43 patients (88%) with SAH due to aneurysm or presumed aneurysm survived their SAH to receive medical attention. Individual analysis of the variables showed that increasing age was related significantly to mortality ($p<0.001$). Each variable was then analyzed individually in conjunction with age. Only the clinical grade on admission and level of consciousness on admission were related significantly to survival in the age-adjusted analysis. For different clinical grades at first medical attention, the age-adjusted relative risks of death within 30 days were 0.8 for grade 2, 3.3 for grade 3, 6.4 for grade 4, and 12.8 for grade 5 ($p<0.01$) (Figure 6); the relative risk was significantly different from 1 only for grade 5. The age-adjusted relative risks of death within 30 days for different levels of consciousness at first medical attention were 1.9 for somnolent, 5.7 for unconscious but responding purposefully to pain ($p=0.03$), and 10.4 for deep coma ($p<0.01$) (Figure 7). No interaction terms were found to significantly affect survival. Because level of consciousness and clinical grade are similar measures of clinical status, they were not combined in a single model. The other variables, including sex, presence of FND on admission, systolic and diastolic blood pressure on admission, evidence of intracerebral or ventricular hemorrhage, time between onset of SAH and the patient’s receiving medical attention, year in which the SAH occurred, and history of hypertension, were not significant predictors of death when each analysis was adjusted for age.

Discussion

A population-based study provides the opportunity to examine the full spectrum of patients with SAH, and it thus avoids the selection bias that is bound to occur in referred patients with a disease process causing high early mortality. Our study extended the period of observation for SAH in Rochester, Minnesota, by 10 years to a total of 40 years (1945–1984) for the only population-based study in North America. There has been essentially no change in the incidence of SAH over these 40 years. This is in sharp contrast to the well-documented decline in the incidence of other types of stroke during the same period.12 Although the incidence rate of SAH increased with age, it did not increase in those over the age of 70 years as we...
noted in an earlier study. This may reflect variability due to relatively few persons in this age group.

After 30 years of average annual mortality rates between 6.3 and 6.8 per 100,000 per year from 1945 through 1974, the rate decreased to 4.3 in 1975–1984. The small number of patients makes it difficult to assess the statistical significance of this observation. The 95% confidence intervals for the different decades overlap slightly, suggesting that the trend has borderline significance. This recent decrease, however, is also evident in the mortality rates for US white females and males in the same interval (Figure 2). The consistently lower mortality rates for the US white population compared with those of the Rochester population probably reflect a difference in case ascertainment. Given the size of the Rochester population and the close surveillance through the medical records and record linkage system at the Mayo Clinic, better case ascertainment might be expected.

Several factors could contribute to the observed decrease in mortality rate. A lower mortality rate would result from a decrease in the incidence of SAH. The incidence rate for 1975–1984 is marginally lower than that of the previous 3 decades and particularly so in males. The incidence rate of SAH may have decreased in this period due to the introduction of CT scanning, which combined with arteriography allowed for more accurate separation of patients with SAH from those with primary intracerebral hemorrhage. Previously some of these patients were misclassified as having SAH, and the misclassified patients may have had a higher mortality rate. This small reduction in numbers, however, would not fully explain the observed decrease in mortality rate.

Lower mortality rates could result from improved case-fatality rates. Although not significantly different ($p=0.10$) by the usual standard, the case-fatality rate decreased from 57% in 1945–1974 to 42% in 1975–1984. This improvement was not the result of an increase in milder cases during the last decade because the percentage of patients whose condition was grade 1, 2, or 3 at first medical attendance was 68% for both periods. Age is a significant predictor of survival, but the average age of 57.5 years for 1945–1974 was not significantly different from the average age of 53.1 years for 1975–1984. Improved management is a possible reason for the improvement in case-fatality rates. A major change in surgical treatment was observed between 1980 and 1984, with the median time from the onset of SAH until surgery decreasing from 12 days for 1975–1979 to 2 days for 1980–1984. The number of patients who survived to receive medical attention and who received some form of medical treatment (e.g., steroids or antivasospasm therapy) increased from 44% in 1975–1979 to 63% in 1980–1984. The small number of cases and the variability of medical and surgical treatment precluded the use of time-dependent covariate analysis, so judgment of treatment can be made only from the outcome of all patients. We were not able to determine whether changes in medical treatment, changes in surgical treatment, both, or neither contributed to the change in case-fatality rates.

In our study, the significant predictors of outcome were the level of consciousness and the clinical grade on admission. That these are both significant is not surprising given that they both estimate neurologic status and that the definitions overlap.

Sex, FND present on admission, systolic and diastolic blood pressure on admission, evidence of intracerebral or ventricular hemorrhage, time between onset of SAH and the patient's receiving medical attention, year in which the SAH occurred, and history of hypertension were not significant predictors of outcome. There were only six patients with FND at first medical assessment from which outcome could be judged. FND developed in 10 other patients later.

Patients who presented for first medical assessment with a delay of >2 days were patients with less severe symptoms and a good clinical grade. That the time between onset of the SAH and first medical assessment was not a significant predictor of outcome is undoubtedly due to only four patients presenting >2 days after onset. Because 81% (35) of 43 patients were seen within the first 8 hours, the small number of patients with a delayed presentation was not enough to establish a significant gradient of difference in times.

We found previously that clinical grade, presence of hematoma, and history of hypertension were significant predictors of outcome. However, in that analysis a different method was used (linear discriminant analysis), and information was available on more patients (100 vs. 43). Also, the number of patients with hematoma may have been overestimated because CT scanning was not available. We did not find that history of hypertension was a significant predictor of outcome in this study. However, a strict definition of hypertension was used, and 17 patients were not included in this part of the analysis because of insufficient information.

Our study has shown a decrease in the 30-day case-fatality rate and in the mortality rate from SAH in Rochester. The reasons behind this decline are not clear, and since it could be related to fluctuations in a relatively small population, further observation is needed to confirm this trend. We also noted a decreased mortality in the US white population, and a study of SAH in New Zealand reported a decline in mortality since the mid-1970s. If changes in management have contributed to the decline in mortality, it is unclear whether it was due to changes in medical treatment, changes in surgical treatment, or a combination.

References


KEY WORDS • incidence • mortality • subarachnoid hemorrhage • epidemiology
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