Evidence for Excess Long-Term Mortality After Treated Subarachnoid Hemorrhage

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Background and Purpose—The purpose of this study was to examine the long-term mortality rate of patients with aneurysmal subarachnoid hemorrhage (SAH) compared with that of the general population.

Methods—Aneurysmal SAH patients who were treated for ruptured aneurysm from 1977 through 1998 in a tertiary referral center (n = 1537) were followed up for a median of 7.5 years. Dates and causes of death were determined. Standardized mortality ratios (observed/expected deaths) according to age, sex, and Glasgow Outcome Scale at 12 months after surgery were calculated.

Results—The mortality rate among patients with good recovery at 12 months was twice that of the general population. The excess mortality appeared to be most evident in younger age groups. Cerebrovascular and cardiovascular diseases were the principal causes of premature death. The result was similar among patients without preexisting cardiovascular diseases at the time of SAH.

Conclusions—Aneurysmal SAH patients have an excess mortality rate even after successful treatment of ruptured aneurysms. Therefore, aneurysmal SAH should be viewed more as one aspect of a chronic general vascular disease, and more attention should be given to treatment of risk factors and long-term follow-up of these patients. (Stroke. 2001;32:2850-2853.)

Key Words: intracranial aneurysm • mortality • outcome • subarachnoid hemorrhage • urban population

Among hemorrhagic strokes, aneurysmal subarachnoid hemorrhage (SAH) causes a high mortality and morbidity in industrialized countries. Even today, nearly half of aneurysmal SAH patients die within a few weeks after bleeding.1–4 The outcome has improved only among those patients who have survived the initial bleeding and are candidates for interventions.5–9 After closure of the ruptured aneurysm, either with clips or coils, patients are believed to be safe from possible aneurysm rebleeding and therefore are believed to have the same life expectancy as the background population. But what is the evidence for this widely held opinion? There are only a few studies that have attempted to compare the long-term mortality rate of aneurysmal SAH patients with that of the general population.10,11

In Finland, the incidence of aneurysmal SAH is high, as is the incidence of cardiovascular diseases in general.12,13 A relatively stable population, comprehensive vital statistics, and a high-quality healthcare system enabled us to compare the long-term survival between treated aneurysmal SAH patients and the corresponding general population.14 In the present study, we have calculated the degree of excess mortality after treatment of aneurysmal SAH by comparing the study cohort with the general population in the same geographic area.

Subjects and Methods

The study population consisted of 1714 patients with aneurysmal SAH who were treated at Kuopio University Hospital, Kuopio, Finland, during the 21-year period from 1977 to the end of 1998. The Department of Neurosurgery at Kuopio University Hospital is the only referral center for aneurysmal SAH in East Finland, with a catchment area of nearly 900 000 inhabitants.

Preoperative clinical status was classified according to the Hunt and Hess classification.15 The diagnosis of SAH in all patients was based on computerized tomography since 1980; before that, it was based on lumbar puncture. A patient was classified as having cardiovascular disease if he or she took medication for or had had a documented diagnosis of cardiovascular disease. After treatment of ruptured intracranial aneurysm, all survivors had at least 2 clinical controls: first, the outpatient visit at 2 months, and second, either an outpatient visit at 12 months or telephone contact of patients or their family members at 12 months. Outcome was assessed with the Glasgow Outcome Scale.16

Mortality Follow-Up

The vital status, dates, and causes of death for the cohort were obtained from the Register of Causes of Death administered by Statistics Finland, which registers all deaths of citizens of Finland. The dates and causes of death through the end of 1998 were available, and therefore, in the analysis of patients with good recovery at 12 months, only those who underwent surgery up to the end of 1997 were taken into account. The validity of stroke diagnosis
in this register has previously been reported to be high.\textsuperscript{7} Survival data were used as either an event or a censored observation.

**Statistical Analysis**

Statistical analysis was performed with SPSS 9.0 for Windows (SPSS). The population of East Finland (provinces of North and South Savo, North Carelia, and Central Finland) was used as a reference population when expected deaths of all causes were calculated. Mortality ratios were standardized in an indirect manner according to age, sex, and year of admission.\textsuperscript{17} Person-years of the cohort were partitioned by sex, age (by 5-year intervals), and calendar year. We calculated the expected deaths for each combination by multiplying the mortality rate of the corresponding general population by the cumulative person-years within each cell. The sum over all combinations of sex, age group, and calendar year yielded an expected number of deaths that took into account variation in national mortality rates according to sex, age, and calendar time. The observed/expected ratio represented the standardized mortality ratio (SMR). Ninety-five percent CIs for SMRs based on the Poisson distribution were estimated. The probability of survival was estimated by the Kaplan-Meier method.

All study patients and those with good recovery at 12 months were divided into age tertiles. All patients in both groups and men and women were separately divided into tertiles. Because the mortality data of the general population were given at 5-year intervals, the age tertiles were rounded to the next 5 years.

**Results**

During the study period, there were 1714 patients with saccular ruptured aneurysms. One hundred seventy-seven patients had no operation or had only ventriculostomy or shunt operation and were excluded from the study. A total of 1537 patients had either surgical (1472 cases, 21 of whom had wrapping or trapping) or endovascular (65 cases) treatment of the ruptured aneurysm. There were 770 women (50.1\%) in the study population. The mean age for the study group was 50.1 years (range, 5.0 to 85.9 years). The characteristics of the study population are shown in Table 1. The Glasgow Outcome Scale assessed at 12 months was based on outpatient visits, and 36 patients were lost to follow-up.

Patients were followed up for a median of 7.5 years (mean±SD, 8.2±6.1 years; range, 0 to 22.3 years). The total number of observed patient-years was 12 537 (for men, 6487; for women, 6050).

By 1998, 415 patients had died. The estimated survival of the entire patient group at 6 months and at 1, 5, 10, 15, and 20 years was 87.4\%, 86.7\%, 81.8\%, 73.9\%, 65.6\%, and 55.7\%, respectively. Among those patients who survived the initial aneurysmal SAH and had a good recovery at 12 months, the risk of death remained elevated and was twice that of the general population (Table 2). Excess mortality tended to be higher in lower age tertiles. Among all patients having definite treatment for ruptured aneurysm, the mortality rate was 4.5 times that of the general population.

The Figure shows the distribution of the causes of death among all deaths after 12 months of follow-up. In the group with good outcomes, nearly 20\% of deaths (24 cases) were caused by cerebrovascular attack. Of these cases, a new SAH was the cause of death in 54.2\% (14 of 24).

There were 925 patients without any history of coexisting cardiovascular diseases at the time of the SAH. Of these, 583 had good recovery at 12 months after surgery. The SMR was 1.86 (95\% CI, 1.45 to 2.28) among these patients. Cerebrovascular diseases accounted for 24\% (15 cases) and other cardiovascular disease for 17\% (11 cases) of all deaths in this patient group. New SAH accounted for 60\% of cerebrovascular deaths (9 of 15).

**Discussion**

Surprisingly little is known about long-term survival after treated aneurysmal SAH. It is commonly believed that patients who have recovered well after successful treatment of ruptured aneurysm will attain the life expectancy of the general population. Therefore, long-term clinical follow-up is rarely recommended for these patients.

The main finding in the present study was that aneurysmal SAH was associated with excess long-term mortality even among those patients who recovered well from the initial bleeding and operation. The excess mortality tended to be higher in younger age groups. What are the background

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reasons that patients who have recovered well from aneurysmal SAH patients have shortened life expectancy? The relatively low number of new SAH events (for example, due to poorly clipped or coiled aneurysms, ruptured fellow aneurysm, or rupture of de novo aneurysms) does not explain the excess mortality. In a long-term outcome study from Iceland, general cerebrovascular causes of death accounted for 27% of all deaths, and other cardiovascular diseases accounted for 32% of all deaths.11 These figures are nearly identical to those in our larger cohort, in which cerebrovascular causes were responsible for 28% of all deaths and other cardiovascular causes for 32%.

Even after those patients with known cardiovascular diseases at time of SAH were excluded, the mortality rate remained twice as high as expected. Systemic cardiovascular disease appears to be the most important cause of death among aneurysmal SAH patients in the long term. The reason for the excess cardiovascular mortality in aneurysmal SAH patients is unclear. One explanation could be that aneurysmal SAH patients may have some genetic factors that expose them to increased risk for cardiovascular disorders. Whatever the background mechanisms, it appears that from the clinical point of view, more attention should be paid to the treatment of cardiovascular risk factors such as smoking and elevated blood pressure in these patients.

Follow-up might have prevented new SAH cases in 24 patients in the present study who were well recovered initially, as suggested by David et al18 and Tsutsumi et al. 19 Because only 36 patients (2.3%) were lost to follow-up and only those with complete follow-up time were included when SMRs were calculated in the group with good recovery at 12 months, missing information is not likely to have caused a bias. When the SMRs are interpreted, the variability in estimation of the mortality rate of the general population may cause bias in the SMRs reported in the present study, and therefore the true CIs for the SMRs may be slightly larger than reported.

In conclusion, aneurysmal SAH patients have excess mortality after successful treatment of ruptured intracranial aneurysm compared with age- and sex-adjusted general populations. Aneurysmal SAH is more of a systemic, chronic vascular disease than a single static event. Long-term follow-up even for SAH patients who have recovered well may be necessary.

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References

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