Life Expectancy After Perimesencephalic Subarachnoid Hemorrhage

Paut Greebe, RN; Gabriël J.E. Rinkel, MD

Background and Purpose—Patients with a perimesencephalic nonaneurysmal subarachnoid hemorrhage are not at risk for rebleeding in the initial years after the hemorrhage. Nevertheless, uncertainty remains on the long-term prognosis after perimesencephalic hemorrhage, and former patients are often considered high-risk cases for health insurance or are denied life insurance. We performed a very long-term follow-up study of a large consecutive series of such patients and compared mortality in this cohort with that in the general population.

Methods—All patients with a perimesencephalic hemorrhage (defined by pattern of hemorrhage on computed tomography within 72 hours after onset and absence of aneurysm) admitted between 1983 and 2005 to our service were followed-up by telephone. For patients who had died, we retrieved age and cause of death. We compared the age- and sex-specific mortality of this cohort with that of the general population by means of standardized mortality ratios with corresponding 95% confidence intervals.

Results—The cohort consisted of 160 patients, with a total number of patient-years of 1213. No new episodes of subarachnoid hemorrhage had occurred. During follow-up 11 patients had died; the expected number of deaths based on mortality rates in the general population (adjusted for age and gender) was 18.1. The standardized mortality ratio was 0.61 (95% confidence interval, 0.34 to 1.1).

Conclusions—Patients with perimesencephalic hemorrhage have a normal life expectancy and are not at risk for rebleeding. No restrictions should be imposed on these patients by physicians or health or life insurance companies.

Key Words: epidemiology ■ perimesencephalic hemorrhage ■ subarachnoid hemorrhage

Patients with a perimesencephalic subarachnoid hemorrhage are not at risk for rebleeding in the first years after the initial bleeding and have no reduced quality of life. Nevertheless, uncertainty remains on the long-term prognosis after a perimesencephalic hemorrhage. Perimesencephalic hemorrhage is a subset of subarachnoid hemorrhage; in recent years, evidence has become available that patients with an aneurysmal subarachnoid hemorrhage have a reduced life expectancy. This reduced life expectancy is not only caused by new episodes of subarachnoid hemorrhage from newly developed or previously undetected aneurysms but also by a higher risk of cardiovascular disease than that of healthy controls. The explanation for the excess mortality from cardiovascular diseases is the finding that smoking and hypertension are important risk factors for subarachnoid hemorrhage. Some studies also found a higher occurrence of hypertension and smoking in patients with perimesencephalic hemorrhage than in the general population, which suggests that these patients may be at increased risk for other cardiovascular diseases. Given these uncertainties, many patients who have had a perimesencephalic hemorrhage are denied life insurances and are considered high-risk cases for health insurance.

We performed a very long-term follow-up study of a large consecutive series of patients with perimesencephalic hemorrhage and compared mortality in this cohort with that in the general population.

Methods

Patients
From a prospectively collected database of patients admitted to the University Medical Center Utrecht with subarachnoid hemorrhage, we retrieved all patients admitted between 1983 and 2005 who met the following criteria: computed tomography scan performed within 72 hours after the onset of headache showing a perimesencephalic pattern of hemorrhage, and absence of a saccular aneurysm on computed tomographic angiography or conventional angiography. Patients who lived outside the Netherlands were excluded.

Follow-Up
First, we contacted the general practitioner of all eligible patients to find out if the patient was still alive. If a patient had died, we asked for the date and cause of death. If death occurred in a hospital or other facility, we reviewed the medical records. Subsequently, we sent a letter to all patients who were still alive. In this letter we announced a telephone call. If a patient had no phone number or an ex-directory one, we sent a letter asking the patient to contact us. During the telephone interview we asked the patients about new
episodes of hemorrhage and new vascular events by means of a standardized interview. We assessed functional outcome by means of 2 simple questions. The first question was whether patients need help from another person for everyday activities. For patients who do not need help, the next question was whether patients feel they have made a complete recovery from their stroke. These questions are practical and accurate, and have reasonable reliability and validity when administered by telephone.8,9

Data Analysis
We registered the number of patients in our cohort who had died during follow-up. We used standardized mortality ratios to investigate possible excess mortality in patients with perimesencephalic hemorrhage compared with the general population. Population-based statistics of The Netherlands were used as reference for the calculation of the total expected number of deaths.10 Mortality ratios were standardized in an indirect manner according to age and sex. Person-years of our cohort were calculated for sex and age (5-year) strata. Because of the long-term follow-up, many patients changed from age stratum during follow-up, for which we adjusted. For example, a patient 37 years of age at time of the hemorrhage and a 12-year follow-up counted for 2 years in the stratum 35 to 39, 5 years in the stratum 40 to 44, and 4 years in the stratum 45 to 49. This adjustment is necessary, because mortality increases with each stratum; therefore, unadjusted calculations would lead to an underestimation of the expected number of deaths in the cohort. The expected number of deaths was calculated by totaling the number of patient-years in each stratum and by multiplying this cumulative number of patient-years per stratum with the age- and sex-specific mortality rates of the reference population in this stratum. The sum of expected deaths per stratum yielded the total number of expected deaths in our cohort. For the reference population, we used mortality rates from 2000, which was the median year of hemorrhage in our cohort. The standardized mortality ratio is the ratio of the observed number of deaths in our cohort to that of the expected number of deaths based on the general population. A standardized mortality ratio >1 means excess mortality in the study cohort compared with the reference population. Ninety-five percent confidence intervals were calculated based on the Poisson distribution. We performed a sensitivity analysis for those patients who were excluded because they resided outside the Netherlands. In a worst-case analysis, these patients were considered to have died in the first year after the hemorrhage.

Results
During the study period, 162 patients with a perimesencephalic hemorrhage had been admitted. One of these patients was a UK resident spending his vacation in the Netherlands; he returned to the UK after discharge. Another patient emigrated soon after the hemorrhage to Australia. Both patients were excluded from the cohort. Therefore, the cohort consisted of 160 patients, 65 (41%) of whom were women. The mean age at time of the hemorrhage was 54.8 years (range, 24 to 90 years). Mean follow-up was 7.5 years (range, 1 to 23 years); the total number of patient-years was 1213.

No new episodes of subarachnoid hemorrhage had occurred (0%; 95% confidence interval, 0% to 0.3%). During follow-up 11 patients had died. Causes of death were myocardial infarction (n = 2), cardiac failure (n = 1), cerebral infarction (n = 1), hepatic failure (n = 1), gastric cancer (n = 2), colon carcinoma (n = 1), and infection at old age (n = 3). In this cohort the expected number of deaths based on mortality rates in the general population (adjusted for age and gender) was 18.1. The standardized mortality ratio was 0.61 (95% confidence interval, 0.34 to 1.1). In the worst-case scenario with the 2 patients living abroad entered as death within the first year after the hemorrhage, the standardized mortality ratio was 0.72 (95% confidence interval, 0.42 to 1.24).

Of the 149 patients who were alive at time of follow-up, one patient, a woman aged 80 years at time of the hemorrhage, had an ischemic stroke at age 86, and was admitted to a nursing home thereafter. A second patient, who had insulin-dependent diabetes and was 74 years of age at time of the hemorrhage, had recovered completely from the hemorrhage but had been admitted to a nursing home at 80 years of age after a humerus fracture. All other 147 patients were independent on activities for daily living, but 39 had symptoms including headaches or dizziness (n = 7), fatigue (n = 7), forgetfulness (n = 12), and irritability (n = 5).

Discussion
This study shows that patients with perimesencephalic hemorrhage have no excess in mortality compared with the general population. Moreover, even on very long-term follow-up no episodes of rebleeding occurred, and all patients regained independence for activities of daily life.

After treatment of a ruptured aneurysm, patients with aneurysmal subarachnoid hemorrhage have a small but definite risk of new episodes after treatment of the ruptured aneurysm from newly developed aneurysms or regrowth aneurysms at the site of the treated aneurysm.11 The development of new aneurysms indicates that having an aneurysm is not a single lifetime event, but a vessel disease that continues during life if patients survive an episode of aneurysmal subarachnoid hemorrhage. In a study from our center, the cumulative risk of a new episode in the first 10 years after the initial hemorrhage was 3.2% and the incidence rate was 286/100 000 patient-years.2 Others have found similar estimates.12 If patients with perimesencephalic hemorrhage would have a similar risk, 3.5 episodes of aneurysmal subarachnoid hemorrhage could have been expected during the follow-up of this cohort. The absence of any episode of aneurysmal subarachnoid hemorrhage indicates that our patients with perimesencephalic hemorrhage are not “missed aneurysm,”13 and that patients with perimesencephalic hemorrhage have a disease process other than intracranial aneurysms.

One of every 4 patients had nonspecific symptoms such as headaches, dizziness, fatigue, and forgetfulness. Unfortunately, we do not have reliable data on the prevalence of such symptoms in the general population. Therefore, we cannot directly compare the prevalence of these symptoms in our cohort with that of the general population, but the impression is that the prevalence in our cohort is higher. Previous studies found similar high rates of nonspecific symptoms and minor cognitive deficits, although none used a proper control group.14,15 The occurrence of these symptoms has been linked to the presence of depression.14 Whether a strategy of strict surveillance for depression and treating it decreases the rate of nonspecific symptoms and minor cognitive deficits remains to be seen.

Our series is the largest with the longest period of follow-up; previous studies have included fewer patients and shorter periods of follow-up, and did not compare long-term outcome with that in the general population.1,14–16 The large number of included patients enabled reliable estimates of the standardized mortality ratio. Another strength of the current study is...
that patients were prospectively collected into our database; thus, no retrieval bias can have occurred. We did not take into account the first year of follow-up. The total number of follow-up years in our calculation is therefore an underestimation of the total number of follow-up years, which leads to an underestimation of the number of expected deaths, and thus to an overestimation of the mortality ratio.

Most patients in our cohort had only computed tomographic angiography to rule out an aneurysm, and repeated studies were not performed unless the initial examination was technically unsatisfactory. In a formal decision analysis that included the risk of angiography and the risk of missing an aneurysm with computed tomographic angiography alone, we found that in patients with a perimesencephalic hemorrhage, computed tomographic angiography alone is the best diagnostic strategy.\textsuperscript{17} Other studies have confirmed the high negative predictive value of computed tomographic angiography for an aneurysm is patients with a perimesencephalic hemorrhage,\textsuperscript{18} and the low yield of repeated angiography in these patients.\textsuperscript{19} Therefore, we feel confident about our diagnostic approach. The absence of catastrophes during the clinical course and long-term follow-up confirms the safety of our strategy.

Because patients with perimesencephalic hemorrhage have a normal life expectancy and are not at risk for rebleeding, no restrictions should be imposed on these patients by physicians or health or life insurance companies.

Disclosures

None.

References

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