Attributable Risk of Common and Rare Determinants of Subarachnoid Hemorrhage

Ynte M. Ruigrok, MD; Erik Buskens, MD; Gabriël J.E. Rinkel, MD

Background and Purpose—Smoking, hypertension, alcohol consumption, autosomal dominant polycystic kidney disease (ADPKD), and positive family history for subarachnoid hemorrhage (SAH) are well-known risk factors for SAH. For effective prevention, knowledge about the contribution of these risk factors to the overall occurrence of SAH in the general population is pivotal. We therefore investigated the population attributable risks of the risk factors for SAH.

Methods—We retrieved the relative risk and prevalence of established risk factors for SAH from the literature and calculated the population attributable risks of these risk factors.

Results—Drinking alcohol 100 to 299 g/wk accounted for 11% of the cases of SAH, drinking alcohol ≥300 g/wk accounted for 21%, and smoking accounted for 20%. An additional 17% of the cases could be attributed to hypertension, 11% to a positive family history for SAH, and 0.3% to ADPKD.

Conclusions—Screening and preventive treatment of patients with familial preponderance of SAH alone will cause a modest reduction of the incidence of SAH in the general population. Further reduction can be achieved by reducing the prevalence of the modifiable risk factors alcohol consumption, smoking, and hypertension. (Stroke. 2001;32:1173-1175.)

Key Words: epidemiology ■ risk factors ■ subarachnoid hemorrhage

Spontaneous subarachnoid hemorrhage (SAH) from rupture of an intracranial saccular aneurysm has an incidence of approximately 6 per 100 000.1 Although outcome after aneurysmal SAH has improved slightly over the last 3 decades, the prognosis remains poor; half the patients die, and 20% remain dependent for activities of daily life.2 The best way to reduce morbidity and mortality is prevention of the occurrence of SAH. Prevention can be achieved by reducing risk factors or by screening and preventive treatment of patients at increased risk of aneurysmal rupture.

Smoking, hypertension, and alcohol abuse are established risk factors for SAH.3 Furthermore, patients with autosomal dominant polycystic kidney disease (ADPKD)4 and first-degree relatives of patients with SAH5 have an increased risk for SAH. However, little is known about the contribution of each risk factor to the overall occurrence of SAH in the general population (the so-called population attributable risk [PAR]). For effective prevention, knowledge about which risk factors have to be targeted is essential. We therefore investigated the PARs of smoking, hypertension, alcohol consumption, ADPKD, and positive family history for SAH.

Methods

Smoking
The relative risk (RR) of SAH for smoking was retrieved from a systematic review of studies on risk factors for SAH; in the review the RR is 1.9 (95% CI, 1.5 to 2.3).5 In the Netherlands, 34.7% of the population older than 16 years smokes; the age-adjusted prevalence is 27.9%.6

Hypertension
We extracted the estimate of the RR of SAH for hypertension (RR, 2.8; 95% CI, 2.1 to 3.6) from the same systematic review.3 The age-adjusted prevalence of men and women with hypertensive blood pressure (≥160/95 mm Hg) from the Monitoring Trends and Determinants in Cardiovascular Disease (MONICA) survey 1989–1990 is 11.4%.8

Alcohol
The estimates on the RRs of SAH for alcohol drinking were retrieved from a longitudinal study on the relationship between alcohol and SAH.9 We could not use the other studies discussed in the systematic review3 because it was impossible to recalculate the data of these studies into the categories of drinking alcohol 100 to 299 and ≥300 g/wk. In the Netherlands, 13.3% of the population consumes ≥3 alcoholic drinks per week, which is approximately ≥100 g/wk. The age-adjusted prevalence of drinking ≥100 g/wk is 10.7%. Consumption of >3 alcoholic drinks daily (approximately ≥300 g/wk) occurs in 7% of the population older than 18 years; the age-adjusted prevalence is 5.9%. The age-adjusted prevalence of drinking 100 to 299 g/wk is 10.7% minus 5.9% and equals 4.8%. The RR of SAH for drinking 100 to 299 g/wk is 3.5 (95% CI, 1.1 to 11.0), and that for drinking ≥300 g/wk is 5.6 (95% CI, 1.9 to 16.7).9

Positive Family History for SAH
For the estimate of the RR of SAH for positive family history we used data from a recent study performed in the Netherlands; in that
study the RR was 6.6 (95% CI, 2.0 to 21.0). Two other studies found similar RRs of 4.1 and 4.5. We could not perform a meta-analysis on the RR of familial preponderance for SAH because we could not extract crude data from these 2 other studies.

The incidence of SAH approximates 6 per 100,000 person-years. This means that in the Netherlands, where the population size approximates 15 million people, 900 new patients have a SAH annually. With a life expectancy at birth of 78 years in the Netherlands, lifetime risk of SAH is 1 per 214 \((6 \times 10^{-5}) \times (15 \times 10^3) \times 78\). Consequently, in the Netherlands 70,093 \((15 \times 10^5)/214\) people had or will have SAH. The mean number of first-degree relatives per family of a patient with SAH is 5. A crude estimate of the total amount of people with a first-degree relative who had or will have SAH is then 350,465 \((5 \times 70,093)\) or 2.3% of the Dutch population.

### Autosomal Dominant Polycystic Kidney Disease

Because no data are available on the RR of ADPKD for SAH, we calculated this RR as follows: the estimated RR of intracranial aneurysms in patients with ADPKD is 4.4 (95% CI, 2.7 to 7.2). If we assume an equal risk of aneurysm rupture given the presence of an aneurysm, the RR would be 4.4. The prevalence for ADPKD in the general population is 1 per 1000.\(^{15,16}\)

### Data Analysis

The PAR is an estimate of the fraction of the total amount of patients with SAH in the population that can be attributed to a particular risk factor. The PAR of a given risk factor is influenced by the prevalence and the RR of this risk factor and is calculated according to the following formula: \( \text{PAR} = \frac{\text{PF}(\text{RR} - 1)}{\text{PF}(\text{RR} - 1) + 1} \), where PF is the population fraction with the risk factor.\(^6\)

### Results

The PARs associated with the risk factors for SAH are shown in the Table. Drinking alcohol 100 to 299 g/wk accounted for 11% of the cases of SAH, drinking alcohol \( \geq 300 \) g/wk accounted for 21%, and smoking accounted for 20%. An additional 17% of the cases were attributable to hypertension, 11% of the cases to a positive family history for SAH, and 0.3% to ADPKD. If all first-degree relatives of patients with SAH are effectively screened and if all aneurysms found during screening are eliminated, then a reduction in incidence of SAH of a maximum of 11% can be achieved.

### Discussion

We found that excessive alcohol consumption and smoking are the major contributors to the incidence of SAH. Secondary contributors are hypertension, modest alcohol consumption, and familial preponderance.

We may have underestimated the PAR of smoking and hypertension for SAH. We extracted the RR of SAH for smoking from a systematic review\(^1\) in which the results of 2 longitudinal cohort studies are combined.\(^8,17\) The diagnosis of SAH was not always confirmed by CT or angiography in these longitudinal studies. Since CT shows sources other than a ruptured aneurysm, most often intracerebral hematomas in up to 20% of patients with the clinical diagnosis of SAH,\(^18\) these studies probably have included patients with primary intracerebral hematoma. Because smoking is a less pronounced risk factor for intracerebral hematoma than for aneurysmal SAH,\(^19\) including patients with intracerebral hematoma dilutes the RR for SAH. Accordingly, the attributable risk of smoking for SAH is probably underestimated in our analysis. For the prevalence of hypertension in the population we defined hypertension as either average systolic blood pressure \( \geq 160 \) mm Hg or diastolic blood pressure \( \geq 95 \) mm Hg. Because the risk of stroke increases with higher blood pressure levels,\(^20\) the actual number of patients with SAH from hypertension is probably larger than we found using a single RR for all people with hypertension. The notion that our results are an underestimation of the PARs of smoking and hypertension for SAH is supported by previous studies that found a PAR of smoking of 40% and a PAR of hypertension of 30% for SAH.\(^21,22\)

We reported the PAR of each risk factor for SAH separately because the data presented in the various articles did not allow us to perform multivariate analyses. However, smoking and alcohol consumption are often combined, and heavy drinking is known to be a risk factor for hypertension.\(^23\) The PARs presented for smoking, alcohol consumption, and hypertension may therefore not be independent. For this reason, it is not justified to add the percentages for smoking and alcohol to one overall atherosclerotic percentage. However, we believe that the estimates provide a good impression of the relative importance of the various risk factors.

The PARs found in our analysis are overall percentages; it was not possible to differentiate for age and sex. The relative contribution of risk factors for SAH probably differs between young and older patients. Genetic factors probably play a more important role in younger patients, and atherosclerotic risk factors probably play a more important role in older patients. Furthermore, SAH is more common in women,\(^1\) while smoking, hypertension, and alcohol use are more common in men.

PARs may differ between different regions and may change over time. In the present analysis the estimates of prevalence of risk factors for SAH were based on studies conducted in Western European countries. In other populations the prevalence of the risk factors for SAH is different and therefore also the corresponding PARs. For example, the incidence of SAH in Finland is almost 3 times higher than in other parts of the world,\(^1\) which may be partly attributed to the high prevalence of hypertension in this country.\(^24,25\) Two studies performed in the late 1980s and the early 1990s found a PAR of smoking of 40% and a PAR of hypertension of 30% for SAH.\(^21,22\) Since that period the prevalences of smoking and hypertension have decreased,\(^26\) which may explain that our PARs of smoking and hypertension for SAH are lower.

The incidence of SAH has remained stable over the last 3 decades.\(^1\) In contrast, the cardiovascular risk factors smoking and hypertension are reduced and, in accordance, the incidence of stroke in general has declined.\(^27\) The reason for not
finding a reduction in the incidence of SAH is probably that the number of patient-years in SAH incidence studies performed is too small to detect such a decline. The highest number of patient-years in an incidence study was found to be 2,800,000. To demonstrate an incidence reduction from 6 per 100,000 to 5 per 100,000 patient-years, 2 incidence studies with a total of 5 million patient-years are needed. Recent data from Finland suggest a decreasing incidence of SAH,28,29 in combination with a decline of cardiovascular risk factors.30,31 We defined patients with a positive family history for SAH as the total amount of people with a first-degree relative who had or who have SAH and found this to be approximately 2.3% of the total Dutch population. Even if screening programs for intracranial aneurysms in first-degree relatives of patients with SAH would result in accurate detection and effective prevention, SAH could only be prevented in those first-degree relatives of whom a family member already suffered SAH. Therefore, the 11% of the SAH cases attributable to a positive family history can never be totally eliminated.

In conclusion, screening and preventive treatment of patients with familial preponderance of SAH alone will cause a modest reduction of the incidence of SAH in the general population. Further reduction can be achieved by reducing the prevalence of the modifiable risk factors alcohol consumption, smoking, and hypertension. Screening programs for intracranial aneurysms in patients with ADPKD will have little influence on the incidence of SAH.

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References

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