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).3 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%.7

Alcohol

The estimates on the RRs of SAH for alcohol drinking were retrieved from a longitudinal study on the relationship between alcohol and SAH.8 The age-adjusted prevalence of drinking ≥300 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;9 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).8

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 ((6×10^3)×(15×10^3)×78). Consequently, in the Netherlands 70,093 (15×10^6/214) 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 (5×70,093) 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. The PARs found in our analysis are overall percentages; it may not be 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, while smoking, hypertension, and alcohol use are more common in men.

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 ≥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 in which the results of 2 longitudinal cohort studies are combined. 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, 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, 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 ≥160 mm Hg or diastolic blood pressure ≥95 mm Hg. Because the risk of stroke increases with higher blood pressure levels, 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. 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. 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, 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, which may be partly attributed to the high prevalence of hypertension in this country. 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. Since that period the prevalences of smoking and hypertension have decreased, 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. In contrast, the cardiovascular risk factors smoking and hypertension are reduced and, in accordance, the incidence of stroke in general has declined. The reason for not
finding a reduction in the incidence of SAH is probably that
the number of patient-years in SAH incidence studies per-
formed is too small to detect such a decline. The highest
number of patient-years in an incidence study was found to be
2 800 000.1 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 will 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 attrib-
utable to a positive family history can never be totally
eliminated.

In conclusion, screening and preventive treatment of pa-
tients 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 consump-
tion, smoking, and hypertension. Screening programs for
intracranial aneurysms in patients with ADPKD will have
little influence on the incidence of SAH.

Acknowledgments

This study was supported in part by an established clinical investi-
gator grant from the Netherlands Heart Foundation to Dr Rinkel
(grant D98.014). We would like to thank Professor L.J. Kappelle,
MD, for his comments on a previous version of the manuscript.

References

2. Hop JW, Rinkel GJE, Algra A, van Gijn J. Case-fatality rates and
functional outcome after subarachnoid hemorrhage: a systematic review.
3. Teunissen LL, Rinkel GJE, Algra A, van Gijn J. Risk factors for sub-
4. Schievink WI, Torres VE, Piepgras DG, Wiebers DO. Saccular intracra-
5. Bromberg JEC, Rinkel GJE, Algra A, Greebe P, van Duyun CM, Hasan D,
ten Berg HWM, Wijdicks EFM, van Gijn J. Subarachnoid haemorrhage in
first and second degree relatives of patients with subarachnoid haem-
Heerlen, Netherlands; 1999.
8. Hense HW, Steher J, Filipiak B, Keil U. Five-year changes in population
blood pressure and hypertension prevalence: results from the MONICA
Augsburg surveys 1984/85 and 1989/90. Am Epidemiol. 1993;3:
410–416.
11. Gaist D, Væth M, Tsirpoulos I, Christensen K, Corder E, Olsen J,
Sørensen HT. Risk of subarachnoid haemorrhage in first degree relatives
of patients with subarachnoid haemorrhage: follow up study based on
national registries in Denmark. BMJ. 2000;320:141–145.
12. Schievink WI, Schaid DJ, Michels VV, Piepgras DG. Familial aneu-
13. Raaymakers TWM, Rinkel GJE, Ramos LMP. Initial and follow-up
screening for aneurysms in families with familial subarachnoid hemor-
rupture of intracranial aneurysms: a systematic review. Stroke. 1998;29:
251–256.
15. Dalgaard OZ. Bilateral polycystic disease of the kidneys: a follow-up of
two hundred and eighty-four patients and their families. Acta Med Scand
Suppl. 1957;328:1–235.
16. Iglesias CG, Torres VE, Offord KP, Holley KE, Beard CM, Kurland LT. Epidemiology of adult polycystic kidney disease, Olmsted County,
18. van Gijn J, van Dongen KJ. Computed tomography in the diagnosis of
subarachnoid hemorrhage and ruptured aneurysm. Clin Neurol Neu-
19. Abbott RD, Yin Y, Reed DM, Yano K. Risk of stroke in male cigarette
21. Javela S, Hillbom M, Nunninen H, Koskinen P. Cigarette smoking and
alcohol consumption as risk factors for aneurysmal subarachnoid hemor-
22. Bonita R. Cigarette smoking, hypertension and the risk of subarachnoid
hemorrhage: a population-based case-control study. Stroke. 1986;17:
831–835.
23. Klatsky AL, Friedman GD, Siegelaub AB, Gérard MJ. Alcohol consump-
24. The WHO MONICA Project, prepared by Pajak A, Kuulasmaa K,
Tuomilehto J, Ruokokoski E. Geographical variation in the major risk
factors of coronary heart disease in men and women aged 35–64 years.
World Health Stat Q. 1988;41:115–140.
25. The WHO MONICA Project, prepared by Tunstall-Pedoe H, Kuulasmaa
K, Amouyel P, Arveiler D, Rajakangas AM, Pajak A. Myocardial
infarction and coronary deaths in the World Health Organization
MONICA Project: registration procedures, event rates, and case-fatality
rates in 38 populations from 21 countries in four continents. Circulation.
Tolonen H, Evans A, Ferrario M, Tuomilehto J. Estimation of contri-
bution of changes in classic risk factors to trends in coronary-event rates
across the WHO MONICA Project populations. Lancet. 2000;355:
675–687.
27. Vartiainen E, Sarti C, Tuomilehto J, Kuulasmaa K. Do changes in cardio-
vascular risk factors explain changes in mortality from stroke in Finland?
BMJ. 1995;310:901–904.
28. Fogelholm R, Hernesniemi J, Vapalahi M. Impact of early surgery on
outcome after aneurysmal subarachnoid hemorrhage: a population-based
incidence and mortality rates of stroke in Finland from 1972 to 1991:
results of three population-based stroke registers. Stroke. 1996;27:
1487–1491.
JO, Puska PM, Nissinen AM. Trends in blood pressure levels and control
of hypertension in Finland from 1982 to 1997. J Hypertens. 1998;16:
1379–1387.
Cardiovascular risk factor changes in Finland, 1972–1997. Int J Epi-
Attributable Risk of Common and Rare Determinants of Subarachnoid Hemorrhage
Ynte M. Ruigrok, Erik Buskens and Gabriël J. E. Rinkel

Stroke. 2001;32:1173-1175
doi: 10.1161/01.STR.32.5.1173

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/32/5/1173

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/