Editorial Comment—Prehemorrhage Risk Factors for Fatal Intracranial Aneurysm Rupture

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Prehemorrhage Risk Factors for Fatal Intracranial Aneurysm Rupture

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Background and Purpose—The goal of this study was to investigate predictive preictal risk factors for fatal subarachnoid hemorrhage (SAH) in a patient population with verified intracranial aneurysms without surgical selection of patients and with complete follow-up.

Methods—A total of 142 patients with 181 unruptured aneurysms diagnosed between 1956 and 1978 were followed up for a total of 2577 person-years until death, SAH, or the years 1997 to 2000. The predictive value of several factors known before SAH was tested for case fatality.

Results—During follow-up, 34 first episodes of hemorrhage from a previously verified unruptured aneurysm occurred. Of these bleeding episodes, 17 were fatal. Patients who died after the bleeding had higher blood pressure values (mean±SD, 148±11/92±8 mm Hg; mean pressure, 111±9 mm Hg) before hemorrhage than did those with nonfatal bleeding (mean±SD, 135±15/83±11 mm Hg; mean, 101±12 mm Hg) ($P<0.05$). Patients with fatal SAH were also older (54±7 versus 47±13 years, $P=0.068$) and had aneurysms larger in diameter (13±8 versus 10±5 mm) than those who survived. They had a higher prevalence of definite hypertension (56% versus 12%, $P<0.05$), more frequently used antihypertensive medication (29% versus 6%) by the end of follow-up, and tended to have higher blood pressure at the beginning of follow-up (140±21/85±11 versus 134±17/80±9 mm Hg). After adjustment for age, aneurysm size, and sex, the only indisputable significant independent risk factor for fatal SAH compared with nonfatal SAH was systolic blood pressure before aneurysm rupture (odds ratio, 1.11 per 1 mm Hg; 95% CI, 1.01 to 1.23; $P=0.032$). The adjusted odds ratio of definite hypertension for fatal SAH was 12.67 (95% CI, 1.53 to 104.70; $P=0.018$).

Conclusions—Increased systolic blood pressure values and long-term hypertension before aneurysm rupture seem to predict fatal SAH independently of aneurysm size or patient age or sex at the time of rupture. **(*Stroke*. 2003;34:1852-1858.)**

Key Words: hypertension ■ intracranial aneurysm ■ natural history ■ outcome ■ subarachnoid hemorrhage

Aneurysmal subarachnoid hemorrhage (SAH), despite improvements in surgical and medical treatment, is a serious disease with high rates of mortality (40% to 50%) and morbidity.[1,2] Outcome of SAH is still determined mainly by severity of initial bleed or early rebleeding[1–3] and, to a lesser extent, by delayed cerebral ischemia, commonly attributed to vasospasm in the large cerebral arteries.[4–6] Hence, identification of modifiable risk factors for SAH and for impaired outcome after the bleeding is important as a means to influence incidence and outcome of this serious disease.

Indisputable modifiable risk factors for SAH seem to be cigarette smoking, alcohol consumption, and hypertension.[7–10] Besides severity of bleeding, outcome after SAH may be influenced by such preictal factors as patient age,[4,11–13] aneurysm site[4] and size (in surgical SAH cases),[4] history of hypertension,[11,13] and heavy alcohol drinking.[11] Patient age,[4,12] aneurysm site,[4] and recent history of heavy alcohol consumption[11] (which is correlated with hypertension) have been reported independently of severity of SAH to predict outcome in hospital-based patient populations. In addition, in a large meta-analysis,[10] cigarette smoking has also been shown to increase risk for symptomatic vasospasm somewhat. Independently of other prognostic factors, high systolic blood pressure (BP) values after aneurysm rupture predict death, poor outcome,[4] and possibly occurrence of early rebleeding.[3]

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Actual risk factors affecting outcome and case fatality, however, may differ from those in hospital-based populations with their usual 20% to 30% case fatality rates because a large proportion of patients with aneurysmal SAH die of primary bleed or early rebleeding soon after SAH before admission to neurological or neurosurgical centers. Before 1979, unruptured intracranial aneurysms were not operated on in our clinic, which, until the late 1960s, was the only neurosurgical center in Finland.[2,14,15] In this long-term cohort study, patients with verified unruptured aneurysms diagnosed before

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1979 were followed up to explore preictal risk factors that predict case fatality after aneurysm rupture.

Patients and Methods

Patient Population

Follow-up and radiological data on patients with unruptured intracranial aneurysms have been collected since the 1950s at the Department of Neurosurgery, Helsinki University Central Hospital. Previous reports[2,14,15] give detailed baseline characteristics and radiological findings of the 142 patients (76 women) whose unruptured aneurysms were diagnosed between 1956 and 1978, as well as inclusion and exclusion criteria. Patients with symptomatic aneurysms were included only if SAH was excluded by lumbar puncture within a few days after onset of symptoms.

Most patients (n=131) were cases with unruptured aneurysms and SAH with only the ruptured aneurysm clipped and occlusion of the aneurysm confirmed by postoperative angiography. Five patients had asymptomatic incidental aneurysms, and 6 had symptomatic aneurysms (5 aneurysms caused a cranial nerve deficit because of space-occupying effect).

Recording of Follow-Up Data

In addition to data obtained during hospital stays or visits in the outpatient department and from follow-up interviews, information on all patients came from medical records at other hospitals and from general practitioners as a double-check on diseases, medications, and BP values. Autopsy reports and official death certificates of all deceased patients were examined.

The follow-up database also included data on patient height and weight; medical history, hospitalizations, and drugs used; approximate intake of ethanol per week; occurrence of heavy drinking (CAGE questionnaire)[2]; current and previous smoking status; and family history of verified intracranial aneurysm cases in first-degree relatives (parents, siblings, and offspring). Location, number, size (maximum diameter and volume), shape, and orientation (direction) of aneurysms in the initial and follow-up angiographies were recorded.[2,14] Each patient's clinical condition on admission to the first hospital after aneurysm rupture was graded according to the World Federation of Neurological Surgeons (WFNS) Grading Scale.[16]

Recording of BP Values

BP values were recorded before diagnosis and during follow-up, excluding the values for those patients with multiple aneurysms obtained within 3 months after SAH because SAH may secondarily increase BP. In patients with multiple BP measurements, values in the first and last quarters (≈5 years) of the follow-up were averaged. BP measurements by healthcare professionals were done during the follow-up on average 7.5±5.8 times (mean±SD) per patient (median, 6; range, 2 to 34) and, during the last quarter of the follow-up, 3.1±2.3 times per patient (median, 3; range, 1 to 15). A BP measurement was missing at the end of follow-up for only 1 patient.

Mean arterial BP was calculated from this formula: diastolic BP+(systolic BP−diastolic BP)/3.

Definite hypertension was defined as a systolic pressure repeatedly >160 mm Hg, diastolic pressure >95 mm Hg, or use of antihypertensive medication.

Statistical Analysis

Data were analyzed with the SPSS statistical package (SPSS for Windows, release 9.0.1.1999, SPSS Inc). Categorical variables were compared by Fisher's exact 2-tailed test, Pearson's χ^2 test, or the test for linear trend. Continuous variables were compared between groups by the Mann-Whitney *U* test, *t* tests, or analysis of variance with corrected multiple pairwise comparisons by use of Dunnett's method. Univariate association of continuous variables was tested by Spearman's rank correlation coefficients (r_s).

Univariate and multivariate odds ratios (ORs) and 95% CIs of risk factors for fatal SAH were analyzed by unconditional logistic regression. The variables tested were age at both the beginning and end of follow-up; sex; body mass index calculated as weight divided by height squared (kg/m^2); size, location, and direction of the largest unruptured aneurysm; diameter of ruptured aneurysm in cases with prior SAH; presence of multiple unruptured aneurysms; aneurysm group (symptomatic or incidental compared with those with prior SAH); cigarette smoking status, current smoking, number of cigarettes smoked daily, and duration of smoking; alcohol consumption and heavy drinking; source of information on the patient's health habits; family history of intracranial aneurysms; definite hypertension; antihypertensive medication; and BP (systolic, diastolic, mean) values during follow-up. A maximum-likelihood stepwise forward elimination procedure was used, with selection of variables to be added based on the magnitude of their probability values (<0.05). A 2-tailed value of $P<0.05$ was statistically significant.

Results

Study Group and Follow-Up

Of a total of 142 patients, 34 (24%) had a hemorrhage from a previously verified unruptured aneurysm, and 17 (50%) of these patients died because of this bleeding. The total follow-up time for patients after diagnosis of unruptured aneurysm was 2577 person-years, an average of 18.2 years per patient (median, 19.7; range, 0.8 to 38.9), yielding an approximate annual aneurysm rupture rate of 1.3%. Baseline characteristics according to occurrence of either a nonfatal or fatal SAH compared with those without aneurysm rupture are shown in Table 1.

Patients with an aneurysm rupture had a shorter follow-up time with no difference in case fatality than did those with no aneurysm rupture. The former were therefore also younger at the end of follow-up ($P<0.01$) because their follow-up was terminated by the SAH. Patients with a fatal SAH were older ($P=0.068$) than those with a nonfatal SAH at the end of follow-up (ie, at the time of SAH), but they were also older at the beginning of follow-up (42.7±9.2 versus 34.3+7.6 years, $P<0.05$).

The mean maximum aneurysm diameter in patients with a fatal SAH (n=10) was not significantly ($P=0.17$) greater than in the nonfatal SAH group (n=17). If aneurysms were estimated to be at least 40% greater before death than was measured at autopsy,[17] this difference was significant ($P<0.05$). In that situation, however, growth rate was not associated with case fatality because patients who died of SAH already had, at the start of follow-up, somewhat larger aneurysms than did those who survived SAH (6.6±7.2 versus 3.9±2.2 mm).

Current smoking was significantly ($P<0.01$) more common in patients with aneurysm rupture but was not associated with case fatality after SAH. Alcohol use per week was greater ($P=0.022$) for patients with fatal SAH than for those without SAH, but there were only 4 patients with fatal SAH who had data on alcohol use.

BP Values

Systolic, diastolic, and mean BP values were significantly higher in patients with fatal than in those with nonfatal SAH before bleeding, as were prevalence of definite hypertension and use of antihypertensive medication (Table 1). During some phase of follow-up, 44 patients (31%) received antihypertensive therapy. BP readings were repeatedly high (sys-

TABLE 1. Baseline Characteristics of Patients at End of Follow-Up According to Later Aneurysm Rupture and Case Fatality

Characteristic	Nonfatal SAH (n=17)	Fatal SAH (n=17)	No SAH (n=108)
Women, n (%)	11 (65)	12 (71)	53 (49)
Age (mean±SD), y	47.0±13.1*	53.8±6.8*	62.9±11.2
Body mass index (mean±SD), kg/m^2	27.6±3.8	26.6±4.2	25.6±3.8
Unruptured aneurysms (mean±SD), n	1.12±0.33	1.35±0.61	1.29±0.55
Aneurysm size (mean±SD, n=87), mm			
Diameter	9.8±4.7†	13.2±8.1*	6.1±4.2
Adjusted diameter	9.8±4.7†	15.3±8.0*‡	6.2±4.3
Location of aneurysms, n (ruptured)			
ICA	11 (9)	6 (5)	62 (−)
ACA+A2	1 (1)	0	6 (−)
ACOA	1 (1)	3 (3)	4 (−)
MCA	6 (6)	14 (9)	62 (−)
BAS+SCA	0	0	5 (−)
Aneurysms, n	19 (17)	23 (17)	139 (−)
Cigarette smoking, n (%)			
Never	5/16 (31)	3/12 (25)	30/95 (32)
Previous	0	0	26/95 (27)
Current	11/16 (69)	9/12 (75)	39/95 (41)
BP, mm Hg	135±15*/83±11	148±11‡/92±8‡	148±17/89±10
Mean BP, mm Hg	101±12†	111±9‡	109±11
Definite hypertension,§ n (%)	2 (12)	9 (56)	45 (42)
Antihypertensive medication,§ n (%)	1 (6)	5 (29)	38 (35)
Alcohol use (mean±SD, n=95), g/wk	132±13	350±135†	107±180
Heavy alcohol consumption (n=111), n (%)	3 (21)	3 (27)	23 (27)
Family history (n=94), n (%)	2 (15)	1 (11)	6 (8)

ICA indicates internal carotid artery; MCA, middle cerebral artery; ACA, anterior cerebral artery; A2, pericallosal artery; ACOA, anterior communicating artery; BAS, basilar tip; and SCA, superior cerebellar artery. Aneurysm size is largest diameter in mm. Definite hypertension was defined as systolic BP repeatedly >160 mm Hg, diastolic BP >95 mm Hg, or use of antihypertensive medication. Family history of aneurysms was defined as ≥1 verified aneurysm cases in first-degree relatives. Adjusted aneurysm diameter is diameter measured at autopsy estimated to have been 40% greater before death.[17]

*$P<0.01$, †$P<0.05$ for difference from patients with no SAH; ‡$P<0.05$ for difference between fatal and nonfatal SAH groups, and §$P<0.05$ for difference between groups.

tolic BP >160 mm Hg or diastolic BP >95 mm Hg) in 17 patients (12%) at the beginning of follow-up and in 30 patients (21%) at the end of follow-up.

BP was significantly associated with age. Systolic BP ($r_s=0.281$, $P=0.001$ in the beginning of follow-up; $r_s=0.356$, $P<0.001$ at the end of follow-up) and mean BP ($r_s=0.268$, $P=0.001$; $r_s=0.208$, $P=0.013$, respectively) values during the entire study period were related to age, but diastolic BP was associated with age only in the beginning of follow-up ($r_s=0.214$, $P=0.011$; $r_s=0.052$, $P=0.54$, respectively). Despite the long follow-up time, there were also high correlation coefficients between BP values obtained in the beginning and at the end of follow-up ($r_s=0.513$, $P<0.001$ for systolic; $r_s=0.453$, $P<0.001$ for diastolic; $r_s=0.500$, $P<0.001$ for mean BP values). After aneurysm rupture in 33 patients, WFNS score correlated with pre-SAH systolic ($r_s=0.339$, $P=0.053$), mean ($r_s=0.332$, $P=0.059$), and diastolic ($r_s=0.327$, $P=0.063$) BP values obtained at the end of follow-up.

Patients with a fatal SAH already had, at the beginning of follow-up, nonsignificantly higher BP values (140±21/85±11 versus 134±17/80±9 mm Hg; mean BP, 103±13 versus 98±11 mm Hg) than did those with a nonfatal SAH. Definite hypertension was also more prevalent ($P=0.064$) at the beginning of follow-up in those with fatal SAH (5 of 17, 29%) than for either those with nonfatal SAH (0 of 17) or those without later SAH (18 of 108, 17%).

Case Fatality and Treatment After SAH

Clinical condition, treatment, and causes of death according to fatality of SAH are shown in Table 2. Most patients with fatal SAH died soon after bleeding because of a severe primary bleed or rebleeding without any specific aneurysm treatment. No patient died from surgical complications. Four patients with fatal SAH had an ultra-early rebleeding in the primary hospital or during transfer. Of all 17 patients who died because of SAH, 7 (41%) had had no motor response to

TABLE 2. Clinical Grade on Admission to First Hospital and Treatment of Aneurysms According to Fatality of SAH

Characteristic	Nonfatal SAH (n=17), n (%)	Fatal SAH (n=17), n (%)
WFNS grade[16] on admission*		
I	9 (53)	0
II	2 (12)	1 (6)
III	6 (35)	2 (12)
IV	0	1 (6)
V	0	13 (76)
Treatment of aneurysm*		
None	2 (12)	16 (94)
Clipping	14 (82)	1 (6)
Coiling	1 (6)	0
Cause of death		
Primary bleed or ultra-early rebleed	...	15 (88)
Late rebleed	...	2 (12)

Ultra-early rebleeding occurred in the primary hospital or during transfer; late rebleeds, at 7 and 21 days from SAH.
*$P<0.001$ for the difference between SAH groups.

pain on admission to the primary hospital, and all of these patients died within a few hours without transfer to a referral hospital.

Prediction of Fatal Aneurysm Rupture

Multiple stepwise logistic regression showed that systolic BP at the end of follow-up before aneurysm rupture was the only indisputably significant ($P<0.05$) predictor for fatal SAH among patients with an aneurysm rupture. Definite hypertension was also a significant ($P<0.05$) risk factor for fatal SAH if BP values were not analyzed. Patient age and maximum diameter of aneurysm (corrected diameter obtained by multiplying by 1.4 if measured only at autopsy) had a borderline direct association with risk for fatal SAH. Univariate and multivariate risk factors for fatal SAH are shown in Table 3.

In multivariate models, the significance of age decreased when either BP values or hypertension was in the models because BP values were correlated with age. If elevated BP (>160/95 mm Hg) regardless of use of antihypertensives was used as a categorical variable in model 1 instead of continuous systolic BP, it was almost a significant predictor for fatal SAH compared with levels of ≤160/95 mm Hg (adjusted OR, 6.81; 95% CI, 0.85 to 54.52; $P=0.071$). In model 2, its corresponding adjusted OR was 7.25 (95% CI, 0.81 to 64.73; $P=0.077$). Borderline hypertension alone (160/95≥BP>140/90 mm Hg) or combined with clear hypertension (BP >160/95 mm Hg) was not a significant predictor for fatal SAH (data not shown).

Similar results were obtained if risk factors for fatal SAH were compared with those of the patients who had no aneurysm rupture during follow-up (Table 4). Because patients without SAH were clearly older than those with SAH, systolic BP values before fatal SAH, but not occurrence of definite hypertension, had only a borderline significance after adjustment for patient age, sex, and aneurysm size. Patients with fatal SAH had, as expected, significantly larger aneurysms than did those without SAH.

Discussion

On the basis of this study, which also includes SAH patients who died soon after the bleeding as a result of the primary bleed or ultra-early rebleeding, systolic BP values and definite hypertension were significant independent predictors for fatal SAH. Aneurysm size and patient age seem also to be important risk factors but had less predictive effect on the severity of bleeding than did BP values.

Part of the deleterious effect of age and alcohol consumption on outcome may be due to hypertension because BP values are directly correlated with age and alcohol use. On the other hand, both of these factors are, independently of severity of bleeding, significant risk factors for poor outcome in hospital-based SAH patient populations.[4,11,12] Patients with ruptured aneurysm of the basilar artery may also have a worse

TABLE 3. Multivariate ORs (95% CIs) of BP, Hypertension, Age, and Size of Aneurysm for Fatal Compared With Nonfatal SAH

	OR (95% CI)				
Characteristic	Univariate	Model 1	Model 2	Model 3	Model 4
Systolic BP at end of follow-up (per mm HG)	1.09	1.11	1.15	...	...
	(1.01–1.18)*	(1.01–1.23)*	(1.01–1.30)*		
Definite hypertension	9.64	...	...	12.67	12.90
	(1.63–56.92)*			(1.53–104.70)*	(1.44–115.35)*
Age at rupture (per y)	1.07	1.00	0.99	1.03	1.03
	(0.99–1.15)	(0.91–1.09)	(0.89–1.10)	(0.94–1.13)	(0.93–1.14)
Size of aneurysm (per mm)	1.10	1.17	...	1.12	...
	(0.95–1.27)	(0.96–1.43)		(0.96–1.30)	
Adjusted size of aneurysm (per mm)	1.17	...	1.30	...	1.18
	(0.99–1.38)		(0.99–1.71)		(0.99–1.40)

In multivariate analysis, ORs were also adjusted for sex.
*$P<0.05$.

TABLE 4. Multivariate ORs (95% CIs) BP, Hypertension, Age, and Size of Aneurysm for Fatal SAH Compared With no SAH

	OR (95% CI)				
Characteristic	Univariate	Model 1	Model 2	Model 3	Model 4
Systolic BP at end of follow-up (per mm HG)					
	1.04	1.06	1.07	...	...
	(0.99–1.09)	(1.00–1.13)	(1.00–1.15)		
Definite hypertension	2.25	...	...	2.34	1.81
	(0.57–8.82)			(0.37–14.88)	(0.25–12.85)
Age at rupture (per y)	0.90	0.86	0.83	0.87	0.86
	(0.83–0.97)†	(0.76–0.97)*	(0.71–0.96)*	(0.79–0.97)*	(0.76–0.97)*
Size of aneurysm (per mm)	1.20	1.24	...	1.18	...
	(1.06–1.36)†	(1.05–1.46)*		(1.00–1.39)*	
Ajusted size of aneurysm (per mm)	1.25	...	1.32	...	1.26
	(1.09–1.42)†		(1.09–1.60)†		(1.06–1.50)†

In multivariate analysis, ORs were also adjusted for sex.
*$P<0.05$; †$P<0.01$.

prognosis than those with aneurysms of other locations.[4] In the present study, the number of patients with such aneurysms was too small (n=5) to detect this association. Furthermore, these aneurysms were also small (3 to 7 mm in diameter), and none ruptured during follow-up.

The results of this study cannot be broadly generalized because this patient population comprised mainly patients with prior SAH and multiple aneurysms, although patients were not selected by surgery. These patients may have an increased risk for aneurysm formation and possibly for rupture of an unruptured aneurysm. They also are younger and more likely to be cigarette smokers than those with an incidental or a single aneurysm.[2,14,15] However, recent updated prospective data from the International Study of Unruptured Intracranial Aneurysms[18] suggest that risk for rupture of incidental unruptured aneurysms is similar to that of unruptured aneurysms in cases with prior SAH among patients >50 years of age at diagnosis of aneurysm.[2] So, it seems quite likely that risk factors for fatal SAH are the same in other SAH populations as in this study, which is also supported by the results of a large hospital-based study.[4]

Risk factors for SAH seem to differ from those for mortality after the bleeding. After bleeding, the outcome is most closely associated with factors like initial clinical condition and amount of subarachnoid and intraventricular blood on CT scan because they are markers, not causes, of severe bleed.[4]

Indisputable modifiable risk factors for SAH seem to be cigarette smoking, alcohol consumption, and hypertension.[7–10] Cigarette smoking is the most important risk factor for SAH but seems, in hospital-based studies, to impair outcome only modestly, mainly through the increased possibility of symptomatic vasospasm.[10,11] Heavy alcohol consumption may also impair outcome through increased severity of the episodes of rebleeding and symptomatic vasospasm.[11]

Although the significance of hypertension as a risk factor for aneurysmal SAH seems to be modest,[7–9] it may be a significant risk factor for impaired outcome after SAH.[4,11,13] High systolic BP values after aneurysm rupture predict, independently of other prognostic factors, death, poor outcome,[4] and possibly occurrence of early rebleeding.[3] Previous outcome studies, however, were hospital-based and thus missed most of the patients who had died of primary bleed and early rebleed.

It is well established that chronic hypertension induces hypertrophy of the arteriolar smooth muscle cells and shifts the cerebral autoregulation curve to the right.[19,20] This shift, together with narrowing of small arteries, may render hypertensive patients more vulnerable to cerebral ischemia during aneurysm rupture when a transient decrease in cerebral circulation occurs. Tolerance of acute decreases in arterial pressure may therefore be impaired in hypertensive patients. This may well be the mechanism by which hypertension or high long-term systolic BP values before aneurysm rupture may lead to increased case fatality and predict poor clinical status after aneurysm rupture.

History of hypertension has also been shown to be a risk factor for post-SAH cerebral infarction and symptomatic vasospasm,[5,6] although no clear association appeared between hypertension and angiographic vasospasm in large cerebral arteries during the second week after aneurysmal SAH.[6] A history of hypertension may thus depend on mechanisms other than large-artery vasospasm by which it would lead to increased risk for infarction and symptomatic vasospasm after aneurysmal SAH. Impaired autoregulation caused by both chronic hypertension and SAH, as well as increased endothelin production by the endothelium, may be mechanisms by which hypertension increases the risk for delayed ischemia after SAH by decreasing the collateral circulation and cerebral blood flow.[6] Although a history of chronic hypertension may worsen outcome and increase risk for post-SAH cerebral infarction, elevation of BP by use of hypervolemic and hypertensive therapy after treatment of the ruptured aneurysm can prevent or even reverse ischemic

symptoms when started immediately after the first signs of ischemia.[21,22] This effect is due to SAH-induced impairment of cerebral autoregulation because elevation of BP can directly improve cerebral blood flow and thus may reverse symptoms.

Conclusions

Increased systolic BP values and long-term definite hypertension (BP >160/95 mm Hg or use of antihypertensive medication), but not borderline hypertension (160/95 mm Hg>BP>140/90 mm Hg), before aneurysm rupture seem to predict fatal SAH independently of aneurysm size or patient age or sex at the time of aneurysm rupture. Because hypertension increases risk for both SAH and fatality after the bleeding, it should be considered 1 of the main risk factors for SAH, in addition to cigarette smoking, female sex, and patient age. Thus, careful treatment of hypertension is important in patients with unruptured aneurysms, and elevated BP levels should be taken into account when decisions on surgical and endovascular aneurysm treatment are made.

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Editorial Comment

Prehemorrhage Risk Factors for Fatal Intracranial Aneurysm Rupture

In another important contribution from the Department of Neurosurgery at the University of Helsinki, where careful records and follow-up on patients with diagnosed intracranial aneurysms have been maintained for decades, evidence is presented that preexisting hypertension is associated with a higher fatality rate when unruptured cerebral aneurysms rupture. When dealing with the issue of unruptured cerebral aneurysms in the clinic, risk factors that may predict a higher risk of future bleeding (death notwithstanding) are assessed, factors that might justify the risk involved in prophylactic aneurysm repair. Previous study of this same captive Finnish population[1] and other reports have suggested that the risk of future hemorrhage increases with aneurysm size,[2,3] the presence of a local mass effect and symptoms resulting from the aneurysm,[3,4] previous bleeding from another intracranial aneurysm,[2,3] an aneurysm location in the posterior circulation,[2,3] a multilobulated[5] or long[6] aneurysm shape, female sex,[3] younger age at diagnosis,[7] a familial history of aneurysm rupture,[8] cigarette smoking,[9,10] and heavy alcohol use.[11] Arterial hypertension is another but perhaps less powerful predictor of rupture, as the authors discuss in this report.

Still, even in the presence of several of the aforementioned risk factors, the annual risk of an unruptured saccular aneurysm rupturing on an annual basis might be only 1% to 3%,[12] a reassuringly low figure especially for older patients. Balancing this low annual bleeding rate, and especially for younger patients who bear a far greater cumulative lifetime risk of rupture, is the very high mortality and morbidity

attached to each and every aneurysm rupture, a figure probably greater than 50%.[2,7] This Finnish series indicates that the presence of arterial hypertension might make this risk even higher. One hundred forty-two patients with 181 unruptured aneurysms were followed for as long as 2 decades, for a total of 2577 person-years. Thirty-four aneurysm ruptures occurred, one half of which were fatal. Multiple stepwise logistic regression analysis revealed that systolic blood pressure values at follow-up before aneurysm rupture was the only indisputably significant predictor of death among patients with aneurysm rupture.

Clearly, hypertension requires aggressive treatment in patients harboring unruptured intracranial aneurysms, and the presence of hypertension (especially in patients whose blood pressure is difficult to control) can be reasonably applied along with other considerations in formulating a recommendation for or against aneurysm repair.

As important as the information contained in this report is, it still constitutes only level III evidence (data from nonrandomized, concurrent cohort studies), making it difficult to draw up unequivocal treatment guidelines regarding the management of unruptured intracranial aneurysms. As Weir concluded in a recent and comprehensive review of the subject, many patients fall into "a gray zone in which both components of medicine—art and science—must be brought to bear."[13]

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