

# Prognostic Factors for Outcome in Patients With Aneurysmal Subarachnoid Hemorrhage

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**Background and Purpose**—The purpose of this study was to describe prognostic factors for outcome in a large series of patients undergoing neurosurgical clipping of aneurysms after subarachnoid hemorrhage (SAH).

**Methods**—Data were analyzed from 3567 patients with aneurysmal SAH enrolled in 4 randomized clinical trials between 1991 and 1997. The primary outcome measure was the Glasgow outcome scale 3 months after SAH. Multivariable logistic regression with backwards selection and Cox proportional hazards regression models were derived to define independent predictors of unfavorable outcome.

**Results**—In multivariable analysis, unfavorable outcome was associated with increasing age, worsening neurological grade, ruptured posterior circulation aneurysm, larger aneurysm size, more SAH on admission computed tomography, intracerebral hematoma or intraventricular hemorrhage, elevated systolic blood pressure on admission, and previous diagnosis of hypertension, myocardial infarction, liver disease, or SAH. Variables present during hospitalization associated with poor outcome were temperature  $>38^{\circ}\text{C}$  8 days after SAH, use of anticonvulsants, symptomatic vasospasm, and cerebral infarction. Use of prophylactic or therapeutic hypervolemia or prophylactic-induced hypertension were associated with a lower risk of unfavorable outcome. Time from admission to surgery was significant in some models. Factors that contributed most to variation in outcome, in descending order of importance, were cerebral infarction, neurological grade, age, temperature on day 8, intraventricular hemorrhage, vasospasm, SAH, intracerebral hematoma, and history of hypertension.

**Conclusions**—Although most prognostic factors for outcome after SAH are present on admission and are not modifiable, a substantial contribution to outcome is made by factors developing after admission and which may be more easily influenced by treatment. (*Stroke*. 2007;38:2315-2321.)

**Key Words:** cerebral infarction ■ outcome ■ subarachnoid hemorrhage ■ vasospasm

Several studies have examined factors that affect outcome after aneurysmal subarachnoid hemorrhage (SAH), but only 3 included sufficient patients to allow analysis of the effect of multiple independent factors.<sup>1-3</sup> Two of these studies described patients who were not treated with nimodipine, were frequently given antifibrinolytics, did not uniformly undergo early aneurysm obliteration, and were not treated for the most part with contemporary measures used in SAH patients.<sup>1,2</sup> Analysis of factors affecting outcome in the timing study also was never published in detail.<sup>2</sup> A recent update of guidelines for management of aneurysmal SAH noted deficiency in knowledge about this issue.<sup>4</sup> The purpose of this study was to analyze prognostic factors for clinical outcome in 3567 patients with aneurysmal SAH who were entered into 4 randomized clinical trials of tirilazad at neurosurgical centers around the world between 1991 and

1997.<sup>5-8</sup> Although there have been changes in management of SAH since these studies, principally introduction of endovascular treatments, these patients were treated with more modern methods than prior reports. In particular, they underwent early aneurysm surgery and were treated with nimodipine and more contemporary medical management.

## Materials and Methods

### Patient and Clinical Variables

Data on 3567 patients with aneurysmal SAH entered into 4 randomized, double-blind, placebo-controlled clinical trials of tirilazad were analyzed. Patients were entered between 1991 and 1997 at 162 centers from 21 countries in Europe, Australia, North America, and Africa.<sup>5-8</sup> Inclusion criteria were  $\geq 18$  years of age, SAH on computed tomographic (CT) scan or lumbar puncture, and angiographically-confirmed saccular aneurysm as the cause of the hemorrhage. Patients had to receive study drug or placebo within 48

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hours of onset of SAH. Exclusion criteria were traumatic SAH, fusiform or mycotic aneurysm, severe, concomitant medical, neurological, or psychiatric illness, serious cardiovascular illness such as myocardial infarction within 6 months, uncontrolled hypertension or any Q-wave myocardial infarction, serious cardiac arrhythmia, or congestive heart failure. Pregnant or lactating patients were excluded and patients who were taking corticosteroids or calcium antagonists other than nimodipine before randomization, or who had a known intolerance to calcium antagonists, were excluded. Almost all patients were treated with nimodipine. Timing of surgery was decided by site investigators. Patients treated with Guglielmi or other detachable coils were excluded.

Baseline demographic and clinical data included age, gender, race, admission Glasgow coma score,<sup>9</sup> World Federation of Neurologic Surgeons (WFNS) grade,<sup>10</sup> admission systolic and diastolic blood pressures, time from ictus to admission and admission to surgery, weight, and body temperature. History of hypertension, myocardial infarction, diabetes, liver disease, thyroid disease, migraine headaches, and previous SAH were recorded. Body temperature was documented again 8 days after SAH.

Data on in-hospital complications included symptomatic vasospasm, cerebral infarction, hydrocephalus, and pulmonary edema. Symptomatic vasospasm was defined as a  $\geq 2$  point decrease in Glasgow coma score or a 2 point increase in the motor score of the National Institutes of Health Stroke Scale<sup>11</sup> lasting for at least 8 hours. Other causes of deterioration, including but not limited to electrolyte imbalance, hydrocephalus, postoperative brain swelling or hemorrhage, seizures, had to be excluded. Confirmation with transcranial Doppler ultrasound or cerebral angiography was recommended but not mandatory. Determination of these complications was made at each center and there was no central review, although central review of some cases showed good agreement between diagnoses made at the sites and at central review (N. Kassell, personal communication, 2006). Therapeutic interventions recorded included aneurysm clipping, anticonvulsant use, cerebral angioplasty, and whether or not prophylactic or therapeutic hemodilution, hypervolemia, or induced hypertension were used.

Outcome was assessed 3 months after SAH using the 5-point Glasgow outcome scale (GOS).<sup>12</sup> Unfavorable outcome was defined as dead, vegetative, or severely disabled. Time from admission to death or recording of the GOS was recorded.

### Radiological Variables

There was no central radiology review. The amount of subarachnoid blood on the admission CT scan was graded as none, diffuse or localized thin, or diffuse or localized thick. Grading was by the treating physician, and no specific definitions could be agreed on so they were not defined further. Intracerebral hemorrhage, intraventricular hemorrhage, and hydrocephalus were recorded as present or absent on admission CT scans. Intrathecal fibrinolytic therapy was not allowed. The location of the ruptured aneurysm was recorded. When multiple aneurysms were observed, the pattern or blood on CT scan was used to determine the aneurysm most likely to have ruptured. The maximum angiographically demonstrated diameter of the ruptured aneurysm was recorded as  $\leq 12$  mm, 13 to 24 mm, or  $\geq 25$  mm. Vasospasm on the initial angiogram was noted and denoted acute vasospasm.

### Statistical Analysis

Of 3567 patients randomized, 3-month follow-up was recorded in 3498 (98%). Patients with missing data on any of the factors examined were deleted, leaving 2695 patients. The only frequent missing values were temperature on admission (293 patients) and on day 8 (340 patients). From 1 to 54 patients were missing data from 26 other variables. Deletion of the patients was handled by analyzing the 2695 patients with complete data and all patients with the missing values imputed by best subset regression. Cox proportional hazards regression was done only on patients with complete data. Because of concern over the frequency of missing values, the effect of the most common missing variables (admission and day 8 temperatures) were examined by entering variables coding for presence or absence of the

temperature values into the regression.<sup>13</sup> Sensitivity analysis was done by coding the temperatures as binary variables and varying the numbers of missing values in each category by 10% to determine if this affected their contribution to the models.

Univariate analysis was performed first using the 3-month GOS outcome as the dependent variable. The 33 demographic, clinical, radiographic, treatment-related, and in-hospital complication variables described above were the independent variables. Outcome was considered as favorable or unfavorable. Categorical variables were analyzed using  $\chi^2$  tests and continuous variables were analyzed by 2 sample *t* tests or Wilcoxon rank sum tests. The relative difference between outcomes was expressed as an odds ratio (OR, with 95% confidence interval [CI]) and significance was taken at  $P < 0.05$ . Log odds were examined for continuous variables to assess the linearity of the effect and variables that were not normally distributed were proposed for transformation, although this was unnecessary. Log rank tests were performed for each variable using time to death or recording of the GOS as the measure of survival.

Unconditional logistic regression with stepwise backward selection was then used to adjust for variables identified in univariate analysis to be significantly different between the outcomes. The probability value for removal in logistic regression was set at 0.15. Adjusted ORs with 95% CI were calculated. Independence of variables was tested using the likelihood ratio test on reduced models. We constructed receiver operating characteristic curves for all models and estimated the area under the curve and standard characteristics. The relative importance of factors associated with outcome in logistic regression was estimated using bootstrap resampling of the  $R^2$  value based on squared raw residuals to calculate marginal and partial proportions of explained variation.<sup>14</sup> Multivariable logistic regression with the dependent variable defined as the 5-point GOS was done next. Proportional odds modeling was done first but was abandoned because many variables did not meet the proportional odds assumption. Therefore, polytomous logistic regression was used first to select significant variables based on maximum likelihood estimation. Next, the significant independent variables were entered into a multivariable polytomous logistic regression. Relative risk ratios and 95% CI were calculated.

We conducted Cox proportional hazards modeling entering variables found to be significantly related to survival time by the log rank test. Adjusted ORs and 95% CI were derived and variables considered significant if  $P < 0.05$ . The proportional hazards assumption was tested by analysis of Schoenfeld residuals.<sup>15</sup>

Interactions were assessed in all models by determining the significance of variables for which a relation might logically be thought to be present and important (age with time to surgery, WFNS grade, clot thickness, and vasospasm with cerebral infarction and clot thickness). Although tirilazad had no significant effect on outcome, models were fitted with tirilazad dose forced into the final model to confirm the acceptability of using patients treated with tirilazad and placebo in the analysis. This did not alter the results in any case, so we provide data omitting tirilazad dose. We also performed a logistic regression on only placebo patients, which found the same significant factors as the primary results shown, which justified use of the entire dataset. When necessary, the reference group for calculation of odds ratios was male, age 18 to 29, WFNS grade 1 with no or local thin SAH on admission CT scan, and a ruptured aneurysm  $\leq 12$  mm in size located on the internal carotid artery. All values are means  $\pm$  SD.

## Results

### Predictors of Outcome in Univariate Analysis

When outcome was assessed as a binary variable in patients with complete data, univariate analysis found multiple significant variables (supplemental Tables I and II, available online at <http://stroke.ahajournals.org>;  $P < 0.05$ ). Imputation of missing values resulted in loss of significant association between admission temperature and outcome. 2 analyses using the 5-point GOS as the dependent variable were

**TABLE 1. Significant Variables in Multivariable Logistic Regression Using the GOS as a Binary Outcome**

Variable	Preoperative Factors			All Factors		
	Odds Ratio*	95% CI	P Value	Odds Ratio	95% CI	P Value
Age by decade	1.53	1.47–1.63	<0.0001	1.50	1.37–1.64	<0.0001
Admission neurological grade						
Overall	1.74	1.60–1.90	<0.0001	1.74	1.60–1.88	<0.0001
Clot thickness	1.18	1.07–1.31	0.002	1.15	1.04–1.27	0.006
Aneurysm location	1.21	1.10–1.34	<0.0001	1.09	0.99–1.21	0.113
Aneurysm size	1.42	1.17–1.74	0.001	1.43	1.18–1.74	0.002
Systolic blood pressure, mm Hg						
Overall	1.01	1.00–1.01	0.006	1.01	1.00–1.01	0.003
Prior SAH	1.53	1.07–2.19	0.019	1.51	1.04–2.18	0.044
Myocardial infarction	1.87	0.99–3.56	0.055	1.58	1.15–2.18	0.003
History of hypertension	1.50	1.19–1.88	<0.0001	1.41	1.12–1.78	0.011
Acute vasospasm	1.43	0.93–1.21	0.107	not significant		
Liver disease	not significant	1.31	0.97–1.77	0.088		
Diabetes mellitus	1.57	0.93–2.65	0.090	1.15	0.88–1.51	0.112
Intracerebral hemorrhage	1.21	0.94–1.56	0.14	1.49	1.14–1.96	0.050
Intraventricular hemorrhage	1.33	1.07–1.66	0.011	1.28	1.02–1.62	0.005
Anticonvulsant use				1.37	1.08–1.74	0.002
Hypertension, prophylactic				0.76	0.52–1.12	0.090
Hypervolemia, therapeutic				0.74	0.49–1.11	0.084
Hypervolemia, prophylactic				0.65	0.51–0.82	0.001
Symptomatic vasospasm				1.75	1.21–2.53	0.004
Temperature on day 8 $\geq 38^{\circ}\text{C}$				1.81	1.45–2.26	<0.0001
Cerebral infarction				5.38	4.24–6.82	<0.0001

\*Odds ratios (=1) for reference group, which was age  $\leq 29$ , WFNS grade 1, internal carotid aneurysm  $\leq 12$  mm in size, no subarachnoid clot, systolic blood pressure  $\leq 129$  mm Hg, no history of SAH, diabetes, myocardial infarction, hypertension, or liver disease, no intracerebral or intraventricular hemorrhage, surgery within 24 hours of admission, no anticonvulsant use, no hemodynamic maneuvers, no vasospasm or cerebral infarction, and temperature  $< 38^{\circ}\text{C}$  on day 8.

performed on patients with complete data, giving similar results to the binary GOS except that time from SAH to admission and prophylactic hemodilution became significant ( $P < 0.05$ ) and admission temperature and diastolic blood pressure were not significant.

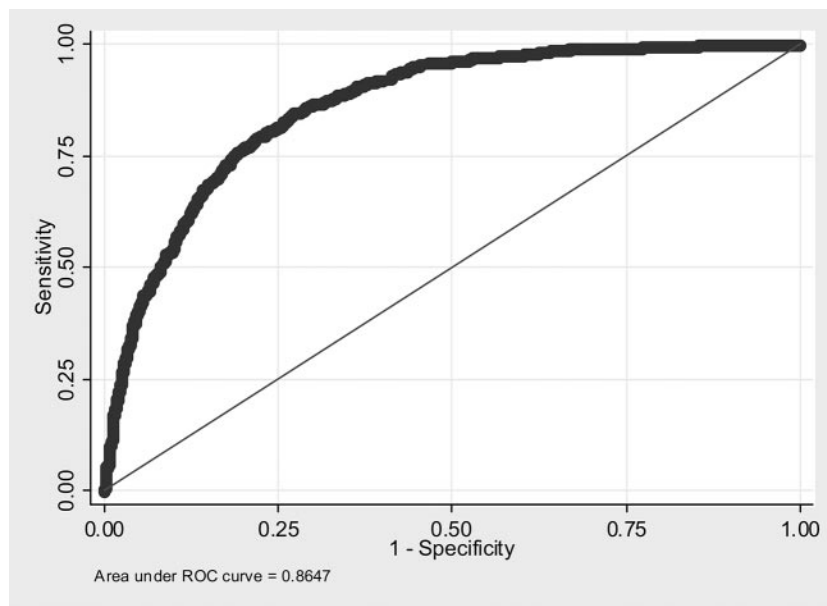
**Predictors of Outcome in Multivariable Analysis**

Multivariable analysis of patients with complete data using the binary GOS found that unfavorable outcome was associated with increasing age, worse admission WFNS grade, greater SAH thickness on admission CT scan, posterior circulation ruptured aneurysm location, larger ruptured aneurysm, intraventricular hemorrhage, intracerebral hematoma, higher systolic blood pressure on admission, history of hypertension, prior SAH, myocardial infarction and liver disease, temperature on the 8th day  $\geq 38^{\circ}\text{C}$ , anticonvulsant use, not using prophylactic or therapeutic hypervolemia or prophylactic induced hypertension, symptomatic vasospasm, and cerebral infarction (Table 1). The same factors were identified when only placebo patients were analyzed. Multivariable analysis was done on all patients with imputed values. The only differences were that liver disease and

diabetes mellitus, which was of marginal significance in the first analysis, were no longer significant.

Analysis of preoperative and admission characteristics only among patients with complete data found acute vasospasm to be significant in addition to the other factors (Table 1). Sensitivity analysis of admission temperature and temperature on the 8th day  $\geq 38^{\circ}\text{C}$  had no effect on either variable.

To assess the importance of missing values further, we generated variables coding admission temperature as present or missing and included these in the regression. This showed that patients missing admission temperatures were significantly more likely to have unfavorable outcome. This suggests imputation was not an optimal method for handling missing values, although the only effect was to make liver disease and diabetes mellitus insignificant. This maneuver was not done for temperature on the 8th day because 256 of the missing values were attributable to death before day 8, which made missing day 8 temperature significant because it basically represented death. Entering variables for the particular study and tirilazad dose found both factors to be insignificant in all models ( $P = 0.2$  to  $0.5$  depending on the model). There was no correlation or interaction of tirilazad



Receiver operating characteristic curve for the full multivariable logistic regression model of factors predicting outcome on the GOS defined as a binary variable. The area under the curve was 86%.

use or dose with variables that were significant in multivariable analysis.

Interaction variables were entered into a multivariable regression using the patients with complete data. This was based on significant ( $P < 0.05$ ) relationships between each of these variables using linear correlation or  $\chi^2$  analysis. These variables were age times WFNS grade, age times clot thickness, vasospasm times clot thickness, and vasospasm times cerebral infarction but none of these were significant. There was no significant relation between age and time to surgery nor was an interaction term age times time to surgery significant in logistic regression.

Multivariable logistic regression also was conducted using the 5-point uncollapsed GOS. Ordinal logistic regression using the proportional odds assumption was not appropriate because of variability in odds ratios between 5-point GOS levels ( $\chi^2$  statistic  $< 0.001$ ). Therefore, multinomial and stereotype logistic regression were carried out. The significant factors were identical to those using a binary GOS (Table 1) except that not using prophylactic-induced hypertension became insignificant.

The ability of these factors to predict outcome was estimated several ways. First, the McFadden  $R^2$  value for the full multivariable logistic regression model using a binary GOS was 0.31. 81% of patients were correctly classified assuming a predicted probability of the outcome of  $> 0.5$ , giving sensitivity of 48% and specificity of 92%. A receiver operating characteristic curve fitted to this model had an area under the curve of 86% (Figure). The proportion of explained variance for each variable in the model was assessed to rank variables in order of relative importance. The most important factors were cerebral infarction, age, WFNS grade, temperature on the 8th day  $\geq 38^\circ\text{C}$ , and symptomatic vasospasm (Table 2). The variables included in logistic regression only explained 36% of the variance in outcome.

### Cox Proportional Hazards Models

Whether some variance in outcome could be explained by rebleeding was addressed using Cox proportional hazards

regression because time from admission to death, surgery, and recording of the GOS was known. Time from admission to surgery should adversely affect prognosis by permitting more rebleeding. Of the 33 independent variables, the log rank test showed factors significant among the patients with complete data were the same as in the above analysis except that there was a significant relation between survival time and time from admission to surgery ( $P = 0.0065$ ) and that liver disease and prophylactic-induced hypertension were not sig-

**TABLE 2. Proportion of Explained Variation (PEV) by Stepwise Selection in a Multivariable Logistic Regression<sup>14</sup>**

Prognostic Factor	Marginal PEV	Partial PEV
Age, 10 years	6.65%	3.54%
Admission neurological grade	13.3%	5.80%
Clot thickness	2.37%	0.19%
Ruptured aneurysm location	0.51%	0.46%
Ruptured aneurysm size	0.86%	0.46%
Intraventricular hemorrhage	3.66%	0.07%
Intracerebral hemorrhage	2.89%	0.47%
Temperature $> 38^\circ\text{C}$ on day 8	4.49%	0.80%
Systolic blood pressure, 10 mm Hg	1.45%	0.29%
History of hypertension	2.43%	0.21%
Anticonvulsant use	0.52%	0.39%
Prophylactic hypervolemia	0.34%	0.69%
Therapeutic hypervolemia	0.32%	0.16%
Prophylactic induced hypertension	0.48%	0.23%
Symptomatic vasospasm	3.18%	0.27%
Previous SAH	0.50%	0.30%
Myocardial infarction	0.64%	0.28%
History of myocardial infarction	0.28%	0.31%
History of liver disease	0.25%	0.16%
Cerebral infarction	14.2%	6.79%
Overall model	36.1%	...

nificant. In the complete dataset, the findings are identical apart from inclusion of prophylactic-induced hypertension and lack of significance of prophylactic hemodilution.

Multivariable Cox modeling on patients with complete data found admission and preoperative factors significantly associated with unfavorable outcome were advancing age, worse WFNS grade, more SAH on admission CT scan, posterior circulation aneurysm, larger aneurysm, increased admission systolic blood pressure, history of SAH, myocardial infarction, hypertension or diabetes mellitus, intracerebral hemorrhage, intraventricular hemorrhage, and acute vasospasm. When all variables were included, additional significant factors were increased time from admission to surgery, use of anticonvulsants, vasospasm, cerebral infarction, temperature  $>38^{\circ}\text{C}$  8 days after SAH, and not using prophylactic hypervolemia whereas history of hypertension became insignificant (Table 3). For both models the proportional hazards assumption tested by analysis of Schoenfeld residuals was valid. For interactions, when assessing only admission and preoperative variables, age times WFNS grade and age times subarachnoid clot thickness were significant (hazard ratio of 0.99 for both,  $P=0.036$  and  $0.017$ , respectively, 95% confidence intervals of 0.99 to 1.00 and 0.99 to 1.00, respectively). No interaction terms were significant when examining all factors together.

### Discussion

We have identified unfavorable outcome on the GOS 3 months after surgical treatment of aneurysmal SAH as associated with increased age, worse admission WFNS grade, greater SAH clot thickness on admission CT scan, posterior circulation and larger aneurysm, intraventricular hemorrhage, intracerebral hemorrhage, admission systolic hypertension, history of hypertension, SAH and myocardial infarction, temperature  $\geq 38^{\circ}\text{C}$  8 days after SAH, anticonvulsant use, not using prophylactic hypervolemia, symptomatic vasospasm, and cerebral infarction. Some factors were significant in some but not other models, such as history of liver disease and diabetes mellitus, acute vasospasm, time from admission to surgery, and not using prophylactic-induced hypertension or therapeutic hypervolemia. We also estimated the relative importance of these factors, which has not been done before. The most important factors were cerebral infarction, WFNS grade, age, temperature on the 8th day  $\geq 38^{\circ}\text{C}$ , and symptomatic vasospasm. The significant factors identified explained only a small portion of variance in outcome.

This analysis expands on prognostic factors identified in 3 prior studies of aneurysmal SAH patients that performed multivariable analyses.<sup>1-3</sup> Others have examined prognostic factors for outcome after aneurysmal SAH but results are limited because of small sample sizes and univariate statistical analyses. Factors significantly related to death in 1114 patients entered into a cooperative aneurysm study between 1970 and 1977 were admission neurological grade, diastolic blood pressure, interval to treatment, vasospasm, and medical condition.<sup>1</sup> Only 119 (11%) patients died so the analysis was based on small numbers. These patients did not undergo aneurysm treatment. That aneurysm site and size were not significantly associated with death suggests that the negative

impact of these factors on outcome is related to treatment of the aneurysm. A treatment associated with less risk, therefore, could improve outcome and would be consistent with results of randomized clinical trials of surgical clipping versus endovascular coiling.<sup>16</sup> Age was not significant, which could be because of bedrest elevating risk of death among young patients or surgical intervention increasing the risk of poor outcome among older patients. Another multivariable analysis was reported in a single table from the cooperative timing study.<sup>2</sup> Death and disability were associated with reduced consciousness on admission, increasing age, preexisting medical conditions, intracerebral hematoma, intraventricular hemorrhage, systolic blood pressure, basilar aneurysm, more SAH on admission CT scan, and vasospasm on admission angiography. The notable differences compared with the present study are the lack of significance of delayed vasospasm, aneurysm size, use of anticonvulsants, and hemodynamic maneuvers.

929 patients with aneurysmal SAH admitted to the only neurosurgical center in Western Finland were analyzed in a third study.<sup>3</sup> Multivariable models to predict poor outcome using logistic regression were created. Factors associated with poor outcome among a subset of 620 patients were increased age, worse neurological grade, more blood on CT scan, intraventricular hemorrhage, and angiographic vasospasm. Inclusion of pre- and postoperative factors also identified preoperative rebleeding, interval from bleeding to surgery, ligation of a major artery, temporary clipping, hypodense areas on postoperative CT, postoperative intracranial hemorrhage, and cardiopulmonary event.

Some of the factors we identified were robust in that they were significant in all models whereas the significance of others varied depending on the model. This suggests that the latter variables, such as history of diabetes mellitus and liver disease and time from admission to surgery, exert a relatively small influence on outcome. Rebleeding is a prognostic factor in some<sup>17</sup> but not other studies.<sup>2,18</sup> Time from admission to surgery, which would incorporate some effect of rebleeding, was important prognostically in Cox proportional hazards analysis but not logistic regression. The mean time from admission to surgery was short (mean of  $50 \pm 112$  hours) which might reduce the impact of rebleeding compared with some studies.<sup>18</sup> Other factors not included in the analysis, such as inflammatory responses, physiological parameters, and apolipoprotein E allele isoforms, also may contribute to outcome.<sup>19-21</sup>

Limitations of this analysis include lack of central clinical and radiology review and of more quantitative measurements of some factors such as SAH on CT scan, intraventricular hemorrhage, and intracerebral hematoma. The diagnosis of cerebral vasospasm was not based on the gold standard which is digital subtraction angiography so some patients may have deteriorated for other reasons. This is not a population-based study. Patients entered into clinical trials may be in better clinical grades and have more favorable outcomes. On the other hand, comparison of these patients to those of Niskanen et al, who were admitted from Eastern Finland to the only neurosurgical unit, shows that clinical grades on admission and outcomes were very similar with grades 4 and 5 com-

**TABLE 3. Significant Variables in Cox Proportional Hazards Regression**

Variable	Preoperative Factors			All Factors		
	Hazard Ratio	95% CI	P Value	Hazard Ratio	95% CI	P Value
Age	1.02	1.02–1.04	<0.0001	1.03	1.02–1.04	<0.0001
Admission neurological grade						
2	1.55	1.19–2.01	0.001	1.33	1.02–1.73	0.034
3	2.81	2.11–3.76	<0.0001	2.48	1.87–3.30	<0.0001
4	3.31	2.46–4.46	<0.0001	2.68	1.99–3.62	<0.0001
5	4.48	3.59–6.47	<0.0001	3.40	2.52–4.59	<0.0001
Clot thickness						
Local thin	2.18	0.84–5.61	0.11	1.60	0.61–4.19	0.34
Diffuse thin	2.33	0.93–5.83	0.07	1.86	0.73–4.72	0.19
Local thick	2.72	1.10–6.78	0.03	2.19	0.87–5.49	0.097
Diffuse thick	3.08	1.23–7.45	0.016	2.32	0.93–5.80	0.071
Aneurysm location						
Anterior cerebral	1.15	0.92–1.44	0.23	0.97	0.77–1.22	0.80
Middle cerebral	0.87	0.66–1.15	0.34	0.82	0.63–1.10	0.19
Posterior circulation	1.53	1.14–2.04	0.004	1.23	0.92–1.65	0.17
Other	2.23	1.03–4.85	0.043	2.41	1.10–5.23	0.027
Aneurysm size						
13–24 mm	1.23	1.01–1.49	0.042	1.16	0.95–1.42	0.15
≥25 mm	1.86	1.18–2.93	0.007	1.53	0.97–2.44	0.07
Systolic blood pressure, mm Hg						
130–139	0.98	0.73–1.31	0.89	0.95	0.71–1.27	0.72
140–159	1.29	1.03–1.63	0.026	1.37	1.09–1.73	0.008
160–179	1.21	0.92–1.59	0.18	1.23	0.93–1.62	0.15
180–209	1.25	0.89–1.77	0.20	1.33	0.94–1.90	0.11
≥210	1.47	0.81–2.65	0.20	1.24	0.68–2.26	0.48
Time admission to surgery (hours) not significant				1.20	1.00–1.45	0.047
Prior SAH	1.49	1.14–1.94	0.004	1.54	1.17–2.01	0.002
Myocardial infarction	1.54	0.98–2.41	0.063	1.73	1.09–2.74	0.021
Diabetes mellitus	1.39	0.94–2.05	0.095	1.39	0.94–2.06	0.097
Intracerebral hemorrhage	1.21	0.98–1.49	0.08	1.26	1.02–1.56	0.034
Intraventricular hemorrhage	1.34	1.10–1.63	0.003	1.31	1.08–1.59	0.006
Acute vasospasm	1.55	1.12–2.15	0.009	not significant		
Anticonvulsant use				1.33	1.09–1.63	0.005
History of hypertension	1.32	1.10–1.58	0.003	not significant		
Hemodilution, therapeutic				not significant		
Hemodilution, prophylactic				not significant		
Hypertension, therapeutic				not significant		
Hypervolemia, therapeutic				not significant		
Hypervolemia, prophylactic				0.80	0.66–0.98	0.028
Symptomatic vasospasm				1.72	1.30–2.29	<0.0001
Temperature on day 8 ≥38°C				1.57	1.31–1.89	<0.0001
Cerebral infarction				3.29	2.73–3.96	<0.0001

\*Hazard ratios (=1) for reference group, which was age ≤29, WFNS grade 1, internal carotid aneurysm ≤12 mm in size, no subarachnoid clot, systolic blood pressure ≤129 mm Hg, no history of SAH, diabetes, myocardial infarction, hypertension, or liver disease, no intracerebral or intraventricular hemorrhage, surgery within 24 hours of admission, no anticonvulsant use, no hemodynamic maneuvers, no vasospasm or cerebral infarction, and temperature <38°C on day 8.

prising 23% in this study and 17% in the Finnish study and good outcome achieved in 70% and 68%, respectively.<sup>3</sup> The data were collected 10 to 15 years ago and advances in treatment, such as endovascular aneurysm treatment and better medical management, may influence prognostic factors.

### Conclusion

Factors prognostic for unfavorable outcome at 3 months among a large population of patients with aneurysmal SAH were determined. The findings provide information about what variables need to be stratified for in clinical trials, raise questions about various treatment strategies such as use of anticonvulsants, and point out the need for further studies to find factors influencing outcome after aneurysmal SAH.

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### Disclosures

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