

Improved outcome after rupture of anterior circulation aneurysms: a retrospective 10-year review of 224 good-grade patients

PETER D. LE ROUX, M.D., J. PAUL ELLIOTT, M.D., LOIS DOWNEY, DAVID W. NEWELL, M.D., M. SEAN GRADY, M.D., MARC R. MAYBERG, M.D., JOSEPH M. ESKRIDGE, M.D., AND H. RICHARD WINN, M.D.

Department of Neurological Surgery, University of Washington School of Medicine, Seattle, Washington

✓ Several significant diagnostic and therapeutic advances in the management of subarachnoid hemorrhage have emerged during the last 10 years. The present study was undertaken to determine whether these advances have improved overall outcome in patients of low surgical risk and what factors predict outcome. The authors retrospectively reviewed the management of good-grade patients seen at the Harborview Medical Center at the University of Washington, who suffered ruptured anterior circulation aneurysms between 1983 and 1993. The results in this series demonstrate that favorable outcomes occurred in 96.8% of patients designated Hunt and Hess Grade I, 88.3% of those assigned Grade II, and 81.3% of those deemed Grade III after rupture of anterior circulation aneurysms. On the basis of clinical and radiographic factors present at admission, correct prediction can be made about all favorable, but only 17% of unfavorable outcomes. During the decade under investigation, the authors observed a significant ($p = 0.002$) increase in the number of favorable outcomes: 74.5% of patients treated during the first management period (1983–1987); 87% of patients treated during the second period (1987–1990); and 93.5% of patients treated during the third management period (1990–1993) experienced favorable outcomes. Improvements in critical-care techniques and the management of vasospasm may be associated with the improved outcome observed during this series.

KEY WORDS • aneurysm • angioplasty • outcome • subarachnoid hemorrhage

OUTCOME following subarachnoid hemorrhage (SAH) is influenced by many variables including aneurysm location and the patient's clinical grade. Most patients who harbor anterior circulation aneurysms^{4,13,14,26,29} and fall into good clinical grade categories^{4,6,8,10,13,28,33} experience little surgical morbidity. Management results, however, demonstrate that there is still potential for improvement in the overall care of patients suffering aneurysmal SAH, including those at low surgical risk.^{3,13,20–23,32}

During the last decade several advances in the management of SAH, such as early surgery,⁷ transcranial Doppler,³⁰ hypervolemia,² calcium channel blockers,²⁷ balloon angioplasty,^{18,24} identification of secondary cerebral insults,^{16,31,35} invasive monitoring, and aggressive intensive care,¹⁷ have provided opportunities to improve overall outcome after SAH. These advances have been incorporated into our SAH management policy, successful implementation of which requires a dedicated, knowledgeable team and a large commitment of resources. We therefore undertook this retrospective study to examine the management of 224 good-grade (Hunt and Hess¹⁰

Grades I to III) patients who suffered ruptured anterior circulation aneurysms during the last 10 years. We wanted to test the hypothesis that aggressive, comprehensive management has improved overall outcome for patients at low surgical risk. We also examined what factors are associated with outcome, because our ability to improve outcome further and to make effective use of resources in the future depends, in part, on identifying the patient at most risk for the deleterious consequences of SAH.

Our overall management results indicate that the number of patients who experienced a favorable outcome significantly increased as management evolved during the period reviewed. This improved patient outcome appears to be associated with vigorous critical-care techniques and aggressive vasospasm management.

Clinical Material and Methods

Patient Population

During a 10-year period (September 1983 to August 1993), 543 patients admitted to Harborview Medical Cen-

Good-grade anterior circulation aneurysms

ter at the University of Washington received treatment for cerebral aneurysms. All patients were considered surgical candidates regardless of their clinical status. We retrospectively evaluated all of these patients using the following inclusion criteria: 1) diagnosis of SAH, 2) an anterior circulation aneurysm, and 3) good clinical grade, defined as Hunt and Hess¹⁰ Grade I, II, or III at admission. Changes in grade were not made for systemic disease or for the presence of vasospasm. Subarachnoid hemorrhage was confirmed by computerized tomography (CT) or, in rare instances, by lumbar puncture. The severity of the SAH was classified radiologically from the CT appearance according to a modification of the Fischer⁵ grade. The presence of an aneurysm was diagnosed by four-vessel angiography. Information was obtained from patient charts, operative reports, review of radiological investigations (including CT scans and angiographic films), clinic visits, and telephone interviews.

Management of Cases

All patients were managed according to a standardized policy¹⁶ that included aggressive preoperative resuscitation, early surgery, and aggressive prevention and treatment of vasospasm. Patients were cared for in the Neurosurgery Intensive Care Unit with routine intracranial pressure and invasive hemodynamic monitoring. Frequent head CT and single-photon emission CT scans supplemented the clinical evaluation. Patients were routinely administered dilantin to therapeutic levels, dexamethasone (4 mg every 6 hours), and since 1987, nimodipine (60 mg every 4 hours). Volume expansion and hemodilution were initiated prophylactically in all patients. Since 1987, all patients have undergone daily transcranial Doppler examination to diagnose vasospasm and to predict which patient might develop ischemic symptoms. The diagnosis of vasospasm was confirmed by angiography. Patients who developed symptomatic vasospasm were treated with induced hypertensive therapy, and since 1990, transluminal angioplasty has been routinely used when other means of therapy were ineffective.²⁴

Patient Outcome

Outcome was assessed at least 6 months after the SAH, by clinic visit or telephone interview, according to the Glasgow Outcome Scale¹² (GOS). Patients with a GOS score of "good" or "moderately disabled" live independently, caring for all their needs, and participate in a normal social life; for statistical comparison, these patients were classified as a favorable outcome. The classification of unfavorable outcome was assigned to those patients who died or were not capable of independent existence.

Statistical Analysis

Data analyses for this report included several bivariate techniques selected for their appropriateness to the measurement level and distributional properties of the available data. Data are expressed as the mean \pm the standard deviation of the mean or, in the case in which samples depart substantially from normal distributions, are summarized as the median. Two-sample significance of data that departed from a normal distribution and rank-order

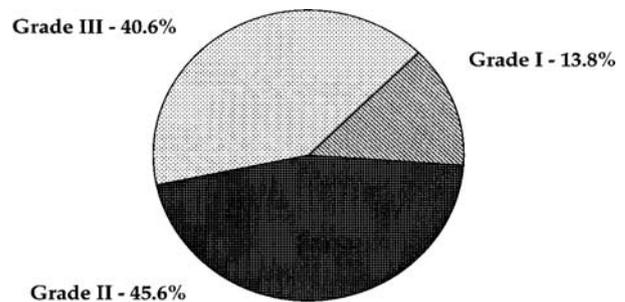


FIG. 1. Pie graph depicting the distribution of patients on admission according to Hunt and Hess¹⁰ clinical grades.

variables were tested by the Mann-Whitney U-test procedure; Spearman rank-order correlations were used to relate ordered variables to one another. The Student's t-test was used to test for differences between groups in which the samples were normally distributed. Sub-sample differences on categorical variables were tested by Pearson chi-square statistics or for 2×2 tables with expected frequencies less than five by the Fisher's exact two-tailed test. All univariate and bivariate statistical analyses were performed using a commercially available software package (SPSS/PC+, Version 4.0, SPSS, Inc., Chicago, IL).

Multivariate analysis of outcome was accomplished through a three-stage process. First, a pool of potential outcome predictors was constructed, including all variables whose unadjusted association with outcome, determined by the techniques described above, were significant at or beyond the 0.05 probability level without correction for multiple tests. In addition to the total predictor pool, a subset including only admission and preoperative predictors was formed. Second, three stepwise logistic regression models were constructed using the three predictor pools established in stage one. At each step in model construction, variables remaining in the pool were evaluated using score tests, and the variable with the most significant score test was added to the existing model. Model building ceased when no variables remaining in the pool had score tests with probability values less than 0.05. Probability values and confidence intervals (CIs) for the final model are based on likelihood ratio tests. Logistic regression modeling was performed using EGRET software (Statistics and Epidemiology Research Corp., (SERC), Seattle, WA).

Results

Clinical Data

Over the 10-year period, 224 patients (87 men and 137 women, mean age 50.6 ± 14.7 years) were admitted to Harborview Medical Center in good clinical grade (Hunt and Hess¹⁰ Grade I, II, or III) following rupture of anterior circulation aneurysms. The distribution of neurological grade at admission is shown in Fig. 1; presentation and clinical characteristics are listed in Table 1.

Preoperative Diagnostic Studies

All patients underwent preoperative CT and four-vessel

TABLE 1

Clinical presentation of 224 patients and findings at admission

Presentation or Finding	No. (%)
sentinel bleed	54 (24.1)
headache	216 (96.4)
seizure	35 (15.6)
transient loss of consciousness	53 (23.7)
neck stiffness	151 (67.4)
pupillary abnormality	10 (4.5)
cranial nerve palsy	31 (13.8)
motor weakness	28 (12.5)

angiography. The CT characteristics are summarized in Table 2 and Fig. 2. The severity of the SAH (Spearman $r = 0.319$; $p < 0.00001$), but not that of intracerebral hemorrhage (ICH) as it appeared on CT, correlated with the patient's clinical grade. The distribution of ruptured aneurysms is summarized in Table 3. The median aneurysm size was 8 mm; five aneurysms exceeded 25 mm in diameter. Multiple aneurysms were observed in 71 patients (31.7%). On admission angiogram, vasospasm and intracranial atherosclerosis were demonstrated in 39 (17.4%) and 26 (11.6%) patients, respectively.

Preoperative Course

Twenty-one patients received ventricular drainage because of significant ventricular enlargement. Intracranial pressure (ICP) monitors were inserted in 50 patients preoperatively; the median maximum ICP was 18 mm Hg. Overall, nine patients (4%) demonstrated clinical improvement, whereas 29 patients (12.9%) deteriorated before surgery. Aneurysm rebleeding, confirmed by head CT scan, was observed in 11 (4.9%) of the patients; no factors that predicted rebleeding were identified.

Surgical Findings

The timing of surgery following SAH is illustrated in Fig. 3. Two aneurysms were wrapped; the remaining aneurysms were occluded by application of a single (81.7%) or multiple clips. Suction or internal decompression was used to facilitate the obliteration of eight aneurysms. Moderate hypotension (systolic blood pressure 80 mm Hg) was used in 47 patients (21.0%) and temporary clips were applied in 42 patients (18.8%). Aneurysm rupture or minor leak occurred in 52 patients (23.2%). The timing of surgery did not correlate with intraoperative aneurysm rupture.

TABLE 2

Ruptured anterior circulation aneurysms: computerized tomography features in 224 good-grade patients*

Features	No. (%)
subarachnoid hemorrhage	209 (93.3)
intraventricular hemorrhage	101 (45.1)
ventricular enlargement	99 (44.2)
intracerebral hemorrhage ≤ 3 cm	31 (13.8)
intracerebral hemorrhage > 3 cm	7 (3.1)

* Good grade = Hunt and Hess¹⁰ Grades I to III.

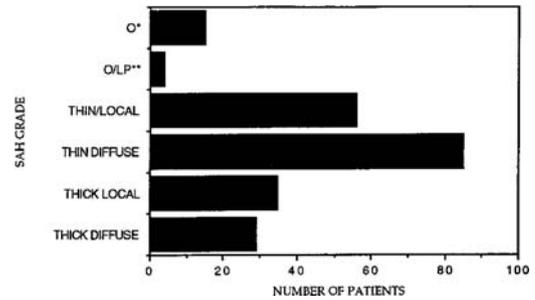


FIG. 2. Bar graph showing subarachnoid hemorrhage (SAH) grade on computerized tomography (CT) obtained at admission. * SAH not visible on admission CT; only intracerebral or intraventricular hemorrhage present; ** SAH not visible on admission CT; diagnosed by lumbar puncture.

Postoperative Course

Patients were cared for in the neurosurgery intensive care unit between 7 and 14 days after SAH. The following secondary cerebral insults were identified: hypotension (systolic blood pressure < 80 mm Hg) in 33 patients (14.7%); elevated ICP (> 20 mm Hg for at least 15 minutes) in 106 patients (47.3%); hypoxia ($PaO_2 < 70$ mm Hg on two consecutive arterial blood-gas samples) in 99 patients (44.2%); or hyperglycemia (blood glucose > 200 mg/dl on two consecutive samples) in 94 patients (42.0%). Postoperative surgical, medical, and infectious complications are listed in Table 4.

All patients underwent postoperative four-vessel angiography; complete obliteration of the ruptured aneurysm was confirmed in 208 patients (92.9%). In 16 patients, aneurysm remnants were observed on postoperative angiogram; only one patient required further surgery. Angiographically confirmed vasospasm was observed in 117 patients. Thirty-nine patients (17.4%) developed symptomatic vasospasm. The severity of the SAH demonstrated by preoperative CT did not predict the development of symptomatic vasospasm; however, a worse clinical grade at admission was associated with the onset of delayed ischemic deficits (Mann-Whitney $z = -2.2$; $p = 0.03$). Angioplasty was performed in 22 symptomatic patients; 21 (95.5%) of whom demonstrated a clinical response and experienced favorable outcomes. The patient who did not respond to angioplasty did poorly.

TABLE 3

Location of ruptured anterior circulation aneurysms in 224 good-grade patients*

Location	No. (%)
pericallosal	8 (3.6)
anterior cerebral artery	1 (0.4)
anterior communicating artery	83 (37.1)
middle cerebral artery bifurcation	43 (19.2)
middle cerebral artery trunk	4 (1.8)
posterior communicating artery	57 (25.4)
cavernous carotid	3 (1.3)
internal carotid artery	19 (8.5)
carotid ophthalmic artery	6 (2.7)

* Good grade = Hunt and Hess¹⁰ Grades I to III.

Good-grade anterior circulation aneurysms

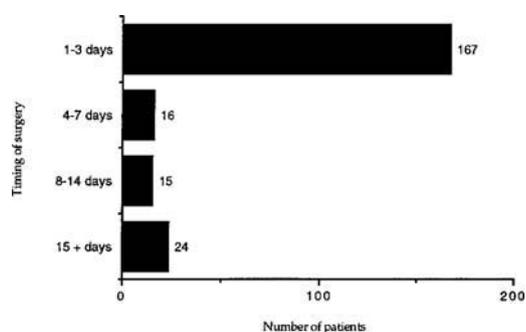


FIG. 3. Bar graph displaying timing of surgery. Two patients died before surgery could be attempted; the remaining 222 patients underwent surgical obliteration of their aneurysm. Aneurysm obliteration was achieved within 3 days of subarachnoid hemorrhage in 75.2% of patients. Day 1 = day of hemorrhage.

Immediately postoperative and subsequent follow-up CT scans were obtained in all patients; an area of low density consistent with cerebral infarction was documented in 54 patients (24.1%). Low-density changes were transient in 15 patients. The development of CT low-density changes did not correlate with the development of either angiographic or symptomatic vasospasm.

Thirty-five patients required insertion of a shunt, including seven patients who underwent ventriculostomies preoperatively. The severity of intraventricular hemorrhage (IVH) (Mann-Whitney $z = 3.4$; $p = 0.0008$) and the severity of ventricular enlargement (Mann-Whitney $z = -4.2$; $p < 0.0001$) observed on preoperative CT scan correlated with the need for a long-term shunt procedure.

TABLE 4

Postoperative complications in 224 patients with ruptured anterior circulation aneurysms

Complications*	No. (%)
surgical	
new IH	5 (2.2)
new IH, surgery†	10 (4.5)
wound dehiscence	5 (2.2)
CSF leak	4 (1.8)
medical	
deep vein thrombosis	9 (4.0)
pulmonary embolus	2 (0.9)
cardiac	24 (10.7)
pulmonary	25 (11.2)
renal	8 (3.6)
hepatic	2 (0.9)
drug allergy	16 (7.1)
infection	
meningitis	5 (2.2)
pneumonia	33 (14.7)
scalp wound	1 (0.4)
urinary tract	24 (10.7)
line sepsis	21 (9.4)
endocarditis	1 (0.4)
enterocolitis	2 (0.9)

* IH = intracerebral hematoma; CSF = cerebrospinal fluid.

† New IH requiring surgical evacuation.

TABLE 5

Clinical grade of 224 patients with ruptured anterior circulation aneurysms at admission and outcome*

Clinical Grade†	Outcome		
	Favorable	Poor	Dead
Grade I (31 patients)	96.8%	3.2%	—
Grade II (102 patients)	88.3%	3.9%	7.8%
Grade III (91 patients)	81.3%	7.7%	11.0%

* Clinical grade at admission was determined according to the Hunt and Hess¹⁰ scale. Outcome was assessed at 6 months according to the Glasgow Outcome Scale¹² with "good" or "moderate disability" classified as a favorable outcome and "severe disability" or "vegetative" classified as a poor outcome.

† Increasing clinical grade predicted a worse outcome (Spearman correlation: $r = 0.15$; $p = 0.03$).

Patient Outcome

Overall, 194 patients (86.6%) experienced a favorable outcome and were found to be fully independent at their 6-month follow-up examination. The distribution of outcome according to grade is depicted in Table 5. Eighteen patients (8%) died; the causes of death are listed in Table 6.

To determine which factors predicted or correlated with outcome, we evaluated a variety of pre-SAH conditions, clinical factors, radiological features, operative findings, and postoperative characteristics (Table 7). The significant results of univariate analysis are summarized in Table 8. Notable are the following observations:

1) Several factors identified at admission, including age, a history of hypertension or vascular disease, clinical grade at admission, elevated blood glucose, the presence of IVH or thick SAH observed on admission CT, and atherosclerosis identified on preoperative angiogram, were associated with an unfavorable outcome. 2) During the preoperative course, rebleed, insertion of a ventricular shunt, or clinical deterioration predicted an unfavorable outcome. All patients who improved preoperatively demonstrated favorable outcomes. 3) Timing of surgery and other surgical factors did not demonstrate an association with outcome. However, surgical complications, such as a postoperative ICH, were associated with an unfavorable outcome. 4) During the postoperative course, the development of medical complications (listed in Tables 4 and 8) or secondary insults (such as an episode of hypoxia, hypotension, or hyperglycemia) predicted a poor outcome. The

TABLE 6

Causes of death in 224 patients with ruptured anterior circulation aneurysms

Cause of Death	No. (%)
rebleed prior to surgery	6 (2.7)
vasospasm	2 (0.9)
myocardial infarct	2 (0.9)
respiratory failure	2 (0.9)
sepsis	3 (1.3)
undetermined	3 (1.3)
total	18 (8)

TABLE 7
Factors evaluated for prognostic significance*

Category	Factor
patient characteristics	age, sex, smoking, hypertension, cardiac disease, vascular disease
admission clinical status	consciousness level, Hunt & Hess grade, systolic blood pressure, meningeal signs, blood glucose
admission CT findings	amount of SAH, presence & size of IH, midline shift, ventricle size, IVH
admission angiogram findings	aneurysm size & location, atherosclerosis, vasospasm
preop clinical course	rebleed, clinical course, ventriculostomy, ICP
surgery	timing, aneurysm rupture, use of hypotension, temporary clips, clip application, technique of aneurysm obliteration
postop radiographic studies	aneurysm obliteration, angiographic spasm, new IH, low density changes on CT, ventricle size
postop course	secondary insults (hypoxia, hypotension, hyperglycemia, increased ICP), complications (surgical, medical, or infectious), symptomatic spasm & treatment, shunt for hydrocephalus

* Abbreviations: CT = computerized tomography; SAH = subarachnoid hemorrhage; IH = intracerebral hematoma; IVH = intraventricular hemorrhage; ICP = intracranial pressure.

development of angiographic or symptomatic vasospasm was not correlated with outcome, whereas an area of low density observed on CT scan predicted a poor outcome. Patients who required insertion of a shunt for symptomatic hydrocephalus were three times more likely to have poor outcome than patients who did not require diversion of cerebrospinal fluid.

Multivariate Analysis and Outcome Prediction

To determine which variables were the most predictive of outcome, variables found to have a significant association with outcome in univariate analysis (Table 8) were subjected to multivariate analysis. Three prediction models, which allowed for added factors as the patient's hospital course progressed chronologically, were constructed.

Admission Model. This paradigm used only admission clinical and radiographic factors. Age demonstrated the strongest association with outcome (odds ratio 1.09; 95% CI 1.05–1.13; p = 0.001) and once entered into the model no other factor or combination of factors added significant information. The admission model correctly predicted all favorable outcomes, but only 17% of unfavorable outcomes.

Preoperative Model. This analysis included preoperative variables and admission characteristics. Rebleed exhibited the strongest association with an unfavorable outcome (odds ratio 14.16; 95% CI 2.742–73.17; p = 0.001). Once age and rebleed were added to the model, none of the remaining univariate predictors were able to improve the model's predictive power; however, only 30% of unfavorable outcomes were correctly predicted.

Comprehensive Model. This model added postoperative

TABLE 8
Variables associated with outcome*

Factor	Significance
pre-SAH condition	
age	Student's t test, t = -5.8, df = 222, p < 0.0001
hypertension	$\chi^2 = 4.7$, df = 1, p = 0.03
history of vascular disease	Fisher's exact, p = 0.01
admission clinical status	
Hunt & Hess grade	Mann-Whitney, z = -2.2, p = 0.03
blood glucose	Mann-Whitney, z = -2.3, p = 0.02
admission CT findings	
amount of SAH	Mann-Whitney, z = -1.9, p = 0.05
IVH	$\chi^2 = 6.5$, df = 1, p = 0.01
admission angiogram	
atherosclerosis	Fisher's exact, p = 0.0005
preop course	
rebleed	Fisher's exact, p < 0.0001
ventriculostomy	Fisher's exact, p = 0.01
clinical course	Mann-Whitney, z = -3.6, p = 0.0003
surgery	NS
postop radiographic studies	
new IH	Mann-Whitney, z = -3.9, p = 0.0001
low-density changes on CT	$\chi^2 = 4.8$, df = 1, p = 0.03
nonobliteration of aneurysm	Fisher's exact, p = 0.03
postop course	
hypoxia	$\chi^2 = 9.1$, df = 1, p = 0.003
hypotension	Fisher's exact, p = 0.001
hyperglycemia	$\chi^2 = 4.7$, df = 1, p = 0.03
deep vein thrombosis	Fisher's exact, p = 0.02
cardiac complications	Fisher's exact, p = 0.001
pulmonary complications	Fisher's exact, p < 0.0001
renal complications	Fisher's exact, p < 0.0001
hepatic complications	Fisher's exact, p = 0.02
pneumonia	Fisher's exact, p < 0.0001
line sepsis	Fisher's exact, p < 0.0001
shunt for hydrocephalus	Fisher's exact, p = 0.0004

* Abbreviations: SAH = subarachnoid hemorrhage; IVH = intraventricular hemorrhage; NS = not significant; IH = intracerebral hematoma; CT = computerized tomography.

factors and included all univariate predictors of outcome in a multiplicative model without interactions. Nine factors that made significant prediction were retained from the 21 potential predictors; these are summarized in Table 9. Once postoperative factors were added, age gave way to three other admission factors: clinical grade, IVH on CT, and atherosclerosis on angiogram. Use of the comprehensive model correctly predicted 93% of all outcomes, including 97% of favorable and 67% of unfavorable outcomes.

Change in Outcome From 1983 to 1993

During the 10-year period under review we observed a significant improvement in the number of favorable outcomes that were achieved (Table 10). Three distinct treatment epochs, in part determined by techniques available to manage vasospasm, were observed: 55 patients were treated between 1983 and 1987, 74.5% of whom experienced favorable outcomes; 77 patients were treated between 1987 and 1990, and favorable outcomes were

Good-grade anterior circulation aneurysms

TABLE 9

Multivariate analysis of variables demonstrating potential prognostic significance*

Predictor	Odds Ratio	95% CI	p Value
admission grade	2.87	1.03–9.56	0.04
IVH on admission CT	3.74	1.07–16.04	0.04
atherosclerosis on admission angiogram	10.11	2.68–42.35	0.001
preop rebleed	33.0	5.09–312	0.001
postop hypotension	5.33	1.49–19.83	0.01
postop IH	15.57	3.16–86.49	0.001
postop pulmonary complications	7.21	1.84–29.73	0.005
postop renal complications	48.0	4.34–817.3	0.001
postop shunt for hydrocephalus	5.49	1.63–19.81	0.006

* All variables that predicted outcome from univariate analysis (Table 8) were included in a multiplicative model, without interactions, using logistic regression techniques. Two additional models, which included only characteristics present at admission or admission and preoperative factors, were also created; the findings are summarized in Results. CI = confidence interval; IVH = intraventricular hemorrhage; CT = computerized tomography; IH = intracerebral hematoma.

observed in 87%; and 92 patients were treated between 1990 and 1993, and favorable outcomes were observed in 93.5% of these patients.

We assessed the incidence of factors of possible biological significance (Table 8) and factors associated with outcome in this series (Table 9) according to treatment epoch. Patient demographics and admission characteristics were very similar in each treatment time period. Between 1983 and 1987, however, more patients were classified as Hunt and Hess Grade III at admission, and ICH was observed more frequently on admission CT than during subsequent treatment epochs. When the variables were analyzed for an association with outcome in each treatment epoch, no association between outcome and admission clinical status or ICH was found in the first treatment epoch. Furthermore, when outcome was assessed within each Hunt and Hess grade, an improvement in favorable outcomes with increased time was observed within each category. These observations suggest that advances in management, rather than differences in patient characteristics, may be associated with the improved outcome observed over time. We did not change our surgical technique during the decade reviewed. By contrast, advances in critical-care techniques and vasospasm management were incorporated into our therapeutic protocol. Consequently, we analyzed the impact of these two factors on patient outcome over the decade.

Critical Care Techniques. The frequency of any medical complication (Fig. 4) and the incidence of iatrogenic complications, such as line sepsis (Mann-Whitney $z = -2.4$; $p = 0.02$), declined over each treatment period. In addition, the number of medical complications a patient might develop also decreased over time (Fig. 4). By contrast, no decline in the incidence of intraoperative or postoperative surgical complications associated with outcome was observed in each treatment epoch.

Were we better able to deal with medical complications once they occurred? When composite measures of medical complications (any or none and the total number of systems involved in a patient) were analyzed, the num-

TABLE 10

Improvement in management results of 224 patients over time*

Time Period	Type of Vasospasm Management	No. of Patients	Outcome		
			Favorable	Poor	Dead
1983–1987	hypervolemia induced hypertension	55	74.5%	9.1%	16.4%
1987–1990	hypervolemia induced hypertension TCD, calcium channel blockers	77	87%	7.8%	5.2%
1990–1993	hypervolemia induced hypertension TCD, calcium channel blockers, angioplasty	92	93.5%	1.1%	5.4%

* Spearman correlation: $r = -0.21$, $p = 0.002$. TCD = transcranial Doppler ultrasound.

ber of medical complications were found to be significantly associated with outcome in each treatment epoch (Mann-Whitney Epoch 1: $z = -2.2$, $p = 0.03$; Epoch 2: $z = -3.1$, $p = 0.002$; Epoch 3: $z = -2.0$, $p = 0.05$). Unfavorable outcome correlated with an increased number of systems involved in a patient. These results suggest that once a medical complication occurred it had an adverse effect on outcome. Furthermore, the association of a medical complication and unfavorable outcome did not change over time. By contrast, the frequency of medical complications decreased over time, which suggests that proactive, rather than reactive, attempts to decrease the impact of medical complications on outcome are, in part, associated with improved outcome.

Vasospasm Management. Were advances in vasospasm management associated with the improvement in outcome? Symptomatic vasospasm occurred in 39 patients (17.4%). Five (12.8%) of these patients experienced an unfavorable outcome. Prophylactic hypervolemia was used throughout the series and may have contributed to this relatively low incidence of symptomatic vasospasm. The introduction of routine transcranial Doppler exam-

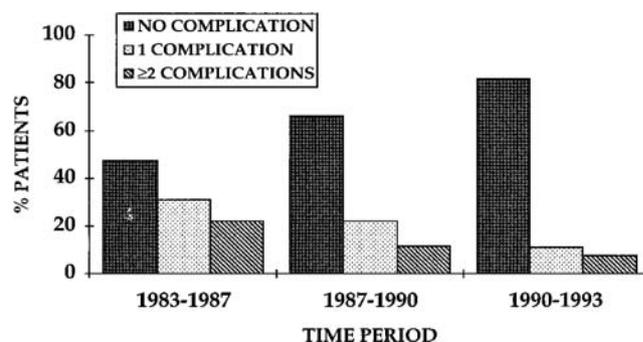


FIG. 4. Bar graph indicating a decrease in the incidence of medical complications following a subarachnoid hemorrhage (SAH) deemed "good grade." The number of patients having any complication (Mann-Whitney $z = -4.27$; $p = 0.0000$) and the number of complications each patient may experience (Spearman correlation $r = -0.29$, $p = 0.00001$) declined each successive treatment epoch (Table 10).

ination and administration of calcium channel blockers during the second treatment time period was associated with improved management outcome (Table 10). With the routine use of angioplasty for the treatment of medically refractory vasospasm after 1989, further improvement in outcome was noted (Table 10). For example, when angioplasty was not used or not available (17 patients), 76.5% of symptomatic vasospasm patients achieved a favorable outcome in contrast to 96.6% when angioplasty was available and used (22 patients). Although these results may reflect advances in critical-care techniques, it is possible that aggressive vasospasm management may correlate with some of the improved outcome observed during the decade.

Hospital Stay. There are many variables that influence utilization of resources; we determined length of hospital stay (excluding rehabilitative care) as an overall estimate of hospital resource utilization. There was significant decrease in the number of days a patient spent in hospital as the series progressed (Spearman correlation $r = -0.16$; $p = 0.02$). The median length of hospitalization was 23 days in the first treatment epoch, 20 days in the second, and 17.5 days in the third treatment epoch.

Discussion

The present retrospective report covers our experience over the past decade in the management of 224 patients who suffered ruptured anterior circulation aneurysms and who were classified as Hunt and Hess¹⁰ Grade I, II, or III at admission. A standardized management policy, including early surgery, aggressive vasospasm management, and intensive care was used to treat all patients. Seventy-five percent of the patients were operated on within 72 hours of their SAH. We observed a significant increase in the number of patients experiencing a favorable outcome as management evolved during the decade. In part, advances in critical care and vasospasm management were associated with the observed improvement in patient outcome.

Population Under Study and Selection Factors

The results in this series demonstrate that favorable outcomes can be expected in approximately 90% of Grade I or II and 81% of Grade III patients following rupture of anterior circulation aneurysms. Outcome is influenced by several variables, including referral and admission policy, patient selection, and therapy. Advances in therapy appear to be associated with the improved outcome observed in this series. Although the influence of selection cannot be entirely excluded, we would discount a significant role of selection bias for the following reasons: 1) this is a single-institution study; 2) Harborview Medical Center is the major emergency Level I medical center for Seattle and the surrounding area and served this function throughout the decade studied; 3) the probability of subsequent survival increases with the passage of time from aneurysm rupture;^{1,34} and the vast majority of patients in this series were admitted within 24 hours of SAH; and 4) all patients admitted with the diagnosis of Hunt and Hess¹⁰ Grade I, II, or III after rupture of an anterior circulation aneurysm are included in the analysis, including those who subsequently deteriorated or died before surgery.

Comparison to Earlier Studies

Whereas historical cohorts, particularly those derived from retrospective analysis, are less relevant than prospective randomized studies, comparison of the results obtained in this series with previous reports provides an indication of the favorable impact of aggressive SAH management. In the pre-CT era, Hunt and Hess¹⁰ observed that 20% of Grade I and II and 36% of Grade III patients died. In our series 6% of Grade I and II and 11% of Grade III patients died. Reports of contemporary large series focusing on surgical⁸ or predominantly late surgical management results²² of mainly anterior circulation aneurysms have cited favorable outcomes in 83% and 72%, respectively, of Grade I and II and III patients. For example, Miyaoka and colleagues²² described 1622 patients, including 1209 categorized as good clinical grade, treated at 12 Japanese centers between 1980 and 1987. One-third of these patients underwent early surgery. Overall, favorable outcomes were observed in 72% of Grade I, II, and III patients.

Previous reports describing early surgery after good-grade SAH suggest management results have improved over the last 10 years, in part, because of newer techniques to manage vasospasm.^{19,29} For example, Ljunggren, *et al.*,¹⁹ observed favorable outcomes in 74% of 160 good-grade patients treated during the early 1980s, whereas Säveland and coworkers,²⁹ in a prospective analysis of 145 Grade I through III patients treated at five centers between 1989 and 1990, observed a favorable outcome in 81% of these patients. This improved outcome was attributed to advances in vasospasm management such as the routine use of nimodipine and hypervolemia. In our series, Grade III patients were most likely to develop symptomatic vasospasm. Consequently, the successful management of vasospasm using contemporary strategies should have the greatest impact on outcome in these patients; overall, 81.3% of Grade III patients in this report experienced favorable outcomes with an improvement observed over the decade. When aggressive vasospasm management is not routine, between 56% and 73% of Grade III patients experience favorable outcomes.^{8,13,15,22} For example, Hernesniemi, *et al.*,⁸ treated 1662 good-grade patients at a single center over a 14-year period; 68% of the Grade III patients experienced a favorable outcome.

Outcome Prediction

In an era of increasing limitations of medical resources, the ability to predict outcome is becoming increasingly important because when outcome can be accurately predicted, treatment is more likely to be geared toward potentially avoidable, deleterious factors. Subarachnoid hemorrhage is a complex pathophysiological event and outcome is determined by many variables. We constructed three simple models to determine which factors best predicted outcome. Our admission model was effective in predicting good outcome but fared poorly in predicting unfavorable results. Our comprehensive model, which included all univariate predictors of outcome, correctly predicted 93% of all outcomes. Two points are important in interpreting these results. First, the relatively small sample size, particularly for rare events such as preoperative rebleed, makes it difficult to estimate the precise magnitude of the

Good-grade anterior circulation aneurysms

association between predictors and outcome. Conservatively, one would estimate that each of the risk factors in the model multiplies the odds of an unfavorable outcome by an amount equal to the lower limit of the confidence interval for the risk factor. Second, because events proximate to, and associated with, outcome are included, adverse events that occur earlier in the causal pathway may be forced out of the model. The early event, however, may have an association with outcome or be a precipitating factor of later occurring events.

Analysis of outcome prediction in this series emphasizes the importance of comprehensive critical care, avoidance of medical complications, and effective vasospasm management. No intraoperative factor was associated with outcome. The occurrence of vasospasm also did not predict outcome, perhaps because it was aggressively prevented and managed. Furthermore, multivariate analysis suggested that more than half of the factors associated with outcome were preventable, unlike the patient characteristics on admission. Nevertheless, following univariate analysis, several patient characteristics, particularly age, clinical grade, the amount of SAH or IVH on admission CT, and atherosclerosis observed on admission angiogram were all found to be associated with outcome. The correlation of these factors and outcome have been previously documented.^{5,6,8,11,14,23,25}

Improved Outcome

Perhaps the most important finding of this study is the significant improvement in outcome over the time period in question. What factors may account for this? Practice effect and increased experience may explain part of the improvement. This effect, however, was probably minimized by the frequent changes in resident staff and variations in attending staff, although one individual (H.R.W.) was responsible for two-thirds of the cases. There was little evidence to suggest that improvement in surgical technique was associated with outcome. We cannot, however, exclude the possibility that advances in neuroanesthesia and a better understanding of the effects of anesthetic agents on cerebral hemodynamics contributed either directly or indirectly to improved outcome.

Improvements in critical-care techniques and, perhaps, the management of vasospasm, appear to correlate with the improvement observed in the present series. Although vasospasm management did not improve outcome independently, several lines of evidence suggest it may be associated with the improved outcome. First, symptomatic vasospasm was relatively uncommon in this series. The routine use of prophylactic hypervolemia may have contributed to this and may also explain the lack of correlation between the severity of SAH identified on CT and the incidence of vasospasm. Second, vasospasm accounted for 16% of unfavorable outcomes in this series. By contrast, before antiischemic treatment was routine, between 32% and 43% of patient morbidity and mortality following SAH was associated with vasospasm.^{13,14,19} Finally, we observed a temporal association between improved outcome and the introduction of calcium channel blockers, transcranial Doppler, and angioplasty. The benefits of each of these techniques in the management of vasospasm have been previously described.^{9,18,24,27,30}

The successful management of SAH not only involves prevention of rebleeding and vasospasm; it also involves careful attention to cardiorespiratory function, volume status, intracranial hemodynamics, and the prevention of secondary cerebral insults or medical complications. An association was observed between outcome and medical complications and secondary insults in this series. Furthermore, improvement in management results was associated with a decrease in the incidence of complications and secondary insults but not in our ability to respond to them. These findings suggest that critical-care monitoring in specialized neurovascular intensive care units and proactive attempts to avoid complications may contribute to improved outcome.

Intensive hospital care and technological advances are frequently portrayed as being responsible for a significant portion of increased health care costs and questions are often raised about their effectiveness. The results of this study demonstrate that improvements in critical-care techniques and advances in vasospasm management are, in part, associated with improved outcome following good-grade SAH. Furthermore, the advances in care are associated with a decrease in the length of time a patient remains in a neurosurgical care unit. Together, these observations suggest that aggressive, state-of-the-art SAH management practiced in specialized cerebrovascular centers may ultimately be cost effective.

Acknowledgments

The authors express their thanks to Ray Baculi, Rose Fontanilla, Galen Ransom, Debbie Schneiderman, and Andrew Zweibel for assistance in data acquisition.

References

1. Alvord EC Jr, Loeser JD, Bailey WL, et al: Subarachnoid hemorrhage due to ruptured aneurysms. A simple method of estimating prognosis. *Arch Neurol* **27**:273-284, 1972
2. Awad IA, Carter LP, Spetzler RF: Clinical vasospasm after subarachnoid hemorrhage: response to hypervolemic hemodilution and arterial hypertension. *Stroke* **18**:365-372, 1987
3. Bamford J, Sandercock P, Dennis M, et al: A prospective study of acute cerebrovascular disease in the community: the Oxfordshire Community Stroke Project—1981-86. 2. Incidence, case fatality rates and overall outcome at one year of cerebral infarction, primary intracerebral and subarachnoid haemorrhage. *J Neurol Neurosurg Psychiatry* **53**:16-22, 1990
4. Deruty R, Mottolese C, Pelissou-Guyotat I, et al: Management of the ruptured intracranial aneurysm—early surgery, late surgery, or modulated surgery? *Acta Neurochir* **113**:1-10, 1991
5. Fischer CM, Kistler JP, Davis JM: Relation of cerebral vasospasm to subarachnoid hemorrhage visualized by computerized tomographic scanning. *Neurosurgery* **6**:1-9, 1980
6. Gerber CJ, Lang DA, Neil-Dwyer G, et al: A simple scoring system for accurate prediction of outcome within four days of a subarachnoid haemorrhage. *Acta Neurochir* **122**:11-22, 1993
7. Haley EC Jr, Kassell NF, Torner JC, et al: The International Cooperative Study on the Timing of Aneurysm Surgery. The North American experience. *Stroke* **23**:205-214, 1992
8. Hernesniemi J, Vapalahti M, Niskanen M, et al: One-year outcome in early aneurysm surgery: a 14 years experience. *Acta Neurochir* **122**:1-10, 1993
9. Higashida RT, Halbach VV, Dowd CF, et al: Intravascular balloon dilatation therapy for intracranial arterial vasospasm:

- patient selection, technique, and clinical results. **Neurosurg Rev** 15:89–95, 1992
10. Hunt WE, Hess RM: Surgical risk as related to time of intervention in the repair of intracranial aneurysms. **J Neurosurg** 28:14–20, 1968
 11. Inagawa T: Management outcome in the elderly patient following subarachnoid hemorrhage. **J Neurosurg** 78:554–561, 1993
 12. Jennett B, Bond RM: Assessment of outcome after severe brain damage: a practical scale. **Lancet** 1:480–484, 1975
 13. Kassell NF, Torner JC, Haley EC Jr, et al: The International Cooperative Study on the Timing of Aneurysm Surgery. Part 1: overall management result. **J Neurosurg** 73:18–36, 1990
 14. Kassell NF, Torner JC, Jane JA, et al: The International Cooperative Study on the Timing of Aneurysm Surgery. Part 2: surgical results. **J Neurosurg** 73:37–47, 1990
 15. Krupp W, Heienbrok W, Mücke R: Management results attained by predominantly late surgery for intracranial aneurysms. **Neurosurgery** 34:227–234, 1994
 16. Lanzino G, Kassell NF, Germanson T, et al: Plasma glucose levels and outcome after aneurysmal subarachnoid hemorrhage. **J Neurosurg** 79:885–891, 1993
 17. Le Roux P, Winn HR: The poor grade aneurysm patient, in Salzman M (ed): **Current Techniques in Neurosurgery**. Philadelphia: Current Medicine, 1993, pp 10.1–10.28
 18. Le Roux PD, Newell DW, Eskridge J, et al: Severe symptomatic vasospasm: the role of immediate postoperative angioplasty. **J Neurosurg** 80:224–229, 1994
 19. Ljunggren B, Säveland H, Brandt L: Causes of unfavorable outcome after early aneurysm operation. **Neurosurgery** 13:629–633, 1983
 20. Maurice-Williams RS, Marsh H: Ruptured intracranial aneurysms: the overall effect of treatment and the influence of patient selection and data presentation on the reported outcome. **J Neurol Neurosurg Psychiatry** 48:1208–1212, 1985
 21. Milhorat TH, Krauthelm M: Results of early and delayed operations for ruptured intracranial aneurysms in two series of 100 consecutive patients. **Surg Neurol** 26:123–128, 1986
 22. Miyaoka M, Sato K, Ishii S: A clinical study of the relationship of timing to outcome of surgery for ruptured cerebral aneurysms. A retrospective analysis of 1622 cases. **J Neurosurg** 79:373–378, 1993
 23. Mohr G, Ferguson G, Khan M, et al: Intraventricular hemorrhage from ruptured aneurysm. Retrospective analysis of 91 cases. **J Neurosurg** 58:482–487, 1983
 24. Newell DW, Eskridge JM, Mayberg MR, et al: Angioplasty for the treatment of symptomatic vasospasm following subarachnoid hemorrhage. **J Neurosurg** 71:654–660, 1989
 25. Öhman J, Servo A, Heiskanen O: Risk factors for cerebral infiltration in good-grade patients after aneurysmal subarachnoid hemorrhage and surgery: a prospective study. **J Neurosurg** 74:14–20, 1991
 26. Ojemann RG, Heros RC, Crowell RM: **Surgical Management of Cerebrovascular Disease**. Baltimore: Williams & Wilkins, 1987, pp 163–177
 27. Pickard JD, Murray GD, Illingworth R, et al: Effect of oral nimodipine on cerebral infarction and outcome after subarachnoid haemorrhage. **Br Med J** 298:636–642, 1989
 28. Ropper AH, Zervas NT: Outcome 1 year after SAH from cerebral aneurysm. Management morbidity, mortality and functional status in 112 consecutive good-risk patients. **J Neurosurg** 60:909–915, 1984
 29. Säveland H, Hillman J, Brandt L, et al: Overall outcome in aneurysmal subarachnoid hemorrhage. A prospective study from neurosurgical units in Sweden during a 1-year period. **J Neurosurg** 76:729–734, 1992
 30. Seiler RR, Newell DW: Subarachnoid hemorrhage and vasospasm, in Newell DW, Aaslid R (eds): **Transcranial Doppler**. New York: Raven Press, 1992, pp 101–107
 31. Solomon RA, Post KD, McMurtry JG III: Depression of circulating blood volume in patients after subarachnoid hemorrhage: implications for the management of symptomatic vasospasm. **Neurosurgery** 15:354–361, 1984
 32. Sundt TM Jr, Kobayashi S, Fode NC, et al: Results and complications of surgical management of 809 intracranial aneurysms in 722 cases. Related and unrelated to grade of patients, type of aneurysms, and timing of surgery. **J Neurosurg** 56:53–765, 1982
 33. Taylor B, Harries P, Bullock R: Factors affecting outcome after surgery for intracranial aneurysm in Glasgow. **Br J Neurosurg** 5:591–600, 1991
 34. Weir BKA: The management of intracranial aneurysms—prospects for improvement. **Clin Neurosurg** 34:154–160, 1988
 35. Wijdicks EFM, Vermeulen M, Hijdra A, et al: Hyponatremia and cerebral infiltration in patients with ruptured intracranial aneurysms: is fluid restriction harmful? **Ann Neurol** 17:137–140, 1985

Manuscript received June 23, 1994.

Accepted in final form February 2, 1995.

This work was supported in part by National Institutes of Health Grant NS 30305. Dr. Le Roux is the New York Academy of Medicine Elsberg Fellow in Neurosurgery.

Current address for Dr. Le Roux: New York University Medical Center, New York, New York.

Address reprint requests to: H. Richard Winn, M.D., Department of Neurological Surgery, University of Washington School of Medicine, 325 Ninth Avenue, ZA-86, Seattle, Washington 98104.