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Marked reduction of cerebral vasospasm with lumbar drainage of cerebrospinal fluid after subarachnoid hemorrhage

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Object. Cerebral vasospasm after subarachnoid hemorrhage (SAH) continues to be a major source of morbidity in patients despite significant clinical and basic science research. Efforts to prevent vasospasm by removing spasmogens from the subarachnoid space have produced mixed results. The authors hypothesize that lumbar cisternal drainage can remove blood from the basal subarachnoid spaces more effectively than an external ventricular drain (EVD). This nonrandomized, controlled-cohort study was undertaken to evaluate the effectiveness of a lumbar drain in patients with SAH compared with those in whom an EVD or no form of cerebrospinal fluid (CSF) drainage was used to prevent the development of clinical vasospasm and its sequelae.

Methods. The authors collected data on 266 patients with nontraumatic SAH who were admitted to the University of Utah Health Sciences Center between January 1994 and January 2003. Of these, 167 met the study entry criteria. The treatment group consisted of 81 patients in whom a lumbar drain had been placed for CSF shunting, whereas the control group was composed of 86 patients who received no form of CSF drainage or who were treated solely with an EVD. Primary outcome measures were as follows: 1) clinically evident vasospasm; 2) the need for endovascular intervention; 3) vasospasm-induced infarction; 4) disposition at time of discharge; and 5) Glasgow Outcome Scale (GOS) score at 1 to 3 months postdischarge. Secondary outcomes included length of stay and the need for CSF shunting.

The presence of a lumbar drain conferred a statistically significant protective and beneficial effect across all outcome measures, reducing the incidence of clinical vasospasm from 51 to 17%, the need for angioplasty from 45 to 17%, and the occurrence of vasospastic infarction from 27 to 7% (all $p \leq 0.001$–0.008). Patients in the treatment group were more likely to be discharged home (54% compared with 25%, $p = 0.002$) and to have a GOS score of 5 at follow up (71% compared with 35%, $p < 0.001$). The mean number of days spent in the intensive care unit and in the hospital overall was also fewer in the treatment group. A similar degree of benefit was found in patients with different Fisher grades and regardless of whether an EVD was needed on presentation, both by subgroup analysis and multivariate logistic regression modeling. There was no statistical difference between the groups in terms of patients requiring a shunt. Complications with lumbar drains were rare and yielded no permanent sequelae.

Conclusions. Shunting of CSF through a lumbar drain after an SAH markedly reduces the risk of clinically evident vasospasm and its sequelae, shortens hospital stay, and improves outcome. Its beneficial effects are probably mediated through the removal of spasmogens that exist in the CSF. The results of this study warrant a randomized clinical trial, which is currently under way.

Key Words • aneurysm • subarachnoid hemorrhage • vasospasm • lumbar drain

Vasospasm continues to be a major cause of morbidity after aneurysmal SAH. Although much has been elucidated regarding its pathophysiology, it remains an incompletely solved problem. As improved emergency medical services, diagnostic testing, and rapid treatment have decreased the mortality rate from aneurysmal SAH, there has been a concomitant increase in the relative contribution of vasospasm to the overall outcome. A number of significant achievements have improved our ability to manage vasospasm, but have not eliminated it as a clinical entity.

Abbreviations used in this paper: CI = confidence interval; CSF = cerebrospinal fluid; CT = computerized tomography; EVD = external ventricular drain; GOS = Glasgow Outcome Scale; ICP = intracranial pressure; ICU = intensive care unit; MCA = middle cerebral artery; OR = odds ratio; rt-PA = recombinant tissue plasminogen activator; SAH = subarachnoid hemorrhage; TCD = transcranial Doppler.

Foremost among these improvements was the introduction of triple-H therapy in the early 1980s.[5,30,51] Nimodipine, which was introduced for widespread clinical use in 1985, reduced the overall percentage of patients with severe vasospasm from 30 to 20%, but it did not seem to decrease the incidence of vasospasm identified on angiography.[2,6,13,49,52,53] In the late 1980s, endovascular techniques such as angioplasty and administration of intraarterial chemical vasodilators such as papaverine enabled the neurological rescue of many patients, thereby further improving their overall outcome.[3,9,11,12,14,17,42,46,47,55,56,60] Despite all these advances, vasospasm still contributes to poor outcome in approximately 10 to 40% of patients with dense SAH.[8,15,31] There is still no effective means to prevent vasospasm, and clinical practice now involves the intensive management of its effects while the disease runs its course. Management of vasospasm currently accounts for a substantial proportion of the duration and cost of the hospital stay.

Research has clearly shown that the pathophysiology of vasospasm is directly related to the presence of blood in the subarachnoid space surrounding the cerebral conductance vessels.[39,76] Fisher, et al.,[18] first noted this relationship in 1980, and their grading scheme remains the mostly widely applied means of predicting vasospasm risk.[19] Because hemolysis of blood is the primary inciting agent for vasospasm, it would follow that strategies to facilitate the clearance of blood from the subarachnoid spaces would decrease cerebral vasospasm. This strategy has been studied by a number of investigators.[16,25,32,35–37,43,44,48,50,64,65,70–72,74,77] Cisternal administration of thrombolytic/fibrinolytic therapy was first introduced in 1991 and has been thoroughly evaluated, including a well-conducted randomized controlled trial.[32,36,43,44,63–65,70,71,74,77] A number of Japanese groups have advocated cisternal irrigation therapy with inflow and outflow catheters placed in the cranial subarachnoid spaces.[35–37,48,72] This is usually coupled with other modalities such as daily "head-shaking" and fibrinolytic therapy. These therapies have not gained widespread acceptance because of mixed results, the potential for morbidity from placing drains within the cisternal spaces, and the fear of hemorrhagic complications.[66,73]

We hypothesized that lumbar CSF drainage may represent a simple and effective way to increase the clearance of blood from the subarachnoid spaces and consequently decrease the incidence of clinically significant vasospasm. Draining CSF from the lumbar cistern would be expected to promote circulation of clear, newly formed CSF from the cerebral ventricles through the subarachnoid spaces, especially if the arachnoidal membranes and/or lamina terminalis were opened at the time of surgery. Moreover, lumbar drainage would also promote removal of the red cell mass from the intrathecal space, which represents the largest of all subarachnoid cisterns. Conversely, CSF drainage directly from the lateral ventricles may contribute to stasis of hemorrhage within the subarachnoid cisterns, so that ventricular drainage in those patients may actually add to the risk that cerebral vasospasm will develop. We have been using lumbar CSF drainage after SAH for the last 9 years, and now report how this affects the incidence of vasospasm in comparison to a group of patients whose SAH was managed with conventional or no CSF drainage.

Clinical Material and Methods

This study was made possible by differences in practice preference between two groups of cerebrovascular surgeons at the University of Utah over a 9-year period. One group used EVDs for CSF drainage in the postoperative period, if they believed it was necessary. The other group preferentially used lumbar CSF drainage in patients with high-grade SAHs according to the Fisher scale when this procedure was not contraindicated by safety concerns. Nearly equal numbers of patients with SAH were treated with one of these two management strategies. All other aspects of care, as described later, were similar.

Patient Population

Patients who suffered nontraumatic SAH between January 1994 and January 2003 were identified from a clinical database maintained in the Department of Neurosurgery at the University of Utah. Clinical records from admission up to the time of discharge were available and were reviewed. The University of Utah's institutional review board authorized all data collection and analysis.

Patient Demographics and Data

Between January 1994 and January 2003, 266 patients with nontraumatic SAH were treated at the University of Utah Health Sciences Center. From this population, 99 patients were excluded from this study for various reasons. Forty-four patients had only Fisher Grade 1 or 2 hemorrhages; clinically evident vasospasm developed in only one, for an overall incidence of 2.3%. We excluded 27 patients who presented in poor neurological condition and either never significantly improved or died early. An additional 12 patients who were in poor neurological condition after aneurysm treatment were excluded. Finally, 16 patients who presented for treatment 4 or more days after their index hemorrhage were also disqualified. This left 167 patients with high-grade hemorrhages (Fisher Grades 3, 3+4, and 4) who were in satisfactory neurological condition before the onset of vasospasm as the core patient population for this study.

Patient Selection and Clinical Management

All patients were assigned a Hunt and Hess grade[24] at the time of admission according to neurological parameters only. The presence of serious systemic disease was not used to upgrade the Hunt and Hess score. On arrival, all patients were systemically and neurologically resuscitated and stabilized, if necessary, with intubation, mannitol, and moderate hyperventilation therapy. An EVD was placed immediately if neuroimaging or clinical features indicative of elevated ICP or symptomatic acute hydrocephalus were present. Patients were also classified according to the density of their SAH on the initial CT scan by using a modified Fisher grading system. This modification creates a new Grade 3+4 category for patients with both dense subarachnoid blood and intraparenchymal/intraventricular hemorrhages of 5 ml or more (diameter > 2 cm). Examples of CT scans obtained in a patient assigned to this Fisher 3+4 category are displayed in Fig. 1.

We excluded from analysis all patients whose neurological condition was too poor to allow clinical recognition of the signs and symptoms of cerebral vasospasm. This included all patients in Hunt and Hess Grade V who failed to improve substantially with either initial resuscitation or surgical intervention, those who died before clinical vasospasm developed, patients who sustained a severe neurological deficit from aneurysm treatment (coma with Glasgow Coma Scale motor score ≤ 4), and those in whom there was a delay of 4 or more days in presenting to our institution after their index SAH. We did not exclude patients who may have sustained a minor sentinel hemorrhage more than 4 days before admission.

With the exception of CSF drainage, all patients received treatment according to a consistent protocol. This included early surgical occlusion of the ruptured aneurysm with clip or coil placement (≤ 36 hours after admission); prophylactic hypervolemic therapy with central venous catheters or Swan-Ganz catheters; administration of nimodipine; daily

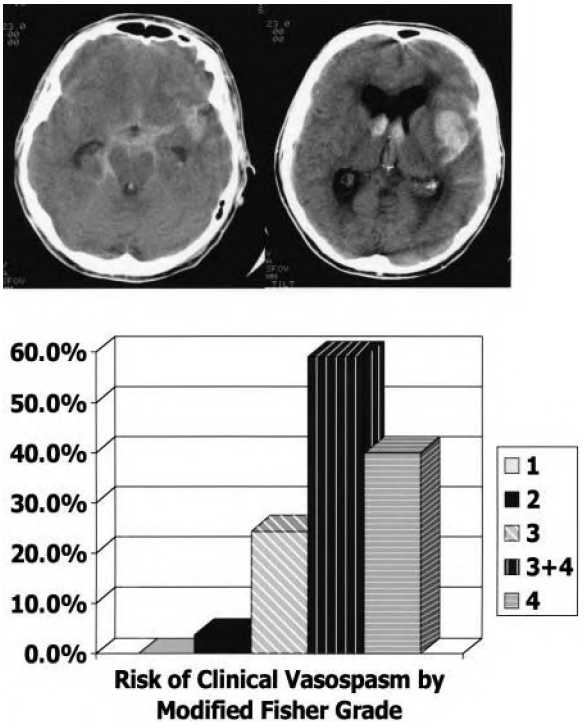

FIG. 1. *Upper:* Noncontrast axial CT scans demonstrating a Fisher Grade 3+4 SAH. There is dense blood within the basal cisterns *(left)* as well as significant intraventricular hemorrhage and a perisylvian intraparenchymal hemorrhage *(right)*. *Lower:* Bar graph showing the risk of suffering clinical vasospasm based on our modified Fisher grading scheme. Patients with Fisher Grade 3+4 are at greatest risk (59%).

TCD ultrasonography examinations; and rigorous monitoring and correction of electrolyte, blood gas, and serum anticonvulsant drug levels and hydrocephalus. In patients who were treated surgically, the accessible basal cisterns were opened and cleaned of blood by suction and irrigation. All patients underwent cerebral angiography if vasospasm was suspected based on clinical evidence. At the onset of a neurological change indicative of vasospasm, patients were given a bolus of crystalloid or colloid and their total fluid intake was titrated to a higher central venous pressure, or to the point of maximum cardiac output on the Starling curve if a Swan-Ganz catheter was used. Vasopressor medications were administered to elevate blood pressure if clinical improvement was not achieved or sustained with hypervolemia. At the discretion of the attending surgeon, in consultation with the interventional radiologist, severe or refractory vasospasm was treated with either balloon angioplasty or repeated intraarterial infusion of papaverine. In three patients (all in the lumbar drainage group), moderate to severe vasospasm was detected on surveillance TCD studies and angiography in the absence of clinically apparent neurological change, and prophylactic endovascular therapy was initiated. For the purpose of data analysis, these patients were scored as having vasospasm. Otherwise, prophylactic angioplasty was not routinely used.

Definition of Vasospasm and Vasospasm-Related Infarction

Vasospasm was diagnosed using the criteria defined in the tirilizad trials:[21,22,29,38] 1) onset of new neurological deficits such as confusion, disorientation, drowsiness, or focal motor deficit during posthemorrhage Days 4 to 14; 2) negative findings on CT scans obtained to rule out other causes of neurological deterioration such as hemorrhage, cerebral edema, or hydrocephalus; 3) no other identifiable cause of neurological deterioration such as hyponatremia ($\leq$ 132 mEq/L), hypoxia, drug toxicity, infection, or seizures; and 4) evidence of vasospasm on serial TCD ultrasonography examinations or a cerebral angiogram demonstrating vascular narrowing affecting a territory concordant with the suspected source of the change in findings on neurological examination. Cerebral infarction caused by vasospasm was diagnosed if either a delayed ischemic deficit became sustained beyond the risk period of cerebral vasospasm (indicated by normal results on TCD examination or angiography) or if imaging studies revealed a region of cerebral infarction in a vascular distribution consistent with the patient's vasospasm.

Cerebrospinal Fluid Drainage Methods

Any patient who presented with intracranial hypertension, which was usually caused by acute symptomatic hydrocephalus, was treated with an EVD in a conventional fashion. Lumbar CSF drainage in these patients was initiated only when it was deemed safe, as evidenced by the presence of an unobstructed ventricular system and the absence of mass lesions (hemorrhage or cerebral edema) causing midline shift. Lumbar drains were typically placed in patients at the time of surgery and were kept closed until postoperative Day 1. At the surgeon's discretion, CSF was diverted using the lumbar drain intraoperatively to facilitate brain relaxation. If the postoperative CT scan demonstrated no contraindication, the lumbar drain was opened. In those patients who initially received EVDs for acute or obstructive hydrocephalus, we would transition the CSF drainage from the ventricular to the lumbar route as the patient's clinical condition and neuroimaging studies allowed, often overlapping the use of both drains for several days.

Lumbar CSF drainage was continued throughout the vasospasm risk period (drain height 5–10 cm above the external auditory canal); the collection rate was targeted at 5 to 10 ml/hour. Lumbar drainage was stopped once the CSF was no longer visibly hemorrhagic and the risk period for vasospasm had passed. For the purposes of data analysis, we considered only patients in whom lumbar CSF drainage was started by posthemorrhage Day 4 and continued for a minimum of 3 days to have undergone an effective trial of lumbar drainage.

Outcome Measures

There were five primary outcome measures in this study: 1) clinically evident vasospasm; 2) use of cerebral angioplasty and/or intraarterial papaverine infusion; 3) vasospasm-related cerebral infarction; 4) disposition of the patient at the time of discharge; and 5) GOS[26] score at 1- to 3-month follow up. Secondary outcome measures included duration of stay in the ICU, overall acute hospital duration of stay (excluding inpatient rehabilitation), and the need for permanent CSF diversion (shunt placement).

Calculations and Statistical Analysis

Tests of associations between the primary outcome mea-

TABLE 1

*Characteristics of the lumbar drain and control groups in 167 patients with SAH**

Variable	Group		p Value
	LD	Control	
no. of patients	81	86	
age in yrs (range)	53 (20–90)	53 (27–83)	NS
Hunt & Hess grade (%)			NS
I	7 (9)	5 (6)	
II	30 (37)	25 (29)	
III	25 (31)	22 (26)	
IV	15 (18)	28 (32)	
V	4 (5)	6 (7)	
Fisher grade (%)			0.001
3	64 (79)	47 (55)	
3+4	17 (21)	34 (39)	
4	0 (0)	5 (6)	
EVD on admission (%)	27 (33)	43 (50)	0.024
source of bleeding (%)			NS
ACoA	18 (22)	30 (35)	
PCoA	15 (19)	11 (13)	
MCA bif	11 (14)	12 (14)	
posterior circ†	11 (14)	14 (16)	
nonaneurysmal	12 (15)	7 (8)	
other‡	17 (21)	12 (14)	
intraop rupture (%)	6 (7)	11 (13)	NS
coil insertion (%)	3 (4)	3 (3)	NS

* ACoA = anterior communicating artery; bif = bifurcation; circ = circulation; LD = lumbar drain; NS = nonsignificant; PCoA = posterior communicating artery.

† Includes basilar, vertebral, posterior inferior cerebellar, and posterior cerebral arteries.

‡ Includes patients with multiple aneurysms in whom the source of the hemorrhage could not be reliably determined (internal carotid artery bifurcation aneurysms, distal anterior cerebral artery aneurysms, and so on).

sures and the method of CSF drainage were performed using chi-square analysis. Statistical significance was set at probability values of less than 0.05. Subgroup-specific analysis was also performed. Potential confounding factors were investigated using multivariate logistic regression. The ORs and their 95% CIs obtained from the logistic regression models are reported. All statistical analysis was performed using commercially available software (Stata Corp., College Station, TX).

Results

The creation of a Fisher Grade 3+4 category (51 patients) proved useful because these individuals had the highest overall risk of vasospasm. Figure 1 *upper* illustrates a typical example of a Fisher Grade 3+4 hemorrhage, and Fig. 1 *lower* illustrates, based on our data, the risk of clinically evident vasospasm as a function of this modified Fisher scale. Among our patients in Fisher Grade 1 or 2, symptomatic vasospasm developed in only one patient, and that patient is believed to have suffered a sentinel hemorrhage 4 days before admission. Regardless of treatment group, 24% of Fisher Grade 3 patients and 59% of Fisher Grade 3+4 patients experienced clinically significant vasospasm. Patients who were assigned a Fisher grade of 4 were relatively few (five patients). Of these individuals vasospasm developed in two, both of whom harbored MCA aneurysms with large perisylvian intraparenchymal hemorrhages and suffered vasospasm in the MCA distribution. We believe that their vasospasm occurred as a result of the surgical evacuation of the hematoma through the sylvian fissure, which placed it in communication with the adjacent subarachnoid space.

FIG. 2. Photograph showing CSF collected in one patient with a Fisher Grade 3 SAH in whom both an EVD and a lumbar drain were placed. Our hypothesis for this study is exemplified in this picture: the CSF from the lumbar drain is markedly bloody compared with the CSF obtained from the EVD.

The methods used for CSF drainage were as follows: an EVD was used in 68 patients (40.7%) and no form of drainage was used in 18 (10.8%); these groups constituted our control cohort of 86 patients. Fifty-eight patients (34.7%) received postoperative lumbar drains and another 23 (13.8%) required EVDs initially but were converted to lumbar drains postoperatively, within 4 days of their hemorrhage. These last two groups composed our lumbar drain cohort of 81 patients. The characteristics of the two cohorts are shown in Table 1. Using chi-square tests, differences in the composition of the two groups were evaluated. There were no differences in patient age, Hunt and Hess grade, source of hemorrhage, intraoperative rupture, or use of endovascular coils. Nevertheless, there were statistical differences between the two groups in the Fisher grade ($p = 0.001$), and whether an EVD was placed on admission ($p = 0.024$). The control group included more Fisher Grade 3+4 patients (39% compared with 21%) and had more patients who required an EVD on admission (51% compared with 33%) compared with the lumbar drain group. All of the nonaneurysmal hemorrhages (19 lesions) included in this study represented patients with densely packed, pan-cisternal hematomas, not the classic perimesencephalic hemorrhage in a patient at low risk for vasospasm. Surgery was performed in 80% of patients in the lumbar drain group compared with 88% in the control group, and only three patients in each group were treated with coil placement.

Primary and Secondary Outcomes

As illustrated in Fig. 2, the effect of lumbar CSF drainage on mobilization of blood from the subarachnoid space was dramatic. Typically, CSF from the lumbar cistern was densely hemorrhagic for the initial days of CSF drainage and then progressively cleared. By contrast, CSF drained

TABLE 2

Primary and secondary outcomes in 167 patients with SAH who underwent CSF drainage

Outcome	Group		p Value
	LD	Control	
no. of patients	81	86	
primary measure			
clinical vasospasm (%)	14 (17)	44 (51)	<0.001
angioplasty/papaverine (%)	14 (17)	39 (45)	0.001
vasospasm-related infarction (%)	6 (7)	23 (27)	0.008
disposition (%)			0.002
home	44 (54)	22 (25)	
inpatient rehabilitation	26 (32)	41 (48)	
extended care facility	9 (11)	19 (22)	
death	2 (3)	4 (5)	
GOS score (%)*			<0.001
1	2 (3)	4 (5)	
2	0	4 (5)	
3	13 (16)	31 (40)	
4	8 (10)	12 (15)	
5	56 (71)	27 (35)	
secondary measure			
LOS (mean no. of days)			
ICU	13	16	0.0077
hospital	17	21	0.0014
shunt (%)	19 (24)	28 (36)	0.145

* Scores were assigned at 1- to 3-month follow-up reviews. The GOS score could not be accurately assessed for two patients in the LD group and eight in the control group. Abbreviation: LOS = length of stay.

from the ventricle was often considerably less hemorrhagic, indicating limited circulation within the subarachnoid space before withdrawal.

Table 2 shows the effects of using lumbar CSF drainage on our various primary outcome measures. For the entire cohort of patients, lumbar CSF drainage significantly reduced the incidence of clinical vasospasm from 51 to 17%, the need for endovascular vasospasm treatment from 45 to 17%, and the risk of cerebral infarction from 27 to 7%. Those patients who did not receive a lumbar drain had a 2.9-, 2.6-, and 3.7-fold greater risk of experiencing clinical vasospasm, requiring endovascular procedures, and suffering a stroke, respectively, than those in whom a lumbar drain was placed. Another means of assessing the effectiveness of a lumbar drain is to calculate the number of patients who needed to be treated to prevent adverse outcomes. The number of patients who need to be treated with a lumbar drain to prevent one case of vasospasm and one of stroke are three and five, respectively. Four patients need to be treated with a lumbar drain before one patient is spared an endovascular procedure for vasospasm.

Lumbar CSF drainage also had a positive influence on patient disposition and functional outcome. As seen in Table 2, the proportion of patients in the lumbar drain group who were discharged directly home was more than twice that of the control group, with corresponding decreases in death, discharge to convalescent facilities, and inpatient rehabilitation. Similarly, twice as many patients in the lumbar drain group had a 1- to 3-month GOS score of 5 compared with the control group. Patients in the control group spent a mean of 16 days in the ICU, compared with 13 days for the lumbar drain group (t-test, $p = 0.0077$). Likewise, the mean hospital stay for the control group was longer than that of the lumbar drain group (21 compared with 17 days, t-test, $p = 0.0014$). Of the possible 162 patients, excluding the five who died before we could determine whether they needed a shunt, 24% in the lumbar drain group and 34% in the control group required a shunt. This difference did not reach statistical significance, however ($p = 0.145$).

TABLE 3

*Results of logistic regression analysis**

Factor	OR (95% CI)	
	Crude	Adjusted
clinical vasospasm	0.20 (0.10–0.41)	0.20 (0.09–0.44)
angioplasty/papaverine	0.25 (0.12–0.52)	0.27 (0.12–0.60)
vasospasm-related infarction	0.21 (0.08–0.57)	0.17 (0.08–0.64)

* The table shows the crude and the adjusted ORs for different outcome measures when the lumbar drain group was compared with the control group. The crude OR was calculated from 2 × 2 tables, whereas the adjusted OR was derived from the logistic regression model. The results were controlled for patient age, Fisher grade, Hunt and Hess grade, intraoperative rupture, need for EVD on admission, and aneurysm location.

Logistic Regression Analysis

Because there were imbalances in Fisher grade (3 compared with 3+4) and in the need for EVD on admission (Table 1), we analyzed for these effects in two different ways. First, we performed a logistic regression analysis to identify factors that predicted the three main binary outcomes: clinically evident vasospasm, endovascular treatment, and stroke. Second, we performed a subgroup analysis to look at the effect of lumbar drains within each of these separate demographic variables. For the logistic regression models, the following factors were tested: the presence of a lumbar drain, patient's age, intraoperative rupture of the lesion, EVD on admission, Fisher grade, Hunt and Hess grade, and source of hemorrhage. Table 3 shows the crude ORs for the outcomes and the adjusted ORs from the logistic regression models and their respective 95% CIs. The protective benefit of a lumbar drain with respect to the outcomes did not change significantly when controlled for the factors listed earlier. Covariates were considered useful in predicting the outcome of interest if their probability value was less than 0.15. The factors that were found to predict the development of clinical vasospasm were as follows: the presence of a lumbar drain ($p < 0.001$), Fisher grade ($p = 0.014$), anterior circulation aneurysm ($p = 0.007$), multiple aneurysms ($p = 0.126$), and posterior circulation aneurysms ($p = 0.114$). Use of a lumbar drain ($p = 0.001$), Fisher grade ($p = 0.008$), Hunt and Hess grade ($p = 0.029$), and anterior circulation aneurysms ($p = 0.009$) were found to predict whether endovascular intervention was needed. Use of a lumbar drain ($p = 0.005$) and presence of anterior ($p = 0.014$) and posterior ($p = 0.024$) circulation aneurysms were predictive of vasospastic stroke. Nonsignificant factors were patient age, intraoperative aneurysm rupture, and the need for EVD on admission. No factor was identified as a confounder or an effect modifier.

Subgroup Analysis

We performed a subgroup analysis to look at the effect of lumbar CSF drainage within individual Fisher grades and among patients who did and did not require preoperative

TABLE 4
Subgroup analysis in patients with SAH who underwent CSF drainage

Outcome	Group		p Value	Risk Reduction (%)	
	LD	Control		Absolute	Relative
Fisher Grade 3 only					
no. of patients	64	47			
clinical vasospasm (%)	8 (13)	19 (40)	0.001	27	68
angioplasty/papaverine (%)	8 (13)	14 (30)	0.024	17	57
vasospasm-related infarction (%)	3 (5)	11 (23)	0.003	18	78
Fisher Grade 3+4 only					
no. of patients	17	34			
clinical vasospasm (%)	6 (35)	23 (68)	0.028	33	49
angioplasty/papaverine (%)	6 (35)	23 (68)	0.028	33	49
vasospasm-related infarction (%)	3 (18)	11 (32)	0.217	16	47
EVD on admission					
no. of patients	27	43			
clinical vasospasm (%)	5 (19)	27 (63)	<0.001	44	70
angioplasty/papaverine (%)	5 (19)	25 (58)	0.001	39	67
vasospasm-related infarction (%)	3 (11)	13 (30)	0.050	21	66
no EVD on admission					
no. of patients	54	42			
clinical vasospasm (%)	9 (17)	17 (40)	0.009	23	58
angioplasty/papaverine (%)	9 (17)	14 (33)	0.058	16	48
vasospasm-related infarction (%)	3 (6)	10 (24)	0.010	18	75

EVDs (Table 4). Within Fisher Grade 3 patients only, lumbar CSF drainage significantly reduced the relative risk of clinical vasospasm, endovascular procedures, and cerebral infarction, by 68, 57, and 78%, respectively. In the Fisher Grade 3+4 group only, the relative risk reduction of clinical vasospasm and the need for endovascular intervention was 49% for both. Although the relative risk of cerebral infarction was decreased by 47%, this did not reach statistical significance. Similar results were found in the analysis of patients who did and did not require an EVD on admission. In the former, the relative risk reduction for clinical vasospasm and endovascular procedures was 70 and 67%, respectively. Again, although there was a dramatic decrease in the risk of cerebral infarction with a lumbar drain (66%), this was not statistically significant ($p = 0.05$). For patients who did not require an EVD, the relative risk reductions for clinical vasospasm, need for endovascular intervention, and stroke were 58, 48, and 75%, respectively. Here, the reduction in endovascular procedures did not reach statistical significance.

Drain Complications

Occasional complications occurred with both lumbar drains and EVDs, as follows. On removal of their EVDs, two patients suffered an intracerebral hemorrhage that required surgical evacuation. There were a number of other patients with small, asymptomatic hemorrhages that did not require treatment. In the lumbar drain group, no patient developed subdural hematomas or hygromas. In two patients in both the lumbar drain and EVD groups, culture-positive meningitis/ventriculitis developed while the drains were in place. In all cases, these infections resolved after treatment with antibiotic drugs and removal or changing of the drain, with no permanent sequelae. In both groups, there were two patients in whom the catheters broke and surgery was required to retrieve the broken end. Three patients in the lumbar CSF drain group were observed to show signs of transient clinical or neurological worsening when CSF drainage was initiated. This consisted of a decreased level of responsiveness in all cases and bradycardia in two, but these signs cleared rapidly after clamping of the drain. We were able to recommence lumbar CSF drainage successfully within 24 to 36 hours, initially at a slow rate and then progressing to our target rate, without further difficulty. None of these three patients suffered vasospasm.

Discussion

Impact of Vasospasm After SAH

The impact of cerebral vasospasm on outcome after SAH has steadily declined over the past two decades, although it is still an important clinical issue. Data from the International Cooperative Study on the Timing of Aneurysm Surgery performed in the early 1980s showed that clinically significant vasospasm permanently affected 13.5% of all patients and accounted for 33% of deaths and disabilities.[31] With advances in the surveillance and management of vasospasm, more recent studies indicate that 5 to 11% of patients continue to suffer permanent disability as a result of vasospasm.[15,59,66,67] The current standard of care consists of triple-H therapy, calcium-channel antagonists, and the use of endovascular reperfusion techniques. Muizelaar, et al.,[46] have suggested the use of preemptive cerebral angioplasty in high-risk patients to halt the onset of vasoconstriction; however, it is not yet clear if the risk/benefit ratio of such an approach is justified. With the exception of preemptive angioplasty, none of these current therapies prevents the occurrence of vasospasm, but they do lessen its clinical impact.

Benefits of Lumbar Drainage

The results of this controlled-cohort study show a marked benefit from lumbar CSF drainage in the following

parameters: clinically symptomatic vasospasm, need for endovascular intervention, occurrence of vasospasm-induced cerebral infarction, disposition at discharge, number of days in the ICU and total acute hospital care days, and GOS score measured at 1 to 3 months after discharge. The only outcome that did not show a statistical improvement with lumbar drainage was the need for a CSF shunt. Despite differences between the lumbar drain and control groups with respect to Fisher grade and placement of an EVD on admission, the degree of protection provided by the lumbar drain was consistent throughout multivariate logistic regression analysis and separate subgroup analyses. The absence of a lumbar drain was consistently the strongest predictive factor for clinically evident vasospasm, need for endovascular procedures, and vasospasm-induced cerebral infarction.

Although we have performed our analysis in a subset of all patients with SAH presenting to the University of Utah Health Sciences Center, the effect of these exclusions was to eliminate patients at low risk for vasospasm (Fisher Grade 1 or 2), and those whose neurological condition after their hemorrhage or treatment was too poor to be impacted by any subsequent vasospasm. The only other group we excluded from analysis was a small number of patients who were admitted with a delay of 4 or more days after their SAH. Although this group was too small to alter our results, we believe that this exclusion was justified on the premise that early initiation of therapy would be necessary to achieve protection. All other patients were included in this study. Even with these exclusions, demographic analysis showed that our patient population represented a typical cross-section of patients with SAH. All patients were treated by specialists in cerebrovascular surgery and with a consistent postoperative vasospasm protocol, so that the only identifiable treatment differences were related to the use of lumbar CSF drains or EVDs.

Causes of and Treatments for Vasospasm

Research on the pathophysiology of cerebral vasospasm has related the occurrence of arterial narrowing to biochemical processes that are initiated as blood undergoes lysis within the subarachnoid space. Factors that have been implicated include oxyhemoglobin, iron, intracellular adhesion molecule-1, endothelins, nitrous oxide, reduced form of nicotinamide-adenine dinucleotide phosphate oxidase, vascular endothelial growth factor, and arachidonic acid derivatives.[10,27,28,34,39–41,45,54,75,76] Several clinical strategies for reducing cerebral vasospasm have been developed based on these mechanisms.[4,16,22,57,68] Fibrinolytic agents, such as urokinase or rt-PA, have been extensively studied.[16,36,43,44,63–65,70,71,74,77] The results from these studies indicate that there may be at best a slightly decreased risk of vasospasm in the treated groups.

A well-designed multicenter randomized trial performed in 1995 did not show a difference in angiographically confirmed or symptomatic vasospasm between patients treated with a single intraoperative injection of rt-PA and their control group.[16] Nevertheless, when only patients with a thick subarachnoid clot were analyzed, there was a 56% relative risk reduction of severe vasospasm in the group treated with rt-PA. In contrast to this study, Kodama and colleagues[35,36] have provided evidence of a significant benefit with fibrinolytic therapy in an uncontrolled, nonrandomized cohort study. They administered urokinase and ascorbic acid into irrigation tubes placed in the sylvian fissure (inlet) and prepontine or chiasmal cisterns (outlet) at the time of aneurysm clip occlusion in 222 consecutive patients with Fisher Grade 3 SAHs. Ascorbic acid was added because it has been shown to degrade oxyhemoglobin into verdohemelike products, which are thought to have no prospasmogenic properties.[37] Clinical vasospasm occurred in only six patients (2.7%), two of whom suffered permanent sequelae (0.9%). Despite these promising results, such treatment has not yet become widely incorporated into current clinical care.

Rationale for CSF Drainage

A number of Japanese surgeons have been using CSF drainage methods, including lumbar drains, since the early 1980s, with mixed results.[32,33,61] The results of our study are consistent with the concept of a CSF-soluble spasmogenic agent(s). The rationale underlying our use of lumbar CSF drainage is that it promotes CSF circulation from the ventricles through the subarachnoid spaces, and that it also evacuates the large reservoir of bloody CSF from the spinal cistern. Conversely, CSF drainage from the ventricles may actually promote stasis within the subarachnoid space. It is our impression that patients who underwent lumbar CSF drainage had more rapid clearance of neuroimaging-depicted blood from the subarachnoid spaces than did control patients, although this aspect was not specifically measured in this study. Moreover, of the few patients with lumbar CSF drainage in whom vasospasm developed, many had loculated pockets of hemorrhage within the subarachnoid cisterns or a delay in clot lysis and clearance. Based on these findings, we believe that it may be possible to enhance the overall effectiveness of lumbar CSF drainage on vasospasm even further if the device was either combined with an irrigation catheter in the ventricles or basal cisterns, or if its use was combined with infusion of thrombolytic agents. We do not believe that the protective effect of the lumbar drain is gained simply through a decrease in the ICP, thus promoting cerebral perfusion. In both our lumbar drain and EVD groups, CSF diversion yielded similar values of ICP and for similar durations, and both TCD data and angiographic results showed decreased vascular narrowing in the lumbar drain group. Another aspect of this therapy that needs further investigation is whether opening the various arachnoidal compartments in the basal cisterns or opening the lamina terminalis facilitates CSF circulation and clearance of subarachnoid blood.

Complications of Lumbar Drainage

Lumbar drains are currently used in a variety of surgical scenarios, and are already commonly used in aneurysm surgery for facilitation of brain relaxation intraoperatively.[7] The published experience with lumbar drains documents that they can be associated with a variety of complications.[1,58,62,69] Catheter breakage and infection are inherent risks of both EVDs and lumbar drains, and this occurred equally in both groups. Lumbar drains, unlike EVDs, cannot be a direct cause of intracranial hemorrhages, but can cause them indirectly, especially if CSF drainage is overly aggressive. Tension pneumocephalus is a complication of lumbar CSF drainage that has been reported after transsphe-

noidal surgery, and could be a risk related to aneurysm surgery if the frontal or ethmoidal sinuses are violated and not adequately repaired.[23] Both spinal nerve root injury and post–dural puncture headache are reported complications of spinal CSF drainage,[20] but were not encountered in our study. Cerebral herniation leading to death or neurological injury is the most feared complication of lumbar CSF drainage, especially in postoperative patients or those with intracranial diseases causing mass effect. We avoided this complication by using a strict protocol requiring a satisfactory postoperative CT scan before CSF drainage was commenced, and by avoiding the use of drains in patients with mass lesions that caused any significant cerebral midline shift.

We encountered several patients who transiently became less responsive at the start of lumbar CSF drainage with immediate resolution of symptoms after clamping of the drain. Two of these patients had posterior fossa SAHs from posterior inferior cerebellar artery aneurysms and one had a partially evacuated large intracerebral hematoma from an MCA aneurysm. In all of these individuals, we were able to resume lumbar CSF drainage safely within 24 hours. None of these patients suffered vasospasm despite having very substantial SAH. In all respects, safe use of postoperative lumbar CSF drainage in patients with aneurysms requires strict attention to detail, close surveillance, and an experienced team of neurologically trained critical care nurses.

Limitations of the Study

There are several limitations in terms of methodology and outcomes in this cohort study. Selection bias is always a potential problem in a nonrandomized study, although case assignment did have a randomizing effect. Thus, patients were assigned randomly by the call schedule to attending physicians who either never used lumbar CSF drainage (control group) or to physicians who always used it as long as it was not contraindicated (treatment group). The only selection bias we could identify was a tendency to use lumbar drains less frequently in the group of patients harboring both dense cisternal subarachnoid blood and intracerebral hemorrhages (our Fisher Grade 3+4 group). As can be seen in Table 1, there were more patients in the control group with a Fisher Grade 3+4 hemorrhage compared with the intervention (lumbar drain) group. This is important because this group has the highest risk of suffering vasospasm. Likewise, lumbar CSF drainage was not used at all in our few patients with exclusively intracerebral and/or intraventricular hemorrhage (Fisher Grade 4). This imbalance occurred because of safety concerns about the use of lumbar CSF drainage in patients with intracerebral hematomas. Lumbar drains were used in some of these patients (the ones whose hematomas had been sufficiently evacuated or did not cause major mass effect), and in these individuals the severity of cerebral vasospasm was significantly reduced (Table 2). Nevertheless, the difference in the Fisher grade composition of the two groups did not prove to be a confounding factor based on our logistic regression modeling. Another limitation in our study was the fact that the data acquisition covered a period of 9 years; therefore, the data are limited by the quantity and quality of the information obtained from the medical records.

In this study we have not presented any data as to whether lumbar CSF drainage prevents neuroimaging-confirmed cerebral vasospasm. This question will be specifically analyzed in a separate study; however, our overwhelming impression so far is that lumbar CSF drainage actually prevents arterial narrowing. The majority of patients with lumbar CSF drainage were noted to display only mild elevation of blood flow velocities on TCD studies, and surveillance angiography between SAH Days 7 and 9 revealed only limited vasospasm on neuroimages. Finally, in this study we primarily evaluated the acute management and sequelae of vasospasm and did not assess any long-term outcome beyond the 1- to 3-month GOS scores. We would expect that early favorable outcomes would be reflected in long-term favorable outcomes as well, but this will need to be confirmed in future studies.

Conclusions

This controlled, nonrandomized cohort study represents our extensive experience with lumbar CSF drainage over the last 9 years. With this technique, we have shown a marked reduction in the risk of suffering clinically symptomatic vasospasm, vasospasm-induced stroke, and in the need for endovascular procedures for neurological rescue. Number of days in the ICU and overall hospital stay were reduced, as was the need for rehabilitation or convalescent care. The risk of chronic hydrocephalus, however, was not significantly changed with use of a lumbar drain, although there was a favorable trend. Lumbar drains are believed to decrease cerebral vasospasm by promoting circulation of CSF and clearance of blood from the subarachnoid spaces. The complication rate with lumbar drains was no greater than that associated with EVDs, but appropriate precautions must be observed when using the former. On the basis of our study, a randomized prospective trial of this therapy is warranted and is currently under way. The present report was primarily a surgical aneurysm series, and this approach should also be investigated to see if it would decrease cerebral vasospasm in endovascularly treated patients as well.

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