Global Cerebral Edema After Subarachnoid Hemorrhage
Frequency, Predictors, and Impact on Outcome

Jan Claassen, MD; J. Ricardo Carhuapoma, MD; Kurt T. Kreiter, MA; Evelyn Y. Du, PhD; E. Sander Connolly, MD; Stephan A. Mayer, MD

Background and Purpose—Cerebral edema visualized by CT is often seen after subarachnoid hemorrhage (SAH). Inflammatory or circulatory mechanisms have been postulated to explain this radiographic observation after SAH. We sought to determine the frequency, causes, and impact on outcome of early and delayed global cerebral edema after SAH.

Methods—We evaluated the presence of global edema on admission and follow-up CT scans in 374 SAH patients admitted within 5 days of onset to our Neurological Intensive Care Unit between July 1996 and February 2001. Using multivariate analysis, we identified predictors of global cerebral edema and evaluated the impact of global edema on outcome 3 months after onset with the modified Rankin Scale.

Results—Global edema was present on admission CT scans in 8% (n = 29) and developed secondarily in 12% (n = 44) of the patients. Global edema on admission was predicted by loss of consciousness at ictus and increasing Hunt-Hess grade. Delayed global edema was predicted by aneurysm size >10 mm, loss of consciousness at ictus, use of vasopressors, and increased SAH sum scores. Thirty-seven percent (n = 137) of the patients were dead or severely disabled (modified Rankin Scale 4 to 6) at 3 months. Death or severe disability was predicted by any global edema, aneurysm size >10 mm, loss of consciousness at ictus, increased National Institutes of Health Stroke Scale scores, and older age.

Conclusions—Global edema is an independent risk factor for mortality and poor outcome after SAH. Loss of consciousness, which may reflect ictal cerebral circulatory arrest, is a risk factor for admission global edema, and vasopressor-induced hypertension is associated with the development of delayed global edema. Critical care management strategies that minimize edema formation after SAH may improve outcome. (Stroke. 2002;33:1225-1232.)

Key Words: brain edema ■ cerebral aneurysm ■ mortality ■ outcome ■ subarachnoid hemorrhage

Subarachnoid hemorrhage (SAH) continues to have a substantial impact on mortality and has long-lasting effects on the functional status and quality of life of patients who survive.1–3 Poor neurological status within 24 hours after the ictus,1,4,5 advanced age,1,4,6 and large aneurysm size7 have been consistently identified as predictors of mortality and poor functional outcome after SAH. The presence of intraventricular hemorrhage (IVH), intracerebral hemorrhage (ICH), and extensive subarachnoid blood after SAH on CT are recognized radiological factors considered predictive of poor neurological outcome and mortality.4,5

The presence of cerebral edema, however, has received little attention as a prognostic variable after SAH. This may be due to the fact that global edema is difficult to appreciate and quantify on CT scans. Global edema after SAH may reflect diffuse ischemic injury due to transient ictal cerebral circulatory arrest, diffuse inflammatory or neurotoxic effects of blood and its degradation products on brain tissue, or abnormal autoregulation due to microvascular damage or dysfunction of vasomotor centers in the brain stem. Global edema was seen in 211 (6%) of 3451 admission CT scans in SAH patients in the International Cooperative Study on the Timing of Aneurysm Surgery but was not identified as a predictor of mortality. In a previous study, we found that global edema had a strong negative impact on cognitive functioning after SAH.8 To our knowledge, no prior study has focused on cerebral edema as a determinant of outcome after SAH. We sought to determine the frequency, causes, and impact on outcome of early and delayed global cerebral edema after SAH.

Subjects and Methods

Subjects
All SAH patients admitted to the Neurological Intensive Care Unit of Columbia-Presbyterian Medical Center between July 1996 and February 2001 were offered enrollment in the Columbia University SAH Outcomes Project. The study was approved by the hospital’s Institutional Review Board, and in all cases, written informed consent was obtained.

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consent was obtained from the patient or a surrogate. The diagnosis of SAH was established by the admission CT scan or by xanthochromia of the cerebrospinal fluid if the CT was not diagnostic. Patients with aneurysmal and spontaneous nonaneurysmal SAH were included; patients with SAH due to trauma, arteriovenous malformation rupture, vasculitis, and other structural lesions were excluded. Only patients meeting the following criteria were included in the present analysis: (1) admission CT imaging available within 5 days of hemorrhage onset and (2) outcome assessment performed at discharge.

Clinical Management
External ventricular drainage was placed in all patients with symptomatic hydrocephalus or IVH with a reduced level of consciousness. All patients were followed with daily or every-other-day transcranial Doppler (TCD) sonography and received oral nimodipine. To maintain central venous pressure >8 mm Hg, patients were treated with 0.9% normal saline and supplemental 5% albumin solution. Vasopressors were given to patients after surgery to maintain systolic blood pressure in the high normal range (140 to 160 mm Hg). Clinical deterioration from delayed cerebral ischemia was treated with hypertensive hypervolemic therapy (HHT) to maintain systolic blood pressure >200 mm Hg. When clinical evidence of delayed cerebral ischemia persisted despite HHT, balloon angioplasty was performed whenever feasible.

Clinical Variables
We recorded baseline demographic data (age, sex, and ethnicity), social history (tobacco and alcohol use), past medical history (cardiovascular and neurological disease and sentinel bleeding), and clinical features at onset (loss of consciousness or seizures at ictus). A study neurologist performed a neurological and general medical evaluation on admission. Neurological status on admission was assessed with the Glasgow Coma Scale,9 the Hunt-Hess scale,10 the World Federation of Neurosurgeons Scale,11 and the National Institutes of Health Stroke Scale (NIHSS).12 We also assessed the Acute Physiology and Chronic Health Evaluation-2 (APACHE-2) scale13 and calculated a physiological subclass by subtracting the Glasgow Coma Scale, age, and chronic health elements from the total score. We recorded whether patients were hyponatremic (<130 mmol/L) on admission or at any time during hospitalization and documented mean arterial pressure on admission. We identified patients with delayed clinical deterioration or infarction potentially attributable to vasospasm after rigorously excluding other possible causes.14 We also recorded angiographic and TCD findings, mode of aneurysm treatment (clipping versus coiling), whether any vasopressors were used after surgery, and whether vasopressors were used specifically to treat symptomatic vasospasm (HHT).

Radiographic Variables
Admission and follow-up CT scans were independently evaluated by a study neurologist for the presence of focal or global cerebral edema, the amount and location of blood,15 the presence and degree of hydrocephalus,16 and the presence of cerebral infarction. We recorded location and size of the aneurysm and the presence and extent of vasospasm on admission and follow-up angiography. Global cerebral edema was diagnosed when both of the following were present: (1) complete or near-complete effacement of the hemispheric sulci and basal cisterns and (2) bilateral and extensive disruption of the hemispheric gray-white matter junction at the level of the centrum semiovale, which was due to either blurring or diffuse peripheral “fingerlike” extension of the normal demarcation between gray and white matter. Patients were classified as having global edema on the admission CT scan (admission global edema), on ≥1 follow-up CT scan (delayed global edema), and on any CT scan (any global edema). Focal cerebral edema was diagnosed when localized brain tissue hypodensities associated with mass effect were present. Focal edema was categorized as (1) hemorrhage-related if the hypodense area surrounded a thick clot in the subarachnoid space or an intraparenchymal hematoma, (2) infarction-related, or (3) related to other causes. When diagnosing edema, infarction, or other radiographic findings, independent confirmation was obtained from the other study physicians. In a prior study, we have shown good to excellent interobserver reliability for SAH (K = 0.61), IVH (K = 0.83), and ICH (K = 0.83) variables in our study population.14 In the present study, we assessed interobserver reliability for global and focal edema by comparing the ratings of 2 independent blinded examiners, each of whom evaluated 36 CT scans selected from our database to provide broad representation as follows: no edema, n = 13; global edema, n = 10; focal edema, n = 7; and global plus focal edema, n = 6.

Outcome Variables
Survival and functional outcomes at discharge and at 3 months were assessed with the modified Rankin Scale (mRS). For patients who died in the hospital, we documented the mode of death (cardiac versus brain death) and whether life support was withdrawn in a patient with do-not-resuscitate status according to the patient’s previously stated wishes. A principal cause of death was determined by the treating study neurologist who identified the predominant process leading to cardiac or brain death or devastating neurological injury followed by withdrawal of life support according to the following classification scheme: direct effects of the hemorrhage, aneurysmal rebleeding, medical complications (ie, sepsis or pulmonary embolism), cerebral infarction, herniation from hydrocephalus, herniation from global cerebral edema, and other. The principal cause of death was retrospectively confirmed in each case in a clinical review conducted by 2 additional study physicians. For the analysis of predictors of the 3-month outcome, death or severe disability was defined as an mRS of 4 to 6.

Statistical Analysis
Data analyses were performed with commercially available statistical software (SPSS, version 9.0, SPSS Inc). Kappa scores (κ values) were calculated to assess interobserver reliability for focal and global edema. Univariate associations between candidate predictor variables and global edema and mortality were tested with binary logistic regression analyses. To assess the validity of this approach, we performed a confirmatory univariate analysis using χ² or Fisher exact tests for categorical variables, 2-tailed t tests for normally distributed continuous variables, and Mann-Whitney U tests for nonnormally distributed continuous variables. Among similar variables that were highly intercorrelated (ie, clinical scales), only the variable with the highest odds ratio (OR) and smallest P value in the binary logistic regression analysis was used as a candidate variable in the final multivariate model. Independent predictors of admission global edema, delayed global edema, any global edema, death at 3 months, and death or severe disability at 3 months were identified with backward stepwise multiple logistic regression analysis. We explored 2-way interaction terms among all variables with independent predictive value. When significant 2-way interactions were identified, we reanalyzed the predictive value of each factor after stratifying the analysis between the 2 levels of the other factor. Because of the large number of statistical tests performed, significance was judged at P < 0.01.

Results
Demographic and Clinical Features
From a consecutive series of 411 patients with nontraumatic SAH enrolled during the 4.5-year study period, 37 were excluded because a CT scan within 5 days of the hemorrhage was not available, leaving 374 patients for analysis. Eighty-three percent (311 of 374) of the admission CT scans were obtained within 24 hours of symptom onset. Mean ± SD age at the time of the hemorrhage was 54 ± 15 years (range 16 to 89 years); 69% (257 patients) were women. Hunt-Hess grades were 1 in 26% (n = 98), 2 in 16% (n = 61), 3 in 30% (n = 112), 4 in 16% (n = 58), and 5 in 12% (n = 45). In 46 (12%) patients,
no aneurysm was found on angiography, and in 21 (6%) patients, angiography was not performed because of poor prognosis. Of the 307 (82%) patients with an identified aneurysm, clipping was performed in 236 patients, and embolization with Guglielmi detachable coils was performed in 56 patients.

Radiological Features
Twenty-nine (8%) patients had global cerebral edema, and 27 (7%) had focal cerebral edema (22 were ICH-related, 4 were SAH-related, and 1 was infarct-related) on the admission CT scan (Figures 1 and 2). Delayed global edema developed in 44 (12%) patients and was first diagnosed on follow-up CT scans performed 2 to 16 days (mean 6.3±3.1 days) after the ictus (Figures 3 and 4). CT interobserver reliability was excellent for focal edema (κ value 0.82) and global edema (κ value 0.89).

Predictors of Admission Global Edema
Six clinical and radiographic variables were associated with global edema on the admission CT scan in the univariate analysis (Table 1). Backward stepwise logistic regression identified loss of consciousness at ictus (OR 3.9, 95% CI 1.0 to 14.9) and a high Hunt-Hess grade (OR 2.3, 95% CI 1.4 to 6.8) as independent predictors of admission global edema (P<0.0001 for the entire model). No interactions were found between these predictors.

Predictors of Delayed Global Edema
Five clinical and radiographic variables were associated with the development of delayed global edema in the univariate analysis (Table 1). Backward stepwise logistic regression identified aneurysm size >10 mm (OR 5.3, 95% CI 2.3 to 12.2), loss of consciousness at ictus (OR 2.7, 95% CI 1.2 to 6.2), the use of vasopressors (OR 2.4, 95% CI 1.0 to 5.7), and SAH sum score (OR 1.1, 95% CI 1.0 to 1.1) as independent predictors of delayed global edema (P<0.0001 for the entire model). No interactions were found between these predictors.
Predictors of Any Global Edema
Nine clinical and radiographic variables were associated with admission or delayed global edema in the univariate analysis (Table 1). Backward stepwise logistic regression identified aneurysm size $>10$ mm (OR 3.3, 95% CI 1.5 to 7.0), loss of consciousness at ictus (OR 2.9, 95% CI 1.4 to 6.3), the use of vasopressors (OR 2.2, 95% CI 1.1 to 4.6), and Hunt-Hess score (OR 1.8, 95% CI 1.3 to 2.4) as independent predictors for the development of any global edema ($P<0.0001$ for the entire model). No interactions were found between these predictors.

Three-Month Outcome
Ninety (24%) patients were dead 3 months after SAH. Mortality was $>40\%$ in patients with admission or delayed global cerebral edema compared with 18% in those without global edema (Table 2). Three-month mRS scores were available in 350 patients; in 24, the 3-month mRS score was not available, and the mRS score at discharge was carried forward (6 severely disabled patients [mRS 4 or 5], 18 patients not severely disabled [mRS 0 to 3]).

Predictors of Mortality
Sixteen variables were associated with death at 3 months in the univariate analysis (Table 3). Backward stepwise logistic regression identified loss of consciousness at ictus (OR 2.8, 95% CI 1.4 to 5.6), any global edema (OR 2.5, 95% CI 1.1 to 5.6), a poor Hunt-Hess score (OR 2.0, 95% CI 1.4 to 2.8), APACHE-2 physiological subscore (OR 1.2, 95% CI 1.0 to 1.3), and old age (OR 1.1, 95% CI 1.0 to 1.1) as independent predictors of mortality ($P<0.0001$ for the entire model). No interactions were found between these predictors. Radiographic predictors of mortality related to SAH, IVH, ICH, and hydrocephalus did not remain in the final model. When admission or delayed global edema was substituted for any global edema in the final model, only delayed global edema remained an independent predictor of death (OR 3.7, 95% CI 1.4 to 9.5).
Predictors of Death or Severe Disability

Sixteen variables were associated with death or severe disability at 3 months in the univariate analysis (Table 3). Backward stepwise logistic regression identified any global edema (OR 2.5, 95% CI 1.2 to 4.6), loss of consciousness at ictus (OR 2.3, 95% CI 1.2 to 4.3), a poor NIHSS score (OR 1.2, 95% CI 1.1 to 1.2), and old age (OR 1.1, 95% CI 1.0 to 1.1) as independent predictors of mortality (P<0.0001 for the entire model). There was an interaction between age and any global
edema (P<0.02 in the multivariate model). Stratified analysis showed that any global edema was predictive of death or disability in patients below the median age of 58 years (OR 3.1, 95% CI 1.2 to 7.9) but not among older patients (OR 1.1, 95% CI 0.4 to 3.1). When admission or delayed global edema was substituted for any global edema in the final model, only delayed global edema remained an independent predictor of death or severe disability (OR 4.5, 95% CI 1.8 to 11.0).

### Discussion

In the present study, CT evidence of global cerebral edema was an independent predictor of mortality and poor functional outcome after SAH. Admission global edema was present in 8% of our patients, a frequency similar to that reported by the International Cooperative Study on the Timing of Aneurysm Surgery (6% of 3451 SAH patients).4 Global edema on the admission CT scan was predicted by loss of consciousness at ictus and poor Hunt-Hess grade on admission, suggesting that ictal circulatory arrest may play a role in its pathogenesis. Delayed global edema was identified an average of 6 days (range 2 to 16 days) after the onset of the hemorrhage in an additional 12% of our patients. The use of vasopressors, large aneurysm size, loss of consciousness at ictus, and extent of SAH were independent predictors of delayed global edema. Importantly, hydrocephalus, admission blood pressure, hypotension, and various measures of vasospasm (angiographic, TCD, and clinical) were not associated with global edema.

A number of different mechanisms may lead to global edema formation after SAH. The observed association between ictal loss of consciousness and early edema suggests that this radiographic finding may reflect tissue or microvascular injury caused by intracranial circulatory arrest. Insufficient cerebral perfusion caused by severe intracranial hypertension immediately after SAH can lead to a state of transient diffuse ischemic encephalopathy.17 This phenomenon is felt to cause the transient loss of consciousness at onset that occurred in 37% of our cohort and has been reported in 44% by others.18 The triad of (1) vasomotor paralysis, (2) increased cerebral blood volume, and (3) elevated intracranial pressure in patients with global brain edema has been identified after SAH17 and traumatic brain injury19 and has been proposed to be a general reflex phenomenon after severe brain injury.17,19 Experimental models indicate that microcirculatory dysfunction after SAH may result from an initial period of global ischemia,20,21 followed by subsequent recovery of cerebral circulation and “rebound” hyperemia in the setting of abnormal autoregulation.20 In punctured artery models of experimental SAH, global edema develops 1 to 6 hours after ictus,20,22 confirming that this type of edema can develop very early after the insult.

### Table 2. Mortality and Severe Disability in Patients With SAH

<table>
<thead>
<tr>
<th></th>
<th>Admission Global Edema (n=29)</th>
<th>Delayed Global Edema (n=44)</th>
<th>No Global Edema (n=301)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital mortality, n (%)</td>
<td>14 (48)</td>
<td>19 (43)</td>
<td>40 (13)</td>
</tr>
<tr>
<td>Time of in-hospital death after onset, d</td>
<td>2 (1–21)</td>
<td>6 (5–28)</td>
<td>8.5 (1–163)</td>
</tr>
<tr>
<td>Mode of in-hospital death, n (%)</td>
<td>Brain 9 (64)</td>
<td>9 (47)</td>
<td>12 (30)</td>
</tr>
<tr>
<td></td>
<td>Cardiac, without withdrawal of support 1 (7)</td>
<td>3 (16)</td>
<td>18 (45)</td>
</tr>
<tr>
<td></td>
<td>Cardiac, with withdrawal of support 4 (29)</td>
<td>7 (37)</td>
<td>10 (25)</td>
</tr>
<tr>
<td>Primary cause of in-hospital death, n (%)</td>
<td>Direct effect of hemorrhage 13 (93)</td>
<td>7 (37)</td>
<td>21 (53)</td>
</tr>
<tr>
<td></td>
<td>Rebleeding 1 (7)</td>
<td>6 (32)</td>
<td>5 (13)</td>
</tr>
<tr>
<td></td>
<td>Medical complications 0 (0)</td>
<td>2 (11)</td>
<td>9 (23)</td>
</tr>
<tr>
<td></td>
<td>Cerebral infarction 0 (0)</td>
<td>1 (5)</td>
<td>4 (10)</td>
</tr>
<tr>
<td></td>
<td>Herniation due to global edema 0 (0)</td>
<td>3 (16)</td>
<td>0 (0)</td>
</tr>
<tr>
<td></td>
<td>Herniation due to hydrocephalus 0 (0)</td>
<td>0 (0)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Three-month outcome,* n (%)</td>
<td>Dead (mRS ≥6) 14 (48)</td>
<td>22 (50)</td>
<td>54 (18)</td>
</tr>
<tr>
<td></td>
<td>Severely disabled (mRS 5–6) 4 (14)</td>
<td>6 (14)</td>
<td>37 (12)</td>
</tr>
<tr>
<td></td>
<td>Not severely disabled (mRS 1–3) 11 (38)</td>
<td>16 (36)</td>
<td>210 (70)</td>
</tr>
</tbody>
</table>

Data are given as number (percentage) or median (range).
*Three-month outcomes were not available for 3 patients with admission cerebral edema, 2 with delayed cerebral edema, and 19 with no cerebral edema; in these patients, discharge mRS scores were carried forward.
edema can be exacerbated by induced hypertension. 26 The edema in the present study (Table 1). However, experimental
measures of large-vessel spasm, as evidenced by angiography, TCD, or clinical findings, were associated with global edema, defined as “mass effect” among a cohort of 1734 SAH patients. 32 However, this variable did not remain

associated with delayed as well as admission edema in the univariate analysis, and several of the cases that we classified as delayed global edema had subtle disruption of the gray-white matter junction on admission that did not meet our strict radiographic criteria for global edema. Follow-up scans in these cases showed apparent progression of these abnormalities.

Vaspressors were given to 45% of our study cohort, and their use was associated with the development of delayed or any global edema. Autoregulation is impaired after SAH,23–25 and in experimental models, the magnitude of vasogenic cerebral edema can be exacerbated by induced hypertension.26 The potential for induced hypertension to cause global edema after SAH has been described by others as well. In a report of 2 patients, HHT for vasospasm after SAH was associated with clinical deterioration attributed to hypertensive encephalopathy.27 The radiographic findings of sulcal effacement, diffuse peripheral fingerlike extension of the normal demarcation between gray and white matter, and hypodensities in the region of the centrum semiovale resembled the findings of our patients with delayed global edema (Figure 3).27

Our findings do not support a role for arterial vasospasm in the pathogenesis of global cerebral edema after SAH. No measures of large-vessel spasm, as evidenced by angiography, TCD, or clinical findings, were associated with global edema in the present study (Table 1). However, experimental evidence suggests that a vicious cycle of increasing generalized edema, compression of capillaries, and diffuse ischemia may play a role in the development of brain edema after SAH.28 The relationship between microvascular compromise and global edema after SAH requires further study.

Experimental ICH models suggest that blood components (eg, thrombin) are capable of inducing inflammation and vasogenic edema.29,30 Although this concept may also apply for SAH, this has not yet been demonstrated. Cerebral edema may also be caused by hypo-osmolality and hyponatremia after SAH. 31 Although this may have played a role in individual patients, hypo-osmolality was not identified as a risk factor for global edema in the present study.

Global edema was an independent predictor of death and severe disability 3 months after SAH in the present study, even after the influence of other well-established prognostic variables, such as age, 1,4,6 aneurysm size, 7 and poor neurological grade on admission, 1,4,6 was taken into account. Patients with admission global edema, compared with those without, died earlier (at 2 versus 8 days, respectively) and more often as a direct effect of the hemorrhage (93% versus 48%). A preliminary report of the Cooperative Aneurysm Study reported a mortality risk ratio of 1.71 for admission global edema, defined as “mass effect” among a cohort of 1734 SAH patients. 32 However, this variable did not remain

### TABLE 3. Predictors of Mortality and of Mortality or Severe Disability 3 mo After SAH

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Dead (n=90)</th>
<th>No (n=284)</th>
<th>P</th>
<th>Dead or Severely Disabled* (n=137)</th>
<th>No (n=237)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>60±16</td>
<td>52±14</td>
<td>0.0001</td>
<td>60±15</td>
<td>51±14</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Neurological and clinical exam on admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss of consciousness at ictus, n (%)</td>
<td>56 (62)</td>
<td>81 (29)</td>
<td>&lt;0.0001</td>
<td>76 (56)</td>
<td>61 (26)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hunt-Hess grade</td>
<td>4.0</td>
<td>2.0</td>
<td>&lt;0.0001</td>
<td>4.0</td>
<td>2.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Glasgow Coma Score</td>
<td>7.0</td>
<td>15.0</td>
<td>&lt;0.0001</td>
<td>9.0</td>
<td>15.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>NIHSS</td>
<td>14.0</td>
<td>0</td>
<td>&lt;0.0001</td>
<td>11.0</td>
<td>0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>APACHE-2 subscore</td>
<td>7±3</td>
<td>5±3</td>
<td>&lt;0.0001</td>
<td>7±3</td>
<td>4±3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Radiographic findings</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>SAH sum score</td>
<td>18±8</td>
<td>14±8</td>
<td>&lt;0.0001</td>
<td>18±8</td>
<td>13±8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cisternal clot present†</td>
<td>72 (80)</td>
<td>157 (55)</td>
<td>0.0001</td>
<td>107 (78)</td>
<td>122 (52)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IVH sum score</td>
<td>3.5</td>
<td>0</td>
<td>&lt;0.0001</td>
<td>3.0</td>
<td>0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IVH present, n (%)</td>
<td>71 (79)</td>
<td>127 (45)</td>
<td>&lt;0.0001</td>
<td>104 (76)</td>
<td>94 (40)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ICH, n (%)</td>
<td>30 (33)</td>
<td>39 (14)</td>
<td>0.0001</td>
<td>42 (31)</td>
<td>27 (11)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Temporal horn diameter, mm</td>
<td>6±4</td>
<td>5±3</td>
<td>0.0073</td>
<td>6±4</td>
<td>5±3</td>
<td>0.0004</td>
</tr>
<tr>
<td>Global edema, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>36 (40)</td>
<td>37 (13)</td>
<td>&lt;0.0001</td>
<td>46 (34)</td>
<td>27 (11)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Admission</td>
<td>14 (16)</td>
<td>15 (6)</td>
<td>0.0024</td>
<td>18 (13)</td>
<td>11 (5)</td>
<td>0.0045</td>
</tr>
<tr>
<td>Delayed</td>
<td>22 (24)</td>
<td>22 (8)</td>
<td>&lt;0.0001</td>
<td>28 (20)</td>
<td>16 (7)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Aneurysm size &gt;10 mm, n (%)</td>
<td>28 (31)</td>
<td>48 (17)</td>
<td>0.0040</td>
<td>42 (31)</td>
<td>34 (14)</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

Data are given as number (percentage), mean±SD, or medians. Binary logistic regression analysis was used to calculate P values; a confirmatory analysis using conventional tests for categorical, ordinal, or continuous data yielded nearly identical results (see Subjects and Methods). Variables that independently predicted mortality or severe disability in a multivariate model are shown in bold (P<0.01).

*Defined as mRS >3.
†Complete filling of at least 1 cistern or fissure (Hijdra score 3).
an independent predictor when evaluated together with level of consciousness, IVH, ICH, and amount of SAH.2,3
Several limitations of the present study deserve mention. The major weakness is that our analysis was based on a dichoto-
mized qualitative assessment of brain edema. Although global brain edema is notoriously difficult to evaluate on CT scans, we demonstrated good interrater reliability, which may reflect the fact that our radiographic criteria were intended to identify only very severe cases. For further determination of the prognostic importance of brain edema in SAH patients, quantitative measures of brain water content should be pursued. Hospital mor-
tality can be influenced by decisions to withdraw life support in critically ill neurological patients,8,9 and it is possible that these decisions may have been biased by radiographic findings. However, the frequency of withdrawing life support was similar in patients with and without global edema (Table 2), and survivors with global edema also had worse functional outcome, suggesting that decisions to withdraw support were based on poor prognosis. Our findings indicate that global brain edema is an impor-
tant predictor of poor outcome after SAH and that this CT finding is not merely an epiphenomenon of extensive SAH or severe hydrocephalus. Further research is needed to elucidate the pathogenesis of this disorder, apply imaging strategies that can quantify brain water content, and develop intensive care management strategies that can prevent or minimize brain edema after SAH.

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