Risk of Rebleeding After Treatment of Acute Hydrocephalus in Patients With Aneurysmal Subarachnoid Hemorrhage

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Background and Purpose—Cerebrospinal fluid drainage is often indicated in patients with acute hydrocephalus after aneurysmal subarachnoid hemorrhage but is believed to increase the risk of rebleeding. We studied the risk of rebleeding in patients with subarachnoid hemorrhage during treatment for acute hydrocephalus.

Methods—We included patients with hydrocephalus treated with external ventricular drainage or lumbar punctures within 4 days after the hemorrhage and before aneurysm occlusion. Each treated patient was matched with a control patient with untreated hydrocephalus and a control patient without ventricular enlargement. Patients and controls were matched for interval since subarachnoid hemorrhage, duration of exposure, use of tranexamic acid, clinical condition on admission, and age. We used Cox regression to calculate hazard ratios and we adjusted for rebleeding that had occurred before starting the cerebrospinal fluid drainage.

Results—In the group treated with external ventricular drainage, rebleeding occurred in seven of 34 patients (21%) with treatment, in seven of 34 controls (21%) with untreated hydrocephalus, and in six of 34 controls (18%) without hydrocephalus. In the group treated with one or more lumbar punctures, rebleeding occurred in one of 21 patients (5%) with treatment, in three of 21 controls (14%) with untreated hydrocephalus, and in none of the 21 controls without hydrocephalus. The hazard ratios for rebleeding were 1.0 (95% CI: 0.4 to 2.7) for external ventricular drainage treatment and 0.7 (95% CI: 0.1 to 6.4) for lumbar puncture treatment.

Conclusion—This study does not confirm an importantly increased risk of rebleeding during external ventricular drainage or lumbar punctures for acute hydrocephalus after aneurysmal subarachnoid hemorrhage. (Stroke. 2007;38:96-99.)

Key Words: aneurysm ■ cerebral aneurysm ■ intracranial aneurysm ■ risk factors ■ subarachnoid hemorrhage

Acute hydrocephalus is a common complication after aneurysmal subarachnoid hemorrhage (SAH). Its reported rate ranges from 9% to 67% depending on the criteria used for the diagnosis.1,2 In case of clinical deterioration from acute hydrocephalus, drainage of cerebrospinal fluid (CSF) often results in immediate clinical improvement, although the risk of poor outcome remains still higher than in patients without hydrocephalus.2–5

There are conflicting reports about the risk of rebleeding from CSF drainage in patients with an unprotected aneurysm.1–3,5–11 It has been suggested that external ventricular drainage (EVD) increases the risk of rebleeding.2,7 Such an increased risk of rebleeding was not found in patients treated with one or more lumbar punctures (LP).5,7–9 These previous studies on the risk of rebleeding during CSF drainage had two major shortcomings. First, the exposure time (the duration of the drainage period during which the aneurysm was not occluded) was not taken into account, and second, no adjustment was made for the interval between the initial hemorrhage and the start of drainage.12 This latter factor is important because the risk of rebleeding decreases over time, especially in the first days after the hemorrhage.13

We therefore studied the risk of rebleeding in patients with SAH during treatment for acute hydrocephalus with adjustment for the exposure time and the interval between the hemorrhage and the start of drainage.

Methods

We retrospectively selected patients from our prospectively collected database who had been admitted with aneurysmal SAH within 72 hours to the University Medical Center Utrecht from 1993 to 2001. Information was retrieved from a prospectively collected database of all the patients with SAH who are admitted to our service. During hospitalization, physicians enter into a proforma data on medical history, clinical condition on admission, clinical course and complications, radiology and laboratory tests, and condition at discharge. After discharge, research nurses check this form against discharge letters and operation reports. In the event of discrepancies, one of the study physicians reviews all data. Only thereafter are data entered into the computerized database. Patients were included only if a first computed tomography scan was made within 72 hours in our hospital; computed tomography scans made within this period at a referring hospital were not included.
The diagnosis of SAH was made from the presence of extravasated blood in the basal cisterns on a computed tomography scan or, if the computed tomography scan was negative, on xanthochromia of CSF. Conventional angiography, computed tomography, or magnetic resonance angiography was performed to detect an aneurysm. If angiography could not be performed, the patient was considered to have an aneurysmal SAH if the computed tomography scan showed a typical aneurysmal pattern of hemorrhage.\textsuperscript{14}

We quantified the size of the frontal horns of the lateral ventricles by means of the bicaudate index on all computed tomography scans made within 72 hours after SAH. To calculate age-adjusted relative sizes, the bicaudate indices were divided by the corresponding upper limit per age group (95th percentile for age). Hydrocephalus was defined as an age-adjusted relative bicaudate index above 1.\textsuperscript{2,6} Acute hydrocephalus was considered present if any of the computed tomography scans performed within the first 72 hours after the hemorrhage met this computed tomography-defined criterion.

All patients who were treated for hydrocephalus within 4 days after SAH and before aneurysm occlusion were included in the study.

Rebleeding was defined as an episode of sudden clinical deterioration with evidence of fresh blood on a computed tomography scan in comparison with a previous scan or evidence of an increased amount of blood on autopsy. An episode of rebleeding before start of the analysis period was defined as either previous computed tomography–confirmed rebleeding or as a highly suggestive clinical history before admission.

The clinical condition on admission was graded by means of the World Federation of Neurological Surgeons grading scale.\textsuperscript{15} A good clinical condition was defined as grade I or II.

All patients were kept under close observation with continuous monitoring of blood pressure, heart rate, electrocardiogram, and arterial oxygen saturation for at least 2 weeks after the onset of SAH. They were treated according to a standardized protocol that consisted of strict bed rest until aneurysm occlusion, administration of nimodipine, cessation of antihypertensive medication, and intravenous administration of fluid aimed at maintaining normovolemia. Aneurysm occlusion was performed as soon as possible, but in case of a poor clinical condition, it was postponed.

### Matching Procedure

Patients treated for hydrocephalus were divided into two groups according to their drainage method: EVD versus LP. Patients who were treated with EVD after LP earlier that day were included in the EVD treatment group. However, when the interval between LP and EVD was more than 24 hours, the patient was included in both groups (in the LP group for the day of LP treatment and in the EVD group for the time of the EVD treatment). Patients from these two treatment groups were compared with two control groups retrieved from the same cohort: patients without acute hydrocephalus and patients with acute hydrocephalus without any drainage. Although hydrocephalus is not believed to be a risk factor for rebleeding,\textsuperscript{7,16–18} this design ensured to take account of the presence of hydrocephalus per se.

Treated patients and control patients were matched for possible confounding factors: interval since SAH, duration of exposure, use of tranexamic acid, clinical condition on admission, age (± 10 years), and aneurysm size.

Interval since SAH was counted in days with the day of the hemorrhage (and not day of admission) as the first day. Exposure time began at the day of starting LP or EVD and lasted until 1 day after the drainage had been stopped or until occlusion of the aneurysm or death. Within this exposure time, all controls had to be at risk for rebleeding; patients with aneurysm treatment or death within the exposure time could not serve as controls. Thus, for a patient with acute hydrocephalus and CSF drainage starting 2 days after the onset of the SAH and lasting through the sixth day, we retrieved a control patient with hydrocephalus but no treatment of the aneurysm and a control patient without hydrocephalus but no aneurysm treatment before the seventh day after the hemorrhage, and compared the risk of rebleeding in these three patients for the second through the seventh day after the onset of the SAH. All patients were matched for use of antifibrinolytics, because this protects the patients against rebleeding.\textsuperscript{19} However, for two patients in the EVD control groups, matching for clinical condition at admission could not be achieved, whereas the World Federation of Neurological Surgeons is a possible risk factor for rebleeding in some studies;\textsuperscript{8} although not in others.\textsuperscript{13,14,17} In the EVD control groups, the age limits were exceeded in nine patients with a mean age difference of 18 years.

Two patients in the LP control groups could not be matched for age, resulting in a mean age difference of 42 years in these patients. This was not considered of great importance because the daily risk for rebleeding does not increase with age.\textsuperscript{16} There are conflicting reports on whether aneurysm size is considered a risk factor for rebleeding.\textsuperscript{7,16,17} In our study, the aneurysm size of the patient was not always documented; therefore, only 11 controls could be matched for this variable in the EVD group and 17 in the LP group.

A previous episode of rebleeding increases the risk for further rebleeding.\textsuperscript{7,20} Because it was not possible to match for this factor, we adjusted for this factor in the analyses.

The amount of subarachnoid blood, the presence of intraventricular blood,\textsuperscript{16,20,21} gender, and the localization of the aneurysm\textsuperscript{16,17} are not considered risk factors for rebleeding; therefore, these factors were not included in the matching procedure.

### Analysis

Episodes of rebleeding were counted as events. Differences in the occurrence of rebleeding between patients and controls were calculated by Cox proportional hazards regression. Kaplan-Meier survival curves were used for graphic comparison.

The log rank test was used to test for overall differences in the risk of rebleeding between the three study groups for patients with EVD as well as for the group treated with LP. A probability value of less than 0.05 was considered statistically significant. We adjusted for risk factors that we could not match completely and for previous rebleeding.

### Results

In the study period, a total of 546 patients with aneurysmal SAH were admitted to our service and had a computed tomography scan within 72 hours after the ictus, of which 271 (50%) had enlarged ventricles according to our predefined computed tomography scan criteria. Of these patients, 54 (20%) underwent CSF drainage in the presence of an unprotected aneurysm. Thirty-four patients were treated with EVD and 21 patients with LP (Table 1).

The average duration of treatment of acute hydrocephalus was 6.3 days (SD: 6) in the EVD group and 2.2 days (SD: 2) in the LP group.

In the EVD treatment group, rebleeding occurred in seven of the 34 patients (21%), in seven of the 34 controls (21%) with hydrocephalus but no treatment, and in six of the 34 controls (18%) without hydrocephalus. In the LP treatment group, rebleeding occurred in one of the 21 patients (5%), in three of the 21 controls (14%) with hydrocephalus but no treatment, and in none of the 21 controls without hydrocephalus. The Kaplan-Meier survival curve of the treatment with EVD and matched control groups is shown in the Figure. There was no statistically significant difference in the proportion of patients with rebleeding between the EVD treatment group and controls ($P=0.93$, pooled log rank test) nor between the LP treatment groups and controls ($P=0.16$, pooled log rank test).

The crude hazard ratio of rebleeding was 1.0 (95% CI: 0.4 to 2.7) for EVD treatment and 0.7 (95% CI: 0.1 to 6.4)
for LP treatment compared with controls with or without hydrocephalus (Table 2).

After adjustment for rebleeding before start of the exposure time, the crude hazard ratios were essentially the same (1.0 [95% CI: 0.4 to 3.0] for EVD and 0.6 [95% CI: 0.1 to 6.1] for LP). Results were also similar after adjustment for clinical condition on admission or age, the two factors for which we did not achieve complete matching.

**Discussion**

The results of this study provide no evidence that treatment of acute hydrocephalus after SAH is associated with a substantially increased risk of rebleeding.

Several factors have been proposed to explain a perceived increase in the risk of rebleeding after ventricular drainage. A common explanation is that by drainage of CSF, the intracranial pressure is lowered, which in turn would result in increased transmural pressure on the aneurysm.3,7 Unfortunately, we do not have sufficient data of the hydrodynamic effects of the procedures such as the change of the intracranial pressure during drainage or the rate of drainage. Other theories include disruption of the blood clot by shrinking of the ventricles and enhancement of intracranial fibrinolytic activity by the ventricular drain.3

Only few studies have addressed the effect of LP on the risk of rebleeding, all of them not showing an increased risk.3,7–9 The explanation for a difference with the putative risk of ventricular drainage was that CSF pressure decreases more gradually with LP.

A possible explanation for the increased risk of rerupture after ventricular drainage reported in previous studies is that these studies did not adjust for possible confounding variables. More importantly, these studies did not take into account the duration of the “period at risk” for rebleeding nor of the interval after SAH.12 In a recent study of ventriculostomy for hydrocephalus, 4.4% of the patients had rebleeding after the procedure against 5.4% of the patients without ventriculostomy.4 These authors compared the mean interval between ventriculostomy and operative occlusion of the aneurysm with the mean time between SAH and operation in patients who did not undergo ventriculostomy and found that the mean exposure time did not significantly differ between patients with or without rebleeding. However, approximately 85% of ventriculostomies were performed between 24 and 48 hours after the hemorrhage. As a consequence, these patients were already less prone to rebleeding, because most episodes of rebleeding occur within the first 24 hours after SAH.13,17 With this experience in mind, we matched patients treated with CSF drainage with controls for interval from the onset of the SAH to achieve an unbiased comparison.

In our study, we found a large proportion of patients with enlarged ventricles (50%). This finding contrasts with an incidence of 20% to 30% found in other studies using the same criteria.1–3,5,6,21 The explanation for this difference probably is that we used the largest bicaudate index of all computed tomography scans performed within 72 hours instead of only the bicaudate index of the admission computed tomography scan.

### Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>EVD Treatment</th>
<th>Controls With Hydrocephalus</th>
<th>Controls Without Hydrocephalus</th>
<th>LP Treatment</th>
<th>Controls With Hydrocephalus</th>
<th>Controls Without Hydrocephalus</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>34</td>
<td>34</td>
<td>34</td>
<td>21</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>Mean age (SD)</td>
<td>59 (14)</td>
<td>59 (14)</td>
<td>57 (16)</td>
<td>61 (12)</td>
<td>61 (11)</td>
<td>56 (15)</td>
</tr>
<tr>
<td>Women (%)</td>
<td>18 (53)</td>
<td>19 (56)</td>
<td>20 (59)</td>
<td>12 (57)</td>
<td>11 (52)</td>
<td>13 (62)</td>
</tr>
<tr>
<td>WFNS I/II on admission (%)</td>
<td>6 (18)</td>
<td>6 (18)</td>
<td>8 (24)</td>
<td>13 (62)</td>
<td>13 (62)</td>
<td>13 (62)</td>
</tr>
<tr>
<td>Mean time to start drainage in days (SD)*</td>
<td>0.5 (0.7)</td>
<td>1.2 (1.2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean duration of drainage in days (SD)†</td>
<td>6.3 (6)</td>
<td>2.2 (2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of patients with rebleeding</td>
<td>7</td>
<td>7</td>
<td>6</td>
<td>1</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

*Counted from initial bleeding; †exposure time.

WFNS indicates World Federation of Neurological Surgeons grading scale.

### Table 2. Crude Hazard Ratios of EVD and LP Treatment

<table>
<thead>
<tr>
<th></th>
<th>Crude Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVD treatment compared with</td>
<td></td>
</tr>
<tr>
<td>All controls</td>
<td>1.04 (0.41 to 2.66)</td>
</tr>
<tr>
<td>Controls with hydrocephalus</td>
<td>0.87 (0.28 to 2.74)</td>
</tr>
<tr>
<td>Controls without hydrocephalus</td>
<td>1.15 (0.39 to 3.42)</td>
</tr>
<tr>
<td>LP treatment compared with</td>
<td></td>
</tr>
<tr>
<td>All controls</td>
<td>0.67 (0.07 to 6.41)</td>
</tr>
<tr>
<td>Controls with hydrocephalus</td>
<td>0.33 (0.04 to 3.21)</td>
</tr>
<tr>
<td>Controls without hydrocephalus</td>
<td>*</td>
</tr>
</tbody>
</table>

*No rebleeding in this control group.
Only half of the patients with enlarged ventricles had clinical signs of hydrocephalus, which explains why many patients were not treated for hydrocephalus before the aneurysm was occluded.

Although the number of patients admitted during the study period was large, the number of patients treated for hydrocephalus was relatively small. An important reason for this small proportion is that the perceived risk of rebleeding made us reluctant to perform CSF drainage in the presence of a patent aneurysm. According to the relatively small number of patients, the confidence intervals are wide, for which reason we cannot rule out an increased risk of rebleeding from CSF drainage. However, a power calculation demonstrates that to prove (more or less) definitively that CSF drainage does not increase the risk of rebleeding, a study would require over 6000 patients.

This study was performed in a retrospective manner, but we used prospectively collected information from our database. Therefore, we hardly encountered any missing values. Only aneurysm size was not documented in all patients.

In conclusion, this study provides no evidence that treatment of acute hydrocephalus in case of an unprotected aneurysm increases the risk of rebleeding importantly, although such a risk cannot be excluded and the advantage of LP over ventricular drainage remains uncertain.

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Disclosures
None.

References
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