Extent of Acute Hydrocephalus After Aneurysmal Subarachnoid Hemorrhage as a Risk Factor for Delayed Cerebral Infarction

Annelies M. Bakker, MD; Sanne M. Dorhout Mees, MD; Ale Algra, MD; Gabriël J.E. Rinkel, MD

Background and Purpose—Delayed cerebral infarction (DCI) is an important cause of poor outcome after subarachnoid hemorrhage. Cerebral perfusion is a predictor for DCI. Because acute hydrocephalus may impair cerebral perfusion, we evaluated the predictive value of the extent of acute hydrocephalus on the development of DCI.

Methods—We retrieved data on 321 patients admitted within 4 days after aneurysmal subarachnoid hemorrhage from our prospectively collected database. Ventricular enlargement was quantified by measuring the bicaudate index and the width of the third ventricle. Ventricular sizes were analyzed as continuous variables and after categorization into quartiles. The relationship between these variables and the development of DCI was analyzed by means of the Cox proportional hazards model.

Results—DCI occurred in 76 patients (23.7%). Hazard ratios for occurrence of DCI of the continuous variables were 1.01 (95% CI: 0.97 to 1.06) for the bicaudate index, 1.00 (95% CI: 1.00 to 1.01) for the age-adjusted bicaudate index, and 0.99 (95% CI: 0.92 to 1.06) for the width of the third ventricle in univariable analysis. The adjusted hazard ratio for the highest quartile of the bicaudate index versus the lowest quartile was 0.9 (95% CI: 0.5 to 1.8). No linear trend could be recognized in consecutive quartiles.

Conclusions—Acute hydrocephalus is not a risk factor for occurrence of DCI, even when the extent of hydrocephalus is taken into account. However, we cannot exclude the possibility that extensive hydrocephalus leading to coma does increase the risk for DCI if no therapeutic intervention were done. (Stroke. 2007;38:2496-2499.)

Key Words: cerebral ischemia ■ hydrocephalus ■ risk factors ■ subarachnoid hemorrhage

Aneurysmal subarachnoid hemorrhage (SAH) still has a poor prognosis; half of the patients die and one of every 5 survivors remains dependent on help for activities of daily life.1 Delayed cerebral infarction (DCI) is an important cause of death and disability after SAH.2 It occurs in approximately one third of patients, mostly between the fourth and the tenth days after the hemorrhage.3,4 Independent predictors for DCI are the neurological condition on admission and the amount of extravasated blood on the initial CT.5–7 In a recent study, we also found that cerebral perfusion on the admission CT is a strong predictor for the development of DCI.8

Because it is plausible that acute hydrocephalus has a negative influence on the cerebral perfusion, hydrocephalus on the admission scan may be a risk factor for DCI as well. In that case, early treatment of hydrocephalus with no or minor symptoms could be important in the prevention of DCI. The predictive value of acute hydrocephalus for the occurrence of DCI has been evaluated in several studies; most found no relationship.5–7,9–11 Yet, all studies classified acute hydrocephalus dichotomously as “present” or “absent,” and some studies even lacked a well-described definition of hydrocephalus.9–11 However, not only the presence, but also the severity of the hydrocephalus may be of great importance for the relationship with cerebral perfusion and subsequently for the development of DCI.

We studied the relationship between the extent of acute hydrocephalus on the admission CT scan and the occurrence of DCI.

Methods

Patients

Data on patients were retrieved from a prospectively collected database on all patients with aneurysmal SAH admitted to the University Medical Center Utrecht. Patients were included in the current study if they had been admitted between February 2002 and February 2006 and if the initial CT scan was performed within 4 days after the onset of SAH. Patients were excluded when they died in the first 24 hours after the hemorrhage or when the initial CT scan was no longer available for reevaluation.

Aneurysmal SAH was diagnosed by the presence of blood on CT or of xanthochromia of the cerebrospinal fluid in combination with an aneurysm confirmed by conventional or CT angiography. Clinical
condition on admission was graded by means of the World Federation of Neurologic Surgeons grading scale. The amount of cisternal blood on the initial CT was graded according to the method described by Hijdra. The Hijdra score has a better interobserver agreement than the Fisher score and is an independent prognostic factor for DCI and clinical outcome.

Ventricular enlargement on the admission scan was quantified by measuring the bicaudate index (BCI) and the width of the third ventricle on the admission CT scan. The BCI is the width of the frontal horns at the level of the caudate nuclei and the foramen of Monro divided by the corresponding diameter of the brain. To calculate age-adjusted relative sizes, the BCIs were divided by the corresponding upper limit (95th percentile) per age group. We measured the widest diameter of the third ventricle in millimeters. The measurements of the bicaudate index and the third ventricle were done blinded as far as knowledge about occurrence of DCI. The third ventricle measurements were done for a subset of the 200 most recent admitted patients for the pragmatic reason that these CT scans could be electronically retrieved. The BCIs in the other patients had been measured previously.

DCI was defined as the occurrence of new clinical features suggestive of DCI (gradually developed focal deficits, decreased level of consciousness, or both) confirmed by a new hypodense lesion on CT compatible with the clinical features.

**Data Analysis**

First, we calculated crude hazard ratios (HR) for the occurrence of DCI for the bicaudate index, the relative bicaudate index, and the width of the third ventricle as continuous variables by means of the Cox proportional hazards model. Subsequently, patients were categorized into quartiles based on the bicaudate index, the relative bicaudate index, and the width of the third ventricle. HRs for the occurrence of DCI were calculated for the higher quartiles in comparison with the lowest quartile. HRs were adjusted for age, because ventricular size increases with age. Also, because hydrocephalus might be of more importance in younger patients, the same analysis was performed for the bicaudate index for patients younger than the median age of all patients. Neurological condition on admission and amount of cisternal blood were adjusted for if bivariable analysis changed the HR more than 5% in at least one quartile.

**Results**

During the study period, 390 patients with an aneurysmal SAH were admitted to our hospital with a CT scan performed within 4 days after the SAH. Forty-six patients were excluded because they had died within 24 hours after admission and another 17 patients because the initial CT scan could no longer be retrieved. In 6 other patients, clinical data were insufficient to rule in or rule out the occurrence of DCI, and these patients were excluded as well. The remaining 321 patients were included in this study. Baseline characteristics of these patients are shown in Table 1.

### Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N=321</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>56 (14)</td>
</tr>
<tr>
<td>Women, %</td>
<td>72</td>
</tr>
<tr>
<td>Poor clinical condition on admission: WFNS IV-V, %</td>
<td>27</td>
</tr>
<tr>
<td>Amount of cisternal blood: Hijdra score &gt;23, %</td>
<td>50</td>
</tr>
<tr>
<td>Bicaudate index</td>
<td>0.17 (0.05)</td>
</tr>
<tr>
<td>Relative bicaudate index</td>
<td>0.92 (0.26)</td>
</tr>
<tr>
<td>Third ventricle width* mm</td>
<td>8 (4)</td>
</tr>
</tbody>
</table>

Values are means (SD) or percentages. *n=200.

WFNS indicates World Federation of Neurologic Surgeons.

The HR for the bicaudate index for the occurrence of DCI was 1.01 (95% CI: 0.97 to 1.06) in the univariable analysis (Table 2). For each increase of 0.1 of the bicaudate index, the risk for DCI increases with 1% with a confidence interval between 3% decrease and 6% increase in risk. Univariable analysis showed a HR of 1.00 (95% CI: 1.00 to 1.01) for the relative bicaudate index and a HR of 0.99 (95% CI: 0.92 to 1.06) for the width of the third ventricle. The HRs were not influenced by other variables in bivariable analyses and so no multivariable analysis was performed.

Table 3 shows the crude and adjusted HRs for the quartiles of the bicaudate index. The adjusted HR for the highest quartile of the bicaudate index versus the lowest quartile for the occurrence of DCI was 0.9 (95% CI: 0.5 to 1.8).

The adjusted HR in patients aged under 56 years of age for the highest quartile of the bicaudate index versus the lowest quartile was 1.1 (95% CI: 0.3 to 2.3). Consecutive quartiles did not show a linear trend in either analysis. Analysis of the relative bicaudate index and the width of the third ventricle divided into quartiles yielded similar results (data not shown).

**Discussion**

This study shows that acute hydrocephalus is not a risk factor for the occurrence of DCI. The analysis of the width of the frontal horns and the third ventricle as continuous variables and analysis of these measures in quartiles all failed to show a relationship with the development of DCI. Moreover, HRs of consecutive quartiles of these measures of ventricular size did not show a linear trend.

We have 2 possible explanations for the absence of a relation between hydrocephalus and occurrence of DCI. First, in contrast with our assumption, there might not be a
relationship between acute hydrocephalus and cerebral perfusion. Second, in our study, we assessed only the extent of the hydrocephalus on the admission CT scan as a determinant and not the duration of the hydrocephalus. The duration of hydrocephalus depends on spontaneous improvement, which can be assessed only by means of repeated CT scans, and therapeutic interventions. In our study, the duration of hydrocephalus and therapeutic interventions were not taken into account. However, in our hospital, acute hydrocephalus is only treated in case of a severely decreased level of consciousness. Thus, our results pertain mainly to moderate degrees of hydrocephalus, and we cannot exclude the possibility that extensive hydrocephalus leading to coma does increase the risk for DCI if no therapeutic intervention were done. Because cerebral perfusion on admission is a risk factor for the development of DCI, irrespective of therapeutic interventions, the absence of a relation between hydrocephalus on admission and DCI further suggests that factors other than hydrocephalus determine the cerebral perfusion on admission.

The large sample size of our study, with 76 patients developing DCI, has the advantage that even small risks would have been detected. Other strengths of our study are the prospective collection of patients and the blinded assessment of ventricular size. The finding that, like in previous studies, neurological condition on admission and the amount of cisternal blood were predictors for the occurrence of DCI (Table 2) further validates our study sample.

A limitation is that the size of the third ventricle was assessed only in the subset of the 200 most recently admitted patients. Nevertheless, it is not likely that an analysis of the width of the third ventricle in all 321 patients would have yielded different results. Another limitation might be the strict definition of DCI, which included the presence of hypodense lesions on CT scan. Therefore, milder forms of DCI might have been missed. However, we do not expect that a possible underestimation of the incidence of DCI would have altered our results.

Previous studies investigated the predictive value of acute hydrocephalus, classified dichotomously as "present" or "absent." Most studies did not find a relation between acute hydrocephalus and DCI, but in one Japanese study, an adjusted odds ratio of 2.3 (95% CI: 1.2 to 4.2) was found. This opposite result could be explained by differences in study population (Japanese and European), time periods of the study (with inherent progress of medical treatment in the last decade), and methodology (with no clear definition of hydrocephalus in the Japanese study). Our study adds additional value to the current literature, because it is the first in which the extent of acute hydrocephalus is taken into account. By applying quartiles in our data analysis, we could differentiate between moderate and severe forms of hydrocephalus. We expected a higher risk for DCI in severe forms of hydrocephalus. However, our results did not show a relationship between the extent of hydrocephalus and the occurrence of DCI.

In conclusion, this study shows convincingly that the presence of acute hydrocephalus has no predictive value for the development of DCI irrespective of the severity of the hydrocephalus. However, we cannot exclude the possibility that extensive hydrocephalus leading to coma does increase the risk for DCI if no therapeutic intervention would be done.

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Disclosures
None.

References


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