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ORIGINAL RESEARCH

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BACKGROUND AND PURPOSE: Acute hydrocephalus after aneurysmal subarachnoid hemorrhage (SAH) may decrease cerebral perfusion by increasing intracranial pressure. We studied cerebral perfusion in patients with and without acute hydrocephalus after SAH.

MATERIALS AND METHODS: We performed noncontrast CT scans, CT perfusion (CTP), and CT angiography on admission in all patients with aneurysmal SAH. Patients were dichotomized at a relative bicaudate index of 1 for the presence or absence of hydrocephalus. Cerebral perfusion was measured in the cortex, basal ganglia, and periventricular white matter. Mean CTP parameters were compared between patients with and without acute hydrocephalus (ie, within 3 days after SAH).

RESULTS: We included 138 consecutive patients with successful CTP measurements, of whom 49 (36%) had acute hydrocephalus. Mean cerebral blood flow (CBF) was lower in patients with hydrocephalus than in those without in the basal ganglia (difference of means, 6.8; 95% CI, 1.6–11.0 mL/100 g/min) and periventricular white matter (difference of means, 3.8; 95% CI, 0.9–6.8 mL/100 g/min) but not in the cortex (difference of means, 1.8; 95% CI, −2.8 to 6.4 mL/100 g/min). In all regions studied, mean transit time (MTT) and time-to-peak (TTP) were statistically significantly longer in patients with hydrocephalus, but cerebral blood volume (CBV) values were similar.

CONCLUSIONS: Acute hydrocephalus after SAH reduces CBF in the deep gray matter and periventricular white matter and delays MTT and TTP in all investigated brain areas. The negative effect of acute hydrocephalus on cerebral perfusion in patients with SAH seems more pronounced in the vicinity of the ventricles than in remote sites.

Acute hydrocephalus is a frequent complication of aneurysmal subarachnoid hemorrhage (SAH)[1] and often leads to clinical deterioration. Spontaneous recovery occurs within 24 hours in approximately half of these patients.[2] Besides a policy of wait and see, other treatment options are external drainage or (serial) lumbar puncture.[3-5] In patients who are not comatose, an initial policy of waiting for spontaneous recovery has been advocated[1] because external drainage carries a definite risk for complications such as infection[3-6] and is possibly associated with an increased risk of rebleeding, though not all studies agree.[7-9] However, hydrocephalus may decrease cerebral blood flow (CBF) by an increase of intracranial pressure,[10] even in patients who are awake. A few small studies in which CBF was measured with xenon-133 (^{133}Xe) or single-photon emission CT (SPECT) found decreased perfusion in patients with acute hydrocephalus after SAH.[11-13]

Our aim was to obtain insight into the effect of acute hydrocephalus on cerebral perfusion. For this purpose, we related hydrocephalus to cerebral perfusion in the cortex, basal ganglia, and periventricular brain tissue in several patients. Cerebral perfusion was measured by means of CT perfusion (CTP), a readily available and valid method to study CBF.[14]

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Materials and Methods

Patients

We included a consecutive series of patients with aneurysmal SAH admitted between September 2003 and June 2006. Since September 2003, all patients in whom SAH is confirmed on the admission noncontrast CT (NCCT) scan undergo CT angiography (CTA) and CTP. The CTP is performed before the CTA and serves as a timing scan. All patients admitted to our service with a nontraumatic SAH are prospectively entered in a data base immediately after admission. From this data base, we retrieved patients with a proved aneurysmal source of the SAH who had been admitted less than 72 hours after onset of the symptoms. Exclusion criteria for the current study were admission to our hospital more than 3 days after SAH, age younger than 18 years, a history of stroke before the SAH, the presence of an intracerebral hematoma causing compression of the ventricular system, no available perfusion scan before the placement of a ventricular drain, and CTP of poor quality. All participants gave written informed consent, and the study was approved by the medical ethics committee of our institution.

Determinants

For included patients, we measured the size of the ventricular system by means of calculating the bicaudate index (BCI); "the width of the frontal horns at the level of the caudate nuclei divided by the corresponding diameter of the brain."[4] The relative BCI was obtained by dividing the patient's BCI by the normal upper limit (95th percentile) for age.[4] Acute hydrocephalus was defined as a relative BCI of more than 1. The amount of cisternal and intraventricular blood on the NCCT scan was graded by means of the Hijdra score.[15] The clinical condition on admission was graded by means of the World Federation of Neurologic Surgeons grading scale.[16]

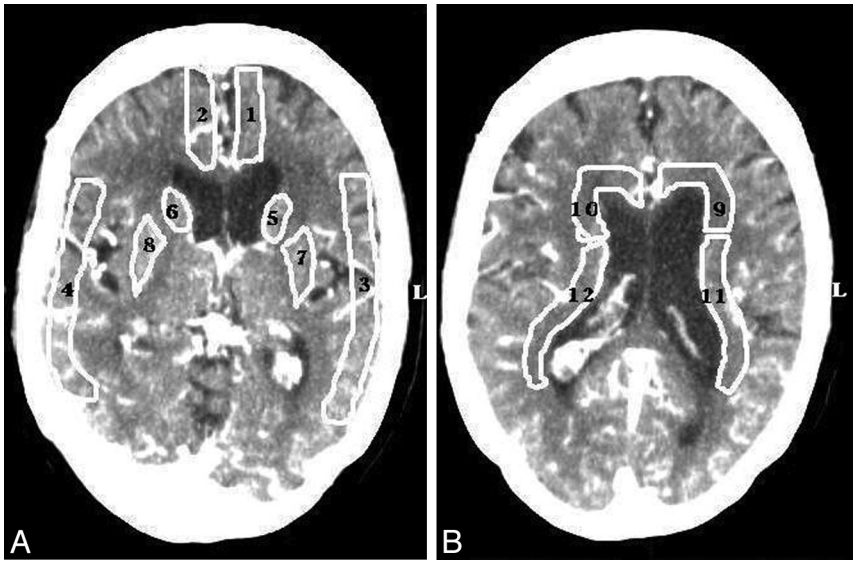

Fig 1. *A,* ROIs that were drawn in the flow territories of the anterior cerebral artery (cortex: ROIs 1 and 2, basal ganglia: ROIs 5 and 6) and the middle cerebral artery (cortex: ROIs 3 and 4, basal ganglia: ROIs 7 and 8). *B,* In the periventricular white matter, ROIs were drawn anterior (ROIs 9 and 10) and on either side (ROIs 11 and 12) of the lateral ventricles.

Table 1: Patient characteristics

Characteristic	Hydrocephalus	No Hydrocephalus
No. of patients (%)	49 (36)	89 (65)
Mean age (SD)	59.8 (13)	54.1 (14)
Women (%)	31 (63)	65 (73)
Admission WFNS score (%)		
I	20 (41)	47 (53)
II	7 (14)	12 (14)
III	7 (14)	9 (10)
IV	11 (22)	12 (13)
V	4 (8)	9 (10)
Day (after SAH) of admission scan (%)		
0	33 (67)	56 (63)
1	10 (20)	24 (27)
2	4 (8)	5 (6)
3	2 (4)	4 (5)
Amount of blood (Hijdra score)		
Median cisternal sum score	24	22
Median ventricular sum score	2	0
Mean bicaudate index (SD)	0.22 (0.3)	0.14 (0.3)
Mean relative bicaudate index (SD)	1.2 (0.1)	0.75 (0.2)
Aneurysm location (%)		
Anterior communicating[a]	22 (45)	41 (46)
Internal carotid artery	6 (12)	14 (16)
Middle cerebral artery	6 (12)	17 (19)
Posterior[b]	15 (31)	17 (19)

Note:—WFNS indicates World Federation of Neurologic Surgeons; SAH, subarachnoid hemorrhage.
[a] Includes the anterior cerebral artery.
[b] Basilar or vertebral arteries.

CTP Technique and Measurements

CTP Technique. The imaging studies were performed on a 16-section spiral CT scanner (Mx8000 IDT; Philips Medical Systems, Best, the Netherlands). The conventional timing scan that is required to perform a CTA was replaced by the CTP scan, which provides the same timing information. With CTP, quantitative data on cerebral blood volume (CBV), CBF, mean transit time (MTT), and time-to-peak (TTP) are obtained. CTP source data were derived from sequential scans covering a slab of 2.4-cm thickness selected 3 cm above the sella turcica and angulated parallel to the meato-orbital line containing the upper parts of the lateral ventricles and the basal ganglia. There was 40 mL of nonionic contrast agent (Iopromide Ultravist, 300 mg iodine/mL; Schering, Berlin, Germany) that was injected into the cubital vein (18-gauge needle) at a rate of 5 mL/s followed by a 40-mL saline flush at a rate of 5 mL/s by use of a dual power injector (Stellant Dual CT injector; Medrad Europe, Beek, the Netherlands). The following parameters were used: 90 kVp, 150 mAs, 8 × 3-mm collimation, 512 × 512 matrix, 200-mm FOV, 1 image per 2 s during 60 s (total, 30 images), brain standard (UB) filter, and standard resolution.

CTP Postprocessing and Measurements. Data were transferred to a Philips workstation (Best, the Netherlands) for postprocessing. The algorithm was based on the central volume principle and CBF was calculated by the deconvolution method.[17] CTP scans were initially reconstructed at 12 mm and at 6-mm contiguous axial images later in the study to reduce partial volume effects. The arterial input function (AIF) and the venous output function (VOF) were obtained semiautomatically, with the user selecting vascular regions of interest (ROIs) and the computer algorithm choosing the optimal AIF and VOF. The major vessels, intracerebral hemorrhage, and CSF were discarded automatically by means of thresholding. Eight ROIs (Fig 1*A*) were drawn in the peripheral (cortical) and deep (basal ganglia) flow territories of the anterior cerebral artery and the middle cerebral artery. Four ROIs were drawn in the periventricular white matter (Fig 1*B*). CTP postprocessing and measurements were performed retrospectively.

Data Analysis

Patients were dichotomized at a relative bicaudate index of 1 for the presence or absence of acute hydrocephalus. We used descriptive statistics for demographic data, clinical condition on admission, scan on the day of admission, and aneurysmal location for patients with and without hydrocephalus. Median values of the cisternal and ventricular sum score of extravasated blood were calculated for patients with and without hydrocephalus.

The CTP variables were normally distributed and were used as continuous variables. Because CBF and CBV differ between gray and white matter,[18] we calculated mean cerebral perfusion values with

Table 2: Cerebral perfusion in patients with and without hydrocephalus

	Hydrocephalus	Cortex	Difference of Means (95% CI; *P* Value)	Basal Ganglia	Difference of Means (95% CI; *P* Value)	Periventricular White Matter	Difference of Means (95% CI; *P* Value)
Mean CBV (mL/100 g) (SD)	No	4.0 (1.2)	−0.1 (−0.4 to 0.1; *P* = .41)	4.1 (1.2)	−0.2 (−0.5 to 0.2; *P* = .35)	3.1 (0.9)	0.1 (−0.2 to 0.3; *P* = .61)
	Yes	4.1 (1.0)		4.3 (1.3)		3.0 (0.9)	
Mean CBF (mL/100 g/min) (SD)	No	53.4 (18.2)	1.8 (−2.8 to 6.4; *P* = .43)	62.7 (21.1)	6.2 (1.6 to 11.0; *P* = .014)	32.4 (11.0)	3.8 (0.9 to 6.8; *P* = .005)
	Yes	51.6 (18.6)		56.5 (17.2)		28.6 (10.3)	
Mean MTT (seconds) (SD)	No	4.9 (1.8)	−0.5 (−1.1 to −0.1; *P* = .048)	4.3 (1.7)	−0.7 (−1.1 to −0.1; *P* = .008)	6.0 (1.9)	−0.9 (−1.6 to −0.2; *P* = .004)
	Yes	5.4 (2.7)		5.0 (1.9)		6.9 (2.8)	
Mean TTP (seconds) (SD)	No	23.4 (5.5)	−1.6 (−3.0 to −0.1; *P* = .28)	23.1 (5.6)	−1.4 (−2.9 to 0.1; *P* = .056)	25.7 (4.6)	−1.7 (−3.1 to −0.3; *P* = .034)
	Yes	25.0 (6.0)		24.5 (5.9)		27.4 (5.4)	

Note:—CI indicates confidence interval; CBV, cerebral blood volume; CBF, cerebral blood flow; MTT, mean transit time; TTP, time-to-peak.

SDs separately for the cortical ROIs (ROIs, 1–4), basal ganglia ROIs (ROIs, 5–8), and periventricular white matter ROIs (ROIs, 9–12). We compared differences in mean values of cerebral perfusion between patients with and without hydrocephalus by calculating the 95% confidence interval (CI) of the mean difference.

Results

Of the 138 patients who met our inclusion criteria, 49 (36%) had acute hydrocephalus on the admission CT scan. Patients without hydrocephalus were younger (54.1 years [SD, 14 years]) than those with hydrocephalus (59.8 years [SD, 13 years]) and were more often women (73%) than those with hydrocephalus (63%) (Table 1).

Perfusion of Cortex. CBV and CBF values were similar in patients with or without acute hydrocephalus (Table 2). In patients with hydrocephalus, MTT was 5.4 s, and in those without hydrocephalus, MTT was 4.9 s (difference, −0.5; 95% CI, −1.1 to 0.1 s). TTP was 25.0 s in patients with hydrocephalus and 23.4 s in those without hydrocephalus (difference, −1.6; 95% CI, −3.1 to −0.1 s).

Perfusion of Basal Ganglia. In the deep gray matter, no statistically significant differences in CBV values were seen between patients with and those without acute hydrocephalus. CBF was 62.7 mL/100 g/min in patients without hydrocephalus and 56.5 mL/100 g/min in those with acute hydrocephalus (difference, 6.2; 95% CI, 1.6 - 11.0 mL/100 g/min). MTT was shorter in patients without hydrocephalus than in those with acute hydrocephalus (4.3 vs 5.0 s; difference, −0.7 s; 95% CI, −1.1 to −0.1 s), as was TTP, though this difference did not reach statistical significance (23.1 vs 24.5 s; difference, −1.4 s; 95% CI, −2.9 to 0.1 s).

Perfusion of Periventricular White Matter. We were not able to draw periventricular ROIs in 20 CTP scans because the periventricular white matter of the lateral ventricles was not visible. In the 118 patients who could be included in the periventricular white matter measurements, 43 (36.4%) had acute hydrocephalus. Patients with and without hydrocephalus had similar CBV values. Patients with hydrocephalus had a significantly lower CBF than patients without hydrocephalus (28.6 vs 32.4 mL/100 g/min; difference, 3.8; 95% CI, 0.9 - 6.8 mL/100 g/min) and a longer MTT (6.9 vs 6.0 s; difference, −0.9 s; 95% CI, −1.6 to −0.2 s) and TTP (27.4 vs 25.7 s; difference, −1.7 s; 95% CI, −3.1 to −0.3 s).

Discussion

Previous studies have found that acute hydrocephalus after aneurysmal SAH affects cerebral perfusion. In this study, we demonstrated that in patients with hydrocephalus, CBF is reduced in the basal ganglia and periventricular white matter but not in the cortex. Therefore, our data suggest that the impact of hydrocephalus is a more local than a global process. The effect seems to be more pronounced in the vicinity of the ventricles than in more remote sites.

Several studies have showed that chronic, so-called normal pressure hydrocephalus reduces cerebral perfusion in patients with SAH.[19,20] Data on the effect of acute hydrocephalus, which often results in very high pressures of the CSF, on cerebral perfusion are scarce. Two studies that used ^{133}Xe to assess CBF found reduced CBF in the hemispheric gray matter or combined gray and white matter in patients with acute hydrocephalus after SAH.[11,12] The results of these 2 studies are not entirely in concordance with our findings because we did not find a significant reduction of CBF in the cortical gray matter of patients with acute hydrocephalus. These different results might be explained by the different control groups used in the ^{133}Xe studies. In the ^{133}Xe studies, the control group consisted of healthy subjects,[11,12] whereas the "nonhydrocephalus" group in our study consisted of all patients with a BCI under the normal upper limit (95th percentile) of age. In some of these patients, the ventricles may have been larger than before the SAH, though no hydrocephalus existed according to our definition. This may have decreased the difference between the 2 groups in our study and may explain the small differences in perfusion parameters that we found in the cortex of patients with acute hydrocephalus vs those without hydrocephalus. Another reason for the discordance might be the limited spatial resolution of the older xenon studies, which made it harder to differentiate between gray and subcortical white matter. Unintended measurement of perfusion in subcortical white matter voxels may have resulted in an apparent decrease in perfusion of "cortical" areas.

A preliminary study that used serial CTP to assess CBF in 15 patients with SAH found a reduction of CBF in either gray and white matter on days 1 to 3 after SAH, but in that study, 14 of the 15 patients were in good clinical condition on admission, and the presence or absence of acute hydrocephalus was not taken into account.[18] It is possible that CBF is not reduced only in patients with SAH and acute hydrocephalus but rather, to some extent, in patients without ventricular enlargement

as well. To investigate the effect of the SAH itself on CBF, we have to compare values of patients with SAH with and without acute hydrocephalus vs CTP values in healthy subjects. However, we could not include such a control group because measurement of CTP in healthy control subjects would be unethical. Although we perform CTP studies in patients with idiopathic thunderclap headache on a regular basis, we chose not to use them as control subjects. It has been suggested that the caliber of small vessels is altered in patients with thunderclap headache[21]; therefore, we cannot rule out the possibility that cerebral perfusion in these patients is compromised.

A SPECT study in 4 patients with acute hydrocephalus showed a decreased uptake of technetium Tc99m mainly in the basal parts of the brain.[13] This suggests a local decrease of CBF instead of a more generalized effect, as we have found in our study.

The maintenance of perfusion in the cortical gray matter compared with the periventricular white matter might be explained by less direct pressure from the dilated ventricles on the cortex than on the periventricular white matter. Another explanation may be related to differences in architecture of the arterial vascularization of the cortex and white matter, both on a macrovascular and microvascular level. Large pial and leptomeningeal vessels are more in the vicinity of the cortical gray matter compared with the periventricular white matter. Also, the attenuation of brain capillaries is significantly higher in the cortex compared with the white matter.[22]

We measured cerebral perfusion in a large consecutive series of patients with SAH with a wide range of clinical conditions on admission. By using CTP, we were able to investigate different perfusion parameters at several predefined regions in gray and white matter. This setting enabled us to study the effect of acute hydrocephalus on perfusion in different brain areas. In the current study, we used a 16-section scanner, which restricted our measurements to the level of the basal ganglia and the lateral ventricles. Because it is likely that acute hydrocephalus causes an upward shift of the cortex at the vertex, it would have been interesting to perform perfusion measurements in this region. With the introduction of 64- or 128-section scanners, more brain tissue can be covered, permitting us in the future to investigate the effect of acute hydrocephalus in more brain areas. Our study gives more insight in the negative effect of hydrocephalus on cerebral perfusion, which seems to affect the deep brain areas predominantly.

A limitation of our study was that we can only speculate about how cerebral perfusion is related to intracranial pressure (ICP) and mean arterial blood pressure because these possible determinants were not taken into account. However, the current techniques to measure ICP are invasive and are not able to measure ICP at several brain regions.

A prospective follow-up on the changes in perfusion after treatment of hydrocephalus may indirectly provide some information on the relationship between pressure and cerebral perfusion.

Conclusions

We observed a negative effect of acute hydrocephalus on cerebral perfusion in patients with aneurysmal SAH. This effect seems to be more pronounced in the vicinity of the ventricles than in remote sites.

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