Vasospasm secondary to subarachnoid hemorrhage (SAH) presents in some 40% to 70% of all cases and is symptomatic in 17% to 40% of patients. Despite preventive medical treatment, vasospasm-related ischemia may become symptomatic. In fact, vasospasm is responsible for numerous deaths or ischemic neurological sequelae and is reported to double the risk of mortality in SAH. Although percutaneous angioplasty can restore artery lumen size, it must be performed immediately after the onset of symptoms if clinical disturbances are to be reversed or averted. This poses the problem of diagnosis. Two methods of investigation are available: angiography, which provides evidence of arterial lumen narrowing, and transcranial Doppler (TCD), which plots and compares circulating blood velocities, thereby providing an indirect diagnosis of vasospasm. Blood flow velocities in the middle cerebral artery (MCA) are considered directly proportional to vasospasm severity; i.e., vasospasm is mild at average speeds of 80 to 120 cm/s, moderate at 130 to 200 cm/s, and severe above that figure. Neither of these modalities provides evidence of the actual status of the parenchyma, however. This is especially important in sedated or comatose patients in whom objective clinical tests are not feasible.

Although TCD performed at regular intervals monitors blood velocities, it would be useful to have indicators of cerebral damage. Cerebral perfusion abnormalities during vasospasm have already been studied with single-photon emission CT, positron emission tomography, xenon-enhanced CT, and perfusion-weighted MRI. Early parenchymal involvement has not been detectable until now, however. Recently developed diffusion- and perfusion-weighted MRI techniques are highly sensitive in the investigation of ischemia. In our view, they may also prove to be a useful diagnostic tool for the investigation of vasospasm. To our knowledge, very few studies so far have been conducted on the diagnostic value of these methods of investigation.

This study aimed to assess the extent to which diffusion-weighted MRI (DWI) detects vasospasm-induced ischemia and to study the correlation between DWI, clinical symptoms,
and blood flow. In addition, patients were followed up to assess whether the abnormalities on DWI progressed over time to become established ischemic lesions or whether they could be reversed.

Subjects and Methods

Patients

All patients in the early stages of SAH (Table 1) who are referred to our hospital receive preventive medical treatment for vasospasm consisting of IV nimodipine. After endovascular treatment of the ruptured aneurysm (day 1), patients undergo TCD at days 5, 10, and 15. In the event of vasospasm, TCD is performed every 48 hours. When blood flow values indicate the presence of vasospasm, MRI is performed within the framework of a study protocol, which has already been approved by our regional Ethics Committee, that aims to assess the usefulness of DWI in SAH with secondary vasospasm.

Inclusion Criteria

Inclusion criteria for the study were as follows: (1) SAH of <8 days; (2) cerebral blood flow values indicative of vasospasm; ie, mean circulatory values >120 cm/s in at least 1 vascular axis of the circle of Willis; (3) patient age >18 years; (4) a clinical condition permitting the patient to be transported and undergo MRI; and (5) informed and signed consent.

So far, we have studied 7 patients within the framework of the protocol (group 1). Five have remained asymptomatic while 2 have presented with neurological deficit. A control group has been formed consisting of 4 patients (group 2) whose circulating blood flow velocities are <120 cm/s. This control group was studied by morphological and DWI investigations. Finally, we compared group 1 with 3 other patients (group 3) who presented during the same period with symptomatic vasospasm and who therefore could not be included in the protocol.

Protocol

Acute Phase

When TCD records blood flows exceeding 120 cm/s in at least 1 vascular axis, MRI is performed within 48 hours. This step is repeated when blood flow exceeds 160 cm/s, when values then rise>

>200 cm/s, or when a clinical episode occurs. In the absence of these events, MRI is repeated 4 to 6 days after the first investigation.

Magnetic Resonance Imaging

All investigations were conducted on a 1.5-T system (Signa imager, General Electric Medical Systems). For the T2 fast spin-echo axial sequence, we used the following parameters: repetition time (TR)=3800 ms, echo time (TE)=95 ms, echo train length=8, 20 slices of 5 mm/1.5 mm, 2 excitations, matrix=512×256, and field of view (FOV)=24×18 cm. For the fluid-attenuated inversion recovery (FLAIR) fast sequence, the following parameters were used: TR=9000 ms, TE=140 ms, TI=2200, matrix=256×256, 20 slices of 5 mm/0 mm, 1 excitation, and FOV=24 cm. For the DWI MRI (spin-echo echo-planar imaging), the following parameters were used: b=0 and b=1000, 1 shot, minimum TE, TR=10 000 ms, 16 overlapping 5-mm slices, FOV=28 cm, matrix=128×128, a diffusion gradient applied on the 3 axes, and acquisition time=1 minute, 20 seconds.

Subsequent Investigations

A follow-up MRI (morphological study and DWI) was performed between 5 weeks and 2 months subsequent to SAH. Patients also underwent a morphological MRI 6 months after the episode as part of our hospital’s routine follow-up program for aneurysms treated with the endovascular procedure (Table 2).

Data Processing

DWI sequence data were fed into an adjacent workstation (Advantage for Windows 3.1, Sun Microsystem) and processed with FUNCTOOL software (General Electric Medical Systems). Diffusion images (B=1000) were scanned for signal abnormalities, after which an apparent diffusion coefficient (ADC) map and quantitative assessment were made.

ADC Calculation

Initially, we devised symmetric regions of interest (ROIs) in the suspect areas on the ADC map. The technique was applied by using ROIs of differing size. This process, however, generated ROIs containing both gray and white matter and even cerebrospinal fluid, often containing blood, in the cortical sulci. To match the ADC values with the different structures, we decided to provide systematic digital readings in predefined regions (ie, the frontal cortex [F2], the

TABLE 1. Characteristics of patients

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Group</th>
<th>Age, y</th>
<th>Aneurysm Location</th>
<th>Treatment Delay/SAH</th>
<th>Secondary Neurological Signs</th>
<th>Clinical Status (6-Month Follow-Up)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>36</td>
<td>LMCA</td>
<td>d1</td>
<td>Transient aphasia (d8–d10)</td>
<td>Normal</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>62</td>
<td>ACoA</td>
<td>d1</td>
<td>Confusion (d7–d15)</td>
<td>Cognitive deficit</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>24</td>
<td>RMCA</td>
<td>d1</td>
<td>None</td>
<td>Normal</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>61</td>
<td>ACoA</td>
<td>d1</td>
<td>None</td>
<td>Normal</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>40</td>
<td>RMCA</td>
<td>d1</td>
<td>None</td>
<td>Normal</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>34</td>
<td>RMCA</td>
<td>d1</td>
<td>None</td>
<td>Normal</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>38</td>
<td>RMCA</td>
<td>d1</td>
<td>None</td>
<td>Normal</td>
</tr>
<tr>
<td>8</td>
<td>2</td>
<td>52</td>
<td>ACoA</td>
<td>d1</td>
<td>None</td>
<td>Normal</td>
</tr>
<tr>
<td>9</td>
<td>2</td>
<td>42</td>
<td>RiCA</td>
<td>d1</td>
<td>None</td>
<td>Normal</td>
</tr>
<tr>
<td>10</td>
<td>2</td>
<td>48</td>
<td>RMCA</td>
<td>d1</td>
<td>None</td>
<td>Normal</td>
</tr>
<tr>
<td>11</td>
<td>2</td>
<td>35</td>
<td>PICA</td>
<td>d1</td>
<td>Minor cerebellar syndrome</td>
<td>Normal</td>
</tr>
<tr>
<td>12</td>
<td>3</td>
<td>36</td>
<td>LMCA</td>
<td>d8</td>
<td>Transient right arm deficit</td>
<td>Normal</td>
</tr>
<tr>
<td>13</td>
<td>3</td>
<td>28</td>
<td>LMCA</td>
<td>d3</td>
<td>Right hemiplegia</td>
<td>Right arm paresis</td>
</tr>
<tr>
<td>14</td>
<td>3</td>
<td>37</td>
<td>ACoA</td>
<td>d10</td>
<td>Left crural deficit</td>
<td>Normal</td>
</tr>
</tbody>
</table>

ACoA indicates anterior communicating artery; ICA, internal carotid artery; and PICA, posteroinferior cerebellar artery.
centrum semiovale, the frontoparietal cortex, thalamus, and lenticular nucleus) by using a series of point-by-point seriated measurements. This is done by defining a reference line against which each pixel is attributed a value. In this way, each ROI is then 5 mm³ (1 voxel). Measurements are performed symmetrically in the 2 hemispheres. When lesions appear on DWI, a more in-depth investigation is conducted in the ROI, either by using the same investigative technique or by enlarging the ROI over the area in both hemispheres.

In the cortex, some ROIs were located in the sulci. After verifying on the b0 images the locations where the sulci would appear as a hyperintense signal, these values were eliminated. In some cases, the presence of blood in the sulci made it difficult to visualize the exact ROI location. This problem can be overcome by using other sequences, ie, FLAIR, to eliminate ROIs in blood-filled sulci. Blood is visualized as a hyperintensity on FLAIR images and as a hypointense signal on T2-weighted images, thus causing a reduction of diffusion.13–15

**Treatment**

Initially, the curves for the 2 hemispheres were compared visually. Subsequently, statistical comparison was made of the values obtained from the Mann-Whitney test (StatView software). The difference was considered significant when \( P < 0.05 \) (Figures 1 through 3).

**Results**

**Patients With No Vasospasm**

The 4 patients without vasospasm (group 2) did not present any evidence of abnormal parenchymal signals either on DWI or on morphological imaging, nor was any significant asymmetry of ADC values found outside the central gray nuclei.

The only zones returning a hyperintense signal on DWI were those affected by SAH (Table 2).

**Patients With Symptomatic Vasospasm**

Patients who presented with symptomatic vasospasm on arrival (group 3) showed abnormal hyperintensity on DWI and marked reduction of the ADC compared with the other hemisphere. These abnormalities were found in the territory affected by vasospasm, with ample involvement of the cortex, subcortical white matter, and the junctional territories of the centrum semiovale, which appeared as small, focal lesions in 2 patients (Nos. 12 and 13). Abnormalities on DWI were

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Group</th>
<th>TCD (d)/SAH, Mean Blood Velocity (cm/s), Artery</th>
<th>MRI, d After Rupture</th>
<th>SP Diff</th>
<th>ADC Decrease/SP Diff</th>
<th>T2 FLAIR/SP Diff</th>
<th>T2 FLAIR (Last MRI)/SP Diff (1st MRI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>d7/160 (LMCA) d10/160 (LMCA)</td>
<td>11, 15, 45</td>
<td>Normal</td>
<td>Diffuse (LMCA territory)</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>d7/200 (RMCA) d9/270 (LACA)</td>
<td>8, 14, 36</td>
<td>Normal, d9</td>
<td>Asymetric measures</td>
<td>=</td>
<td>Small lesions decrease/d14</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>d6/120 (RMCA) d8/120 (RMCA)</td>
<td>11, 18, 38</td>
<td>Normal, d9</td>
<td>Bilateral small lesions (CSO, d14)</td>
<td>=</td>
<td>Normal</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>d7/120 (RMCA) 176 (LMCA)</td>
<td>7, 13</td>
<td>Small lesions (right CSO)</td>
<td>=</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>d6/170 (RMCA) d8/160 (RMCA) 110 (RACA)</td>
<td>8, 14, 55</td>
<td>Normal</td>
<td>Asymmetrical measures</td>
<td>=</td>
<td>Normal</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>d8/117 (RMCA) d11/200 (RMCA)</td>
<td>10, 15, 55</td>
<td>Normal</td>
<td>Diffuse (RMA territory)</td>
<td>=</td>
<td>Normal</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>d8/140 (RMCA) d11/220 (RMCA)</td>
<td>9, 13</td>
<td>Small lesions (CSO, right cortex)</td>
<td>=</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>2</td>
<td>d8/100 (LMCA) d12/90 (LMCA)</td>
<td>6</td>
<td>Hematoma</td>
<td>Normal</td>
<td>=</td>
<td>=</td>
</tr>
<tr>
<td>9</td>
<td>2</td>
<td>d7/90 (RMCA) d14/85 (RMCA)</td>
<td>6</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>10</td>
<td>2</td>
<td>d5/110 (RMCA) d8/105 (RMCA)</td>
<td>8</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>11</td>
<td>2</td>
<td>d8/85 (R, LMCA) d14/60 (RMCA)</td>
<td>11, 15</td>
<td>Hematoma</td>
<td>Normal</td>
<td>=</td>
<td>=</td>
</tr>
<tr>
<td>12</td>
<td>3</td>
<td>d8/200 (LMCA) d11/125 (LMCA)</td>
<td>8, 9, 69</td>
<td>Small lesions (CSO, insula)</td>
<td>=</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>3</td>
<td>d9/≈200 (LMCA) d13/≈200 (LMCA)</td>
<td>11, 16, 58</td>
<td>Frontal lobe F1</td>
<td>=</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>3</td>
<td>d10/150 (RLMCA) d14/188 (RMCA)</td>
<td>11, 16, 61</td>
<td>Right temporofrontal lesions</td>
<td>=</td>
<td>&lt;</td>
<td></td>
</tr>
</tbody>
</table>

SP Diff indicates diffusion-weighted sequence; ACA, anterior cerebral artery; CSO, centrum semiovale; =, size of images are equivalent on different sequences; <, images are smaller on T2 or FLAIR sequences.

**Figure 1.** ADC values in the right (diamonds) and left (squares) frontal cortex for each group 1 patient.
more extensive than those revealed by T2-weighted images or FLAIR sequences. The focal lesions stabilized, regressed, or disappeared altogether. Both patients were treated with angioplasty and subsequently showed improvement (Figure 4).

**Patients Included in the Protocol**

Patients included in the protocol (group 1) presented with vasospasm only on the basis of high blood flow values. Two patients subsequently became symptomatic.

One developed a neurological deficit (patient No. 2). The first MRI performed at the onset of vasospasm in the right MCA (blood flow of 200 cm/s) did not return any abnormal signal. Significant ADC asymmetry in the frontoparietal cortex was observed, however. Vasospasm subsequently progressed markedly, with blood flow rising to 270 cm/s and becoming diffuse and symptomatic (confusion, right crural paresis). At the second MRI 6 days after the first, DWI showed evidence of lesions. Average ADC values were considerably reduced in the right hemisphere ($732 \times 10^{-6}$ mm$^2$/s on the right vs 789 on the left), with more focal areas of lower ADC on the left side and frontal cortex asymmetry ($P=0.0404$, reduction on the right side). Subsequently, ie, 2 months after the first MRI, the significant difference in the centrum semiovale persisted, although ADC had increased in the left hemisphere: $831 \times 10^{-6}$ mm$^2$/s on the left vs 714 on the right ($P=0.003$), reflecting the progression of necrotic areas that appeared as a hyperintensity on the T2 sequence.

Another patient presented with a transient deficit (No. 1) due to modest vasospasm of the left MCA (intermittent phasic disorders). After the regression of signs, no signal anomaly was detected on subsequent DWI. However, the ADC map showed frank asymmetry, with a significant fall of ADC values ($P=0.047$) in the left sylvian territory (−9%). During follow-up, no lesion was observed in the territory previously affected by vasospasm.

Five patients remained asymptomatic (Nos. 3, 4, 5, 6, and 7). No abnormal signals were present on DWI in 2 patients (Nos. 5 and 6) despite average blood flow velocities indicative of moderate to severe unilateral vasospasm (170 and 200 cm/s). However, ADC mapping provided evidence of abnormalities on the affected side. The ADC map of patient No. 6 was pathological, showing a significant drop in ADC values in the territory affected by vasospasm, especially in the centrum semiovale ($P=0.008$). Although patient No. 5 had an apparently normal ADC map, point-by-point calculation and statistical analysis revealed significant asymmetry ($P=0.034$).

In the other 3 cases (patients Nos. 3, 4, and 7), lesions were observed on DWI in the distal areas or junctional territories. On DWI, patient No. 3 presented with a hyperintensity in the temporo-occipital area, distal to a right MCA branch. This region was the site of a fall in ADC that averaged 30%, with peaks of 47% in the central zone ($491 \times 922 \times 10^{-6}$ mm$^2$/s). This patient’s ADC values rose to higher than average at the second MRI performed 7 days later but returned to normal after 1 month. No abnormalities were observed on the T2 and FLAIR morphological sequences during the period of investigation (Figures 5 and 6).

Patient No. 4 presented with an ADC fall of 15% at a focal lesion of the left oval foramen compared with the contralateral
side (663 × 10⁻⁶ mm²/s compared with 771). There was no significant difference in the point-by-point measurements, however. Vasospasm was bilateral, albeit more severe in the left hemisphere.

In patient No. 7, abnormalities on DWI were focal and diffuse, involving areas of the cortex and white matter (right centrum semiovale). ADC was significantly lower on the right side (centrum semiovale P = 0.0003, frontal cortex P = 0.0025, thalamus P = 0.008, lentiform nucleus P = 0.015) and were correlated with a right MCA vasospasm. These abnormalities were still observed on the second MRI performed when vasospasm had progressed, and the difference in centrum semiovale ADC values was even more significant (P = 0.001). Fewer focal lesions were observed on the morphological sequences than were seen on DWI. In conclusion, abnormalities were observed in all patients, either symptomatic or asymptomatic, on either DWI sequences or by ADC calculation.

Discussion

Validity of Measurements

Diffusion increases in fluid structures, and average ADC values range from 2000 to 3000 × 10⁻⁶ mm²/s in cerebrospinal fluid. 16 Although sulcus ADC values have never been studied in SAH patients, some authors have investigated intraparenchymal hemorrhagic lesions and have reported reduced ADC values. 13–15 It follows that ROIs encompassing blood-carrying structures produce misleading results. Average ADC values in the gray matter are 800 × 10⁻⁶ mm²/s. Values are more variable in the white matter, ranging from 300 × 10⁻⁶ mm²/s to 1200 × 10⁻⁶ mm²/s. 16 This variation is due to anisotropy, or the phenomenon whereby diffusion is concentrated along nerve fibers. To minimize these differences, measurements are made on the image generated after diffusion gradients have been applied along the 3 axes (isotropy).

In the literature, studies to measure ADC seldom provide information on ROI size and how white and gray matter structures, which are poorly visible on untreated images with B values of 0 or 1000, are differentiated. In our ADC study, ROIs were given small surface areas (5 mm³) to ensure reliable localization and study of intraparenchymal areas only. ROIs coinciding with the cortical sulci, in other words, with cerebrospinal fluid or SAH blood, were eliminated so as not to distort the calculations.

Control Group

In the control group, measurements were as follows: oval foramen, 730 × 10⁻⁶ mm²/s; frontal cortex, 757 × 10⁻⁶ mm²/s; frontoparietal cortex, 753 × 10⁻⁶ mm²/s; thalamus, 729 × 10⁻⁶ mm²/s; and lentiform nucleus, 740 × 10⁻⁶ mm²/s. Because the very small control group did not justify a comparison of outcomes, we opted for a symmetric comparison between the 2 hemispheres of each patient. However, this was sometimes difficult in the case of diffuse, bilateral vasospasm (eg, patient No. 2). ADCs showed wide variability in certain regions such as the central gray nuclei. Future
Abnormalities Observed on DWI During Vasospasm

DWI has seldom been used in vasospasm. Busch et al reported DWI data in the acute phase of SAH in the rat. In the first 2 hours after hemorrhage, the ADC fell in an initially focal area of the ipsilateral somatosensory cortex. Most abnormalities observed on DWI in rats not receiving heparin regressed (ie, bleeding ceased), whereas abnormalities progressed in the heparin-treated group. Abnormalities were first evidenced in the most distal part of the MCA and may have been associated with acute vasospasm and reduced cerebral blood flow due to the fall in perfusion pressure.

DWI and perfusion-weighted MRI have been used in only 1 clinical study by Rordorf et al, who investigated early ischemic lesions in patients presenting with symptomatic vasospasm after SAH who were managed surgically for ruptured aneurysm. The average time between onset of the neurological deficit and the investigation was 10.5 hours (range, 9 to 12). Rordorf et al compared abnormalities appearing on diffusion and perfusion sequences, suggesting that perfusion abnormalities were more marked than diffusion anomalies in symptomatic vasospasm. Symptomatic patients were also found to have an increased median transit time over wide areas, characterized by small, sometimes multiple, focal ischemic lesions on DWI appearances. In the event of neurological deficit, median transit time anomalies were more extensive than the abnormalities appearing on DWI. MRI was normal in 1 asymptomatic patient diagnosed as having vasospasm (of unquantified severity) on angiography and TCD. There are, therefore, no reports in the literature of DWI abnormalities observed in asymptomatic vasospasm.

Our study showed abnormalities on DWI in the form of hyperintense signals in 7 of our patients (Nos. 2, 3, 4, 7, 12, 13, and 14) whether they were symptomatic or not. In 3 cases (Nos. 4, 2, and 7), hyperintensity was moderate and located in the white matter of the centrum semiovale. One patient (No. 3) presented with abnormalities localized to the distal temporal territory, which includes both white and gray matter. Although the ischemic lesions in symptomatic vasospasm patients as described by Rordorf et al were limited in size, our symptomatic patients presented with fairly extensive cortical lesions together with other smaller lesions in the oval foramen, a phenomenon that has been seldom described.

Many studies have shown that lesions induced by arterial ischemic disease are visible on DWI very soon after arterial occlusion and before abnormalities show up on T2-weighted images. In our study, patient No. 2 presented with abnormalities on DWI before they appeared on the T2-weighted image. Four others (Nos. 4, 7, 12, and 14), however, had lesions on both investigations concomitantly. Their ADC values confirmed that their abnormalities were due to recent ischemic damage.

We also observed ADC anomalies in the absence of any untoward DWI appearances. This was the case in 2 patients (Nos. 1 and 6), who presented with ADC abnormalities in the territory affected by spasm. In a third patient (No. 5), ADC asymmetry was significant only when we systematically calculated the ADC voxel by voxel and compared these series of values. To our knowledge, similar ADC reductions without concomitant anomalies on DWI have not been reported, but mention is often made in the literature of “diffusion anomalies” in stroke accidents. Patients with SAH without vasospasm did not show any ADC map abnormalities nor any statistically significant asymmetry in point-by-point assessment.

Reversibility of Diffusion Anomalies

Patients with isolated ADC reduction had a favorable clinical outcome, without evidence of vascular parenchymal sequelae on subsequent MRI and a return to normal ADC values. In 2 patients (Nos. 3 and 12), the temporal abnormalities observed on DWI regressed, with no evidence of any lesion on the morphological sequences. The ADC reduction concomitant with these lesions had nonetheless initially been 17% to 43% lower than in the contralateral side.

Reversible diffusion abnormalities in arterial ischemic disorders have rarely been described in humans. However, a few recent studies report reversible lesions during acute transient cerebral ischemia, casting doubt on previous assumptions that lesions visible on DWI are areas of cytotoxic edema, which inevitably induces cell death.

The literature does contain anecdotal reports of transient cerebral ischemia in which abnormalities observed on DWI sequences prove to be reversible. In an animal model, Li et al showed that ADC losses could be reversed if occlusion had lasted < 60 minutes. Beyond that time, however, lesions were irreversible. The same authors subsequently reported that early recovery of ADC values after transient arterial occlusion did not exclude further sudden neuronal loss with a second abrupt fall-off of ADC values. Using an ischemia/anoxia model, Harris et al showed that the ADC has to fall 10% to 25% before anoxic depolarization is triggered, ie, before proton pump failure occurs. These findings fire the debate on the pathophysiology of diffusion abnormalities during ischemia and would support the hypothesis that not all lesions observed in diffusion studies are irreversible. ADC and DWI abnormalities have furthermore been observed during epilepsy in comitance with reversible cell membrane changes and fluid movements. In fact, Hasegawa et al suggested that there might be an ADC threshold above which lesions are reversible. In our study, however, patient No. 3 presented with a 43% ADC reduction compared with the contralateral side (minimum = 491 × 10^-6 mm²/s) without suffering any sequelae. Therefore, no reversibility threshold was observed by us. Admittedly, however, our case material is limited and larger studies are necessary.

With What Are DWI Abnormalities Associated?

Even in the first few minutes after acute arterial occlusion, DWI sequences return a hyperintense signal and there is a fall in the ADC. The main pathophysiological explanation is the existence of cytotoxic edema due to proton pump failure. As a result, water moves from the extracellular spaces into the cells. The resultant cellular swelling leads to a drop in ADC. This hypothesis has been corroborated by a study on ADC during acute severe hypoglycemia, which slows proton pump activity and causes energy loss. Other hypotheses put forward include loss of ionic homeostasis, viscosity abnor-
malities, and impoverishment of the extracellular environment, resulting in diffusion pathways going around and not through the cells.28-29

Origin of Abnormal DWIs in Vasospasm

The pathophysiology of vasospasm is still not well known. Some patients remain asymptomatic despite severe vasospasm, while others present with neurological deficits even at only moderate blood flow velocity increases. It would seem, therefore, that patients have manifestly different tolerance thresholds to reduced cerebral blood flow caused by vasospasm. On the other hand, the varying severity of ischemia may also be an explanation, with asymptomatic patients suffering only subacute ischemia. Whatever the differences, however, abnormalities observed on DWI indicate vasospasm-related ischemia due to prolonged reduced blood flow to the brain. Such prolonged ischemia may well disrupt the cell membrane proton pump but need not lead to cell death. Correlation with perfusion imaging may shed new light on this issue.

The pathophysiology of the reversible abnormalities observed on DWI in transient ischemia is not clear. The existence of a reversibility threshold is an alluring hypothesis and, if proved correct, would be key to patient management. Some authors have suggested that the absence of abnormal DWIs in some cases of early stage stroke may be accounted for by maintenance of an “intermediate” cerebral blood flow that is insufficient to avert neuronal dysfunction but is greater than the diffusion loss threshold. It is further suggested that proton pump abnormalities do not occur at cerebral blood flows >10 or 15 mL · 100 g⁻¹ · min⁻¹. This hypothesis still has to be confirmed, however, as does the theory that DWI abnormalities in vasospasm are exclusively associated with proton pump dysfunction.

Although small, this study has provided evidence for abnormalities on DWI that are concomitant with a reduction in the ADC in early stage asymptomatic vasospasm. In some cases, the abnormalities were reversible. In asymptomatic patients, abnormalities were mainly in the white matter, whereas lesions were prevalently cortical in symptomatic vasospasm. Detection of these abnormalities could prove to be a useful patient management tool. It is hoped that a larger study will ascertain whether there is a threshold beyond which lesions become irreversible.

References

Vasospasm After Subarachnoid Hemorrhage: Interest in Diffusion-Weighted MR Imaging

Stroke. 2001;32:1818-1824
doi: 10.1161/01.STR.32.8.1818
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2001 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/32/8/1818

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/