Cerebral vasospasm is a complication with major implications for the further therapeutic management of patients with subarachnoid hemorrhage (SAH). Until now, the only way to establish the time course of vasospasm has been by angiography. This is an invasive procedure, however, and cannot be repeated at frequent intervals to monitor the development and resolution of arterial narrowing following SAH. Transcranial Doppler ultrasonography (TCD) has opened up the possibility of noninvasive diagnosis of cerebrovascular spasm and observation of its time course.

The mean flow velocity has been considered the most important diagnostic parameter in the evaluation of vasospasm by TCD because a clear correlation between the velocity of flow and the diameter of the middle cerebral artery (MCA) measured by angiography has been found in different studies. All patients in whom angiography showed evidence of MCA vasospasm had TCD blood flow velocities of 120 cm/sec or more. The intracranial flow patterns can also be influenced by other factors, in particular by the intracranial pressure (ICP). Partial pCO₂, or the hematocrit. The combined occurrence of vasospasm and increased ICP is of particular importance in the development of neurological deficits, thus making the evaluation of both factors essential for prognosis and therapy.

The TCD blood flow velocities associated with neurological deficits clearly vary from case to case. Compton, et al., observed that deterioration of clinical condition from Grade I to Grade III (according to the Hunt and Hess scale) was accompanied by an increase in the mean flow velocity, whereas patients in clinical Grade IV demonstrated a decrease in mean flow velocity as compared to Grade III patients. Lindegaard, et al., pointed out that classification of MCA spasm by use of flow velocity could be misjudged if blood flow reduction and artery narrowing concur. It was the aim of the present study to evaluate the interdependence of the patient’s clinical grade, vasospasm, ICP, and TCD parameters.

Clinical Material and Methods

Seventy-six patients suffering from spontaneous SAH were included in this study. A clinical summary for this series is shown in Table 1. Angiography was performed
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in all patients. Blood flow velocity in the MCA was measured using a 2-MHz pulsed TCD device. The instrumentation and techniques used for the TCD examination have been described in detail elsewhere. The time-averaged peak frequencies (mean), converted by the built-in computer into blood flow velocities (cm/sec), were noted for the mean flow velocity. The peak systolic and end-diastolic flow velocities were extracted after manual labeling of the TCD recordings. Flow patterns of the MCA were recorded either intermittently at least once a day or (if the patient's clinical condition deteriorated) continuously by means of a specially designed attached probe holder.

Surgery for a verified operable aneurysm was carried out in 26 (34%) of the 76 patients within the first 7 days after SAH. After confirmation of the SAH by bloody or xanthochromic cerebrospinal fluid and/or computerized tomography (CT) scans, the patients received 2 mg/hr nimodipine intravenously for 7 to more than 14 days, depending on the intracranial flow patterns monitored by TCD. The individual timing for changing nimodipine to an oral dose of 60 mg/24 hr was evaluated, again based on the TCD findings. In addition, the usual SAH therapy was performed. The clinical grade according to the classification of Hunt and Hess was evaluated daily by a neurologist experienced in the assessment of cerebrovascular disorders. The Hunt and Hess stages at admission are shown for all patients in Table 2. The degree of SAH on admission CT scans and the resulting distribution of the patients as being at low or high risk for symptomatic vasospasm (Table 2) was determined using the classification of Fisher, et al., as follows: CT Grade I (thin localized layer); CT Grade II (thick layer in two of the three subarachnoid compartments or one subarachnoid compartment and at the cortical surface); and CT Grade III (severe diffuse SAH with thick layers in all three subarachnoid compartments or in two compartments and at the cortical surface).

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**Table 1**

<table>
<thead>
<tr>
<th>Location of Aneurysm</th>
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</tr>
</thead>
<tbody>
<tr>
<td>internal carotid artery</td>
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<tr>
<td>anterior cerebral artery/anterior communicating artery</td>
<td>28</td>
</tr>
<tr>
<td>middle cerebral artery</td>
<td>17</td>
</tr>
<tr>
<td>posterior cerebral artery/posterior communicating artery</td>
<td>5</td>
</tr>
<tr>
<td>no verified aneurysm</td>
<td>15</td>
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</table>

* There were 40 females and 36 males. Mean patient age was 49 years (range 21 to 73 years).

**Table 2**

<table>
<thead>
<tr>
<th>Patient Classification</th>
<th>No. of Cases</th>
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</thead>
<tbody>
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<td>clinical grade</td>
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</tr>
<tr>
<td>I</td>
<td>16</td>
</tr>
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<td>II</td>
<td>22</td>
</tr>
<tr>
<td>III</td>
<td>20</td>
</tr>
<tr>
<td>IV</td>
<td>18</td>
</tr>
<tr>
<td>SAH grade on CT</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>14</td>
</tr>
<tr>
<td>II</td>
<td>25</td>
</tr>
<tr>
<td>III</td>
<td>37</td>
</tr>
</tbody>
</table>

* SAH = subarachnoid hemorrhage. Clinical grade according to Hunt and Hess; SAH grade on computerized tomography (CT) scans according to Fisher, et al. (see text).

Arterial pCO₂ was monitored using blood gas analysis. Mean arterial blood pressure (MABP) was calculated as: MABP = (systolic pressure - diastolic pressure) / 3 + diastolic pressure. According to Pourcelot, the index of cerebral circulatory resistance (R) was calculated from the TCD data as: R = (maximum systolic flow velocity - end-diastolic flow velocity)/maximum systolic flow velocity. The resistance index R is a measure of the peripheral flow resistance; in general, low vascular resistance is characterized by high diastolic flow velocities, whereas low diastolic flow indicates high resistance.

In 41 patients, the ICP was also measured, using an epidural transducer. In all cases with an asymmetrical distribution of the hemorrhage (as determined from the CT scans), the epidural pressure transducer was placed on the side with more blood and the parameters of the ipsilateral MCA were evaluated. If both hemispheres were affected to a similar degree, the parameters of the MCA were evaluated on the side of the implanted epidural device.

To achieve a homogeneous study population, we selected 36 of the 41 patients with ICP measurements who fulfilled the following criteria. The patients' clinical status had to allow for a minimum monitoring period of 8 days following SAH, including ICP measurements. Only data taken at time intervals of at least 12 hours were considered. The maximum flow velocities had to be on the side of the implanted epidural device. The hematocrit had to be in the 30% to 40% range; for the TCD recordings to be considered in this analysis, the heart rate had to be rhythmic and range from 60 to 90 beats/sec. To minimize the influence of varying PaCO₂ on the flow patterns, TCD data were accepted only if the PaCO₂ was in the range of 30 to 40 mm Hg at the time of recording. The data from these 36 patients were divided into two groups: Group A consisting of 14 patients with SAH and normal or only slightly increased...
ICP (<20 mm Hg); Group B including 22 patients with SAH and clearly increased ICP (>20 mm Hg).

Results

Clinical Status and TCD Parameters

The average values of the maximum mean flow velocities (maximum flow velocities for both sides) as well as the corresponding resistance indices of the 76 patients were compared with the clinical grade according to the classification of Hunt and Hess (Fig. 1). Analysis of these values (expressed as mean ± standard error of the mean) demonstrated an increase in the mean flow velocity from Grade I (122 ± 41.8 cm/sec) to Grade III (175 ± 55.5 cm/sec) and a decrease for Grade IV (93 ± 30.1 cm/sec). Paralleling these values, the mean resistance index decreased to 0.46 ± 0.09 in Grade III patients and clearly increased to more than 0.6 in Grade IV patients (results of Student’s t-test analysis are given in the legend to Fig. 1). The decrease of the resistance index in Grade III patients is a result of the greater percentage increase in the diastolic flow velocity compared to the systolic flow velocity.

Interdependence Between Vasospasm, ICP, and TCD Parameters

Qualitative Aspects. Figure 2A demonstrates the time course of a typical patient with vasospasm and ICP lower than 20 mm Hg (Group A), and Fig. 2B presents that of a different patient with vasospasm and ICP greater than 20 mm Hg (Group B). The patient in Group A shows an increase in the mean flow velocity from 54 cm/sec (Day 2 after SAH) to a maximum of 190 cm/sec (Day 9 after SAH). The clinical status at this time corresponded to Grade III. In the following days, the mean flow velocity decreased and returned to normal by Day 25 after SAH. An improvement in clinical status to Grade I was also seen in this phase. The resistance index demonstrated a reciprocal development to the mean flow velocity and fluctuated in the phase of high flow velocities between 0.35 and 0.47. With normalization of mean flow velocity, there was an increase in the resistance index to values over 0.5. During the monitoring phase, the resistance index did not rise over 0.58. Angiography performed for diagnostic purposes on Day 17 after SAH revealed an aneurysm of the right internal carotid artery; this vessel as well as the middle and the anterior cerebral arteries still clearly displayed vasospasm, corresponding to the TCD findings at this time (mean flow velocity 152 cm/sec, resistance index 0.37).

The ICP of the patient in Group B (Fig. 2B) showed pronounced fluctuations. Clinically, he continually presented a Grade IV status. At nearly constant ICP, the patient showed an increase in the mean flow velocity to 160 cm/sec 12 days after SAH. The increase in ICP to 38 mm Hg and drop in MAP to 79 mm Hg on Day 13 was accompanied by a decrease in the mean flow velocity to 98 cm/sec and the appearance of a readily discernible “resistance profile” with an increase in the resistance index to 0.80. This constellation, however, is obviously less a product of reduced vasospasm than of an increased ICP. Following successful drug therapy to reduce the high ICP, the mean flow velocity rose again to 142 cm/sec with a concomitant decrease in the resistance index to 0.65 on Day 15, indicating that vasospasm was still present. The resistance index did not fall below 0.5 during the entire monitoring period.

Quantitative Aspects. The average values of the resistance index in 14 patients from Group A (ICP < 20 mm Hg) and 22 patients in Group B (ICP > 20 mm Hg) are shown in Fig. 3 for the first 12 days after SAH. The highest mean resistance index (0.58 ± 0.09) was found in Group A patients during the first 2 days of the monitoring period. This decreased to a value below 0.5 between Days 9 and 12. The average mean flow velocity in this phase attained values over 140 cm/sec. The resistance index in Group B was greater than 0.6 (ranging from 0.65 ± 0.08 to 0.69 ± 0.09) during the entire monitoring period, indicating clearly increased peripheral flow resistance in this group. The lowest resistance index values were also observed in the phase of

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Fig. 2. Transcranial Doppler ultrasound recordings of the right middle cerebral artery (MCA Rt) of a 51-year-old patient suffering from spontaneous subarachnoid hemorrhage (SAH) and normal intracranial pressure (A) and a 34-year-old patient suffering from spontaneous SAH and pathological intracranial pressure (B), registered on different days after SAH. Mean flow velocity (MFV, cm/sec), resistance index (R), mean systemic arterial pressure (MAP, mm Hg), and mean intracranial pressure (ICP, mm Hg) are presented at various recording times.

The highest flow velocity between Days 7 and 10 after SAH. The lowest mean resistance index was found in both groups on Days 9 and 10. This correlated well with the occurrence of the maximum mean flow velocity (Group A: Day 10.2 ± 3.4 after SAH; Group B: Day 9.8 ± 3.2 after SAH).

During the critical phase in the development of vasospasm, an angiogram was necessary for diagnostic purposes in four Group A patients (ICP < 20 mm Hg) and in five Group B patients (ICP > 20 mm Hg). The four Group A patients exhibited vasospasm in the corresponding MCA, whereby the mean flow velocities at this point were clearly higher than 120 cm/sec (186 ± 34.7 cm/sec). Their mean resistance index was less than 0.5 (0.45 ± 0.06) and the mean ICP was in a normal range (11.0 ± 3.6 mm Hg). In contrast, the five Group B patients in whom the MCA's also showed vasospasm on angiography demonstrated mean corresponding blood flow velocities below 120 cm/sec (97.5 ± 14.5 cm/sec) and a mean raised resistance index of more

Fig. 3. Average values of the resistance index (R) in 14 Group A patients (intracranial pressure (ICP) < 20 mm Hg) and 22 Group B patients (ICP > 20 mm Hg) for the first 12 days after subarachnoid hemorrhage (SAH). Statistical significance (by Student's t-test) of differences between Group A and Group B on Days 1 - 2: not significant; Days 3 - 4: p < 0.005; Days 5 - 6: p < 0.005; Days 7 - 8: p < 0.01; Days 9 - 10: p < 0.001; and Days 11 - 12: p < 0.001.
the degree of vasospasm in Grade IV patients than in patients with Grades I to III. These results seem to contrast with various angiographic studies in which a direct correlation was observed between the incidence and severity of vasospasm and an increase in clinical symptoms. For example, Voldby, et al., found angiographic evidence of vasospasm in all Grade IV patients. The evaluation of vasospasm with TCD is based on the finding of an inverse proportion between vessel diameter and blood flow velocity. Basically, this means that a reduction in vessel lumen is deduced from an increase in flow velocity. However, other factors beside blood vessel diameter might also have an effect on flow velocity and must be regarded in the evaluation of the severity of vasospasm. For example, Compton, et al., pointed out that a decrease in the mean flow velocity in Grade IV patients compared to Grade III patients may result from the simultaneously observed reduction in cerebral blood flow (CBF). Other research groups have been able to demonstrate a 20% to 45% reduction in CBF in Grade IV patients versus Grade III patients.

Our results indicate that the observed reduction in mean flow velocity in Grade IV patients in the present study is not a result of a less pronounced vasospasm but is instead caused by an increased ICP and reduced cerebral perfusion pressure (CPP), respectively. These findings were directly supported by five patients whose MCA’s showed vasospasm on angiography but whose TCD blood flow velocities were clearly less than 120 cm/sec. However, angiography is an invasive procedure and performing it on patients with vasospasm involves an even greater risk of incurring neurological deficits. Thus, during the critical phase in the development of vasospasm, angiography was performed in only nine patients for purposes of special diagnostics. As an indication for the degree of vasospasm to be expected for all patients, the CT scale developed by Fisher, et al., was used. Those and subsequent authors were able to demonstrate a significant correlation between the amount and distribution of subarachnoid blood detected by CT scans early after aneurysmal rupture and the subsequent development of cerebral vasospasm visualized angiographically. Although Group B (ICP > 20 mm Hg) patients showed a significantly higher value for the CT scale score than Group A (ICP < 20 mm
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Hg). Group B demonstrated a significantly lower mean flow velocity. The significantly lower mean flow velocity in Group B patients is probably a result of two factors: 1) the higher ICP in this group causes a reduction of the CPP and therefore a decrease of the mean flow velocity; and 2) the pressure loss caused by the vasospasm leads to a decrease in CBF due to disturbed autoregulation and to a further reduction in blood flow velocity.

Resistance Index

The resistance index as a measure of the peripheral vascular flow resistance was reduced in Group A (R < 0.5). This can be a sign of (still) intact autoregulation. Primarily, the vasospasm results in a pressure loss over the spastically narrowed vessel region. In this situation, the decreased resistance index indicates a reactive dilatation in the arterioles. This dilatation allows a compensation for the pressure loss over the narrowed vessel region and subsequently a nearly constant CBF over a large range. In contrast, the elevation of the resistance index of Group B (R > 0.6) can be considered a symptom of raised peripheral vascular flow resistance due to the clearly increased ICP. Under these conditions, autoregulation may be disturbed.

Aslidi, et al., observed neurological deficits solely in patients with SAH in whom the flow velocities in the extracranial internal carotid artery were simultaneously reduced during the phase of increased mean flow velocity of the MCA. In our study, no irreversible neurological deficits were observed in the examined patients whose resistance index fell below 0.5 in the phase of increased mean flow velocity; on the other hand, in those patients who developed irreversible neurological deficits a resistance index of more than 0.6 was always present during the vasospastic phase. A decrease in CBF obviously occurred in these patients as a result of vasospasm associated with increased ICP. The resistance index in patients with SAH and vasospasm thus delivers valuable information about ICP alterations and about the functional capacity and "vasomotor reserve capacity" of the autoregulatory system.

False Negatives in TCD

Group B patients (ICP > 20 mm Hg) demonstrated a significantly lower mean flow velocity although its CT scale score was significantly higher than that of Group A patients (ICP < 20 mm Hg). These results indicate that a TCD evaluation of the severity of vasospasm based solely upon the mean flow velocity in patients with raised ICP (usually Grade IV patients) can lead to false-negative results (blood flow velocities too low in the presence of a distinct vasospasm). The angiographic findings in the Group B patients on whom an angiography was performed for diagnostic purposes during the critical phase in the development of vasospasm supported this statement. Thus, besides the critical evaluation of the resistance index, an ICP measurement is especially important, particularly in Grade IV patients, to decide whether the decrease in flow velocity occurring during SAH with vasospasm is a result of the decrease in vasospasm or an increase in ICP.

Conclusions

The following statements can be made on the basis of the present study. 1) In patients with a resistance index of less than 0.5, changes in the mean flow velocity seem to reflect sufficiently the actual severity and time course of vasospasm. 2) During the time course of vasospasm, an increase in the resistance index above values of 0.6 with a simultaneously decreased mean flow velocity indicates a rise in ICP or drop in CPP.
respectively, rather than a reduction in vasospasm. 3) With a pronounced increase in ICP, an evaluation of the severity and time course of vasospasm by TCD based solely upon the mean flow velocity can lead to false-negative results.

References

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