Cerebral hemodynamic impairment after aneurysmal subarachnoid hemorrhage as evaluated using transcranial Doppler ultrasonography: relationship to delayed cerebral ischemia and clinical outcome

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Object. In this study the authors evaluated the relative role of cerebral hemodynamic impairment (HDI) in the pathogenesis of delayed cerebral ischemia and poor clinical outcome after aneurysmal subarachnoid hemorrhage (SAH).

Methods. Cerebral hemodynamics were assessed daily with transcranial Doppler (TCD) ultrasonography in 55 consecutive patients with verified SAH. Hemodynamic impairment was defined as blood flow velocity (BFV) values consistent with vasospasm in conjunction with impaired autoregulatory vasodilation as evaluated using the transient hyperemic response tests in the middle cerebral arteries. A total of 1344 TCD examinations were performed, in which the evaluation of HDI was feasible during 80.9% and HDI was registered during 12% of the examinations. It was found that HDI occurred in 60% of patients and was frequently recorded in conjunction with severe vasospasm (p < 0.05) and a rapid increase of BFV values (p < 0.05). Detection of HDI was closely associated with the development of delayed ischemic brain damage after SAH (p < 0.05). Furthermore, because delayed ischemia was never observed in cases in which vasospasm had not led to the development of HDI, its occurrence significantly increased the likelihood of subsequent cerebral ischemia among the patients with vasospasm (p < 0.05). Detection of HDI was independently related to unfavorable clinical outcome according to Glasgow Outcome Scale at 6 months after SAH (p < 0.05).

Conclusions. The results showed that HDI is common after SAH and can be evaluated with TCD ultrasonography in routine clinical practice. Detection of HDI could be useful for identifying patients at high or low risk for delayed ischemic complications and unfavorable clinical outcome after SAH.

KEY WORDS • autoregulation • cerebral hemodynamics • subarachnoid hemorrhage • delayed cerebral ischemia • transcranial Doppler ultrasonography
Fig. 1. Tracing showing example of the changes in the BFV (FV) of the MCA during a THR test. A definition of the parameters used to describe the response and the equation for the calculations are presented. FVS = systolic flow velocity.

Patients with extracranial arterial stenosis has been extensively studied. Most of the studies have revealed a clear association between hemodynamic compromise and increased stroke risk in patients with CA occlusive disease. Application of the concept of HDI in patients with progressive luminal narrowing of major cerebral arteries due to vasospasm might contribute to a better understanding of the pathogenesis of ischemic brain damage after SAH.

The development of TCD ultrasonography has facilitated the early diagnosis and monitoring of cerebral arterial vasospasm after SAH. Although this modality has several limitations, it has enabled the creation of a number of methods to assess cerebrovascular hemodynamic reserve. These methods are based on evaluation of induced or spontaneous changes in cerebral BFV values, and several of them could provide valuable information about the vasodilatory capacity of the cerebral microvasculature. The THR test was introduced by Giller as a simple clinical marker of cerebral autoregulation and was later evaluated by a number of researchers. The THR test is non-invasive, easy to perform at the bedside, and, because it avoids the potential danger from manipulations of arterial blood pressure, it can be used for regular monitoring of cerebral autoregulation. The test allows physicians to evaluate the impairment of autoregulatory vasodilatation in cerebral microcirculation by measuring the hyperemic response of BFV in the MCA following brief ipsilateral CA compression, and it could be applicable for routine evaluation of HDI in patients with SAH.

The objectives of the present study were as follows: 1) to evaluate the practicability of regular HDI monitoring after SAH; 2) to assess the frequency of HDI in patients with SAH; 3) to determine the relationship between the severity of vasospasm and development of HDI after SAH; 4) to compare the association of vasospasm and HDI with the development of delayed cerebral ischemia; and 5) to assess the relevance of HDI as a risk factor for poor clinical outcome after SAH.

Clinical Material and Methods

Seventy-six patients with suspected SAH were admitted to the Department of Neurosurgery at the University Hospital of Tartu, Estonia between December 1998 and May 2000. Twenty patients were subsequently excluded from the study because there was no evidence that an aneurysm was the source of bleeding and/or moribund conditions present on admission, and one patient with a mycotic aneurysm was also excluded. Thus, the final study group was composed of 55 consecutive patients ranging in age from 25 to 82 years (mean 56.3 years) who had verified aneurysmal SAH. The presence of significant extracranial cerebrovascular stenosis or atheroma was excluded by angiography or CA Doppler ultrasonography studies.

All patients were admitted during the acute phase of the disease (78% of them within 48 hours and the others by Day 5 after the suspected bleeding). Each patient’s clinical condition on admission was assessed using the WFNS scale. The diagnosis of SAH was confirmed on CT scans, and the aneurysm location was assessed using digital subtraction angiography (in two patients an aneurysm was revealed during emergency evacuation of ICH). All patients were treated at the neurointensive care unit. Fifty-one patients underwent emergency surgery, preferably via a pterional approach, and the aneurysms were clipped using standard microsurgical techniques. Four patients were excluded from aggressive surgical therapy because of their severe clinical condition. The neurological status of the patients was closely monitored and their levels of consciousness were registered according to the Glasgow Coma Scale. Ventriculostomy was performed and intracranial pressure was monitored continuously through an intraventricular catheter in all patients with significant ventricular enlargement. Frequent laboratory analysis and radiological diagnostic procedures were performed as a cornerstone of therapy. The treatment focused on the control of intracranial pressure and the preservation of normal body physiology. We instituted HHH therapy if vasospasm had been diagnosed. All patients routinely received nimodipine.

Consecutive CT scans were obtained in all patients. Experienced neuroradiologists, who were unaware of the clinical and TCD ultrasonography findings, examined all CT scans. The initial CT scans were evaluated according to a modified Fisher grading system as follows: Grade I, thin diffuse or localized blood layers; Grade II, thick blood layers in at least two of the four subarachnoid compartments (sylvian fissures, cortical surface, basal cisterns, frontal interhemispheric space); and Grade III, thick blood layers in at least three of the four subarachnoid compartments. Acute hydrocephalus was defined as a bicaudate index above the upper limits for age on the initial CT scan. All ICHs and cerebral infarcts were registered. Ischemic changes already visible on the initial CT or on other CTs obtained within 48 hours after the ictus were considered to be related to the initial bleeding, and hypodense lesions visible on a CT scan obtained within 48 hours after surgery and localized in the region of the operation were considered to be related to aneurysm surgery. Follow-up CT scans were performed at discharge. For the patients who died during hospitalization, the last CT obtained before death was used as the follow-up CT. All low-density areas on the follow-up CTs that were not considered related to the initial bleeding or the surgical trauma were recorded as DCIs. The registration of DCIs was classified as present or absent for the purpose of statistical analysis.

Neurological deterioration with delayed onset, that is,
Hemodynamic impairment after SAH

either temporary or permanent decline in the level of consciousness or gradual development of focal neurological signs, was defined as symptomatic vasospasm if all other potential causes, such as surgical complications, hydrocephalus, rebleeding, seizures, infection, metabolic disturbances, or cardiopulmonary complications, were excluded. Symptomatic vasospasm was diagnosed without knowledge of the presence or absence of HDI. All patients with symptomatic vasospasm and/or registration of DCI on the follow-up CT scan were recorded as having DINDs. The occurrence of DIND was classified as present or absent for the purpose of statistical analysis.

The TCD ultrasonography examinations (MultiDop X; DWL, Überlingen, Germany) were performed daily with a 2-MHz handheld probe, starting from the 1st day after admission and continuing throughout the course of intensive care management. The systolic, diastolic, and mean BFV values in the MCAs and the anterior cerebral arteries were recorded bilaterally via the transtemporal approach. The submandibular approach was used to measure the BFV values in the extracranial segment of ICAs and the suboccipital route was used for the BFV measurements in the basilar arteries. The TCD ultrasonography examinations were performed by a single researcher (T.R.) to minimize interobserver variations. Only the highest time-averaged mean BFV values in MCAs and the highest mean BFV ratios of the MCA/ipsilateral extracranial ICA (Lindegaard ratio) were used to evaluate the degree of arterial vasospasm. Moderate vasospasm was diagnosed if a BFV greater than 120 cm/second had been recorded in conjunction with a Lindegaard ratio of greater than 3, whereas severe vasospasm was diagnosed if BFV values greater than 180 cm/second and Lindegaard ratios greater than 5 had been recorded. Rapid increases in BFV values in the MCA (increases of > 50 cm/second in 24 hours) were also registered. The TCD ultrasonography examinations that were consistent with cerebral circulatory arrest were excluded from the study.

The THR tests in MCAs were performed during all TCD ultrasonography examinations. Only the segment of MCA with the highest BFV values was selected as a site for the tests. The THR test results were calculated according to standard formulas: the THR ratio was calculated as systolic BFV values during hyperemia, divided by baseline systolic BFVs (Fig. 1). The heart cycle just preceding CA compression was used to measure baseline systolic BFV. Systolic BFV during CA compression was calculated as the average systolic BFV from the first two heart cycles after the compression. Systolic BFV during hyperemia was calculated as the average systolic BFV from the second and the third heart cycles after the release of the compression. The criteria for acceptable THR tests included the following: 1) a sudden decrease in BFV at the onset of compression; 2) a stable TCD ultrasonography signal during compression; 3) compression duration of 5 seconds or more; 4) compression ratio greater than 30%; and 5) no significant response from baroreceptors. The THR values greater than or equal to 1.10 were considered to indicate a positive response and intact cerebral autoregulatory vasodilation, whereas values less than 1.10 were interpreted as a negative response and indicative of impaired autoregulatory vasodilation. When results were negative, the THR test was repeated at an interval of more than 2 minutes, and only the average value of the two tests was recorded for further analysis.

Cerebral hemodynamic status was evaluated according to BFV values in MCAs and THR test results (Fig. 2). All the examinations in which BFV values indicated vasospasm, in conjunction with negative THR tests, were considered to indicate HDI. For the purpose of data analysis, the occurrence of HDI was classified as present or absent.

The GOS score at 6 months after ictus was used to assess the clinical outcome of the patients. For the purpose of statistical analysis, the GOS score was dichotomized for a favorable outcome, that is, good recovery and moderate disability (GOS Score 5–4), and for an unfavorable outcome, that is, severe disability, vegetative state, and death (GOS Score 3–1).

**Statistical Analysis**

Continuous variables were reported as the means ± standard deviation and checked for normality by using the Kolmogorov statistic. The statistical significance of intergroup differences for continuous variables was assessed using unpaired Student t-tests. Categorical data were compared using the Pearson chi-square test; the Fisher exact test was used if at least one cell in the 2 × 2 tables had an expected value of less than 5. Stepwise multiple logistic regression analysis was applied to determine the factors that might be considered independent predictors of a poor clinical outcome after SAH, whereas a significance level of 0.05 was chosen for variable entry into the model. The odds ratios were calculated and presented with 95% confidence intervals. The analyses were performed with the use of SAS software (version 6.12; SAS Institute, Cary, NC). A probability value of less than 0.05 was considered statistically significant.
Results

The patients’ baseline and clinical characteristics are presented in Table 1.

Protocol for TCD Ultrasonography Examinations

A total of 1344 TCD ultrasonography examinations were performed in 55 patients during a mean of 12 days (2–17 days) after ictus. Blood flow velocity values ranging from 21 to 257 cm/second (91.1 ± 39.7) were recorded; 248 (19%) of the BFV values indicated moderate and 32 (2%) severe vasospasm. The TCD ultrasonography examinations indicated moderate vasospasm in 26 patients (47%) and 41 MCAs (37%) and severe vasospasm in 12 patients (22%) and 13 MCAs (12%). An increase in BFV values of greater than 50 cm/sec/24 hrs was registered in 20 vasospastic MCAs (37%).

In all, 1087 (81.6%) acceptable THR tests were recorded, with 342 (31%) negative test results obtained compared with 745 (69%) positive results (THR ratios 1.14 ± 0.11). Negative results of THR tests were registered in 45 patients (82%) and 77 MCAs (70%), and results remained negative for 1 to 13 days (mean 5.1 and 3.1 days, respectively). Negative THR tests occurred more frequently (> 30% of tests performed) 0 to 3 and 7 to 14 days after ictus (Fig. 3). Whereas registration of negative THR tests 0 to 3 days after ictus was related to a WFNS grade of greater than II on admission (p < 0.05), negative test results obtained 7 to 14 days after ictus were associated with development of arterial vasospasm (p < 0.05).

Practicability of Measurements of HDI

Altogether, it was possible to evaluate the status of cerebral hemodynamics during 1087 (80.9%) of the 1344 TCD examinations. Approximately 20% of the measurements failed because of unacceptable THR tests due to difficulties in performing adequate CA compression or increased psychomotor activity of the patients, and occasionally because of suboptimal temporal bone windows. The evaluation of HDI was feasible in 52 (95%) of 55 patients and 103 (94%) of 110 MCAs. The development of HDI was always possible to assess in 20 patients (36%) and 51 MCAs (46%), but the examinations failed at least once in 35 patients (64%) and 59 vessels (54%). The patients in whom measurements failed did not differ significantly from the others by age, severity of clinical conditions on admission, development of vasospasm, and registration of delayed cerebral ischemia or unfavorable clinical outcome. Data from the three patients in whom and the seven vessels in which all the measurements failed were excluded from further calculations.

Presence of HDI: Frequency, Time of Occurrence, and Relationship to Severity of Vasospasm

As shown in Fig. 4, HDI was registered during 130 (12%) of the 1087 measurements; HDI was recorded in 31 (60%) of 52 patients and 40 (39%) of 103 MCAs, and lasted 1 to 10 days (mean 3.9 and 3.3 days, respectively). As seen in Fig. 5, HDI occurred more frequently (> 15% of examinations performed) 7 to 12 days after ictus.

Because 257 TCD ultrasonography studies demonstrated vasospasm, the development of this condition was not accompanied by HDI in 49% of the examinations. Values for BFV were significantly higher in the studies indicating HDI (160.2 ± 30.9) compared with the examinations in which vasospasm without HDI was indicated (142.6 ± 21.6, t = 5.54; p < 0.0001). As shown in Fig. 6, HDI was registered more frequently in cases of severe compared with moderate vasospasm: 48% of TCD ultrasonography studies in patients with moderate and 72% of studies in those with severe vasospasm indicated HDI (p < 0.05).

TABLE 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of Patients (%)</th>
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<tr>
<td>sex</td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>13 (24)</td>
</tr>
<tr>
<td>F</td>
<td>42 (76)</td>
</tr>
<tr>
<td>age &gt;60 yrs</td>
<td>22 (40)</td>
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<tr>
<td>aneurysm location</td>
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<tr>
<td>MCA</td>
<td>18 (33)</td>
</tr>
<tr>
<td>anterior communicating artery</td>
<td>20 (36)</td>
</tr>
<tr>
<td>ICA</td>
<td>8 (14)</td>
</tr>
<tr>
<td>anterior cerebral artery</td>
<td>3 (5)</td>
</tr>
<tr>
<td>basilar artery</td>
<td>3 (5)</td>
</tr>
<tr>
<td>other</td>
<td>3 (5)</td>
</tr>
<tr>
<td>WFNS grade</td>
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<td>I</td>
<td>30 (54)</td>
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<tr>
<td>II</td>
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<tr>
<td>III</td>
<td>2 (4)</td>
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<td>IV</td>
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</tr>
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<td>18 (33)</td>
</tr>
<tr>
<td>III</td>
<td>16 (29)</td>
</tr>
<tr>
<td>hydrocephalus</td>
<td>17 (31)</td>
</tr>
<tr>
<td>intraventricular hemorrhage</td>
<td>27 (49)</td>
</tr>
<tr>
<td>ICH</td>
<td>16 (29)</td>
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</table>
Although HDI was recorded in 74% of the vasospastic MCAs, the TCD examinations showed HDI in 72% of vessels with moderate and 92% with severe vasospasm (p < 0.05); however, the HDI was not registered in 14 (26%) of 54 MCAs and in seven (18%) of 38 patients with vasospasm. Development of HDI in a vasospastic MCA frequently occurred in conjunction with rapidly rising BFV values (> 50 cm/sec/24 hrs). From the MCAs in which vasospasm had been recorded, HDI was registered in 90% of vessels with, and in 65% of vessels without the rapid increase of BFV (p < 0.05).

Vasospasm and HDI: Relationship to Development of DCIs

Sixteen DCIs were registered in 13 patients (25%) on follow-up CT scans. Twelve DCIs were discovered ipsilaterally to the registration of vasospasm (Fig. 7), and the relationship between the detection of vasospasm in MCAs and the development of DCIs was not significant (p > 0.05). Because no DCIs were recorded if vasospasm had not been accompanied by HDI, the associations between HDI and detection of DCI were statistically significant (p < 0.05; Table 2). At the same time, the registration of HDI was closely related to the development of ipsilateral DCIs in the group of vasospastic MCAs (p < 0.05, Fisher exact test; specificity 33%, sensitivity 100%).

Vasospasm and HDI: Relationship to Development of DINDs

Nine patients (17%) experienced symptomatic vasospasm, and in six of them DCIs were registered; 16 patients (31%) had DINDs. We detected DINDs in 14 of 38 patients with vasospasm and in 14 of 31 patients with HDI (Fig. 8). Detection of vasospasm was not significantly related to the registration of DINDs (p > 0.05, specificity 33%, sensitivity 88%); however, the associations between HDI and DINDs were statistically significant (p < 0.05, specificity 53%, sensitivity 88%). Among the patients with vasospasm, the development of DINDs was registered only if vasospasm had been associated with the detection of HDI (p < 0.05, Fisher exact test; specificity 29%, sensitivity 100%).

Relationship of HDI to Clinical Outcome After SAH

The clinical outcome according to the GOS in the 52 patients included in the final analysis revealed a good recovery in 18 (35%), moderate disability in five (10%), severe disability in 13 (25%), and death in 16 (31%). Thus, the group with a favorable outcome consisted of 23 patients (44%) and the group with an unfavorable outcome of 29 patients (56%).

An unfavorable outcome was detected in 21 of 31 patients with HDI and in 22 of 38 patients with vasospasm (Fig. 9). The registration of HDI, in contrast with the registration of vasospasm, was found to be significantly related to the development of a poor outcome after SAH (p < 0.05; Table 3). By univariate analysis, an unfavorable outcome was also related to the patients older than 60 years of age, severity of SAH according to the CT grade on the modified Fisher system, SAH severity according to the WFNS clinical grading system, and the detection of acute hydrocephalus (p < 0.05).

Last, all the factors significantly related to a poor outcome were entered into a stepwise multiple logistic regression model; the result was that older age, the detection of HDI, and the registration of a poor WFNS grade on admission were found to be independently related to the development of an unfavorable clinical outcome after SAH.

Discussion

In this study we analyzed prospectively the occurrence of HDI distal to the spastic cerebral arteries in a group of consecutive patients with verified SAH. The examinations were performed during routine TCD ultrasonography measurements, and HDI was found in the majority of vessels with arterial vasospasm. Although the detection of HDI after SAH was significantly related to delayed isch-
emic brain damage, the registration of arterial vasospasm without HDI never led to the development of delayed cerebral ischemia. Therefore, HDI was established as an independent predictor of an unfavorable clinical outcome in patients with SAH.

The THR Test: a Simple Measure of Cerebral Autoregulation

Utilization of the THR test has been advocated in a number of studies.7,13,27,31,40–42 The theoretical basis for the test was provided by Czosnyka, et al.,7 in a modeling study in which they described the phenomenon of THR in a mathematical model of CBF and the cerebrospinal fluid circulation. The test results have been compared successfully with intraoperative assessment of autoregulation and hypotensive challenges,13 standard Aaslid’s leg-cuff tests,41 and TCD waveform-derived indexes of cerebral autoregulation.42 The reliability and reproducibility of the test results for detection of the changes in cerebral autoregulation at different CO2 levels have been assessed.31,41 Smielewski, et al.,42 monitored cortical microcirculation by means of laser Doppler flowmetry during the THR tests and confirmed that the test reflects blood flow responses occurring at the level of small resistance vessels of the brain. These findings indicate that the test could be used for evaluation of HDI after SAH.

The THR test has been described as a noninvasive and simple method for repeated measurements of cerebral autoregulation. Because the magnitude of the hemodynamic challenge induced by CA compression is unknown, the test can be used only as a dichotomized index, indicating intact or absent autoregulation. The THR test, as in TCD ultrasonography examinations in general, is subject to operator-dependent variations. Despite these considerations, however, the simplicity and safety of the test favor its routine use, especially in situations in which the majority of autoregulation tests are impossible to perform because of unstable clinical conditions in the patients. Even though the THR test is recommended as easy to perform at the bedside, we failed to complete the tests at least once in approximately half of our patients. Nevertheless, eventually only three patients had to be excluded from the analysis because of unacceptable test results, which had a negligible effect on the results of our study.

Frequency of HDI After SAH

We observed HDI in 39% of the examined MCAs and in 60% of the patients. Detection of HDI was clearly related to the severity and rate of progression of arterial vasospasm. To date, in contrast with the extensive knowledge about the incidence of vasospasm, the occurrence of HDI after SAH has not been clarified. Still, several studies have been focused on the development of microcerebrovascular changes after SAH, and deranged autoregulation has often been related to the degree of arterial vasospasm, severity of clinical conditions, and the development of delayed cerebral ischemia or poor clinical outcome after SAH.25,36,46,51 It is clear that a complicated pathophysiological process, composed of a number of systemic and intracranial alterations, follows the rupture of a cerebral aneurysm, and regular evaluations should be conducted for adequate monitoring of aberrations in cerebral microvasculature. Yet, due to the lack of a good screening test for autoregulatory status, most of the earlier investigators have used only a single or a limited number of tests to measure the cerebral autoregulatory reserve in patients with SAH. Several authors have found evidence about the impact of vasospasm on the capacity of autoregulatory vasodilation in the small intraparenchymal vessels by using positron emission tomography19,32,58 or radioisotope tracer methods.27 In 1985, Voldby, et al.,41 reported defective autoregulation in most patients with slight and in all patients with severe angiographic vasospasm after SAH. In 1993,

![Table 2](image)

<table>
<thead>
<tr>
<th>Factor</th>
<th>Values Compared</th>
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<tr>
<td></td>
<td>yes</td>
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<tr>
<td>ipsilateral DCIs</td>
<td>(16 vessels)</td>
<td>(87 vessels)</td>
</tr>
<tr>
<td>HDI</td>
<td>12</td>
<td>28</td>
</tr>
<tr>
<td>vasospasm</td>
<td>12</td>
<td>42</td>
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<tr>
<td>patients w/ DINDs</td>
<td>(16 patients)</td>
<td>(36 patients)</td>
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<td>HDI</td>
<td>14</td>
<td>17</td>
</tr>
<tr>
<td>vasospasm</td>
<td>14</td>
<td>24</td>
</tr>
</tbody>
</table>

* CI = confidence interval; NS = not significant.

![Figure 8](image)

Fig. 8. Bar graph showing the incidence of DINDs in patients with vasospasm or with HDI after SAH.

![Figure 9](image)

Fig. 9. Bar graph showing the frequency of favorable and unfavorable outcome at 6 months after SAH according to the detection of vasospasm and development of HDI. Unfavorable outcome is defined as death, vegetative state, or severe disability; favorable outcome as moderate disability or good recovery.
Kimura, et al.,

used single-photon emission CT scanning
to document reduced cerebral vasodilatory capacity in
71% of patients by Day 18 after SAH. Although the severity
of vasospasm was not reported in their paper, the fre-
quency of deranged autoregulatory vasodilation is com-
parable to the incidence of HDI in our study. According
to our data, however, the development of vasospasm is
not inevitably associated with hemodynamic compromise,
and registration of HDI is not always guaranteed, even in
patients with severe vasospasm after SAH.

### Relationship Between HDI and Delayed Cerebral Ischemia

We found that the detection of HDI was clearly associ-
ated with the development of delayed cerebral ischemia
after SAH, but no ischemic complications followed the
registration of vasospasm without HDI. Although a posi-
tive correlation between arterial vasospasm and the de-
velopment of delayed ischemia has been confirmed in a
number of studies, several authors have reported on
patients who tolerated severe angiographically confirmed
vasospasm,
as well as extreme increases in BFV val-
ues, with no neurological deterioration. At the same
time, a number of injurious complications besides vaso-
spasm have been associated with DCI and poor clinical
outcome after SAH. Recently, Lam, et al.,
have tried to predict the development of delayed cerebral
ischemia by using TCD ultrasonography and serial THR
tests in a group of patients with no immediate postopera-
tive neurological deficits after SAH. Although the authors
have not analyzed the occurrence of HDI in this study,
they have found that patients with primarily impaired au-
toregulation are at a higher risk for the development of
delayed cerebral ischemia due to vasospasm after SAH.
According to our data, the development of brain damage
from vasospasm is closely regulated by the status of com-
pensatory mechanisms, which can respond to maintain
optimal CBF during the narrowing of the cerebral arter-
es. Furthermore, vasospasm, even if severe, could be a
rather benign phenomenon if it does not lead to the de-
velopment of HDI. It does seem likely, however, that the pro-
cess of neurological deterioration in patients with vaso-
spasm is complex, because several factors can increase the
risk of cerebral ischemia by impairing cerebral autoregu-
latory mechanisms and contributing to the development
of HDI.

It was found in more than half of the patients that the
status of HDI was not associated with delayed cerebral
ischemia. In previous studies investigators have reported
on the alterations in cerebral tolerance for ischemia after
consecutive insults to the brain. The enhanced isch-
emic vulnerability of the brain might be intermediated by
impaired cerebral autoregulation, but it might also involve
cellular processes that render the brain more susceptible
to ischemic cerebral perfusion. These factors might serve
to explain why some patients seem to be more prone to the
development of cerebral ischemia due to HDI after SAH.
On the other hand, many patients could probably escape
cerebral ischemia because of an abundant collateral blood
supply to the vascular bed of the spastic arteries. More-
ever, even in patients with HDI, the cerebral blood supply
could be preserved by HHH therapy. In fact, the derange-
ment of autoregulation might even increase the effect of
HHH therapy by permitting sustained CBF through pas-

tive filling of the nonautoregulating small resistance ves-
sels of the brain. Thus, even if aggressive HHH therapy
could be harmful on certain occasions, optimal volume
expansion and induced hypertension could avoid the de-
velopment of Stage II hemodynamic failure (misery per-
fusion) and thereby prevent delayed cerebral ischemia
in many patients with HDI after SAH.

### Associations Between HDI and Clinical Outcome

We determined that the detection of HDI was independ-
ently associated with an unfavorable clinical outcome
after SAH. The clinical outcome after an intracranial an-
eurysm rupture is put at risk by multiple factors. The age
of the patients, aneurysm rebleeding, and the develop-
ment of delayed arterial spasm have frequently been identi-
ced as risk factors for a poor outcome after SAH. The impact of
vasospasm on management outcome after SAH has arguably
been reduced recently because of new therapeutic modal-
ities like HHH therapy and nimodipine. Although the de-
velopment of vasospasm was not significantly related to the
clinical outcome in the present study, our results clear-
ly indicate the sustained importance of the hemodynamic
factors in the prognosis of SAH.

### Potential Implications of HDI Monitoring After SAH

In this study the measurement of HDI was proven to be
deurable during routine TCD ultrasonography monitoring

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**TABLE 3**

**Determinants of unfavorable clinical outcome according to the GOS score at 6 months post-SAH***

<table>
<thead>
<tr>
<th>Factor</th>
<th>GOS Score</th>
<th>Univariate Analysis</th>
<th>Multivariate Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥4 (23 patients)</td>
<td>&lt;4 (29 patients)</td>
<td>Odds Ratio (95% CI)</td>
</tr>
<tr>
<td>age &gt;60 yrs</td>
<td>6</td>
<td>16</td>
<td>3.49 (1.07–11.39)</td>
</tr>
<tr>
<td>HDI</td>
<td>10</td>
<td>21</td>
<td>3.41 (1.07–10.87)</td>
</tr>
<tr>
<td>vasospasm</td>
<td>16</td>
<td>22</td>
<td>1.38 (0.40–4.70)</td>
</tr>
<tr>
<td>WFNS Grade &gt;II</td>
<td>3</td>
<td>12</td>
<td>4.71 (1.14–19.48)</td>
</tr>
<tr>
<td>Fisher CT Grade ≥2</td>
<td>11</td>
<td>22</td>
<td>3.43 (1.05–11.16)</td>
</tr>
<tr>
<td>ICH</td>
<td>8</td>
<td>18</td>
<td>3.07 (0.98–9.59)</td>
</tr>
<tr>
<td>hydrocephalus</td>
<td>6</td>
<td>8</td>
<td>1.08 (0.31–3.72)</td>
</tr>
<tr>
<td>IVH</td>
<td>4</td>
<td>13</td>
<td>3.86 (1.05–14.21)</td>
</tr>
</tbody>
</table>

* IVH = intraventricular hemorrhage.
in the majority of patients with SAH. No therapeutic activities based on the detection of HDI have been undertaken in the present study; however, there might be several clinical implications of regular evaluation of HDI after SAH. In patients with CA occlusion, the concept of hemodynamic staging has been proposed as an opportunity to identify patients best suited for the investigation of novel management strategies. In patients with SAH, close evaluation of HDI while analyzing the administration of HHH therapy could be considered, and it could be useful for selecting a target population for scientific assessment of advances in the management of vasospasm. Further research on the specific indications for and clinical benefits of HDI monitoring after SAH may provide an opportunity to improve the overall outcome after aneurysm rupture.

Conclusions

Cerebral HDI is a common occurrence after SAH. The development of HDI can be evaluated noninvasively in daily clinical practice by using TCD ultrasonography. Hemodynamic insufficiency occurs in a majority of patients with cerebral vasospasm and is related to the severity and rapid progression of vasospasm. Compared with vasospasm per se, HDI should be considered to be a more ominous prognostic sign for the development of delayed ischemic brain damage and an unfavorable clinical outcome in patients with SAH. Therefore, HDI monitoring could increase the value of simple BFV recordings, and an aggressive management strategy could be advocated to counteract the development of delayed cerebral ischemia after SAH.

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