Cerebral Venous Flow Velocity Predicts Poor Outcome in Subarachnoid Hemorrhage

Wolf-Dirk Niesen, MD; Michael Rosenkranz, MD; Wolfram Schummer, MD; Cornelius Weiller, MD; Ulrich Sliwka, MD

Background and Purpose—Predictors of clinical outcome in aneurysmal subarachnoid hemorrhage (SAH) vary in reliability. Measurement of cerebral venous hemodynamics by transcranial color-coded duplexsonography (TCCS) has become of increasing interest lately, and correlation with intracranial pressure (ICP) seems to be high. The aim of the presented study was to assess changes of cerebral venous hemodynamics in SAH and evaluate its relationship with clinical outcome.

Methods—We performed sequential TCCS of venous peak flow velocities (vp-FVs) in the transversal sinus in 28 consecutive patients with aneurysmal SAH (Hunt and Hess scale 1 to 5). Measurement was initiated at onset of arterial vasospasm up to 5 days after SAH. All patients had a continuous ICP monitoring. Clinical outcome was evaluated with the modified ranking scale (MRS) 30 days after SAH. Patients were divided according to outcome: group I good recovery (MRS 0-III) and group II poor outcome (death or MRS IV-V). Maximum vp-FV, time-averaged vp-FV (mv-FV), and ICP were compared between groups.

Results—Vp-FV and mv-FV as well as ICP of group II exceeded values of group I (P<0.001 for all 3 parameters). Vp-FV showed a positive correlation with ICP (r=0.63; P<0.001). A vp-FV exceeding 35.4 cm/s (sensitivity 100%; specificity 90.9%), an mv-FV exceeding 27.3 cm/s (sensitivity 94.1%; specificity 81.8%), and an ICP exceeding 24 mm Hg (sensitivity 87.5%; specificity 81.8%) predicted poor outcome (receiver operating characteristic analysis).

Conclusions—Increased ICP values correlate with increased venous flow velocities. In SAH, increased ICP and increased venous flow velocities are associated with poor outcome. Flow velocity of the transversal sinus is a highly sensitive, reliable, and early predictor of outcome in SAH. (Stroke. 2004;35:1873-1878.)

Key Words: outcome ■ subarachnoid hemorrhage ■ ultrasonography, Doppler, transcranial ■ brain edema

Spontaneous subarachnoid hemorrhage (SAH) due to a ruptured cerebral aneurysm accounts for 3% of all strokes.1 Despite advanced techniques of aneurysm occlusion to prevent rebleeding, SAH is still associated with an overall mortality of 45%. Another 30% of patients experience a variable degree of persistent disability.2 Mortality and permanent neurological sequelae are mainly attributable to secondary and tertiary complications of SAH.

There are several factors that have been identified as outcome predictors in SAH.3–8 The most important is the neurological state at onset.9,10 Except for the initial Glasgow Coma Scale, predictors show a variable relationship with outcome in SAH. Assessment of neurological status at symptom onset may be difficult and is dependent on experience.11 Besides initial clinical scoring, the prognostic value of initial and delayed brain edema seems to be high.12 However, there is a need for outcome predictors that are more reliable and can be assessed easily.

The measurement of flow velocities of the deep cerebral veins by means of transcranial color-coded duplexsonography (TCCS) has been reported recently, and normal values have been published.13,14 Moreover, there are several studies that describe the influence of increased intracranial pressure (ICP) on the cerebral venous system.15 Changes of venous hemodynamics result from ICP changes, changes of cerebral perfusion pressure, or from venous outflow resistance.16 We hypothesize that secondary changes of ICP in SAH might influence venous hemodynamics.

This study evaluates prospectively the changes of venous cerebral hemodynamics in patients with SAH and its correlation with ICP increase. Venous hemodynamics and ICP are evaluated concerning prognostic impact to find a reliable and valid early outcome predictor. We also evaluated common predictors of poor outcome within the studied patient group.

Methods and Patients

Inclusion and Exclusion Criteria

Patients with aneurysmal SAH were included in the study. Inclusion was performed after surgical or interventional occlusion of the aneurysm and within 3 days of SAH.
Patients were excluded from the study in cases of insufficient transtemporal bone window, traumatic SAH, or SAH resulting from pathologies other than aneurysm, pre-existing pathologies of cerebral veins, or systemic disease influencing venous hemodynamics (e.g., venous thrombosis, jugular vein thrombosis, arteriovenous malformation, dural fistulas, as well as massive right ventricular insufficiency and pulmonary hypertension). Also, patients were excluded if patients or their relatives did not consent to participation.

Baseline Assessment and Procedures
Demographic data of patients liable for the study were assessed and included gender, age, concomitant morbidities with a special emphasis on vascular risk factors, neurological status after SAH, aneurysm localization, and therapeutic intervention.

At hospital admission, patients were classified according to the Hunt and Hess (H&H) scale. Diagnosis of SAH was based on cerebral CT (CCT), and in case of uncertainty, CCT diagnosis was approved by examination of the cerebrospinal fluid. If trauma was ruled out, patients underwent digital subtraction angiography (DSA) of the cerebral vessels within 24 hours to localize the ruptured aneurysm. According to localization and shape of the aneurysm, occlusion was performed surgically or by endovascular intervention. Decision on the placement of ventricular drainage was based on initial or postinterventional CCT. In patients without ventricular drainage, a parenchymal probe was placed to monitor ICP.

After surgical or interventional procedures, patients were monitored for secondary brain damage (e.g., delayed ischemic neurological deficit [DIND], hydrocephalus, and brain edema). Monitoring included online assessment of ICP, sequential CCT, and transcranial Doppler monitoring of the basal cerebral arteries.

Transcranial Duplexsonography
Monitoring for Cerebral Vasospasm
Patients were monitored for cerebral vasospasm at least every 12 hours. TCCS was performed with a 2.5-MHz sector array transducer (Sonos 5500; Philips) transtemporally. Basal cerebral arteries were identified using published criteria, and both peak middle cerebral artery flow velocities (MCA-FVs) were assessed. Angle correction was performed if possible (visible vessel over a length of ≥1.5 cm). Cerebral vasospasm was suspected if MCA-FV exceeded 160 cm/s. For further analysis, the MCA with the higher MCA-FV was used.

Venous Hemodynamics
Assessment of venous cerebral hemodynamics was performed by TCCS using a 2.5-MHz sector array transducer (Sonos 5500, Philips, Hamburg). The transversal sinus as well as the basal vein of Rosenthal (BVR) were insonated transtemporally using the meatoorbital plane. Vessels were identified using published criteria. Flow velocities of both transversal sinuses were measured on the side contralateral to the probe, whereas BVR flow velocity (BVR-FV) was measured ipsilaterally. Flow velocities of the transversal sinus were corrected for angulation using the proximal part of the transversal sinus, which is directed away from the ultrasound probe, and may be depicted for ≥3 cm, allowing correction of insonation angulation <70° (Figure 1). BVR-FV was also corrected for angulation. For analysis of venous hemodynamics, the maximum venous peak flow velocity (vp-FV) of the transversal sinus was used as well as time-averaged vp-FV (mv-FV) and maximum BVR-FV. Assessment of vp-FV was performed if MCA-FV or FV of other basal cerebral arteries indicated cerebral vasospasm, but on the fifth day after onset of SAH at latest. Venous flow velocities were monitored every other day over a period of 6 days. Measurement was performed using the same part of the vessel in all follow-up examinations.

ICP Monitoring
ICP was assessed continuously, either via a parenchymal probe (Codman ICP monitoring device) or via an intraventricular drain. ICP peak values recorded independently of patient manipulation or pulmonary manipulation were used for statistical analysis.

Figure 1. Depiction of transversal sinus with contrast imaging (top) and flow velocity of transversal sinus in near-normal ICP of 20 mm Hg (middle) and ICP crisis of 60 mm Hg (bottom).

Modified Rankin Scale
Early clinical outcome was assessed on day 30 after SAH. Outcome was measured using the modified Rankin scale (MRS), which describes the grade of disability and case fatality. Outcome was classified as good in case of MRS 0-III (outcome group I) and as poor in case of death or MRS IV and V (outcome group II).

Statistical Analysis
For statistical analysis, maximum vp-FV, mv-FV, BVR-FV, ICP, and MCA-FV were compared between outcome groups. Vp-FV, mv-FV, and BVR-FV were correlated with ICP. Common predictors
of poor outcome (ie, age, DIND, H&H grade, and occurrence of brain edema) were compared between groups. After testing for normal distribution (Shapiro–Wilk test), continuous data were compared using Student t test (normal distribution) or Mann–Whitney U test (absent normal distribution). Correlation was computed using Pearson correlation coefficient and Spearman correlation coefficient for nonparametric testing. Dichotomous variables were compared using Fisher exact test. In a receiver operating characteristic (ROC) analysis, cut-off values for vp-FV, mv-FV, and ICP were computed to distinguish between patients with good and poor outcome (10.1 version; SPSS).

**Results**

Twenty-eight consecutive patients with aneurysmal SAH of all H&H grades were included in the study. Aneurysms of the basilar cerebral arteries were identified in 23 patients. Aneurysms were treated with coil embolization in 16 patients and with neurosurgical clipping in 7 patients. No aneurysm could be detected in 1 patient in outcome group I, but distribution of SAH on CCT suggested an aneurysmal bleeding. Moreover, in 4 patients of outcome group II, DSA was omitted because of poor prognosis at admission. Medical history as well as CCT findings hinted at aneurysmal SAH. All patients but 1 received ICP monitoring: parenchymal probe in 6 patients and ventricular drain in 21 patients. A total of 16 patients were treated with Trippe-H-therapy, and 20 patients received intravenous catecholamines during monitoring. Mean arterial pressure was generally kept >80 mm Hg.

Secondary complications occurred in 25 of 28 patients. The 30-day outcome was poor in 17 of 28 patients (outcome group II). Within outcome group II, 9 of 17 patients had died, and 2 patients presented with a persistent vegetative state 30 days after SAH onset. Eleven of 28 patients had a good recovery (outcome group I; Table 1).

**Common Predictors of Poor Outcome**

Outcome groups I and II did not differ concerning age and presence of onset seizure (Table 1). The mean H&H grade was significantly higher in outcome group II (ie, initial clinical condition was worse in outcome group II [P=0.003]). Prevalence of cerebral vasospasm (P=0.13) and DIND (P=0.44) did not differ between groups. Brain edema was present in outcome group II only (P<0.001). Thirteen of the 17 patients in group II showed brain edema (Table 1).

**MCA Flow Velocity**

Cerebral vasospasm occurred in 18 patients. In 7 patients, vasospasm was asymptomatic, and in 11 patients, vasospasm resulted in DIND. Prevalence of vasospasm and DIND did not differ between groups (Table 1). MCA-FV as a marker of cerebral vasospasm was higher in group II compared with group I (Table 2). In an ROC analysis, MCA-FV of 219 cm/s had a sensitivity of 71.4% and a specificity of 81.8% in identifying outcome group II (Figure 2).

**Venous Hemodynamics and ICP**

In all patients, the transversal sinus and the BVR could be depicted, and venous flow velocities were measured. Maximum ICP was measured in all but 1 patient. There was a significant positive correlation of vp-FV and ICP

<table>
<thead>
<tr>
<th>TABLE 1. Patient Data</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
</tr>
<tr>
<td>Female, n (%)</td>
</tr>
<tr>
<td>Age (y), mean±SD</td>
</tr>
<tr>
<td>H&amp;H grade, mean±SD</td>
</tr>
<tr>
<td>Initial seizure, n (%)</td>
</tr>
<tr>
<td>Complication, n (%)</td>
</tr>
<tr>
<td>Vasoaspsm</td>
</tr>
<tr>
<td>DIND</td>
</tr>
<tr>
<td>Hydrocephalus</td>
</tr>
<tr>
<td>Ventricular blood</td>
</tr>
<tr>
<td>Secondary bleeding</td>
</tr>
<tr>
<td>Brain edema</td>
</tr>
<tr>
<td>Localization of aneurysm, n (%)</td>
</tr>
<tr>
<td>MCA</td>
</tr>
<tr>
<td>ACOMA</td>
</tr>
<tr>
<td>Anterior cerebral artery</td>
</tr>
<tr>
<td>PCOMA</td>
</tr>
<tr>
<td>Basilar artery</td>
</tr>
<tr>
<td>Therapeutic intervention, n (%)</td>
</tr>
<tr>
<td>Trippe-H-therapy</td>
</tr>
<tr>
<td>Catecholamines</td>
</tr>
</tbody>
</table>

Demographic data, complications, localization of aneurysms, therapeutic intervention in outcome groups. Outcome Group I, good recovery with MRS 0-III; Outcome Group II, poor outcome (ie, death, MRS IV-V).

ACOMA indicates anterior communicating artery; PCOMA, posterior communicating artery.

(r=0.63; P<0.001) and of mv-FV and ICP (r=0.64; P<0.001; Figures 1 and 2). There was no significant correlation between ICP and BVR-FV. BVR-FV did not differ between groups (Table 2).

To test for influence of Trippe-H-therapy, venous flow velocities were compared according to the presence of Trippe-H-therapy, which did not reveal a difference. To rule out influence of catecholamine treatment, we compared venous flow velocities according to catecholamines in group I, which did not differ.

Comparing flow velocities of the transversal sinus between the 2 outcome groups, vp-FV was highly increased in outcome group II. Mv-FV and ICP were increased in outcome group II compared with outcome group I (Table 2). When

<table>
<thead>
<tr>
<th>TABLE 2. Flow Velocities and ICP According to Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome Group I</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>MCA-FV</td>
</tr>
<tr>
<td>BVR-FV</td>
</tr>
<tr>
<td>ICP</td>
</tr>
<tr>
<td>vp-FV</td>
</tr>
<tr>
<td>mv-FV</td>
</tr>
</tbody>
</table>

Peak MCA-FV, BVR-FV, vp-FV, and mv-FV and ICP according to outcome. Level of significance is displayed. Outcome Group I, MRS 0-III; Outcome Group II, death, MRS IV-V. Values are presented as mean±SD.
comparing vp-FV of outcome group II, according to the presence of brain edema, there was no difference of vp-FV between patients with and without brain edema.

In an ROC analysis, pv-FV of 35.4 cm/s revealed a sensitivity of 100% and a specificity of 90.9% in identifying outcome group II (Figure 3). Odds ratio (OR) for poor outcome in case of vp-FV exceeding 35.4 cm/s was 11.0 (95% CI, 1.7 to 71.3). Mv-FV of 27.3 cm/s had a sensitivity of 94.1% and specificity of 81.8%, and an ICP of 24 mm Hg had a sensitivity of 87.5% and a specificity of 81.8% in identifying poor outcome (ie, outcome group II [Figure 3]). OR for poor outcome in case of ICP exceeding 24 mm Hg was 5.2 (95% CI, 1.5 to 18.2).

**Discussion**

The aim of this study was to evaluate the impact of venous hemodynamics in SAH on clinical outcome. Assessment of cerebral venous hemodynamics has become of increasing interest lately. Monitoring venous flow velocity with transcranial duplexsonography has been evaluated sufficiently, and normal values have been published with excellent agreement between the different studies and a high interobserver and intraobserver reliability.

The expected close relationship between venous flow velocity and increasing ICP makes the method intriguing. In adults, cerebral compliance depends on the compressibility of the CSF compartment and of the venous segment, which carries 70% of the cerebral vascular volume. Thus, increasing ICP should influence cerebral venous hemodynamics. We found a positive linear relationship between flow velocity within the transversal sinus and ICP. A similar relationship was demonstrated in predominantly traumatic brain injury. Stasis within the bridging veins (the vessels most sensitive to elevated ICP) during the early phase of ICP rise leads to secondary blood pooling toward the larger venous vessels, with consecutive increase of venous blood flow velocity. Flow velocity increases further with progressive compression of the venous system.

Increased ICP and consecutive increase of venous flow velocity in patients with aneurysmal SAH is probably attributable to global cerebral edema, which may occur during the acute phase or with onset delay. Acute edema is caused by SAH-induced vasoplegia in conjunction with increased intracerebral blood volume. In addition, experimental data suggest ischemic microcirculatory dysfunction, followed by subsequent recovery with rebound hyperemia resulting in brain edema. In contrast, delayed onset may be due to autoregulatory breakthrough in hypertensive phases, diffuse microvasculature spasm with consecutive ischemia, inflammation induced by blood products, and water shift caused by hyponatremia.

We found global brain edema only to be present in the group with poor outcome. Accordingly, flow velocity within the transversal sinus was increased significantly in patients with poor outcome with highly predictive cut-off values. Because there was a significant linear relationship with ICP, ICP cut-off value is highly predictive of poor outcome as well. Increased flow velocity within the transversal sinus is probably a result of global brain edema, which, in SAH, is associated with poor outcome or death with an OR of 4.5. Although hemispheric edema may influence venous hemodynamics differently, data of venous hemodynamics in malignant stroke underline these findings as well. Midline shift resulting from space-occupying stroke leads to increase of flow velocities within the vein of Galen and the straight sinus, which was associated with poor outcome. Contrary to increase of flow velocity within the straight sinus and the vein of Galen, flow velocity within BVR was reduced. This phenomenon might best be explained by partial compression of the rigid sinuses with consecutive stenosis, which results in reduced flow velocity in the preceding vessel. These findings have been shown in SAH as well as in brain trauma and are in accordance with our data.

Additionally, increase of venous hemodynamics might represent a pathophysiological phenomenon that affects outcome by itself. Venous hemodynamics may be impaired in insufficient venous outflow with consecutive congestive edema. Furthermore, pathological studies in transtentorial herniation revealed that distribution of mesencephalic lesions was influenced primarily by venous compression. This
might explain the high predictive power of flow velocities within the transversal sinus in SAH.

Looking for differences caused by vasospasm MCA flow velocities of patients with poor outcome exceeded flow velocities in patients with good recovery. Despite this, there was no difference concerning prevalence of vasospasm nor DIND. Moreover, occurrence of vasospasm did not influence venous flow velocities. These findings are in accordance with data on global edema in SAH, although experimental data suggest that diffuse ischemia caused by vasospasm might play a role in the development of brain edema influencing outcome. We also were not able to detect differences concerning onset seizure and age. These results contradict findings of others and thus probably need further confirmation. Comparing initial neurological status, H&H grade indicated poorer initial neurological state of patients with poor outcome, which is in accordance with others.

Comprising our results, we found increased venous flow velocity within the transversal sinus in poor outcome after SAH, which is probably attributable to global edema. Occurrence of global edema is an important predictor of poor outcome after SAH, which has also been shown by others. Moreover, flow velocities within the transversal sinus as well as maximum ICP are highly predictive of poor outcome when exceeding the presented cut-off values. Flow velocity within the transversal sinus is linearly correlated with ICP and is a highly sensitive, reliable, and early predictor of outcome in SAH.

References


Cerebral Venous Flow Velocity Predicts Poor Outcome in Subarachnoid Hemorrhage
Wolf-Dirk Niesen, Michael Rosenkranz, Wolfram Schummer, Cornelius Weiller and Ulrich Sliwka

Stroke. 2004;35:1873-1878; originally published online June 3, 2004;
doi: 10.1161/01.STR.0000132195.17366.2b
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2004 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/35/8/1873