Correlations Between Cerebral Arterial Velocities, Blood Flow, and Delayed Ischemia After Subarachnoid Hemorrhage

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Background and Purpose: Elevated middle cerebral erythrocyte velocities and tissue hypoperfusion have been correlated with delayed ischemia after subarachnoid hemorrhage, but few studies have compared serial arterial velocities with cerebral blood flow and neurological deficits.

Methods: Serial measurements of middle cerebral velocities, using transcranial Doppler ultrasonography, were performed in 34 patients after subarachnoid hemorrhage and correlated with cerebral blood flow, measured in 20 of the 34 using single-photon emission computed tomography with technetium-99m hexamethylpropylene amine oxime and neurological evidence of delayed ischemia.

Results: In 16 patients without delayed ischemia, eight had evidence of vasospasm (>120 cm/sec), but only one of seven had hypoperfusion, suggesting that vasospasm might be more common than hypoperfusion in this group (p=0.1). In 10 patients with delayed ischemia and a lateralizing deficit, both asymmetrical middle cerebral vasospasm (eight of nine with vasospasm) and hypoperfusion (six of six studied) were concordant with the clinically ischemic hemisphere (p<0.05). Vasospasm occurred with nonlateralized delayed ischemia in seven of eight patients and with hypoperfusion in five of six, affecting the anterior cerebral territory in three.

Conclusions: Concordant vasospasm and hypoperfusion were most often present in patients with delayed ischemia and lateralizing neurological deficits. Discordant results reflect inherent limitations and the different levels of the circulation monitored by the two techniques. (Stroke 1992;23:492–497)

KEY WORDS • blood flow velocity • cerebral blood flow • subarachnoid hemorrhage
Patients. Compton et al12 found that both CBF and arterial velocities correlated with the clinical grade of the patients. In contrast, Romner et al20 found a poor correlation between hemispheric CBF, reactivity, and TCD velocities in preoperative patients.

Measurements of arterial velocities do not necessarily equate with cerebral tissue perfusion. Cerebral blood flow measurements using TCD would necessitate measurements of vessel caliber. Moreover, TCD measures erythrocyte velocities in the large basal arteries, whereas the perfusion methods measure CBF at the microcirculatory level. Measurements of cerebral hemodynamics using both TCD and SPECT after SAH might be expected to produce discordant results in some patients. We therefore set out to analyze the relationship between arterial vasospasm and tissue perfusion after SAH, correlating these hemodynamic measurements with neurological evidence of delayed ischemia.

Subjects and Methods

We studied 37 consecutive patients with SAH, proven on CT scan or lumbar puncture, aged 44±2 (mean±SE) years. All patients had an initial CT scan and four-vessel angiography. Daily neurological examination was performed without knowledge of the TCD and SPECT results, using the Hunt-Hess scale,21 which involves assessment of conscious state and the presence and severity of any focal deficits. A clinical diagnosis of delayed ischemia was made when a patient showed delayed neurological deterioration (particularly depression of conscious state), with or without focal neurological deficits, after other causes had been excluded by investigations including repeat CT scan, but usually not repeat angiography. Lateralizing hemispheric neurological deficits1 were recorded, including dysphasia, hemiplegia, hemianesthesia, visual field deficit, or neglect. A diagnosis of delayed ischemia without lateralizing deficits1 was made when a patient showed decline in conscious state or confusion with or without other nonlateralizing signs, such as frontal lobe dysfunction with disturbances of sensorium, incontinence, and grasp reflexes.

Serial TCD measurements of mean MCA velocities were performed using a 2-MHz pulsed Doppler probe via the transtemporal windows, using the method described by Aaslid et al.2,3 The proximal segments of the right and left MCAs were each insonated three times at each examination, and mean values were established for the time-averaged mean erythrocyte velocities. Serial MCA velocities were successfully recorded in 34 of the 37 patients (30 with aneurysmal SAH, four with SAH and normal angiography) on 235 occasions, an average seven (range 3–14) studies per patient over an average 16 (range 4–38) days.

Insonation was unsuccessful in three patients because of poor bone windows. Two had aneurysmal and one nonaneurysmal SAH. None of the three developed delayed ischemic deficits. We used an averaged mean MCA velocity value of >120 cm/sec as the criterion for vasospasm, but also analyzed those with multiple as opposed to isolated velocity elevations at this level and also those with progressively rising velocity values.

We used the same protocol to measure arterial velocities in 30 normal volunteers and neurological patients without any cerebral abnormality or known cerebrovascular risk factors, age-matched (42±3 [mean±SE] years) to the SAH patients. To determine interhemispheric MCA asymmetry, the absolute difference for right and left mean MCA velocities was calculated and divided by the mean MCA velocity for the two sides.

Cerebral blood flow was measured in 20 of the 34 SAH patients 8±1 (mean±SE) days after SAH, using the ⁹⁹Tc HM-PAO SPECT technique previously described,17 with regional count data displayed on colored tomographic maps. The performance of the CBF studies in only 20 of the 34 patients was due to restricted access to the SPECT technique, but included a similar proportion of patients with and without delayed deterioration as the total group. The studies were performed within 4 hours of a correlative TCD study and neurological examination. Interhemispheric asymmetry in the anterior cerebral, middle cerebral, or posterior cerebral arterial territories was determined by visual inspection and by using homologous 16-pixel square regions of interest, without knowledge of the clinical data or TCD results. Each pixel was 3 mm on a side, and the regions of interests were 12×12 mm. An interhemispheric difference of >12% for homologous regions indicated abnormal blood flow asymmetry.19

Percent interhemispheric MCA absolute asymmetry was evaluated in the control subjects using histogram analysis to determine the level of absolute asymmetry which 95% of subjects were below. We used logistic regression to test whether the proportion of patients with delayed ischemia was increased with higher TCD values. Other tests of proportion were performed by logistic regression and binomial tests for p=0.5.

Results

For the 30 age-matched control subjects, mean±SD MCA velocity was 62±15 cm/sec (Table 1). Interhemispheric percentage MCA asymmetry was <20% in 95% of subjects.

Of the 34 patients successfully studied by TCD, the 30 patients with aneurysms were treated by craniotomy and aneurysm clipping, in <72 hours in 22 of the 30 patients. Eleven of these were treated with intravenous nimodipine. Eighteen of the 34 patients (53%) developed clinical signs of delayed ischemia, with lateralizing deficits in 10 (29%) and nonlateralizing neurological deterioration documented in the remaining eight patients (24%).

There was no evidence of MCA vasospasm (>120 cm/sec) in any patient in the first 72 hours after subarachnoid hemorrhage. Vasospasm was identified in 24 of the 34 patients (71%), in 16 of the 18 (89%) with delayed ischemia (four before clinical deterioration), but also in eight of the 16 without delayed ischemia (50%). Delayed deterioration was present in two of 10 patients with MCA velocities <120 cm/sec, in six of 10 in the range 120–160 cm/sec, and in 10 of 12 with velocities >160 cm/sec. The proportion of patients with delayed ischemia increased across the three categories (one-tailed, p = 0.05), indicating that higher MCA velocities correlated with delayed ischemia.

Of the 30 patients with aneurysmal SAH, 13 had midline (anterior communicating or basilar tip) and 17 had lateralized (internal carotid/posterior communicating or middle cerebral) aneurysms. Asymmetrical MCA vasospasm (>20% side-to-side difference) was present

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in a similar proportion of patients in the two groups (nine of 13 midline, 11 of 17 lateralized aneurysms). Of the 11 patients with lateralized aneurysms and asymmetrical vasospasm, 10 of 11 had higher velocities ipsilateral to the side of the aneurysm, whereas higher velocities were contralateral in one. Using a binomial test, this has a nominal probability value of <0.01. Of the 18 patients with delayed ischemia, 13 had SPECT scans that were abnormal in 11 (85%) and normal in two. In 16 patients without delayed ischemia, only one of seven SPECT studies was abnormal (14%).

Further analysis was performed by categorizing the patients into three groups, based on the presence or absence of delayed neurological deterioration and any lateralizing deficits (Table 1). Group 1 comprised 16 patients without delayed deficits. Eight of 16 had normal serial TCD studies. However, bilateral symmetrical vasospasm was present in two and asymmetrical vasospasm in six patients. Only one of the seven SPECT studies performed in this group showed regional hypoperfusion, concordant with asymmetrical MCA vasospasm. Of the six patients with normal SPECT, three had abnormal TCD studies, two with a progressive rise in velocities and multiple measurements >120 cm/sec. These results suggest that MCA vasospasm is more common than hypoperfusion in patients without delayed ischemia (p=0.125), although the difference did not reach statistical significance.

Group 2 comprised 10 patients who developed lateralizing neurological deficits (Figure 1, top and bottom panels). Vasospasm was identified in nine patients, significantly higher velocities ipsilateral to the clinically ischemic hemisphere in eight of the nine cases. Using a binomial test, asymmetrical vasospasm and higher MCA velocities correlated with the clinically ischemic hemisphere (p<0.05).

One patient had normal serial TCD studies although middle cerebral hypoperfusion was present on SPECT, concordant with the clinically ischemic hemisphere. Seven of these 10 patients were studied with SPECT. One was studied before the onset of the delayed deficit and had normal perfusion. The remaining six patients all had middle cerebral hypoperfusion concordant with the clinically ischemic hemisphere, one with bilateral regions of hypoperfusion. These patients all had MCA vasospasm with a progressive rise in velocities and multiple measurements >120 cm/sec. Using a binomial test, hypoperfusion correlated with clinical ischemia (p<0.05).

Group 3 comprised eight patients who showed delayed deterioration without a lateralizing deficit. In seven of the eight, MCA vasospasm was identified, symmetrical in one and asymmetrical in six patients. Six of these eight patients had correlative SPECT scans. One SPECT study was normal in a patient with bilateral, symmetrical MCA vasospasm with progressively rising velocities and multiple measurements >120 cm/sec. In a second patient, there was frontal lobe hypoperfusion with normal serial MCA velocities (Figure 2, top and bottom panels).

Three patients had regional hypoperfusion in the hemisphere ipsilateral to higher MCA velocities, two of the three with rising velocities and all three with serial measurements >120 cm/sec. One patient had right frontal hypoperfusion, rising MCA velocities and serial measurements >120 cm/sec, and higher velocities present in the contralateral hemisphere. In the five patients with regional hypoperfusion, CBF was depressed in the anterior cerebral territory in three and in the middle cerebral artery in the remaining two.

**Discussion**

Patients without delayed neurological deterioration after subarachnoid hemorrhage usually have normal cerebral blood flow, as shown by this and our previous investigations using the $^{99m}$Tc HM-PAO SPECT technique. In contrast, TCD evidence of symmetrical or asymmetrical vasospasm was present in approximately 50% of our patients, often with rising values and serial measurements in the vasospasm range, consistent with previous reports. Angiographic studies have also demonstrated a substantially higher frequency of vasospasm after SAH than of clinical signs of delayed ischemia.

In the early stages of cerebral vasospasm and lowered perfusion pressure, autoregulation with vasodilatation of small blood vessels will increase cerebral blood volume and hence maintain cerebral blood flow. Although this and previous studies have correlated the

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**Table 1. Correlations Between Delayed Ischemic Deficits, Middle Cerebral Velocities, and Cerebral Blood Flow After Subarachnoid Hemorrhage**

<table>
<thead>
<tr>
<th>Clinical course</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>No delayed ischemia</td>
<td>16</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>MCA vasospasm on TCD</td>
<td>8/16</td>
<td>9/10</td>
<td>7/8</td>
</tr>
<tr>
<td>Number SPECT studies</td>
<td>7</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Hypoperfusion on SPECT</td>
<td>1/7</td>
<td>6/7†</td>
<td>5/6§</td>
</tr>
<tr>
<td>Concordance clinical course, SPECT, TCD</td>
<td>3/7</td>
<td>5/7</td>
<td>4/6§</td>
</tr>
<tr>
<td>Concordance clinical course, SPECT, discordant TCD</td>
<td>3/7</td>
<td>1/7</td>
<td>1/6</td>
</tr>
<tr>
<td>Concordance clinical course, TCD, discordant SPECT</td>
<td>...</td>
<td>1/7*</td>
<td>1/6</td>
</tr>
<tr>
<td>Concordance SPECT, TCD, discordant with clinical course</td>
<td>1/7</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

TCD, transcranial Doppler ultrasonography; MCA, middle cerebral artery; SPECT, single-photon emission computed tomography.

*SPECT study performed before clinical onset of lateralized ischemic deficit in 1 case.
†All middle cerebral territory hypoperfusion.
§Concordant for the finding of abnormal SPECT, TCD, but different vascular territories affected in 2 of these 4 patients.
The likelihood of "symptomatic vasospasm"1 with the severity of erythrocyte velocity increases,4,5 these compensatory mechanisms can prevent delayed ischemia in some patients with very high maximum MCA velocities, including those with rising values on serial examinations.

One patient, without clinical signs of delayed ischemia, had middle cerebral hypoperfusion and concordant MCA vasospasm. With less severe hypoperfusion, neuronal function can be maintained by increased oxygen extraction and maintenance of regional oxygen metabolism.13 The 99mTc HM-PAO SPECT technique does not permit quantification of CBF and, hence, estimation of the quantitative severity of hypoperfusion.17 The differentiation of reversibly ischemic tissue from infarcted tissue requires paired metabolic and CBF measurements using positron emission tomography.13

Concordant MCA vasospasm and hypoperfusion were most often found in the group of patients with delayed ischemia and lateralizing deficits. The 99mTc HM-PAO SPECT demonstrated regional MCA hypo-
perfusion, correlating with the focal deficits, as we have previously reported. These patients usually had asymmetrical MCA vasospasm with rising velocities and serial measurements in the vasospasm range, higher velocities concordant with both the hypoperfusion and clinically ischemic hemisphere. One patient with a delayed lateralized deficit had normal serial MCA velocities yet middle cerebral hypoperfusion on a correlative SPECT study. This discordant result could be explained by vasospasm in small distal vessels not insonated by TCD or by frank infarction.

Soucy et al found an excellent correlation between hypoperfusion using Tc HM-PAO SPECT and the angiographic distribution of vasospasm. Jakobsen et al also found a correlation between the angiographic distribution of vasospasm and regional hypoperfusion using intra-arterial xenon-133, but additionally reported cases with focal vasospasm yet diffuse hypoperfusion. They concluded that factors other than vasospasm could depress cerebral perfusion.

Interhemispheric MCA asymmetry did not predict aneurysm lateralization in our series, although higher velocities correlated with the side of lateralized ruptured aneurysms, as previously reported. We did not detect MCA vasospasm in any patient in the first 72 hours after subarachnoid hemorrhage. Rommer et al studied patients in the first 12 hours after SAH and found no evidence of a biphasic course of cerebral vasospasm.
Patients with delayed ischemia without lateralizing neurological deficits also had evidence of MCA vasospasm, except in one case where the correlative SPECT study showed hypoperfusion in the anterior cerebral artery territory. The finding of anterior cerebral hypoperfusion in three patients could explain the lack of lateralized deficits and also the discordant result in the patient without evidence of vasospasm yet with regional hypoperfusion. Anterior cerebral artery vasospasm causes prominent alterations in sensorium, the emergence of primitive reflexes, incontinence, and akinesia, in contrast to the more readily recognized lateralized motor, sensory, visual, and speech deficits that typify vasospasm affecting the MCA. Vasospasm in the anterior cerebral arteries cannot be adequately diagnosed by the TCD method. This has been attributed to the technical difficulties involved in insomatizing the distal portion of the anterior cerebral arteries and the effects of collateral circulation via the anterior communicating artery.

One patient with nonlateralized delayed deterioration and an apparently normal SPECT study had bilateral and symmetrical MCA vasospasm. Because the 99mTc HM-PAO SPECT technique is not quantitative, interpretation being reliant on the comparison of interhemispheric count ratios in homologous regions, bilateral symmetrical or diffuse hypoperfusion could be misinterpreted as a "normal" SPECT result.

Of the 20 patients studied by the two hemodynamic techniques, the frequencies of MCA vasospasm and hypoperfusion were similar in those with delayed deterioration. Concordant results were most often found in the middle cerebral territory of the clinically ischemic hemisphere in those with lateralized deficits. However, the finding in patients of regional hypoperfusion after SAH appears to be a more specific indicator of cerebral ischemia than does the demonstration of erythrocyte velocities in the vasospasm range. In monitoring cerebral hemodynamics after SAH, these two techniques provide complementary information about the state of the basal middle cerebral vessels and microvascular perfusion. Transcranial Doppler is a valuable bedside monitoring technique, but the present study has shown that even rising velocity values and serial measurements in the vasospasm range do not necessarily indicate tissue hypoperfusion. The demonstration of regional hypoperfusion by SPECT could be used in the evaluation of new and potentially invasive therapies for vasospasm, such as balloon arterial dilatation in patients with delayed ischemia who are unresponsive to medical treatment. The discordant results found in this study reflect the different levels of the cerebral circulation being monitored, the complex consequences of vasospasm and distal blood flow changes, and the inherent limitations of the two methodologies.

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References

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