The Prognostic Value of Noninvasive CBF Measurement in Subarachnoid Hemorrhage

Gilles Géraud, M.D., Michel Tremoulet, M.D., Antonio Guell, M.D., and André Bes, M.D.

SUMMARY Seventy-four measurements of cerebral blood flow (CBF) were performed using the Xenon 133 inhalation method in 50 cases of spontaneous subarachnoid hemorrhage. This method is non-traumatic, reproducible and dependable. A correlation was found between clinical condition and CBF values, but in a number of cases which cannot be dismissed, very low mean CBF values or ischemic foci were revealed where clinical state gave no indication of same. A poor correlation appeared between vasospasm seen by angiography and ischemic foci detected by isotopic technique. Patients' age influenced CBF values but not clinical evolution.

CBF values, measured in the first two weeks of illness, were significantly higher in those patients having favorable outcome, whatever their clinical state at the time of CBF measurement (comas excluded). The figure of 60 ml/100g/min. for mean cortical flow seemed to be a critical level below which risk of complications was greater. Conversely, in every case where mean cortical flow measured above 70 ml, outcome was favorable. Thus, CBF measurement promises to be a valuable prognostic tool, playing an important role in the therapeutic strategy for this type of patient.

PREVIOUS CBF STUDIES in subarachnoid hemorrhage have established relations between CBF values and the level of consciousness, focal neurological symptoms and vasospasm seen by angiography. Although these studies are of significant physiopathological interest, they have proved of limited practical application, as establishing the prognostic value of this method was not an objective. Nilsson¹¹ alone indicated that a reduction greater than 40% in pre-operative CBF was related to unfavorable outcome. In a more recent study, Ishii⁷ came to the same conclusion.

The development of noninvasive measurement of CBF by inhalation or intravenous injection of Xenon 133 and the recent perfection of dependable and easy to handle apparatus have stimulated renewed interest in this problem and have resulted in new publications in the last few years.¹ ³ ⁹ ¹⁰ ¹⁶

The main question remaining is whether atraumatic measurement of CBF has prognostic value, and if so, what role should it play in regard to clinical evaluation and angiographic results? The present study, then, centers on this practical problem.

Materials and Methods

Fifty patients (20 men, 30 women) with subarachnoid hemorrhage were studied. Mean age of the subjects was 48 ± 12 years (ranging from 21 to 68 years of age). The neurological condition of the patients was graded according to the Hunt and Hess criteria:² Grade I and II, asymptomatic headache without alteration of consciousness or neurological deficit (29 cases); Grade III, drowsiness or confusion (14 cases); Grade IV stu-

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TABLE 1

Correlation Between Clinical Grade and CBF Values (74 Measurements Were Made in 50 Patients)

<table>
<thead>
<tr>
<th>Clinical grade</th>
<th>n</th>
<th>Age (years)</th>
<th>F1 (ml/100 g/mn)</th>
<th>ISI</th>
<th>pCO2 (mm Hg)</th>
<th>MABP (mm Hg)</th>
<th>Oligemic focus (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I—II</td>
<td>35</td>
<td>47.2 ± 12.3</td>
<td>65.5 ± 13.6</td>
<td>38.2 ± 6.6</td>
<td>32.3</td>
<td>97.3 ± 10.0</td>
<td>24 (70)</td>
</tr>
<tr>
<td>III</td>
<td>23</td>
<td>46.1 ± 13.6</td>
<td>67.4 ± 17.9</td>
<td>38.8 ± 12.3</td>
<td>31.8 ± 12.2</td>
<td>98.5 ± 13.2</td>
<td>10 (43)</td>
</tr>
<tr>
<td>IV</td>
<td>16</td>
<td>53.1 ± 11</td>
<td>51.3 ± 11.3</td>
<td>30.3 ± 7.9</td>
<td>30.4 ± 3.2</td>
<td>98.6 ± 9.8</td>
<td>3 (19)</td>
</tr>
</tbody>
</table>

Statistical test: F = 0.79, t = 6.65, F = 5.20, F = 1.55, F = 0.12
χ² = 11.76

*Mean ± SD.
NS = non-significant.

TABLE 2

Influence of Patients' Age on Clinical, Hemodynamic and Angiographic Parameters

<table>
<thead>
<tr>
<th>Age</th>
<th>Clinical grade</th>
<th>First rCBF</th>
<th>pCO2 (mm Hg)</th>
<th>MABP (mm Hg)</th>
<th>Oligemic focus (%)</th>
<th>Vasospasm (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50 years</td>
<td>I—II 13</td>
<td>70.5 ± 18.1†</td>
<td>41.5 ± 11.8</td>
<td>32.1 ± 2.9</td>
<td>98.7 ± 10.3</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>III 9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥50 years</td>
<td>I—II 16</td>
<td>60.9 ± 11.6</td>
<td>36.3 ± 5.8</td>
<td>32.2 ± 2.8</td>
<td>101.8 ± 11</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>III 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Statistical test: χ² = 1.60, t = 2.24, t = 1.98, t = 0.14, t = 1.03, χ² = 0, χ² = 0.59

†Mean ± SD.
NS = not significant.
were initially classified in grades I–II and III; moreover the 7 grade IV patients were equally divided among the 3 outcome groups.

On the other hand, initial CBF was greater in those patients having good recovery compared with those either suffering disabilities or dying (fig. 1). Mean values were significantly different for F1, which represented cortical flow. The same tendency, although less marked, was observed for ISI. Taking the value of 60 ml/100g/min. as the cortical level for F1 and 35 as that for ISI, it appeared that below this level the risk of complications was much greater; of the 18 patients with complications or who died, regardless of classification in grades I–II and III; more–over the 7 grade IV patients were equally divided among the 3 outcome groups.

Table 4 presented cortical flow. The same tendency, although less marked, was observed for ISI. However, marked decrease of initial cortical CBF was noted in those subjects experiencing complications. Similarly, focal oligemia occurred more frequently in this group than in those patients with uncomplicated postoperative evolution.

**Discussion**

As many other authors3, 7, 9, 13 have found, a certain correlation was observed between CBF values and the clinical state of patients: those with both alteration of consciousness and motor deficit showed a mean CBF decrease of 30% compared with the others. However, it seemed more valuable to emphasize the discords which may exist between clinical and hemodynamic parameters: among grade I–II patients, certain subjects showed abnormally low CBF values: 31% had a CBF value less than 60 ml/100g/min. Conversely, 57% of grade III or IV patients had results above this critical level. It would appear that the study of cerebral hemodynamics in these patients could furnish additional results and particularly, as Ferguson has noted,9 such investigation could permit detecting those risk-prone subjects with insufficient cerebral perfusion whose clinical condition gave no indication of same.

Analysis of regional CBF can also provide valuable information: each of the 7 patients with localized clinical symptoms presented a concordant ischemic or oligemic territory. The advantage of this type of atraumatic measurement is that of following the evolution of such focal ischemic and comparing it with the patient’s clinical outcome. However, discords could also exist between clinical and hemodynamic re-

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**Table 3 Correlations Between the 50 Patients’ Outcome and Clinical, Angiographic and Hemodynamic Parameters**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>n</th>
<th>Age (years)</th>
<th>Clinical grade</th>
<th>Vasopasm</th>
<th>First rCBF</th>
<th>Oligemic focus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recovery</td>
<td>31</td>
<td>46.5 ± 12.77</td>
<td>I II III IV</td>
<td>21 10</td>
<td>71.9 ± 16</td>
<td>41 ± 11.2</td>
</tr>
<tr>
<td>Disability</td>
<td>13</td>
<td>50.2 ± 12.5</td>
<td>I II III IV</td>
<td>7 6</td>
<td>52.8 ± 8.4</td>
<td>36.9 ± 4.3</td>
</tr>
<tr>
<td>Death</td>
<td>6</td>
<td>49.3 ± 12.1</td>
<td>I II III IV</td>
<td>2 4</td>
<td>50.1 ± 8</td>
<td>32.6 ± 4.4</td>
</tr>
</tbody>
</table>

| Statistical test | F = 0.45 | NS | $\chi^2 = 8.14$ | $\chi^2 = 3.24$ | NS | $\chi^2 = 6.89$ | $p < 0.05$ | $p < 0.01$ | NS | $p < 0.05$ |

**Table 4 Correlations Between the 27 Surgical Patients’ Outcome and Clinical, Angiographic and Hemodynamic Parameters**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>n</th>
<th>Age (years)</th>
<th>Clinical grade</th>
<th>Vasopasm</th>
<th>CBF (F1) (ml/100 g/min)</th>
<th>Oligemic focus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favorable</td>
<td>19</td>
<td>47.4 ± 13.2</td>
<td>I II III-IV</td>
<td>12 7</td>
<td>68.8 ± 11.6</td>
<td>15</td>
</tr>
<tr>
<td>Unfavorable</td>
<td>8</td>
<td>51.6 ± 11</td>
<td>I II III-IV</td>
<td>6 2</td>
<td>52.7 ± 8.6</td>
<td>1</td>
</tr>
</tbody>
</table>

| Statistical test | t = 0.80 | NS | $\chi^2 = 0.22$ | $\chi^2 = 0.36$ | NS | $t = 3.54$ | $\chi^2 = 10.30$ | $p < 0.01$ | $p < 0.01$ | NS | $p < 0.01$ |

†Mean ± SD. NS = not significant.
Results: thus, in 30% of the grade I–II patients and 57% of those in grade III, the first CBF measurement showed clinically silent focal oligemia. In 4 patients this oligemic focus was seen a few days before the concordant clinical deficit appeared. An example illustrating this is given in figure 3. The existence of such clinically silent oligemic foci could explain ischemic strokes following arteriography or surgery in patients showing no clinical or arteriographic symptoms of high risk.

Meyer et coll. have recently stressed the influence of patients' age: they reported decreased CBF and less favorable outcome in subjects over 50. Similarly, the present study established an inverse correlation between age and blood flow. But unlike the work of the former authors, this study does not emphasize relation between patients' age and their outcome (Table III): subjects 50 years or older did not evolve in a significantly different way than the others. It may thus be concluded in this sample that decreased CBF in those subjects with poor outcome was not a function of more advanced age.

Most of the earlier studies establish a relationship between spasm and decreased CBF. The present study also revealed decreased mean CBF in subjects with spasm, but it was not possible to correlate this decrease with spasm intensity. Nevertheless, having excluded comatose patients from this study, only three cases of severe, extensive spasm were observed. As well, there was no systematic correlation between spasm seen by angiography and focal oligemia revealed through hemodynamic examination: these two methods do not explore the same vascular territory.

![Figure 1. Initial cerebral blood flow values for the 50 patients in terms of their outcome. F1 represents cortical flow. ISI is an index of mean flow.](image)

![Figure 2. Comparative prognostic value of clinical grade and initial CBF measurements evaluated in the early days following meningeal hemorrhage (mean 9.7 ± 9.6 days).](image)

![Figure 3. A 56-year-old woman. Aneurysm of left middle cerebral artery (MCA) bifurcation. Arteriography performed on the 6th day showed no spasm. At the time of CBF measurement on the 10th day, the patient was in grade II, showing neither confusion nor deficit. This flow reading revealed major focal oligemia in the left MCA territory. Five days later, this patient became aphasic. Surgery took place on the 33rd day once mean CBF had returned to a normal value. Post-operative evolution was uncomplicated, but the patient retained aphasic deficit.](image)
angiography shows mainly the basal and cortical arteries; Xenon 133 inhalation measures tissue perfusion, i.e. distal circulation. It is known that the narrowing of arterial lumen must be greater than 80% before distal circulation is affected. That is why angiographic vasospasm and focal ischemia may be dissociated, and why angiographic results do not provide an exact picture of tissue perfusion and consequently, of the risk of ischemia.

Finally, the essential focus of this study remains patients’ outcome and the search for prognostic factors. It was observed that neither the patients’ age, nor the presence of vasospasm, nor the extent of bleeding, nor the location of the aneurysm seemed to be determinant in patients’ evolution (table 3). Nor was significant correlation found between initial clinical grade and outcome. It is not to be inferred, nonetheless, that clinical state has no predictive value, particularly for surgical results. To do so would be to oppose well-established ideas and daily experience. Like most other medical-surgical teams, ours does not consider operable those patients with alteration of consciousness or significant neurological deficit. Spontaneous improvement must occur before surgery is indicated. Nonetheless, it must be stated that, in this study, a significant correlation appeared between CBF measured in the first two weeks of illness and patient’s outcome on leaving hospital (fig. 1). Such a correlation was not evident with initial clinical condition at the time of CBF measurement (fig. 2). This observation stands when considering solely the 27 patients later undergoing surgery (table 4).

The prognostic value of cerebral hemodynamic measurements in subarachnoid hemorrhage has been suggested by several authors. 

The studies record lower CBF values in those subjects having poor outcome. The decrease falls between 25 and 40% depending on the study, absolute values varying widely according to the method of CBF measurement. Ishii, by intracarotid method, and Meyer et coll., by inhalation method, place the critical level at 30 ml/100g/min.; this value corresponding to mean flow rather than cortical flow. Our study seemed to indicate the critical level as 60 ml/100g/min. for cortical flow and 35 for flow, as evaluated by ISI.

This study thus confirm the significant prognostic value of CBF measurement in subarachnoid hemorrhage. Thanks to its atraumatic nature, measurement by inhalation can be repeatedly performed on the same patient with no ill effect. The approach we presently adopt in cases of spontaneous subarachnoid hemorrhage is performing the first CBF measurement as soon as possible. Mean cortical flow values less than 60 ml/100g/min. and/or focal oligemia temporarily contraindicate surgery. In these conditions, we prefer delaying angiography and repeating CBF measurements until hemodynamic and clinical improvement safety permit further investigation.

References

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