ISI Values and Interhemispheric Differences in Patients with Ischemic Cerebrovascular Disease; Correlations with Clinical and Angiographic Findings

P. C. M. Mosmans, M.D., M. M. Veering, M.D., and E. J. Jonkman, M.D.

SUMMARY Xenon 133 inhalation CBF studies of one hundred patients with ischemic cerebrovascular disease in the territory of the carotid artery were compared in an attempt to gain more insight into the collateral capacity, especially in those with a stenosis or occlusion of one of the major arteries. Asymmetry of the ISI values for the two hemispheres was expressed as a ratio. High ratios (greater ISI asymmetries) were found for patients with an occlusion of the internal carotid or middle cerebral artery, especially — but not exclusively — those with the more severe clinical symptoms. It also appeared that even when the patient is in a good clinical condition, an elevated ratio reflects insufficiency of the collateral supply to the affected side. The ISI values for individual patients seem to be less useful, partly due to the variable age dependency of this flow parameter.

IN A NUMBER OF PATIENTS suffering from ischemic cerebrovascular disease (CVD) the clinical symptoms are due to hemodynamic changes which led to an insufficient supply of blood to some parts of the brain. In selected cases of extracranial vascular stenosis, which has a hemodynamic impact, endarterectomy is the treatment of choice. In the past few years patients with an occlusion of the internal carotid artery or an occlusion or stenosis of one of the major intracranial arteries have received a so-called extra-intracranial bypass. A collaborative study on the clinical effectiveness (i.e. stroke prevention) of this type of operation is still in progress. Both the development and the severity of the clinical symptoms in patients with one-sided stenosis or occlusion of one of the major arteries depend to a large extent on the capacity of the collateral circulation. In such cases information about this capacity might indicate the need for surgical intervention. This can be important for the group with a slight or no neurological deficit in particular since these patients should be considered for surgical treatment. There is therefore a need for a method of examination which not only provides the information required with a high degree of reliability but is also harmless to the patient. If the collateral circulation between the two carotid artery territories is sufficient in a patient with a severe one-sided stenosis or occlusion of a carotid artery, then the blood flow in the two hemispheres will probably be equal or almost equal.

In this study we tried to determine whether different parameters (absolute ISI values and differences in ISI values between the hemispheres) of blood flow studies (Xe 133 inhalation method) could provide a better insight into the efficiency of the collateral circulation. Using 100 patients suffering from ischemic CVD the clinical condition of the patient, the angiographic findings and the results of the CBF were evaluated. For this purpose the patients studied were divided into several groups: patients with a normal angiogram, those with a stenosis and those with an occlusion of a major artery.

Methods

The CBF studies were carried out using the Xe 133 inhalation method. An array of 16 detectors was placed against the head of the patient on each side. Each probe contained a ½ × ¼ inch NaI crystal. The collimator had a width of 22 mm and a depth of 18 mm. The exact position of each detector and further details concerning the method are described elsewhere. Blood pressure was measured immediately after the flow study. The end-tidal pCO₂ was registered during the flow study. One CBF study was carried out per patient. During the study the patient was in a supine position in a quiet environment with eyes closed. The Initial Slope Index (ISI), as defined by Risberg et al (1979) and calculated according to Jablonski et al, (1979) was used as the parameter for cerebral blood flow. The mean ISI for each hemisphere was calculated for every patient. For reasons described in a previous study values registered by the three detectors located in the lower temporal area were not included in the calculations. The difference between the mean ISI values for the two hemispheres was expressed as the R/L ratio or % asymmetry:

\[
R/L\text{ ratio or } %\text{ asymmetry:}\]

\[
\frac{\text{ISI noninvolved hemisphere}}{\text{mean ISI of both hemispheres}} - \frac{\text{ISI involved hemisphere}}{100}\]

The involved hemisphere is the clinically affected side. A negative R/L ratio indicates that the lower ISI value was found for the clinically normal hemisphere. A ratio ≥5 was considered to be abnormal. This value is based on flow values published in the literature and is in accordance with the values found for 5 nor-
In total 100 patients, ranging in age from 23 to 70 years, were investigated. In all cases the diagnosis of an ischemic CVD was based on the history, a clinical examination and the electroencephalogram. Usually a computerized axial tomogram (CT scan) of the brain was also made. Selective angiograms of both carotid arteries were always made; often one or both vertebral arteries were investigated as well. Only those patients with a vascular accident confined to the territory of one carotid artery were included in this study. According to the results of the angiographic studies the patients were divided into 4 groups:

- Group 1 (n = 33): patients without or with only minor abnormalities on the angiogram.
- Group 2 (n = 19): patients with a stenosis of 50% or more of the lumen of one of the internal carotid arteries. In 3 cases there was a stenosis of the proximal part of the ipsilateral middle cerebral artery as well.
- Group 3 (n = 10): patients with one-sided occlusion of the middle cerebral artery.
- Group 4 (n = 38): patients with one-sided occlusion of the internal carotid artery.

The clinical condition of the patients examined was indicated as follows:

- Status 0: no complaints and no clinical symptoms at the time of the CBF study. In most cases these patients had suffered amaurosis fugax or transient ischemic attacks (TIA).
- Status 1, II, III and IV: according to the classification system of the Ad-hoc Committee on Cerebrovascular Diseases. Status 1 indicates no significant impairment while Statuses II, III and IV refer to mild, moderate and severe impairments, respectively.

Patients with Status IV were excluded from the study because from a technical point of view, CBF studies were often not possible in these cases.

For patients who had suffered several TIAs the time between onset of the symptoms and CBF studies was difficult to estimate. In most cases the time lapse ranged from one week to two months.

### Results

The results for the patients investigated are presented in Table 1. For each group of patients the results as well as the number of patients and the mean ages are given separately for the four categories of clinical status. Figure 1 shows the relation between the clinical status and the R/L ratio for each patient. The four columns in the Figure represent the four different groups. As can be seen, no patients with Status III are to be found in groups 1 and 2; moreover there were no patients with Status 0 in group 3. In Table 2 the mean ISI values and ratios are presented for the different groups and different clinical conditions. Only small differences were found in Mean Arterial Blood Pressure (MABP, ⅓ systolic blood pressure + ⅔ diastolic blood pressure, range 110-117 mm Hg) between the different groups; endtidal pCO₂ range: 4.5-5.6 vol%.

In order to evaluate the significance of the mean ISI (mean of the ISI values for each hemisphere) it was important to determine first whether the age of the patients influenced the ISI values for the non-involved and the involved hemisphere in the four groups of patients. For this purpose the regression lines (age versus ISI non-involved hemisphere and age versus ISI involved hemisphere) for all patients with Status 0 and all patients with Status I + II from each group were

### Table 1

<table>
<thead>
<tr>
<th>Status</th>
<th>n</th>
<th>Age (mean ± SD)</th>
<th>ISI (mean ± SD)</th>
<th>Ratio (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>12</td>
<td>49.2 ± 10.1</td>
<td>62.4 ± 10.5</td>
<td>1.6 ± 1.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(31.0-62.0)</td>
<td>(48.7-78.6)</td>
<td>(-1.4-4.4)</td>
</tr>
<tr>
<td>I</td>
<td>18</td>
<td>47.3 ± 13.0</td>
<td>52.1 ± 10.7</td>
<td>1.8 ± 1.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(23.0-70.0)</td>
<td>(37.7-73.5)</td>
<td>(-4.6-4.6)</td>
</tr>
<tr>
<td>II</td>
<td>3</td>
<td>54.6</td>
<td>46.1</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(50.0-58.0)</td>
<td>(40.7-49.3)</td>
<td>(-5.6-7.4)</td>
</tr>
<tr>
<td>III</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Status</th>
<th>n</th>
<th>Age (mean ± SD)</th>
<th>ISI (mean ± SD)</th>
<th>Ratio (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>10</td>
<td>59.0 ± 9.5</td>
<td>52.9 ± 11.0</td>
<td>0.0 ± 2.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(41.0-68.0)</td>
<td>(35.5-68.0)</td>
<td>(-2.0-3.6)</td>
</tr>
<tr>
<td>I</td>
<td>5</td>
<td>57.8</td>
<td>52.6</td>
<td>3.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(49.0-64.0)</td>
<td>(42.6-70.6)</td>
<td>(-4.0-7.8)</td>
</tr>
<tr>
<td>II</td>
<td>4</td>
<td>63.5</td>
<td>47.5</td>
<td>9.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(61.0-65.0)</td>
<td>(42.0-56.4)</td>
<td>(4.8-12.4)</td>
</tr>
<tr>
<td>III</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

### Table 2

<table>
<thead>
<tr>
<th>Status</th>
<th>n</th>
<th>Age (mean ± SD)</th>
<th>ISI (mean ± SD)</th>
<th>Ratio (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>9</td>
<td>51.3</td>
<td>53.9</td>
<td>4.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(39.0-63.0)</td>
<td>(40.7-67.1)</td>
<td>(0.6-10.8)</td>
</tr>
<tr>
<td>I</td>
<td>19</td>
<td>59.9 ± 5.5</td>
<td>47.0 ± 9.4</td>
<td>10.4 ± 6.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(51.0-69.0)</td>
<td>(23.0-70.4)</td>
<td>(1.2-23.0)</td>
</tr>
<tr>
<td>II</td>
<td>8</td>
<td>58.2</td>
<td>41.7</td>
<td>13.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(45.0-70.0)</td>
<td>(27.3-55.9)</td>
<td>(8.2-19.4)</td>
</tr>
<tr>
<td>III</td>
<td>2</td>
<td>50.0</td>
<td>42.5</td>
<td>25.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(42.0-58.0)</td>
<td>(40.8-44.4)</td>
<td>(22.0-28.8)</td>
</tr>
</tbody>
</table>

For the groups with n < 10 no SD is calculated. Ranges are indicated by numbers in parentheses.
calculated separately. Patients with Status III were excluded from this calculation because their number was too small. The results are presented in table 3. The regression coefficients obtained were compared with the one published by Matsuda et al. They calculated the regression line for age versus ISI using 90 normals (age range: 19 to 80 years, 125 CBF studies). Their ISI values, derived in the same manner as described in this paper, were also not corrected for pCO₂.

Linear regression analysis showed that there was no significant correlation between age and the ISI values for patients with Status 0 or Status I + II from the four different groups. The results of the analysis of age versus ISI are given below.

Group I (n = 33). From table 3 it can be seen that in group 1 there is a weak correlation between age and the ISI values (non-involved and involved hemisphere) for patients with Status 0 and those with Status I + II. The fact that a significance level of \( p < 0.05 \) is not reached may be caused by the rather small number of patients in the group and the relatively low variance of the age distribution. No pronounced difference exists between the ISI values for group 1 and the values found for normals by Matsuda et al. Only two patients had a ratio that was too high (both with clinical Status II, fig. 1). It should be noted that one of these two patients had a negative ratio, i.e. the lower ISI value was for the normal hemisphere. There was no significant difference between the mean ratios found for Status 0 and Status 1 + II patients.

Group 2 (n = 19). The angiogram revealed in most cases a severe stenosis (80–90% lumen diameter) on the side related to the clinical symptoms. Stenoses of lesser severity were often seen on the contralateral side. In three patients the ipsilateral middle cerebral artery showed an important stenosis as well.

For reasons that are not quite clear no correlation between age and either ISI non-involved or ISI involved hemisphere could be found for group 2 patients with Status 0 and with Status 1 + II (table 3). This may be due to the fact that most of the patients were concentrated within a small age group.

The patients with Status 0 had a normal ratio in all cases. An elevated ratio was found for five patients with Status I or II (fig. 1). In five other patients the lower ISI value was found for the asymptomatic hemisphere. All of these patients had a ratio within normal limits. In one case (Status I, CT scan normal) the most severe stenosis was on the side of the asymptomatic hemisphere. However the lower ISI value was for the symptomatic side.

The mean ratio for Status 0 patients differed significantly from the mean ratio for patients with Status I + II (\( p < 0.01 \)).

Group 3 (n = 10). As a rule the clinical symptoms are severe in patients with an occlusion of the middle cerebral artery. This is probably due to the lack of possibilities for developing an adequate collateral supply. A significant correlation was found between age

### Table 2: Mean ISI Values ± SD and Ratios ± SD for the Different Groups, Irrespective of Clinical Status (A) and for the Clinical Status Irrespective of Group (B)

<table>
<thead>
<tr>
<th>A Group</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>33</td>
<td>19</td>
<td>10</td>
<td>38</td>
</tr>
<tr>
<td>ISI</td>
<td>55.3±11.5 (37.7–78.6)</td>
<td>51.0±10.0 (35.5–70.6)</td>
<td>49.8±13.1 (36.5–81.0)</td>
<td>47.3±10.1 (23.3–70.4)</td>
</tr>
<tr>
<td>Ratio</td>
<td>1.4±2.4 (-5.6–7.4)</td>
<td>3.3±4.3 (-4.0–12.4)</td>
<td>7.5±8.7 (-14.8–15.4)</td>
<td>10.8±6.6 (0.6–28.8)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B Status</th>
<th>0</th>
<th>I</th>
<th>II</th>
<th>III</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>31</td>
<td>45</td>
<td>19</td>
<td>5</td>
</tr>
<tr>
<td>ISI</td>
<td>56.0±11.2 (35.5–78.6)</td>
<td>49.6±10.0 (23.3–73.5)</td>
<td>46.5±11.4 (27.3–81.0)</td>
<td>44.9 (36.5–55.5)</td>
</tr>
<tr>
<td>Ratio</td>
<td>2.4±2.8 (-2.0–10.8)</td>
<td>6.1±6.3 (-4.6–23.0)</td>
<td>8.3±8.2 (-14.8–19.4)</td>
<td>18.6 (13.2–28.8)</td>
</tr>
</tbody>
</table>

Ranges are indicated by numbers in parentheses.
INTERHEMISPHERIC ISI DIFFERENCES IN ISCHEMIC CVD/Mosmans et al

TABLE 3 Regression Coefficients for the Correlation Between Age and ISI Non-involved Hemisphere (non-involv) and Age and ISI Involved Hemisphere (involv) for Each Group and Patients with Clinical Status I + II.

<table>
<thead>
<tr>
<th>Group</th>
<th>Status</th>
<th>n</th>
<th>Age</th>
<th>ISI</th>
<th>Slope</th>
<th>95% c.i.</th>
<th>Interc.</th>
<th>Corr. coeff.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>12</td>
<td>49.2</td>
<td>63.04</td>
<td>-0.51</td>
<td>±0.63</td>
<td>88.24</td>
<td>-0.49</td>
</tr>
<tr>
<td></td>
<td>involv</td>
<td>12</td>
<td>49.2</td>
<td>62.08</td>
<td>-0.53</td>
<td>±0.62</td>
<td>88.43</td>
<td>-0.50</td>
</tr>
<tr>
<td></td>
<td>I+I</td>
<td>21</td>
<td>47.8</td>
<td>51.51</td>
<td>-0.34</td>
<td>±0.40</td>
<td>68.04</td>
<td>-0.38</td>
</tr>
<tr>
<td></td>
<td>I+II</td>
<td>21</td>
<td>47.8</td>
<td>51.08</td>
<td>-0.31</td>
<td>±0.39</td>
<td>65.90</td>
<td>-0.35</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>10</td>
<td>59.0</td>
<td>53.00</td>
<td>-0.18</td>
<td>±0.64</td>
<td>63.65</td>
<td>-0.15</td>
</tr>
<tr>
<td></td>
<td>involv</td>
<td>10</td>
<td>59.0</td>
<td>52.98</td>
<td>-0.12</td>
<td>±0.62</td>
<td>60.60</td>
<td>-0.11</td>
</tr>
<tr>
<td></td>
<td>I+I</td>
<td>9</td>
<td>60.3</td>
<td>52.03</td>
<td>0.59</td>
<td>±1.34</td>
<td>16.38</td>
<td>0.36</td>
</tr>
<tr>
<td></td>
<td>I+II</td>
<td>9</td>
<td>60.3</td>
<td>48.96</td>
<td>0.35</td>
<td>±1.34</td>
<td>27.37</td>
<td>0.23</td>
</tr>
<tr>
<td>3</td>
<td>I+I</td>
<td>7</td>
<td>46.5</td>
<td>52.07</td>
<td>-0.69</td>
<td>±0.53</td>
<td>84.20</td>
<td>-0.83</td>
</tr>
<tr>
<td></td>
<td>involv</td>
<td>7</td>
<td>46.5</td>
<td>50.61</td>
<td>-0.86</td>
<td>±0.91</td>
<td>91.04</td>
<td>-0.73</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>9</td>
<td>51.3</td>
<td>55.50</td>
<td>-0.98</td>
<td>±1.20</td>
<td>106.05</td>
<td>-0.59</td>
</tr>
<tr>
<td></td>
<td>involv</td>
<td>9</td>
<td>51.3</td>
<td>52.77</td>
<td>-1.02</td>
<td>±1.01</td>
<td>105.36</td>
<td>-0.67</td>
</tr>
<tr>
<td></td>
<td>I+I</td>
<td>27</td>
<td>59.5</td>
<td>47.70</td>
<td>-1.01</td>
<td>±0.42</td>
<td>107.93</td>
<td>-0.69</td>
</tr>
<tr>
<td></td>
<td>I+II</td>
<td>27</td>
<td>59.5</td>
<td>42.35</td>
<td>-0.89</td>
<td>±0.41</td>
<td>95.49</td>
<td>-0.66</td>
</tr>
<tr>
<td></td>
<td>Matsuda (normals)</td>
<td>125</td>
<td>42.5</td>
<td>55.05</td>
<td>-0.30</td>
<td>±0.06</td>
<td>67.8</td>
<td>-0.67</td>
</tr>
</tbody>
</table>

Bottom line: results of 125 CBF studies in 90 normals (Matsuda et al).
95% c.i.: 95% confidence interval.

and the ISI values (non-involved and involved hemisphere), see table 3.

The ratios were abnormal in all cases, except one. This patient was the only one who had an extensive collateral vascular supply via the leptomeningeal arteries. One patient had a high negative ratio (-14.8) two days after the development of the clinical symptoms. A luxury perfusion syndrome could be demonstrated angiographically and on the CT scan at that time. A repeat study four weeks later showed the lower ISI value on the occluded side.

Group 4 (n = 38). Every clinical status is represented in this group, which is in accordance with data reported in the literature.16,17 There is an extremely variable clinical picture among patients with a one-sided carotid artery occlusion. The mean ISI values are lower than those found for groups 1 and 2 with the same clinical status except for Status 0 (table 1). Nearly all ISI values for the patients in group 4 were within the normal range given by Matsuda et al. The regression coefficient (age versus ISI) was the same for the non-involved and the involved hemisphere for Status 0 and Status I + II patients. None of the patients in group 4 had a negative ratio. In all cases the clinical symptoms were in accordance with the side of the occluded internal carotid artery. Patients with Status II and III in particular were found to have a high ratio (fig. 1). Nine patients had a normal ratio: five with Status 0 and four with Status I. The remaining four patients with Status 0 had an abnormal ratio. The mean ratio for patients with Status 0 differed significantly from that found for patients with Status I + II (p < 0.01).

As far as the mean ISI for each individual patient is concerned, it can be concluded that a relationship exists between the age and the ISI for both the non-involved and the involved hemisphere for the patients in the different groups - except for the patients in group 2. However none of the groups had a mean ISI value that exceeded the normal limits calculated by Matsuda et al.15 From table 4 it is apparent that the difference between the ratios for the different groups is significant, except for that between groups 1 and 2 Status 0.

Discussion

Before basing any conclusions on the results described in this study, one should be aware of several factors which may have influenced these results. Such factors may be:

a) The patients investigated were preselected: in all cases angiography was necessary, both on clinical grounds and to evaluate whether the vascular abnormalities were suitable for surgical intervention. Only patients suffering from an ischemic CVD in the region of the carotid artery were investigated.

b) The division of the patients into four groups on the basis of the angiogram is not quite accurate in all cases. It is well known that a number of patients with cerebral ischemia suffer from multiple arterial abnormalities of the extracranial and the intracranial vascular system.18 Some of our patients exhibited multiple arteriosclerotic changes. Furthermore

TABLE 4 Differences in the Ratio between Groups 1, 2 and 4

<table>
<thead>
<tr>
<th>Groups</th>
<th>Status 0</th>
<th>Status I + II</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>NS</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>1-4</td>
<td>p &lt; 0.05</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>2-4</td>
<td>p &lt; 0.01</td>
<td>p &lt; 0.05</td>
</tr>
</tbody>
</table>

No significant difference was found between groups 1 and 2 (Status 0).
some also suffered from diabetes mellitus, hypertension, myocardial infarction etc.

c) The ISI values were the only parameter of the cerebral blood flow. The methods of investigation and calculation used in this investigation have several drawbacks that are inherent in the two-dimensional CBF methods. 19, 20

d) No attention was paid to focal CBF abnormalities. However with the method used focal abnormalities will probably not be detected very accurately. 21 It is quite likely that the ratio used in this study is influenced by so-called cross talk. 22

e) Only CBF studies taken during rest were investigated. Corrections for pCO₂ were not made. This may be a point of criticism but corrections for pCO₂ can give rise to incorrect ISI values for patients with CVD. 23

In order to answer the question formulated in the Introduction a correlation was sought between a particular flow pattern and a specific clinical condition and/or angiographic pattern. The mean ISI for both hemispheres and the ratio were used as the parameters of the cerebral blood flow.

The ISI. It is well known that a relation exists between the clinical condition of the patient and the cerebral blood flow. Lower flow values can be found in clinically more disabled patients. 15, 34, 35 Patients suffering from TIA can have lower flow values than normals. 26, 27 The ISI values can be influenced by the time lapse between the development of the cerebrovascular accident and the measurement of flow. Flow can change in the period immediately after the accident due to edema, changes in intracranial pressure, luxury perfusion, 24, 28, 29 etc. The influence of the time lapse on the ISI values and the ratio is demonstrated by the patient in group 3. This patient had a high negative ratio shortly after the accident; a second study one month later showed a positive ratio. In contrast to Meyer et al, 30 Demeurisse et al 31 observed no change in blood flow over a longer period after the stroke. However, the studies are not truly comparable. Tables 1 and 2 give the impression that lower ISI values are found for patients of groups 3 and 4, especially among those with a more severe clinical status. However it is highly likely that the age of the patients influenced the ISI values. The blood flow through the brain decreases with increase in age in normals. 15, 32, 33 In patients with risk factors for atherothrombotic stroke (for example hypertension, diabetes mellitus, hyperlipidemia) the decrease in blood flow with increasing age is even more pronounced. 40 It has been demonstrated that the relation between age and cerebral blood flow was preserved under pathological conditions, for example in the case of cerebrovascular disease 41 and subarachnoidal hemorrhage. 42

In this study it was found that in most of the groups there was a correlation between age and ISI. The regression lines were more or less parallel to the regression line calculated by Matsuda et al (table 3). The lines for the group 4 patients were steeper. Rather high values were found for the younger patients and lower values for the elderly. Only 13% of all patients investigated had a lower mean ISI value below the 95% lower limit of Matsuda et al, only one being a patient with Status 0.

In summary many factors may influence the ISI. For that reason it is very difficult to draw any conclusions from the ISI values found for an individual patient. Moreover comparison of the different groups of patients according to clinical status is only possible if the age distributions for each group are comparable. Therefore the absolute ISI values do not seem to provide a better insight into the efficiency of the collateral circulation in the patients studied.

The ratio. In normals the different parameters for the cerebral blood flow (e.g. ISI, flow grey matter, total blood flow, etc.) remain symmetrical in both hemispheres with increasing age. 34, 35 So it is understandable that no correlation could be found between the age and the ratio for the different groups. From the figure it can be seen that the ratio for most of the patients with Status 0 and I from groups 1 and 2 is low. The highest ratios were found for patients with arterial occlusion (groups 3 and 4). Patients with a more severe clinical status (II or III) had higher ratios compared to those in a better clinical condition, as can be seen in the figure and tables 1 and 2. In the case of stenosis of the internal carotid artery the flow to the ipsilateral hemisphere is probably determined mainly by the hemodynamic effect of the stenosis and the capacity of the developing collateral supply. It is well known that the hemodynamic effect of an arterial stenosis is barely predictable. 46, 51 Furthermore it is not easy to estimate the degree of stenosis from the angiograms. 22 A simple correlation between clinical symptoms and angiographic findings cannot be found for all patients suffering from ischemic CVD. 51 However, patients with obstructive lesions in the afferent arteries of the brain run a greater risk of developing a stroke than patients without an obstructive lesion. 54 In the case of a severe arterial stenosis or complete occlusion of a major artery a reduced supply of blood to the involved hemisphere can be expected, even if an infarction has not yet occurred. This is in accordance with the paper by Awad et al 55 who demonstrated by intravenous digital subtraction angiography a less well developed collateral flow to the hemisphere on the occluded side in patients with a greater difference in flow between both hemispheres in contrast to those with a smaller difference. A larger volume of infarcted brain tissue could be demonstrated in patients with a very poor collateral supply to the hemisphere ipsilateral to the occluded internal carotid artery. 56 In the case of a brain infarction it is likely that the decreased need for blood causes the diminished blood flow to the pathological hemisphere. 57, 58

A significant difference in ratios between Status 0 and Status 1 + II patients was demonstrated for groups 2 and 4 (no patients Status 0 in group 3). It is highly likely that a high ratio is indicative of an insufficient collateral supply to the occluded side in group 2 and 4 patients Status 0 and I. In these patients no or only
small areas of infarction could be demonstrated by CT scan which is in agreement with the results known from the literature on similar patients.\(^5,6\) For that reason it is unlikely that in such cases the ISI values and/or ratio will be greatly influenced by a decreased metabolic demand or by the time lapse between the development of the clinical symptoms and the blood flow study. Factors mentioned earlier like changes in intracranial pressure, luxury perfusion, etc. can also cause changes in the flow pattern. Diaschisis lowers the blood flow in the non affected hemisphere resulting in a less pronounced difference in ISI between both hemispheres. Especially methods which measure both hemispheres simultaneously (intravenous, inhalation) reveal the phenomenon of diaschisis clearly.\(^12, 25, 30, 61-63\) Contrary to the expectations none of the patients of group 3 showed the high ratios as found in some patients of group 4. An explanation can be that in case of internal carotid artery occlusion not only the territory of the middle cerebral artery has a diminished supply of blood but the anterior and posterior cerebral arterial territories as well, which may result in a lower mean flow in the affected hemisphere. Moreover 9 patients in group 3 showed more or less extended infarctions on CT scans probably accompanied by phenomena like luxury perfusion, diaschisis and decreased metabolic demand. These phenomena may result in a lesser difference of flow between the hemispheres. Nine out of the 38 patients of group 4 had a normal ratio. Therefore a normal ratio does not exclude the existence of a one-sided internal carotid artery occlusion.

From table 4 it can be seen that the differences between the ratios found for the different groups are statistically significant, except for those between the patients of group 1 and 2 with Status 0. The data seem to be in accordance with the presumption that the ratio is of significance in providing information about the capacity of the collateral vascular system. Although there is a correlation between the ratio and the clinical symptoms, a functional deficit will only develop when the regional flow values drop below a critical value.

Furthermore there is a correlation between both the angiographic findings and the ratio and the clinical condition of the patient and the ratio.

Therefore it can be stated that the ISI ratio, as derived from CBF studies in which both hemispheres are measured simultaneously, seems to be a valuable but complex parameter. Further studies are required to determine whether an elevated ratio indicates a cerebral infarction and/or reduced collateral capacity in patients suffering from more severe clinical symptoms (Status II and III). CT scan investigations may be useful in this respect.

One should be aware of the fact that this method of CBF investigation only provides information about hemodynamic aspects of circulation; it will be of little help in case of vascular accidents due to emboli.\(^64\)

In a series of patients with one-sided occluded internal carotid arteries Thomas et al\(^20\) did not observe changes in the asymmetry of blood flow between the hemispheres over a period of 2-5 years. It would be interesting to do follow up studies on the patients of groups 2 and 4 especially those with slight symptoms in order to determine whether asymmetry between ISI values will develop, increase or even decrease in this period.

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