Leukoaraiosis and Ventricular Enlargement in Patients With Ischemic Stroke

Albert Hijdra, MD and Bernard Verbeeten Jr., MD

We studied the relationship between ventricular size and nonspecific periventricular lucency on computed tomograms (leukoaraiosis) in 192 patients with ischemic stroke. Leukoaraiosis did not occur in 21 patients <50 years of age; ventricular size could not be measured in an additional 29. Leukoaraiosis was graded from 0 to 4 on a semiquantitative scale; bicaudate, frontal horn, and posterior horn indices were used as measures of ventricular size. Patients with leukoaraiosis were older (difference between means 7 years, \( t=5.3, df=140, p<0.0001 \)) and had larger bicaudate indices (difference between means 0.023, \( t=3.54, df=140, p=0.0007 \)) than patients without leukoaraiosis. Multiple regression analysis demonstrated that the effects of age and leukoaraiosis were independent. No effect of lesion type (cortical or lacunar infarct, or both) on bicaudate index could be demonstrated. Larger values for the bicaudate index were associated with a predominantly anterior location of leukoaraiosis. The frontal horn and occipital horn indices increased with age, but we could not find an effect of leukoaraiosis on these indices. (Stroke 1991;22:447-450)

Non-specific periventricular white matter lucency on a computed tomogram (CT scan) (leukoaraiosis\(^1\)) does not always have clinical significance, but if severe it may be associated with mental decline, gait disturbances, and urinary incontinence,\(^2-6\) reminiscent of the clinical signs of normal pressure hydrocephalus. Periventricular white matter lucency may also be found in patients with hydrocephalus, and the lateral ventricles may be dilated in patients with severe white matter changes.\(^7-8\) This diagnostic problem may be a cause of the failure of shunts to improve the condition of patients with presumed normal pressure hydrocephalus.\(^7,8\)

It is therefore important to know whether leukoaraiosis on a CT scan may lead to ventricular dilatation. In a retrospective analysis, we first studied the relationship between leukoaraiosis and ventricular size, without reference to cognitive status. We studied patients with ischemic cerebrovascular disease because leukoaraiosis is often found in such patients.\(^9,10\)

Subjects and Methods

We included all patients admitted to our department during 2 years with a diagnosis of cerebral infarction and a relevant lesion on a CT scan. Clinical data on age, sex, hypertension, diabetes, and vascular disease as previously defined\(^10\) were retrieved from the patient files. Cognitive status could not be reliably assessed retrospectively for most patients and was not attempted.

All CT scans had been made ≤1 week after admission. Hard copies of noncontrast-enhanced scans were studied jointly by us. We excluded patients with compressed ventricles, infarcts of the caudate nucleus, or focal dilatation of a ventricle. Infarcts were defined as cortical or lacunar (<2 cm).\(^10\) The criterion for leukoaraiosis was ill-defined hypodense areas (density between that of the normal white matter and that of the cerebrospinal fluid) around the frontal or posterior parts of the lateral ventricles, and leukoaraiosis was assessed separately in these two regions.\(^11-13\) Abnormal white matter was graded as 1 when only the region adjoining the ventricles was abnormal and as 2 when the entire region from the ventricle to the cortex was abnormal. When the two hemispheres were not equally affected, the score of the more abnormal side was used. The anterior and posterior scores were added to give a sum score ranging from 0 to 4. As measures of ventricular size we used the bicaudate index, the frontal horn index, and the occipital horn index (i.e., the width of the frontal horns at the level of the caudate nuclei, the width of the frontal horns at the level of their maximal width, and the width of the occipital horns at their...
maximal width, each divided by the inner skull diameter at the same level, respectively).

### Results

Of the 192 patients, 73 (38%) had leukoaraiosis. It did not occur in 21 patients aged <50 years, and in another 29 patients ventricular measurements were not possible because of compressed ventricle(s) or a caudate infarct. Exclusion of patients aged <50 years and those without ventricular measurements left 142 patients, 64 (45%) of whom had leukoaraiosis. The mean age of these 142 patients was 71 (range 50-94) years; 77 (54%) were men. Hypertension was present in 71 (50%), diabetes in 35 (25%), and vascular disease in 37 (26%). Of the 142 patients 29 had only cortical, 65 had only lacunar, and 45 had both types of infarct; three had large (>2 cm) subcortical infarcts.

The difference between the bicaudate indices of patients with and those without leukoaraiosis proved to be highly significant (Table 1), and this was analyzed in more detail. A scatterplot of the bicaudate indices versus age is presented in Figure 1. There was considerable overlap of values for patients with and without leukoaraiosis over the complete range of ages. Patients with leukoaraiosis were older than those without; the difference between the mean ages was 7 years ($t=5.3$, $df=140$, $p<0.0001$). In Figure 2 the mean bicaudate indices of patients with and without leukoaraiosis are compared in four arbitrary age classes between 50 and 90 years.

To account for possible mutual dependence of the variables age, leukoaraiosis grade, and several interactions between these two, we performed multiple regression analyses with these variables. This led to the following model: $\text{Bicaudate index} = 0.104 + 0.0009 \times \text{Age} + 0.0168 \times \text{Leukoaraiosis}$. The constant and both coefficients were significantly different from 0, and analysis of variance for the model yielded an $F$ ratio of 9.30 ($df=139$, $p<0.0001$). Leukoaraiosis in this model was entered as absent (0) or present (1), and introduction of separate grades (0-4) did not improve the model. Regression analysis demonstrates that the two curves drawn in Figure 2 are significantly different. Two regression lines are drawn in Figure 1.

The mean bicaudate index of patients with more frontal than parietal leukoaraiosis was greater than that of the patients for whom the reverse was true (Table 2). The difference between these means is 0.031 ($t=2.50$, $df=30$, $p=0.018$).

When ventricular dilatation is defined as a bicaudate index greater than the 95th percentile for age, the conclusions derived from the analysis above are essentially confirmed. Ventricular dilatation occurred in 13 (17%) of the 78 patients with normal white matter and in 22 (34%) of the 64 patients with leukoaraiosis (Fisher's exact test, $p=0.0146$). Mean age in both groups with ventricular dilatation was 71 years.

### Table 1. Ventricular Measures in 142 Patients With Ischemic Stroke

<table>
<thead>
<tr>
<th>Measure</th>
<th>Leukoaraiosis Absent (n=78)</th>
<th>Leukoaraiosis Present (n=64)</th>
<th>95% confidence limits of difference</th>
<th>$p$ (t test)</th>
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<tbody>
<tr>
<td>Bicaudate index</td>
<td>0.164</td>
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Values are mean unless noted.

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**TABLE 1. Ventricular Measures in 142 Patients With Ischemic Stroke**

- **Bicaudate index**: Measured as the maximal width of the lateral ventricles, each divided by the inner skull diameter at the same level.
- **Frontal horn index**: Measured as the maximal width of the frontal horn divided by the inner skull diameter at the same level.
- **Occipital horn index**: Measured as the maximal width of the occipital horn divided by the inner skull diameter at the same level.

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Since lacunar infarcts are located mainly in the basal ganglia region, lesion type may also be an important determinant of the bicaudate index. However, enlarged ventricles did not occur more often in patients with lacunar infarcts, and for all lesion types patients with leukoaraiosis tended to more often have dilated frontal horns than patients without leukoaraiosis (Table 3).

Discussion

Leukoaraiosis in patients with ischemic stroke is associated with a significant increase of the bicaudate index. From Figure 2 it may be inferred that this may be less so in the 50–59 years and 80–95 years age classes, but this may also be caused by the relatively small sample sizes for these classes. Regression analysis (Figure 1) suggests that the effect is constant in all persons aged >50 years. Leukoaraiosis is not necessarily related to ventricular dilatation; 13 (37%) of the 35 patients with abnormal age-corrected bicaudate indices had no white matter lucency on CT scans. On the other hand, 42 (66%) of the 64 patients with leukoaraiosis had normal bicaudate indices. The finding that frontal and not parietal leukoaraiosis was associated with higher values for the bicaudate index suggests a close relation between the two. The most likely explanation is that diffuse tissue loss causes both ventricular dilatation and white matter lucency on CT scans and that the variability in this relation may be explained by the differences in the pathological changes underlying the white matter changes related to vascular disease.5–8–20

Ventricular enlargement related to leukoaraiosis could not be demonstrated with the frontal horn and occipital horn indices, and it is not easy to explain this. We found the difference between bicaudate indices and the significance level of this difference (Table 1) large enough to permit a post hoc analysis of bicaudate indices alone. Our findings, however, should be interpreted with caution and confirmation should be sought, preferably with more sophisticated methods of ventricular measurement.

We did not address the question of the clinical significance of leukoaraiosis and ventricular dilatation. Leukoaraiosis is not necessarily associated with mental deterioration. Since in patients with dementia caused by Alzheimer's disease or vascular disease the severity of mental deterioration is associated with increasing ventricular size, ventricular dilatation in patients with leukoaraiosis may distinguish those with mental changes from those without. This hypothesis is supported by pathological and CT findings of ventricular dilatation in patients with a clinical diagnosis of subcortical arteriosclerotic encephalopathy5–6 but should still be prospectively investigated.

Acknowledgments

The statistical advice of A.A.M. Hart and J. Oosting (Department of Medical Physics, Academisch Medisch Centrum, Amsterdam) and the fruitful discussions with John van Swieten, Saskia Teunisse, Pim van Gool, and Jan Stam are gratefully acknowledged.

References

![Graph of mean values of bicaudate index for four age classes in 142 patients with ischemic strokes with (•-•) or without (△-△) leukoaraiosis. Number of patients in successive age classes with and without leukoaraiosis are four and 13, 11 and 30, 24, and 19 and 10, respectively. For statistical analysis, see “Results.”](http://stroke.ahajournals.org/)

**Figure 2.** Graph of mean values of bicaudate index for four age classes in 142 patients with ischemic strokes with (•-•) or without (△-△) leukoaraiosis. Number of patients in successive age classes with and without leukoaraiosis are four and 13, 11 and 30, 24, and 19 and 10, respectively. For statistical analysis, see “Results.”

**TABLE 2. Mean Bicaudate Indices Related to Frontal and Partial Leukoaraiosis in 142 Patients With Ischemic Stroke**

<table>
<thead>
<tr>
<th>Frontal leukoaraiosis grade</th>
<th>Partial leukoaraiosis grade</th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>Index</td>
<td>No.</td>
<td>Index</td>
<td>No.</td>
</tr>
<tr>
<td>0</td>
<td>78</td>
<td>0.164</td>
<td>6</td>
<td>0.171</td>
</tr>
<tr>
<td>1</td>
<td>15</td>
<td>0.185</td>
<td>21</td>
<td>0.193</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>0.204</td>
<td>3</td>
<td>0.231</td>
</tr>
</tbody>
</table>

Three patients with large (>2 cm) subcortical infarcts excluded.

**TABLE 3. Relation Between Lesion Type, Leukoaraiosis, and Presence of Ventricular Dilatation In 139 Patients With Ischemic Stroke**

<table>
<thead>
<tr>
<th>Lesion type</th>
<th>Absent Dilatation</th>
<th>Present Dilatation</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Cortical infarcts</td>
<td>23</td>
<td>5</td>
</tr>
<tr>
<td>Lacunar infarcts</td>
<td>27</td>
<td>5</td>
</tr>
<tr>
<td>Both types</td>
<td>26</td>
<td>3</td>
</tr>
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18. Awad IA, Johnson PC, Spetzler RF, Hodak JA: Incidental subcortical lesions identified on magnetic resonance imaging in the elderly. II. Postmortem pathological correlations. *Stroke* 1986;17:1090–1097

**KEY WORDS**  •  cerebral infarction  •  leukoencephalopathy  •  hydrocephalus
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