Nuclear Magnetic Resonance Image White Matter Lesions and Risk Factors for Stroke in Normal Individuals

Helmuth Lechner, MD, Reinhold Schmidt, MD, Götz Bertha, MD, Erwin Justich, MD, Hans Offenbacher, MD, and Gerhard Schneider, MD

The incidence, average number, and localization of lesions of the white matter detected by the T2-weighted nuclear magnetic resonance images among volunteers without cerebrovascular symptoms have been correlated with the number of risk factors for stroke. Accepted risk factors were arterial hypertension, diabetes mellitus, smoking, hypercholesterolemia, and cardiac disease. The 42 subjects examined were divided into Group A (0–1 risk factor, mean age 59.36 ± 5.73 years), Group B (2 risk factors, mean age 61.54 ± 8.33 years), and Group C (≥ 3 risk factors, mean age 62.57 ± 9.83 years). Multiple risk factors among the age-matched groups was accompanied by a highly significant increase (p < 0.001, Group A versus Group B; p < 0.01, Group A versus Group C) of the incidence of white matter lesions. The average number of white matter lesions was increased (p < 0.001) when Group A was compared with Groups B and C. Ninety-two percent of the white matter lesions were localized in watershed zones. Only 11 of the 155 abnormalities of the white matter detected by nuclear magnetic resonance imaging could be detected by computed tomography. White matter lesions in T2-weighted images appear to be an early stage of cerebrovascular disease.

Nuclear magnetic resonance imaging (NMRI) demonstrates lesions of the white matter on T2-weighted images among 30% of individuals aged ≥ 60 years.1 There are positive correlations with advancing age but also with the occurrence of risk factors for stroke and cerebrovascular symptoms as described in retrospective studies.2,3 So far, there has been no prospective study comparing age-matched groups showing a relation between white matter lesions in subjects free of cerebrovascular symptoms and the number of coexisting factors for stroke.

Subjects and Methods

A prospective study of 42 volunteers was undertaken to establish the incidence of cerebrovascular risk factors in the Styrian population that lives in Graz, Austria, and the surrounding region. This cohort was divided into three groups according to the number of risk factors for stroke. Group A (22 persons, mean age 59.36 ± 5.73 years) exhibited zero to one risk factor for stroke, Group B (13 persons, mean age 61.54 ± 8.33 years) had two risk factors for stroke, and Group C (7 persons, mean age 62.57 ± 9.83 years) had three or more risk factors. The age distribution was in Group A 53 – 70 years, in Group B 44 – 76 years, and in Group C 44 – 72 years. Accepted risk factors for stroke were arterial hypertension (≥ 160 mm Hg systolic), diabetes mellitus (≥ 160 mg/dl empty stomach blood sugar level), hypercholesterolemia (≥ 250 mg/dl), smoking (≥ 10 cigarettes/day), and heart disease (coronary heart disease, arrhythmias, myocardial infarction).

All volunteers were examined twice over an interval of 17.8 ± 6.7 months. NMRI was carried out on all 42 persons using a superconducting magnet with a field strength of 1.5 T (Gyroscan s 15, Phillips). Using a multislice technique, the brain was imaged in the axial plane at 5-mm intervals. The spin-echo technique uses a pulse repetition time (TR) of 2,500 msec and echo times (TEs) of 30 and 60 msec. In addition, images were made in the sagittal plane with short pulse frequencies (spin-echo, TR/TE 600/30). The matrix was 128 × 256 pixels and the rest with a 512 × 512-pixel matrix. All white matter lesions except caps and periventricular lines of hyperintensity were recorded with respect to their number and location.

Computed tomography (CT) was carried out on Somatom DR3, DR5, and DRH systems without the use of any contrast material. The slice thickness in the posterior fossa was 4 mm and in the suprventricular compartment 8 mm. Sixty percent of the investigations were accomplished with a 256 × 256-pixel matrix and the rest with a 512 × 512-pixel matrix.

To analyze the results, the Wilcoxon-Mann-Whitney U test and the Fisher test were applied.
various groups. Eighteen (42.9%) of the 42 investigated persons (92%), and in Group C they were present in all seven persons (32%) (Table 2). There were significant differences between Groups A and B (p < 0.001) and seven (100%) (Table 2). There were significant differences between Groups A and B (p < 0.001) and seven (100%) (Table 2).

Results

Table 1 displays the risk factor distribution in the various groups. Eighteen (42.9%) of the 42 investigated persons had arterial hypertension, the most frequent cerebrovascular risk factor. The second most frequent risk factor was hypercholesterolemia (16 persons, 38.1%), followed by cardiac disease (14 persons, 33.3%). Six persons (14.3%) suffered from diabetes mellitus, and 3 (7.1%) smoked cigarettes. Twelve persons examined (28.6%) had no cerebrovascular risk factors. The most frequently occurring risk factors in the two groups characterized by multiple risk factors (Groups B and C) were arterial hypertension (69.2 and 100%), hypercholesterolemia (46.2 and 85.7%), and cardiac disease (53.8 and 57.1%). Four of the six persons with diabetes mellitus were in Group C; the other two were in Group B.

NMRI results analyzed according to the number of risk factors for stroke showed lesions of the white matter among seven persons (32%) in Group A. In Group B, white matter lesions were present in 12 persons (92%), and in Group C they were present in all seven (100%) (Table 2). There were significant differences between Groups A and B (p < 0.001) and between Groups A and C (p < 0.001). As the number of risk factors increased, the number of white matter lesions increased. The average number of white matter lesions in Group A was 1.86 ± 3.8, in Group B 5.62 ± 4.98, and in Group C 6.86 ± 8.55. Compared with Group A, significant differences exist for both Groups B and C at the 1% level. The fewest lesions present in a single subject was one, the most was 24.

In twenty-four (92.3%) of the 26 subjects with white matter lesions, these were found in the watershed zones between the middle and anterior and/or the middle and posterior cerebral arteries (Figure 1). In the distribution of the middle cerebral artery, white matter lesions were present in 17 persons (65.4%). In the supply of the anterior cerebral artery, white matter lesions were found among five persons (19.2%), and in the distribution of the posterior cerebral artery among four (15.4%). In addition, four persons (15.4%) showed lesions in the basal ganglia and three (11.5%) in the brainstem. Among 14 subjects (53.8%), white matter lesions were present in at least two of the above-mentioned territories. Punctate foci in the periventricular zone were found in six (23.1%) of the persons examined. They were all associated with lesions of the white matter of other locations as well.

Of 155 lesions identified by NMRI, only 11 were diagnosed by the use of the CT scanner. There were three false-positives diagnosis by CT and 144 false-negatives. None of the lesions detected by either method was smaller than 0.5 cm in diameter. Of the 11 lesions detected by both methods, six were in the area of the internal capsule, two in the thalamus, two in the region of the middle cerebral artery territory, and one in the posterior watershed or border zone. None of the three brainstem changes proved by NMRI were shown by CT.

Discussion

When white matter lesions are noted by T2-weighted NMRI in the elderly, several differential diagnoses should be considered. Certain similarities with the lesions seen in multiple sclerosis raise the question of a focus of demyelination; however, lesions of high water content causing structural changes of myelin in deep white matter also occur with cerebral ischemia. The age and the absence of widespread symptoms in

**Figure 1.** Multiple small white matter lesions located in right hemisphere watershed zone between middle and posterior cerebral arteries detected by T2-weighted nuclear magnetic resonance imaging (1.5 T, repetition time 1,800 msec, echo time 60 msec).
Middle cerebral artery watershed area
Anterior-middle cerebral artery watershed area
Middle-posterior cerebral artery
Anterior cerebral artery
Posterior cerebral artery
Basal ganglia
Brainstem

TABLE 3. Localization of White Matter Lesions (n = 26)

<table>
<thead>
<tr>
<th>Location</th>
<th>No. with lesions</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Middle cerebral artery watershed area</td>
<td>17</td>
<td>65.4</td>
</tr>
<tr>
<td>Anterior-middle cerebral artery watershed area</td>
<td>15</td>
<td>57.7</td>
</tr>
<tr>
<td>Middle-posterior cerebral artery</td>
<td>9</td>
<td>34.6</td>
</tr>
<tr>
<td>Anterior cerebral artery</td>
<td>5</td>
<td>19.2</td>
</tr>
<tr>
<td>Posterior cerebral artery</td>
<td>4</td>
<td>15.4</td>
</tr>
<tr>
<td>Basal ganglia</td>
<td>4</td>
<td>15.4</td>
</tr>
<tr>
<td>Brainstem</td>
<td>3</td>
<td>11.5</td>
</tr>
</tbody>
</table>

the persons examined as well as the rare localization of vascular lesions in the juxtaventricular zones oppose the diagnosis of multiple sclerosis. Gerard and Weisberg describe "patchy periventricular white matter lesions" as well as periventricular bands and/or foci of high signal intensity in the frontal and posterior horn among 31% of those investigated with risk factors for stroke but without cerebrovascular symptoms, independent of age. Patients with risk factors plus cerebrovascular symptoms showed changes of this type in 78.5% of the age group 50-59 years of age and in 84% of those ≥ 60. Awad et al positively correlated incidental subcortical lesions with a history of ischemic cerebrovascular disease and hypertension and considered these two factors together with an elderly age as major predictors of the vascular lesions of the white matter. Foci around the frontal and posterior horns, appearing as periventricular bands, were ignored in our study because histologic investigation showed that they are not pathologic changes.

Our study of white matter lesions was carried out prospectively and is concerned only with volunteers free of cerebrovascular symptoms to examine the role of risk factors for stroke compared across age-differentiated groups. When two risk factors for stroke were present, white matter lesions could be found among 92%; when three or more risk factors were present, lesions were present in 100% of those examined. The present frequency of white matter lesions in the age group > 60 years old is higher than among patients examined by Gerard and Weisberg, who found both risk factors for stroke and cerebrovascular symptoms, despite the fact that all the volunteers in our study were free of clinical manifestation of cerebrovascular disease. Gerard and Weisberg mentioned no breakdown of the type and number of existing risk factors. In the study of Awad et al a direct relation of the incidence of arterial hypertension was identified. In our investigation arterial hypertension and diabetes mellitus, both of which are certain risk factors for stroke, were found nearly exclusively as the risk factors characterizing Groups B and C. This underlines the enhancing effect of these two factors when they occur together or in combination with other risk factors.

Three factors appear important for correlating white matter lesions with the occurrence of cerebrovascular risk factors. These are 1) a highly significant increase of white matter lesions in the groups with multiple risk factors compared with age-matched groups with no or a single risk factor, 2) the average number of lesions correlates positively with the increase in the number of associated risk factors, and 3) a predominant localization (92.3%) of the lesions in watershed areas that are known to be subject to chronically reduced perfusion in the presence of cerebrovascular disease.

Regarding a small group of patients with bilateral stenosis of the internal carotid arteries, Kinkel et al discussed reversible developments of white matter changes in T2-weighted images after endarterectomies confined to the boundary zones of their arterial supply and concluded this to be a reliable sign of reversible perfusion reduction. None of these changes were observed by CT scan. We too have noted that CT is inferior to NMRI in showing these changes. Only 11 of 155 lesions detected by NMRI were diagnosed by CT scanning.

Positive correlations were found with lesions of the white matter observed by NMRI scanning and risk factors for stroke, which supports the view that these changes are an early stage of cerebrovascular disease. As mentioned above, these lesions do not preclude their reversibility.

References


Key Words: cerebrovascular disorders • nuclear magnetic resonance • risk factors
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