Brain Magnetic Resonance Imaging and Neuropsychologic Evaluation of Patients With Idiopathic Dilated Cardiomyopathy

Reinhold Schmidt, MD; Franz Fazekas, MD; Hans Offenbacher, MD; Johann Dusleag, MD; and Helmut Lechner, MD

We compared brain magnetic resonance imaging and neuropsychologic performance in 20 neurologically asymptomatic patients suffering from idiopathic dilated cardiomyopathy (mean age 41 [range 18–49] years) and 20 age-matched controls (mean age 38 [range 28–49] years). Patients exhibited a significantly higher rate of cerebral infarcts (20% versus 0%, p<0.05) and cortical (50% versus 5%, p<0.01) and ventricular (55% versus 15%, p<0.02) atrophy than controls. Accordingly, semiquantitative volumetric measurements yielded a significantly increased ventricular-to-intracranial cavity ratio in the patients (6.2±2.9% versus 4.1±1.3%, p<0.01). This ratio and the cortical atrophy ratings correlated positively with disease duration (r=0.63 and 0.54, p<0.05). Cognitive test performance was significantly worse in patients than in controls and was most impaired in those patients with morphologic cerebral abnormalities. (Stroke 1991;22:195–199)

Cardiac disorders rank third, following age and arterial hypertension, as a risk factor for stroke.1 Arrhythmias, valvulopathies, and heart wall disorders are potential sources for cerebral emboli,2,3 and brain integrity may be threatened by a chronically reduced cardiac output.4 These conditions are also likely to induce subclinical cerebral changes. Evidence of their frequent occurrence underscores the importance of preventive measures, but such data have, to the best of our knowledge, been collected only for atrial fibrillation.5

Looking for such unrecognized brain damage in other cardiac diseases, we first focused on idiopathic dilated cardiomyopathy since it encompasses both low cardiac output and the risk of emboli. We used magnetic resonance imaging (MRI), with its high sensitivity for ischemic damage, to document parenchymal abnormalities and assessed the presence of cognitive and behavioral disturbances by using a neuropsychologic test battery.

Subjects and Methods

Patients were recruited from the Division of Cardiology of the Department of Internal Medicine at the Karl Franzens University, Graz. All suffered from idiopathic dilated cardiomyopathy classified according to the report of the ISCF Task Force on the definition and classification of cardiomyopathies.6 The diagnosis was based on chest roentgenography, two-dimensional M-mode echocardiography (SSH-65A, Toshiba, Tokyo, Japan), and left ventricular catheterization. Coronary arteriography using Judkin's technique and electrocardiography were also performed. To keep possibly confounding factors at a minimum, we selected only patients aged <50 years who were free of any neurologic, psychiatric, or systemic disease including arterial hypertension and diabetes as assessed by history and examination. A history of head injury or alcohol or drug abuse was further reason for exclusion.

Within 1 year 20 patients (19 men, one woman) agreed to participate in this study. The duration of cardiac disease ranged from 1 to 92 months. The clinical severity of cardiomyopathy on the New York Heart Association Criteria Committee scale7 was grade II in 10, grade III in seven, and grade IV in three patients. Left ventricular ejection fraction ranged from 14% to 45%, with a mean of 27.9% (normal range 55–75%). Electrocardiography revealed sinus rhythm in 16 patients and atrial fibrillation in four. Sixteen patients received drug treatment, five digoxin (0.2–0.4 mg/day) alone and the other 11 digoxin (0.2–0.4 mg/day) plus diuretics (four furosemide 40 mg/day, three amiloride hydrochloride 5 mg/day and hydrochlorothiazide 50 mg/
TABLE 1. Demographic Data of Controls and Patients With Idiopathic Dilated Cardiomyopathy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Controls (N=20)</th>
<th>Patients (N=20)</th>
<th>Normal MRI (n=8)</th>
<th>Abnormal MRI (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>37.9±4.7</td>
<td>40.5±7.8</td>
<td>41.9±7.4</td>
<td>39.6±8.3</td>
</tr>
<tr>
<td>Education (yrs)</td>
<td>9.8±2.8</td>
<td>9.1±1.7</td>
<td>8.6±1.5</td>
<td>9.4±2.0</td>
</tr>
<tr>
<td>New York Heart Association</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cardiac impairment score</td>
<td>. . .</td>
<td>2.5±0.6</td>
<td>2.4±0.5</td>
<td>2.7±0.6</td>
</tr>
</tbody>
</table>

MRI, magnetic resonance imaging. Values are mean±SD.

day, and four spironolactone 50 mg/day and butizide 5 mg/day). The control group consisted of 20 volunteers (13 men, seven women) participating in a field study on the incidence of cerebrovascular risk factors in Graz. The controls met the same selection criteria as the patients except the controls had no history of cardiac disease and a normal electrocardiogram. Age and length of education were comparable in both groups (Table 1). All subjects were right-handed.

The MRI studies were performed using a 1.5-T superconducting magnet (Gyroscan S 15, Philips, Eindhoven, The Netherlands) and the spin/echo technique. Axial mixed and T2-weighted (repetition time [TR] 1,800–2,500 msec; echo time [TE] 30, 60–80 msec) and sagittal T1-weighted (TR/TE 600/30 msec) scans were generated with a slice thickness of 5 mm. The matrix used was 128×256 pixels. All scans were reviewed for signal abnormalities and cerebral atrophy by one investigator without knowledge of the clinical diagnosis. Cortical and ventricular atrophy were graded as none, mild, moderate, or severe. Relative volumetric indexes of ventricular enlargement were obtained by calculating a ventricular-to-intracranial cavity ratio using software routines available with the Philips system. Beginning at the bottom of the third ventricle, the ventricular cavities and the outer margin of the subarachnoid space were traced on five subsequent T2-weighted slices displayed on the MRI console (Figure 1). The ventricular-to-intracranial cavity ratio was then calculated by dividing the sum of the ventricular volumes by that of the intracranial cavities and multiplying the result by 100. Measurements were performed by three investigators, and their results were highly correlated (r=0.98–0.99). The mean of these results was used for further statistical analysis.

Neuropsychological testing assessed memory and learning abilities (Baeumler's Lern- und Gedächtnistest LGT-39), attention (d2 test9), vigilance (computerized system of Quatember and Maly10), and mood (adjective list of Janke and Debus11). This battery, more extensively described elsewhere,12 was always administered in the same order and under the same laboratory conditions by one neuropsychologist unaware of the individual's diagnosis and MRI findings.

Data were analyzed with the microcomputer version of SPSS.13 One-way analysis of variance was used first, and Duncan's test was used thereafter to ascertain significant differences between groups. Kendall's tau-b test served for correlations of ordinal data, and we computed Pearson's correlation coefficient to assess interobserver agreement of ventricular-to-intracranial cavity ratio measurements. Frequency distributions were compared by means of Fisher's exact test.

Results

The MRI findings in the controls and patients are listed in Table 2. Three of the four patients with cerebral infarcts had two or more lesions, which were bilateral in two patients (Figure 2). All lesions were incomplete territorial infarcts (six in the middle cerebral artery territory and two in the posterior cerebral artery territory). Two infarcts were located cortically; the other six involved both the cortex and the adjacent white matter. Electrocardiography revealed atrial fibrillation in only one of these four patients, but all were rated as at least grade III on the New York Heart Association scale. Their ejection

![Figure 1. Illustration of ventricular-to-intracranial cavity ratio measurement technique. Lateral ventricles (1) and outer cerebrospinal fluid margin (2) at level of centrum semiovale are outlined in representative patient.](https://stroke.ahajournals.org/Archive/1991/22/2/196/Figure1.png)
fractions were 20%, 25%, 30%, and 45%. The duration of cardiomypathy in the four patients with infarcts ranged from 23 to 84 months, and the mean±SD duration of cardiac symptoms was significantly longer in those with cerebral infarcts than in those without (59.0±28.9 versus 24.4±26.3 months, p<0.02).

Eleven patients (55%) and three controls (15%, p<0.02) showed brain atrophy. Cortical and ventricular cerebrospinal fluid space enlargement were rated as moderate or severe in four and six patients, respectively, while a similar extent of atrophy was present in only one control.

The mean±SD ventricular-to-intracranial cavity ratio was 6.2±2.9% in the patients and 4.1±1.3% in the controls (p<0.01, Figure 3). Ratios exceeding the control mean by >2 standard deviations were found in seven patients. Both the cortical atrophy rating and the ventricular-to-intracranial cavity ratio correlated significantly with the duration of cardiac symptoms (r=0.54 and 0.63, p<0.05 each) but not with the severity of symptoms, age, or left ventricular ejection fraction.

The incidence of white matter lesions was similar in the patients and controls (Table 1). The hyperintensities were all of the punctate type\textsuperscript{14} and ranged in number from 1 to 3 (mean 1.8) in the patients and from 1 to 4 (mean 2.3) in the controls.

Both the entire patient group and the patient subgroup with MRI abnormalities performed significantly worse than the controls on verbal memory, total learning and memory performance, and vigilance tests (Table 3); there were no significant differences with respect to attention. A trend toward memory impairment was also noted in the patient subgroup with normal MRI scans; the vigilance test results of this subgroup were similar to those of the controls, however, and thus were significantly better than those of the subgroup with MRI abnormalities. Both patient subgroups scored worse than the controls on four of the six subscales of the mood questionnaire (Table 3). Correlations between neuropsychologic test results and morphologic abnormalities detected in the patients were not performed because of the diversity of the MRI findings and the limited number of patients.

Discussion

This study demonstrates cerebral infarcts and cortical and ventricular enlargement unsuspected by history and clinical examination in patients with idiopathic dilated cardiomyopathy. Although atrial fibrillation was evident in only one patient with brain infarcts and echocardiography did not reveal left ventricular thrombi in any patient, the territorial type and multiplicity of infarcted areas are strongly indicative of an embolic origin for these lesions. Left atrial or left ventricular thrombi are found at autopsy in as many as 50% of individuals suffering from idiopathic dilated cardiomyopathy\textsuperscript{15}.
and Segal et al.\textsuperscript{16} reported a 14\% incidence of symptomatic systemic or cerebral embolism during a 5-year follow-up. Not surprisingly, therefore, our findings also point toward a high rate of silent cerebral infarction in such patients. The probability of cerebral damage increases with the duration of disease and the severity of cardiac symptoms.

Brain atrophy was the most common MRI abnormality noted. Both the incidence and extent of sulcal and ventricular enlargement were significantly greater in the patients than in the controls. To our knowledge, this fact has not gained attention so far. Although we cannot offer an explanation as to the exact mechanisms involved, chronic perfusion reduction could play at least some role. Regional cerebral blood flow was found to be reduced in patients with chronic atrial fibrillation,\textsuperscript{4} and low-output cardiac diomyopathy and the need for strategies preventing the embolic risks associated with this disease. For the first time, data also indicate an unexpectedly high correlation between the extent of cerebral atrophy and the duration of cardiac disease noted in this study may support this assumption.

White matter lesions are an incidental finding in many MRI studies of patients and asymptomatic individuals,\textsuperscript{17-19} and a relation with cardiac disease has been reported.\textsuperscript{20,21} From the observation of a decreased cerebral blood flow when such high-signal foci are present,\textsuperscript{20} impaired cardiac output might be expected to be an important pathogenetic factor. However, our patients revealed significant differences to controls in neither the incidence nor the number of white matter lesions. This finding, together with more recent histopathologic studies\textsuperscript{22} that ascribe white matter lesions to zones of atrophic perivascular demyelination resulting from focally disturbed microcirculation, indicate a low cerebral blood flow to be the consequence of small-vessel disease rather than a cause of punctate white matter lesions.

Neuropsychologic testing revealed subtle impairment of mnemonic abilities and vigilance in individuals with idiopathic dilated cardiomyopathy that had not been suspected by clinical interview. These deficits cannot be explained by a difference in either age or length of education, nor are the drugs and dosages used by these patients likely to have produced neuropsychologic effects.\textsuperscript{23} While a depressed mood, probably related to the cardiac disease itself, may produce deterioration in cognitive performance in general, it is not unexpected that organic brain damage impairs neuropsychologic functions. In our study, this was most obvious with respect to vigilance.

These data underline the necessity of closely monitoring patients suffering from idiopathic dilated cardiomyopathy and the need for strategies preventing the embolic risks associated with this disease. For the first time, data also indicate an unexpectedly high

### Table 2. Incidence of Abnormal Magnetic Resonance Imaging Findings in Controls and Patients With Idiopathic Dilated Cardiomyopathy

<table>
<thead>
<tr>
<th>Findings</th>
<th>Controls (n=20)</th>
<th>Patients (n=20)</th>
<th>Fisher’s exact test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral infarcts</td>
<td>0 0 4 20</td>
<td>0 0 4 20</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Cortical atrophy</td>
<td>1 5 10 50</td>
<td>0 0 2 0</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Ventricular enlargement</td>
<td>3 15 11 55</td>
<td>3 15 11 55</td>
<td>p&lt;0.02</td>
</tr>
<tr>
<td>White matter lesions</td>
<td>4 20 6 30</td>
<td>4 20 6 30</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS, not significant.

### Table 3. Neuropsychologic Test Scores of Controls and Patients With Idiopathic Dilated Cardiomyopathy

<table>
<thead>
<tr>
<th>Test</th>
<th>Controls (n=20)</th>
<th>Total (n=20)</th>
<th>Normal MRI (n=8)</th>
<th>Abnormal MRI (n=12)</th>
</tr>
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<tbody>
<tr>
<td>Memory and learning ability\textsuperscript{a}</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visuospatial memory</td>
<td>43.8±11.9</td>
<td>38.9±11.5</td>
<td>39.6±12.4</td>
<td>38.5±11.6</td>
</tr>
<tr>
<td>Verbal memory</td>
<td>35.9±9.1</td>
<td>29.4±7.2*</td>
<td>31.1±8.0</td>
<td>28.3±6.8*</td>
</tr>
<tr>
<td>Total learning and memory performance</td>
<td>33.8±9.5</td>
<td>27.6±9.3*</td>
<td>28.4±9.2</td>
<td>27.1±9.8*</td>
</tr>
<tr>
<td>Attention\textsuperscript{c}</td>
<td>25.2±19.9</td>
<td>25.3±24.2</td>
<td>30.4±37.6</td>
<td>22.1±11.0</td>
</tr>
<tr>
<td>False reacts identified (no.)</td>
<td>4.2±2.7</td>
<td>9.8±11.1*</td>
<td>5.3±3.4</td>
<td>12.3±13.1*</td>
</tr>
<tr>
<td>Reaction time (msec)</td>
<td>413.1±60.8</td>
<td>446.4±83.1*</td>
<td>402.8±40.7</td>
<td>470.3±92.0*</td>
</tr>
</tbody>
</table>

MR\textsubscript{I}, magnetic resonance imaging. Values are mean±SD.

\textsuperscript{a}tp<0.05, 0.001, 0.01, respectively, different from controls by Duncan’s t test.

\textsuperscript{c}tp<0.05 different from normal MRI by Duncan’s t test.
rate and extent of cerebral atrophy, which could be hemodynamically mediated. Further exploration of these aspects is warranted to understand better the mechanisms involved and, potentially, to help prevent the neuropsychologic consequences of idiopathic dilated cardiomyopathy.

Acknowledgments

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References


KEY WORDS • cardiomyopathy, congestive • cognition • magnetic resonance imaging
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