Embolic Lesion Pattern in Stroke Patients With Patent Foramen Ovale Compared With Patients Lacking an Embolic Source

Marek Jauss, MD; Tiemo Wessels, MD; Susan Trittmacher, MD; Jens Allendörfer, MD; Manfred Kaps, MD

Background and Purpose—Multiple acute ischemic lesions on diffusion-weighted magnetic resonance imaging (DWI-MRI) are thought to be of embolic origin. However, in several patients with multiple ischemic lesions on DWI-MRI, no embolic source was detected, despite a thorough clinical work-up. Stroke etiology in such cases is then classified as cryptogenic. In other patients, a potential embolic source is limited to a patent foramen ovale (PFO) that may act as an embolic source of unsure relevance. We therefore examined the prevalence of the multiple-lesion pattern in patients with cryptogenic stroke compared with patients with PFO.

Methods—We screened 650 stroke patients by DWI-MRI. For the subsequent evaluation, we excluded patients with a cardiac embolic source other than PFO, symptomatic carotid artery disease, and other apparent stroke causes, such as dissection or vasculitis, and patients whose diagnostic work-up was incomplete. For the remaining 106 patients, we found DWI lesions in 73, who were subjected to further evaluation.

Results—There were no differences in the occurrence of the multiple-lesion pattern in patients with cryptogenic stroke compared with patients with PFO, either for the entire group or for the subgroup of young stroke patients who were <50 years old. Patients with PFO showed a significantly higher incidence of multiple lesions in the posterior circulation.

Conclusions—The multiple-lesion pattern on DWI-MRI is not uncommon, even when extensive testing does not reveal any embolic source. Therefore, it is not possible to discriminate between cryptogenic stroke and stroke from an assumed paradoxical embolism. (Stroke. 2006;37:2159-2161.)

Key Words: foramen ovale, patent □ magnetic resonance imaging, diffusion-weighted

In many patients, multiple acute ischemic lesions on diffusion-weighted, magnetic resonance imaging (DWI-MRI) are associated with detection of an embolic source, such as a ventricular thrombus or atrial fibrillation.1 However, in some patients, despite a thorough examination including transesophageal echocardiography (TEE) and Holter ECG, no embolic source can be revealed. In other patients, the only pathological finding is a patent foramen ovale (PFO) that might act as an embolic source of unsure relevance. The aim of this study was to compare the prevalence of the multiple ischemic lesion pattern in patients with cryptogenic stroke and patients with PFO and to examine whether the distribution of ischemic lesions differs between these groups. In addition, we examined whether recurrent infarctions on DWI-MRI, as has been described to occur in ~40% of acute stroke patients,2 are more common in patients with PFO than in patients who lack an embolic source.

DWI-MRI already has had a substantial impact on early stroke diagnosis and therapy. In contrast to computed tomography and MRI without DWI, detection of lesions in the first hours after the onset of clinical symptoms is possible with DWI. Furthermore, DWI is superior in detecting very small ischemic lesions because of the high signal-to-noise ratio and its capacity of differentiating between chronic and acute lesions.3 Small, clinically “silent” lesions may influence the diagnosis of stroke subtype in ischemic stroke when multiple lesions are detected on DWI.4 The presence of multiple ischemic lesions suggests embolism from the heart or the aortic arch or, if confined to 1 vascular territory, from stenosis of an extracoronary or intracranial large artery. Multiple infarcts in >1 vascular territory, especially bilateral lesions, strongly argue for a proximal source or a systemic cause.1 These may be also present when caused by a lacunar syndrome on clinical grounds that an arteriosclerotic stroke etiology is assumed.5

Patients and Methods

We examined 650 stroke patients who underwent DWI-MRI and who were consecutively admitted to the Department of Neurology, University Hospital, Giessen, Germany, during a 3-year period. For the subsequent evaluation, we excluded patients with carotid stenosis...
(n=118), other apparent stroke causes such as dissection or vasculitis (n=20), or an apparent embolic source (atrial fibrillation, n=105; aortic plaques, n=44; dilated ventricle, n=40; other cardiac embolic sources, n=41). One hundred seventy-seven patients were excluded because the work-up data were incomplete. For the remaining 106 patients, we found DWI lesions in 73 patients who were subjected to further evaluation. In the group with negative MRI findings, the PFO incidence was 36% (n=12) compared with 49% PFO-positive patients in the patient group with DWI lesions on MRI.

Patients underwent DWI-MRI usually within 72 hours of symptom onset by a 1.5-T whole-body scanner (General Electric) with echoplanar imaging data capability. The study protocol has been published previously.6 Because the aim of DWI-MRI was to disclose stroke etiology rather than to search for early infarct signs, the time between onset of symptoms and MRI scan was at least 8 hours. All MRI-scans were assessed by both a neuroradiologist and a neurologist who were blinded to the clinical findings.

Ischemic DWI lesions were classified as (1) single lesions, (2) multiple lesions (see the Figure) in 1 vascular territory (anterior or posterior circulation), and (3) multiple lesions in >1 vascular territory, as suggested in previous studies wherein multiple lesions were considered to be of embolic origin.1,4,7 The presence of cardiac right-to-left shunting was examined by TEE with an intravenous contrast agent (Echovist) and confirmed by a transcranial Doppler test for right-to-left shunt.8 Only patients with positive results on both tests were considered as having a right-to-left shunt on the cardiac level. Statistical analysis was performed with Fisher’s exact test.

**Results**

The mean age of the study patients was 53.1±16.1 (range, 18 to 88) years, and 28 patients (38%) were female. The time from onset of symptoms to MRI examination was 2.2±1.4 (range, 1 to 8) days.

There was no significant difference in the occurrence of the multiple ischemic lesion pattern in patients with cryptogenic stroke compared with patients with PFO, either for the entire group or for the subgroup of young stroke patients who were ≤50 years old. Patients with the multiple ischemic lesion pattern showed significantly more lesions in the posterior circulation (the Table), with a positive prediction value for PFO in cases of multiple emboli in the posterior circulation of 0.99 (0.51 to 1), a specificity of 0.99 (0.88 to 1), and a sensitivity that was low, 0.20 (0.07 to 0.35).

**Discussion**

We report on a selected group of patients from a cohort of stroke patients who often present with the problem of determined stroke etiology. The failure to disclose an embolic source of stroke in patients with an embolic stroke pattern by MRI is not uncommon, despite extensive testing. Therefore, the multiple ischemic lesion pattern is not limited to patients with stroke and PFO. Only in young patients (≤50 years) was there a remarkably high positive predictive value of 75% for the presence of PFO in cases of the multiple ischemic lesion pattern on MRI. The observation that stroke due to paradoxical embolism affects mainly the posterior circulation is supported by a single-photon emission computed tomography study and is possibly a specific feature of paradoxical embolism.9

The limitations of this study are possible bias due to patient selection for DWI-MRI, because cooperation of the patient is required for this examination, and a possible bias in patient selection for TEE, because TEE, though part of our stroke work-up program, was performed as an invasive procedure only in patients who would have been expected to derive a possible therapeutic consequence.

In conclusion, the multiple ischemic lesion pattern is common in PFO patients, but it can also be demonstrated in a subgroup of patients in whom no obvious source of embolic stroke can be demonstrated. The multiple ischemic lesion pattern in the posterior circulation is associated with the presence of PFO.

<table>
<thead>
<tr>
<th>Lesion pattern (all patients)</th>
<th>PFO</th>
<th>No Embolic Source</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single lesion</td>
<td>20</td>
<td>24</td>
<td>NS</td>
</tr>
<tr>
<td>Multiple lesions in 1 territory</td>
<td>12</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Multiple lesions in different territory (same side)</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Multiple lesions in different territory (different side)</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Lesion pattern (&lt;50 years old)</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single lesion</td>
<td>10</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Multiple lesions in 1 territory</td>
<td>4</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Multiple lesions in different territory (same side)</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Multiple lesions in different territory (different side)</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

Fisher’s exact test showed significant differences between these patient groups only for the distribution of lesions favoring those in the posterior circulation in the case of PFO (marked with asterisk).

**Figure 1**

Two representative DWI-MRI slices for a patient with PFO and multiple lesions in the posterior territory.
Disclosures

None.

References

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