Diffusion-Weighted Imaging-Negative Patients With Transient Ischemic Attack Are at Risk of Recurrent Transient Events

Jean-Martin Boulanger, MD, FRCPC; Shelagh B. Coutts, MD, FRCPC; Michael Eliaziw, PhD; Suresh Subramaniam, MD; James Scott, MD, FRCPC; Andrew M. Demchuk, MD, FRCPC

Background and Purpose—Among patients presenting with a transient ischemic attack (TIA), some clinical features predispose to recurrent TIA, whereas others predispose to subsequent strokes. We assessed the implication of negative diffusion-weighted imaging on a baseline MRI in predicting subsequent TIA.

Methods—We prospectively studied patients presenting in the emergency department within 12 hours of a TIA (motor or speech). All patients had a MRI within 24 hours of the index event. The primary outcome was TIA within 1 year of study entry. The 1-year risk of stroke was also evaluated.

Results—A total of 85 patients had a MRI, among which 35 patients (41.2%) had a diffusion-weighted imaging lesion. The mean time from symptom onset to MRI was 12.1 hours. Patients without a diffusion-weighted imaging lesion on baseline MRI were 4.6 times (27.4% versus 5.9%; \(P < 0.05\)) more likely to have a subsequent TIA at 1 year than patients with a diffusion-weighted imaging lesion, but 4.3 times (2.1% versus 9.1%; \(P = 0.19\)) less likely to have a subsequent stroke.

Conclusions—The absence of a diffusion-weighted imaging lesion on the baseline scan predicts recurrent transient events rather than stroke. (Stroke. 2007;38:2367-2369.)

Key Words: brain infarction ischemic stroke magnetic resonance imaging transient ischemic attack

Among patients with transient ischemic attack (TIA), some clinical features help identify those at risk of TIA recurrence (history of multiple TIAs, short duration of symptoms, and isolated sensory abnormalities), whereas others are useful in predicting the early risk of new stroke (age, diabetes mellitus, hypertension, longer duration of symptoms, large-artery disease, and weakness or speech impairment at presentation).

We sought to determine whether a negative diffusion-weighted imaging (DWI) study could identify patients with TIA at risk of TIA recurrence but not at risk of subsequent stroke.

Methods

Patients

Patients were prospectively enrolled if they had a motor hemiparesis or aphasic TIA lasting longer than 5 minutes within the previous 12 hours. Each patient had a complete neurological evaluation by a stroke neurologist at baseline, 24 hours, and 3 months. A diagnosis of TIA was made if no deficit persisted at 24 hours independently of imaging findings. The TOAST classification was used to determine the etiology of the qualifying event. Telephone follow up was done at 6 months and every 6 months thereafter using the Questionnaire for Verifying Stroke-Free Status. Patients with positive answers to the Questionnaire for Verifying Stroke-Free Status were assessed in person by a stroke neurologist. Stroke during follow up was defined clinically as a functional neurological deterioration of vascular origin or a new sudden focal neurological deficit of vascular origin lasting \(>24\) hours. TIA was defined as rapidly developing clinical signs of focal or global disturbance lasting \(<24\) hours without any apparent nonvascular cause.

The study was approved by the local ethics committee. All participants provided written informed consent.

Imaging

Three-Tesla MRI was performed within 24 hours of symptoms onset. All scans were reviewed by a neuroradiologist who was blind to clinical data other than symptom(s) side.

Statistical Analysis

The primary outcome was the first TIA within 1 year of study entry. The risk of stroke was also evaluated. The 1-year risk of stroke and TIA were derived from Kaplan-Meier curves and the log-rank test was used to assess whether the differences between groups were statistically significant. Cox proportional hazards regression modeling was used to assess whether any baseline factors were potential confounders. Differences between proportions were assessed for statistical significance using a \(\chi^2\) test.

Results

One hundred sixty-seven patients were eligible for enrolment from May 2, 2002, to June 29, 2004. Seventy-six patients...
were excluded because of a clinical diagnosis other than TIA and 6 because they received thrombolytic therapy. Therefore, 85 patients were analyzed and 35 patients (41.2%) had DWI lesions. The mean (SD) time from symptom onset to MRI was 11.4 hours (6.9) for patients with a DWI lesion and 12.6 (6.9) hours for patients without a DWI lesion. The median follow up was 13 months (range, 1 day to 24 months) in both groups. The presence of large-artery disease was the only factor associated with the presence of DWI lesions (Table). None of the factors listed in the Table were identified as confounders. A total of 12 (14.1%) patients had a subsequent TIA and 4 (4.7%) patients had a subsequent stroke within 12 months of study entry. The Figure summarizes the 1-year risks of TIA and stroke, respectively. Patients without a DWI lesion on baseline MRI had more TIA than patients with a DWI lesion (24.7% versus 5.9%; OR, 4.6; CI, 1.3 to 12.5; \( P < 0.05 \)) but less stroke (2.1% versus 9.1%; OR, 0.24; CI, 0.03 to 1.8; \( P = 0.19 \)) at follow up. Most patients (10 of 12 [83.3%]) with recurrent TIA had symptoms attributable to the same vascular territory as the index event.

**Discussion**

In patients presenting with a TIA, an MRI has discriminative value in predicting the risk of new TIA. The absence of a DWI lesion at baseline is associated with a high risk for subsequent TIA but a small risk of future stroke.

Our results are concordant with the literature. First, DWI lesions were observed in 41.2% of our patients but others with similar rates among TIs.9,10 Previous studies have already demonstrated that a baseline DWI lesion is a risk factor for new strokes.9,11 but the implications of a negative DWI study has not been studied previously in regard to TIA recurrence.

We studied a population with a high vascular risk according to clinical features (speech or motor TIA)2,5 but despite this, the prognosis was good in most patients without a DWI lesion. Furthermore, their pattern of outcome events (new TIA but not new stroke) was similar to the isolated sensory TIA. Some of these events may represent atypical cases of migraine, seizure, or functional disorder, all of which are likely to recur and are sometimes difficult to differentiate from TIA using clinical features alone. An acutely performed DWI complements the clinical evaluation. False-negative cases should also be considered because a negative MRI scan does not completely exclude an ischemic origin.10,12–14 One should not refrain from treating (including secondary prevention) if the clinical suspicion of a vascular disease is significant, but rather consider and investigate alternate diagnoses in patients with TIA with no DWI lesion. Patients should also probably be informed that they are at risk of recurrent transient events.

Our study has some limitations. First, the median follow up in our study was 13 months and a longer follow up may be required to identify some recurrent events. Second, the Questionnaire for Verifying Stroke-Free Status was used as a screening tool for new TIA, and despite previous validation,7 it remains an imperfect tool. Last, the implications of a negative MRI in predicting recurrent TIA compared with stroke in patients with nonspeech TIA or very short TIA (a group already prone to recurrent TIA compared with stroke)1,2 remains unknown because these patients were excluded from our study.

In summary, in a population of patients with TIA, the absence of a DWI lesion on a baseline MRI is predictive of recurrent TIA at 12 months.

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**Characteristics of Patients According to the Presence and Absence of DWI Lesions**

<table>
<thead>
<tr>
<th>Present, n (%)</th>
<th>Absent, n (%)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age &gt;75 years</strong></td>
<td>14 (40.0)</td>
<td>17 (34.0)</td>
</tr>
<tr>
<td><strong>Male sex</strong></td>
<td>14 (40.0)</td>
<td>17 (34.0)</td>
</tr>
<tr>
<td><strong>Large-artery disease</strong></td>
<td>11 (31.4)</td>
<td>4 (8.0)</td>
</tr>
<tr>
<td><strong>Antiplatelet medications</strong></td>
<td>8 (22.9)</td>
<td>14 (28.0)</td>
</tr>
<tr>
<td><strong>Systolic blood pressure &gt;160 mm Hg</strong></td>
<td>15 (42.9)</td>
<td>18 (36.0)</td>
</tr>
<tr>
<td><strong>Diastolic blood pressure &gt;90 mm Hg</strong></td>
<td>6 (17.1)</td>
<td>16 (32.0)</td>
</tr>
<tr>
<td><strong>Glucose &gt;7 mmol/L</strong></td>
<td>7 (20.0)</td>
<td>11 (22.0)</td>
</tr>
<tr>
<td><strong>Current smoker</strong></td>
<td>7 (20.0)</td>
<td>5 (10.0)</td>
</tr>
<tr>
<td><strong>TIA duration &gt;60 minutes†</strong></td>
<td>17 (48.6)</td>
<td>24 (48.0)</td>
</tr>
<tr>
<td><strong>History of</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke or TIA</td>
<td>12 (34.3)</td>
<td>12 (24.0)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>18 (51.4)</td>
<td>24 (48.0)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>12 (34.4)</td>
<td>12 (24.0)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>9 (25.7)</td>
<td>12 (24.0)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>7 (20.0)</td>
<td>9 (18.0)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>3 (8.6)</td>
<td>5 (10.0)</td>
</tr>
<tr>
<td><strong>Symptoms to MRI &gt;12 hours†</strong></td>
<td>14 (40.0)</td>
<td>24 (48.0)</td>
</tr>
</tbody>
</table>

*Mean (SD) age of patients: 71.3 (7.7) and 65.8 (12.5) years, respectively.
†Mean TIA duration (SD): 292 (400) and 201 (272) minutes, respectively.
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References

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