Detection of Diffusion-Weighted MRI Abnormalities in Patients With Transient Ischemic Attack
Correlation With Clinical Characteristics

Ralph A. Crisostomo, BS; Madelleine M. Garcia, BS; David C. Tong, MD

Background and Purpose—Although diffusion-weighted MRI (DWI) has demonstrated clear superiority over other conventional imaging modalities in the detection of hyperacute cerebral ischemia, its value in the evaluation of patients with transient symptoms has received only limited attention. We assessed the utility of DWI in patients with transient ischemic attack (TIA) to further evaluate the usefulness of this technique in these individuals.

Methods—A retrospective analysis was performed on all patients entered in the Stanford Stroke Center database during 1997–2001 who were clinically diagnosed with a TIA and who had also undergone a DWI scan ≤3 days after symptom onset. The relationship between DWI-detected findings and patients’ clinical presentation was then analyzed.

Results—Seventy-five patients experiencing 78 TIAs who also underwent DWI within 3 days of symptom onset were identified. DWI-detected abnormalities were present in 16 of 78 cases (21%). Patients with positive DWI scans were 9.6 times more likely to have had symptom duration ≤1 hour, 16 times more likely to have had motor deficits, and 25 times more likely to have had aphasia than patients with negative DWI scans. The combination of all 3 symptoms was 100% specific for an abnormality on DWI. In 7 of 16 cases (44%), a DWI abnormality was present on both DWI and conventional imaging (T2-weighted imaging or fluid-attenuated inversion recovery [FLAIR]). In all of these cases the DWI clarified the extent or acuity of the lesion (n=7) or identified additional lesions not detected by conventional imaging (n=9).

Conclusions—In TIA patients, symptom duration ≤1 hour, motor deficits, and aphasia were each independently correlated with detecting an abnormality with DWI. DWI was also helpful in differentiating between chronic versus acute lesions. These data may be of value in identifying those TIA patients for whom MRI evaluation with DWI is of greatest clinical utility. (Stroke. 2003;34:932-937.)

Key Words: ischemic attack, transient ■ magnetic resonance imaging, diffusion-weighted

A transient ischemic attack (TIA) can be defined as a sudden loss of neurological function lasting <24 hours due to occlusive thromboembolic cerebrovascular disease.4 However, because TIAs are usually diagnosed exclusively by history, determining whether an individual experiencing transient neurological symptoms is actually having a TIA can be quite challenging, and definitive diagnosis may be difficult. Thus, any method that could improve our diagnostic accuracy in this situation would be greatly appreciated.

Diffusion-weighted MRI (DWI) is an established MRI technique that is very sensitive to acute cerebral ischemia.2-4 In clinical practice, DWI has been shown to be superior to conventional MRI and CT.5-7 In addition, DWI has the ability to differentiate between acute and chronic ischemia,8-10 which could be of substantial value in patients with prior cerebrovascular disease and new transient neurological symptoms. In contrast, conventional MRI cannot differentiate between acute and chronic infarcts, making it difficult to distinguish acute from chronic lesions in patients with previous infarction.11

DWI is now frequently used in the evaluation of patients who have experienced cerebral ischemia. However, while the superiority of using DWI over other imaging modalities in acute stroke has been studied extensively, its value in the evaluation of patients experiencing TIA has received significantly less attention.12-15

The use of DWI in this situation could be of substantial clinical benefit because it is often difficult to determine by conventional means whether a patient has actually suffered from a TIA. Clinical history, examination, and conventional imaging frequently cannot accurately determine whether transient symptoms are due to cerebral ischemia, making determination of the exact nature of an individual patient’s transient symptoms problematic.

In this study we sought to determine the utility of DWI in patients with a clinical diagnosis of TIA. In addition, the
relationship between specific TIA characteristics and DWI positivity was explored in an effort to identify those features associated with an increased probability of DWI positivity. This information could be of significant value in optimizing the use of DWI in the assessment of TIA patients.

**Subjects and Methods**

A retrospective analysis was performed on all patients entered in the Stanford Stroke Center database during 1997–2001 who were clinically diagnosed with a TIA and who had also undergone a DWI scan ≤3 days after symptom onset. This comprehensive database consists of all patients evaluated by the Stroke Service at Stanford University Medical Center. Entries into the database are completed at the time of hospital discharge.

Data were gathered regarding age; sex; symptom type, number, and date; time of symptom onset; time to symptom resolution; history of previous TIA(s) or stroke(s); and presence of vascular risk factors (eg, hypertension, diabetes mellitus, hypercholesterolemia, history of tobacco use). The date and time of DWI and the presence of a DWI abnormality were also recorded. Symptom duration was defined as the summation of time for all neurological episodes for a given patient.

DWI scans were performed as previously described. In brief, MRI was performed with the use of echo-planar imaging on a 1.5-T magnet (Signa; General Electric). Multislice whole-brain DWI was performed with the following variables: 16 slices; repetition time, 8100 ms; echo time, 110 ms; slice thickness, 5 mm; gap, 2.5 mm; 128×128 matrix; and field of view, 24 cm. B values were 0 and 829 s/mm². Diffusion-weighted images were acquired in the x, y, and z directions and were processed to generate trace apparent diffusion coefficient maps. A DWI scan was considered positive if the scan revealed an area of hyperintensity on DWI and hypointensity on apparent diffusion coefficient maps relative to the normal brain, signifying acute cerebral ischemia. All scans were reviewed by the treating neurologist and a board-certified neuroradiologist during the patient’s hospitalization. All MRI readers had extensive experience with the interpretation of DWI scans.

**Statistical Analysis**

Symptom duration, number, and time from symptom onset to MRI between patients with positive and negative DWI scans were compared. The Mann-Whitney test was used for these analyses. Yates corrected χ² and Fisher exact analyses were used for analysis of contingency tables as appropriate. Logistic regression analysis was used to test for independence among predictors for positive DWI. Significance was determined at the P<0.05 level. Sensitivity, specificity, and positive and negative predictive value for a positive DWI scan were assessed by cross tabulation. We calculated 95% CIs using the efficient-score method, corrected for continuity. Statistical analyses were performed with the use of a commercially available computer program (SPSS 10.0; SPSS Inc).

**Results**

During 1997–2001, 75 patients experiencing 78 TIAs who also underwent acute DWI evaluation within 3 days of symptom onset were identified. The mean age was 67±15 years. The mean duration of symptoms was 3.3±6.3 hours (range, 3 seconds to 24 hours). Multiple recurrent symptoms (range, 2 to 10) were reported within the 3 days before MRI in 45% (n=35) of cases. DWI was performed between 0 and 76 hours after symptom onset (mean, 23±9.2 hours). One patient had a TIA while in the MRI scanner.

DWI was positive in 16 of 78 cases (21%). Patients with positive DWI scans had a significantly longer duration of symptoms than patients with negative DWI scans (Table 1; P=0.025). The mean duration of TIA symptoms for patients with a positive DWI scan was 5.2±8.0 hours (median, 2.0 hours). The mean duration of symptoms in patients with a negative DWI scan was 2.8±5.7 hours (median, 0.5 hour). The shortest total symptom duration in a patient with a positive DWI scan was 40 seconds. Patients with TIAs lasting ≤1 hour were significantly more likely to have a positive scan than those with symptoms lasting >1 hour (Figure 1, Table 2; P=0.007). By univariate analysis, patients with positive DWI scans experienced significantly more frequent motor symptoms (Table 2; P=0.027) and aphasia (Table 2; P=0.005) during their TIAs than patients with negative DWI scans.

A stepwise multiple logistic regression analysis was performed with positive DWI scans as the outcome variable and duration of symptoms (continuous and dichotomous), motor symptoms, and aphasia as potential predictors of DWI positivity. Longer symptom duration, motor symptoms, and aphasia were found to be independently correlated with a positive DWI scan. Patients with a positive DWI scan were 9.6 times more likely (95% CI, 1.7 to 56; P=0.011) to have had symptom duration ≥1 hour, 16 times more likely (95% CI, 1.8 to 140; P=0.014) to have had motor deficits, and 25 times more likely (95% CI, 3.3 to 190; P=0.0018) to have had aphasia.

The combination of symptoms lasting ≥1 hour, motor deficits, and aphasia was 100% specific (95% CI, 93% to 100%) for a positive DWI scan, with a 100% positive predictive value (95% CI, 46% to 100%). Similarly, having either symptoms lasting ≥1 hour, motor deficits, or aphasia was 100% sensitive (95% CI, 76% to 100%) for DWI positivity with a 100% negative predictive value (95% CI,
TABLE 2. Symptom Types and Risk Factors in DWI Positive Versus Negative Scans: Univariate Analyses

<table>
<thead>
<tr>
<th>Symptom types</th>
<th>Positive Scan</th>
<th>Negative Scan</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases with:</td>
<td>n=16</td>
<td>n=62</td>
<td></td>
</tr>
<tr>
<td>Aphasia</td>
<td>8 (50)</td>
<td>9 (15)</td>
<td>0.005†</td>
</tr>
<tr>
<td>Symptom duration ≥1 hour</td>
<td>13 (81)</td>
<td>24 (39)</td>
<td>0.007*</td>
</tr>
<tr>
<td>Motor symptoms</td>
<td>14 (88)</td>
<td>33 (53)</td>
<td>0.027*</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>1 (6.3)</td>
<td>15 (24)</td>
<td>0.17†</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>0 (0)</td>
<td>6 (9.7)</td>
<td>0.34†</td>
</tr>
<tr>
<td>Headache</td>
<td>0 (0)</td>
<td>5 (8.1)</td>
<td>0.58†</td>
</tr>
<tr>
<td>True vertigo</td>
<td>0 (0)</td>
<td>4 (6.5)</td>
<td>0.58†</td>
</tr>
<tr>
<td>Dizziness, NOS</td>
<td>1 (6.3)</td>
<td>4 (6.5)</td>
<td>0.59*</td>
</tr>
<tr>
<td>Sensory symptoms</td>
<td>4 (25)</td>
<td>21 (34)</td>
<td>0.71*</td>
</tr>
<tr>
<td>Diplopia/other visual problems</td>
<td>3 (19)</td>
<td>15 (24)</td>
<td>0.77†</td>
</tr>
<tr>
<td>Gait ataxia</td>
<td>2 (6.3)</td>
<td>8 (13)</td>
<td>0.82*</td>
</tr>
<tr>
<td>Syncope/presyncope</td>
<td>1 (6.3)</td>
<td>6 (9.7)</td>
<td>0.95*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>n=15</th>
<th>n=60</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients with:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2 (13)</td>
<td>12 (20)</td>
<td>0.72†</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>7 (47)</td>
<td>27 (45)</td>
<td>0.86*</td>
</tr>
<tr>
<td>History of previous stroke/TIA</td>
<td>6 (40)</td>
<td>23 (38)</td>
<td>0.86*</td>
</tr>
<tr>
<td>Sex, M</td>
<td>8 (53)</td>
<td>35 (58)</td>
<td>0.95*</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10 (67)</td>
<td>38 (63)</td>
<td>0.95*</td>
</tr>
<tr>
<td>Smoking</td>
<td>8 (53)</td>
<td>29 (48)</td>
<td>0.95*</td>
</tr>
<tr>
<td>Age, mean y</td>
<td>66</td>
<td>68</td>
<td>0.60‡</td>
</tr>
</tbody>
</table>

n=number of cases  
*Fisher corrected χ² test  
†Fisher exact, 2-tail  
‡Mann-Whitney test  
NOS=not otherwise specified. Numbers in parentheses are percentages.  

72% to 100%). In addition, the absence of each of these clinical characteristics was 100% specific (95% CI, 76% to 100%) for a negative DWI scan (Table 3).

There was no difference in the presence of sensory symptoms between the 2 groups (Table 2; P=0.71). In addition, there was no association between having a positive or negative DWI scan and the presence of dysarthria, ataxia, headache, vertigo, syncope/presyncope, dizziness not otherwise specified, nausea/vomiting, diplopia, and other visual disturbances (Table 2). Risk factors for experiencing a TIA such as increasing age, male sex, diabetes, hypertension, high cholesterol, smoking, and prior history of stroke or TIA were not significantly associated with DWI scan results (Table 2).

There was no difference in the rate of DWI positivity between patients with single versus multiple symptom episodes (Table 1; P=0.95). Furthermore, there was no significant difference in mean time from symptom onset to MRI between positive and negative DWI groups (Table 1; P=0.89). Positive scans were identified as early as 1.3 hours and as late as 42 hours after symptom onset (Figure 2).

In 7 of 16 cases (44%), the DWI abnormality was present on both DWI and conventional imaging (T2-weighted imaging or fluid-attenuated inversion recovery [FLAIR]). However, in all cases the DWI clarified the extent or acuity of the lesion (n=7) or identified additional lesions not detected by conventional imaging (n=9).

Discussion

To our knowledge, this study is the first to specifically analyze the clinical characteristics associated with positive DWI scans in TIA patients. We found that symptom duration ≥1 hour, motor weakness, and aphasia independently predict positive DWI lesions. Moreover, in this analysis the combination of all 3 symptoms was always associated with a lesion on DWI.

Our results substantiate the hypothesis that longer symptom duration is associated with an increased likelihood of a positive DWI scan, consistent with some prior studies. Similar observations have been reported for CT imaging. A relationship between symptom duration and DWI positivity makes theoretical sense since longer duration of symptoms would be expected to result in a higher probability of persistent parenchymal damage that could be detected by MRI.

However, symptom duration alone may be an inadequate determinant of DWI positivity. For example, the minimum symptom duration in a patient with positive DWI scan reported in our study was 40 seconds. This is significantly lower than the shortest duration of 10 minutes previously reported. In addition, 10% of patients with symptom duration of <5 minutes demonstrated a positive DWI scan. Thus, symptom duration alone appears to be an imperfect predictor of DWI scan positivity.

Although there was no difference in time from symptom onset to scan for positive and negative DWI groups, we found that after 42 hours all scans were negative. These data suggest that the yield of DWI scanning is optimal if <2 days pass between symptoms and MRI scanning. This is consistent with previous studies that reported a lack of a corresponding lesion on conventional follow-up MRI in at least one fifth of TIA patients with acute DWI abnormalities, particularly in those with brain stem ischemia. This suggests that early imaging of TIA patients may significantly increase diagnostic yield and that it may be appropriate to rapidly perform DWI in TIA patients presenting early after symptom onset.

We found that sensory symptoms were not associated with a positive DWI scan. They are often viewed as "soft" symptoms because they are subjective. In addition, sensory symptoms may be associated with a broad range of possible etiologies such as hyperventilation, seizure, migraine, or multiple sclerosis. This may explain why patients presenting with sensory symptoms did not have a greater likelihood of abnormal DWI imaging. The same reasoning may hold true for other nonspecific symptoms such as dizziness or nausea that were not associated with positive DWI scans. In addition, the latter symptoms are often associated with brain stem lesions, which are known to be more difficult to detect with MRI than hemispheric abnormalities.

Somewhat surprisingly, there was no relationship between the number of neurological symptoms and the probability of DWI positivity. Theoretically, it would seem that more...
frequent symptoms would lead to a greater chance of DWI-detected abnormalities. Repeated ischemia would be expected to result in a higher probability of permanent MRI-detectable neurological injury because of the cumulative damage believed to occur after recurrent ischemic insults. However, it has recently been reported that brief ischemic insults may actually be associated with ischemic tolerance. This leads to greater resistance to permanent ischemic injury and thus could lead to a lower likelihood of detecting ischemia by MRI.

We also found that DWI is frequently helpful even in patients in whom conventional MRI could detect the symptomatic lesion. This finding expands on prior data from acute stroke studies that have reported that DWI helps to accurately determine acuity of an ischemic lesion. This unique characteristic of DWI may be particularly helpful in the frequent scenario of recurrent transient symptoms in patients with a preexisting neurological deficit related to a prior stroke. In these cases, DWI is uniquely able to clarify the diagnosis, significantly aiding the clinician to arrive at the correct diagnosis. Moreover, DWI frequently detects additional lesions not seen on conventional imaging, which could influence subsequent management.

DWI may also detect lesions not directly associated with the patient’s clinical presentation. For example, in Figure 3, the patient presented with sensory symptoms, yet several lesions are evident that would not usually be associated with the patient’s symptoms. This could lead to alterations in the diagnostic impression and subsequent management of the patient. One study reported that more than one third of their positive DWI scans led to a change in the suspected anatomic location, vascular location, or mechanism of the TIA. Thus, as with acute stroke, DWI may help to optimize management of TIs by altering the diagnostic impression of both the location and mechanism of ischemia.

Our study is subject to some limitations. Caution is always required when interpreting data obtained retrospectively from a database because of the possibility of selection bias. The relatively small size of this study could also result in type II error when analyzing subgroups. In addition, the number of patients with positive DWI scans may have been underestimated because the treating clinician could have categorized a patient with transient symptoms as a stroke if the DWI were positive even if clinically the patient’s symptoms lasted <24 hours. Such misclassifications could artificially lower the number of TIA patients with positive DWI scans detected in our study.

Indeed, the incidence of positive DWI scans in our study is lower than in prior reports. We found that 21% of our TIA patients had DWI abnormalities versus 48%, 35%, 67%, and 37% of patients in other studies. However, such a bias should also tend to identify a greater population of bona fide TIA patients, thereby increasing the accuracy of the findings by reducing the number of individuals with transient neurological symptoms not due to cerebral ischemia. However, only prospective studies with complete case ascertainment can hope to clarify this issue.

| TABLE 3. Diagnostic Values of Various TIA Clinical Characteristics for a Positive DWI Scan |
| Time from symptom onset to scan and percentage of cases with positive DWI findings. There was no significant relationship between time from symptom onset to DWI scan and DWI positivity. |

| TIA symptom +1 h AND motor symptom AND aphasia | n = 5 (100%) | n = 0 (0%) |
| TIA symptom <1 h OR no motor symptom OR no aphasia | 73 | 11 (15%) | 62 (85%) |

| Sensitivity | 31% | 12%–59% |
| Specificity | 100% | 93%–100% |
| PPV | 100% | 46%–100% |
| NPV | 85% | 74%–92% |

| TIA symptom +1 h OR motor symptom OR aphasia | 65 | 16 (25%) | 49 (75%) |
| TIA symptom +1 h AND no motor symptom AND no aphasia | 13 | 0 (0%) | 13 (100%) |

| Sensitivity | 100% | 76%–100% |
| Specificity | 21% | 12%–34% |
| PPV | 25% | 15%–37% |
| NPV | 100% | 72%–100% |

n = number of cases; PPV = positive predictive value; NPV = negative predictive value.
Other explanations for differences in the prevalence of DWI-detected abnormalities in our series include differences in the patient populations studied, differences in the time to MRI scan, and variations in both the type and severity of neurological symptoms between different studies. As illustrated in this study, the type of neurological symptom may have a profound effect on the probability of DWI positivity. Similarly, the relationship between symptom severity and DWI positivity has not been adequately evaluated. It seems likely that symptom severity would have a substantial effect on DWI positivity. However, this hypothesis is difficult to test retrospectively. Prospective studies quantifying the severity of the transient neurological deficit may be better able to adequately assess this possibility.

Finally, it should be emphasized that the observations in this study are preliminary and require prospective validation. Because of the multiple comparisons performed, the possibility of a false-positive relationship is increased. Therefore, the associations identified should be considered hypothesis generating only and validated prospectively. Nevertheless, a number of the relationships identified appear biologically plausible and potentially clinically useful.

Conclusions
In conclusion, we found that symptom duration ≥1 hour, motor deficits, and aphasia were associated with DWI positivity. In addition, DWI substantially aided in identifying new lesions in patients with chronic cerebral ischemia. These relationships may help in clinical decision making regarding the use of acute neuroimaging in TIA patients. However, further studies with larger study populations and prospective case ascertainment will be needed to validate these observations. Such studies may also help to identify additional clinical characteristics associated with DWI positivity. Additional studies will also be necessary to determine whether DWI alone can help to differentiate patients with TIAS versus other causes of transient neurological symptoms. Such studies are currently under way at our institution. Only in this way can the true utility of DWI in patients with transient neurological symptoms be fully elucidated. Nevertheless, our data suggest that DWI is a powerful tool that can be of substantial value in the evaluation of patients experiencing TIAS.

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References


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