When to Expect Negative Diffusion-Weighted Images in Stroke and Transient Ischemic Attack

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Background and Purpose—The frequency of DWI negative cerebral ischemia and clinical factors associated with such a circumstance is not well understood.

Methods—We performed MRI including diffusion-weighted imaging (DWI) in patients with stroke and transient ischemic attack (TIA) within 24 hours of symptom onset and again at 30 days.

Results—Of 401 patients, 103 (25.6%) had an initial negative DWI study. In the DWI negative group, among the stroke patients, 6/26 (23.1%) had infarcts on follow-up MRI (4 lacunar and 2 posterior circulation syndromes) and 1 had a rMTT deficit. Among the TIA patients, 4/63 (6.3%) showed rMTT deficits and 2/63 (3.2%) had infaracts on follow-up MRI.

Conclusions—Baseline perfusion weighted imaging sequences may detect ischemia in a small proportion of DWI negative cases. Only those with brain stem location or lacunar syndrome were DWI negative initially and yet had a follow-up imaging confirmation of infarct or a final clinical diagnosis of stroke. (Stroke. 2008;39:1898-1900.)

Key Words: magnetic resonance imaging ■ stroke ■ transient ischemic attack ■ diffusion-weighted imaging ■ cerebral ischemia

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ough the sensitivity of diffusion-weighted imaging (DWI) for acute cerebral ischemia is high, false-negative DWI cases occur.1–4 Transient ischemic attack (TIA) patients show DWI abnormalities in only half of the patients.5 Factors associated with false-negative DWI in acute cerebral ischemia would be useful for clinicians in decision making. Our aim was to estimate the rate of negative DWI studies in patients with stroke and TIA and to study clinical associations.

Subjects and Methods
We performed MRI including DWI in patients with stroke and TIA within 24 hours of symptom onset with the follow-up MRI at 30 days. The study was approved by the institutional ethics committee, and all patients provided written informed consent. Patients were enrolled between March 2002 and March 2005. Patients were excluded for contraindications to MRI, attributable to lack of MRI availability, or for premorbid modified Rankin scale (mRS) > 2, CT scan showing hemorrhage, serious comorbid illness, age <18 years, or an obvious nonischemic diagnosis. Before MRI all patients underwent clinical evaluation by stroke neurologist within 12 hours of symptom onset. A final clinical diagnosis was made after review of the initial and the follow-up clinical data at 30 days. A diagnosis of TIA was made when the clinical symptoms lasted less than 24 hours according to the WHO definition. MR imaging was acquired using a GE 3 Tesla MR scanner as described in a previous study.6 The diffusion gradients were applied in 3 orthogonal directions to generate isotropic DWI using the parameters: TR/TE 7000/73.1 ms, matrix 192×115, b values 0 and 1000s/mm², thickness/gap 5/2 mm.

Those with an initial negative baseline DWI were reviewed with regard to their timing of MRI, vascular distribution of the event (Oxford Community Stroke Project classification), the National Institute of Health Stroke Scale (NIHSS) score, and review of the diagnosis to identify the variables that predicted initial DWI negativity. Among DWI negative patients, the 30-day follow-up DWI and ADC maps, and fluid attenuated inversion recovery (FLAIR) sequences were reviewed by a neuroradiologist to identify an infarct corresponding to the initial clinical localization. Data are reported using standard descriptive statistics.

Results
Of 401 patients, 103 (25.6%) had an initial negative DWI study. In the DWI negative group the final clinical diagnosis was stroke in 26 (25.2%), TIA in 63 (61.2%), and nonischemic in 14 (13.6%) patients (6 seizures, 3 migraine, 2 functional, 2 hypoglycemia, 1 syncope). Of the stroke patients, 6/26 (23.1%) had infarcts on 30-day follow-up MRI on FLAIR sequences in clinically relevant regions (4 lacunar and 2 posterior circulation syndromes). Reassessment of the baseline DWI demonstrated a subtle hyperintensity in the same location as seen on follow-up FLAIR imaging in 3 cases (Figure 1). Of the 20 patients with stroke with no evidence of infarction on the follow-up imaging, 13 (65%) had either brain stem or lacunar strokes as the clinical diagnosis. Seven patients with clinical diagnosis of stroke had significant deficits, (median NIHSS 6 [range 6 to 24], despite DWI negativity of which four received tPA. Of them, 2 had a poor

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1898
Among the 7 patients, 2 had a brain stem stroke and 2 had lacunar stroke. One patient had weakness with aphasia and NIHSS of 24 with cortical deficits. Two patients had hemianopia with sensory motor deficit, which may have been subcortical. Of the TIA patients, 4 (6.3%) showed a rMTT deficit and 2 (3.2%) had infarcts on follow-up MRI (Figure 2). No clinical variables predicted a follow-up ischemic lesion in the baseline DWI negative group.

**Discussion**

We found that 25% of the patients with mild stroke or stroke-like deficits had DWI negative studies which was higher than the 3.5% previously reported. We found several reasons for DWI negative studies in our patients. In patients with a clinical diagnosis of stroke or TIA, 5.6% (5/89) showed evidence of rMTT deficits, with no infarcts on follow-up imaging. This small proportion of the patients might have had reduced perfusion not severe enough to produce a diffusion abnormality. Resolving deficits are intuitively most likely to show this phenomenon, emphasizing the need for a timely perfusion imaging. Perfusion imaging at 3T shows greater skull base susceptibility artifacts and may not be as sensitive as perfusion imaging at lower field strengths, potentially making it difficult to observe a small brain stem perfusion lesion in the absence of a diffusion lesion.

Several case series have shown that false-negative DWI occurs in brain stem strokes. Similarly, 30% of our patients with DWI negative scans had either an imaging or clinical diagnosis of brain stem stroke location. Technical concerns including the magnetic susceptibility artifacts and slice gap thickness may be key reasons for this observation. Follow-up imaging for clinically suspected brain stem strokes is critical. The relationship between DWI negativity and brain stem location has been confirmed in a large prospective study.

We found that lacunar strokes excluding the brain stem locations are also an important cause for DWI negativity; 50% of the DWI negative stroke patients had clinical or follow-up imaging evidence of lacunar stroke. It is not possible for us to reliably predict the localization of a clinical lacunar syndrome; some of these were in the posterior circulation potentially accounting for their initial failure to show on the baseline diffusion weighted image. Such lesions may be beyond the resolution of the echoplanar sequence or
the signal to noise ratio may be insufficient to pick up faint early DWI lesions.\textsuperscript{9,10} In the 4 patients with significant deficits who received tPA, DWI negativity might have been attributable to DWI reversal caused by early recanalization.\textsuperscript{12}

Nonischemic causes can produce stroke-like deficits as seen in 13% of our patients. A DWI negative study should also alert a clinician to search for nonischemic conditions.

Because many of the lesions are very small, high-resolution imaging with thinner sections and combined axial and coronal DWI sequences may increase the sensitivity of lesion identification.\textsuperscript{9}

Our study describes the characteristics of patients in whom no DWI lesions were detected despite a “stroke-like neurological deficit”. Such information may aid the clinician in interpreting DWI negative scan.

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Disclosures
None.

References
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