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

P.N. Sylaja, MD; Shelagh B. Coutts, MD, FRCPC; Andrea Krol, BSc; Michael D. Hill, MD, MSc, FRCPC; Andrew M. Demchuk, MD, FRCPC; for the VISION Study Group

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 infarcts 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

Though 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.

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 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.
functional outcome (mRS >1). 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.7 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.1,4,7,8 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.11

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. In the 4 patients with significant deficits who received tPA, DWI negativity might have been attributable to DWI reversal caused by early recanalization.

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.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.

Sources of Funding
This study was funded by Canadian Institute of Health Research, Heart and Stroke Foundation of Alberta, NWT and Nunavut, and Alberta Foundation for Health Research.

Disclosures
None.

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

P.N. Sylaja, Shelagh B. Coutts, Andrea Krol, Michael D. Hill and Andrew M. Demchuk
for the VISION Study Group

*Stroke*. 2008;39:1898-1900; originally published online April 17, 2008;
doi: 10.1161/STROKEAHA.107.497453

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2008 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/39/6/1898

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Stroke* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Stroke* is online at:
http://stroke.ahajournals.org//subscriptions/