SENSITIVITY OF DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING IN THE DIAGNOSIS OF ACUTE LACUNAR INFARCTS

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Background and purpose: Heightened interest in the early diagnosis and treatment of acute stroke challenges neuroimaging specialists to optimize available modalities and to develop new techniques for the evaluation of cerebrovascular disease. The purpose of this study was to evaluate the sensitivity of diffusion-weighted (DW) magnetic resonance (MR) imaging in detecting early small infarcts and in differentiating acute from nonacute small infarcts when conventional MR imaging demonstrates multiple small infarcts.

Methods: Thirty-eight consecutive patients with a clinical diagnosis of lacunar infarcts (20 men and 18 women, aged 50–79 yr) who underwent DW MR imaging within 3 days of symptom onset were enrolled in this study. All patients underwent both conventional fast spin-echo (FSE) MR imaging and DW MR imaging. Apparent diffusion coefficient (ADC) maps were also acquired. All patients had at least one of the following classic lacunar syndromes: pure motor hemiparesis, ataxic hemiparesis, dysarthria-clumsy hand, pure sensory stroke, and sensorimotor stroke.

Results: Thirty-six patients (40 acute lesions) had focal areas of high intensity on DW MR imaging associated with their clinical symptoms. Acute lacunar infarcts were seen on DW MR imaging as bright areas of decreased ADC ratio (range 0.31–0.85, mean 0.64). Lesion conspicuity with DW MR imaging was superior to that with FSE in 33 acute lesions. In four patients with small hyperacute (within 6 hours) infarcts, DW MR imaging was particularly sensitive for infarcts that were not visible on FSE sequences. The sensitivity of DW MR imaging and ADC map for acute lacunar infarcts was 95%, specificity 94%, positive predictive value 97%, negative predictive value 90%, and accuracy 95%. In 15 patients with both acute and nonacute old small infarcts, DW MR imaging and ADC map could easily distinguish the new infarct from adjacent old ones, although this distinction was difficult to make with FSE.

Conclusions: DW MR imaging accompanied by ADC map is a sensitive diagnostic modality for hyperacute and acute lacunar infarcts. It is also sensitive in distinguishing fresh small infarcts from adjacent multiple old infarcts.

Lacunar infarcts are small brain lesions (0.2–15 mm^3) caused by occlusion of arteries that arise at abrupt angles from the large arteries of the circle of Willis or from the basilar artery [1, 2]. Conventional magnetic resonance (MR) imaging lacks sensitivity for very early cerebral infarction, and is also handicapped by its poor ability to differentiate between acute and chronic lesions.

Recent studies have suggested that diffusion-weighted (DW) MR imaging may have a high sensitivity for early cerebral infarction [3–10]. The purpose of this study was twofold: to evaluate the sensitivity of DW
MR imaging in the detection of early small infarcts, and in differentiating acute from nonacute small infarcts when conventional MR imaging demonstrates multiple small infarcts.

Materials and Methods

From February 1999 to May 2000, 38 consecutive patients with a clinical diagnosis of lacunar syndrome underwent both conventional fast spin-echo (FSE) MR imaging and DW MR imaging with a 1.5-T MR scanner within 3 days of symptom onset. Each patient was examined by a neurologist within 6 hours after arrival at the hospital. All patients presented with at least one of the following classic lacunar syndromes: pure motor hemiparesis, ataxic hemiparesis, dysarthria-clumsy hand, pure sensory stroke, and sensorimotor stroke [11–14]. For comparison, we also studied the imaging data for 18 control patients presenting with acute neurologic symptoms (other than those of classic lacunar syndrome) who had undergone DW MR imaging.

Routine imaging studies performed in all patients included axial T1-weighted spin-echo [500/30/2 (repetition time/echo time/excitations)], T2-weighted FSE (4,000/100/2) with echo train length 8, and fast fluid-attenuated inversion recovery (FLAIR) [9,000/2,200/135/1 (repetition time/inversion time/echo time/number of excitations)] sequences. For all scans, 5-mm-thick sections with 2.5-mm interslice gaps, a 24-cm field of view, and a 256 x 192 matrix were used. Postcontrast T1-weighted images were also acquired. The conventional T2-weighted FSE and fast FLAIR images were assessed without knowledge of DW MR imaging results.

The sequence for DW MR imaging was a single-shot spin-echo echo-planar imaging [10,000/93 (repetition time/echo time)] with diffusion sensitivity (b) set at 0 s/mm² and 1,000 s/mm². The diffusion gradients were applied sequentially in three orthogonal directions to generate three sets of axial DW images. For all scans, 5-mm-thick sections with 2.5-mm interslice gaps, a 24-cm field of view, and a 128 x 256 matrix were used, with a scan time of 40 seconds. A composite isotropic trace image was measured by multiplying the three DW images together and taking the cube root of the result. All T2-signal intensities were read by two radiologists, who were unaware of the patient’s neurologic findings but knew the patient had suffered an acute stroke. Criteria for the diagnosis of acute infarction on DW MR imaging included high focal intensity on all three DW images, judged not to be due to normal anisotropic diffusion or magnetic susceptibility artifact. In all cases, the precise neuroanatomic locations of such lesions were noted. The maximum diameter of DW MR imaging hyperintensity lesions was measured. All diagnoses were made by consensus of the two readers. The association between the location of lesions and clinical symptoms was determined by a neurologist who had personally examined the patient before the imaging study.

Analysis of diffusion changes was performed by calculating the apparent diffusion coefficient (ADC) based on the Stejskal and Tanner equation [15], as the negative slope of the linear regression line best fitting the points for diffusion sensitivity b versus ln (SI), where ln is the natural logarithm and SI is the signal intensity from a region of interest of the images acquired at the two diffusion sensitivity b values. We developed a software package written in Matlab to generate ADC maps from DW images on a pixel-by-pixel basis to avoid T2 shine-through effect. Measurements of ADC were made in regions of interest in the ischemic core and in comparable contralateral regions. Intersubject comparisons were made after computing the ADC ratio of the lesion to an identical region in the control subject. Data processing required approximately 20 minutes and could be performed in a clinical setting. The results of the DW MR imaging accompanied by ADC maps were compared with those of conventional MR imaging.

Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated. These values were estimated from 2 x 2 tables based on DW MR imaging accompanied by the ADC map and the final diagnosis.

Results

Of the 38 patients (20 men and 18 women, aged 50–79 years, mean 67.2 yr) with classic lacunar syndrome, 36 (40 acute lesions) had focal areas of high intensity on DW MR imaging that were associated with all or part of the patient’s clinical symptoms. Four patients had two hyperintense lesions in the corona radiata and 32 patients had a single hyperintense lesion in various areas including the corona radiata (19 patients), lentricular nucleus (3), internal capsule (3), thalamus (2), and brainstem (9). The dimensions of these lesions on DW MR imaging ranged from 3 to 20 mm. Two patients with acute lacunar syndrome had negative DW MR imaging.
imaging; one underwent imaging within 15 hours and the other within 28 hours of ictus. Both patients had resolution of motor deficits within several days after admission, and follow-up MR imaging still showed no evidence of ischemic infarction.

Of the 18 control patients (aged 59–78 yr, mean 70 yr), 14 had a history of hypertension. The clinical manifestations consisted of ataxia (9 patients), apraxia (2), language impairment (2), behavioral changes (3), memory impairment (1), and vision deficits (1). In 17 patients with true-negative results for lacunar infarct, cortical infarction was found in nine patients, brain tumors in six, and encephalitis in two. The one patient with a false-positive result for lacunar infarct presented with acute ataxia and no limb weakness, and had an acute lacunar infarction in the corona radiata identified on DW MR imaging and ADC images. Overall, the sensitivity of DW MR imaging and ADC map for acute lacunar infarcts was 95%, specificity was 94%, positive predictive value 97%, negative predictive value 90%, and accuracy 95%.

Acute lacunar infarcts (within 3 days of onset of symptoms) were identified with DW MR imaging as bright areas of decreased ADC ratio (range 0.31–0.85, mean 0.64). Lesions were more conspicuously detailed on DW MR imaging compared with FSE and FLAIR (Fig. 1) in 33 lesions. In four patients with small hyperacute (within 6 hours) infarcts of the brainstem, DW MR imaging was particularly useful for showing such infarcts not visible with FSE and FLAIR.

Fig. 1. Images of acute lacunar infarct in the brainstem 8 hours after onset of right hemiplegia and dysarthria in a 62-year-old patient. (A) T2-weighted fast spin-echo and (B) fast fluid-attenuated inversion recovery images showing no hyperacute ischemic lesion. (C) Small ischemic lesions of the brainstem on isotropic diffusion-weighted magnetic resonance imaging. (D) Apparent diffusion coefficient (ADC) map depicting slightly decreased ADC ratio (0.67) in the same area.
In 15 patients with both acute and nonacute old small infarcts, differentiation of new infarcts from adjacent old infarcts was difficult with FSE or FLAIR. However, this differentiation was readily accomplished with DW MR imaging and ADC imaging (Fig. 2). In these patients, there were multiple areas with increased signal on T2-weighted FSE and FLAIR images, representing acute, old lesions and diffuse white matter hyperintensities.

A total of 57 lesions of small chronic infarcts were identified by DW MR imaging and ADC map. Of these, 30 lesions had an iso- or low signal on DW MR imaging and increased ADC ratio on ADC images. The other 27 lesions had a high signal on DW MR imaging and nearly normal or increased ADC ratio on ADC images. Chronic infarcts appeared as a high signal on DW MR imaging and mildly increased ADC ratio as shown in the ADC images in Figure 3.

Discussion

DW MR imaging is a relatively new technique in which strong diffusion-sensitizing gradients are added to spin-echo pulse sequences. Since DW MR imaging is extremely sensitive to any translational movements of water molecules, even very slight movements of the head during image acquisition will severely reduce the quality of the images and invalidate diffusion measurements. The introduction of newer fast techniques such as echo-planar imaging may extend the clinical application of DW MR imaging [3–8]. DW MR imaging is an increasingly popular technique for the diagnosis of acute ischemic stroke.

Lovblad et al reported positive findings in 32 of 34 infarctions (94% sensitivity) examined with DW MR
imaging within 6 hours of symptom onset [3]. The false-negative findings were either in patients with a final clinical diagnosis of stroke attributed to small lesions below the limits of scanning resolution or in patients who had resolving neurologic deficits [3, 4]. Our results show that conventional imaging is of limited value in the early stage of acute lacunar infarct. We could not demonstrate any lacunar lesion in four patients by conventional FSE or FLAIR in the hyperacute stage (within 6 hours). In most patients with acute stroke in the corona radiata, multiple areas with increased signal on FSE and FLAIR images, representing a combination of acute, old lesions and diffuse white matter hyperintensities, were noted (Fig. 2). These white matter changes are due to the aging process in elderly people [16] and the differentiation between new and old lesions is, therefore, difficult. In our study, only one of 19 patients with corona radiata lesions had a single lesion. This finding indicates that, in most patients, it is difficult to define a specific lesion responsible for the acute stroke.

DW MR imaging differs from computerized tomography and conventional MR imaging in that it provides information about a multiplicity of cerebral infarctions and also establishes a temporal association between symptoms and lesions. In acute brain ischemia, infarcts show a decrease in the ADC of water, which contributes to the increased signal on DW MR imaging [9, 10]. In the subacute period, after approximately 1 to 2 weeks, initially reduced ADC values return to baseline [9, 10]. Commonly, acute to subacute lesions appear hyperintense on DW MR imaging. This characteristic allows differentiation of new lesion from old infarctions (Fig. 2). Moreover, DW MR imaging identifies small subcortical and brainstem lesions better than conventional MR imaging because of the high lesion-to-back-
ground ADC ratio (Fig. 1) [6]. The rate of change of the ADC depends on the degree of residual perfusion, such that the diffusion abnormality reflects both degree and duration of ischemia [4, 9, 10].

The mechanism responsible for the decrease in water diffusion in acute stroke is multifactorial and poorly understood, but primarily reflects a relative shift in water from extracellular space to intracellular space [4, 8–10]. A shift of water from the extracellular space, where diffusion is relatively unrestricted, to the more restricted intracellular space reduces water mobility [4, 8–10]. Hypersensitivity on DW MR imaging is not specific for acute ischemia. Differential considerations for diffusion restriction include not only acute ischemia, but also abscess and highly cellular tumors [17].

Signal intensity of DW images can be affected by diffusion anisotropy and the amount of regional hyperintensity on images without diffusion weighting. First, if the white matter tracts are perpendicular to the diffusion gradient, there is hyperintensity on the image, so-called diffusion anisotropy [18, 19]. Diffusion anisotropy will obscure or overestimate acute lesions and lead to misinterpretation of anisotropy as an acute lesion. One method to compensate for this white matter anisotropy is to simultaneously view the set of three images with DW MR imaging. True tissue infarction is demonstrated by matched focal hyperintensity on all three DW images. A more robust method to remove the effects of diffusion anisotropy is to calculate an average composite isotropic diffusion image. This composite image was included in our protocol. Second, DW MR imaging has considerable T2-weighting, because it requires a relatively long echo-time by the addition of a large pair of strong gradient pulses. Hyperintensity on DW MR imaging is thus not necessarily indicative of acute ischemia with slower water diffusion, since an abnormality with long T2 will also cause a bright signal. This effect is known as T2 shine-through (Fig. 3) [20, 21]. Thus, DW MR imaging by itself is ambiguous without knowledge of the T2-weighted images or ADC map. The calculated ADC is the standard way to document diffusion changes in stroke [21, 22], and we calculated ADC in all cases to detect regions of differing tissue damage within the lesions. This change from low ADC in the acute state to high ADC in the chronic state is very helpful in the diagnosis of acute cerebral ischemia [9, 10, 21].

The recent development of thrombolytic and neuroprotective agents has raised the significance of accurate detection of acute infarction to new levels, since the real possibility of early intervention to limit the extent of damage from ischemic events exists. However, because the therapy is not without significant risk, it is important to distinguish patients who have evidence of new ischemic damage from those who do not have acute ischemic lesions.

In conclusion, DW MR imaging combined with ADC map has a high sensitivity in detecting lesions in hyperacute and acute stroke, even when the lesions are small, and the association with clinical findings is strong. Conventional MR imaging is of limited value for diagnosis in the early stage of acute ischemic stroke, while DW MR imaging plus ADC map can differentiate acute from nonacute small infarctions.

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References