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Comparison of the 2010 and 2005 versions of the McDonald MRI criteria for dissemination-in-time in Taiwanese patients with classic multiple sclerosis

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ABSTRACT

In 2010, the International Panel on the Diagnosis of Multiple Sclerosis revised the 2005 version of the McDonald criteria. The revisions to MRI dissemination-in-time criteria include adoption of a new criterion by demonstration of simultaneous asymptomatic gadolinium-enhancing and nonenhancing lesions on baseline MRI scans. The purpose of this study was to demonstrate the diagnostic validity of the modified MRI dissemination-in-time criteria. We collected 80 patients with an initial clinical attack suggestive of an acute central nervous system demyelinating disease. The patients were followed for at least two years or until the development of definite multiple sclerosis. The nonconverters were taken as negative cases. Their baseline and follow-up brain MRI studies were retrospectively reviewed by two neuroradiologists. The 2010 version had higher sensitivity (68.2% vs. 45.5%), slightly lower specificity (80.6% vs. 83.3%), and higher accuracy (73.8% vs. 62.5%) than the 2005 version, but the differences were without statistical significance. The new criteria are more sensitive and accurate and specific just as the old criteria. They allow the diagnosis of definite multiple sclerosis in 34.1% patients at first presentation of the clinically isolated syndrome.

1. Introduction

According to McDonald criteria, multiple sclerosis (MS) is diagnosed based on the objective demonstration of central nervous system (CNS) demyelinating lesions disseminated in space (DIS) and time (DIT) after exclusion of alternative diagnoses that might mimic the disease [1–3]. Magnetic resonance imaging (MRI) findings can substitute for clinical evidence of one lesion and one clinical attack if they fulfill the MRI DIS and DIT criteria, respectively [1–3]. In 2010, the International Panel on the Diagnosis of Multiple Sclerosis adopted a new MRI DIS criterion proposed by Swanton et al. (i.e., at least one T2-lesion in two or more of the following CNS regions: periventricular, juxtacortical, infratentorial, and spinal cord) [4,5]. Our previous study found that the specificity and sensitivity of this criterion were comparable to those of the MRI DIS criterion included in the 2005 version of the McDonald criteria when applied to Taiwanese patients with classic MS [3–6]. In addition, the panel revised the 2005 McDonald criteria by adopting a new criterion proposed by Rovira et al. [3,7]. The new MRI DIT criteria emphasized the early diagnosis of MS based on a single baseline MRI demonstrating simultaneously the presence of asymptomatic gadolinium-enhancing and nonenhancing lesions indicative of demyelinating plaques in different stages of evolution [7,8]. The two sets of MRI DIT criteria (from 2005 to 2010) are summarized in Table 1.

Clinically isolated syndrome (CIS) refers to a single clinical attack of CNS inflammatory demyelinating symptoms suggestive of MS. CIS presentations can be monofocal or multifocal, and typically involve the optic nerve, brainstem, cerebellum, spinal cord, or cerebral hemispheres. Although CIS may represent the first manifestation of definite multiple sclerosis (DMS), some patients (i.e., nonconverters) may not develop a second clinical relapse. The purpose of this study is to validate the diagnostic ability of the two sets of MRI DIT criteria in DMS patients and nonconverter patients.

2. Methods

2.1. Patient selection

The study protocol was approved by the local institutional review board (TSGH IRB 1-101-05-004). From January 2001 to June 2010, we collected 80 patients with an initial clinical attack suggestive of an

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Table 1
The 2005 and 2010 revisions to the McDonald criteria for MRI DIT.

2005 revisions	Detection of gadolinium enhancement at least 3 months after the onset of the initial clinical event, if not at the site corresponding to the initial event or detection of a new T2 lesion if it appears at any time compared with a reference scan done at least 30 days after the onset of the initial clinical event
2010 revisions	A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, with reference to a baseline scan, irrespective of the timing of the baseline MRI or simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions at any time

MRI = magnetic resonance imaging; DIT = dissemination-in-time.

Table 2
Comparison of MRI findings in DMS patients and nonconverters.

	Simultaneous Gd+ and Gd− lesions on baseline MRI	New T2-lesion on F-U MRI	New Gd+ lesion on F-U MRI	Fulfill 2005 MRI DIT	Fulfill 2010 MRI DIT
DMS (n = 44)	17 (38.6%)	20 (45.5%)	5 (11.4%)	20 (45.5%)	30 (68.2%)
Nonconverter (n = 36)	1 (2.8%)	6 (16.7%)	0 (0%)	6 (16.7%)	7 (19.4%)

MRI = magnetic resonance imaging; DMS = definite multiple sclerosis; Gd+ = gadolinium-enhancing; Gd− = gadolinium-nonenhancing; F-U = follow-up; DIT = dissemination-in-time.

acute CNS demyelinating disease (i.e., CIS). They had clinical follow-up of at least two years or until the development of DMS. Some of the subjects were in the cohort we studied previously [6,9]. All 80 patients met the following inclusion criteria: (1) age of 15 to 50 years; (2) baseline brain MRI obtained within three months of symptom onset; (3) follow-up brain MRI available; (4) MRI sequences containing gadolinium enhancement; and (5) no use of disease-modifying agents before the second clinical episodes (except for corticosteroid therapy). The exclusion criteria were: (1) clinical suspicion of acute disseminated encephalomyelitis (ADEM); and (2) symptoms and MRI abnormalities confined to optic nerves and spinal cord fulfilling the diagnostic criteria of neuromyelitis optica proposed by Wingerchuk et al. [10]. (3) other CNS white matter diseases were excluded through clinical work-ups.

2.2. MRI sequences and imaging analysis

The MRI studies were performed on 1.5-T MR scanners. The brain MRI sequences included spin echo (SE) or fast spin echo (FSE) T1-weighted imaging (T1WI), T2-weighted imaging (T2WI), and fluid-attenuated inversion recovery (FLAIR) in the axial plane, T2WI or T2-FLAIR in the sagittal plane, and contrast-enhanced T1WI in axial, coronal, and sagittal planes. Follow-up MRI scans were compared with the baseline scans. Spinal cord MRI studies were not included in this analysis because most patients received no or only one study and therefore DIT could not be demonstrated. Two neuroradiologists who were blind to the final diagnosis retrospectively reviewed the MRI scans and reached a consensus agreement on whether the two sets of MRI DIT criteria were fulfilled.

2.3. Statistical analysis

Patients who finally converted to DMS were considered positive cases and the nonconverters after at least two years of follow-up were considered negative cases. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of the two sets of MRI DIT criteria were calculated. The significance of differences was determined with 95% confidence intervals (95% CI), and the absence of overlapping was considered an indicator of difference.

3. Results

The recruited 80 patients consisted of 28 men and 52 women (mean age, 33.4 years; range, 15–50 years). Finally, 44 (55%) patients converted to DMS with a mean interval of 9.6 months after the onset of initial clinical events (range, 2–24 months) and 36 patients did not convert. The diagnosis of DMS in 44 patients was made by experienced neurologists and based on clinical grounds (two or more clinical attacks of CNS demyelinating events and objective clinical evidence of two or more lesions as defined in McDonald criteria). The mean clinical follow-up duration of the whole cohort was 66.4 months (range, 24–130 months). Clinical features at first presentation among the 80 patients included: unilateral optic neuritis (n = 24 [30.0%]), brainstem symptoms (n = 18 [22.5%]), multifocal symptoms (n = 23 [28.8%]), and spinal cord symptoms (n = 22 [27.5%]).

All of the baseline brain MRI studies were performed within three months after initial symptom onset. Twenty-seven patients had more than one follow-up brain MRI scan (range, 1–4 scans). The mean interval between the baseline and follow-up MRI scans was 6.7 months (range, 3–28 months).

Table 2 summarizes the MRI findings of the DMS patients and nonconverters. Among the 44 patients with DMS, 17 had simultaneous asymptomatic gadolinium-enhancing and nonenhancing lesions on baseline brain MRI; 20 had new T2-lesions, and five had new gadolinium-enhancing lesions on follow-up MRI scans. Some patients had more than one of these findings on MRI. Overall, 30 patients fulfilled the 2010 version of the McDonald criteria for MRI DIT and 20 patients fulfilled the 2005 version of these criteria.

Among the 17 patients who had simultaneous asymptomatic gadolinium-enhancing and nonenhancing lesions on baseline brain MRI (with a mean interval of 15 days from symptom onset), 15 patients also fulfilled the MRI DIS criteria of 2010, which means that the diagnosis of DMS could be established in 34.1% (15/44) patients based on early clinical events and baseline brain MRI studies without the need for a second clinical attack or follow-up MRI according to the new criteria. The other 13 patients fulfilled the 2010 MRI DIT criteria based on follow-up MRI scans (with a mean interval of 168 days from symptom onset). Four of them already had a second clinical attack before follow-up MRI scans and thus had been diagnosed as DMS.

Among the 36 nonconverters, one had simultaneous asymptomatic gadolinium-enhancing and nonenhancing lesions on baseline brain MRI; six had new T2-lesions and none had new gadolinium-enhancing lesions on follow-up scans (i.e., six nonconverters fulfilled the MRI DIT criteria of 2005 and seven fulfilled those of 2010).

Table 3
Performance of the 2005 and 2010 revisions to the McDonald criteria for MRI DIT.

	TP	FP	TN	FN	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
2005 revisions	20	6	30	24	45.5	83.3	76.9	55.6	62.5
95% CI					30.7–60.2	71.2–95.5	60.7–93.1	42.3–68.8	51.9–73.1
2010 revisions	30	7	29	14	68.2	80.6	81.1	67.4	73.8
95% CI					55.4–81.9	67.6–93.5	68.5–93.7	53.4–81.5	64.1–83.4

MRI = magnetic resonance imaging; DIT = dissemination-in-time; TP = true positive; FP = false positive; TN = true negative; FN = false negative; PPV = positive predictive value; NPV = negative predictive value; 95% CI = 95% confidence interval.