

Low sensitivity of McDonald MRI criteria in the diagnosis of multiple sclerosis among Asians

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Abstract

Background: Multiple sclerosis (MS) in Asia manifests differently with lower prevalence, higher female preponderance, fewer cortical lesions but more severe spinal cord disease. **Methods:** We retrospectively reviewed the first brain and spinal cord MRI in patients with clinical or laboratory-supported definite MS under the Poser criteria across Asia to ascertain the sensitivity of the Barkhof and McDonald MRI dissemination in space criteria. **Results:** The Barkhof criteria were only 49% sensitive in 101 patients, classical MS 62%, optic-spinal MS 35%. Similarly, revised McDonald MRI criteria have a sensitivity of only 52%, classical MS 67%, optic-spinal MS 37% in 101 patients. **Conclusion:** The sensitivity of McDonald MRI criteria in the diagnosis of multiple sclerosis among Asians is low.

INTRODUCTION

Multiple sclerosis (MS) in Asia has long been noted to have significant differences with that in the western countries. The differences include lower prevalence, rare positive family history, higher female prevalence, more frequent and severe optic nerve and spinal cord but fewer cortical and cerebellar relapses, with higher frequency of paroxysmal tonic spasm and greater functional disabilities; higher prevalence of the optic-spinal form, lower rate of oligoclonal bands in the cerebrospinal fluids, and longer spinal cord lesions on magnetic resonance imaging (MRI).¹⁻⁷ In patients with classical MS among Asians, spinal cord lesions were reported to be 2.5 ± 2.3⁷ to 5.3 ± 2.58⁸ vertebral bodies high, and 4.2 ± 3.6⁷ to 5.8 ± 3.2⁸ vertebral bodies high in the optic-spinal patients.

In 2001, the International Panel on MS Diagnosis⁹ proposed a new guideline for the diagnosis of MS, which was revised in 2005.¹⁰ The basis of the new guideline remains similar

to the criteria set down by Poser *et al*¹¹ with the inclusion of MRI evidence of dissemination in time and space. The MRI criteria were based on Barkhof *et al*'s study.¹² This has the potential to enable early diagnosis. It has been shown to almost triple the rate of diagnosis of MS within a year of presentation in patients with clinically isolated syndromes from 7-11% to 20-37%, with high sensitivity (74-83%), specificity (83-86%), positive and negative predictive values (75% and 89% respectively) and accuracy (80-83%).^{13,14} For the spinal cord, the lesions should be less than 2 vertebral bodies high, should have little or no swelling, occupy part of the cross section of the cord. The spinal cord lesion can substitute for brain infratentorial lesion, and enhancing spinal cord lesion is equivalent to an enhancing brain lesion.^{9,10} Patients who fulfilled 3 out of 4 MRI criteria were diagnosed as having MRI findings consistent with the diagnosis of MS. The criteria's sensitivity, specificity and accuracy are not known outside the western countries. As Asian MS

patients have fewer brain but more common and severe spinal cord disease, it is hypothesized that the Barkhof criteria would be less sensitive among Asians. It is also thought that excluding spinal cord lesions of more than 2 vertebral bodies high would exclude patients with optic-spinal form of MS. We retrospectively applied Barkhof criteria¹² and the MRI dissemination in space criteria in McDonald *et al* and Polman *et al*^{9,10} to patients who were diagnosed to have clinical or laboratory supported definite MS under Poser criteria¹¹ across Asia to determine its sensitivity, and to assess the importance of spinal cord MRI in the diagnosis of MS outside western countries.

METHODS

We conducted a retrospective survey on the first brain and/or spinal cord MRI done according to clinical indication in 7 regions across Asia (Malaysia, Korea, India, Singapore, Thailand, Taiwan and Hong Kong). The patients were diagnosed to have clinical definite MS according to the Poser criteria.¹¹ The optic-spinal form of MS was defined clinically in patients with recurrent myelitis and/or optic neuritis without clinical involvement of other parts of the central nervous system; while those with classical form had clinical involvement beyond optic nerve and spinal cord. The MRI was done in various centers on at least a 1.5 Tesla machine, with the minimal of T1, T2 and FLAIR weighted images, but preferably with gadolinium enhancement. The spinal cord section was 3 mm or less. The images were read by at least two neuroradiologists/neurologists and the interpretation reached by consensus. Where there was dissenting view, the opinion of the third neuroradiologist/neurologist was accepted as final. The results were collated and analyzed centrally.

Parametric variables were analyzed with ANOVA, and non-parametric with Fisher's exact test, chi square (with Yates' correction when necessary) or Mann-Whitney statistics. All p values of less than 0.05 were accepted as significant.

RESULTS

Demography

Of the 136 patients who were initially enrolled in the study, 121 patients had sufficient clinical details to be included in the analysis. There were 101 first MRI of the brain and 86 of the spinal cord; 66 of whom had both first brain and spinal

cord MRI. On average, the brain MRI was done 2.2 ± 4.9 years and the spinal cord MRI 2.7 ± 5.6 years after diagnosis. The mean age was 38 ± 11 years, with 100 (87%) female. Forty seven percent were ethnic Chinese, 22% Indian, 14% Thai, 12% Korean, 4% Malay, and 1% Taiwanese aborigines. Out of these, 68 (58%) had optic-spinal MS. There was no difference in the age and sex of the two groups, though Chinese is overrepresented in the optic-spinal group ($p=0.04$). The clinical course of the patients was relapsing remitting (89%), secondary progressive (5%), progressive relapsing (3%), and primary progressive (4%), with no significant difference in the optic-spinal and classical groups.

Brain MRI

Overall about half of the 101 patients fulfilled Barkhof criteria.¹² Classical MS patients fulfill more of Barkhof criteria¹¹ than optic-spinal patients (median of 3 criteria versus 1, $p=0.036$), but 34% of the latter still fulfilled 3 or more of Barkhof criteria¹², as compared to 61% for the classical MS group (Table 1).

Spinal MRI

Of the 66 patients who had first MRI spine with the brain, 30 were classical and 36 were optic-spinal MS patients. There were a total of 90 spinal lesions. Table 2 lists the details of the lesions. Thirteen patients (43%) with classical MS and 23 optic-spinal patients (64%) had large spinal cord lesions of more than 2 vertebral bodies. There was no significant difference in the size of spinal cord lesions between those who fulfilled Barkhof criteria¹² and those who did not (3.4 ± 3.1 versus 3.7 ± 4.0 vertebral bodies, $p=0.86$).

Overall, 35 out of the 66 patients who had both brain and spinal MRI (53%), 20/30 (67%) classical and 15/36 (42%) optic-spinal MS fulfilled the MRI criteria by McDonald *et al* and Polman *et al*.^{9,10} However, if large spinal cord lesions were included then 36 patients (55%) satisfied McDonald MRI criteria (20/30 or 67% classical and 16/36, 44% optic-spinal MS patients).

DISCUSSION

Overall, the proportions of the clinical or laboratory-supported definite MS patients in Asia who fulfilled the Barkhof¹² and McDonald^{9,10} were less than reported^{13,14}, particularly so among the patients with optic-spinal MS. Barely half of our patients fulfilled the Barkhof criteria, compared

Table 1: Patients fulfilling Barkhof and McDonald dissemination in space criteria^{9,10,12}

	All patients (N=101)	Classical (N=52)	Optic-spinal (N=49)	p values
Gadolinium enhancement (%)	29 (29%)	19 (37%)	10 (20%)	0.11
≥ 9 T2 lesions (%)	52 (53%)	36 (69%)	17 (35%)	0.001
Infratentorial lesion (%)	59 (58%)	38 (73%)	21 (43%)	0.004
Juxtacortical lesion (%)	62 (61%)	37 (71%)	25 (51%)	0.06
≥ 3 periventricular lesion (%)	43 (43%)	29 (56%)	14 (29%)	0.01
Barkhof criteria ¹²				
1. Fulfilled ≥ 1 criterion (%)	83 (82%)	49 (94%)	34 (69%)	0.0027
2. Fulfilled ≥ 2 criteria (%)	64 (63%)	41 (79%)	23 (47%)	0.0018
3. Fulfilled ≥ 3 criteria (%)	49 (49%)	32 (62%)	17 (35%)	0.012
4. Fulfilled all 4 criteria (%)	29 (29%)	21 (40%)	8 (16%)	0.014
McDonald Criteria ⁹				
1. Fulfilled ≥ 1 criterion	83 (82%)	49 (94%)	34 (69%)	0.0027
2. Fulfilled ≥ 2 criteria	66 (65%)	43 (83%)	23 (47%)	0.0003
3. Fulfilled ≥ 3 criteria	49 (49%)	32 (62%)	17 (35%)	0.012
4. Fulfilled all 4 criteria	29 (29%)	21 (40%)	8 (16%)	0.014
Revised McDonald Criteria ¹⁰				
1. Fulfilled ≥ 1 criterion	94 (93%)	52 (100%)	42 (86%)	0.0050
2. Fulfilled ≥ 2 criteria	77 (76%)	45 (87%)	32 (65%)	0.023
3. Fulfilled ≥ 3 criteria	53 (52%)	35 (67%)	18 (37%)	0.0040
4. Fulfilled all 4 criteria	31 (31%)	21 (40%)	10 (20%)	0.050

Barkhof criteria¹² consist of fulfilling 3 of 4 of the following: 1. One gadolinium-enhancing lesion of 9 or more T₂ lesions if there is no gadolinium enhancing lesions; 2. At least one infratentorial lesion; 3. At least one juxtacortical lesion; 4. At least 3 periventricular lesions.

Table 2: Spinal cord MRI features

	Total	Classical	Optic-spinal	p values
No. of lesions/patient	1.4 ± 1.1	1.5 ± 1.5	1.3 ± 0.7	NS*
Size (no. vertebral bodies)	3.5 ± 3.5	2.5 ± 2.4	4.5 ± 4.2	0.0079
No. of large lesions**	39/90 (43%)	13/44 (30%)	26/46 (57%)	0.018
Swelling	23/79 (29%)	5/35 (14%)	18/44 (41%)	0.019
Complete cross section	12/75 (16%)	3/36 (8%)	9/39 (23%)	0.15

*NS = not significant, **Large lesion = lesions larger than 2 vertebral body segments.

with the reported figures of 74 – 83%.¹²⁻¹⁴ Each of the components of Barkhof criteria was also less sensitive among optic-spinal MS patients.¹⁴ Among patients with classical MS in Asia, the criteria on the total number of lesions and juxtacortical lesions were comparable, but the criteria on infratentorial lesions were more sensitive, as this study reported a 74% sensitivity

compared with 58% in Barkhof *et al.*¹² The criteria on gadolinium enhancement might be falsely low due to the long interval between the time of the last attack and the time when the MRI were done. This study suffers from the drawback of a retrospective study done relatively late after diagnosis. However this should bias the results towards higher sensitivity. A prospective

study done on patients with clinically isolated syndromes as by Barkhof *et al*¹² would likely to yield even lower sensitivity.

Among our patients, spinal cord lesions of more than 2 vertebral bodies in size were relatively common, even among those with classical MS. Similarly cord swelling and complete cross section involvement. Large spinal cord lesions were also just as common among those who fulfilled Barkhof criteria as those who did not. This points to the lack of correlation between the parameters of brain and spinal cord lesions on MRI, a fact demonstrated elsewhere.^{15,16} Kira *et al*⁸ similarly reported that the average size of spinal cord lesions among Japanese patients who fulfilled Poser criteria were 5 to 6 vertebral bodies in size. Thielen *et al*¹⁷ and Honig *et al*¹⁸ also reported spinal cord lesions of up to 60 mm to 5 vertebral segment longitudinally among their MS patients from the West. Therefore, exclusion of large spinal cord lesions would reduce further the sensitivity of the diagnostic criteria by McDonald *et al* and Polman *et al*.^{9,10}

It was recently suggested that optic-spinal MS among Asians is identical to neuromyelitis optica, a disease said to be distinct from MS because of the severe spinal cord lesions and the relative absence of brain involvement.¹⁹ However this study demonstrated that among optic-spinal MS patients, a third of them fulfilled Barkhof criteria as having typical brain MRI changes, and 69% fulfilled at least one of his 4 criteria, each was relatively specific to MS.¹² Moreover, large spinal cord lesions is common in both classical and optic-spinal MS patients. There was also no significant difference in the size of spinal cord lesions between those who fulfilled Barkhof criteria and those who did not. Saida *et al*²⁰ reported that interferon beta-1b is effective in Japanese relapsing remitting MS patients, the magnitude of improvement being similar in both optic-spinal and classical groups of patients, suggesting that the optic-spinal and classical MS are basically similar disease.

In conclusion, McDonald MRI criteria should be modified to increase its sensitivity to diagnosis of MS among Asians.

ACKNOWLEDGEMENTS

Our gratitude to Dr YY Seetoh, National Neuroscience Institute Singapore, and Serono Asia Pacific for their various assistances.

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