MULTIPLE SCLEROSIS JOURNAL | MSJ

Original Research Paper

Brain and spinal MRI features distinguishing MS from different AQP4 antibody serostatus NMOSD at disease onset in a cohort of Latin American patients

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Abstract

Objective: We aimed to evaluate magnetic resonance imaging (MRI) previously used criteria (Matthews's criteria, MC) for differentiating multiple sclerosis (MS) from neuromyelitis optica spectrum disorders (NMOSD) in Caucasian and non-Caucasian populations (Argentina, Brazil and Venezuela) with positive (P-NMOSD), negative (N-NMOSD), and unknown (U-NMOSD) aquaporin-4 antibody serostatus at disease onset and to assess the added diagnostic value of spinal cord MRI in these populations.

Methods: We reviewed medical records, and MRIs were assessed by two blinded evaluators and were scored using MC. Short-segment transverse myelitis (STM) was added as a new criterion. MC sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were determined.

Results: We included 282 patients (MS = 188 and NMOSD = 94). MC applied to the entire cohort showed 97.8% sensitivity, 82.9% specificity, 92.0% PPV, and 95.1% NPV for differentiating MS from NMOSD. A subanalysis applied only to non-Caucasian (MS = 89 and NMOSD = 47) showed 100% sensitivity, 80.8% specificity, 90.8% PPV, and 100% NPV. Similar sensitivity, specificity, PPV, and NPV of MC for MS versus P-NMOSD ($n = 55$), N-NMOSD ($n = 28$), and U-NMOSD ($n = 21$) were observed.

Conclusion: MC distinguished MS from NMOSD of all serostatus in a Latin American cohort that included non-Caucasian populations. Addition of STM to MC did not raise the accuracy significantly.

Keywords: Latin America population, multiple sclerosis, neuromyelitis optica spectrum disorders, Matthews's criteria

Date received: 30 January 2019; revised: 4 April 2019; accepted: 6 April 2019

Multiple Sclerosis Journal

1–10

DOI: 10.1177/1352458519849517

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†This paper is dedicated to the memory of our wonderful colleague, Dr. Amilton Antunes Barreira (Head of Department of Neurosciences and Behavioral Sciences, Hospital das Clínicas, Ribeirão Preto Medical School, University of de São Paulo), who recently passed away.

Introduction

Neuromyelitis optica spectrum disorders (NMOSD) and multiple sclerosis (MS) are both idiopathic, autoimmune, and inflammatory diseases of the central nervous system (CNS) that typically follow a relapsing course.[1,2] At disease onset, relapsing–remitting multiple sclerosis (RRMS) and NMOSD may present with similar or overlapping clinical, paraclinical, and neuroradiological features, and it may be difficult to differentiate these two entities and to establish a specific treatment.[2–4]

In 2004, aquaporin-4 antibodies (AQP4-abs)[5] were found to be the key to early distinction between NMOSD and MS, since AQP4-abs are rarely found in other inflammatory CNS diseases or in healthy controls.[6–8] However, AQP4-abs are not available worldwide; the results may take many weeks to obtain, and these could be negative or unknown, particularly if the recommended methods are not used.[4] Likewise, MS may be misdiagnosed as NMOSD (especially in patients who are AQP4-ab-negative). Moreover, the diagnosis of NMOSD may sometimes only be made

after patients' conditions worsen through MS treatments (using disease-modifying therapy such as natalizumab,[9–11] fingolimod,[12] or interferon[13–14]).[1] Thus, establishing the correct diagnosis may have a positive impact in terms of disease-specific immunotherapy and clinical prognosis, especially when diagnosis and treatment are not delayed.[3]

In addition, brain and spinal magnetic resonance imagings (MRIs) have an important role in making the differential diagnosis and are excellent tools for identifying patients with MS or NMOSD.[15–17] In this regard, brain MRI findings (location and configuration of lesions) that differentiate MS from AQP4-ab-positive NMOSD in everyday clinical practice across centers and scanners have previously been described. These brain lesions distribution criteria have originally been proposed by Matthews et al. (2013), and they have also been named as Matthews's criteria (MC)[18] in some recent studies.[19,20] MC presents 92% sensitivity, 96% specificity, 98% positive predictive value (PPV), and 86% negative predictive value (NPV) for distinguishing patients with MS from AQP4-ab-positive NMOSD, based on a Caucasian population. Moreover, silent spinal cord lesions may contribute toward making the diagnosis of MS, and therefore, spinal cord MRI is recommended at symptom onset, as described in the 2017 McDonald criteria for MS.[21,22] However, spinal cord assessment was not included in previously used criteria (MC), and only AQP4-ab-positive NMOSD patients in a Caucasian population were evaluated in the original cohorts.[18–25]

The objectives of this study were to evaluate previously used criteria (MC) in a cohort of Latin American patients (Caucasian and non-Caucasian populations) with positive (P-NMOSD), negative (N-NMOSD), and unknown (U-NMOSD) AQP4-abs status at disease onset and to assess the added diagnostic value of spinal cord MRI among these patients.

Methods

We conducted a retrospective multicenter study in Argentina (MS = 92, NMOSD = 38), Brazil (MS = 55, NMOSD = 27), and Venezuela (MS = 29, NMOSD = 41). We retrospectively reviewed all the medical record databases of patients who were evaluated between 2010 and 2017, and the features of the first brain and spinal MRIs at presentation (disease onset) were assessed by two blinded evaluators. These features were scored using MC as follows: lesions adjacent to the body of the lateral ventricle, lesions in the inferior temporal lobe, S-shaped/curved U-fiber lesions, and Dawson's fingers.[18–25] Short-segment transverse myelitis (STM) was defined as <3 segment lesions on sagittal MRI with partial (lateral/posterior) cross-sectional involvement[21] added as a new criterion for the analysis (thus modifying MC),[20] as illustrated in Figure 1.

Patients with MS and NMOSD who had previously been diagnosed using the current validated diagnostic criteria, in accordance with the 2010 McDonald criteria for MS[26] and the International Consensus diagnostic criteria for NMOSD 2015[4] (used as the gold standard), were included in this study. The demographic data that were gathered included age, gender, and ethnicity. Ethnicity was analyzed by direct genealogical interview that recorded the place of birth of antecessors up to the great-grandparents and also by paternal and maternal surnames as culturally transmitted markers to confirm ancestry origin.[27] For the analysis, ethnicity was separated into the following: Caucasian (individuals of European descendant), mixed (people of mixed European and Amerindian ancestry living in the region of Latin America), Afro-American (individuals of mixed native American and African descendants), Asian (a person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam), and Aboriginal (unmixed native American ancestry).

The first clinical attack (core clinical characteristic for NMOSD or clinically isolated syndrome for MS) was defined as follows:[4,28] acute transverse myelitis (ATM), optic neuritis (ON), area postrema syndrome (APS), brainstem syndrome (BSS), narcolepsy or diencephalic syndrome (DS), and cerebral syndrome (CS). AQP4-ab status was measured using a cell-based assay (CBA)[8,29] in 78% and indirect immunofluorescence (IIF)[5] in 22%. Thus, patients with NMOSD were classified as follows: AQP4-ab positive (P-NMOSD), negative (N-NMOSD), or unknown (U-NMOSD).

Oligoclonal bands (OCB) were determined by means of isoelectric focusing on cerebrospinal fluid (CSF). Positive findings of antinuclear antibodies (ANAs, tested with IIF using Hep-2 cell culture) were defined as titers $\geq 1/160$. Brain (coronal, axial, and sagittal) and cervical and thoracic spinal cord (axial and sagittal) MRI scans were performed, including T2-weighted sequences, fluid-attenuated inversion recovery (FLAIR), and short-tau inversion recovery (STIR, for spinal cord). These were acquired in all patients using a 1.5 T or 3 T scanner with 3 mm slice thickness.

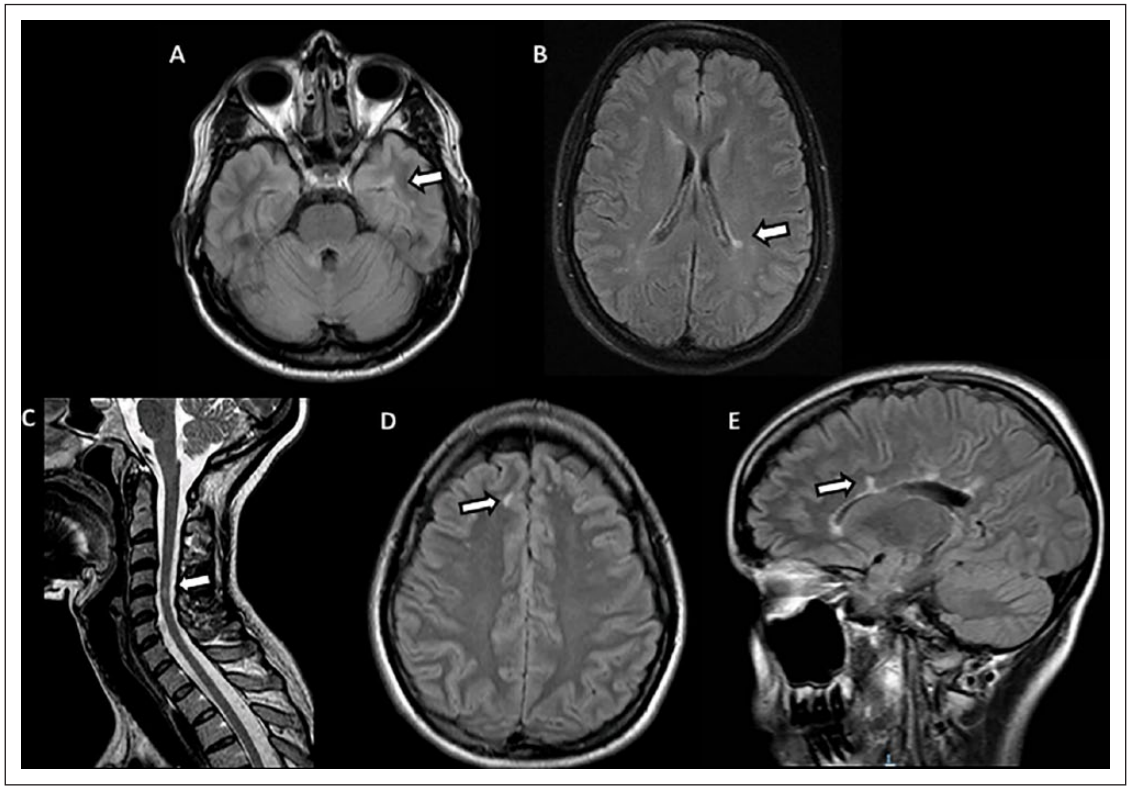

Figure 1. Brain and spinal cord MRIs from five NMOSD patients who fulfilled MC and the modified MC. Lesions are showed with white arrows. Patients A and B had lesions in the inferior part of the left temporal lobe and adjacent to the body of a lateral ventricle, patient C had a spinal cord lesion (short myelitis), patient D had a curved U-fiber juxtacortical lesion, and patient E had callosal lesions that were compatible with Dawson's fingers.

The 2017 McDonald criteria[21] for dissemination of MS lesions in space (DIS) were applied to the brain and spinal cord MRI scans. In addition, the 2016 MAGNIMS criteria[30,31] for DIS (including optic nerve lesions) were also documented.

All patients and MRI scans were evaluated for scoring by at least one of the authors (neurologist) and one neuroradiologist (all of them with expertise in demyelinating diseases such as MS and NMOSD) of each participating center. These evaluators were blinded to the diagnosis, but they were not blinded to the objective of the study. Thus, the sensitivity, specificity, PPV, and NPV of MC and the modified MC were determined.

This study was approved by the local ethics committee of each participating center, and written informed consent was obtained from all participants.

Statistical analyses

Statistical analyses were performed using the GraphPad Prism 6 and SPSS v 22 software. The results were presented as percentages, mean values, and standard deviations (±SD) or medians. The Kolmogorov–Smirnov test was performed to evaluate the distribution of the variables. Comparisons on continuous data among the groups were analyzed using the *t*-test or the Mann–Whitney *U* test, and categorical data were analyzed using the Pearson chi-square test or Fisher's exact test, as appropriate. For all the analyses, the significance level was established as $p < 0.05$.

Based on the diagnosis of MS or NMOSD, both the MC results (MRI findings) and the modified MC results (including spinal cord MRI) were classified as true positive (TP, criteria fulfilled; diagnosis of MS), true negative (TN, criteria not fulfilled; diagnosis of NMOSD), false positive (FP, criteria fulfilled; diagnosis of NMOSD), or false negative (FN, criteria not fulfilled; diagnosis of MS). Thus, specificity was determined as the ratio TN/(TN + FP) and sensitivity as TP/(TP + FN). In addition, PPV was calculated as TP/(TP + FP) and NPV as TN/(TN + FN).

Results

We included 282 patients (MS = 288 and NMOSD = 94; ratio 2:1). The demographic data and clinical and

Table 1. Demographics and paraclinical features.

Characteristics	NMOSD	MS	*P* value
N	94	188	
Mean age at onset, years (±SD)	37.6 (±14.6)	34.09 (±11.7)	0.041
Median (IQR = Q1–Q3)	37.5 (27–46)	33.5 (24–41)	0.07
Female, *n* (%)	76 (80.8)	142 (75.5)	0.36
Ethnicity			
Caucasian	47	97	0.70
Afro-American	2	4	1
Mixed race	42	85	1
Aboriginal	2	0	0.11
Asian	1	2	1
Paraclinical features			
Aquaporin-4 antibodies			
Positive	55 (58.5)	0	<0.0001
Unknown	21 (22.3)	162 (87.5)	
Antinuclear antibodies			
Positive	18 (19.1)	23 (12.2)	0.47
Unknown	10 (10.6)	54 (28.7)	
Oligoclonal bands			
Positive	16 (32.6)	112 (83.5)	<0.0001
Unknown	45 (47.8)	54 (29.1)	

NMOSD: neuromyelitis optica spectrum disorders; MS: multiple sclerosis; SD: standard deviation; IQR: interquartile range.

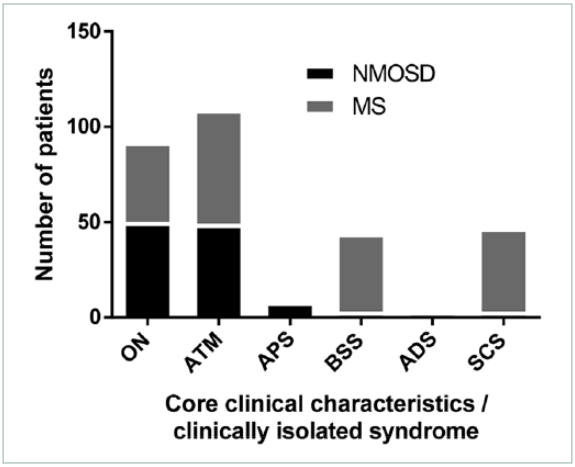

Figure 2. Symptoms at disease onset.
ON: optic neuritis; ATM: acute transverse myelitis; APS: area postrema syndrome; BSS: brainstem syndrome; ADS: acute diencephalic syndrome; SCS: symptomatic cerebral syndrome.

paraclinical features at disease onset are summarized in Table 1 and Figure 2. In addition, the brain and spinal cord MRI findings from the patients with MS and NMOSD at disease onset are shown in Table 2.

As shown in Table 3, MC applied to the entire cohort (Latin American patients) at disease onset showed 97.8% sensitivity, 82.9% specificity, 92.0% PPV, and 95.1% NPV for differentiating MS from NMOSD. Compared with MC, the modified MC showed less specificity, but greater sensitivity and NPV (100% sensitivity, 75.5% specificity, 88.8% PPV, and 100% NPV) for distinguishing MS from NMOSD.

Table 4 shows comparisons between MS and the different categories of NMOSD. For MS versus P-NMOSD ($n = 55$), the sensitivity, specificity, PPV, and NPV of previously used criteria (MC) were 97.8%, 70.9%, 92.0%, and 90.6%; and addition of STM (modified MC) showed 100%, 58.1%, 89.0%, and 100%, respectively. For differentiating MS from N-NMOSD ($n = 28$), MC showed 97.8% sensitivity, 82.1% specificity, 97.3% PPV, and 95.1% NPV; and modified MC showed 100%, 82.1%, 97.4%, and 100%, respectively. Finally, for distinguishing MS from U-NMOSD ($n = 21$), MC showed 97.8% sensitivity, 85.7% specificity, 98.3% PPV, and 81.8% NPV. In addition, values for the modified MC were 100%, 76.1%, 97.4%, and 100%, respectively.

Table 5 shows that when MC were evaluated in the non-Caucasian population (MS = 89 and NMOSD = 47), they had 100% sensitivity, 80.8% specificity, 90.8% PPV, and 100% NPV for differentiating MS from NMOSD. In addition, when the modified MC were

Table 2. Brain MRI findings of MS and NMOSD patients at disease onset.

MRI distribution	NMOSD	MS	*P* value
N	94	188	
Number of lesions			
Mean (±SD)	8.4 (21.8)	34.1 (31.9)	<0.0001
Median (IQR = Q1–Q3)	2 (1–5)	20 (10–48)	<0.0001
⩾1 periventricular lesions	22 (24.4)	178 (94.6)	<0.0001
Adjacent to lateral ventricle	9	22	
Perpendicular aspect to lateral ventricle	13	156	
⩾1 juxtacortical lesions	14 (14.8)	138 (73.8)	<0.0001
U-fiber lesions	8 (8.5)	106 (56.3)	<0.0001
⩾1 Dawson's finger lesions	9 (9.5)	154 (81.1)	<0.0001
⩾1 temporal inferior lesions	4 (4.6)	113 (60.1)	<0.0001
⩾1 posterior fossa lesions	32 (34.0)	137 (72.8)	<0.0001
Brainstem/cerebellum	10/9 (20.2)	56/81 (72.8)	
Area postrema	13 (13.8)	0	
⩾1 optic nerve lesions	23 (24.4)	31 (16.4)	0.11
Typical for MS	4 (16.7)	27 (91.4)	0.07
Atypical for MS	19 (83.3)	4 (8.6)	
⩾1 spinal cord lesions	64 (68.0)	106 (56.3)	<0.0001
STM	19 (29.6)	100 (94.3)	<0.0001
LETM	45 (69.4)	6 (5.7)	

MRI: magnetic resonance imaging; MS: multiple sclerosis; NMOSD: neuromyelitis optica spectrum disorders; SD: standard deviation; IQR: interquartile range; STM: short-segment transverse myelitis (lesions affecting less than 3 spinal segment); LETM: longitudinally extensive transverse myelitis, as described in footnotes (lesions affecting equal or more than 3 spinal segment).
Optic nerve lesions: atypical for MS was defined as ⩾1 unilateral or bilateral lesion extending over half optic nerve length or involving optic chiasm. LETM (lesion ⩾ 3 spinal segments) and STM (lesion < 3 spinal segments). Area postrema lesions were defined as dorsal medulla or contiguous with an upper cervical spinal cord lesion and brainstem/cerebellum lesions as hemispheres and cerebellar peduncle involvement.

Table 3. Evaluation of previously used criteria among RRMS and NMOSD patients with addition of short-segment transverse myelitis (STM) as a new criterion for differentiating MS from NMOSD.

	N = 282	Criterion 1 *PV lesions*	Criterion 2 *Temporal*	Criterion 3 *U-fibers*	Criterion 4 *Dawson's*	Criterion 5 *STM*	Full criteria (1, 2, 3, or 4/1, 2, 3, 4, or 5)
RRMS	188	178	113	106	154	100	184/188
NMOSD	94	22	4	8	9	19	16/23
Sensitivity, %	–	94.6	60.1	56.3	81.9	53.1	97.8/100
Specificity, %	–	76.5	95.7	91.4	90.4	79.7	82.9/75.5
PPV, %	–	94	96.5	92.9	94.4	84.03	92.0/88.8
NPV, %	–	87	54.5	51.1	71.4	46.01	95.1/100

RRMS: relapsing–remitting multiple sclerosis; NMOSD: neuromyelitis optica spectrum disorders; MS: multiple sclerosis; PPV: positive predictive value; NPV: negative predictive value; PV: periventricular lesions. STM: short-segment transverse myelitis.

used, they showed 100% sensitivity, 68.0% specificity, 97.4% PPV, and 100% NPV for discriminating MS from NMOSD. Interestingly, MC and the modified MC showed higher sensitivity and specificity for differentiating MS from NMOSD than in the Caucasian population: 95.9% sensitivity, 68.0% specificity, 86.3% PPV, and 88.8% NPV; and 100% sensitivity, 61.7% specificity, 84.6% PPV, and 100% NPV, respectively.

On the contrary, when we applied the 2017 McDonald criteria and MAGNIMS criteria for DIS to the entire cohort, we observed that 19 (20.2%) and 20 (21.2%) of the NMOSD patients fulfilled these criteria at

Table 4. Evaluation of previously used criteria among RRMS patients, compared with these criteria among patients with AQP4-ab-positive NMOSD (P-NMOSD), AQP4-ab-negative NMOSD (N-NMOSD), and AQP4-ab-unknown NMOSD (U-NMOSD), with addition of short-segment transverse myelitis (STM) as a new criterion for differentiating MS from NMOSD.

	N = 282	Criterion 1 *PV lesions*	Criterion 2 *Temporal*	Criterion 3 *U-fibers*	Criterion 4 *Dawson's*	Criterion 5 *STM*	Full criteria (1, 2, 3, or 4/1, 2, 3, 4, or 5)
RRMS	188	178	113	106	154	100	184/188
P-NMOSD	55	16	4	5	7	15	16/23
Sensitivity, %	–	94.6	60.1	56.3	81.9	53.1	97.8/100
Specificity, %	–	70.9	92.7	90.9	87.2	79.7	70.9/58.1
PPV, %	–	91.7	96.5	95.4	95.6	84.03	92.0/89.0
NPV, %	–	79.5	40.4	37.8	58.5	46.01	90.6/100
RRMS	188	178	113	106	154	100	184/188
N-NMOSD	28	4	0	2	1	2	5/5
Sensitivity, %	–	94.6	60.1	56.3	81.9	53.1	97.8/100
Specificity, %	–	85.7	100	92.8	96.4	92.8	82.1/82.1
PPV, %	–	97.8	100	98.1	99.3	98.0	97.3/97.4
NPV, %	–	70.5	27.1	30.9	77.1	22.8	95.1/100
RRMS	188	178	113	106	154	100	184/188
U-NMOSD	21	2	0	1	1	2	3/5
Sensitivity, %	–	94.6	60.1	56.3	81.9	53.1	97.8/100
Specificity, %	–	90.4	100	95.2	95.2	92.8	85.7/76.1
PPV, %	–	98.8	100	99.1	99.3	98.0	98.3/97.4
NPV, %	–	75.5	21.8	21.0	37.0	22.8	81.8/100

RRMS: relapsing–remitting multiple sclerosis; AQP4-ab: aquaporin-4 antibodies; NMOSD: neuromyelitis optica spectrum disorders; N-NMOSD: negative NMOSD; U-NMOSD: unknown NMOSD; P-NMOSD: positive NMOSD; PPV: positive predictive value; NPV: negative predictive value; MC: Matthews's criteria; PV: periventricular lesions; STM: short-segment transverse myelitis.
Positivity of previously used criteria, also known as MC was defined as full criteria 1, 2, 3, or 4 and for the modified MC was defined as full criteria 1, 2, 3, 4, or 5.

disease onset, respectively. In addition, the McDonald criteria and the MAGNIMS criteria for DIS showed higher sensitivity and specificity for differentiating MS from NMOSD: 100% sensitivity, 79.7% specificity, 90.8% PPV, and 100% NPV and 100% sensitivity, 78.9% specificity, 90.3% PPV, and 100% NPV, respectively (Supplementary Table 1).

Discussion

MC have become an important tool for differentiating patients with MS from those with NMOSD in daily clinical practice.[18–25] Nonetheless, new data and consensuses have pointed out that there is a need to evaluate their appropriateness in populations that differ from the largely Western Caucasian adult populations from which the criteria were derived.[22,23]

In this study, almost 50% of the population included comprised non-Caucasian patients. When we applied previously used criteria (MC) to the entire cohort, we observed that they had 97.8% sensitivity and 82.9% specificity for differentiating MS from NMOSD; and when we applied MC to the non-Caucasian population, we observed that they had 100% sensitivity and 80.8% specificity. When we applied the modified MC to the analysis (by adding the spinal cord), we observed a decrease in the specificity (75.5%), but an increase in the sensitivity (100%) for distinguishing MS from NMOSD. No significant differences in the accuracy of MC regarding the AQP4-ab status of the patients included were observed in trying to differentiate MS from NMOSD.

Our findings are in line with those of previous studies conducted in other regions.[18–25] In a multicenter study conducted in Europe that included patients with RRMS, AQP4-ab-positive NMOSD, myelin oligodendrocyte glycoprotein antibodies (MOG-abs)-positive NMOSD and AQP4-ab-negative NMOSD/MS, Jurynczyk et al.[22,23] showed that MC distinguished RRMS from AQP4-ab-positive NMOSD with a sensitivity of 90.9% and a specificity of 87.1%. In another study, Hyun et al.[25] evaluated the usefulness of MC for

Table 5. Evaluation of previously used criteria among RRMS and among both Caucasian and non-Caucasian NMOSD patients, with addition of short-segment transverse myelitis (STM) as a new criterion for differentiating MS from NMOSD.

	N = 282	Criterion 1 *PV lesions*	Criterion 2 *Temporal*	Criterion 3 *U-fibers*	Criterion 4 *Dawson's*	Criterion 5 *STM*	Full criteria (1, 2, 3, or 4/1, 2, 3, 4, or 5)
Caucasian RRMS	99	94	56	59	78	55	95/99
Caucasian NMOSD	47	14	3	5	6	10	15/18
Sensitivity, %	–	94.9	56.5	59.5	78.7	55.5	95.9/100
Specificity, %	–	70.2	93.6	89.3	87.2	78.7	68.0/61.7
PPV, %	–	87.0	94.9	92.1	92.8	84.6	86.3/84.6
NPV, %	–	86.8	50.5	51.2	66.1	46.8	88.8/100
Non-Caucasian RRMS	89	84	57	47	76	45	89/89
Non-Caucasian NMOSD	47	8	1	3	3	9	9/15
Sensitivity, %	–	94.3	64.0	52.8	85.3	50.5	100/100
Specificity, %	–	82.9	97.8	93.6	93.6	80.8	80.8/68.0
PPV, %	–	91.3	98.2	94.0	96.2	83.3	90.8/97.4
NPV, %	–	88.6	58.9	48.8	65.6	46.3	100/100

RRMS: relapsing–remitting multiple sclerosis; NMOSD: neuromyelitis optica spectrum disorders; MS: multiple sclerosis; PPV: positive predictive value; NPV: negative predictive value; PV: periventricular lesions; STM: short-segment transverse myelitis.

differentiating MS from AQP4-ab-positive NMOSD in an Asian cohort. After 214 patients had been evaluated, MC showed sensitivity, specificity, PPV, and NPV of 79.8%, 87.5%, 90.4%, and 74.7%, respectively, for differentiating MS from NMOSD at disease onset. Thus, it was shown that MC were highly accurate in a population that differed from the Caucasian population that had initially been tested.

Recently, Bensi et al.[20] evaluated the ability of MC to differentiate NMOSD from MS in an Argentinean population, along with the value that spinal cord MRI might add to the criteria. Through evaluation of 150 patients (23 with AQP4-ab-positive NMOSD, 20 with AQP4-ab-negative NMOSD, and 48 adults with RRMS), these authors showed that MC had 79% sensitivity, 96% specificity, 97% PPV, and 69% NPV for differentiating MS from AQP4-ab-positive NMOSD. On the contrary, when spinal MRI was added, the accuracy regarding separating adult-onset RRMS from AQP4-ab-positive NMOSD was observed to be 100% and 87% (sensitivity and specificity, respectively). No information about ethnicity or about the timing of MRI scans was reported in that study.

On the contrary, new criteria for NMOSD (2015) based on the serostatus, clinical presentation, and typical MRI lesions were recently published. Studies from Asia, Europe, and Latin America reported that the application of the 2015 rather than 2006 revised NMO criteria increased the diagnostic rate (sensitivity) by 85%, 76%, and 62.5%, respectively, showing the utility of these new criteria.[16,32,33] Similarly, exclusion of alternative diagnoses is required for diagnosing NMOSD, including MS.[4] We are aware that exclusion of MS-typical lesions on MRI is required for the diagnosis of NMOSD, but MS-typical lesions may fulfill the McDonald criteria in 10%–42% of the NMOSD patients.[34–36] The importance of the MC currently in use is that they provide neurologists with tools that are easy to implement and have high sensitivity and specificity for distinguishing MS from NMOSD, starting from the early stages of these diseases. In addition, the lack of MC should lead neurologists to perform AQP4-abs in order to enable early diagnosis of NMOSD, thus making it possible to implement aggressive initial treatment and preventive long-term treatment. Despite this recognized characteristic, MC still had not been validated in any Latin American cohorts, which are populations that differ from the one that was initially evaluated. Therefore, to evaluate the utility of previously used criteria (MC) at disease onset could provide additional data for distinguishing MS from NMOSD.

In this study, we showed that among non-Caucasian patients with seropositive, seronegative, and unknown serostatus NMOSD, the accuracy of previously used criteria (MC) is high, thereby enabling reliable differentiation between MS and NMOSD. Addition of data regarding spinal cord involvement (modified MC) did not contribute significantly in this study toward increasing accuracy due to a less specificity, as compared with MC. This could be explained because STM is observed in up to 30% of the NMOSD patients.[37–39] These findings provide tools to disseminate the use of previously used criteria (MC) within our environment with confidence, but with caution, with the aim of seeking to expand the power of the observations that have been made so far.

This study had several limitations. First, this was a retrospective study with all the bias that a retrospective study could have. Second, the study included referrals to MS centers in Latin America, which may have generated an analysis bias. Third, recently advances require knowledge of MOG-abs serostatus between NMOSD patients who are seronegative for AQP4-abs. However, MOG-abs are not available in all centers, therefore, they were not studied, although several studies recommend that patients who are seronegative for AQP4-abs should be tested.[40] Finally, we did not perform any inter-rater agreement analysis to evaluate the operator variability in this MRI analysis. However, the Cohen's kappa values reported from other published cohorts were high.[18–25]

In summary, we observed that previously used criteria (MC) distinguished MS from seropositive, seronegative, and unknown serostatus NMOSD at presentation in a Latin American cohort that included a non-Caucasian population. We did not find any significant increase in the accuracy of the criteria through adding spinal cord MRI data. Currently, in Latin America, assessment using AQP4-abs is available only in a few centers and the results may take many weeks to be produced. This makes this differential diagnosis difficult in some countries in this region. MC can be used in everyday clinical practice to differentiate MS from NMOSD because only conventional T2-weighted and FLAIR sequences are required. Further testing on prospective and retrospective data sets that include other centers and areas in Latin America will confirm our initial validating process for MC in this region.

Acknowledgement

We would like to thank to David George Elliff for reviewing the English-language content of the article.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Supplemental Material

Supplemental material for this article is available online.

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