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Prediction of conversion to multiple sclerosis using the 2017 McDonald and 2016 MAGNIMS criteria in patients with clinically isolated syndrome: a retrospective single-centre study

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Until 2018, the 2010 McDonald criteria were the most widely used criteria in the diagnosis of multiple sclerosis (MS), defining dissemination in space (DIS) and time (DIT).[1] In the evaluation of DIS and DIT, clinical and MRI findings are taken into account.[1] Considering new scientific insights and advances in diagnostic techniques, two adaptations of the 2010 McDonald criteria were published in short sequence: (1) the 2017 McDonald criteria and (2) the 2016 MAGNIMS criteria.[2,3] In predicting the conversion from clinically isolated syndrome (CIS) to clinically definite MS (CDMS), the 2016 MAGNIMS and 2010 McDonald criteria demonstrated similar sensitivity and specificity.[4] In contrast, the 2017 McDonald criteria demonstrated a higher sensitivity but a lower specificity than the 2010 McDonald criteria.[5,6] Considering the recency of the publication of the 2017 McDonald criteria, the prediction of conversion to MS and CDMS using this set of criteria has not yet been compared to the 2016 MAGNIMS criteria. Therefore, it is our aim to assess and compare the predictive properties of conversion to MS and CDMS by retrospectively applying the 2017 McDonald and the 2016 MAGNIMS criteria to a single-centre cohort of patients diagnosed with CIS according to the 2010 McDonald criteria. Furthermore, we evaluate the influence of modifications and differences between the 2017 McDonald and the 2016 MAGNIMS criteria on the prediction of conversion to MS and CDMS.

In total, 153 patients who had been diagnosed with CIS according to the 2010 McDonald criteria were retrospectively identified by screening medical records from the neurologic department of the Bern University Hospital (Switzerland) for the diagnosis 'clinically isolated syndrome'. This retrospective study was approved by the local ethics committee (ethic registration no. KEK-BE 2017-01369). The committee waived informed consent due to the large sample size and the retrospective nature of the study. Patients who did not convert to MS or CDMS and also had a follow-up duration of less than 3 months were excluded, which resulted in a study cohort of 127 patients. We evaluated whether at the time point of CIS diagnosis patients already fulfilled the following sets of diagnostic criteria: (1) 2017 McDonald criteria; (2) 2017 McDonald criteria including the optic nerve as an additional location for the demonstration of DIS; (3) 2017 McDonald criteria requiring ⩾3 periventricular lesions for the definition of periventricular involvement; (4) 2016 MAGNIMS criteria; and (5) 2016 MAGNIMS criteria including cerebrospinal fluid-specific oligoclonal bands (OCB) as an additional substitute for demonstration of DIT as OCBs are an independent risk factor for an additional clinical episode in patients with CIS.[7,8] The MRI protocol is described in the supplement. CIS patients were followed up until conversion to MS and CDMS, or in non-converters for a maximum of 5 years. Conversion to MS was defined either (1) as a relapse lasting more than 24 h and occurring at least 1 month after the first clinical event with evidence of two different lesions; or (2) as a new T2-hyperintense or new Gd-enhancing MRI lesion fulfilling DIS and DIT criteria and being

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Table 1. Sensitivity and specificity analysis of conversion to MS and CDMS.

Conversion to MS and CDMS*	Value	95% CI	*n*
2017 McDonald → MS			
Sensitivity	0.89	0.78–0.95	127
Specificity	0.31	0.20–0.44	127
2017 McDonald → CDMS			
Sensitivity	0.85	0.69–0.94	127
Specificity	0.23	0.15–0.33	127
2017 McDonald + optic nerve involvement → MS			
Sensitivity	0.89	0.78–0.95	127
Specificity	0.26	0.16–0.39	127
2017 McDonald + optic nerve involvement → CDMS			
Sensitivity	0.85	0.69–0.94	127
Specificity	0.20	0.12–0.30	127
2017 McDonald + ⩾3 periventricular lesions → MS			
Sensitivity	0.78	0.66–0.87	127
Specificity	0.35	0.24–0.49	127
2017 McDonald + ⩾3 periventricular lesions → CDMS			
Sensitivity	0.70	0.53–0.83	127
Specificity	0.28	0.19–0.38	127
2016 MAGNIMS → MS			
Sensitivity	0.6	0.47–0.72	127
Specificity	0.5	0.37–0.63	127
2016 MAGNIMS → CDMS			
Sensitivity	0.55	0.39–0.70	127
Specificity	0.45	0.34–0.56	127
2016 MAGNIMS + OCBs → MS			
Sensitivity	0.83	0.71–0.91	127
Specificity	0.27	0.17–0.40	127
2016 MAGNIMS + OCBs → CDMS			
Sensitivity	0.78	0.61–0.89	127
Specificity	0.22	0.14–0.32	127

*: Conversion to MS was defined using clinical and MRI parameters. Conversion to CDMS was defined using clinical parameters only (see methods section).
95% CI, 95% confidence interval; CDMS, clinically definite multiple sclerosis; MRI, magnetic resonance imaging; MS, multiple sclerosis; OCB, oligoclonal band.

Table 2. Cox regression analysis of conversion to MS and CDMS.

	aHR	95% CI	*p* value	*n*
Cox regression analysis of conversion to MS*				
2017 McDonald	3.27	1.42–7.55	0.005	127
2017 McDonald + optic nerve involvement	2.89	1.24–6.71	0.014	127
2017 McDonald + ⩾3 periventricular lesions	2.19	1.14–4.18	0.005	127
2016 MAGNIMS	1.45	0.87–2.41	0.15	127
2016 MAGNIMS + OCBs	1.78	0.89–3.59	0.11	127
Cox regression analysis of conversion to CDMS*				
2017 McDonald	1.82	0.73–4.56	0.20	127
2017 McDonald + optic nerve involvement	1.65	0.66–4.16	0.29	127
2017 McDonald + ⩾3 periventricular lesions	1.12	0.54–2.33	0.77	127
2016 MAGNIMS	1.00	0.54–1.89	0.98	127
2016 MAGNIMS + OCBs	1.09	0.49–2.41	0.84	127

*: Cox regression analysis was adjusted for age, sex, immunotherapy, and EDSS score. 95% CI: 95% confidence interval; aHR, adjusted hazard ratio; CDMS, clinically definite multiple sclerosis; EDSS, Expanded Disability Status Scale; MS, multiple sclerosis; OCB, oligoclonal band.

attributable to demyelination.[4] In contrast, conversion to CDMS exclusively followed the clinical relapse definition.

Sensitivity and specificity are presented as mean and 95% confidence interval (95% CI) and were calculated using VassarStats (Poughkeepsie, NY, USA). To generate adjusted hazard ratios (aHRs), Cox regression analyses were performed separately for each of the five diagnostic criteria using SPSS 25 (IBM, Armonk, NY, USA). The setup of the Cox regression analysis consisted of the duration until MS or CDMS conversion as the outcome variable and the following independent variables: the respective set of diagnostic criteria, age, sex, Expanded Disability Status Scale (EDSS) score, and immunotherapy.

The baseline characteristics are presented in the supplementary table. In total, 67/127 (52.8%) patients converted to MS after a median of 1.1 years (25th–75th: 0.6–2.1). Conversion to CDMS was less frequent (40/127; 31.5%) and occurred after a median of 0.9 years (25th–75th: 0.5–2.0). From the five different sets of diagnostic criteria, the 2017 McDonald criteria had the highest sensitivity for predicting the conversion to MS and CDMS at 0.89 (95% CI: 0.78–0.95) and 0.85 (95% CI: 0.69–0.94), respectively (Table 1). Individual modifications did not improve the predictive performance of the 2017 McDonald criteria (Tables 1 and 2). The 2016 MAGNIMS criteria were more specific than the 2017 McDonald criteria. However, specificity of all five sets of criteria was ⩽0.50 regarding the conversion to MS or CDMS (Table 1). The Cox regression analysis, which was adjusted for the influence of age, sex, EDSS score, and immunotherapy, confirmed the predictive value of the 2017 McDonald criteria for the conversion from CIS to MS (aHR: 3.27 (95% CI: 1.42– 7.55), $p = 0.005$; Table 2). Using Cox regression analysis to assess the prediction of converting to CDMS, resulted in no significant results for all five sets of criteria (Table 2).

In a large single-centre cohort of patients diagnosed with CIS according to the 2010 McDonald criteria, we demonstrated that the 2017 McDonald criteria had the highest sensitivity and the highest aHR for predicting the conversion to

MS in comparison to the 2016 MAGNIMS and three combined diagnostic criteria (2017 McDonald criteria including optic nerve; 2017 McDonald criteria requiring ⩾3 periventricular lesions; 2016 MAGNIMS criteria including OCBs). Interestingly, when considering the conversion to CDMS, none of the five criteria sets demonstrated significant findings in the Cox regression analyses. This finding may be explained primarily by the lower number of patients converting to CDMS ($n = 40$) than MS ($n = 67$), and the rather short median follow-up duration of 2 years in non-CDMS converters. In contrast to the Cox regression analysis, the calculation of sensitivity and specificity was not adjusted for age, sex, EDSS score, and immunotherapy. From these parameters, especially the high number of patients treated with immunotherapy after CIS diagnosis (68/127) might have influenced the analysis. Other weaknesses of our study are the retrospective design, the incomplete spinal cord MRI data and the two different scanners used for MRI acquisition (see supplemental material). In comparison with other recently published studies investigating the diagnostic value of the 2017 McDonald criteria,[9–11] which demonstrated more frequent and even earlier diagnosis of MS if the 2017 McDonald criteria were used, our study highlighted differences in diagnostic accuracy between the 2017 McDonald criteria, the 2016 MAGNIMS criteria, and the respective modifications of these criteria. Our research contributes to a better understanding of how different modifications of MS diagnostic criteria affect their diagnostic properties.

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Conflict of Interest Statement

The authors declare no conflict of interest in preparing this article.

Supplemental material

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