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Predictors of conversion from possible to defined multiple sclerosis: a multi-center, retrospective study

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INTRODUCTION AND AIM

In 85% of cases, multiple sclerosis (MS) presents at onset with an isolated episode of focal neurological deficit, the clinically isolated syndrome or CIS [1]. Approximately 2/3 of CIS patients converts, during their life, to MS [2]. According to the 2010 revision of the McDonald criteria, a diagnosis of MS can be made if CIS patients satisfy clinical and/or MRI criteria of both disseminations in time (DIT) and space (DIS) [3]. The presence of DIS without DIT or vice versa configures a diagnosis of possible MS [3].

The aim of the present study was to retrospectively analyze the follow-up data of patients with CIS and DIS in order to obtain information on their risk of conversion.

PATIENTS AND METHODS

We performed a retrospective, multicenter study across 2 Italian MS centers (*, **).

- Inclusion criteria were:
  - (i) a diagnosis of CIS with DIS according to the 2010 McDonald criteria [3];
  - (ii) demographic, clinical, laboratoristic and MRI data available;
  - (iii) a follow-up period lasting until conversion to MS or at least 1 year.
- All the patients underwent brain and spinal cord MRI as part of the usual workup (after 3, 6 and 12 months after the onset and then yearly if asymptomatic).
- MRI lesion load was categorized according to the Barkhof-Tintoré criteria (Bc) [4, 5] .
- Conversion to MS was defined both clinically and radiologically.
- Predictors of time to conversion to MS were assessed using univariate and multivariate Cox proportional hazards regression models.
- A p-value lower than 0.05 was considered to indicate statistical significance for all the analyses.

RESULTS – Overall characteristics of the patients

- 137 patients were enrolled.
- Mean follow-up time was 1348 days (median 1148, min 186, max 7525 days).
- 58 patients (42.3%) had Gd+ symptomatic lesions; according to the proposal of revision of the diagnostic criteria (MAGNIMS) [6] they should be considered as MS patients.

Table 1 shows demographics, clinical and MRI features at baseline.

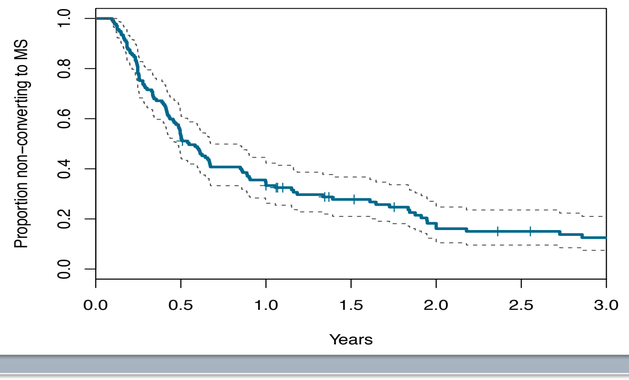
Table 1

Demographics	
N	137
Sex (female)	102 (74%)
Age at onset	31.4 ± 10.5
CIS type	
• Multifocal	7 (5.1%)
• Myelitis	49 (35.8%)
• Brainstem/cerebellar syndrome	34 (24.8%)
• Optic neuritis	33 (24.1%)
• Hemispheric syndrome	14 (10.2%)
CSF features	
• IgG index (mean ± SD)	0.56 ±0.33
• OCB positive	105 (79%)
Mean EDSS at onset	1.62 ± 0.93
MRI Barkhof Tintoré criteria for DIS	
• ≥ 1 Gd+ lesions or ≥ 9 T2 lesions	81 (59.1%)
• ≥ 1 infratentorial lesion	55 (40.2%)
• ≥ 1 juxtacortical lesion	92 (67.2%)
• ≥ 3 periventricular lesions	121 (88.3%)
Number of satisfied MRI Barkhof Tintoré criteria	
• 1	18 (13.1%)
• 2	49 (35.8%)
• 3	43 (31.4%)
• 4	27 (19.7%)
MRI 2010 revised McDonald criteria for DIS	
• Periventricular lesions	93 (67%)
• Juxtacortical lesions	123 (89.8%)
• Infratentorial lesions	57 (41.6%)
• Spinal cord lesions	73 (53.3%)
Patients with Gd+ symptomatic lesion	58 (42.3%)

RESULTS – Conversion to MS

During the follow-up period, 116 patients (84.7%) converted to MS.

- Mean time to conversion was 335 days (median 170, min 26, max 5100).
- 91 patients out of the 116 converters (78.4%), converted within 1 year (**Figure 1**).



Survival curve reporting the proportion of patients that did not convert to MS during the follow-up period.

Figure 1

RESULTS – Predictors of conversion to MS

Table 2 shows the results of the univariate Cox proportional hazard models investigating the role of demographics, clinical and MRI features at baseline for predicting the time to conversion to MS. HR (95% CI).

Table 2

Variable	HR (95% CI)	p-value
Sex (male)	0.98 (0.64-1.50)	0.92
Age at diagnosis	**0.98 (0.96-1.00)**	**0.021**
EDSS at onset	**1.08 (1.00-1.17)**	**0.038**
CIS type		
• Multifocal	1.46 (0.68-3.16)	0.330
• Hemispheric syndrome	**0.50 (0.27-0.93)**	**0.029**
• Brainstem/cerebellar syndrome	**1.86 (1.24-2.80)**	**0.003**
• Optic neuritis	0.88 (0.58-1.34)	0.560
• Myelitis	1.05 (0.72-1.53)	0.790
CSF OCB	1.29 (0.81-2.06)	0.28
MRI Barkhof Tintoré criteria for DIS		
• ≥ 1 Gd+ lesions or ≥ 9 T2 lesions	1.44 (0.98-2.10)	0.061
• ≥ 1 infratentorial lesion	**1.71 (1.18-2.50)**	**0.005**
• ≥ 1 juxtacortical lesion	1.26 (0.85-1.86)	0.250
• ≥ 3 periventricular lesions	0.76 (0.43-1.33)	0.330
Number of Barkhof Tintoré criteria satisfied		
• 1	0.57 (0.32-1.00)	0.052
• 2	0.91 (0.62-1.35)	0.650
• 3	1.07 (0.72-1.58)	0.750
• 4	**1.74 (1.11-2.74)**	**0.017**
MRI 2010 revised McDonald criteria for DIS		
• ≥ 1 periventricular lesion	1.26 (0.85-1.86)	0.250
• ≥ 1 juxtacortical lesion	0.81 (0.45-1.44)	0.470
• ≥ 1 infratentorial lesion	**1.63 (1.12-2.37)**	**0.011**
• ≥ 1 spinal cord lesion	0.80 (0.55-1.15)	0.230
Gd+ symptomatic lesion	1.40 (0.97-2.03)	0.074

Table 3 shows the results of the multivariate Cox proportional hazard models investigating the role of demographics, clinical and MRI features at baseline for predicting the time to conversion to MS. HR (95% CI).

Table 3

Variable	HR (95% CI)	p-value
Age at diagnosis	**0.98 (0.96-1.00)**	**0.003**
Brainstem/cerebellar syndrome	**2.00 (1.32-3.04)**	**0.001**
> 3 Barkhof Tintoré criteria	**1.67 (1.06-2.64)**	**0.028**

Figure 2A shows the survival curve reporting the proportion of patients that did not convert to MS during the follow-up period stratified by having or not a brainstem/cerebellar CIS. **Figure 2B** shows the survival curve reporting the proportion of patients that did not convert to MS during the follow-up period stratified by the number of satisfied Barkhof Tintorè criteria.

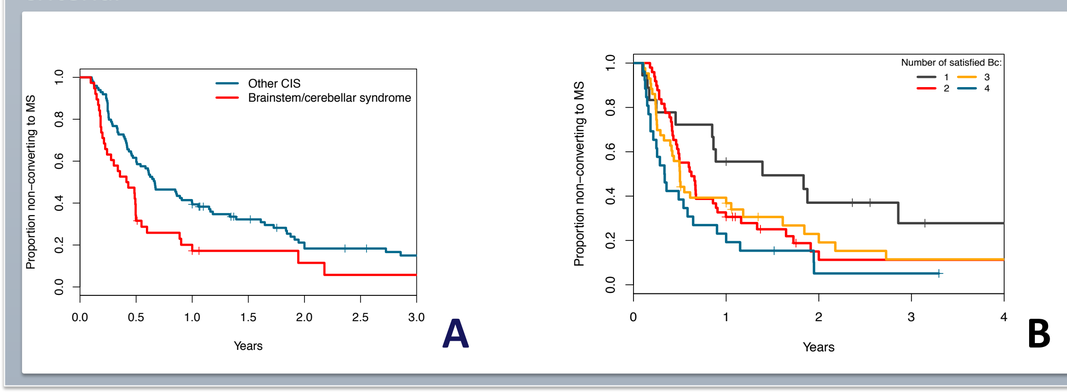


Figure 2

CONCLUSIONS

- Patients with CIS and DIS are at very high risk for an early conversion to MS.
- The onset with a brainstem/cerebellar syndrome doubles the risk for an early conversion.
- The presence at baseline MRI of all the 4 Bc increases the risk for an early conversion.

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