A 6-years follow-up of relapsing remitting multiple sclerosis identifies Word List Generation test and EDSS as best predictors of progressive disease phase

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Introduction

Preventing the entry in the progressive phase constitutes the most important therapeutic goal in Multiple Sclerosis (MS). Thus, the early identification of relapsing remitting MS (RRMS) patients at high risk to rapidly enter in the progressive disease phase could help to personalise the therapy.

Aim of the study

To analyse the value of Brief Repeatable Battery of Neuropsychological Tests (BRB-NT) in predicting RRMS to entry in the progressive disease phase.

Methods

Since 2008, RRMS patients diagnosed and treated at the MS Centre in Padua were routinely evaluated by means of EDSS and the BRB-NT, and asked to participate in a prospective follow-up study. Ninety-nine patients reached the 6th year of follow-up in 2016 and were included in this analysis. Progression was defined as a steadily increase and objectively documented neurologic dysfunction/disability, without unequivocal recovery, confirmed at 6 month in absence of new clinical or radiological evidence of disease activity. The entry into the secondary progressive disease (SPMS) phase was applied as dependent variable in a multivariate Kaplan Mayer analysis, which considered clinical (EDSS at T0, disease duration at T0 and on-going disease-modifying therapies), demographic (age at T0 and gender) and neuropsychological (BRB-NT item z-scores) as independent variables.

Results

During the 6-year follow-up, 15 patients (15.2%) entered the progressive disease phase after a mean interval of 3.9±1.9 years. At baseline, they did not differ from non-progressive patients in gender (p=0.8), disease duration (10.4±6.4 years vs 10.0±8.0 years, p=0.8), EDSS score (2.5 vs 1.5, p=0.2), but differed in age (43.4±11.1 vs 37.4±10.6, p<0.05). Kaplan Meier analysis revealed that age (p<0.05), EDSS (p<0.0001), pathological SDMT z-scores (p<0.005) and pathological WLG z-scores (p<0.05) were predictive of progression at T0 (Fig. 1).

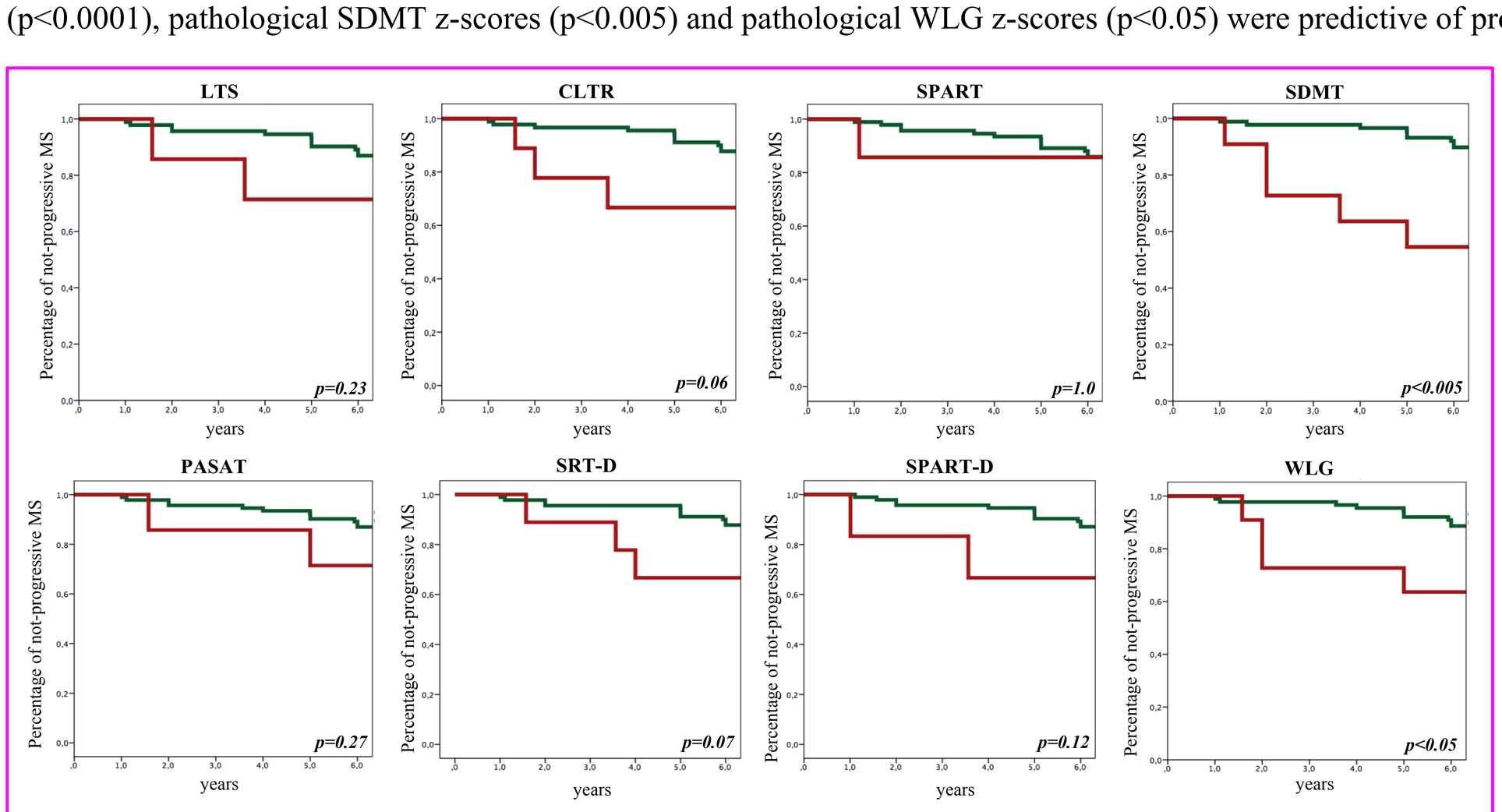

Figure 1. Disease progression and baseline BRB-NT values.

Abbreviations:
LTS: Long Term Storage; **CLTR**: Consistent Long-Term Retrieval; **SPART**: 10/36 Spatial Recall Test; **SDMT**: Symbol Digit Modalities Test; **PASAT**: Paced Auditory Serial Addition Test; **SRT-D**: Selective Reminding Test-Delayed; **SPART-D**: 10/36 Spatial Recall Test Delayed; **WLG**: Word List Generation

However, regression analysis confirmed the predictive value of EDSS (p<0.0001) and pathological WLG z-scores (p<0.05) at T0 (r:0.39, p<0.001) (Table 1).

Independent Variable	Beta	IC95%	p
EDSS at T0	2.6	1.5-4.4	<0.001
Pathological WLG at T0	4.9	1.1-22.6	<0.05

Table 1. Logistic regression analysis values.

Conclusions

At baseline and independently of EDSS, WLG assessment may help to identify RRMS patients with higher risk of disease progression in the following six years. To these patients, whose therapeutic window should be considered reduced, a higher effective disease-modifying therapy should be promptly administered.

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