Cognitive impairment does not predict short term clinical outcome in early onset multiple sclerosis.

R Lanzillo[1], A Carotenuto[1], T Costabile[1], E Signoriello[2], M Moccia[1], AM Barbarulo[2], M Simone[3], RG Viterbo[3], D Paolicelli[3] , G Lus[2], V Brescia Morra[1].

[1] Department of Neurosciences, Reproductive and Odontostomatological Sciences, Federico II University, Naples, Italy
[2] Multiple Sclerosis Center,II Division of Neurology, Department of Clinical and Experimental Medicine, Second University of Naples, Italy
[3] Department of Basic Medical Sciences, Neuroscience and Sense Organs, University of Bari "Aldo Moro", Bari, Italy.

Background

Cognitive impairment (CI) can be highlighted in more than 50% of pediatric and juvenile multiple sclerosis (MS) onset patients.
In adult onset MS, it predicts a worse clinical outcome.
We aimed at evaluating the role of CI as predictor of disease severity in early-onset MS.

Patients & Methods

This is a retrospective study including pediatric (<=18 years) and juvenile (<=25 years) onset RR-MS followed up prospectievely. Socio-demographic and clinical data (age, sex and education level, age at onset, disease duration, expanded disability status scale [EDSS], disease modifying therapy, DMT, lesion load at brain MRI) were collected at baseline. Patients were assessed through the Brief Repeatable Battery (BRB) and the presence of CI has been defined when patients failed in 1 or more tests. Clinical outcomes were the occurrence of a relapse, a therapeutic switch, the achievement of EDSS 4.0, the sustained increase in the EDSS of at least 1 point and the conversion to SP over 5 years of follow-up. Lesion load increase at brain MRI (presence of new T2 lesions) was also considered as an outcomeThe time to the occurrence of each of these clinical outcomes was collected. Binary logistic models and Cox models were run to explore the presumptive role of CI as predictor for each of the clinical outcomes.

Results

Mean follow up period was 32.2 ± 22.5 months. Clinical and demographic characteristics of enrolled patients are shown in table 1 for baseline data and table 2 for follow up assessment.
At NPS evaluation 32/51 (62.75%) patients showed a CI at baseline.
EDSS was the only variable related to the presence of CI (mean EDSS in cognitively preserved and impared patients was 2.3 ± 0.14 vs 3.1 ± 0.47 respectively, p=0.03) at baseline.
The presence of CI at baseline as well as single NPS score were not associated to clinical (Figure 1) or radiological outcomes at 5 years follow-up.

Characteristic		
Subjects	Total	51
	Federico II', N (%)	36 (70.6)
	Policlinico Bari", N (%)	9 (17.6)
	"Sun", N (%)	6 (11.8)
Sex	Male, N (%)	25 (49)
	Female, N (%)	26 (51)
Age, mean ± SD (Range) (years)		19.8 ± 3.8 (13 - 26)
Age at onset, mean ± SD (Range) (years)		17.2 ± 3.9 (9 - 25)
Disease duration, median (Range) (years)		2 (0 - 12)
EDSS, median (Range)		2.5 (1 - 6)
Disease modifying therapy	No DMT , N (%)	2 (3.9)
	First line therapy, N (%)	35 (72.5)
	Second line therapy, N (%)	14 (27.5)
Lesional Load	Low, N (%)	7 (20)
	Medium, N (%)	16 (45.7)
	High, N (%)	12 (42.3)
Age at onset, subgroup	≤18y, N (%)	33 (65)
	18y<x<25y, N (%)	18 (35)

Table 1. Clinical and demographic characteristics at baseline

Follow-up 32.2 ± 22.5 months		N	%
Switch of DMT		25	50%
	inefficacy	16	64%
	tolerability	8	32%
	pregnancy	1	4%
EDSS 1 point increase		6	12%
SP		2	4%
EDSS 4		6	13%
Relapses		27	53%
Lesion load increase (39 pts)		9	26%

Table 2. Clinical and radiological follow-up

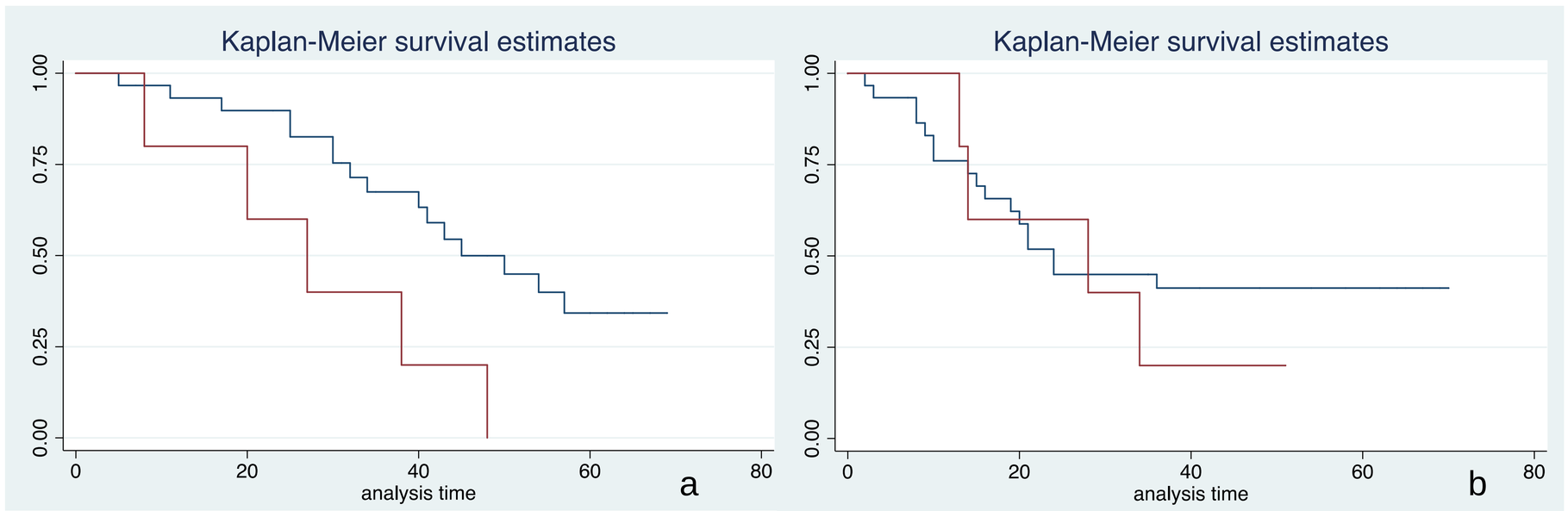

Figure 1.
The figure shows the Kaplan-Meier curves for DMT switch (a) (HR 2.15, p=0.19) and the occurrence of a relapses (b) (HR 1.43, p=0.48) according to the presence (curves in red) or absence (curves in blue) of CI at baseline.

Conclusions

Cognitive impairment is frequent in pediatric and juvenile onset MS patiens and is related to disability. However, in the short-medium term the presence of CI does not predict a worse clinical outcome in this subtype of MS patients. These results seem to confirm the previous findings for adult MS patients, in which CI began to influence clinical outcome only after 5 years from baseline evaluation. However, we can not exclude that juvenile MS is charactezixed by a more marked inflammatory process than neuro-degeneration, which is strictly related to cognitive functions. Also a more aggressive treatment in this patients, with a high percentage could have influenced clinical outcome. Cognitive follow up and extension of observation time is on-going.

References

Lanzillo R, Chiodi A, Carotenuto A, Magri V, Napolitano A, Liuzzi R, Costabile T, Rainone N, Freda MF, Valerio P, Brescia Morra V. Quality of life and cognitive functions in early onset multiple sclerosis. Eur J Paediatr Neurol. 2016 Jan;20(1):158-63.
•Moccia M, Lanzillo R, Palladino R, Chang KC, Costabile T, Russo C, De Rosa A, Carotenuto A, Saccà F, Maniscalco GT, Brescia Morra V. Cognitive impairment at diagnosis predicts 10-year multiple sclerosis progression. Mult Scler. 2016 Apr;22(5):659-67. doi: 10.1177/1352458515599075. Epub 2015 Sep 11. PubMed PMID: 26362896.