Intrathecal IgM synthesis: is really a prognostic factor?

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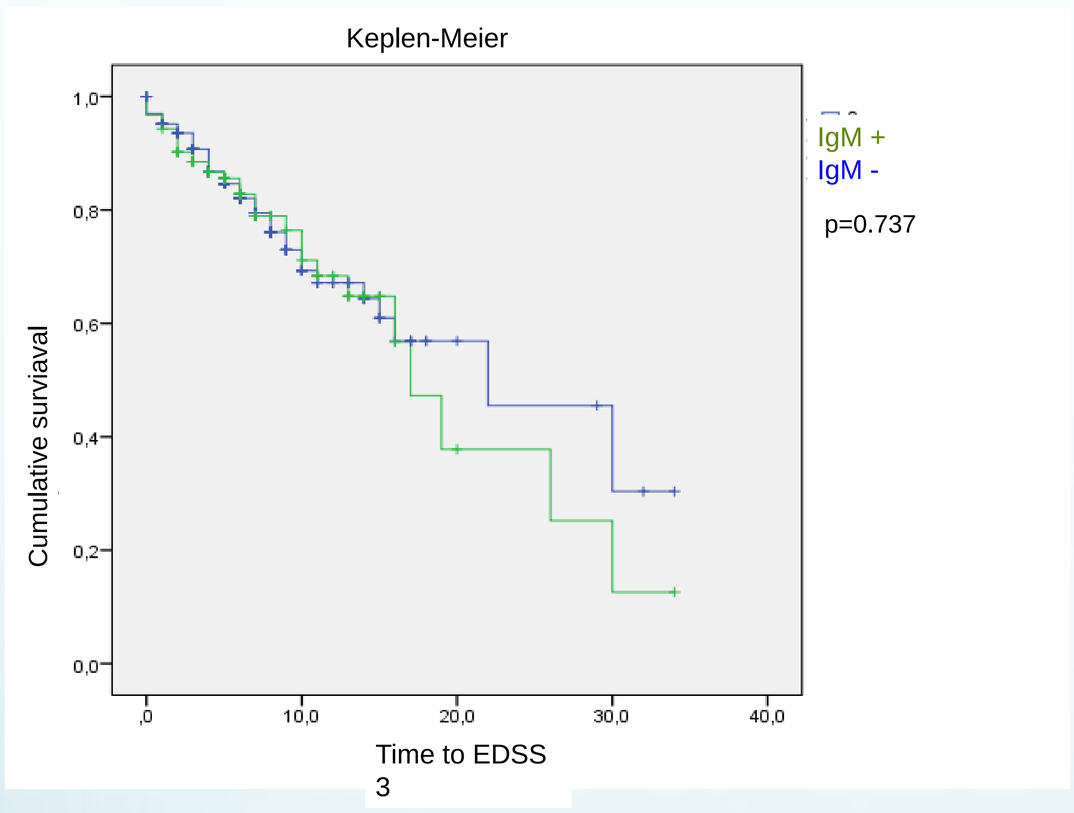
Objectives. Intrathecal IgM synthesis (ITMS) was found associated with poor MS prognosis in studies performed in small samples of patients. (1,2) It was associated to conversion in clinically definite MS after the first relapse, higher EDSS index, secondary progressive course, and higher number of relapses. The evaluation of ITMS in a pediatric group, using a different laboratory method, did not confirm this datum. (3) The aim of our study was to evaluate the prognostic value of ITMS in a higher sample of Sardinian patients.

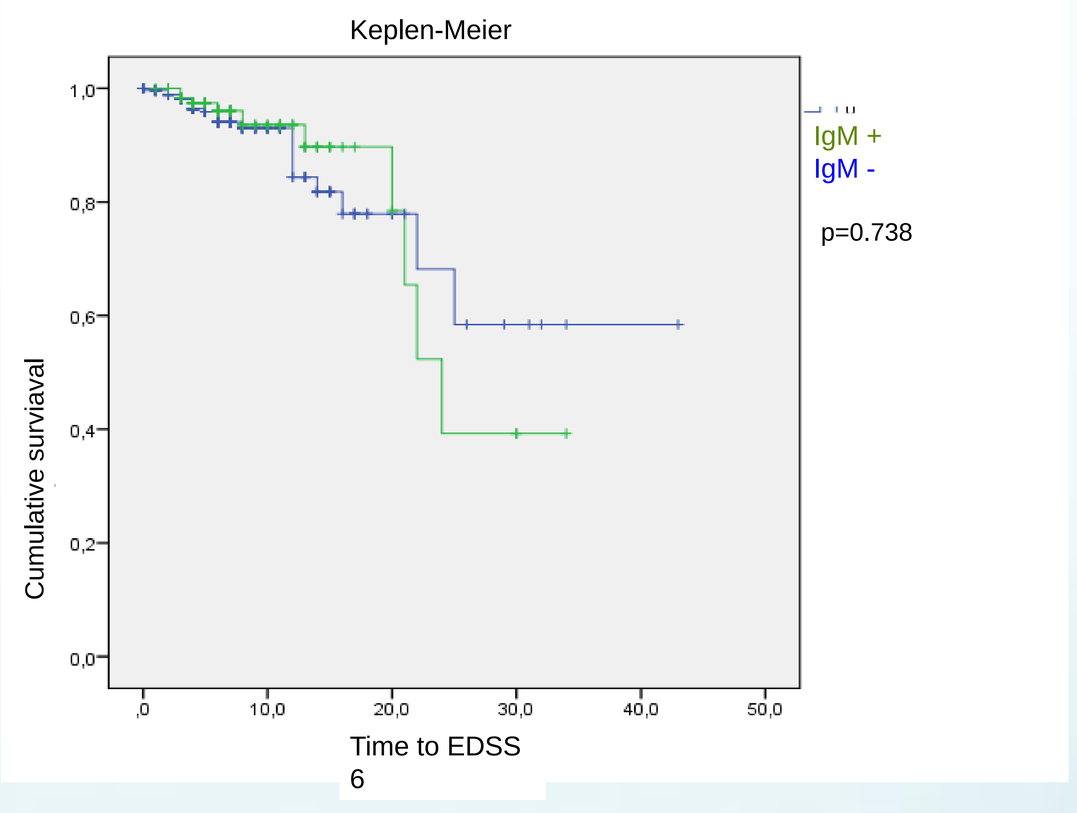
Matherials. In the study were enrolled MS patients (according to McDonald 2010). All of them were recruited from the MS Centre of the University of Cagliari from 2007 until to 2013 and underwent lumbar puncture (LP) for diagnostic purpose.

Methods. For each patient were recorded demographic data, clinical course at LP, time to reach EDSS 3, 6, 8, 10, EDSS at last follow-up (2016), MS treatments until the last follow-up. The analysis of ITMS was performed by isoelettrofocusing and immunoblotting, using specific anti-human IgM antibodies, as descripted by Villar et al in 2011. Fisher test was used to analyse the association of ITMS with clinical course, while with Kaplan-Meier was studied the time to reach EDSS 3 and 6.

Results. The enrolled subjects were 404, 390 relapsing-remitting (RR) and 14 primary progressive (PP); 314 patients started a MS treatment. In 126 patients ITMS were found, in particular IgM were in 120 RR and 6 PP (p=0.38) subjects. The relationship between EDSS and IgM is showed in the table. The time to reach EDSS 3 and 6 is not modified by the presence of IgM.
It is to note that in 9 patients with ITMS the analysis of intrathecal IgG was negative.

EDSS	Totale	IgM +	IgM -	p
3	100	34	66	0.7
6	33	10	23	0.7
8	3	0	3	
10	0			





Discussion and conclusions. Our study did not confirm the prognostic value of IgM in terms of clinical course and time to reach the main EDSS milestones. It is to note that a high percentage of patients started very quickly after the diagnosis immunomodulating or immunosuppressive drugs, which could modify the course of the disease. Moreover, to explain the contrasting result, we could hypothesize a role of genetic factors, having MS Sardinian patients peculiar predisposing and protective HLA. We will study in the next future this aspect. To our knowledge, our study has the higher sample size in literature, but our purpose is to increase the number of enrolled patients.

References:
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