Neurofilament-Light Chain Levels Are Predictive of On-going Disease Activity in Radiologically Isolated Syndrome

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Objective: To evaluate the predictive value of neurofilament-light chain (sNfL) on the risk of evidence of disease activity (EDA) and of clinical conversion (CC) in patients with radiologically isolated syndrome (RIS).

Background: EDA (new MRI lesions and/or a clinical event) is a characteristic feature of multiple sclerosis (MS), associated with an increased risk of relapse. In addition to younger age, male sex and spinal cord lesion(s), elevated cerebrospinal fluid (CSF) NfL and presence of immunoglobulin G oligoclonal bands (OCB) were recently identified as predictive of CC in RIS subjects.

Design/Methods: We measured sNfL and CSF NfL levels by single molecule array (Simoa, Quanterix) in RIS patients as defined by 2009 RIS criteria. We analysed the influence of age, sex, 2005 dissemination in space (DIS) criteria, spinal cord lesion, gadolinium-enhanced lesion, OCB, sNfL and CSF NfL on the risk of EDA and of CC using Kaplan-Meier analysis and Cox regression models.

Results:
62 RIS patients were included from 4 MS centres. Mean follow-up time was 45 months. CSF NfL and sNfL levels at inclusion were highly correlated (Spearman, r=0.783). Kaplan-Meier analysis revealed that presence of OCB, CSF NfL>400pg/mL, sNfL>6.5pg/mL and presence of 4/4 2005 DIS criteria were predictive of disease activity (log rank, p=0.017, p=0.022, p=0.025 and p=0.45, respectively). Especially, patients with 4/4 2005 DIS criteria and/or sNfL>6.5pg/mL had an 86% risk of EDA compared to 54% without these characteristics. Only CSF NfL levels predicted CC during follow-up (log rank, p=0.033). Multivariate Cox regression model revealed that OCB, MRI criteria and sNfL>6.5pg/mL were independent factors of EDA (HR=1.87, p=0.047; HR=2.21, p=0.025 and HR=2.19, p=0.019, respectively), but not of CC.
Conclusions:
Elevated sNfL, OCB and 2005 MRI criteria are predictive of EDA in RIS. If replicated in larger datasets, these biomarkers may inform on treatment decisions in this highly relevant population.

On behalf of RISC and SFSEP.