CSF Neurofilament Light Chain Testing as an Aid to Determine Treatment Strategies in MS

**Objective** To evaluate the use of CSF neurofilament light chain (NfL) measurements in clinical practice as well as their effect on treatment strategies and outcomes in patients with MS.

**Methods** This was an observational cohort study of patients with MS who had a CSF NfL measurement between December 2015 and July 2018 as part of their routine clinical care. Treatment strategies were classified as “No Treatment/No Escalation” (no treatment or no escalation of treatment) or “Treatment/Escalation” (first-line injectable/oral disease-modifying therapies (DMTs), highly active DMTs, or treatment escalation). Change in Expanded Disability Status Scale (EDSS) scores was evaluated after the 1-year follow-up.

**Results** Of 203 patients with MS, 117 (58%) had relapsing-remitting MS. Disease activity was most frequently indicated by elevated CSF NfL (n = 85), followed by clinical (n = 81) and MRI activity (n = 65). CSF NfL measurements were independently associated with clinical (p = 0.02) and MRI activity (p < 0.001). Of those with elevated CSF NfL as the only evidence of disease activity (n = 22), 77% had progressive MS (PMS). In patients with PMS, 17 (20%) had elevated CSF NfL as the sole indicator of disease activity. Elevated CSF NfL resulted more frequently in Treatment/Escalation than normal CSF NfL (p < 0.001). Median EDSS change at follow-up was similar between patients receiving No Treatment/No Escalation and Treatment/Escalation decisions (p = 0.81).

**Conclusions** CSF NfL measurements informed treatment strategies, alongside clinical and MRI measures. CSF NfL levels were the only indicator of disease activity in a subset of patients, which was more pronounced in patients with PMS. Elevated CSF NfL was associated with more Treatment/Escalation strategies, which had an impact on EDSS outcomes at 1 year.

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Serum Neurofilament Light Chain: No Clear Relation to Cognition and Neuropsychiatric Symptoms in Stable MS

**Objective** To explore the hypothesis that serum neurofilament light chain (sNfL) indicative of neuroaxonal damage may improve precise disease profiling with regard to cognition and neuropsychiatric symptoms, we analyzed potential associations of sNfL levels with cognitive test scores, fatigue, depression, and anxiety.

**Methods** Patients with relapsing-remitting and secondary progressive MS (SPMS) underwent an elaborated assessment including MRI, various cognitive tests, and patient-reported outcomes. We determined sNfL levels by single molecule array (Simoa) assay. Relationships between sNfL, cognition, neuropsychiatric symptoms, and demographical data were analyzed using correlations, group comparisons, and regressions.

**Results** In 45 clinically stable patients with MS (Expanded Disability Status Scale = 2.73 ± 1.12, disease duration = 10.03 ± 7.49 years), 40.0% had relapsing-remitting MS. Disease activity was most frequently indicated by elevated CSF NfL (n = 85), followed by clinical (n = 81) and MRI activity (n = 65). CSF NfL measurements were independently associated with clinical (p = 0.02) and MRI activity (p < 0.001). Of those with elevated CSF NfL as the only evidence of disease activity (n = 22), 77% had progressive MS (PMS). In patients with PMS, 17 (20%) had elevated CSF NfL as the sole indicator of disease activity. Elevated CSF NfL resulted more frequently in Treatment/Escalation than normal CSF NfL (p < 0.001). Median EDSS change at follow-up was similar between patients receiving No Treatment/No Escalation and Treatment/Escalation decisions (p = 0.81).

**Conclusions** CSF NfL measurements informed treatment strategies, alongside clinical and MRI measures. CSF NfL levels were the only indicator of disease activity in a subset of patients, which was more pronounced in patients with PMS. Elevated CSF NfL was associated with more Treatment/Escalation strategies, which had an impact on EDSS outcomes at 1 year.

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