

Plasma neurofilament light levels are associated with risk of disability in multiple sclerosis

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Study objective

To investigate the association between plasma NfL (pNfL) levels and risk of reaching sustained disability in patients with multiple sclerosis (MS).

What is known and what this paper adds

CSF NfL levels are useful for predicting long-term outcomes in patients with MS. This study suggests that plasma NfL levels may be a substitute less invasive predictor.

Participants and setting

The analysis includes data from 4,385 individuals with MS and 1,026 randomly selected sex- and age-matched controls enrolled in 2 Swedish cohort studies: the Epidemiologic Investigation of MS and the Immunomodulation and MS Epidemiology study. The median duration of follow-up was 5 years.

Design, size, and duration

Highly sensitive Single Molecule Array (Simoa™) NF-light Advantage kit was used to quantify baseline plasma NfL levels. Disability was assessed with the Expanded Disability Status Scale (EDSS) at annual or biannual follow-up assessments.

Main outcome

Association of pNfL levels and risk of reaching sustained EDSS score milestones 3.0 (moderate disability), 4.0 (significant disability) and 6.0 (severe disability) and conversion to secondary progressive (SP) MS.

Main results

The median pNfL was 7.5 pg/mL in controls and 11.4 pg/mL in MS patients ($p < 0.001$). Elevated pNfL levels at the time of MS diagnosis are associated with risk of long-term sustained disability development (see table). High pNfL was associated with the risk of reaching a sustained EDSS score of 3.0 with adjusted rates ranging between 1.5 (95% CI, 1.2–1.8) and 1.55 (95% CI, 1.3–1.8) over all percentile cut-offs (all $p < 0.001$).

Table Associations between elevated plasma NfL levels and the risk of reaching a sustained EDSS score ≥ 3.0

Plasma NfL levels as percentiles ^a	Adjusted hazard ratio (95% confidence interval)
>80	1.53 (1.26–1.85)
>95	1.55 (1.29–1.87)
>99	1.5 (1.2–1.87)

^a Defined based on age-stratified NfL levels from the controls.

Similar increases were observed for risk of sustained EDSS score 4.0. In contrast, the risk for reaching sustained EDSS score 6.0 and conversion to SP MS was not consistently significant.

Bias, confounding, and other reasons for caution

The present study found considerable overlap in plasma NfL scores between the patients and the controls.

Generalizability to other populations

The present study's reliance on data from Sweden may limit the generalizability of the results.

Study funding/potential competing interests

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A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The corresponding author(s) of the full-length article and the journal editors edited and approved the final version.

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