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Diabetic Peripheral Neuropathy: It's in the Blood

Aim: Diabetic peripheral neuropathy (DPN) lacks a blood-based biomarker to aid diagnosis and evaluate treatment response.
Methods: In this cross-sectional study, 423 adult participants with recently diagnosed type 1 / type 2 diabetes (<1 year duration) from the German Diabetes Study cohort were included. Neurofilament light (NfL) chain was measured in fasting serum samples using the Olink Target 96 Neuro Exploratory multiplex assay panel. Participants underwent assessment of their DPN status by means of nerve conduction studies (NCS), quantitative sensory testing, signs and symptoms. Presence of DPN was defined according to the Toronto consensus criteria. Additionally, demographic, anthropometric, and biochemical information were collected.
***Results*:** Sixty-six (16%) participants fulfilled the criteria for DPN, and 354 (84%) did not. Participants with DPN were more likely to be older, with higher waist circumference, and taller than participants without DPN. Serum NfL was significantly higher in participants with DPN ($P<0.0001$) and in each DPN stage compared to those without DPN. Correlation analysis showed a positive association of NfL with age ($P<0.0001$). Regression modelling showed a positive association between higher NfL and DPN ($P<0.0001$) after adjusting for age and sex. Sensitivity analysis showed that this relationship remained consistent when height and waist circumference were substituted by BMI; and when restricted to type 2 diabetes and those with cardiovascular disease. Higher serum NfL was associated with slower motor ($P<0.0001$) and sural nerve conduction velocity ($P\leq0.03$), sural nerve amplitude ($P=0.0004$), lower nerve conduction velocity sum scores ($P<0.0001$), and higher thermal detection threshold to warm stimuli in the hand ($P=0.023$) and foot ($P=0.004$).
***Conclusions*:** These results underpin the potential of serum NfL as a blood-based biomarker in trials of DPN.

Comments. Neuroaxonal damage is a hallmark of many neurological disorders. Its quantification is important to aid diagnosis, prognosis, and drug development. Latest-generation ultra-sensitive assays allow the detection of blood neurofilament levels even in mild disease. Neurofilaments are considered critical for radial growth and axonal stability thereby enabling high conduction velocity. When an axon is damaged, neurofilaments are released into the extra-cellular space and subsequently into the cerebrospinal fluid and blood. The present study is the first to show that higher serum NfL concentrations are associated with increased prevalence of DPN in recently diagnosed diabetes. Furthermore, the association between serum NfL concentration and slower NCS and higher warm thermal threshold implies that large myelinated fibers and small unmyelinated C fibers rather than thinly myelinated Aδ fibers contribute to this relationship. Larger and longer studies are needed to investigate the clinical and analytical validity of serum NfL in the setting of DPN. Nevertheless, the present results highlight its potential as a monitoring biomarker for DPN in routine clinical care.

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Reference. Maalmi H, Strom A, Petrera A, Hauck SM, Strassburger K, Kuss O, Zaharia OP, Bönhof GJ, Rathmann W, Trenkamp S, Burkart V, Szendroedi J, Ziegler D, Roden M, Herder C; GDS Group. Serum neurofilament light chain: a novel biomarker for early diabetic sensorimotor polyneuropathy. Diabetologia. 2022 Dec 6. doi: 10.1007/s00125-022-05846-8. Epub ahead of print. PMID: 36472640.
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