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Serum Neurofilament Light Chain as a Biomarker for CIDP Diagnosis, Severity, and Treatment Outcome

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Abstract

Background and Objectives

The aim of this study was to characterize serum neurofilament light chain (sNFL) levels in a large cohort of patients with autoimmune neuropathies to provide every-day clinical practice recommendations.

Methods

In this retrospective cohort study, we recruited 191 patients with immune-mediated neuropathies from 2 referral centers. sNFL was measured using the Simoa NF-light kit (Quanterix), and age-corrected and BMI-corrected z-scores (zNFL) were calculated. Clinical data were correlated with zNFL and adjusted for different disease subsets. A receiver operator characteristic analysis was performed. Treatments and longitudinal disease course of patients with typical chronic inflammatory demyelinating polyneuropathy (CIDP) in early disease stage were analyzed.

Results

One hundred ten patients had typical CIDP, and 67 had atypical CIDP. Fourteen patients had other immune neuropathies. zNFL of all patients correlated significantly with the Inflammatory Neuropathy Cause and Treatment Scale–overall disability sum score (r = 0.160), Medical Research Council Scale for Muscle Strength score (r = −0.242), modified Rankin Scale score (r = 0.151), and distal tibial compound muscle action potential (r = −0.151). The correlations remained only in the cohort of typical CIDP. zNFL >2 within the first 24 months of illness differentiated patients with atypical and typical CIDP with a sensitivity of 93%. Patients with early-stage typical CIDP with zNFL >2 (n = 9) presented with the most severe manifestation and did not respond to first-line (p < 0.0001) but to second-line treatments.

Discussion

We established sNFL as a promising biomarker for assessing disease activity in patients with typical CIDP. Elevated zNFL in early-stage typical CIDP indicate severe inflammatory-mediated axonal damage that requires aggressive immunotherapy.

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Supplementary Material

Introduction

Neurofilaments are components of the peripheral nervous system, playing a crucial role in neuronal growth, stability, and electrical conduction. Recent research has focused on their potential as markers of disease activity and progression for chronic inflammatory demyelinating polyneuropathy (CIDP). This is particularly critical given the need for timely

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Glossary

CIDP = chronic inflammatory demyelinating polyneuropathy; **CMAP** = compound muscle action potential; **DADS** = distal acquired demyelinating symmetric polyneuropathy; **GBS** = Guillain-Barré syndrome; **INCAT-ODSS** = Inflammatory Neuropathy Cause and Treatment Scale–overall disability sum score; **INCAT-ISS** = Inflammatory Neuropathy Cause and treatment Sclae- sensory sum score; **IQR** = interquartile range; **MADSAM** = multifocal acquired demyelinating sensory and motor neuropathy; **MMN** = multifocal motor neuropathy; **MRC-SS** = Medical Research Council Scale for Muscle Strength; **mRS** = modified Rankin Scale; **NCSs** = nerve conduction studies; **RODS** = Rash-built overall disability scale; **sNFL** = serum neurofilament light chain; **zNFL** = serum neurofilament light chain z-score.

immunomodulatory first-line interventions, preventing effectively the transition from a neuroinflammatory to a neurodegenerative phase.[1] Still, with the current treatment options, up to 20% of patients experience first-line treatment failure in CIDP.[2] Accurate assessment of axonal damage can, therefore, aid clinicians in determining the optimal timing for therapies and monitoring treatment response. This need for reliable biomarkers in CIDP is emphasized in the EAN/PNS guidelines.[3] Currently, CSF protein is the only available semiquantitative biomarker, although its specificity is limited by comorbidities, age, and sex.[4]

Interest in serum neurofilament light chain (sNFL) is growing regarding their clinical implementation.[5-7] Existing studies have demonstrated elevated sNFL concentrations in patients with CIDP[8,9] and Guillain-Barré syndrome (GBS)[10] compared with healthy controls, a decrease with successful treatment,[11] and a correlation with unspecific clinical scores[12] and tried to analyze their prognostic value.[13,14] These studies use raw sNFL values, which are susceptible to biases depending on age (concentrations increase with age) and body mass index (concentrations decrease with higher BMI), and are characterized by low sample sizes and lack of practical recommendations. Further insights regarding disease prognosis, correlation with disease-specific clinical scores, and the role of sNFL in treatment monitoring are still lacking. The introduction of age-corrected and BMI-corrected z-scores offers a more robust approach to sNFL analysis.[15] We aim to characterize sNFL in a large, bicentric, cross-sectional study of autoimmune neuropathies and provide practical recommendations for its clinical implementation.

Methods

Patients

We included 191 patients diagnosed with autoimmune neuropathies between 2019 and 2024 from 2 centers of the German Neuritis Network (Bochum n = 166, Cologne n = 35). CIDP was diagnosed in accordance with the European Federation of Neurological Societies/Peripheral Nerve Society criteria.[16] As an exclusion criterion, we specifically defined other neurologic disorders in which an increase in sNFL is to be expected. These include the following clinical conditions: amyotrophic lateral sclerosis, MS, and neurodegenerative diseases such as dementias and Parkinson syndrome, as well as acute cerebral ischemia or hemorrhage. In our cohort, 3 patients were excluded because of cerebral ischemia (n = 2) and hemorrhage (n = 1). Data collection included sociodemographic data (age, sex, date of first manifestation/diagnosis), diagnosis (typical CIDP; atypical CIDP and subgroups: distal acquired demyelinating symmetric polyneuropathy (DADS), multifocal acquired demyelinating sensory and motor neuropathy (MADSAM), and other atypical manifestations), GBS, (para-)nodopathies, multifocal motor neuropathy (MMN)), clinical scores, treatments, nerve conduction studies (NCSs), and sNFL measurements.

Clinical Assessments

All patients underwent a comprehensive neurologic examination with the following scores:

- Inflammatory Neuropathy Cause and Treatment Scale–overall disability and sensory sum score (INCAT-ODSS/-ISS)
- Adjusted Medical Research Council Scale for Muscle Strength (MRC-SS) score
- Grip strength (Martin Vigorimeter)
- Rasch-built Overall Disability Scale (RODS)
- Modified Rankin Scale (mRS)

Based on time since manifestation, the subcohorts of early CIDP (<24 months) and late CIDP (>24 months) disease stages were build. Standard-of-care (SOC) therapy response of patients with typical CIDP in early disease course was evaluated at the time point of sNFL measurement and 1 year before/later. SOC was defined as treatment with corticosteroids and intravenous/subcutaneous immunoglobulins (IVIg/SCIg) and SOC-refractory patients receiving second-line (i.e., azathioprine) or escalation (i.e., rituximab) treatments. Longitudinal clinical disease courses (3 annual follow-ups) of 9 severely affected patients with typical CIDP in early disease course were displayed.

Electrophysiologic Assessment

The NCSs were conducted using a Dantec Keypoint Focus electromyographic device (Natus Medical GmbH, Planegg, Germany). Standard techniques were used for percutaneous supramaximal stimulation and positioning of the surface electrode with skin temperatures of at least 33°C at the palm and 30°C at the external malleolus. Bilateral NCSs were performed on the median, ulnar, radial, tibial, fibular, and sural nerves as described before.[17] Results were translated into a comprehensive electroneurography score (ENG-score, eTable 1).[18]

Blood Sampling, sNFL Measurements, and z-Score Transformation

Peripheral blood sampling and blood processing were performed according to a standardized protocol. Serum samples were stored at −80°C. sNFL measurements were performed at the Center for Protein Diagnostics, Ruhr-University Bochum, Germany, using the commercially available Simoa NF-light kit (Quanterix) according to the manufacturer's instructions. sNFL z-scores (zNFL) normalized by age and body mass index were calculated by the Department of Clinical Research, University Hospital Basel, Switzerland. Based on a receiver operating characteristic (ROC) analysis and use of the Youden index, subcohorts with high (>2) and low (<2) zNFL were built.

Ethical Approval

All procedures performed in this study were in accordance with the ethical standard of the institutional and national research committee as well as with the 1964 Helsinki Declaration and its later amendments. The INHIBIT register was approved by the local ethics committee (vote no. 18-6534-BR, Ruhr-University Bochum, and vote no. 21-1079, University Cologne, Germany) and registered in the German Register of Clinical Studies (Deutsches Register Klinischer Studien [DRKS], register number: DRKS00024494).

Statistics

The statistical analysis was conducted using IBM SPSS Statistics (version 27.0.0.0). All data are presented as mean with SD. Nominal and dichotomous variables are presented as counts and percentages and ordinal variables as median with interquartile ranges (IQRs). The Student *t* test was used for comparisons of numerical normally distributed variables, the Mann-Whitney *U* test for numerical non-normally distributed values, and the χ^2 test for nominal variables. Multiple comparisons were performed with post hoc Bonferroni correction. Missing values reduced n for statistical analysis. Correlations were performed using Spearman rank correlation for non-normally and Pearson correlation for normally distributed variables. ROC analysis was performed to determine specificity and sensitivity of zNFL. Individuals with missing values were excluded from the specific analysis. The statistically significant threshold was set at p value <0.05. If not stated otherwise, 2-tailed p values are displayed.

Data Availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available because of information that could compromise the privacy of research participants.

Results

Distribution of sNFL and zNFL in Different Autoimmune Neuropathies and Clinical Characteristics

A total of 191 serum samples were collected. One hundred and seventy-seven patients (92%) were diagnosed with CIDP, of whom 110 suffered from typical CIDP and 67 from atypical CIDP. DADS was the most frequent atypical manifestation (n = 39), followed by MADSAM (n = 21) and other atypical CIDP (n = 7). 14 patients were diagnosed with other immune neuropathies such as MMN; GBS; vasculitic polyneuropathy; and (para-)nodopathies with antibodies against neurofascin 155 (*NF-155*), pan-neurofascin (*NF-155* + *NF-186*), and *contactin-1*. Owing to the small sample size, these neuropathies were not statistically compared with CIDP but sNFL and zNFL concentrations in patients with GBS and paranodopathies are higher compared with the CIDP cohort. In general, no significant differences in zNFL between disease entities were observed (p = 0.326) in multiple comparison tests. Patients with paranodopathies had the highest mean raw sNFL levels, followed by those with GBS, CIDP, and MMN. The lowest raw sNFL concentrations were observed in patients with vasculitic neuropathies (p > 0.05) (Figure 1). The CIDP cohorts of both centers differed only in their disease duration since initial diagnosis (Bochum: 41 ± 46 months, Cologne: 67 ± 58 months, p = 0.003) and the INCAT-ISS (Bochum: 7.0 ± 4.0, Cologne: 5.3 ± 6.8, p = 0.001). Details and n-values of patients with CIDP are presented in Table 1; additional data of centers and other immune neuropathies are presented in eTables 2 and 3.

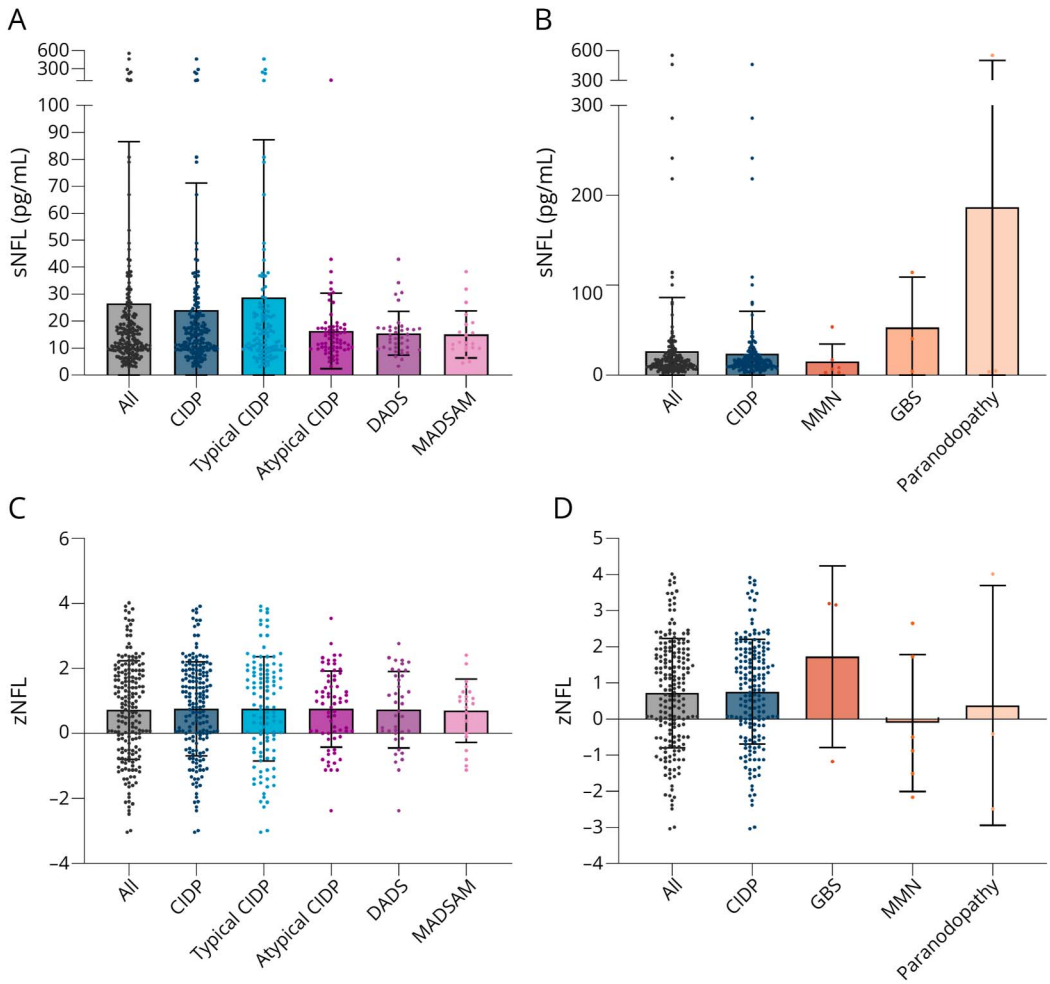
zNFL Correlate With Clinical Disease Severity Scores

Because zNFL were normalized for age and body mass index, these values were used for correlations with clinical data. For all patients, zNFL correlated with INCAT-ODSS (r = 0.160, p = 0.002), ENG-score (r = 0.140, p = 0.027), tibial CMAP (r = −0.151, p = 0.039), mRS score (r = 0.151, p = 0.014), and MRC-SS sum score (r = −0.242, p = 0.001). Patients diagnosed with typical CIDP showed correlations of zNFL with INCAT-ODSS (r = 0.226, p = 0.017), MRC-SS score (r = −0.268, p = 0.005), mRS score (r = 0.202, p = 0.041, one-tailed), time since diagnosis (r = −0.199, p = 0.038), and manifestation (r = −0.219, p = 0.022). In case of atypical CIDP, no significant correlations were found. Similarly, no correlation was found between RODS sum score and ISS with zNFL. Main correlations are displayed in Figure 2 with additional data available, including raw sNFL correlations, in eTable 4.

zNFL Differ Between Typical and Atypical CIDP Only in Early Disease Stages

Because correlations revealed a negative dynamic of zNFL with time only in our typical CIDP cohort, we proceeded to investigate the background of this finding. Within 24 months after first manifestation, patients with typical CIDP had significantly higher zNFL (1.6 ± 1.7, n = 27) compared with the atypical CIDP cohort (0.4 ± 1.4, n = 14, p = 0.028). As expected based on the above-reported correlations, the zNFL differ significantly between early and late disease stages in typical CIDP (n = 75, p = 0.002, Figure 3). Details are provided in Table 2. INCAT-ODSS (p = 0.036), CMAP (p = 0.0399), and RODS sum score (p = 0.0012) were significantly

Figure 1 sNFL [pg/ml] and sNFL z-Scores in CIDP Subsets and Other Autoimmune Neuropathies



(A) sNFL in all patients 26.63 ± 59.88, CIDP 24.07 ± 47.16, typical CIDP 28.75 ± 58.43, atypical CIDP 16.38 ± 14.01, DADS 15.48 ± 8.11, MADSAM 15.11 ± 8.7, other atypical CIDP 25.25 ± 37.24. (B) sNFL in MMN 15.34 ± 19.43, GBS 52.92 ± 56.18, paranodopathy 186.77 ± 316.13. (C) sNFL z-score in all patients 0.72 ± 1.51, CIDP 0.75 ± 1.45, typical CIDP 0.76 ± 1.6, atypical CIDP 0.75 ± 1.17, DADS 0.73 ± 1.18, MADSAM 0.7 ± 0.97. (D) sNFL z-score in MMN -0.11 ± 1.9, GBS 1.73 ± 2.51, paranodopathy 0.37 ± 3.32. Sample sizes: all n = 191, CIDP n = 177, typical CIDP n = 110, atypical CIDP n = 67, DADS n = 39, MADSAM n = 21, MMN n = 6, GBS n = 3, paranodopathy n = 3. CIDP = chronic inflammatory demyelinating polyneuropathy; DADS = distal acquired demyelinating symmetric polyneuropathy; GBS = Guillain-Barré syndrome; MADSAM = multifocal acquired demyelinating sensory and motor neuropathy; MMN = multifocal motor neuropathy.

worse in patients with typical CIDP compared with the atypical CIDP cohort.

We asked the question whether zNFL could distinguish between typical and atypical CIDP in an early disease stage and performed a receiver operating characteristic (ROC) analysis of all patients with CIDP within 24 months since first manifestation and tested for typical CIDP; a positive test was considered above the measurement threshold. A zNFL threshold of 2.04 was identified with 93% specificity and 37% sensitivity. The test for atypical CIDP showed a sensitivity of 93% and a specificity of 37% for zNFL measurements below the threshold of 2.04.

Patients With Typical CIDP With High (>2) zNFL Show More Severe Disease Than the Atypical CIDP Cohort

Considering the identified cutoff's ability to differentiate typical from atypical CIDP, we proceeded to examine the clinical profiles of patients above and below this point. To maintain consistency and in line with our hypothesis that increased zNFL indicate higher clinical severity, we used the identical cutoff for differentiation of clinical severity, rather than using separate cutoffs.

Disease was more severe for patients with high zNFL (>2) in the group of all patients with CIDP (high zNFL: n = 34, low zNFL: n = 143; INCAT-ODSS: $p = 0.01$; MRC-SS score $p = 0.006$, RODS sum score $p = 0.048$) and those with typical CIDP (high zNFL: n = 24; low zNFL: n = 86, INCAT-ODSS $p = 0.016$; MRC-SS score $p = 0.006$, RODS sum score $p = 0.047$), but not in the atypical CIDP cohort (high zNFL: n = 10, low zNFL: n = 57). Patients with high zNFL (>2) presented with a more severe disease but did not have worse axonal markers in the nerve conduction studies because distal tibial CMAP amplitudes of neither typical nor atypical CIDP patients with high zNFL (typical: 1.99 ± 0.62 mV, atypical:

Table 1 Clinical and Paraclinical Data of Disease Groups Including sNFL and zNFL Values

			Patients with CIDP					
					Atypical CIDP			
Data	All	Other neuropathies	Sum	Typical CIDP	Sum	DADS	MADSAM	Other atypical
n (total%)	191 (100)	14 (7)	177 (92)	110 (58)	67 (35)	39 (25)	21 (14)	7 (5)
Female (group%)	49 (31)	4 (29)	45 (25)	30 (27)	15 (22)	7 (18)	3 (14)	5 (71)
Male (group%)	142 (69)	10 (71.4)	132 (74.6)	80 (73)	52 (78)	32 (82)	18 (86)	2 (28)
Age, y ± SD	58 ± 12	51 ± 16	58 ± 12	59 ± 12	58 ± 11	59 ± 9	58 ± 12	50 ± 18
Time since diagnosis, mo ± SD	35 ± 48	41 ± 81	35 ± 44	35 ± 48	35 ± 37	30 ± 30	43 ± 48	37 ± 36
Time since manifestation, mo ± SD	80 ± 67	67 ± 114	81 ± 63	84 ± 64	76 ± 61	76 ± 59	83 ± 69	54 ± 50
sNFL, mean ± SD	26.63 ± 59.88	58.97 ± 145.17	24.07 ± 47.16	28.75 ± 58.43	16.38 ± 14.01	15.48 ± 8.11	15.11 ± 8.7	25.25 ± 37.24
zNFL, mean ± SD	0.72 ± 1.51	0.27 ± 2.19	0.75 ± 1.45	0.76 ± 1.6	0.75 ± 1.17	0.73 ± 1.18	0.7 ± 0.97	1.03 ± 1.75
Tibial CMAP [mV], mean ± SD	2.89 ± 3.26	5.03 ± 4.49	2.72 ± 3.1	2.4 ± 3.04	3.22 ± 3.14	2.16 ± 2.34	4.77 ± 3.55	4.5 ± 4.0
INCAT-ODSS, median (IQR)	3 (2)	3 (4)	3 (2)	3 (2)	2 (2)	2 (2)	3 (2)	4 (4)
INCAT-ISS, mean ± SD	6.5 ± 4.7	4.6 ± 4.6	6.7 ± 4.7	6.8 ± 5.1	6.5 ± 4.1	6.7 ± 3.5	5.5 ± 4.3	7.7 ± 6.2
RODS sum score, mean ± SD	63 ± 22	70 ± 23	62 ± 22	56 ± 21	72 ± 20	81 ± 17	62 ± 19	58 ± 14
Vigorimetry [kPa], mean ± SD	65 ± 32	61 ± 41	65 ± 31	58 ± 28	73 ± 32	81 ± 28	66 ± 36	52 ± 28
MRC-SS score, mean ± SD	72 ± 10	69 ± 15	72 ± 10	70 ± 10	74 ± 8	76 ± 7	72 ± 9	71 ± 10
ENG-score, mean ± SD	3 ± 1.4	2.6 ± 1.9	3.1 ± 1.3	3.2 ± 1.2	3 ± 1.4	3.1 ± 1.2	2.6 ± 1.7	3.1 ± 1.5
mRS score, median (IQR)	2 (1)	1.5 (2)	2 (1)	2 (2)	1 (1)	1 (1)	2 (1)	3 (1)

Abbreviations: CIDP = chronic inflammatory demyelinating polyneuropathy; CMAP = compound muscle action potential; ENG-score = electroneurography score; INCAT-ISS = Inflammatory Neuropathy Cause and Treatment Scale–sensory sum score; INCAT-ODSS = Inflammatory Neuropathy Cause and Treatment Scale–overall disability sum score; MRC-SS = Medical Research Council Scale for Muscle Strength; mRS = modified Rankin Scale; RODS = Rasch-built Overall Disability Scale; sNFL = serum neurofilament light chain; zNFL = serum neurofilament light chain z-score.

2.7 ± 0.9 mV) differed from those of patients with low zNFL (typical: 2.51 ± 0.33 mV, atypical: 3.31 ± 0.42 mV). As expected, patients with typical CIDP with high zNFL (>2) also experienced a significantly more severe disability compared with atypical patients. This was evidenced in MRC-SS sum score (typical: 64 ± 12, atypical: 75 ± 5, $p = 0.0067$) and RODS sum score (typical: 48 ± 22, atypical: 71 ± 18, $p = 0.0032$). Although not reaching statistical significance, the INCAT-ODSS showed a trend toward higher disability in patients with typical CIDP (typical: 4 (5); atypical: 2.5 (2); $p = 0.068$). Details are provided in eTable 5.

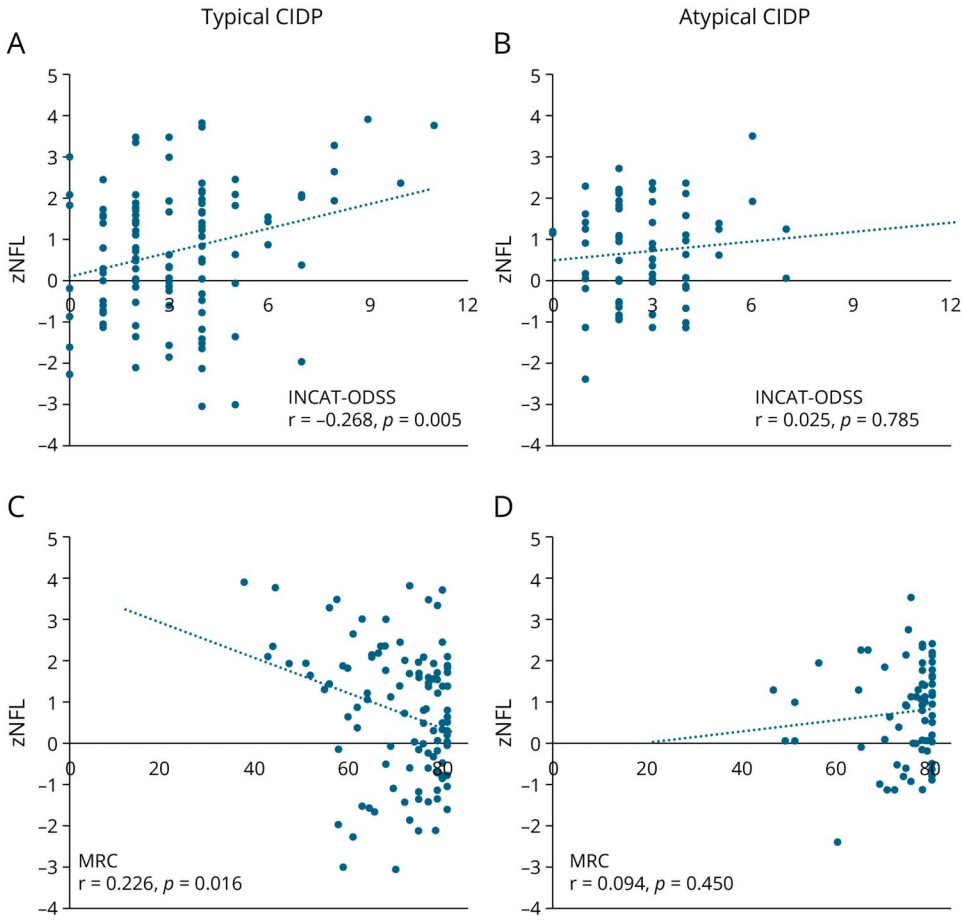
High zNFL Primarily Identify Motor Dysfunction

To evaluate whether high zNFL values are related primarily to motor dysfunction, we divided our cohort based on ISS and MRC-SS score. An ISS ≥10 was considered as strong sensory involvement. MRC-SS score below 70 was chosen for motor impairments. 44 patients had an ISS >10 of whom 19 had a motor impairment. All patients with motor impairments had significantly ($p = 0.0035$) higher zNFL (1.29 ± 1.45) compared with patients with preserved motor function (0.11 ± 1.03). Patients with motor impairments compared with patients with preserved motor function had significantly higher zNFL in typical ($p = 0.0262$, n = 9 vs 17, mean zNFL1.45 ± 1.57 vs 0.19 ± 1.00) but not in the atypical CIDP cohort ($p = 0.7034$, n = 7 vs 6, mean zNFL 0.30 ± 1.09 vs 0.51 ± 0.73).

Identifying Potential Patients at Risk With High zNFL Concentrations in Early (<24 months) Disease Stage

Based on the findings that high zNFL values in early disease stages demonstrate severe disability, we analyzed patients with a time since manifestation of maximum 24 months (all n = 49, CIDP n = 41, typical CIDP n = 27, atypical CIDP n = 14) and compared patients with high (>2) zNFL (all n = 14, CIDP n = 11, typical CIDP n = 10, atypical CIDP n = 1) and low (<2) zNFL (all n = 34, CIDP n = 30, typical CIDP n = 17, atypical CIDP n = 13).

Figure 2 Correlations of zNFL in Different Disease Subsets With Clinical Parameters



r Values and *p* values are provided in the figure. (A) zNFL correlation with INCAT-ODSS in patients with typical CIDP, n = 110. (B) zNFL correlation with INCAT-ODSS in patients with atypical CIDP, n = 67. (C) zNFL correlation with MRC-SS score in patients with typical CIDP, n = 110. (D) zNFL correlation with MRC-SS score in patients with atypical CIDP, n = 67. CIDP = chronic inflammatory demyelinating polyneuropathy; INCAT-ODSS = Inflammatory Neuropathy Cause and Treatment Scale–overall disability sum score; MRC-SS = Medical Research Council Scale for Muscle Strength.

Patients with high zNFL in an early disease stage had significantly worse tibial CMAP ($p < 0.001$), INCAT-ODSS ($p < 0.001$), RODS sum score ($p < 0.001$), and MRC-SS score ($p < 0.001$). Patients with typical CIDP showed significantly worse INCAT-ODSS ($p = 0.029$) and MRC-SS score ($p = 0.007$) in the subgroup with high zNFL. The small number of patients with atypical CIDP with early disease course (n = 14) and high zNFL (n = 1) allowed no comparisons. Details are provided in Table 3.

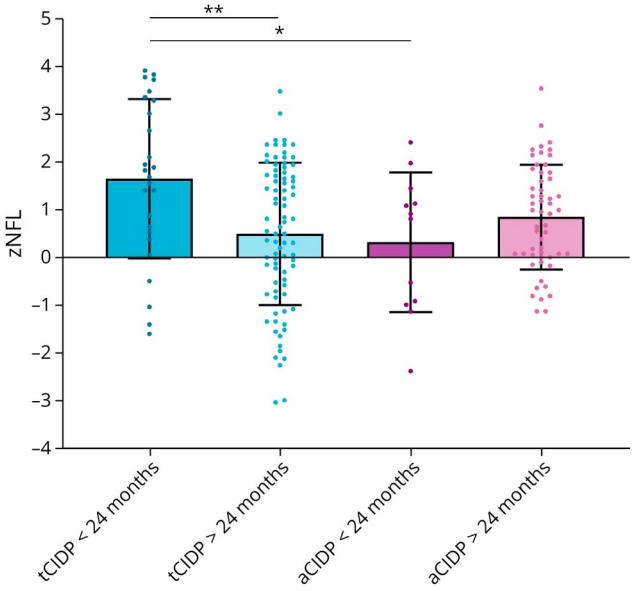
Patients With Typical CIDP in Early Disease Stage and With High zNFL Concentration Are SOC-Refractory

To answer the question whether patients with typical CIDP with high zNFL in early disease stage received more intensive treatment, we analyzed SOC status as defined before and compared patients with high (n = 10) and low (n = 17) zNFL. Data were evaluated before zNFL measurement, at the time point of measurement, and 1 year later and compared with the χ^2 test. Before zNFL measurements, 30% of patients with high and 12% with low zNFL were SOC-refractory ($p = 0.24$). At the time point of measurements, 80% of patients with high and 6% with low zNFL were SOC-refractory ($p < 0.0001$). One year later, 90% of patients with high and 8% of patients with low zNFL were SOC-refractory ($p = 0.0001$).

Longitudinal Course for Aggressive Typical CIDP With High zNFL

Finally, we investigated longitudinal clinical disease course of patients with early-stage typical CIDP with high (>2, n = 10) zNFL, to answer whether these patients show ongoing disease activity after intensive treatment. Nine patients with early-stage typical CIDP had minimum longitudinal data of 2 follow-ups. One patient was observed for 2 years, and 5 patients had follow-up data until year 3. The baseline ODSS was 5.78 ± 3.46 and improved (*ns*) after one (4.11 ± 1.91), 2 (3.17 ± 0.9), and 3 (2.8 ± 0.75) years. The RODS sum score improved significantly in comparison with baseline after 2 ($p = 0.026$) and 3 ($p = 0.023$) years. Patients' improvements in MRC-SS score were less strong (baseline: 56 ± 13, 1-year follow-up: 69 ± 9, $p = 0.056$; 2-year follow-up: 71 ± 9, $p = 0.059$; 3-year follow-up: 69 ± 10). Tibial CMAP did not improve (baseline: 1.9 ± 3.2 mV, 1 year: 2.8 ± 3.3 mV, 2 years: 2.0 ± 2.1 mV; 3 years: 1.8 ± 1.6). Longitudinal disease courses are displayed in Figure 4.

Figure 3 Comparison of zNFL in Typical and Atypical CIDP Cohorts in Early (<24 Months) and Late (>24 Months) Disease Stages Since Manifestation



Typical CIDP <24 m (n = 27, zNFL = 1.6 ± 1.7); typical CIDP >24 m (n = 83, zNFL 0.5 ± 1.5); atypical CIDP <24 m (n = 14, zNFL = 0.4 ± 1.4); atypical CIDP >24 m (n = 53, zNFL = 0.9 ± 1.1); typical CIDP >24 m vs typical CIDP <24 m (p = 0.002); typical CIDP <24 m vs atypical CIDP <24 m (p = 0.028). CIDP = chronic inflammatory demyelinating polyneuropathy.

Discussion

In this study, we provide novel insights and recommendations for using sNFL as a disease marker for CIDP.

Our findings demonstrate that sNFL concentrations vary across different autoimmune neuropathies, with the highest levels observed in paranodopathies and GBS, which show an acute severe manifestation with high probability to cause axonal damage.

Because this study was a cross-sectional study with diverse disease stages, the timing of sNFL measurements may have influenced the results. The high deviation of sNFL and zNFL in the group of paranodopathies might be treatment-related because 2 patients were included early after disease manifestation and had high sNFL concentrations while one patient was included 1 year after disease onset and was treated with rituximab. This is in line with existing literature of treatment-related decrease of sNFL in paranodopathies.[19] The high sNFL concentration in patients with paranodopathies represents early axonal involvement, probably through antibody-directed cytotoxic interactions because most paranodopathies show IgG4 types, which show no complement activation.[20] In case of our patients with GBS, it might be intriguing that these still show elevated zNFL levels 12 months since disease manifestation. Of the 3 patients with GBS presented here, one patient was in an early stage of the disease (3 months since initial diagnosis). This patient still had a very high z-score of 4 and was clinically severely affected with an ODSS of 12. The serum of the other 2 patients was collected after 11 and 20 months since disease manifestation and already showed a lower z-score and a concomitantly low ODSS of 3. We suspect that this difference was due to sufficient therapy as well. The same applies to patients with MMN. These patients even show a negative z-score. However, their time since manifestation and diagnosis was the longest.

Of interest, vasculitic polyneuropathies seem to have the lowest sNFL concentrations in our cohort. In this disease,

Table 2 Clinical Data and sNFL z-Scores in Patients With Different Disease Stages

	All patients		All patients with CIDP		Patients with typical CIDP		Patients with atypical CIDP	
Data	**Early**	**Late**	**Early**	**Late**	**Early**	**Late**	**Early**	**Late**
n (%)	49 (26)	142 (74)	41 (23)	136 (77)	27 (25)	83 (75)	14 (21)	53 (79)
Age, y ± SD	55 ± 12	59 ± 12	55 ± 11	59 ± 12	55 ± 10	60 ± 13	55 ± 12	58 ± 11
zNFL ± SD	1.1 ± 1.8[1]**	0.57 ± 1.38[1]**	1.2 ± 1.7[2]*	0.6 ± 1.4[2]*	1.6 ± 1.7[3]**[4]*	0.5 ± 1.5[3]**	0.4 ± 1.4 [4]*	0.9 ± 1.1
Time since manifestation, mo ± SD	12 ± 7	103 ± 63	12 ± 7	101 ± 57	11 ± 7	107 ± 56	13 ± 7	107 ± 56
Time since diagnosis, mo ± SD	7 ± 7	45 ± 51	6 ± 6	43 ± 47	6 ± 5	44 ± 52	7 ± 7	44 ± 52
Tibial CMAP [mV], mean ± SD	3.35 ± 3.7	2.73 ± 3.09	3.43 ± 3.69	2.49 ± 2.87	2.66 ± 3.49[1]*	2.32 ± 2.89	4.92 ± 3.73[1,2]*	2.77 ± 2.84[2]*
INCAT-ODSS, median (IQR)	3 (3)	3 ± 2	3 (3)	3 (2)	4 (4)[1]*	3 (2)	2 (2)[1]*	3 (2)
RODS sum score, mean ± SD	61 ± 25	63 ± 22	61 ± 25	63 ± 22	52 ± 23[1]*	57 ± 21	78 ± 18[1]*	71 ± 21
MRC-SS score, mean ± SD	70 ± 12	72 ± 9	70 ± 12	72 ± 9	68 ± 13	71 ± 9	75 ± 5	74 ± 9

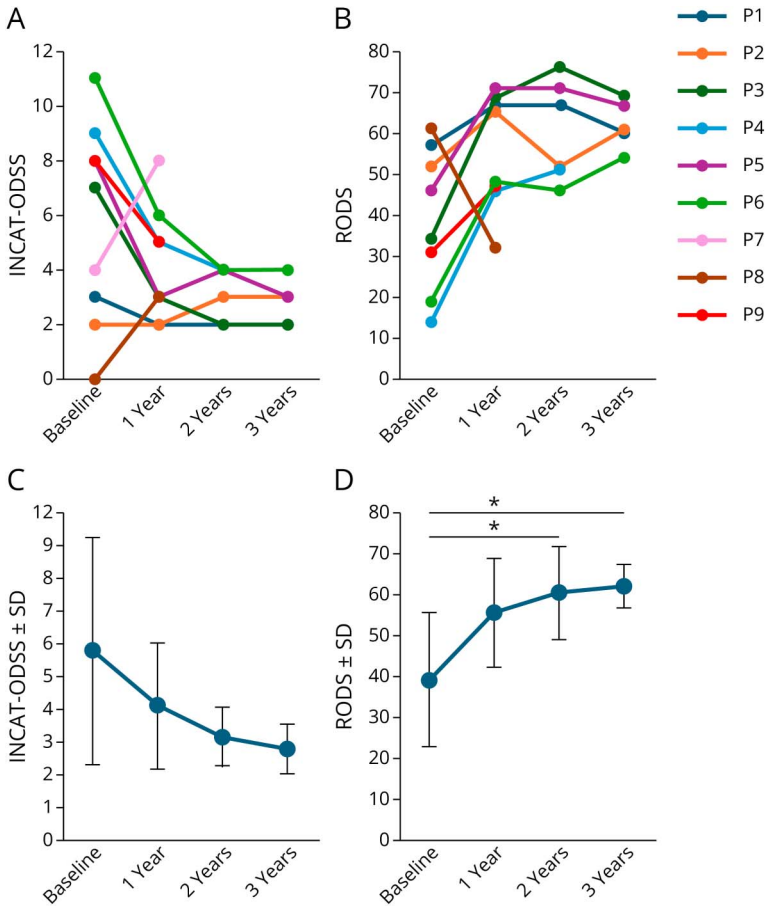
Abbreviations: CIDP = chronic inflammatory demyelinating polyneuropathy; CMAP = compound muscle action potential; INCAT-ISS = Inflammatory Neuropathy Cause and Treatment Scale–sensory sum score; INCAT-ODSS = Inflammatory Neuropathy Cause and Treatment Scale–overall disability sum score; MRC-SS = Medical Research Council Scale for Muscle Strength; mRS = modified Rankin Scale; RODS = Rasch-built Overall Disability Scale; sNFL = serum neurofilament light chain; zNFL = serum neurofilament light chain z-score.
*p < 0.05; **p < 0.01; ***p < 0.001, superscript numbers marking corresponding significant differences in the row. Early disease stage was defined as less than 24 mo since first manifestation. Late disease stage was defined as more than 24 mo since disease manifestation.

Table 3 Clinical Data of Patients in the Early Disease Stage (<24 m) With and Without z-Score >2

	All patients		All CIDP patients		Typical CIDP patients		Atypical CIDP patients	
Data	**zNFL >2**	**zNFL <2**	**zNFL >2**	**zNFL <2**	**zNFL >2**	**zNFL <2**	**zNFL >2**	**zNFL <2**
n (%)	15 (31)	34 (69)	11 (27)	30 (73)	10 (37)	17 (63)	1 (7)	13 (93)
Age, y ± SD	54 ± 12	56 ± 12	51 ± 9	56 ± 11	52 ± 9	57 ± 10	43	56 ± 12
zNFL ± SD	3.24 ± 0.58	0.21 ± 1.28	3.23 ± 0.62	0.39 ± 1.22	3.31 ± 0.58	0.53 ± 1.19	Feb 41	0.21 ± 1.28
Time since manifestation, mo ± SD	7 ± 7	14 ± 6	8 ± 7	13 ± 6	7 ± 7	14 ± 5	18	12 ± 7
Time since diagnosis, mo ± SD	4 ± 5	8 ± 7	5 ± 5	7 ± 6	4 ± 4	8 ± 6	16	7 ± 7
Tibial CMAP [mV], mean ± SD	1.6 ± 2.98[1]**	4.11 ± 3.76[1]**	1.55 ± 2.95[2]*	4.13 ± 3.73[2]*	1.66 ± 3.08	3.26 ± 3.66	0.41	5.26 ± 3.64
INCAT-ODSS, median (IQR)	7 (6)[1]***	2 (2)[1]***	4 (5)[2]**	2 (3)[2]**	5.5 (6)[3]*	3 (4)[3]*	4	2 (2)
RODS sum score, mean ± SD	42 ± 18[1]***	68 ± 23[1]***	44 ± 19[2]**	67 ± 24[2]**	42 ± 18	58 ± 24	65	79 ± 19
MRC-SS score, mean ± SD	59 ± 15[1]***	74 ± 7[1]***	60 ± 15[2]**	74 ± 7[2]**	59 ± 15[3]**	73 ± 8[3]**	78	75 ± 6

Abbreviations: CIDP = chronic inflammatory demyelinating polyneuropathy; CMAP = compound muscle action potential; INCAT-ISS = Inflammatory Neuropathy Cause and Treatment Scale–sensory sum score; INCAT-ODSS = Inflammatory Neuropathy Cause and Treatment Scale–overall disability sum score; MRC-SS = Medical Research Council Scale for Muscle Strength; mRS = modified Rankin Scale; RODS = Rasch-built Overall Disability Scale; sNFL = serum neurofilament light chain; zNFL = serum neurofilament light chain z-score.
*p < 0.05; **p < 0.01; ***p < 0.001, superscript numbers marking corresponding significant differences in the row.

Figure 4 Longitudinal Clinical Observation of Patients With Typical CIDP With zNFL >2 and Early Disease Stage (<24 m) Individually (A and B) and Combined (C and D)



Significant disease amelioration of RODS sum score (B and D) after 2 years (56 ± 13; p = 0.023) and 3 years (63 ± 5; p = 0.026) in comparison with baseline (39 ± 16). n = 9. CIDP = chronic inflammatory demyelinating polyneuropathy; INCAT-ODSS = Inflammatory Neuropathy Cause and Treatment Scale–overall disability sum score; RODS = Rasch-built Overall Disability Scale.

function is not hampered by direct nerve inflammation, but patency of microvascularization is crucial for axonal survival. These findings may be a powerful tool to distinguish vasculitic neuropathy from neuritis *sensu stricto* and should be addressed in future studies. However, it must also be considered that disease stability here had a crucial influence on the low sNFL values, as it has been reported before.[21]

The CIDP cohort showed relatively high sNFL concentrations but below the level of GBS and paranodopathies. This is in line with existing literature but also might be due to a longer disease duration.[22] Nevertheless, the high sNFL concentrations represent an axonal involvement in our cohort, which is also represented in decreased distal tibial CMAP. Because CIDP is a rare disease, differences between typical and atypical manifestations were not evaluated in literature yet.

In general, timing of sNFL measurements varies across the observed disease entities with higher z-scores observed in early disease stages. In addition, stability of disease and treatments might have influenced the results as well.

The benefit of using zNFL instead of raw sNFL concentrations is that these values were adjusted for age and BMI. Correlations of raw sNFL values with clinical scores showed plenty of significant relationships, but bias is crucial here because sNFL is increasing with age and decreasing with BMI.[15] Analyzing the same correlations with zNFL values, however, still showed significant correlations with INCAT-ODSS and MRC-SS score in typical CIDP, but not in atypical CIDP. It has to be considered that these disease subtypes might differ significantly in their respective underlying pathophysiology, indicating to be potential different disease entities. In a previous study, we demonstrated that typical CIDP is more frequently associated with axonal damage then atypical CIDP.[18] In addition, Italian colleagues demonstrated a more moderate disease course of patients with atypical CIDP.[23] It may be disconcerting that the effect of the correlations demonstrated here is weak. In previous work, stronger correlations were found using raw sNFL values in a smaller number of patients.[9,12] However, given that our cohort is very heterogeneous and we have eliminated the influence of BMI and age using z-scores, the weakness of the correlation is not surprising. Other influencing factors such as disease stability, disease duration, and previous therapies may also have contributed to the weak correlations.[24] To not distort the overall picture of the zNFL correlations, we decided against such an approach. zNFL did not show significant correlations to axonal damage in NCS in ENG-score or to distal tibial CMAP. When using raw sNFL, the correlation with distal tibial CMAP was weak with $r = -0.131$ and 2-tailed p value of 0.51 in patients with typical CIDP (eTable 3). We believe that the timing of the measurement might be the reason for these results. The heterogenicity of the cohort with a long history of disease and pretreatments might have weakened the correlations. It might be necessary to recruit much more patients in early disease stages without treatment to demonstrate that zNFL and sNFL correlate with decreased CMAP.

In our cohort, already at an early stage of disease, significant differences between typical and atypical CIDP were observed, with a severe motor affection of patients with typical CIDP. In line with this, these patients had higher sNFL concentrations. Possible explanations can be found in the clinical phenotype. Typical CIDP is characterized by symmetric, distal, and proximal muscle weakness, affecting both large and small muscles, whereas atypical CIDP presents with predominantly distal (DADS) or multifocal (MADSAM) weakness. It is plausible that typical CIDP predominantly affects larger nerves or more nerve fascicles, which contain more neurofilaments, while atypical CIDP involves smaller or simply fewer nerves. When differentiating patients with high sensory involvement as represented by a high ISS, for motor dysfunction and for preserved motor function, it becomes evident that increased zNFL values are primarily attributable to motor nerve damage, which is mostly present in patients with typical CIDP. This is particularly highlighted by the fact that patients with an elevated ISS and preserved motor function exhibit a z-score comparable with that of healthy individuals. Of interest, patients with atypical CIDP with motor dysfunction had lower zNFL than patients with preserved motor functionality, indicating that motor dysfunction in atypical CIDP might be less caused by axonal degeneration but more by demyelination.

zNFL may be a useful biomarker for differentiating between these subtypes. A zNFL threshold of 2 yielded a specificity of 93% for typical CIDP, but a sensitivity of only 37%. Conversely, a zNFL value less than 2 demonstrated high sensitivity (93%) but low specificity (37%) for atypical CIDP, suggesting that zNFL <2 can reliably confirm atypical CIDP when atypical CIDP is suspected. In addition, patients with typical CIDP with zNFL >2 in the early disease stage exhibited the most severe disease course, identifying them as patients at risk.

A negative correlation was observed between zNFL and time since initial diagnosis and manifestation in typical CIDP, suggesting that elevated zNFL may primarily occur during early disease stages that are characterized by high inflammatory activity and subsequent axonal damage. Otherwise, decreasing zNFL could be contributed to therapy response as discussed before.

Longitudinal observation of 9 of 10 patients with typical CIDP with zNFL >2 and early disease onset revealed a significant increase in the RODS score over time. Although no significant changes were observed in the ODSS and MRC-SS score, a trend toward improvement was noted. We hypothesize that these trends reflect the positive impact of treatment because analysis of SOC response showed that these patients received significantly more often second-line and escalation treatments in comparison with patients with typical CIDP

with low zNFL. A "hit hard and early" treatment regime should be discussed for patients with zNFL >2 because our data and existing literature are showing better outcomes for aggressively early-treated patients.[25,26]

Of interest, patients with zNFL >2 at early disease course already had decreased tibial CMAP and showed neither improvements nor deterioration in NCSs over time, maybe due to successful stabilization of the disease. Contrary to the prevailing view that axonal degeneration occurs primarily in the later stages of typical CIDP, our findings indicate that significant axonal damage is present early in the disease course. This underlines the value of zNFL as an early marker of severity, which demands for consequent treatment. Especially at time of disease onset, zNFL might be of high value to determine whether patients are in need of aggressive treatment. While clinical examination provides insights into the patient's disease severity, zNFL can further objectify the pathophysiologic disease activity and offer clinicians crucial assistance in making treatment decisions at the time of initial diagnosis.

In summary, our data demonstrate that zNFL are elevated in typical CIDP compared with atypical CIDP in early disease stages, can effectively differentiate between these subtypes, reflect disease activity, and identify patients with most severe disease stages, where aggressive treatment can improve the clinical course. Therefore, we postulate the following clinical practice recommendations:

1. sNFL should be measured at time of diagnosis and expressed as z-score (zNFL).
2. zNFL can help differentiate between typical and atypical CIDP at time of diagnosis (threshold of 2).
3. zNFL >2 in typical CIDP can identify "patients at risk" with high disease activity.
4. Early aggressive treatment of patients with typical CIDP with zNFL measurements >2 at time of diagnosis should be considered.

Our study also has some limitations: zNFL measurements from different time points are not included, hindering a comprehensive assessment of longitudinal disease progression. The small sample size of especially patients with atypical CIDP with zNFL >2 and early disease onset limits the reproducibility of our findings in this specific subgroup. Furthermore, our analysis does not take into account patient stability and therapy, both of which can influence zNFL. Longitudinal sNFL measurements with additional correction for age in multivariant models over a prolonged period might be necessary to elucidate this impact.

Author Contributions

R. Klimas: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data. F. Kohle: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; analysis or interpretation of data. L. Horstkemper: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. P. Benkert: major role in the acquisition of data. A. Rehm: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. A. Seibert: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. M. Riesner: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. M. Sgodzai: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. T. Grüter: drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data. N. Rilke: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. B. Gisevius: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. L. Beyer: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. K. Gerwert: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. J. Kuhle: drafting/revision of the manuscript for content, including medical writing for content. M. Schroeter: drafting/revision of the manuscript for content, including medical writing for content. H.C. Lehmann: drafting/revision of the manuscript for content, including medical writing for content. R. Gold: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. A.L. Fisse: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; analysis or interpretation of data. J. Motte: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; analysis or interpretation of data. K. Pitarokoili: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data.

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References

1. Klimas R, Kordes A, Huckemann S, et al. The multiple roles of nerve biopsy in the diagnosis and prognosis of suspected immune neuropathies. *J Neurol*. 2024;271(8):5109-5121. doi:10.1007/s00415-024-12456-4
2. Fisse AL, Motte J, Grüter T, Sgodzai M, Pitarokoili K, Gold R. Comprehensive approaches for diagnosis, monitoring and treatment of chronic inflammatory demyelinating polyneuropathy. *Neurol Res Pract*. 2020;2:42. doi:10.1186/s42466-020-00088-8
3. European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint Task Force-Second revision. *J Peripher Nerv Syst*. 2022;27(1):94. doi:10.1111/jns.12479
4. Seeliger T, Gingele S, Güzeloglu YE, et al. Comparative analysis of albumin quotient and total CSF protein in immune-mediated neuropathies: a multicenter study on diagnostic implications. *Front Neurol*. 2023;14:1330484. doi:10.3389/fneur.2023.1330484
5. Wieske L, Smyth D, Lunn MP, Eftimov F, Teunissen CE. Fluid biomarkers for monitoring Structural changes in polyneuropathies: their use in clinical practice and trials. *Neurotherapeutics*. 2021;18(4):2351-2367. doi:10.1007/s13311-021-01136-0
6. Andersen NE, Boehmerle W, Huehnchen P, Stage TB. Neurofilament light chain as a biomarker of chemotherapy-induced peripheral neuropathy. *Trends Pharmacol Sci*. 2024;45(10):872-879. doi:10.1016/j.tips.2024.08.001
7. Velasco R, Marco C, Domingo-Domenech E, et al. Plasma neurofilament light chain levels in chemotherapy-induced peripheral neurotoxicity according to type of anticancer drug. *Eur J Neurol*. 2024;31(9):e16369. doi:10.1111/ene.16369
8. Hayashi T, Nukui T, Piao JL, et al. Serum neurofilament light chain in chronic inflammatory demyelinating polyneuropathy. *Brain Behav*. 2021;11(5):e02084. doi:10.1002/brb3.2084
9. Stascheit F, Hotter B, Klose S, Meisel C, Meisel A, Klehmet J. Calprotectin in chronic inflammatory demyelinating polyneuropathy and variants-a potential novel biomarker of disease activity. *Front Neurol*. 2021;12:723009. doi:10.3389/fneur.2021.723009
10. Altmann P, De Simoni D, Kaider A, et al. Increased serum neurofilament light chain concentration indicates poor outcome in Guillain-Barré syndrome. *J Neuroinflammation*. 2020;17(1):86. doi:10.1186/s12974-020-01737-0
11. van Lieverloo GGA, Wieske L, Verhamme C, et al. Serum neurofilament light chain in chronic inflammatory demyelinating polyneuropathy. *J Peripher Nerv Syst*. 2019;24(2):187-194. doi:10.1111/jns.12319
12. Fukami Y, Iijima M, Koike H, Yamada S, Hashizume A, Katsuno M. Association of serum neurofilament light chain levels with clinicopathology of chronic inflammatory demyelinating polyneuropathy, including NF155 reactive patients. *J Neurol*. 2021;268(10):3835-3844. doi:10.1007/s00415-021-10537-2
13. Godelaine J, De Schaepdryver M, Bossuyt X, van Damme P, Claeys KG, Poesen K. Prognostic value of neurofilament light chain in chronic inflammatory demyelinating polyneuropathy. *Brain Commun*. 2021;3(1):fcab018. doi:10.1093/braincomms/fcab018
14. Kodal LS, Witt AM, Pedersen BS, Aagaard MM, Dysgaard T. Prognostic value of neurofilament light in blood in patients with polyneuropathy: a systematic review. *J Peripher Nerv Syst*. 2024;29(1):17-27. doi:10.1111/jns.12608
15. Benkert P, Meier S, Schaedelin S, et al. Serum neurofilament light chain for individual prognostication of disease activity in people with multiple sclerosis: a retrospective modelling and validation study. *Lancet Neurol*. 2022;21(3):246-257. doi:10.1016/S1474-4422(22)00009-6
16. van den Bergh PYK, Hadden RDM, Bouche P, et al. European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society - first revision. *Eur J Neurol*. 2010;17(3):356-363. doi:10.1111/j.1468-1331.2009.02930.x
17. Stöhr M, Pfister R, Reilich P. *Klinische Elektromyographie Und Neurographie: Lehrbuch Und Atlas*. Kohlhammer Verlag; 2022.
18. Grüter T, Motte J, Bulut Y, et al. Axonal damage determines clinical disability in chronic inflammatory demyelinating polyradiculoneuropathy (CIDP): a prospective cohort study of different CIDP subtypes and disease stages. *Eur J Neurol*. 2022;29(2):583-592. doi:10.1111/ene.15156
19. Appeltshauser L, Junghof H, Messinger J, et al. Anti-pan-neurofascin antibodies induce subclass-related complement activation and nodo-paranodal damage. *Brain*. 2023;146(5):1932-1949. doi:10.1093/brain/awac418
20. Delmont E, Manso C, Querol L, et al. Autoantibodies to nodal isoforms of neurofascin in chronic inflammatory demyelinating polyneuropathy. *Brain*. 2017;140(7):1851-1858. doi:10.1093/brain/awx124
21. Bischof A, Manigold T, Barro C, et al. Serum neurofilament light chain: a biomarker of neuronal injury in vasculitic neuropathy. *Ann Rheum Dis*. 2018;77(7):1093-1094. doi:10.1136/annrheumdis-2017-212045
22. Keddie S, Smyth D, Keh RYS, et al. Peripherin is a biomarker of axonal damage in peripheral nervous system disease. *Brain*. 2023;146(11):4562-4573. doi:10.1093/brain/awad234
23. Doneddu PE, Cocito D, Manganelli F, et al. Atypical CIDP: diagnostic criteria, progression and treatment response. Data from the Italian CIDP Database. *J Neurol Neurosurg Psychiatry*. 2019;90(2):125-132. doi:10.1136/jnnp-2018-318714
24. Llauradó A, García-Carmona C, Restrepo-Vera JL, et al. Usefulness of serum neurofilament light chain in chronic inflammatory demyelinating polyradiculoneuropathy. *J Neurol Sci*. 2025;470:123397. doi:10.1016/j.jns.2025.123397
25. Schumacher A, Hieke A, Spenner M, et al. Early therapy initiation is crucial in chronic inflammatory demyelinating polyneuropathy: prospective multimodal data from the German INHIBIT registry. *J Neurol*. 2025;272(1):100. doi:10.1007/s00415-024-12860-w
26. Quint P, Schroeter CB, Kohle F, et al. Preventing long-term disability in CIDP: the role of timely diagnosis and treatment monitoring in a multicenter CIDP cohort. *J Neurol*. 2024;271(9):5930-5943. doi:10.1007/s00415-024-12548-1