



Siriraj Medical Journal

The Official Journal of Faculty of Medicine Siriraj Hospital, Mahidol University

The World-leading Biomedical Science of Thailand

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Siriraj Medical Journal
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MONTHLY
ORIGINAL ARTICLE
REVIEW ARTICLE

Neurofilament

Neurofilament	Subunit	Approximate Size
NFH	Rod	200 kDa
NFM	Rod	155 kDa
NFL	Rod	68 kDa
g-Int	Rod	66 kDa
	Tail	
	E	
	KSP	
	KSP2	
	SP4E	

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Full Issue

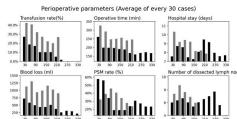
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Original Article



(<https://he02.tci-thaijo.org/index.php/sirirajmedj/article/view/259456class=1>)

Paradigm Shift from Open Surgery to Minimally Invasive Surgery in Three Approaches for Radical Prostatectomy: Comparing Outcomes and Learning Curves (<https://he02.tci-thaijo.org/index.php/sirirajmedj/article/view/259456>)

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Risk Factor of Proximal Lag Screw Cut-Out After Cephalomedullary Nail Fixation in Trochanteric Femoral Fractures: A Retrospective Analytic Study (<https://he02.tci-thaijo.org/index.php/sirirajmedj/article/view/259455>)

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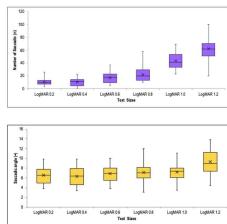
TABLE 1: Years of experience at Siriraj Hospital of administrators, surgical staff, and surgical residents.

Year	N	%	Experience at Siriraj Hospital			
			As an administrator	As a surgical staff	As a surgical resident	
≤ 5	4	10.0	6	25.0	1	25.0
6-10	6	15.0	2	7.7	2	33.3
11-15	6	15.0	5	18.8	3	50.0
16-20	2	5.0	5	18.8	4	33.3
≥ 21	6	15.0	7	26.7	5	33.3
Total	30	100.0	30	100.0	14	100.0

(<https://he02.tci-thaijo.org/index.php/sirirajmedj/article/view/259452class=1>)

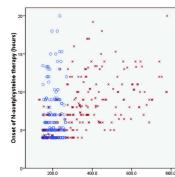
Comparative Study Regarding Autonomy of Final-Year Surgical Residents: A Case Study of Perception among Surgical Residents, Surgical Staff, Administrators, and Patients at Siriraj University Hospital (<https://he02.tci-thaijo.org/index.php/sirirajmedj/article/view/259452>)

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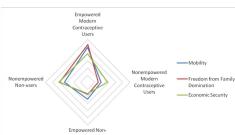
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Predicting the Need for Continuation of N-acetylcysteine Treatment among Acute Paracetamol Overdose Patients with Psi Parameter (<https://he02.tci-thaijo.org/index.php/sirirajmedj/article/view/259444>)

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Determinants of Modern Contraceptive Usage among Married Women A Mixed-Methods Study in a Rural Community of India (<https://he02.tci-thaijo.org/index.php/sirirajmedj/article/view/259553>)

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Simulated Surgical Model Design for Myringotomy and Tympanostomy Tube Insertion in Children using Medical Image Processing and 3D-Printing Technologies (<https://he02.tci-thaijo.org/index.php/sirirajmedj/article/view/259452>)



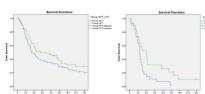
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Survival Analysis of and Prognostic Factors for Metastatic Epidural Spinal Cord Compression Compared between Preoperative Known and Unknown Primary Tumors (<https://he02.tci-thaijo.org/index.php/sirirajmedj/article/view/259573>)

Nitiwut Saenmanot, Monchai Ruangchainikom, Thanase Ariyawatkul, Ekkapoj Korwutthikulrangsri, Soraya Saenmanot, Panya Luksanapruksa, Werasak Sutipornpalangkul, Sirichai Wilartratsami, Chatupon Chotigavanichaya
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Variable	Laparoscopy		Direct Colostomy		Total (n=180)	P-value
	n (%)	p (%)	n (%)	p (%)		
Gender, n (%)	90 (50.0%)	90 (50.0%)	90 (50.0%)	90 (50.0%)	180 (100.0%)	0.711
Age, years	30.0 (18.0-48.0)	30.0 (18.0-48.0)	30.0 (18.0-48.0)	30.0 (18.0-48.0)	30.0 (18.0-48.0)	0.107
Level of obstruction, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.107
Anorectal Transposition	3 (1.7%)	0 (0.0%)	3 (1.7%)	0 (0.0%)	3 (1.7%)	0.107
Descending	2 (1.1%)	1 (0.6%)	2 (1.1%)	1 (0.6%)	3 (1.7%)	0.107
Urgency	1 (0.6%)	0 (0.0%)	1 (0.6%)	0 (0.0%)	1 (0.6%)	0.107
Type of Metastasis, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.107
Metastatic Colorectal Tumors	30 (16.7%)	30 (16.7%)	30 (16.7%)	30 (16.7%)	30 (16.7%)	0.107
Perirectal	12 (6.7%)	0 (0.0%)	12 (6.7%)	0 (0.0%)	12 (6.7%)	0.107
Extensive	18 (10.0%)	0 (0.0%)	18 (10.0%)	0 (0.0%)	18 (10.0%)	0.107
Hepatocellular Carcinoma	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.107
Hepatocarcinoma	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.107
Pancreatic Carcinoma	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.107
Pancreatic Adenocarcinoma	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.107
Pancreatic Ductal Adenocarcinoma	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.107
Pancreatic Cystic Tumor	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.107
Pancreatic Carcinoma	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.107
Pancreatic Adenoma	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.107
Pancreatic Carcinoid	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.107
Gastric Cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.107

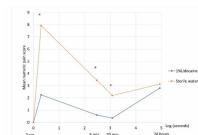
Types and Levels of Colostomy in Children with Anorectal Malformation (<https://he02.tci-thaijo.org/index.php/sirirajmedj/article/view/259551>)

Ravit Ruangtrakool, Cholapa Pintawekiat
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Lidocaine Reducing Pain from Benzathine Penicillin Injection: A Controlled Trial (<https://he02.tci-thaijo.org/index.php/sirirajmedj/article/view/259550>)

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Review Article

TABLE I. Differential diagnosis of postoperative cognitive dysfunction.			
Parameters	Definition	POCO	Normal
Age	Older than 60 years	Normal to 6 months	Normal to 6 years
Location	Direct to remote	Worse in memory	Memory to intact
Associated	None	Normal	Normal
Coincident Symptom	Altered	Normal	Normal
Postoperative	Persistent after the surgery	Memory decline or cognitive	Mental decline associated with the surgery
	or transient	disturbance	before and within
			immediately after the procedure
Activities of Daily Living	Normal and functional	No rise of functional decline	No rise of functional decline
Assessment POCO = Postoperative cognitive dysfunction			

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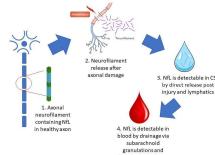
An Overview on Postoperative Cognitive Dysfunction; Pathophysiology, Risk Factors, Prevention and Treatment (<https://he02.tci-thaijo.org/index.php/sirirajmedj/article/view/259558>)

Thanathip Suenghataiphorn, Sakdipat Songwisit, Surapa Tornsatitkul, Pawit Somnuke
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Serum Neurofilament Light Chain: A Potential Biomarker for Peripheral Neuropathy (<https://he02.tci-thaijo.org/index.php/sirirajmedj/article/view/259448>)

I Putu Eka Widhyadharma, Eric Hartono Tedyanto
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Serum Neurofilament Light Chain: A Potential Biomarker for Peripheral Neuropathy

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ABSTRACT

In some neurological diseases, advanced examinations can be used as diagnostic tools. Several indicators have also been discovered that can be used to assess the severity of neuronal damage and neurological disease progression. Neurofilament light chain (NfL) is a cytoskeleton protein that makes up the structure of neuron axons and is released when a neuron is injured, allowing it to assess neuronal injury severity. NfL was first used to diagnose central nervous system disorders like dementia, multiple sclerosis, and other neurodegenerative diseases. But, NfL levels have also been elevated in peripheral nervous system disorders, like in several neuropathic conditions, including amyloid neuropathy, HIV-associated neuropathy, diabetic peripheral neuropathy, leprosy neuropathy, and other neuropathy, according to various investigations. Theoretically, all abnormalities induced by axonal injury will increase blood NfL levels, allowing NfL testing to be utilized as a measurement tool. NfL levels can also be a predictive indicator to monitor treatment efficacy and peripheral neuropathy progression.

Keywords: Biomarker; neurofilament light chain; peripheral neuropathy; prognostic (Siriraj Med J 2022; 74: 714-720)

INTRODUCTION

In recent years, neurology has made significant technological innovations. A variety of neuroimaging methods can generate accurate images of the brain. Moreover, various biomarkers have been developed which may be used in clinical trials to estimate the level of neuronal damage. One of them is the neurofilament light chain (NfL). NfL is released into the CSF and bloodstream whenever there is damage to neurons.¹

Since it is an indicator of axonal damage, the serum neurofilament light chain (NfL) is a potential diagnostic in neurological diseases. Previously, NfL has only been detected in CSF. The NfL can still be detected in the blood due to the new advanced technologies, making it simpler to detect and avoiding traumatic procedures like a lumbar puncture. A neurologist can use NfL as a prospective diagnostic as an accurate sign of nerve

injury. If the cardiologist has troponin, the neurologist has the neurofilament light chain (NfL).²

NfL concentrations in the normal population are rarely reported. Tobias et al revealed that NfL levels in normal populations are 7.3 (± 3) pg/mL in serum and 416 (± 191) pg/mL in CSF. In patients with Multiple Sclerosis, NfL levels are 16.4 (± 14.4) pg/mL in serum and 2368 (± 1947) pg/mL in CSF. The levels of NfL are affected by age, BMI, and renal function. The association between age and NfL concentration was positive ($r = 0.325$; p-value <0.0001), while the correlation between BMI and NfL concentration was negative ($r = 0.227$; p-value <0.0001). No significant differences exist between NfL concentration and gender. In addition, there was a strong correlation between NF-L levels and renal function. NfL concentration and eGFR were also found to have a very strong connection ($r = -0.492$; p-value <0.0001).³⁻⁵

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CSF and serum NfL levels were higher in patients with a central or peripheral nervous system injury. This increase has been linked to neurological diseases, according to certain studies. The NfL can also be used to predict future outcomes. Because it can be easily detected and non-invasively in the blood, NfL is a promising biomarker for monitoring the progression of neurological diseases and evaluating the efficacy of therapy.⁶

Peripheral neuropathy affects approximately 2.4 percent of the population, with symptoms varying depending on what type of nerve fiber is affected, the type of neuron injury, and the severity of the injury. Peripheral neuropathy is most commonly caused by diabetes. However, HIV can also directly or indirectly induce peripheral neuropathy through antiretroviral (ARV) medications. Systemic disease, infection, and malnutrition are also all potential causes of peripheral neuropathy.⁷

A neurologist might conduct an electrophysiological evaluation of nerve conduction velocity to diagnose peripheral neuropathy. However, nerve conduction velocity may not be able to accurately assess the severity and progression of neuropathy in some conditions, requiring the use of additional biomarkers to determine prognostic value. On the other hand, NfL has lately undergone massive research and can be utilized as a biomarker for peripheral nerve injury. Serum NfL levels are known to be elevated in cases of peripheral neuropathy and correlate with disease severity.⁸ In this review, we provide the role of the neurofilament light chain (NfL) as a biomarker of peripheral neuropathy.

Neurofilament light chain (NfL)

The essential features of neurons are neurofilaments, built up of protein triplets and present on nerve axons (Fig 1). The neurofilament core cannot functionally work without the neurofilament light chain (NfL) subunit. Almost every neuron component contains the protein neurofilament light chain (NfL). The diameter and speed of nerve conduction from peripheral nerves are determined by NfL accumulation, linked to axon growth during myelination.⁹ Depending on the severity of axonal damage in peripheral nerves, NfL can be released into the extracellular space and bloodstream. An apophagocytic process releases NfL into the CSF and bloodstream when neurons in the central nervous system are damaged. NfL will enter the CSF through direct drainage and then enter the bloodstream through arachnoid granulation and lymphatic flow in the subarachnoid space, making it detectable in both the CSF and the blood.¹⁰ According to some studies, the amount of NfL in CSF is 500 times higher than in blood because CSF is directly related to the central nervous system. NfL concentrations in the blood are too low to be detected by an ELISA test. Thanks to recent technological advancements, a new method, SIMOA (Single-Molecule Assay (SiMoA), has been developed to detect NfL down to a single-digit picogram per millimeter unit.¹¹

NfL in neurological cases

Axonal damage in the central and peripheral nervous systems, such as stroke, head trauma, multiple sclerosis, ALS, Alzheimer's disease, frontotemporal dementia,

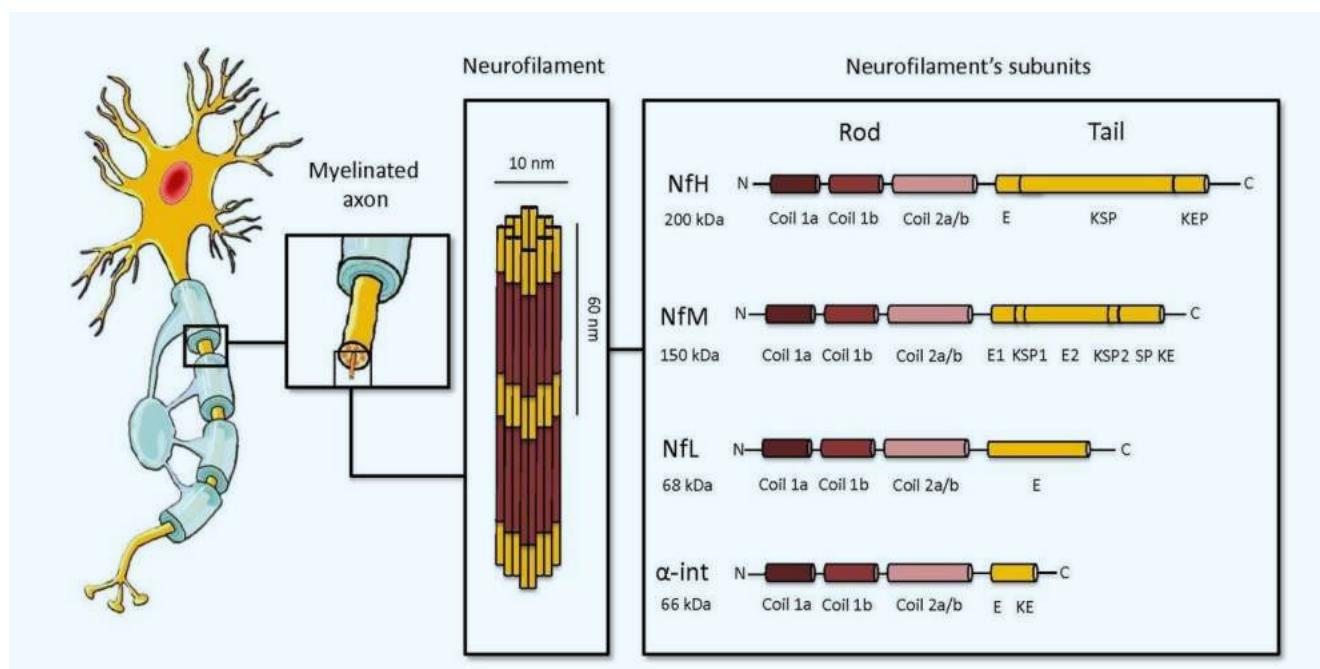


Fig 1. Structure of neurofilament.⁶

and peripheral neuropathy, can be identified by NfL measurement. Previous studies linked increased NfL levels in CSF and serum to neurodegenerative and neuroinflammatory processes, indicating demyelination and axonal damage.¹²⁻¹⁶

Neurological patients have much greater NfL levels in their CSF and blood than healthy or non-neurological patients. NfL is a test that can identify neurological problems caused by axonal damage. It can tell the difference between varying degrees of axonal damage, progression, and whether or not it is a neurodegenerative condition. As a result, the NfL examination is utilized as a biomarker to validate the diagnosis after a full neurological examination or other biomarker and neuroimaging procedures.⁶ In the event of peripheral neuropathy, NfL can be utilized as a non-invasive diagnostic technique to determine therapy success and progression.⁸

It is unclear how long the duration of NfL levels increases in patients with peripheral neuropathy. In studies on multiple sclerosis, traumatic brain injury, and stroke, NfL levels peak 3–4 weeks after a clinical relapse and remain elevated for 6–12 months. Further studies on how long NfL levels increase in peripheral neuropathy need to be done for prognostic purposes.¹⁷

NfL in peripheral neuropathy

Peripheral neuropathy has become a global health concern, affecting 2.4 percent of the world's population, or around 10 million people in the European Union and 7 million in the United States. Measurement of nerve conduction velocity is the gold standard for diagnosing

peripheral neuropathy. However, it cannot be used as a monitor for the success of therapy or disease progression in some cases. As a result, a peripheral nerve damage biomarker is required. On the other hand, NfL has recently undergone extensive research and can be used as a biomarker for peripheral nerve damage. NfL levels have been shown to increase in peripheral neuropathy patients' blood and correlate with disease severity, implying that the NfL is involved in disease progression and can be used as a prognostic factor in peripheral nerve damage.^{8,18}

Neuronal neurofilament breakdown is thought to use a combination of ubiquitin-mediated proteasomal and apophagocytotic mechanisms. Based on the transport of other CNS-degraded proteins, it is likely that neurofilament fragments drain directly into CSF and blood via numerous pathways. These include lymphatic outflow into subarachnoid and perivascular regions and direct draining into CSF and blood via arachnoid granulations. Once NfL enters the bloodstream, the half-life is a crucial factor with consequences for disease activity monitoring frequency. In a longitudinal study of NfL levels before and after implantation of an intrathecal catheter, NfL levels in both CSF and serum peaked one month after surgery and returned to baseline six to nine months later.²

Other biomarkers besides NfL can be used to diagnose peripheral neuropathy, including Brain Derived Neurotrophic Factor (BDNF), Nerve Growth Factor (NGF), and other inflammatory markers such as IL-1, 6,10, 18, and TNF-alpha. Low BDNF levels were correlated with CIPN in 91 multiple myeloma patients treated

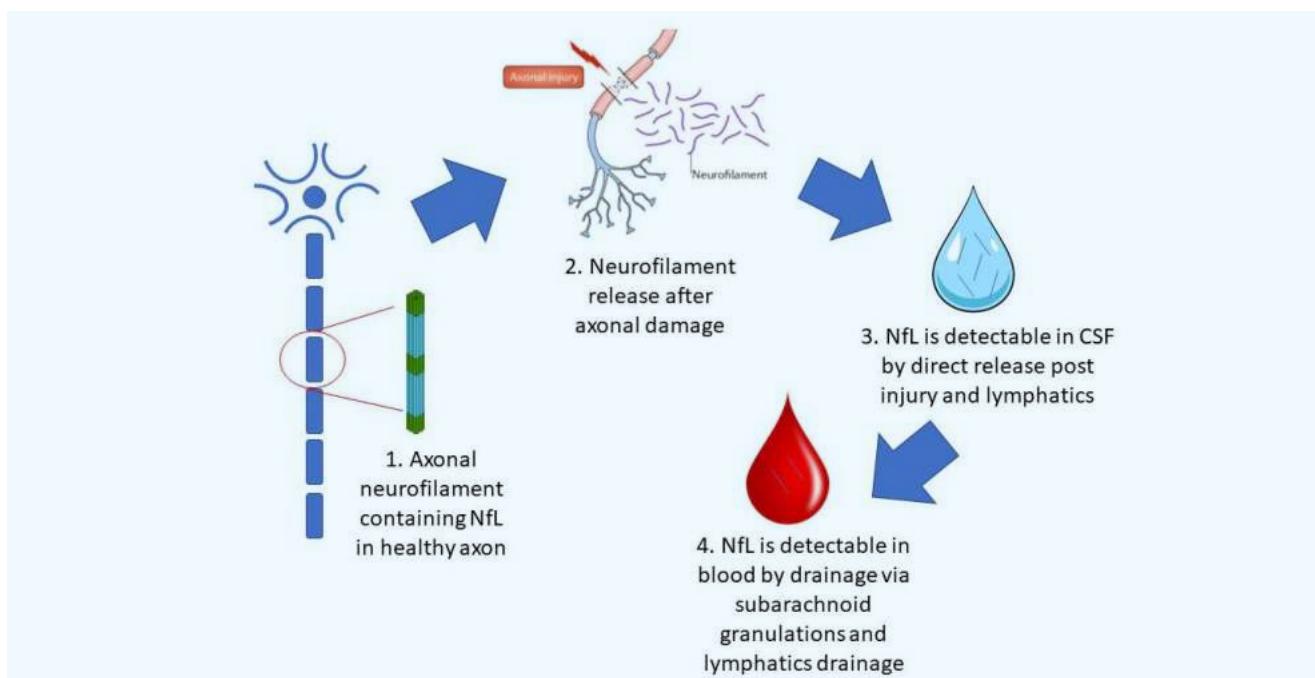


Fig 2. Pathophysiology of neurofilament light chain in cerebrospinal fluid (CSF) and blood.

with bortezomib, and a cut-point of 9.11 ng/ml was 76% sensitive and 71% specific for identifying Chemotherapy-induced Peripheral Neuropathy (CIPN). Nonetheless, another study found no correlation between BDNF and the incidence of CIPN. In one investigation, a correlation was shown between decreasing NGF and the severity of neuropathy as measured by nerve conduction velocity testing. High levels of IFN-, IL-1, and IL-8, but low levels of IL-10 and IL-6, were linked to peripheral neuropathy symptoms. Due to the inconsistency and expense of these biomarkers, NfL testing is recommended to monitor peripheral neuropathy.¹⁹

Sandelius et al. suggested that the cut-off value of NfL for peripheral neuropathy was 20 pg/mL with a sensitivity of 71% and specificity of 75%. Increased serum NfL concentration is not specific to peripheral neuropathy because other neurological disorders such as multiple sclerosis, Alzheimer's disease, stroke, and Amyotrophic Lateral Sclerosis (ALS) also reported increases. NfL is not useful for diagnosis, but it may be useful to measure axonal damage and could serve as a biomarker of progressivity of the disease for monitoring and response to treatment. NfL is sensitive to detecting axonal damage and correlates with disease severity and progressivity.¹⁸

Several studies have reported elevated levels of NfL in amyloid neuropathy, HIV-associated neuropathy, diabetic peripheral neuropathy, chemotherapy-induced peripheral neuropathy, and pyridoxine-induced sensory neuropathy.

Amyloid neuropathy

Amyloidosis patients with polyneuropathy experience axonal degeneration, which results in elevated serum NfL levels. Axonal degeneration is caused by the accumulation of amyloid fibrils in the endoneurium and direct toxicity to the nerve's prefibrillar oligomers.²⁰⁻²² Patients with symptomatic polyneuropathy, as well as those who are asymptomatic, have elevated serum NfL levels. Serum NfL levels can be used as a marker for early-stage axonal damage in asymptomatic or subclinical amyloidosis, making it essential to diagnose, treat, and monitor the progress and success of amyloidosis therapy.²³ The AUC between asymptomatic and symptomatic amyloid neuropathy patients was 0.99 (p .001), and a NfL concentration of 10.6 pg/mL distinguished these individuals with a sensitivity of 96.2% and a specificity of 93.8%.²⁰ Serum NfL levels increase the most in patients with abnormal EMG results. This demonstrates that serum NfL is a sensitive marker for early detection of polyneuropathy and is strongly associated with the disease.¹⁴

HIV-associated neuropathy

HIV-associated neuropathy manifests as distal symmetrical polyneuropathy and toxic antiretroviral neuropathy (ATN), which is difficult to distinguish clinically and electrophysiologically regardless of the use of antiretroviral drugs or the onset of symptoms. HIV-associated neuropathy is linked to the patient's viral load and CD4+ cell count. The use of dNRTIs like stavudine, didanosine, or zalcitabine has been linked to ATN. After antiretroviral therapy, the symptoms of HIV-related polyneuropathy improve as the viral load decreases. After a year of ARV treatment, the symptoms of ATN will worsen.²⁴

NfL is a structural component of myelinated axons that have been used as a marker of axonal damage in neurodegenerative diseases in several studies. Axonal damage also occurs in HIV-associated neuropathy, but research on elevated serum NfL levels in HIV-associated neuropathy is uncommon. The HIV in Dementia study is the most widely conducted. Compared to HIV patients without dementia, NfL levels were significantly higher in HIV patients with dementia. The levels of plasma NfL and CSF NfL did not differ significantly. Damian et al. conducted a study to see if NfL levels were elevated in HIV-associated neuropathy patients. The researchers discovered an increase in NfL levels in both CSF and serum in 26 of 54 patients with neuropathy, which correlates to the severity of the neuropathy.²⁵ NfL levels are not only used as markers of damage to the central nervous system but also in the peripheral nervous system, such as neuropathy, according to these studies.²⁶

Chemotherapy induced peripheral neuropathy (CIPN)

CIPN is a side effect of chemotherapy in some cancers. Proper diagnosis, treatment, and dosage adjustments are required to avoid permanent nerve damage. Because CIPN is an axonopathy, it can mimic the symptoms of polyneuropathy. Previous research has discovered that elevated serum NfL levels are linked to peripheral neuropathy and the severity of nerve damage, allowing NfL levels to be measured in CIPN patients. In a mouse model given the cytostatic drug vincristine (VCR) 0.2 mg/kg intravenously four times per week, serum NfL levels increased fourfold, with signs of axonopathy on neurophysiological and pathological examinations. The presence of the NfL in the blood can determine the severity of CIPN.²⁷⁻²⁹

Other chemotherapy drugs, such as oxaliplatin, can cause neuronal cell death and neuropathy in the dorsal ganglion. One study found a link between serum NfL levels and changes in nerve amplitude after treatment with

oxaliplatin. Serum NfL levels were significantly higher in 5 patients with grade 3 OIPN (oxaliplatin-induced peripheral neuropathy) than in grades 0-2 (80 percent sensitivity and 86 percent specificity with a cut-off value of 195 pg/mL). Based on the findings of these studies, serum NfL can be used as a monitor for the severity of OIPN.³⁰

Diabetic peripheral neuropathy (DPN)

An observational study used Serum NfL as a non-invasive diagnostic tool to detect diabetic peripheral neuropathy and its progression. NfL levels are related to the neuropathy disability score (NDS) and decreased nerve conduction velocity in some nerves. The AUC for serum NfL was 0.564, and the DPN cut-off point was 12.6 pg/ml. NfL is also associated with the hyperalgesia phenotype and is positively correlated with the severity of DPN.^{31,32}

NfL mRNA levels have also been elevated in prediabetic patients with peripheral neuropathy. This supports the hypothesis that NfL mRNA levels are significantly higher in prediabetic patients when small-diameter nociceptive afferent C fibers are interfered with in hyperglycemic conditions, causing axon damage and neuropathic pain symptoms. This level is positively correlated with DN4 questionnaire score.^{9,33}

Leprosy neuropathy

Mycobacterium leprae can damage both myelinated and unmyelinated nerve fibers. Patients with leprosy may

develop painful neuropathy symptoms. The pathogenesis of neuropathy in leprosy includes infection of the Schwann cells, demyelination, and damage to the axons, leading to atrophy. In tuberculoid and borderline leprosy, axon damage is caused by inflammation of the endoneurial membrane, which destroys nerve structures and causes nerve damage. According to the results of a nerve biopsy, axons and myelin are lost in patients with leprosy. Electromyography also revealed axonal polyneuropathy. Axon damage is a focus of research into the mechanism of leprosy neuropathy. Biomarkers such as NfL can be used with other tests to help determine prognosis and treatment success.^{35,36}

Post-herpetic neuralgia

After the reactivation of the varicella-zoster virus, which damages the cell body and axons, post-herpetic neuralgia (PHN) develops. The pathology of PHN is associated with peripheral axonal damage, sensory neuron degeneration, and dorsal horn atrophy. However, several theories suggest that after viral reactivation, axonal damage occurs due to inflammation in PHN. The role of NfL in post-herpetic neuralgia has rarely been studied. More research on the NfL as a biomarker of post-herpetic neuralgia is needed.³⁷

Pyridoxine-induced sensory neuropathy (PISN)

According to a study, NfL levels in the CSF and blood increased on day four after rats received pyridoxine therapy. Pyridoxine's primary target is the cell body of

TABLE 1. Summarize how NfL is used in various peripheral neuropathy diseases.

Disease	NfL levels	Indication	Sensitivity	Specificity	AUC	Reference
Peripheral neuropathy	20 pg/mL	Prognostic	71%	75%	0.755	¹⁸
Amyloid neuropathy	10.6 pg/mL	Prognostic	96.2%	93.8%	0.99	²⁰
CIPN	195 pg/mL	Prognostic, treatment response	80%	86%	N/A	³⁰
Diabetic peripheral neuropathy	12.6 pg/ml	Prognostic, treatment response	77.6%	86.3%	0.564	³²
ALS	93 pg/ml	Prognostic	80.5%	90.9%	0.85	³⁸
Post-stroke cognitive impairment	46.12 pg/ml	Prognostic	71%	81.5%	0.785	³⁹

DRG neurons, which is followed by secondary nerve fiber degeneration. NfL is released directly from the DRG to the CSF via the subarachnoid space from the neuronal cell body and surrounding nerve fibers.³⁴

Summarize

As described above, NfL can help determine the progression and response to peripheral neuropathy treatment. Here we provide a table summarizing how NfL is used in various peripheral neuropathy diseases discussed in the manuscript (**Table 1**). We also compared diseases such as ALS and post-stroke cognitive impairment. No studies determine the cut-off value for some types of peripheral neuropathy. Further research on cut-off NfL levels needs to be done.

CONCLUSION

Serum NfL can be used as a diagnostic tool for peripheral neuropathy after a careful history and physical examination. In addition, NfL levels can also be used as a monitor for the success of therapy and the progression of peripheral neuropathy to be used as a prognostic value. Further studies regarding when serum NfL levels begin to elevate, how long they last, and clear cut-off points for each type of peripheral neuropathy are needed to strengthen the diagnostic value and specificity of serum NfL.

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REFERENCES

1. Barro C, Chitnis T, Weiner HL. Blood neurofilament light: a critical review of its application to neurologic disease. *Ann Clin Transl Neurol.* 2020;7(12):2508-23.
2. Thebault S, Booth RA, Freedman MS. Blood neurofilament light chain: The neurologist's troponin? *Biomedicines.* 2020;8(11): 1-11.
3. Sejbaek T, Mendoza JP, Penner N, Madsen JS, Olsen DA, Illes Z. Comparison of neurofilament light chain results between two independent facilities. *BMJ Neurol Open.* 2020;2(2):e000063.
4. Ladang A, Kovacs S, Lengelé L, Locquet M, Reginster JY, Bruyère O, et al. Neurofilament light chain concentration in an aging population. *Aging Clin Exp Res.* 2022;34(2):331-9.
5. Bäckström D, Linder J, Jakobson Mo S, Riklund K, Zetterberg H, Blennow K, et al. NfL as a biomarker for neurodegeneration and survival in Parkinson disease. *Neurology.* 2020;95(7):e827-38.
6. Gaetani L, Blennow K, Calabresi P, Di Filippo M, Parnetti L, Zetterberg H. Neurofilament light chain as a biomarker in neurological disorders. *J Neurol Neurosurg Psychiatry.* 2019; 90(8):870-81.
7. Benn M. Peripheral Neuropathy-Time for Better Biomarkers? *Clin Chem.* 2020;66(5):638-40.
8. Remiche G, Kadhim H, Maris C, Mavroudakis N. Peripheral neuropathies, from diagnosis to treatment, review of the literature and lessons from the local experience. *Rev Med Brux.* 2013;34(4):211-20.
9. Celikbilek A, Tanik N, Sabah S, Borekci E, Akyol L, Ak H, et al. Elevated neurofilament light chain (NFL) mRNA levels in prediabetic peripheral neuropathy. *Mol Biol Rep.* 2014;41(6): 4017-22.
10. Thebault S, Tessier DR, Lee H, Bowman M, Bar-Or A, Arnold DL, et al. High serum neurofilament light chain normalizes after hematopoietic stem cell transplantation for MS. *Neurol Neuroimmunol Neuroinflammation.* 2019;6(5):e598.
11. Wilson DH, Rissin DM, Kan CW, Fournier DR, Piech T, Campbell TG, et al. The Simoa HD-1 Analyzer: A Novel Fully Automated Digital Immunoassay Analyzer with Single-Molecule Sensitivity and Multiplexing. *J Lab Autom.* 2016;21(4):533-47.
12. Jordanova A, De Jonghe P, Boerkel CF, Takashima H, De Vriendt E, Ceuterick C, et al. Mutations in the neurofilament light chain gene (NEFL) cause early onset severe Charcot-Marie-Tooth disease. *Brain.* 2003;126(3):590-7.
13. Kuchel GA, Poon T, Irshad K, Richard C, Julien JP, Cowen T. Decreased neurofilament gene expression is an index of selective axonal hypotrophy in ageing. *Neuroreport.* 1996;7(8):1353-9.
14. Perrot R, Berges R, Bocquet A, Eyer J. Review of the multiple aspects of neurofilament functions, and their possible contribution to neurodegeneration. *Mol Neurobiol.* 2008;38(1):27-65.
15. Disanto G, Barro C, Benkert P, Naegelin Y, Schädelin S, Giardullo A, et al. Serum Neurofilament light: A biomarker of neuronal damage in multiple sclerosis. *Ann Neurol.* 2017;81(6):857-70.
16. Landqvist Waldö M, Frizzell Santillo A, Passant U, Zetterberg H, Rosengren L, Nilsson C, et al. Cerebrospinal fluid neurofilament light chain protein levels in subtypes of frontotemporal dementia. *BMC Neurol.* 2013;13.
17. Ferreira-Atuesta C, Reyes S, Giovanonni G, Gnanapavan S. The Evolution of Neurofilament Light Chain in Multiple Sclerosis. *Front Neurosci.* 2021;15:642384.
18. Sandelius Å, Zetterberg H, Blennow K, Adiutori R, Malaspina A, Laura M, et al. Plasma neurofilament light chain concentration in the inherited peripheral neuropathies. *Neurology.* 2018;90(6): e518-24.
19. Rodwin RL, Siddiq NZ, Ehrlich BE, Lustberg MB. Biomarkers of Chemotherapy-Induced Peripheral Neuropathy: Current Status and Future Directions. *Front Pain Res. (Lausanne).* 2022;3:864910.
20. Maia LF, Maceski A, Conceição I, Obici L, Magalhães R, Cortese A, et al. Plasma neurofilament light chain: an early biomarker for hereditary ATTR amyloid polyneuropathy. *Amyloid.* 2020;27(2): 97-102.
21. Kapoor M, Foiani M, Heslegrave A, Zetterberg H, Lunn MP, Malaspina A, et al. Plasma neurofilament light chain concentration is increased and correlates with the severity of neuropathy in hereditary transthyretin amyloidosis. *J Peripher Nerv Syst.* 2019;24(4):314-9.
22. Reilly MM, King RHM. Familial Amyloid Polyneuropathy. *Brain Pathol.* 1993;3(2):165-76.
23. Shin SC, Robinson-Papp J. Amyloid neuropathies. *Mt Sinai J Med.* 2012;79(6):733-48.
24. Amruth G, Praveen-kumar S, Nataraju B, Nagaraja BS. HIV associated sensory neuropathy. *J Clin Diagn Res.* 2014;8(7): MC04-7.
25. Damian A, Skolasky R, Demsky C, McArthur J, Sacktor N, Zetterberg H, et al. Neurofilament light chain protein levels in HIV positive subjects with neuropathy. *Neurology.* 2019;92(15)

- Supplement 1).
26. Gisslén M, Price RW, Andreasson U, Norgren N, Nilsson S, Hagberg L, et al. Plasma Concentration of the Neurofilament Light Protein (NFL) is a Biomarker of CNS Injury in HIV Infection: A Cross-Sectional Study. *EBioMedicine*. 2015;3:135-40.
 27. Cavaletti G, Marmiroli P. Chemotherapy-induced peripheral neurotoxicity. *Nat Rev Neurol*. 2010;6(12):657–66.
 28. Cavaletti G, Cornblath DR, Merkies ISJ, Postma TJ, Rossi E, Frigeni B, et al. The chemotherapy-induced peripheral neuropathy outcome measures standardization study: From consensus to the first validity and reliability findings. *Ann Oncol*. 2013;24(2): 454–62.
 29. Meregalli C, Fumagalli G, Alberti P, Canta A, Carozzi VA, Chiorazzi A, et al. Neurofilament light chain as disease biomarker in a rodent model of chemotherapy induced peripheral neuropathy. *Exp Neurol*. 2018;307:129-32.
 30. Kim SH, Choi MK, Park NY, Hyun JW, Lee MY, Kim HJ, et al. Serum neurofilament light chain levels as a biomarker of neuroaxonal injury and severity of oxaliplatin-induced peripheral neuropathy. *Sci Rep*. 2020;10(1):7995.
 31. Cai L, Huang J. Neurofilament light chain as a biological marker for multiple sclerosis: A meta-analysis study. *Neuropsychiatr Dis Treat*. 2018;14:2241-54.
 32. Morgenstern J, Groener JB, Jende JME, Kurz FT, Strom A, Göpfert J, et al. Neuron-specific biomarkers predict hypo- and hyperalgesia in individuals with diabetic peripheral neuropathy. *Diabetologia*. 2021;64(12):2843-55.
 33. Singleton JR, Smith AG, Bromberg MB. Increased prevalence of impaired glucose tolerance in patients with painful sensory neuropathy. *Diabetes Care*. 2001;24(8):1448-53.
 34. Sano T, Masuda Y, Yasuno H, Shinozawa T, Watanabe T, Kakehi M. Blood Neurofilament Light Chain as a Potential Biomarker for Central and Peripheral Nervous Toxicity in Rats. *Toxicol Sci*. 2021;185(1):10-8.
 35. Nascimento OJM. Leprosy neuropathy: Clinical presentations. *Arq Neuropsiquiatr*. 2013;71(9 B):661-6.
 36. Hassan R, Hui M, Sireesha Y, Afshan J, Meena AK, Uppin MS. Understanding demyelination in leprosy neuropathy: A nerve biopsy analysis. *Ann Indian Acad Neurol*. 2020;23(6): 829-32.
 37. Bennett GJ, Peter CPN. Herpes zoster and postherpetic neuralgia: Past, present and future. *Pain Res Manag*. 2009;14(4):275-82.
 38. Verde F, Otto M, Silani V. Neurofilament Light Chain as Biomarker for Amyotrophic Lateral Sclerosis and Frontotemporal Dementia. *Front Neurosci*. 2021;15:679199.
 39. Wang Z, Wang R, Li Y, Li M, Zhang Y, Jiang L, et al. Plasma Neurofilament Light Chain as a Predictive Biomarker for Post-stroke Cognitive Impairment: A Prospective Cohort Study. *Front Aging Neurosci*. 2021;13:631738.