Title: Blood Neurofilament Light Chain Measurement toward Clinical Application: A Review

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Abstract

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paved the way for assessing neuroaxonal injury using blood tests [3-5].

Blood NFL level in neurological disease

According to previous reports, blood NFL levels are elevated in various neurologic conditions, including multiple sclerosis (MS), stroke, amyotrophic lateral sclerosis (ALS), frontotemporal dementia (FTD), and traumatic brain injury (TBI). Blood NFL levels can also be used to monitor disease severity and predict long-term outcomes. In speci c situations, it may help support a di erential diagnosis. e most studied neurological disease with blood NFL analysis is MS.

e current role of biomarkers to monitor neuronal injury is limited. Usually, it is evaluated by MRI, but its high cost and long scan time limit its utility. Blood NFL level elevation is reported to be correlated with relapse of symptoms, as well as new lesions on MRI scans, in both progressive and relapsing MS in many studies [3, 5-10]. e decrease in blood NFL levels was observed a er treatment, indicating its potential for monitoring treatment e ect. [8,11,12] Blood NFL level responds to anti-in ammatory therapies 3 to 6 months a er their initiation, with its degree of di erence re ecting treatment e cacy. [7] Blood NFL level is also elevated a er stroke. It takes several days to rise, is correlated with symptom severity and lesion size, and can predict functional outcomes and the onset of postinfarct depression. e elevation can take several hours to more than a week, and it remains elevated for several months. Patients with ALS have higher blood NFL levels 1 year before symptom onset, thus helping in predicting incidence. Blood NFL levels can di erentiate ALS from its mimics, and it can be an independent predictor of clinical prognosis. In FTD, a higher blood NFL level is

observed at symptom onset when compared to that in healthy controls. It can be used as a predictor of prognosis and di erentiate FTD with behavioral symptoms from primary psychiatric disorders. TBI is also reported to be related to elevated blood NFL levels. In this case, blood NFL correlates with the number of head impacts and is associated with the outcome a er a year. An increase in blood NFL is also observed in patients with Parkinson's disease (PD) and Alzheimer's disease (AD); however, the overlap of the levels with healthy controls is

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