NEJM Journal Watch

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Plasma Biomarkers May Identify Risk for Dementia

Plasma amyloid and neurofilament levels were associated with dementia risk in a population-based cohort.

Assessment of plasma biomarkers is emerging as a potential noninvasive way to determine risk for dementia. To further evaluate the utility of plasma biomarkers in this setting, researchers analyzed whether plasma amyloid-β40, amyloid β42, total tau, and neurofilament light chain (NfL) levels were associated with all-cause dementia and Alzheimer disease (AD) risk in 4444 participants without dementia in the Rotterdam population-based cohort study. At baseline, the average age of participants was 72 years, 9% had mild cognitive impairment (MCI), 58% were female, and 26% were apolipoprotein ε4 carriers.

During a median follow-up of ≈7 years, key results were as follows:

- ≈12% of participants developed incident dementia, among whom 68% had AD.
- In adjusted analyses, higher plasma NfL levels were associated with a 54% greater risk for all-cause dementia and a 49% greater risk for AD dementia.
- Higher amyloid-β42 levels were associated with a 40% decreased risk for all-cause dementia and AD.
- The associations between plasma NfL and amyloid-β42 levels and dementia risk remained present after excluding participants with low baseline-screening cognitive test results or MCI.
- Baseline total tau and amyloid-β40 levels were not significantly associated with risk for dementia.
- A combination of the highest-quartile NfL levels and the lowest-quartile amyloid-β42 levels conferred a nearly 10-fold increased risk for all-cause dementia and a nearly 16-fold increased risk for AD compared with a combination of the lowest-quartile NfL levels and the highest-quartile amyloid-β42 levels.
- Faster rates of change in NfL levels were seen in those who developed AD and had begun to deviate from a dementia-free cohort approximately 10 years before AD diagnosis.
- Rates of decline in plasma amyloid-β42 levels were not significantly different between those who developed AD and those who did not.

COMMENT

Assessing plasma biomarker levels continues to show promise as a noninvasive way to identify risk for dementia. Interestingly, contrary to a prior report (*NEJM JW Neurol* Jun 2019 and *JAMA Neurol* 2019; 76:598), plasma total tau levels were not associated with incident dementia. As the researchers suggest, total tau levels may be more prominent during later stages of the disease. The results of this study also support following NfL levels in neurodegenerative disease (*NEJM JW Neurol* Feb 2019 and *JAMA Neurol* 2019; 76:318). Higher plasma NfL levels and lower amyloid-β42 levels in combination may be particularly useful in determining dementia and AD risk. Correlating these results with trajectories of cognitive performance also may be helpful clinically. ***— Jennifer Rose V. Molano, MD***

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de Wolf F et al. Plasma tau, neurofilament light chain and amyloid-β levels and risk of dementia; a population-based cohort study. **Brain** *2020 Apr 1; 143:1220. (https://doi.org/10.1093/brain/awaa054)*