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Cerebrospinal Fluid Aβ$_{42}$, Total Tau, and Phosphorylated Tau in the Evaluation of Alzheimer's Dementia: Experience from a Commercial Reference Laboratory

Background

- Alzheimer disease (AD) is characterized by Aβ amyloid plaques and tau neurofibrillary tangles in the brain. These changes may play a role in AD-associated neurodegeneration.[1]
- The biomarkers Aβ$_{42}$, total tau (T-tau), and phosphorylated tau$_{181}$ (P-tau) in cerebrospinal fluid (CSF) are used to help diagnose AD.[2]
- **Objective:** In this study, the investigators assessed use of the Aβ$_{42}$/T-tau index (ATI) and P-tau among patients presumably being evaluated for suspected AD.

Methods

- Investigators analyzed CSF specimens from patients with suspected AD submitted to Athena Diagnostics, a large commercial reference laboratory, for measurement of Aβ$_{42}$ and T-tau, and P-tau.
- Each biomarker was measured using a sandwich ELISA−based assay.
- ATI was determined as Aβ$_{42}$/(240 + (1.18 X T-tau)).
- AD was classified according to a combination of ATI and P-tau thresholds:
  – AD: ATI <0.8 or P-tau >68 pg/mL
  – Borderline: ATI 0.8-1.2 and/or P-tau 54-68 pg/mL
  – Not AD: ATI >1.2 and P-tau <54 pg/mL
  – Indeterminate (possible non-AD dementia [NADD]): ATI <0.8 and P-tau <54
  – Other: highly elevated ATI
- Age differences among AD classification groups at the time of testing were assessed by analysis of variance (ANOVA) followed by Tukey pairwise testing.

Results

- The study included 42,030 CSF specimens (mean patient age, 66 years; 49.1% from women).
- Testing yielded a classification of either AD or not-AD in almost half (46.3%) of patients:
  – AD: 30.0%
  – Borderline: 30.2%
  – Indeterminate-NADD: 21.7%
  – Not AD: 16.3%
  – Other: 1.9%
- The proportion of women was higher in the AD than in the non-AD group (55.6% vs 42.8%).
- Patient age at testing was significantly greater in the AD group than the not-AD group (mean age: 66.8 vs 62.5 years; P<0.001); similar age differences between AD and not-AD groups were found for both women and men.

Conclusions

- CSF ATI and P-tau results were consistent with either AD or not-AD in almost half of specimens tested, demonstrating the potential value of the biomarkers for diagnosing suspected AD.
- The older age among patients classified as having AD is consistent with a higher pretest probability with increasing age.

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