Impact of Biomarkers On Diagnostic Confidence in Clinical Assessment of Patients with Suspected Alzheimer's Disease and High Diagnostic Uncertainty: An EADC Study

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Background

NIA-AA and IWG diagnostic criteria for Alzheimer's Disease (AD) include core structural, functional, and CSF biomarkers. The impact of core biomarkers in clinical settings is still unclear. This study aimed at measuring the impact of core biomarkers on the diagnostic confidence of uncertain AD cases in a routine memory clinic setting.

Methods

356 patients with mild dementia (MMSE = 20) or Mild Cognitive Impairment possibly due to AD were recruited in 17 European Alzheimer's Disease Consortium (EADC) memory clinics. The following variables were collected: age; sex; MMSE; neuropsychological evaluation including long term memory, executive functions, language and visuospatial abilities. Core biomarkers were collected following local practices: Scheltens's visual assessment of medial temporal atrophy (MTA) on MR scan; visual assessment of hypometabolism/hypoperfusion on FDG-PET/SPECT brain scan; CSF Aß1-42, tau and phospho-tau levels. At diagnostic workup completion, an estimate of confidence that cognitive complaints were due to AD was elicited from clinicians on a structured scale ranging from 0 to 100. Only cases with uncertain diagnoses (confidence between 15% and 85%) were retained for analysis. Generalized linear models were used to describe the relationship between the collected measures and the diagnostic confidence of AD.

Results

Neuropsychological assessment was carried out in almost all cases (98% of the cases). Medial temporal atrophy ratings were done in 40% of cases, assessment of cortical hypometabolism/hypoperfusion in 34%, and CSF Aß and tau levels in 26%. The markers that better explained the variability of diagnostic confidence were CSF Aß1-42 level ($R^2=0.46$) and hypometabolism/hypoperfusion ($R^2=0.45$), followed by CSF tau level ($R^2=0.35$), MTA assessment ($R^2=0.32$) and. All figures were highly significant, at $p<<0.001$. The diagnostic confidence variability due to neuropsychological tests for different domains was lower: MMSE ($R^2=0.29$); long term memory ($R^2=0.23$); executive functions ($R^2=0.05$); language ($R^2=0.02$); visuospatial abilities ($R^2=0.04$) even if significant ($p<0.01$).

Conclusions

The use of core biomarkers in the clinical assessment of subjects with suspected AD and high diagnostic uncertainty is still limited. However, when assessed, these biomarkers show a higher impact on diagnostic confidence of AD than the most widespread clinical measures