

Clinical And Biomarker Features Of Mixed Alzheimer’s-vascular Dementia: A Cohort Study

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Neither clinical and neuropsychological features nor fluid biomarkers helped distinguish AD from AD-CVD, suggesting that these conditions may exist along a shared continuum in which CAA is common.

INTRODUCTION

Although Alzheimer’s disease associated to cerebrovascular disease (AD-CVD) is estimated to be highly prevalent, it is relatively understudied. We aimed to characterize individuals with AD-CVD, including those with cerebral amyloid angiopathy (CAA), in comparison with individuals with Alzheimer’s disease (AD), and to identify features that may aid in differentiating AD-CVD from AD.

METHODS

Individuals with mild AD confirmed by cerebrospinal fluid (CSF) biomarkers, either with (AD-CVD) or without (AD) significant cerebrovascular disease, were prospectively recruited and underwent blood tests and neuropsychological and neuroimaging assessments.

CSF biomarkers included Aβ42, p-tau181, and t-tau. Blood biomarkers (BMs) included Aβ40, Aβ42, Aβ42/Aβ40, p-tau181, t-tau, GFAP, NfL, sTREM2, ucMGP, and ApoE genotype.

Classification into AD-CVD required 1) temporally related onset with a cerebrovascular event, 2) probable CAA, or 3) fulfilment of VASCOG criteria, consisting in at least one of: ≥1 strategic or large infarct, ≥2 intracranial haemorrhages, >2 lacunar infarcts, extensive and confluent white matter hyperintensities.

RESULTS

121 participants (73 AD, 48 AD-CVD) were recruited between July 2021 and July 2023 at Vall d’Hebron University Hospital, Barcelona, Spain (median age 74.1 years; 59.5% women). Additionally, 28 hypertensives individuals without stroke nor cognitive symptoms from the ISSYS cohort [1] were included as a reference control group for the blood BMs analyses.

The median follow-up was 12 months (interquartile range: 10-14). 50.5% of participants had cerebral infarcts, and 34 accomplished Boston 2.0. criteria for possible (n=24) or probable (n=10) CAA.

As compared with the AD group, the AD-CVD group had more:

- Ischaemic infarcts (71.1% vs 21.9%; p=0.04)
- Lobar microbleeds (44.5% vs 10%; p=0.01)
- ApoE ε4 homozygous individuals (14.6% vs 4.1%; p=0.01)
- Higher CSF NfL levels (2304.5 [1987.0–2944.9] vs 1957.5 [1578.0–2735.8]; p=0.03)

Additionally, a non-statistically significant trend towards lower blood total Tau in the AD-CVD group as compared with the AD group was observed (p=0.056) (Figure 1. There were no significant differences in any other aspects.

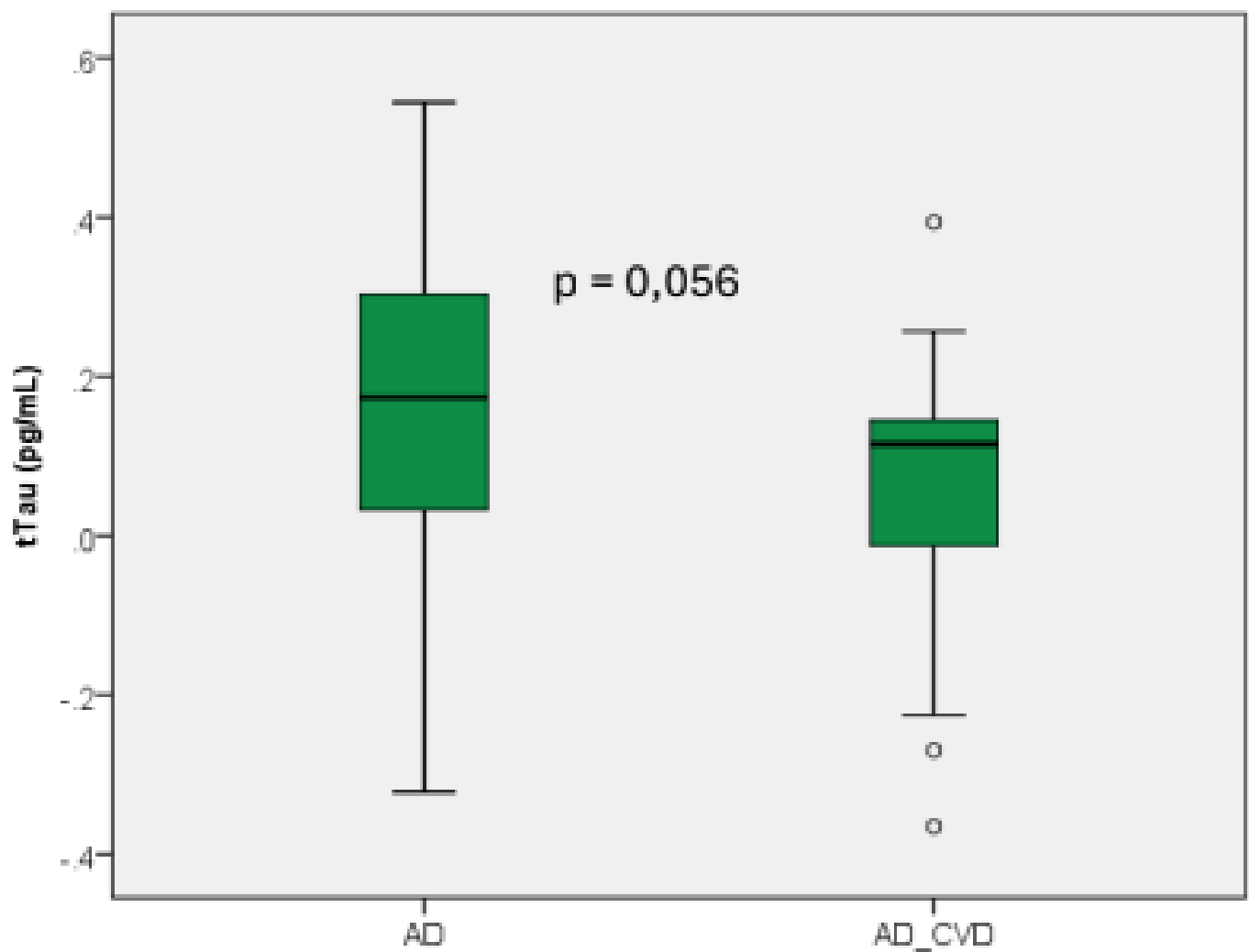
Plasma ucMGP showed modest discriminative capacity (AUC 0.71).

CONCLUSIONS

The high prevalence of ApoEε4 and CAA lesions in individuals with AD, and the even higher prevalence of both in individuals with AD-CVD, aligns with prior knowledge [2-6].

AD and AD-CVD appear to exist along a shared continuum in which CAA is common. The role of biofluid BMs to differentiate both entities within this continuum warrant further investigation, ideally considering the limitations of this study (mainly, possible lack of statistical power).

Figure 1. Blood t-tau levels (mean+/-2 SD) in AD and AD-CVD



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