Cerebrospinal fluid biomarkers in Alzheimer's disease and other neurodegenerative disorders: diagnostic accuracy and discriminatory power for the differential diagnosis

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BACKGROUND

The differential diagnosis between Alzheimer's disease (AD) and other forms of dementia can be challenging for the neurologist, due to the possible overlapping of clinical and neuropathological features. Convergent findings support the utility of cerebrospinal fluid (CSF) biomarkers in the diagnosis of dementias. Low amyloid-β1-42 (Aβ42) and high total tau (T-tau) and phosphorylated tau (P-tau) levels configure the typical CSF pattern of AD. Moreover, the ratio of Aβ42 to T-tau and the ratio of Aβ42 to P-tau can increase the diagnostic accuracy.

OBJECTIVE

Our aim was to evaluate the accuracy of CSF biomarkers and their ratios in discriminating AD from other dementias in patients with cognitive impairment. Furthermore, we aimed at establishing a cutoff value for each biomarker and ratio to be used in the differential diagnosis between AD and other non-AD dementias.

METHODS

Concentrations of Aβ42, T-tau, P-tau, and ratios (Aβ42/T-tau and Aβ42/P-tau) were determined in CSF samples from 60 older adults referred to our centre for cognitive disturbances, including 30 patients fulfilling the diagnostic criteria for AD and 30 subjects affected by other neurodegenerative disorders (non-AD group). For each CSF biomarker and ratio, we determined the sensitivity and the specificity in distinguishing AD from Non-AD patients and calculated the cut-off value that best discriminated among the two groups.

AD group (30 subjects)

Typical AD
(IWG-2 criteria) n. 24

Atypical AD
(IWG-2 criteria) n. 6
Posterior, biparietal variant n. 1
Logopenic variant n. 2
Frontal variant n. 3

Non-AD group (30 subjects)
Progressive Supranuclear Palsy
(NINDS-SPSP criteria) n. 7
Corticobasal Syndrome
(Armstrong et al., 2013) n. 2
Behavioural variant of frontotemporal dementia
(Rascovsky et al, 2011) n. 7
Dementia with Lewy bodies
(DLB consortium, third report) n. 3
Vascular Dementia
(NINDS AIREN criteria) n. 7
Normal pressure hydrocephalus
(clinical and neuroradiological diagnosis) n. 5

RESULTS

There were no significant differences in age and gender distribution between the diagnostic groups. Subjects with AD had significantly lower CSF concentration of Aβ42 and significantly higher concentrations of T-tau and P-tau compared with the Non-AD group; likewise, the Aβ42/T-tau and Aβ42/P-tau ratios were lower in AD compared to Non-AD patients (Tab. 1; Fig. 1). Receiver Operating Characteristic (ROC) curves were carried out to determine, for each CSF biomarker and combinations, the cut-off scores that best discriminated AD from non-AD patient based on sensitivity and specificity values. In our population, the Aβ42/T-tau and Aβ42/P-tau ratios differentiated AD from Non-AD group better than any other CSF parameter. In particular, Aβ42/P-tau ratio >11 discriminated non-AD from AD group with the best sensitivity (96%) and specificity (83%) (Tab. 2).

	Mean ± SD (30 AD)	*Mean ± SD (30 Non-AD)*	*p-value*
Age	67y ± 6.8	67y ± 6.9	N.A (p > 0.9)
Sex	16 F	17 F	N.A (p > 0.8)
T-tau	559 ± 439	235 ± 168	p < 0.0001*
P-tau	83 ± 44	37 ± 13	p < 0.0001*
Aβ42	385 ± 109	597 ± 224	p < 0.0001*
Aβ42/T-tau	1.07 ± 0.76	3.46 ± 2.01	p < 0.00001*
Aβ42/P-tau	5.4 ± 2.3	18 ± 8	p < 10E-10*

Tab.1 Demographic characteristics and concentrations of cerebrospinal fluid biomarkers according to baseline diagnosis.

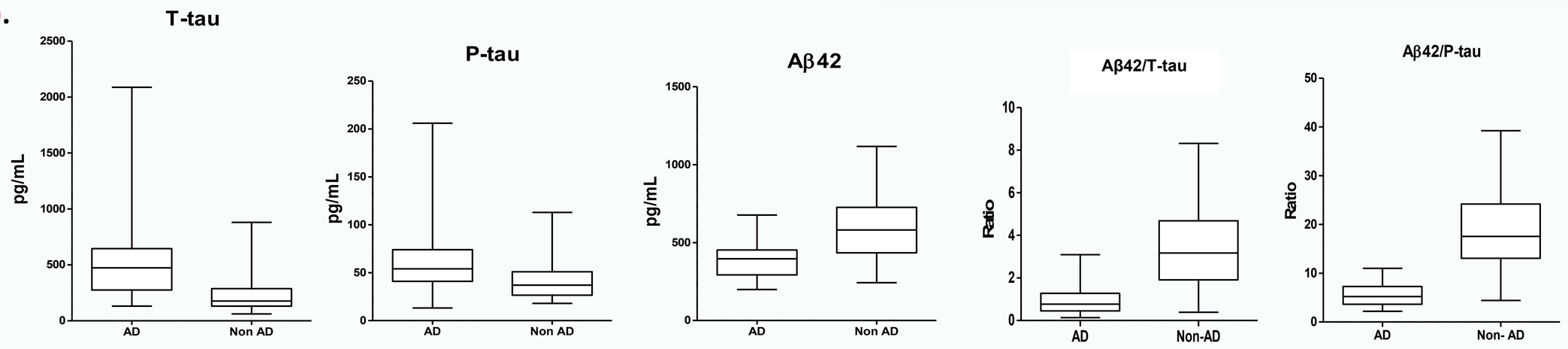

Fig.1 Box plots displays differences in concentrations of T-tau, P-tau, Aβ 42 and their ratios among the group AD and Non-AD.

	Cut-off	*Sensibility*	*Specificity*
T-tau	----		
P-tau	----		
Aß42	469 pg/mL	83%	73%
Aß42/T-tau	1.449	83%	83%
Aß42/P-Tau	11	96%	83%

Tab.2 Cutoff scores and sensitivity/specificity values of cerebrospinal fluid biomarkers

CONCLUSIONS

Our results are in line with available evidences and strongly support the usefulness of CSF biomarkers in the differential diagnosis between AD and other dementias. In particular, we recommend the current use of CSF ratios to better discriminate AD from non-AD patients, Aβ42/P-tau being the most powerful marker.

References

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