

AD Clinicopathological Staging In A Cohort Of Greek Individuals Across The Spectrum Of Impairment



Nikos Giagkou¹, Iliana Gkelmpesi¹, Faidra Kalligerou^{1,2}, Panagiota Zoi², Kostas Patas¹, Chatzipanagiotou Stylianos¹, Angeliki Tsapanou¹, Eirini Mamalaki¹, Eva Ntanasi¹, Mary Yannakoulia³, Efstratios Karavasilis⁴, Georgios Velonakis⁵, Nikolaos Scarmeas^{1,6}

1 Eginitio Hospital NKUA; 2 Athens Alzheimer Association; 3 Harokopio University of Athens; 4 Democritus University of Thrace; 5 Research Unit of Radiology and Medical Imaging, NKUA; 6 Taub Institute for Research in Alzheimer's Disease and the Aging Brain, The Gertrude H. Sergievsky Center, Columbia University

INTRODUCTION AND METHODS

We applied the new Alzheimer’s Association Workgroup Criteria for the diagnosis and staging of AD in individuals aged ≥40 across the spectrum of cognitive health.

- CSF or plasma (ptau217) AD biomarkers
- Clinical Stage 2 was defined as Mild behavioral impairment (MBI= NPI≥1) OR Subjective cognitive decline (all z-scores on neuropsychological examination >[-1.5])
- Stages 3 and 4-6 defined according to established criteria
- MRI: Vascular co-pathology [Fazekas ≥2] and non-specific neurodegeneration [MTA ≥2 for ages <75; MTA ≥3 for ages ≥75]
- Ordinal regression was used to assess the independent associations of clinical stage with markers of pathology, neurodegeneration and demographics

RESULTS

- AD pathology was assessed in N=414 using CSF (n=358) or plasma (n=56) biomarkers
AD(+) n=166; AD(-) n=248
- AD positive participants were older and had more frequent presence of vascular co-pathology and non-specific neurodegeneration (Table 1)

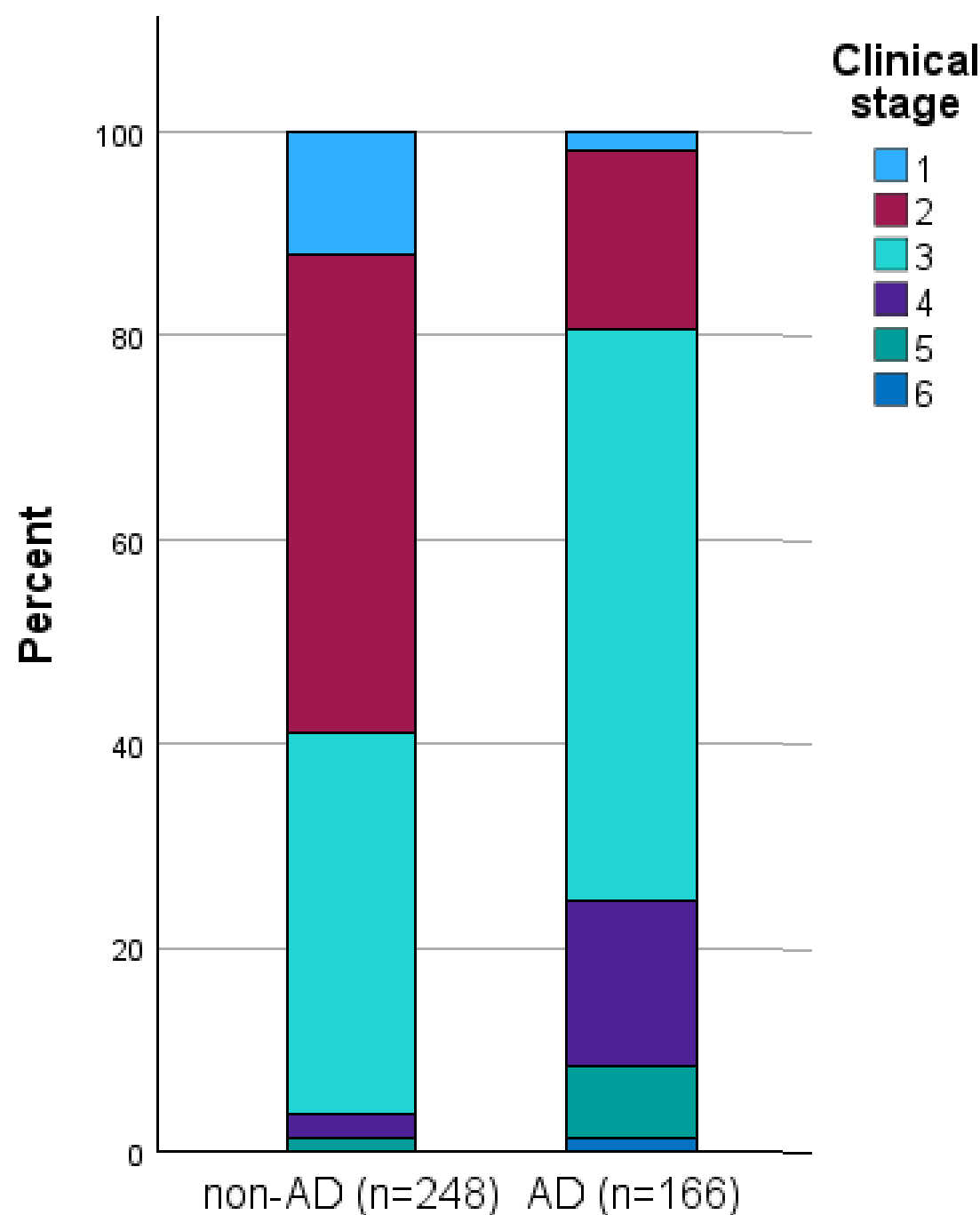
	Non-AD	AD	P-value
Age	61.7 (9.6)	72.0 (8.2)	<0.001
Sex (male, %)	39.9%	47%	NS
Vascular co-pathology (present, %)	20.0%	41.5%	<0.001
Neurodegeneration (present, %)	9.7%	23.3%	0.003

Table 1 – Demographics

- AD positivity was associated with higher clinical stages (p<0.001) (Table 2, Fig)
- AD pathology, age and non-specific neurodegeneration were independent predictors of increased clinical stage

Stage	Non-AD (%)	AD (%)
1	12.1	1.8
2	46.8	17.5
3	37.5	56
4	2.4	16.3
5-6	1.2	8.4
All	100	100

Table 2 – Clinical stage distribution



Predictors	Coefficient	95% CI	P-value
AD pathology	1.2	0.6, 1.8	<0.001
Vascular co-pathology	-0.3	-0.9, 0.3	0.33
Neurodegeneration	0.9	0.1, 1.7	0.026
Age	0.3	0.04, 0.6	0.022
Sex	0.2	-0.3, 0.7	0.34

Table 3 – Ordinal regression. Outcome= Clinical stage

- Most participants classified as Stage 2 had subjective cognitive decline (Tables 4 and 5)
- A minority had isolated mild behavioral impairment

Non-AD		Subjective only cognitive decline	
		Yes	No
MBI	Yes	21.9%	4.4%
	No	56.2%	17.5%

Table 4 – Prevalence of SCD and MBI in Stage 2 non-AD participants

AD		Subjective only cognitive decline	
		Yes	No
MBI	Yes	29%	3.2%
	No	61.3%	6.5%

Table 5 – Prevalence of SCD and MBI in Stage 2 non-AD participants

CONCLUSIONS

- AD positivity was associated with higher clinical stages.
- Age, amyloid pathology and non-specific neurodegeneration on MRI were independently associated with increased clinical stage. Sex and visual assessment of white matter hyperintensities were not.
- Classification as clinical Stage-2 is mainly driven by subjective cognitive complaints.