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Title: **Factors associated to disease duration in Alzheimer's patients: a clinicopathological study.**

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Abstract: Introduction: Length of survival and progression rate is poorly understood in Alzheimer's disease (AD). Diverse progression rates have been related to different phenotypes of cortical atrophy, and to the type of combined pathology (e.g. Lewy bodies or vascular lesions). The aim of this study is to analyze this variability and associated factors in a cohort of demented patients from the brain donation program at Alzheimer's Center Queen Sofía Foundation. Materials and Methods: Ninety two patients with detailed postmortem neuropathological study and relevant Alzheimer's type pathology were included. Three groups of disease duration (DD) were defined: short, ≤ 7 yrs. (sD, n=20); intermediate, 7-11 yrs. (iD, n=29); and long, ≥ 12 yrs. (lD, n= 43). Sociodemographic, clinical, cognitive, functional, neuropathological and genetic data were compared among groups through multivariant statistics. Results: Although mean age at death was not significantly different between groups, a younger age of onset was associated to longer DD. Shorter times to reach GDS=7 or Semantic Fluency Test=0 were associated to shorter survivals. No difference was observed between groups in vascular risk factors, cause of death or number of medical comorbidities. Groups did not differ either in macroscopic findings. Among variables defining Alzheimer's and common combined pathologies, only the intensity of amyloid angiopathy, the presence of hippocampal sclerosis and the stage of TDP-43(+) pathology were associated to longer DD. Conclusion: In our cohort of pathologically diagnosed AD patients the DD is determined neither by core features of Alzheimer's pathology nor by the main clinical, cognitive or functional traits. The main determinant of DD seems to be age at onset of clinical disease. Alzheimer's disease shows a homogeneous pattern of evolution over a time period whose duration is age dependent.