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Neuropathology in the LifeAfter90 study: A new ethnically diverse cohort study of oldest-old

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Abstract

Background: Persons over the age of 90 are the fastest growing segment of the population in the US, yet there is a dearth of studies investigating the underlying neuropathology of cognitive impairment and dementias, in ethnically diverse, non-white decedents.

Method: The Life after 90 study began enrollment in July 2018 and is an ongoing cohort study of members of Kaiser Permanente Northern California aged 90+ with targeted recruitment of individuals across different racial/ethnic groups with no prior diagnosis of dementia in their medical record. Participants are examined every 6 months. Brain donation was available to all interested consenting participants. Neuropathology was assessed using the National Alzheimer's Coordinating Center Neuropathology form v. 10.

Result: As of January 2021, 173 (26%) participants enrolled in autopsy (18% Asian, 12% African American, 12% Latino, and 10% as multiracial) with 8 deceased and neuropathological evaluations completed. Average age of death was 96 years (range 91 to 105), 5 (62.5%) were female, 3 Latino, 3 Caucasian, and 2 multiracial. At the final clinical exam, which was on average 4 months before death (range: 2-8), 2 participant had dementia (25%), 3 questionable/mild cognitive impairment (37.5%), and 3 cognitively normal (37.5%). With respect to a neuropathologic diagnosis of Alzheimer's disease (AD), 2 met criteria for intermediate likelihood (25%), 4 low (50%), and 2 were considered not to have AD (25%). Notably, none had high likelihood of AD. All participants had some level of neurofibrillary tangles with Braak stages between II and IV. Two participants lacked plaques (Amyloid-Beta or neuritic types), and the highest Thal phase was 4. Four participants (50%) had Lewy bodies (LBs), 1 in olfactory bulb/tract only, 2 Transitional, and 1 with Diffuse. Hippocampal sclerosis was not seen in any whereas TDP-43 inclusions were detected in 2 participants (25%). Diffuse LB, TDP-43 inclusions, and intermediate AD co-occurred in one (50%) of the dementia participants while all lacking in the other.

Conclusion: Preliminary results of the first 8 deaths in this multiethnic cohort of oldest-old individuals indicate that numerous brain pathologies are present with advanced age. Further work with this study will examine the clinical impact of this pathological heterogeneity.