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Authors

Neuville, Raumin

Ho, Chu-Ching

Sajjadi, S Ahmad

et al.

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One Hundred Centenarians: Brain Pathology and Relationship to Dementia in The 90+ Study (P1-1.Virtual)

Raumin Neuville, Chu-Ching Ho, S. Ahmad Sajjadi, Roshni Biswas, Thomas Montine, Maria Corrada, and Claudia Kawas

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Abstract

Objective:

To determine prevalence of dementia-related neuropathologic changes and examine their association with dementia risk and severity in centenarians, and compare findings with nonagenarians from the same cohort.

Background:

Centenarians worldwide are projected to increase 50-fold by 2100 with dementia incidence estimated ~40%. Brain autopsy studies in this population are highly limited.

Design/Methods:

Participants were individuals who agreed to autopsy from The 90+ Study, a longitudinal study of aging. Cognitive diagnoses were assigned during a multidisciplinary conference blinded to autopsy results. Using standardized protocols, dementia-related neuropathologic changes (NCs) were assessed blinded to clinical information and dichotomized for analyses: +Alzheimer's disease (AD) neuropathologic change (ADNC;intermediate/high), +cerebral amyloid angiopathy (moderate/severe), +arteriosclerosis (moderate/severe), +Lewy body disease (limbic/neocortical), +TDP-43 (hippocampal/cortical), +age-related tau astrogliopathy (ARTAG;present), +microinfarcts (≥ 2), and +hippocampal sclerosis (present). Mini-Mental State Exam (MMSE) scores nearest to death were used to examine dementia severity. Prevalence and associated odds of dementia were determined for each NC and for the presence of multiple NCs.

Results:

388 participants (100 centenarians and 288 nonagenarians) with completed brain autopsies were included. In centenarians, ADNC was most prevalent (75%; vs. 71% in nonagenarians), followed by arteriosclerosis (69%; vs. 55% in nonagenarians) and ARTAG (66%; vs. 60% in nonagenarians). In centenarians, arteriosclerosis (69%) and TDP-43 (39%) were significantly more prevalent compared to nonagenarians (55% and 28% respectively; $P=0.01$ and $P=0.05$ respectively). 83% centenarians had 2+NCs and number of NCs was strongly associated with dementia risk. Odds ratio increased from 2.9 (95% Confidence interval (CI):0.49–16.9) for 2NCs, to 12.7 (95%CI:2.34–68.31) for 3, and 63.8 (95%CI:8.78–463.67) for 4NCs. Number of NCs was also associated with dementia severity.

Conclusions:

Prevalence of dementia-related NCs is exceptionally high in centenarians and greater for arteriosclerosis and TDP-43 compared to nonagenarians. Multiple NCs are typical in centenarians and strongly associated with cognitive impairment, with risk and severity increasing with higher numbers of NCs.

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