Sex-specific Biomarkers in Alzheimer’s Disease Progression: Framingham Heart Study

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Abstract

Background: Research shows that women have a higher risk of developing Alzheimer’s disease (AD) than men. This study seeks to identify sex-specific risk profiles linked to the development of AD.

Method: We analyzed multiple blood biomarkers for risk of development of AD as well as with cognitive decline in the community-based longitudinal Framingham Heart Study Offspring Cohort. A total of 2962 participants (mean age 60 year, 55% women) without any type of dementia were followed up to a median of 12 years with cognitive testing, blood sampling and dementia assessments. This study analyzed participants 60 years and older. Proportional hazards models were performed to investigate associations between biomarkers and the time to incident AD. Linear models were used to quantify the associations between biomarkers and annualized, domain-specific cognitive decline. Covariates included age, sex, education, and baseline cognitive measurement.

Result: During the follow-up, 7.3% (119/1631) women and 4.7% (63/1331) men developed AD; 8.6% (141/1631) women and 7.1% (94/1331) men developed all-cause dementia. We found that women were 41% more likely than men to be diagnosed with AD ($P = 0.029$) while found no gender differences in the time to develop all-cause dementia ($P = 0.16$). We found that lower plasma amyloid-beta42 level was significantly predictive for the future risk of AD in women ($P = 0.0018$) and not in men ($P = 0.069$), while the hazards ratio were not significantly different between men and women ($P_{\text{diff}} = 0.92$). Further, lower plasma amyloid-beta42 was significantly associated with annualized memory decline in women ($P = 0.00023$) but not in men ($P = 0.55$) ($P_{\text{diff}} = 0.026$ between men and women for regression estimates). Several vascular risk factors, such as fasting glucose levels, were predictive of AD/dementia in both men and women.

Conclusion: Our study may offer new insights into how blood tests can be better personalized for predicting future AD risk in women versus men.