

Epidemiology / Risk and protective factors in MCI and dementia

Stroke, genetic risk and incidence of dementia

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Abstract

Background: Stroke is a strong, independent and modifiable risk factor for all-cause dementia. However, the extent to which stroke adds to or moderates genetic risk is unknown.

Method: In this cohort study, we used data from UK Biobank including adults aged 60 years and older of European ancestry without cognitive impairment or dementia at baseline. Participants joined the study between 2006 and 2010 and were followed until 2016 or 2017. Genetic risk was estimated using a polygenic score for dementia incorporating 249,273 single-nucleotide polymorphisms with low (lowest quintile), intermediate (quintiles 2-4), and high (highest quintile) categories. Stroke was a binary variable based upon history of stroke occurring before dementia diagnosis or end of follow-up in participants who remained dementia-free. The outcome was incident all-cause dementia, ascertained through hospital inpatient and death records.

Result: 196,383 individuals (mean [SD] age, 64.1 [2.9] years; 52.7% were women) were followed up for 1,545,433 person-years (median [interquartile range] follow-up, 8.0 [7.4-8.6] years). Overall, 3.8% of participants had a history of stroke. 20.0% had high polygenic risk scores, 60.0% had intermediate risk scores, and 20.0% had low risk scores. Of the participants with high genetic risk, 1.2% developed dementia compared with 0.63% of the participants with low genetic risk (adjusted hazard ratio, 1.94 [95% CI, 1.66-2.27]). Of the participants with stroke, 2.7% developed dementia compared with 0.8% of participants without a stroke (adjusted hazard ratio, 2.73 [95% CI, 2.35-3.17]). Of the participants with a high genetic risk and stroke, 3.4% developed dementia compared with 0.57% of participants with low genetic risk and no stroke (adjusted hazard ratio, 5.02 [95% CI, 3.67-6.86]). There was no significant interaction between genetic risk and stroke ($P = 0.633$). Among participants with high genetic risk, 1.2% of those without stroke developed dementia compared with 3.4% of those with stroke (hazard ratio, 0.40 [95% CI, 0.29-0.53]).

Conclusion: Among older adults without cognitive impairment or dementia, both stroke and high genetic risk were significantly associated with higher dementia risk. Stroke prevention should be a key element of risk reduction strategies for the prevention of dementia, particularly amongst those with a high genetic risk.