Can We Escape Stroke and Alzheimer Disease?

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Stroke and Alzheimer disease are major public health burdens that account for substantial disability and extensive cost. In addition, these diseases currently tie as the third most common cause of death in the United States, and both will become more important as life expectancy increases. Annually, 15 million people worldwide experience a stroke, of which 5 million are fatal and an equal number are left permanently disabled and in need of assistance for activities of daily living. In the United States alone, approximately 700,000 people have a stroke each year, of which 500,000 are first stroke events. Recent evidence suggests that stroke is at least as frequent as acute coronary events.

Alzheimer disease accounts for ~60% to 70% of cases of progressive cognitive impairment in elderly patients in Western societies. The prevalence of Alzheimer disease exceeds 4 million in the United States alone, and each year, >400,000 new cases are diagnosed. Assuming current trends, the numbers are expected to more than triple over the next 50 years.

Increasing age is the strongest predictor for both stroke and Alzheimer disease. Atherosclerosis is an established risk factor for stroke, but over the last decade, the evidence has accumulated that Alzheimer disease is also associated with vascular risk factors and atherosclerosis independent of age. For example, various measures of atherosclerosis including vessel wall thickness, plaques of the carotid and coronary arteries, and the ratio of ankle-to-brachial systolic blood pressure have all been associated with Alzheimer disease. In addition, older adults with cardiovascular disease other than stroke are at increased risk of Alzheimer disease compared with those without. Processes that involve cholesterol mechanism and inflammation have also been associated with Alzheimer disease and atherosclerosis.

The lifetime risk method is used to estimate the probability that a person will develop a specific disease during his or her lifespan. In contrast to cumulative risk or age-adjusted incidence measures, lifetime risk estimates do not depend on survival to a given age. This measure is based on methods that use life table information, which accounts for competing risk of death. Thus, unlike other incidence measures, lifetime risk estimates do not overestimate the risk of developing a specific disease when the competing risks of death from other causes are high and the condition under study is common, as for example stroke and Alzheimer disease in the very elderly. In addition, lifetime risk estimates are important because such estimates provide easier and more comprehensive information compared with isolated prevalence, incidence, or relative risk measures. Furthermore, using this method, different diseases can be directly compared in the same cohort for various age groups.

In this issue of Stroke, Seshadri et al report the lifetime risk of stroke and Alzheimer disease as estimated from the community-based prospective Framingham study. During 51 years of follow-up, 875 (18%) of the participants developed a first-ever stroke, mostly ischemic stroke, whereas during 29 years of follow-up, 400 (14%) participants developed dementia, mostly Alzheimer disease. The risk for stroke and Alzheimer disease was higher among women, primarily because of their longer life expectancy. When stroke and dementia/Alzheimer disease were combined, the lifetime risk was 1 in 3 for women and 1 in 4 for men. This underscores the importance of both diseases for populations with increasing life expectancy.

The shape of the association between the lifetime risk of stroke and Alzheimer disease reveals interesting features. First, the lifetime risks of stroke and Alzheimer disease are fairly parallel and, in addition, level off in the oldest age groups. This may be explained by the fact that the life expectancy decreases with increasing age, and thus the probability of developing stroke and Alzheimer disease is reduced. It is also plausible that those individuals who survive until a very advanced age are less susceptible to developing stroke or Alzheimer disease (ie, a healthy survivor effect) and that they will escape both diseases even if they live longer. On the other hand, the flattening of the lifetime risk estimates of stroke and Alzheimer disease in the oldest age groups may be attributable to a change of exposure-specific effects on the occurrence of these diseases. For example, the presence of the apolipoprotein-ε4 allele is associated with a higher risk of Alzheimer disease, but it is not a predictor of its occurrence after age 85 in populations that are characterized by long life expectancy. If this scenario of changing effect of exposures across the lifespan is true, different age groups may require different preventive strategies.

In stratified analyses, Seshadri et al also evaluated the lifetime risk of stroke by blood pressure classes, suggesting that lower blood pressure in any age group is associated with lower lifetime risk of stroke, although the effect seems less apparent in older age groups. In contrast, blood pressure categories were not associated with the lifetime risk of Alzheimer disease.
dementia/Alzheimer. In other studies, it has been shown that elevated blood pressure in midlife is related to increased risk of Alzheimer disease. However, in late life, the relationship of blood pressure and risk for subsequent Alzheimer disease is controversial.

Projections based on lifetime risk estimates are strongly determined by the expectation of life in a given age of the cohort under study. Because the Framingham cohort is a population-based study of a relatively small town in the northeastern United States and includes mostly whites, the findings may not necessarily extrapolate to population with other ethnic backgrounds or with different socioeconomic status. However, because the lifetime risk of stroke and Alzheimer disease does not further increase in older age groups, interventions that could delay the onset of these diseases even a few years could have a substantial impact on their incidence in the general population.

References

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