CLINICAL RESEARCH STUDY

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Healthy Lifestyle and Functional Outcomes from Stroke in Women

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ABSTRACT

PURPOSE: While a healthy lifestyle has been associated with reduced risk of developing ischemic stroke, less is known about its effect on stroke severity.

METHODS: We performed a prospective cohort study among 37,634 women without stroke or missing risk factor data at baseline. The healthy lifestyle index was composed of smoking, physical activity, body mass index, alcohol consumption, and diet (range 0-20, with 20 representing healthiest lifestyle). Possible functional outcomes were no stroke or stroke with modified Rankin Scale score of 0-1 (mild), 2-3 (moderate), or 4-6 (severe). Multinomial logistic regression was used to analyze the association between healthy lifestyle and functional outcomes from stroke.

RESULTS: Over 17.2 years of follow-up, 867 total strokes were confirmed. Compared with the lowest category (0-4), the highest category (17-20) was associated with reductions in risk of total stroke with mild (odds ratio [OR] 0.43; 95% confidence interval [CI], 0.20-0.90), moderate (OR 0.53; 95% CI, 0.27-1.06), and severe (OR 0.48; 95% CI, 0.20-1.18) functional outcomes. Even a modest healthy lifestyle index (5-8 points) was associated with significant decreases in total stroke with severe and moderate functional outcomes. Similar results were seen for ischemic but not hemorrhagic strokes.

CONCLUSIONS: Highest vs lowest scores on the healthy lifestyle index were associated with reductions in risk of total and ischemic strokes with mild, moderate, and severe functional outcomes among women. The evidence that even modest healthy lifestyle index scores reduced risks of total and ischemic stroke with moderate and severe functional outcomes suggests modest lifestyle changes may reduce risk of disabling stroke events.

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Stroke is a leading cause of morbidity and mortality worldwide.[1,2] There is growing interest in determining whether a "healthy lifestyle" reduces the risk of stroke events. Previous studies among women have shown a decreased risk of the development of total and ischemic stroke with healthier lifestyles.[3-6] However, research on healthy lifestyle and functional outcomes from stroke in initially healthy populations is limited. Most research on functional stroke outcomes has focused on the effect of single risk factors[7-23] and has not considered how a combination of factors may interact to influence total and ischemic stroke functional outcomes. Given the morbidity and mortality consequences of stroke, it is important to determine if healthy lifestyles also decrease stroke severity.

Results for the effect of healthy lifestyle on hemorrhagic stroke are mixed. One study observed a decreased risk with healthier lifestyles,[6] while other studies have observed no association[5] or suggested a U-shaped association where healthier lifestyle was associated with a nonsignificant

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increase in the risk of hemorrhagic stroke.[3] None of these studies examined the impact of healthy lifestyle on functional outcomes from hemorrhagic stroke.

To determine the associations between healthy lifestyle and the risks of functional outcomes from total, ischemic, and hemorrhagic stroke, we used data from the Women's Health Study, a large prospective cohort of initially healthy women with available information on lifestyle factors and functional outcomes after incident stroke.

CLINICAL SIGNIFICANCE

- Highest vs lowest scores on the healthy lifestyle index were associated with reductions in risk of total and ischemic strokes with mild, moderate, and severe functional outcomes among women.
- The evidence that even a modest healthy lifestyle index score reduced risks of total and ischemic stroke with moderate and severe functional outcomes suggests that modest lifestyle changes may translate to reductions in risk of a disabling stroke event.

METHODS

The Women's Health Study (WHS) was a randomized, placebo-controlled trial of the effects of low-dose aspirin and vitamin E in the primary prevention of cardiovascular disease and cancer. The design, methods, and main findings have been published.[24,25] Briefly, at baseline (1992-1996), the study randomized 39,876 US female health professionals ages 45 years or older without a history of cardiovascular disease, cancer, or other major illnesses to receive low-dose aspirin or vitamin E (vs placebo) in a 2-by-2 factorial design. After the end of the trial in March 2004, women continue to be followed on an observational basis. Twice during the first year and yearly thereafter, women were sent follow-up questionnaires asking about demographic, lifestyle, and health information, including the occurrence of stroke events.

The WHS was approved by the Institutional Review Board at Brigham and Women's Hospital; all subjects provided written informed consent.

Exposure

We used a healthy lifestyle index previously developed in the WHS,[3] which contains components similar to other lifestyle indices associated with stroke risk,[4-6] to evaluate the relationship of healthy lifestyle with incident stroke. The healthy lifestyle index incorporates information from the baseline questionnaire on smoking, physical activity, body mass index (BMI), alcohol consumption, and diet. For each variable we created 5 categories and assigned scores from 0 to 4, with higher scores indicating healthier behaviors. Smoking was categorized as: current smoker who smokes $\geq$15 cigarettes per day (0 points), current smoker who smokes <15 cigarettes per day (1 point), past smoker who smoked $\geq$20 pack-years (2 points), past smoker who smoked <20 pack-years (3 points), and never smoker (4 points). Physical activity was categorized based on frequency of strenuous exercise: rarely or never (0 points), <1 time per week (1 point), 1 time per week (2 points), 2 to 3 times per week (3 points), or $\geq$4 times per week (4 points). Body mass index was categorized as $\geq$35.0 kg/m^2 (0 points), 30.0-34.9 kg/m^2 (1 point), 25.0-29.9 kg/m^2 (2 points), 22.0-24.9 kg/m^2 (3 points), and <22.0 kg/m^2 (4 points). To reflect the J-shaped relationship between alcohol consumption and cardiovascular disease risk,[26] we assigned the least number of points to those who rarely or never drank alcohol and the highest number of points to those who consume light to moderate amounts of alcohol. Alcohol intake was categorized as never (0 points), <1 drink/week (1 point), 1 to 3 drinks/week (3 points), 4 to <10.5 drinks per week (4 points), and $\geq$10.5 drinks per week (2 points). The construction of our diet score has been described in detail previously.[3] Briefly, women completed a 161-item standardized food frequency questionnaire at baseline.[27] We examined intake of cereal fiber, folate, ratio of polyunsaturated to saturated fat, omega-3 fatty acids, *trans* fats, and glycemic load. Each item was grouped into deciles and scored from 0 (least healthy) to 9 (healthiest) (*trans* fat and glycemic load were scored inversely). The scores were summed to create a total diet score, which was then grouped into quintiles. The lowest quintile (representing the least healthy diet) received 0 points, while the highest quintile (representing the healthiest diet) received 4 points.

The individual scores from the 5 components were summed to create a total final healthy lifestyle index ranging from 0 to 20. We categorized the final score into 5 categories for our total and ischemic stroke analyses: 0 to 4 (least healthy category and the reference category), 5 to 8, 9 to 12, 13 to 16, and 17 to 20 (healthiest category). Due to the small number of hemorrhagic strokes among those with the lowest healthy lifestyle index scores, our exposure categories for our hemorrhagic stroke analyses were 0 to 8 (least healthy category and the reference category), 9 to 12, 13 to 16, and 17 to 20 (healthiest group).

Outcome Ascertainment

If a woman reported a stroke on her follow-up questionnaire, we asked for permission to review her medical records. An Endpoints Committee of physicians, including a board-certified vascular neurologist (CSK) blinded to randomized treatment assignment, reviewed medical records and determined if the self-reported stroke was confirmed. A nonfatal stroke was defined as a focal neurologic deficit of sudden or rapid onset and vascular mechanism that lasted >24 hours. Fatal strokes were confirmed using all available sources, including death