Does lifetime exposure to estrogen affect risk of stroke?

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People with a higher cumulative estrogen exposure throughout their life may have a lower risk of stroke, according to a new study published in the February 1, 2023, online issue of *Neurology*. The lower risk was

found for both ischemic stroke and intracerebral hemorrhage.

An ischemic stroke is caused by a blockage of blood flow to the brain and is the most common type of stroke. An intracerebral hemorrhage is caused by bleeding in the brain.

"Our study suggests that higher estrogen levels due to a number of reproductive factors, including a longer reproductive life span and using hormone therapy or contraceptives, are linked to a lower risk of ischemic stroke and intracerebral hemorrhage," said study author Peige Song, Ph.D., of the Zhejiang University School of Medicine in Hangzhou, China. "These findings might help with new ideas for stroke prevention, such as considering screenings for people who have a short lifetime exposure to estrogen."

The study involved 122,939 postmenopausal female participants with a median age of 58 living in China without stroke at the start of the study.

Participants answered questions on personal factors, such as age, sex, and occupation, as well as lifestyle factors, such as smoking, alcohol use, exercise and medical history. They also answered questions on reproductive health information, including age at first menstruation and start of menopause, number of pregnancies and miscarriages and oral contraceptive use.

Researchers looked at health insurance and disease registry data to determine which participants had a stroke. During an average follow-up period of nine years, 15,139 had a stroke. Of those,12,853 had ischemic stroke, 2,580 had intracerebral hemorrhage and 269 had subarachnoid hemorrhage, which is bleeding between the brain and the membrane that covers it.

Participants were divided into four groups determined by their

reproductive life span, the number of years from first menstruation to menopause. Participants in the group with the shortest reproductive life span had up to 31 reproductive years. Participants in the group with the longest reproductive lifespan had 36 reproductive years or more.

As a percentage, participants in the longest group had slightly more strokes than those in the shortest group, 13.2% compared to 12.6%. But when researchers adjusted for other factors that could affect stroke risk, such as age, smoking, physical activity and high blood pressure, they found that participants in the longest group had a 5% lower risk of all kinds of stroke.

When looking at different types of stroke, female participants with the longest reproductive life span had a 5% lower risk of ischemic stroke and a 13% lower risk of intracerebral hemorrhage when compared to women with the shortest reproductive life span.

Researchers also looked at other factors affecting estrogen levels, such as number of births and use of oral contraceptives, both of which are associated with higher levels, and length of breastfeeding, which is associated with lower levels based on the hypothesis that pregnancy and oral contraceptive use represent relatively higher sustained blood estrogen levels. They found that higher estrogen levels led to a lower risk of all types of stroke, as well as ischemic stroke and intracerebral hemorrhage.

"Estrogen exposure throughout life could potentially be a useful indicator of a person's risk of different types of stroke following menopause," said Song. "However, more research is needed on the biological, behavioral, and social factors that may contribute to the link between estrogen exposure and stroke risk across a woman's lifespan."

A limitation of the study was that information on reproductive factors

was collected mainly based on participants' ability to recall events, and participants may not have remembered such events correctly.

More information: Leying Hou et al, Lifetime Cumulative Effect of Reproductive Factors on Stroke and Its Subtypes in Postmenopausal Chinese: A Prospective Cohort Study, *Neurology* (2023). DOI: 10.1212/WNL.0000000000206863 , dx.doi.org/10.1212/WNL.0000000000206863

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