

REPRODUCTIVE ENDOCRINOLOGY

Women with early menopause have an increased risk of ischemic stroke

Women who begin natural menopause before 42 years of age have twice the risk of ischemic stroke as other women, found a prospective study published in *Stroke* that included participants of the Framingham Heart Study.

Women live longer than men do and, as a consequence, more women than men will experience a stroke during their lifetime. Furthermore, women experience increased functional impairment after stroke compared with men. Increased knowledge of women's risk factors for stroke is, therefore, essential to design prevention strategies. Limited data has suggested a link between age at natural menopause and risk of stroke, but prospective evidence is lacking, which prompted the current research by Lisabeth and coworkers.

The study included 1,430 women who had survived stroke-free until the

age of 60 years, experienced natural menopause and had not used estrogens before menopause. Follow-up was until first ischemic stroke, death or end of follow-up. The women's average age at natural menopause was 49 years, and 234 incident ischemic strokes occurred. Women experienced stroke at an average age of 80 years. After adjustment for a range of confounders known to affect stroke risk, women with menopause at age <42 years had an increase stroke risk compared with women who experienced menopause between 42 years and 54 years or at ≥55 years. A secondary analysis investigated the relationship between BMD—an alternative measure of cumulative endogenous estrogen exposure—and risk of ischemic stroke. The subgroup analysis, which included 654 women, showed that women in the lowest quintile of BMD had an elevated

risk of ischemic stroke compared with those in the middle quintiles. However, women in the highest quintile of BMD also had an elevated risk of stroke, a surprising finding the researchers speculate might be artifactual.

Reasons for increased stroke risk with early menopause are unclear. Estrogen deficiency could be an important factor, although existing evidence of this hypothesis is conflicting. Changes in levels of androgens and other hormones with menopause could also influence stroke risk; the researchers suggest that future stroke studies should include measurements of endogenous hormones to explore possible mechanisms.

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Original article Lisabeth, L. D. *et al.* Age at natural menopause and risk of ischemic stroke: The Framingham Heart Study. *Stroke* 40, 1044–1049 (2009).