

Association between genetic condition, hormonal factors, and risk of endometrial cancer

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For women with Lynch syndrome, an association was found between the risk of endometrial cancer and the age of first menstrual cycle, having given birth, and hormonal contraceptive use, according to a study in the July 7 issue of *JAMA*. Lynch syndrome is a genetic condition that increases the risk for various cancers.

Endometrial cancer is the most common type of gynecologic cancer in developed countries. Between 2 percent and 5 percent of all endometrial cancer cases are associated with a hereditary susceptibility to cancer, mainly Lynch syndrome, which is caused by a germline mutation in one of the DNA mismatch repair (MMR) genes. Depending on the mutated gene, cumulative risk of developing endometrial cancer by age 70 years for women is thought to be between 15 percent and 30 percent. Apart from hysterectomy, there is no consensus recommendation for reducing endometrial cancer risk for women with an MMR gene mutation. Studies in the general population have shown that hormonal factors are associated with endometrial cancer risk, according to background information in the article.

For Lynch syndrome, the association between hormonal factors and endometrial cancer risk has not been clear. Aung Ko Win, M.B.B.S., Ph.D., M.P.H., of the University of Melbourne, Victoria, Australia, and colleagues conducted a study that included 1,128 women with an MMR gene mutation identified from the Colon Cancer Family Registry. Participants were recruited between 1997 and 2012 from centers across the United States, Australia, Canada, and New Zealand.

Endometrial cancer was diagnosed in 133 women. The researchers found that later age at menarche (first menstrual cycle, age 13 or older), parity (has had one or more live births), and hormonal

contraceptive use (for one year or longer) were associated with a lower risk of endometrial cancer. There was no statistically significant association between endometrial cancer and age at first and last live birth, age at menopause, and postmenopausal hormone use.

"In this study, an inverse association was observed between the risk of endometrial cancer for women with an MMR gene mutation and later age of menarche, increased parity, and use of hormonal contraceptives. The directions of the observed associations are similar to those that have been reported for the general population, suggesting a possible protective effect of these factors," the authors write.

"If replicated, these findings suggest that women with an MMR gene mutation may be counseled like the <u>general population</u> in regard to hormonal influences on <u>endometrial cancer</u> risk."

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