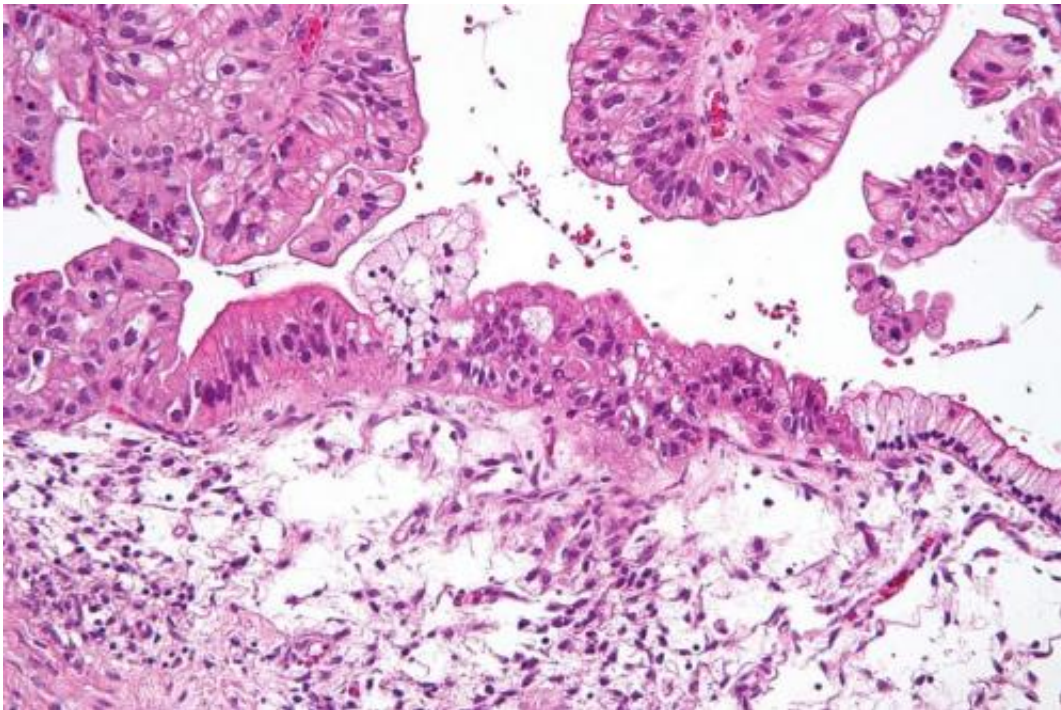


Preventive surgery for women at high risk of breast and ovarian cancer

February 3 2016



Intermediate magnification micrograph of a low malignant potential (LMP) mucinous ovarian tumour. H&E stain. The micrograph shows: Simple mucinous epithelium (right) and mucinous epithelium that pseudo-stratifies (left - diagnostic of a LMP tumour). Epithelium in a frond-like architecture is seen at the top of image. Credit: Nephron /Wikipedia. CC BY-SA 3.0

In a review article published in the Feb. 4 issue of the *New England Journal of Medicine*, a pair of Mayo Clinic Cancer Center researchers provide an in-depth look at the issues associated with the care of women

in families with hereditary breast and ovarian cancer syndrome who have not yet developed cancer themselves. The article addresses optimal risk assessment for breast and ovarian cancers, the usefulness of risk-reducing surgery, side effects of these procedures, alternative strategies for cancer prevention and the best ways to help with the decision-making process.

"Women whose families have been marked by excess [breast](#) and ovarian cancer are at higher risk of developing those diseases over their lifetime," says lead author and Mayo Clinic oncologist Lynn Hartmann, M.D. "Although these women can reduce their risk considerably through preventive mastectomies and or the removal of their [fallopian tubes](#) and ovaries, these procedures come with their own complications and psychosocial effects."

In the article Dr. Hartmann and co-author, Noralane Lindor, M.D., a pathologist and genetics expert, argue for greater support for women grappling with complex and emotionally charged decisions, and more research to devise improved treatment approaches for hereditary breast and ovarian cancer syndrome.

"Most of the research thus far examined whether or not these procedures could actually prevent cancer and to what extent," says Dr. Hartmann. "Now that we have evidence of the efficacy of the surgeries, there has been a shift toward looking at the psychological impact of these procedures on women. The studies that have been done thus far indicate that most women are satisfied with the choice that they make, but more research is needed to figure out how we can help them sort through their options in the most helpful manner."

Each year, more than 200,000 women in the U.S. are diagnosed with breast cancer, and more than 20,000 are diagnosed with ovarian cancer. Women who have hereditary breast and ovarian cancer syndrome have

had either (or both) disease arise over and over again in their family tree. Mutations in BRCA1 and BRCA2 are the most common genetic defects in these women, though they are still responsible for only a minority of cases.

Women who carry BRCA1 and BRCA2 mutations are often lumped under the single heading BRCA1/2, as if they face the same risks and are susceptible to the same types of cancer. However, Drs. Hartmann and Lindor explain that the diseases spawned by mutations in these two genes can be very different. BRCA1 carriers face an average cumulative risk of 67 percent for [breast cancer](#) and 45 percent for ovarian cancer by age 80. For BRCA2 carriers, those average cumulative risks are 66 percent and 12 percent, respectively.

Most of the breast cancers that develop in BRCA1 carriers are high-grade, "triple-negative" breast cancers (negative for estrogen receptor, progesterone receptor and HER-2). In contrast, breast cancers in BRCA2 carriers are mostly ER-positive, like those seen in the general population. Dr. Hartmann says these differences have significant prognostic and treatment ramifications for these women, because risk-reducing medications are available for women with ER-positive disease but not for those with ER-negative disease.

In addition, ovarian cancer typically strikes earlier and with greater frequency in BRCA1 carriers than in BRCA2 carriers. Current guidelines recommend that BRCA1 and BRCA2 carriers who are done having children have their ovaries and fallopian tubes removed—through a procedure known as a salpingo-oophorectomy—between the ages of 35 and 40 years. The authors believe that women who are BRCA2 carriers can delay this procedure until they are 45 years of age, since their risk of ovarian cancer by 50 years of age is only one percent.

"Many of the studies we discuss were published recently, so we are

taking advantage of the increased knowledge of the types of cancers that these women develop and the ages at which they occur to suggest how we can change our thinking around their management," says Dr. Hartmann. "It is part of medicine today to try to individualize recommendations whenever possible."

For women with strong family histories of breast and [ovarian cancers](#) in whom mutations in the BRCA genes are not present, consideration of testing rarer, less well-understood genes is now an option. Dr. Lindor says that women with mutations discovered in non-BRCA genes or those with no known mutations identified in their family at all face even more difficult decisions when it comes to clinical care as individual cancer risks and treatment benefits are often challenging to define.

To improve recommendations for high-risk women, Drs. Hartmann and Lindor propose future studies that investigate how women weigh their options and studies that follow the short- and long-term psychosocial and medical effects of [women's](#) decisions to undergo surgery, take risk-reducing medications, or pursue surveillance.

Provided by Mayo Clinic

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