Surveillance of women at high or potentially high risk of ovarian cancer

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1. Ovarian cancer surveillance is not recommended for women at high or potentially high risk.
2. Evidence shows that ultrasound or CA125, singly or in combination, is not effective at detecting early ovarian cancer.
3. The most effective risk reducing strategy for ovarian cancer is bilateral salpingo-oophorectomy.

Background

Familial clusters of ovarian cancer have been recognised for many years and family history has been identified as a risk factor in epidemiological studies that have investigated its role.\(^1\) Up to 15% of all cases of invasive ovarian cancers involve the inheritance of a mutated gene.\(^2\) Women born with a mutation in one of several genes have an increased risk of breast and/or ovarian cancer. These include the breast cancer susceptibility genes BRCA1 and BRCA2, p53 and mismatch repair genes. There may be other genes, as yet undiscovered, in which mutations are also associated with a risk of breast or ovarian cancer.

Women who have inherited mutations in the BRCA1 or BRCA2 genes have substantially elevated risks of breast and ovarian cancer, with estimates risks for ovarian cancer, ranging from 36% to 46% for BRCA1 mutation carriers and from 10% to 27% for BRCA2 mutation carriers.\(^3\) The vast majority of affected women do not carry an inherited mutation in a known breast or ovarian cancer predisposing gene. Those women most likely to have inherited a mutation are those with the strongest family history of breast or ovarian cancer, but family history does not necessarily imply an inherited genetic cause.

Definition of potentially high risk

The category of potentially high risk of ovarian cancer covers less than 1% of the female population. As a group, lifetime risk of ovarian cancer ranges between 1 in 30 and 1 in 2. This risk is more than 3 times the population average. Individual risk may be higher or lower if genetic test results are known.\(^4\) Women who have had a genetic fault identified through testing are regarded as being at high risk. Women have been defined as being at potentially high risk of developing ovarian cancer\(^5\) if they:

- Are at high or potentially high risk of breast cancer
- Have one 1° relative diagnosed with epithelial ovarian cancer in a family of Ashkenazi Jewish ancestry*.
- Have one woman in the family with ovarian cancer at any age, and another with breast cancer before the age of 50, where the women are 1° or 2° relatives of each other
- Have two 1° or 2° relatives on the same side of the family diagnosed with epithelial ovarian cancer, especially if one or more of the following features occurs on the same side of the family:
  1. additional relative(s) with breast or ovarian cancer.
  2. breast cancer diagnosed before the age of 40.
3. bilateral breast cancer.
4. breast and ovarian cancer in the same woman.
5. breast cancer in a male relative.

- Have three or more 1° or 2° degree relatives on the same side of the family diagnosed with any cancers associated with hereditary non-polyposis colorectal cancer (HNPCC): colorectal cancer (particularly if diagnosed before the age of 50), endometrial cancer, ovarian cancer, gastric cancer, and cancers involving the renal tract.
- Are a member of a family in which the presence of a high-risk ovarian cancer gene mutation has been established.

*High-risk ovarian and breast cancer mutations are more common in people of Ashkenazi Jewish ancestry.*

**Surveillance for ovarian cancer**

To date, women at high or potentially high risk for ovarian cancer have been offered surveillance using measurement of CA 125 and transvaginal ultrasound (TUVS), should they choose not to have risk-reducing surgery. The effectiveness and potential harms of such surveillance, however, have being questioned by the results of recent studies.

Retrospective and prospective cohort studies of annual surveillance of women at high risk for ovarian cancer using CA 125 and TUVS, have reported low positive predictive values, limited sensitivity with a high number of false positive findings and an inability to detect early stage ovarian cancer. A recent study of women with BRCA1 or BRCA2 mutations, concluded that annual surveillance with CA 125, TVUS and pelvic examination was not effective. The positive predictive values and sensitivities were low and the ovarian cancers found were at an advanced stage.

A meta-analysis of ovarian cancer screening in women at high risk has shown that they tend to develop high-grade serous cancer for which there is no recognisable precursor, so are detected at a later stage for which screening may be of limited value.

**Ongoing Clinical Trials**

**Gynecologic Oncology Group (GOG) 199** is an international, prospective, non-randomised, cohort study of women at increased risk of ovarian cancer, based on a strong family history of breast and/or ovarian cancer, or a personal or family history of a mutation in the BRCA1 or BRCA2 genes. Accrual to the trial was completed in November 2006, having enrolled over 2,500 women, 85 of whom were recruited in Australia. After discussion with their health care provider, women chose to either undergo RRSO or surveillance with CA125, using the Risk of Ovarian Cancer Algorithm (ROCA). Women with a rising trend in CA125 levels over time will undergo additional studies. Tissue removed at the time of RRSO will be examined to assess if examination of the ovaries after surgical removal can provide better information about cancer-related tissue changes. Women who enrol in the surveillance arm can switch to the surgical arm during the course of the study. Primary endpoints are the incidence of breast and ovarian cancer and the feasibility and selected performance characteristics of ROCA. It will also assess Quality of Life and non-oncologic morbidity related to various interventions. Follow up of both arms will continue until November 2011.

**UK Familial Ovarian Cancer Screening Study (UK-FOCCS)** This study commenced in 2000 in the UK and aims to assess and refine screening amongst women with a strong family history of ovarian cancer (involves two or more close relatives with ovarian cancer or one relative with ovarian cancer and a relative with breast cancer that occurred at a young age). Screening will be provided using a CA 125 test every four months and an annual ultrasound scan. An observational study of 145 mainly pre-menopausal, high-risk women, registered with the UK-FOCCS was conducted between 1998 and 2003. The follow-up period was too short to reach any conclusions about the benefits for yearly screening for this group of women. The study will report after 2011.
References

1. The Australian Cancer Network and National Breast Cancer Centre**. Clinical practice guidelines for the management of women with epithelial ovarian cancer. 2004 National Breast and Ovarian Cancer Centre*, Camperdown, NSW.


** In February 2008, National Breast Cancer Centre (NBCC), incorporating the Ovarian Cancer Program, changed its name to National Breast and Ovarian Cancer Centre (NBOCC). On 30 June 2011, NBOCC amalgamated with Cancer Australia to form a single national agency, Cancer Australia, to provide leadership in cancer control and improve outcomes for Australians affected by cancer.

Resource status:

- Greater than 5 years

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