Anxiety or Death?

Uneasy Feelings About Ovarian Cancer Screening

Dr. Lizabeth Brydon, MD, FRCSC

As presented at Pediatrics Obstetrics and Gynecology Overview, Regina, Saskatchewan (February 2006).

Kim's case

- Kim is a 40-year-old woman requesting your advice about her risk of ovarian cancer. Her mother was recently diagnosed with ovarian cancer at age 67 and also had breast cancer at age 42
- Her mother's doctors have asked her if she wishes to have genetic testing. Kim is her only daughter and wonders if she should encourage her mother to also have genetic testing

What is Kim's risk of developing ovarian cancer?

Should Kim have surgery to remove her ovaries?

If not, what other options should she consider?

Table 1
Genetic risk factors for ovarian cancer[1]

Genetic factors	Breast cancer < age 85	Ovarian cancer < age 85
2 normal BRCA genes	11%	1% to 2%
Altered BRCA-1 gene	50% to 70%	20% to 40%
Altered BRCA-2 gene	55% to 80%	10% to 20%

Ovarian cancer is the leading cause of gynecologic cancer death in Canada. Ovarian cancer is usually found in late stage when cure is unlikely. Perhaps 5% to 10% of ovarian cancers result from a hereditary predisposition. Of these, about 50% are linked to either BRCA-1 or BRCA-2 genes (Table 1).

Risks of screening

The aim of screening is to diagnose ovarian cancer in the early stage; however, there are risks involved. The incidence and prevalence of this disease is low. Therefore, if a positive screen leads to surgery and if the false positive rate is high, a large number of healthy women will undergo unnecessary surgery. A screening protocol should have a positive predictive value of at least 10%, meaning no more than nine women with false positive screens would undergo unnecessary surgery for each case of ovarian cancer detected.

Thus, the major dilemma is the emotional cost to a woman who is found to have a positive screen, but does not actually have cancer. She has to undergo numerous investigations, await surgery and then undergo surgery, only to potentially find out that she does not have ovarian cancer. Needless to say, there is a huge potential cost to the health care-system if we attempt to operate on

what would be thousands of women to try to find ovarian cancer, unless the screening test for ovarian cancer becomes more accurate.

The aim of screening is to diagnose ovarian cancer in the early stage; however... if a positive screen leads to surgery and if the false positive rate is high, a large number of healthy women will undergo unnecessary surgery.

Screening tests:

CA-125

CA-125, a serum protein, is elevated in > 80% of women with ovarian cancer, but in only half of those whose ovarian cancer is at stage-I. The sensitivity of CA-125 testing is 70% to 80%, while the specificity is 98.6% to 99.4%. In an average-risk population, 30 women would undergo surgery to detect one case of cancer.

A change in CA-125 levels may be more specific. In one study, the specificity was 99.9% if the CA-125 was > 35 U/mL and doubled in six months.[2] However, there are no trials yet that show reduced mortality.

Transvaginal ultrasonograph (TVUS)

Of 4,526 high-risk women screened with TVUS, only stage-III cancers were found in a total 12,709 scans; no stage-I (*i.e.*, curable) cancers were found.[3]

A study of women at lower-risk was more favourable. Of 14,469 women > 50 years of age with a positive family history for ovarian cancer, 180 patients with persistent TVUS abnormalities underwent surgery, 11 of whom were determined to have stage-I cancer. Thus, 16 women underwent surgery for each stage-I cancer detected.[4]

Multimodal screening

In a feasibility study, 22,000 post-menopausal, average-risk women had their CA-125 level measured. If the level was > 35 U/mL, a TVUS was done. If the TVUS was abnormal, surgery was done. Four women had surgery for every case of ovarian cancer found.[5]

Recommendation of expert groups

The Canadian Task Force on the Periodic Health Examination, the National Institutes of Health Consensus Conference on Ovarian Cancer, the US Preventive Services Task Force, the American College of Obstetricians and Gynecologists and the American College of Physicians all recommend against routine screening at this time.

Final thoughts

There is insufficient support at this time to justify screening women who are at average-risk for ovarian cancer. Considerations for women at increased-risk should be made according to two main factors:

1. High-risk family history

Women with suspected hereditary ovarian cancer syndrome should be referred for genetic counseling. Screening protocols include combinations of the pelvic exam, CA-125 and TVUS. The optimal screening interval is unknown, but most physicians screen every six months. Prophylactic oophorectomy, at the completion of child-bearing or at age 35, has been recommended. A 30-year-old woman with either BRCA-1 or BRCA-2 genes gains 0.3 to 1.7 years of life from prophylactic oophorectomy. Gains in life expectancy decline with age, with no gain by age 60. There was little loss in life expect-ancy if the surgery was performed at age 40, rather than at age 30.

2. Low-risk family history

If there is a family history, but no evidence of a high-risk pattern and the woman is post-menopausal, she may be a candidate for screening. The usual strategy is annual CA-125 testing with TVUS, if the CA-125 is > 35 U/mL.

Dr. Brydon is an Assistant Professor, Department of Obstetrics and Gynecology, University of Sasktachewan; and the Chair of the Gynecologic Cancer Group, Allan Blair Cancer Centre, Regina, Saskatchewan.

References

1. Penson RT, Shannon KE, Sharpless NE, et al: Ovarian cancer: An update on genetics and therapy. Compr Ther 1998; 24(10):477-87.
2. Zurawski VR Jr, Orjaseter H, Andersen A, et al: Elevated serum CA-125 levels prior to diagnosis of ovarian neoplasia: Relevance for early detection of ovarian cancer. Int J Cancer 1988; 15;42(5): 677-80.
3. Fishman DA, Cohen L, Blank SV, et al : The role of ultrasound evaluation in the detection of early-stage epithelial ovarian cancer. Am J Obstet Gynecol 2005; 192(4):1214-21.
4. van Nagell JR Jr, DePriest PD, Reedy MB, et al: The efficacy of transvaginal sonographic screening in asymptomatic women at risk for ovarian cancer. Gynecol Oncol 2000; 77(3):350-6.
5. Jacobs I, Davies AP, Bridges J, et al: Prevalence screening for ovarian cancer in postmenopausal women by CA-125 measurement and ultrasonography. BMJ 1993; 306(6884):1030-4.

Recommended patient information resources

1. The National Cancer Institute Cancer Information Service: 1 (800) 4-CANCER.
2. Women's Cancer Network at www.wcn.org. This site is sponsored by the Society of Gynecologic Oncologists. It is designed to educate the public about cancers of the reproductive system. There is a confidential questionnaire allowing users to assess their individual risk of developing cancer of the ovary.
3. Ovarian Cancer Alliance Canada at www.ovariancancercanada.ca. A Canadian website for public information, supported by the Gynecologic Oncologists of Canada.