

CLINICAL INQUIRIES FROM THE FAMILY PRACTICE INQUIRIES NETWORK

Should we screen for ovarian cancer?

Pamela M. Wiseman, MD

Tulane University School of Medicine, New Orleans, La;

Kathleen Puglia, MLS

Tulane Medical Library, New Orleans, La

■ EVIDENCE-BASED ANSWER

Ovarian cancer screening using pelvic examination, CA-125 serum tumor marker, transvaginal ultrasound (TVU), or any combination of tests is not recommended in average-risk women, or in women with only 1 first-degree relative with ovarian cancer (strength of recommendation [SOR]=**B**). There is insufficient evidence to recommend for or against screening women with 2 or more first-degree relatives with ovarian cancer. A careful discussion of risks and benefits to screening is suggested, with referral to specialists as needed to assist in the decision-making (SOR=**C**).

■ EVIDENCE SUMMARY

The low incidence of ovarian cancer in the general population (40/100,000) makes it a challenge for successful screening. Current screening methods include pelvic examination, CA-125 levels, TVU, or a combination of modalities. Very limited data exist on the usefulness of the bimanual pelvic exam. Palpation can detect some ovarian cancers, but those cancers are usually advanced and associated with a poor prognosis.¹ In general, pelvic exam is not thought to be a useful screening procedure for ovarian cancer in asymptomatic women.

Estimates of the performance of other screening tests are extremely imprecise due to study limitations.² CA-125 has a reported sensitivity of about 80%, a high specificity of 98%–99%, and a false-positive rate of 0.1%–0.6%. Ultrasound has a sensitivity approaching 100%, a lower specificity, and a higher false-positive rate of 1.2%–2.5%. Using ultrasound, more cancers would be identified, but more women would face unnecessary intervention or surgery. Use of multimodal screening (CA-125 followed by TVU if abnormal) can increase specificity to 99.9% but has a lower sensitivity (58%–79%).³ Use of multimodal screening results in a higher rate of false negatives and could therefore create a false sense of security.

Between 5%–17% of women who undergo initial screening with ultrasound and 0.9%–4% of those who undergo multimodal screening will be recalled for further testing, potentially resulting in distress and anxiety. With ultrasound screening, 7–60 women will undergo diagnostic surgery for every 1 cancer detected. Using multimodal screening, 2.5–15 women will undergo diagnostic surgery for every cancer detected.

Before screening is implemented, there should be evidence that early detection and treatment of the disease results in improved outcomes. Several ongoing randomized controlled trials address screening of average-risk women, including one sponsored by the National Institutes of Health (NIH).⁴ There is indirect evidence that early detection prolongs survival, as well as evidence that screening results in an increase in diagnosing a tumor at stage 1.²

A large pilot study showed improved median survival in a screened group compared with a control group (72.9 months vs 41.8 months), but there was no significant difference in either mortality from ovarian cancer or all-cause mortality.³ This is consistent with earlier evidence that screening brings forward the diagnosis of ovarian cancer by about 8 months,¹ but raises the possibility that earlier diagnosis may simply reflect a lead-time bias without any actual improvement in outcome.

Women with 2 or more first-degree family members with ovarian cancer are at risk for one of the rare hereditary cancer syndromes, with lifetime risk of ovarian cancer of 40%. Although there is interest in identifying and screening these very high-risk women, there is no evidence that screening benefits this group in terms of median

■ RECOMMENDATIONS FROM OTHERS

No organization currently recommends routine ovarian cancer screening of average-risk women. The US Preventive Services Task Force (USPSTF),¹ American College of Obstetricians and Gynecologists (ACOG), American College of Physicians,^{5,6} and the Canadian Task Force on Preventive Health Care (CTF)⁷ all recommend against routine use of serum tumor markers or ultrasound for women at average risk.

USPSTF and CTF found insufficient evidence for or against screening women at increased risk. An NIH Consensus Conference recommends comprehensive family history and annual pelvic exam for all women, referral to a specialist for risk counseling for women with 2 or more first-degree relatives, and annual screening with pelvic examination, CA-125, and TVS in women with known hereditary ovarian cancer syndrome.⁸

ACOG recommends an annual pelvic examination for all women as part of routine preventive care.⁹ While the USPSTF does not recommend the use of pelvic exam for ovarian cancer screening, it states it is prudent to do a bimanual examination when performing a gynecologic examination for other reasons.^{1,9}

CLINICAL COMMENTARY

Better screening tests are needed

Ellen Beck, MD

University of California at San Diego School of Medicine

The fear that one's ovaries may contain undetected cancer is one many women share. Currently only 25% of ovarian cancers are found in early stages. A screening test to diagnose early stage disease is clearly needed. CA-125 is not a sufficient screening test

because it may also be elevated in hepatic disease, renal failure, and pancreatitis. The new field of proteomics, the study of precise protein patterns of cancer cells, holds promise to develop a blood test for ovarian cancer screening.

Studies have identified patterns unique to ovarian cancers. Physicians should have a high index of suspicion for cancer clusters in families. For example, Jewish women in America are mainly Ashkenazi (family from Eastern Europe), and 1 in 40 Ashkenazi Jewish women carry the BRCA-1 or -2 gene. Women having both breast and ovarian cancer, or with first-degree relatives with these diseases, may carry these genes, which put them at risk for colon cancer, oropharyngeal cancer, and melanoma as well.

Women in families with a high incidence of colon cancer at an early age should be followed closely for breast or ovarian cancer. Those women with potential hereditary nonpolyposis colorectal cancer syndrome (3 family members with colon cancer, 1 younger than age 50, and in 2 generations) are at risk for other cancers, including uterus, ovaries, stomach, and pancreas.

REFERENCES

1. US Preventive Services Task Force. *Guide to Clinical Preventive Services: Report of the US Preventive Services Task Force*. 2nd ed. Baltimore: Williams & Wilkins, 1996.
2. Bell R, Petticrew M, Sheldon T. The performance of screening tests for ovarian cancer: results of a systematic review. *Br J Obstet Gynaecol* 1998;105:1136–1147.
3. Jacobs IJ, Skates SJ, MacDonald N, et al. Screening for ovarian cancer: a pilot randomised controlled trial. *Lancet* 1999;353:1207–1210.
4. Prorok PC, Andriole GL, Bresalier RS, et al. Design of the Prostate, Lung, Colorectal and Ovarian (PLCO) cancer screening trial. *Control Clin Trials* 2000;21 (6 Suppl):273S–309S.
5. Carlson KJ, Skates SJ, Singer DE. Screening for ovarian cancer. *Ann Intern Med*. 1994;121:124–132.
6. Screening for ovarian cancer: recommendations and rationale. American College of Physicians. *Ann Intern Med* 1994;121:141–142.
7. Gladstone CQ. Screening for ovarian cancer. In: *Canadian Task Force on the Periodic Health Examination*. Canadian Guide to Clinical Preventive Health Care. Ottawa: Canada Communication Group; 1994;870–881.
8. National Institutes of Health Consensus Development Conference Statement. Ovarian cancer: screening, treatment and follow-up. *Gynecol Oncol* 1994;55:S4–S14.
9. ACOG Committee Opinion No. 280, December 2002. The role of the generalist obstetrician-gynecologist in the early detection of ovarian cancer. *Obstet Gynecol* 2002;100:1413–1416.

