ATTENTION

This Policy was reaffirmed by the ACPM Board of Regents on 1/31/2005 and is effective through 1/31/2010.

Screening Asymptomatic Women for Ovarian Cancer: American College of Preventive Medicine Practice Policy Statement

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Burden of suffering

Ovarian cancer is the fourth leading cause of cancer death in women in the United States. In 1997, it is estimated that 26,800 new cases will be diagnosed and 14,200 women will die of ovarian cancer. (1) Ovarian cancer has a prevalence of 50/100,000 and an annual incidence rate of 14/100,000. (2) Despite advances in treatment and attempts at early diagnosis, long-term survival is bleak, with only 46% of Caucasian patients surviving five years. (1) Most patients with epithelial ovarian cancer, the predominant form, are asymptomatic in early-stage disease and usually present with stage III or IV disease. Their five-year survival is less than 25%, with lower survival among African-American women. (1) The minority of patients discovered with early-stage disease have a five-year survival rate of 80%-90%. (1) In the absence of a family history of ovarian cancer, lifetime risk of ovarian cancer is 1/70. Risk factors include familial cancer syndromes (risk of up to 82% by age 70 in women with hereditary breast/ovarian syndrome); family history (1.4% lifetime risk with no affected relatives, 5% with one affected relative, 7% with two affected relatives); (3) nulliparity; advancing age; obesity; personal history of breast, endometrial, or colorectal cancer; fewer pregnancies; or older age (>35 years) at first pregnancy. However, 95% of all ovarian cancers occur in women without risk factors. Use of hormonal contraceptives, oophorectomy, and tubal sterilization reduce risk of ovarian cancer; (3-5) however, even bilateral ooperectomy may not be completely effective in preventing ovarian cancer.

Description of preventive measures

Techniques that may be used for ovarian cancer screening include history and bimanual examination, ultrasonography (transabdominal, transvaginal, and color flow Doppler imaging), and serum tumor markers. Bimanual examination involves insertion of one or two examiner fingers into the vaginal vault with simultaneous palpation of the lower abdomen to characterize the size and shape of the uterus and adnexa; a recto-vaginal examination may also be included. Ultrasonography involves the use of sound waves to delineate internal structures; transducers may be placed on the abdomen or in the vagina, and other imaging modalities, such as color flow, may enhance visualization. Biochemical markers include CA 125 and other antigens that are usually increased (nonspecifically) in ovarian cancer. Genetic or molecular biomarkers have only been recently discovered; currently their use in screening is limited to research purposes. When an abnormality is detected with one modality, others are frequently employed to assist in diagnosis; however, laparoscopy or laparotomy, is required for definitive diagnosis.

Evidence of effectiveness

Sensitivity of pelvic examination for detection of ovarian cancer is unknown; however, it is thought to be quite low due to the anatomic location of the ovary. Cancers detected by pelvic examination are often far advanced. Ultrasound is widely used for diagnostic testing for pelvic masses, but is limited in its usefulness as a screening tool by high rates of false-positive results and low positive predictive value. One study reported a relatively high sensitivity (100%) and specificity (94.6%) of routine ultrasound of asymptomatic women, but positive predictive value was low (2.6%). (6) Because transvaginal ultrasound provides a higher level of detail than transabdominal ultrasound, it maintains a higher sensitivity (100%) and allows a higher specificity (98.7%) for ovarian cancer. (7) However, due to high rates of false-positive interpretations, positive predictive value is still low (22%). (8) Color flow Doppler imaging, in combination with transvaginal ultrasonography, improves specificity and ability to discriminate benign and malignant tumors, but its value in screening is unknown.

Studies on the effectiveness of ultrasound for screening are limited by small sample sizes, limited follow-up, and the use of nonrandomized volunteers. Routine ultrasound screening of asymptomatic women generates a high proportion of false-positive results, which require laparoscopy or laparotomy. One study of 805 high-risk women yielded 39 laparotomies, 1 ovarian cancer, and 8 other tumors (2 borderline tumors, 1 cecal cancer, 5 cystadenomas). (10)

Another study of 5,489 asymptomatic women with or without a family history of breast or gynecologic cancer reported the detection of 5 cancers in 14,356 ultrasound screens performed over 3 years. (11) It has been estimated that ultrasound screening of 100,000 women over age 45 would detect 40 cases of ovarian cancer, with 5,398 false-positive results and more than 160 complications from laparoscopy. (12)

Biochemical markers, particularly CA 125, are useful in monitoring patients with ovarian cancer and have been suggested for screening, either alone or in combination with ultrasound. Although CA 125 is detectable in 80% of epithelial ovarian cancers, (13) it is elevated in less than half. (14) Following a single elevated CA 125 measurement with abdominal ultrasound yielded a sensitivity of 58%-79%, specificity approaching 100%, and positive predictive value of 27% in one series. (14) Molecular biomarkers, such as BRCA1, a genetic marker for familial breast/ ovarian cancer syndrome, may be useful in certain cases for detection of those at particularly high risk of ovarian cancer; however, use is still experimental.

The high association between stage of diagnosis and survival from ovarian cancer suggests that screening or early detection could decrease mortality association with ovarian cancer, but the role of lead and length-time bias remains unresolved. However, to date, no large-scale, prospective randomized trial with adequate follow-up comparing screening modalities to clinical observation has been completed. Such an investigation is underway, under the auspices of the National Institutes of Health (NIH) as part of the Prostate, Lung, Colorectal, and Ovary randomized clinical trial comparing CA 125 and transvaginal ultrasound screening to routine care.

Public policy considerations

Screening for ovarian cancer is expensive because of low prevalence of disease, high rate of surgical intervention for noncancerous disease, and high costs of tests and follow-up. Many experts suggest that the possible benefits of lowered mortality or years of life saved do not justify the costs of screening. The low positive predictive value associated with currently available screening modalities suggests that more women without cancer will be subject to laparoscopy or laparotomy than will those with cancer. Even a test with 99% specificity and 100% sensitivity would yield only 1 in 21 women with a positive screen actually having the disease. (15) Modeling studies of annual screening with CA 125, with or without a single screening with transvaginal ultrasound, found an increase in life expectancy of less than one day per woman screened. (16,17)

Recommendations of other groups

An NIH consensus panel recommends family history and annual pelvic examination for ovarian cancer screening. The American Cancer Society, National Cancer Institute, American Academy of Family Physicians, American College of Obstetricians and Gynecologists, American Medical Association, American Nurse's Association, and American Medical Women's Association recommend annual pelvic exams (along with Pap smears) for women starting when sexual activity commences or age 18. The US Preventive Services Task Force does not recommend routine pelvic examination for the detection of ovarian cancer. No organization currently recommends either ultrasound or cancer marker screening in asymptomatic women, and multiple organizations (including the American College of Physicians, the Canadian Task Force on the Periodic Health Examination, and the American College of Obstetricians and Gynecologists) recommend against it. Regarding women at higher risk (e.g., hereditary cancer syndromes), the NIH consensus conference recommends annual CA 125 measurements, pelvic exam, and transvaginal ultrasound until childbearing is completed; at age 35, women should be referred for bilateral oophorectomy. The US Preventive Services Task Force and Canadian Task Force on the Periodic Health Examination find insufficient evidence to define or screen high-risk women, although the U.S. Task Force suggests specialist referral for women with hereditary cancer syndromes.

Rationale

With a high mortality and survival advantage from early-stage detection and treatment, ovarian cancer is a potential candidate for population-based screening. However, because of its low prevalence, even with relatively high sensitivity and specificity estimates for proposed screening tests, predictive value of a positive test is too low. The evidence is insufficient at this time to recommend physical examination, ultrasonography, biochemical markers, or genetic screening for asymptomatic women for early detection of ovarian malignancy. Results of studies thus far indicate that, even in a high-risk population, many women must undergo surgical procedures to diagnose relatively few cancers. Although sensitivity and specificity may improve with combinations of available tests or in some subpopulations of women, research has not convincingly demonstrated that screening will reduce morbidity or mortality from ovarian cancer or improve the health status of women.

American College of Preventive Medicine Recommendation For Ovarian Screening

The American College of Preventive Medicine does not currently recommend routine pelvic exams for the detection of ovarian cancer (although pelvic examinations may be performed for diagnostic purposes) or the use of CA 125 or ultrasound to screen asymptomatic women. These same recommendations apply to women with either none or one first degree relative with ovarian cancer. Screening of women with familial cancer syndrome may be appropriate, due to their elevated risk of cancer, but direct evidence of effectiveness is lacking. Clinicians should therefore take a thorough family history regarding breast, ovarian, and other cancers, and women at high risk should be counseled about the benefits and risks of ovarian cancer screening. Until prospective, randomized clinical trials are completed, the American College of Preventive Medicine cannot recommend population-based screening apart from participation in clinical investigations.

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