IV. Ovarian Cancer

A. Epidemiology of ovarian cancer (Nelson article)
   1. Recognize need for and associated problems with early diagnosis
   2. Basic risk factors
      a. Advancing age
      b. Reproductive history
      c. Family history and the BRCA1 and BRCA2 genes
      d. Post hysterectomy/oophorectomy

B. Screening techniques available (ACOG Committee Opinion)
   1. Review techniques available including specificity and positive predictive value
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      b. Annual pelvic ultrasound
      c. Bimanual examination
   2. Cost-effectiveness
   3. Recognize gene testing controversy

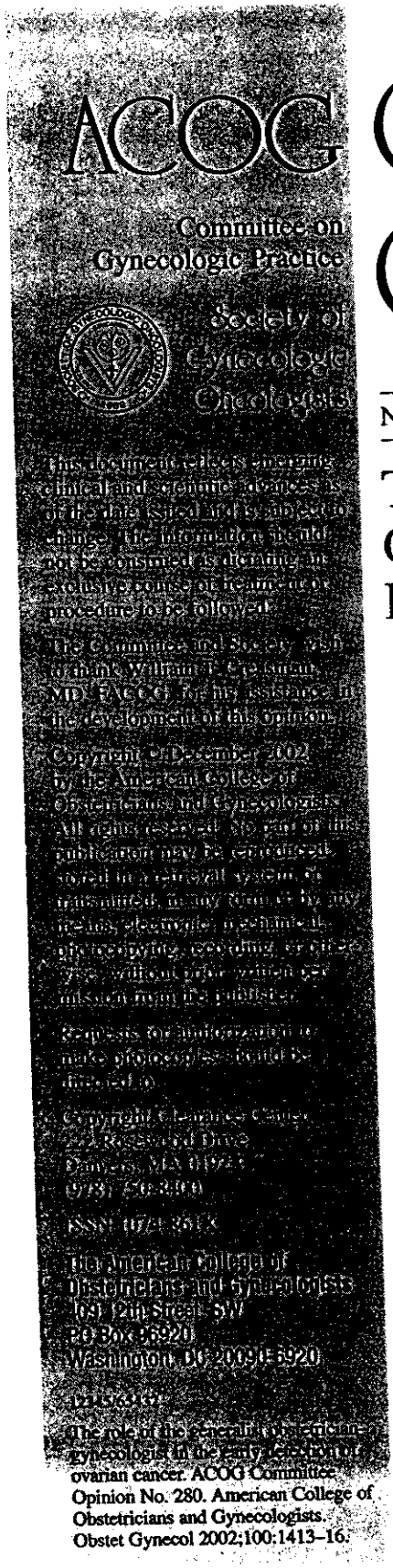
.C. Additional resources
   1. Gilda Radner Familial Ovarian Cancer Registry (http://www.ovarianancer.com)
   2. National Ovarian Cancer Coalition (http://www.ovarian.org)
   3. Medline Plus – patient tutorial available in Spanish

Resources

ACOG Committee Opinion. December, 2002. Number 280.

Carcio HA. . Advanced Health Assessment of Women. (1999) Philadelphia: Lippincott, Chapter 4, pp. 52-70

Nelson HD et al. Screening for ovarian cancer. US Preventive Services Task Force. 2004, May.



Committee Opinion

Number 280, December 2002

The Role of the Generalist Obstetrician–Gynecologist in the Early Detection of Ovarian Cancer

ABSTRACT: The purpose of this Committee Opinion is to define the role of the generalist obstetrician–gynecologist in the early detection of ovarian cancer. Currently, it appears that the best way to detect early ovarian cancer is for both the patient and her clinician to have a high index of suspicion of the diagnosis in the symptomatic woman. In evaluating symptoms, physicians should perform a physical examination, including a pelvic examination. In premenopausal women with symptoms, a CA 125 measurement has not been shown to be useful in most circumstances. In postmenopausal women with a pelvic mass, a CA 125 measurement may be helpful in predicting a higher likelihood of a malignant tumor than a benign tumor, which may be useful in making consultation or referral decisions or both. A woman with a suspicious or persistent complex adnexal mass requires surgical evaluation by a physician trained to appropriately stage and debulk ovarian cancer. Data suggest that currently available screening tests do not appear to be beneficial for screening low-risk, asymptomatic women. An annual gynecologic examination with an annual pelvic examination is recommended for preventive health care.

Although ovarian cancer is the second most common female reproductive cancer, preceded by cancer of the uterine corpus, more women die from ovarian cancer than from cervical and uterine cancer combined. In the United States, it is estimated that ovarian cancer will be diagnosed in 23,300 women, and 13,900 women will die from this malignancy in 2002. The principal reason for these poor outcomes is the advanced stage of disease at diagnosis in 70–75% of cases and an overall 5-year survival of only 20–30%. However, women with a diagnosis of stage I disease achieve a 90–95% probability of cure. The purpose of this Committee Opinion is to define the role of the generalist obstetrician–gynecologist in the early detection of ovarian cancer.

The poor prognosis of ovarian cancer often is attributed to the fact that it is a "silent" cancer, with symptoms appearing only late in the disease process. This is a misconception, in that studies have shown that women with ovarian cancers are symptomatic often several months before the diagnosis, even with early-stage disease. In a survey of 1,725 women with ovarian cancer, 70% recalled having symptoms for 3 months or longer before the diagnosis, and

35% recalled having symptoms for at least 6 months (1). About three fourths of these women had abdominal symptoms and half had pain or constitutional symptoms. Overall, only 5% were asymptomatic, including only 11% of those with stage I and stage II disease. Pelvic examinations and tests to evaluate symptoms in these women were done more frequently by obstetrician–gynecologists than by other primary care physicians, resulting in earlier disease diagnosis.

Currently, it appears that the best way to detect early ovarian cancer is for both the patient and her clinician to have a high index of suspicion of the diagnosis in the symptomatic woman. This requires education of both as to the symptoms commonly associated with ovarian cancer. Persistent symptoms such as an increase in abdominal size, abdominal bloating, fatigue, abdominal pain, indigestion, inability to eat normally, urinary frequency, pelvic pain, constipation, back pain, urinary incontinence of recent onset, or unexplained weight loss should be evaluated with ovarian cancer being included in the differential diagnosis. Because ovarian cancer occurs most frequently in the postmenopausal woman (median age, approximately 60 years), these symptoms should not be ignored in these women. Unfortunately, many women and clinicians are quick to attribute such symptoms to menopause, aging, dietary changes, stress, or functional bowel problems. As a result, delays of weeks or months often occur before medical advice is sought or diagnostic studies are performed.

In evaluating these symptoms, physicians should perform a physical examination, including a pelvic examination. Imaging studies (including vaginal ultrasonography) may be helpful before making the diagnosis of irritable bowel syndrome, depression, stress, or other diagnoses. In premenopausal women with symptoms, a CA 125 measurement has not been shown to be useful in most circumstances because elevated levels of CA 125 are associated with a variety of common benign conditions, including uterine leiomyomata, pelvic inflammatory disease, endometriosis, adenomyosis, pregnancy, and even menstruation. In postmenopausal women with a pelvic mass, a CA 125 measurement may be helpful in predicting a higher likelihood of a malignant tumor than a benign tumor, which may be useful in making consultation or referral decisions or both; however, a normal CA 125 measurement alone does not rule out ovarian cancer because up to 50% of early-stage cancers and 20–25% of advanced cancers are associated with normal values. The longer the delay in evaluating symptoms or suspicious findings by either the patient or the clinician, the more likely advanced disease will be found.

Diagnostic criteria based on physical examination and imaging techniques that should be used to consider referral to or consultation with a gynecologic oncologist are as follows:

- Postmenopausal women who have a pelvic mass that is suspicious for a malignant ovarian neoplasm, as suggested by at least one of the following indicators: elevated CA 125 level; ascites; a nodular or fixed pelvic mass; evidence of abdominal or distant metastasis; a family history of one or more first-degree relatives with ovarian or breast cancer
- Premenopausal women who have a pelvic mass that is suspicious for a malignant ovarian neoplasm, as suggested by at least one of the following indicators: very elevated CA 125 level (eg, >200 U/mL); ascites; evidence of abdominal or distant metastasis; a family history of one or more first-degree relatives with ovarian or breast cancer

A woman with a suspicious or persistent complex adnexal mass requires surgical evaluation. In these circumstances, a physician trained to appropriately stage and debulk ovarian cancer, such as a gynecologic oncologist, should perform the operation. This should be done in a hospital facility that has the necessary support and consultative services (eg, pathology) to optimize the patient's outcome. When a malignant ovarian tumor is discovered and the appropriate operation cannot be properly performed, a gynecologic oncologist should be consulted.

Of particular concern is the observation that many women with early-stage disease do not undergo appropriate surgical staging. Patients whose comprehensive surgical staging confirms early-stage disease have a much better prognosis than those patients who were thought to have early-stage disease but did not undergo comprehensive surgical staging, presumably because occult disease was missed. In the absence of clinically apparent malignant disease, intraoperative pathology consultation should be obtained if cancer remains a concern. If an apparent early-stage malignancy is present, comprehensive surgical staging should be performed, preferably during the same operation. At the time of surgery for a pelvic mass, samples for peritoneal cytology should be obtained when the abdomen is entered. The mass should be removed intact through an incision that permits thorough staging and surgical management of the primary tumor and possible

sites of metastasis. After the liver, spleen, and all peritoneal surfaces, including both hemidiaphragms, are inspected and palpated, a bilateral pelvic and paraaortic lymphadenectomy is performed along with an omentectomy, peritoneal biopsies, removal of the uterus and adnexa, and biopsies or removal of any suspicious lesions. When the cancer appears to be confined to one ovary, especially if it is low grade, it may be appropriate to modify the staging procedure by leaving the uterus and the uninvolved ovary in place for younger women who wish to preserve their fertility.

Unfortunately, there is no screening test for ovarian cancer that has proved effective in screening low-risk asymptomatic women. Measurement of CA 125 levels and completion of pelvic ultrasonography (both abdominal and transvaginal) have been the two tests most thoroughly evaluated. One group of researchers evaluated 22,000 women with CA 125 screening, followed by pelvic ultrasonography if an elevated tumor marker was present (2, 3). More than 98% of women had normal CA 125 values. Of the remaining group, 41 (0.1%) had both increased CA 125 values and abnormal ultrasonograms and underwent surgical assessment. Only 11 women (0.05% of women screened) had ovarian cancer, which was stage III in 7 women. The false-positive rate among those undergoing surgery was 73%. Another group of researchers evaluated 14,469 asymptomatic women with transvaginal ultrasonography, performing 57,214 scans over a period of several years (4). During the period of evaluation, only 11 of 180 women who had surgery for abnormal adnexal masses (6% of operations and 0.07% of women screened) had primary epithelial ovarian cancers, 6 of whom had cancers beyond stage I. Unfortunately, 4 additional women developed primary epithelial ovarian cancers (stage II and stage III) within 12 months of a normal scan. In a mass screening study of 51,500 women conducted over several years using transvaginal ultrasonography, 324 women were identified with abnormalities requiring surgery (5). Only 17 of these women (5% of operations and 0.03% of women screened) were found to have primary epithelial ovarian cancers.

Data suggest that currently available tests do not appear to be beneficial for screening low-risk, asymptomatic women because their sensitivity, specificity, positive predictive value, and negative predictive value have all been modest at best. Because of the low incidence of disease, reported to be approximately one case per 2,500 women per year, it has been estimated that a test with even 100% sensitivity and 99% specificity would have a positive predictive value of only 4.8%, meaning 20 of 21 women undergoing surgery would not have primary ovarian cancer. Unfortunately, no test available approaches this level of sensitivity or specificity.

Hereditary ovarian cancer is estimated to represent only 5–10% of all ovarian cancers. Based on current data, a woman with a germline mutation of *BRCA1* or *BRCA2* has a lifetime risk of 15–45% of developing ovarian cancer. There are no data demonstrating that screening improves early detection of ovarian cancer in this population. These women should be offered genetic counseling to address issues that relate to their high risk of breast and ovarian cancer and the potential impact of these genetic mutations on their offspring. Even if this group were screened for ovarian cancer on a regular basis, more than 90% of all potential ovarian cancer patients would remain unscreened.

Despite varying recommendations regarding the frequency of cervical cytology screening, the Committee on Gynecologic Practice and the Society of Gynecologic Oncologists still believe that an annual gynecologic examination with an annual pelvic examination is recommended for preventive health care. Although newer tumor markers and proteomics are undergoing investigation and appear promising for screening, it is unclear whether they will help identify high-risk women or facilitate the early diagnosis of more women with ovarian cancer. Currently, there are no techniques that have proved to be effective in the routine screening of asymptomatic low-risk women for ovarian cancer.

References

1. Goff BA, Mandel L, Muntz HG, Melancon CH. Ovarian carcinoma diagnosis. Cancer 2000;89:2068–75.
2. Jacobs IJ, Skates SJ, MacDonald N, Menon U, Rosenthal AN, Davies AP, et al. Screening for ovarian cancer: a pilot randomized controlled trial. Lancet 1999;353:1207–10.
3. Jacobs I, Davies AP, Bridges J, Stabile I, Fay T, Lower A, et al. Prevalence screening for ovarian cancer in postmenopausal women by CA 125 measurement and ultrasonography. BMJ 1993;306:1030–4.
4. van Nagell JR Jr, DePriest PD, Reedy MB, Gallion HH, Ueland FR, Pavlik EJ, et al. The efficacy of transvaginal sonographic screening in asymptomatic women at risk for ovarian cancer. Gynecol Oncol 2000;77:350–6.
5. Sato S, Yokoyama Y, Sakamoto T, Futagami M, Saito Y. Usefulness of mass screening for ovarian carcinoma using transvaginal ultrasonography. Cancer 2000;89:582–8.

Brief Evidence Update

Screening for Ovarian Cancer

U.S. Preventive Services Task Force (USPSTF)

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Background

Systematic reviews of the evidence serve as the basis for U.S. Preventive Services Task Force (USPSTF) recommendations on clinical prevention topics. The Task Force tailors the scope of these reviews to each topic. The USPSTF determined that a brief, focused evidence review was needed to update its 1996 recommendations on screening for ovarian cancer.[1]

To assist the USPSTF, the Oregon Evidence-based Practice Center (under contract to the Agency for Healthcare Research and Quality) performed a targeted review of the literature published on this topic from 1995 to 2002.

In 1996, the USPSTF stated that routine screening for ovarian cancer by ultrasound, the measurement of serum tumor markers, or pelvic examination was not recommended (a D Recommendation).[1] There was insufficient evidence to recommend for or against the screening of asymptomatic women at increased risk for developing ovarian cancer (a C Recommendation). In addition, the USPSTF indicated that although there was no direct evidence from prospective studies that women with early-stage ovarian cancer detected through screening have lower mortality from ovarian cancer than do women with more advanced disease, indirect evidence supported this rationale. Available screening tests,

however, were found to be inadequately sensitive/specific for screening and had not been adequately tested for this purpose.

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Epidemiology

Ovarian cancer is the fifth leading cause of cancer death among women in the U.S., accounting for an estimated 23,400 new cases and 13,900 deaths in 2001.[2] Risk for ovarian cancer increases with age and peaks in the eighth decade.[2] The overall age-adjusted incidence rate is 16.8 cases per 100,000 (95 percent confidence interval [CI], 16.6-17.1) and the age-adjusted rate for women aged 50 and older is 44.4 per 100,000 (95% CI, 43.5-45.2).[3] Approximately 90 percent of malignant ovarian tumors are of epithelial origin.

The 5-year relative survival rate for all stages of ovarian cancer in the U.S. is 50 percent, but may improve to 95 percent for women whose disease is detected and treated at stage I.[2] However, up to 75 percent of women with ovarian cancer have non-localized disease at the time of diagnosis because early stages are often asymptomatic. Five-year relative survival rates for women with regional and distant disease are 79 percent and 28 percent, respectively.[2] Efforts to develop screening methods and strategies are focused on increasing the proportion of cases detected in early stages, particularly stage I.

A number of risk factors have been associated with ovarian cancer. The strongest associations related to reduced risk include oral contraceptive use (relative risk [RR] 0.66; 95% CI, 0.55-0.78) and any term pregnancy (RR 0.47; 95% CI, 0.4-0.56).[4] The strongest association with increased risk is family history. Existence of 1 first- or second-degree relative with ovarian cancer increases the RR to 3.1 (95% CI, 2.2-4.4); 2 or 3 relatives with ovarian cancer increases the RR to 4.6 (95% CI, 1.1-18.4).[5] Some studies suggest that postmenopausal estrogen use is a risk factor for ovarian cancer,[6,7] while others do not.[8] It has not yet been determined how to use these risk factors in a screening strategy.

In some families, the pattern of cancers suggests the presence of a dominantly inherited gene (*BRCA1*, *BRCA2*). Carriers of the BRCA1 gene in such linkage families may have a risk of up to 60 percent for developing ovarian cancer by the age of 70, as well as an increased risk for breast cancer.[9] Carriers of the *BRCA2* gene are at increased risk for ovarian, colorectal, endometrial, stomach, and possibly pancreatic cancer.[9] A growing literature focuses on the identification of women who carry these genes by genetic testing for the purposes of initiating measures to prevent ovarian and related cancers (i.e., surveillance, prophylactic oophorectomy).

Current screening methods include transvaginal or transabdominal ultrasound scanning of the ovaries and measurement of the tumor-marker cancer antigen 125 (CA 125) in serum. Although several other tumor markers have been associated with ovarian cancer, they have not been widely tested for screening purposes. When used for screening, CA 125 measurement is usually followed by ultrasound scanning in women with abnormal levels. The definition of abnormal level varies with menopausal status. The presence of rising CA 125 levels obtained by serial measurements has also been used to indicate possible tumor activity. There are no universally-accepted criteria for distinguishing between benign and malignant conditions on the basis of ultrasound findings. Several systems for classifying and scoring abnormalities have been described.[10-12] Women with persistently abnormal findings on these

tests are referred for diagnostic abdominal surgery usually including oophorectomy. Treatment of diagnosed cancers includes surgery and chemotherapy or other adjuvant therapy for tumors that have extended beyond the ovaries.

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Methods

In conjunction with a medical librarian, we conducted literature searches using MEDLINE® (January 1995-December 2002) (search terms are listed in the Appendix) and the Cochrane Controlled Trials Register (www.cochrane.org), yielding 685 abstracts. Additional articles were obtained by reviewing reference lists of pertinent studies, reviews, and editorials. We also reviewed results of a systematic review on screening for ovarian cancer by the Health Technology Assessment (HTA) program in the United Kingdom.[13] Studies were included if they addressed the key questions for the target population of asymptomatic women. Studies were excluded if the population was selected according to prior test results. Papers related to genetic testing were also excluded because they are beyond the scope of screening recommendations for the general population. This topic will be addressed in an upcoming recommendation from the USPSTF.

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Analytic Framework

The analytic framework indicates the target population, interventions, and health outcome measures examined (Figure 1, 15 KB). This update will focus on studies of screening and performance of detection technologies available since the last USPSTF review. Numbered arrows in the figures correspond to the key questions considered, as listed in Key Questions and Results.

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Key Questions and Results

1. Does Screening for Ovarian Cancer among Asymptomatic Women Result in Early Detection and, with Effective Treatment, Reduce Premature Death and Disability?

Screening Studies with Early Detection Outcomes

The HTA systematic review reported that both CA 125-based multimodal screening (CA 125 followed by ultrasound if CA 125 levels are high) and ultrasound screening alone can detect a higher proportion of ovarian cancers at stage I than the 25 percent currently observed in the U.K.[13] This report estimated that approximately 50 percent (95% CI, 23-77) of ovarian cancers are diagnosed at stage I in the 4 CA 125-based multimodal screening studies examined,[14-17] and approximately 75 percent (95% CI, 35-97) in the 8 ultrasound screening studies.[18-25] For women with a family history of ovarian cancer, 60 percent (95% CI, 32-84) are diagnosed at stage I based on 8 studies using either of the techniques. However, the studies for which all of

these estimates are based reported small numbers of cancer cases, varied in methods, and enrolled mostly self-selected women.

Three prospective studies of screening published after the systematic review are consistent with these findings. A 10-year study of 183,034 asymptomatic pre- and postmenopausal women in Japan, undergoing primary screening with transvaginal ultrasonography in a voluntary community screening program, reported that 58.8 percent of 85 ovarian cancers detected were stage I.[26] Another study of transvaginal ultrasonography screening in the U.S. enrolled over 14,000 asymptomatic women, including normal risk women aged 50 and older, and women with a family history of ovarian cancer aged 25 and older.[27] Women meeting criteria for abnormal sonograms were further evaluated by repeat scans. Those with persistently abnormal scans were referred for surgery. Approximately 65 percent of tumors in this study were stage I. A pilot randomized controlled trial (RCT) to determine feasibility of multimodal screening (CA 125 followed by ultrasound if CA 125 levels were high) was recently conducted in nearly 22,000 women in screening and control groups in the U.K.[28] Results indicated that 50 percent of cancers detected by screening, and 5 percent of those in the control group, were stage I.

Screening Studies with Mortality Outcomes

No RCTs of screening for ovarian cancer in the general population with mortality outcomes have been completed, although some are currently in progress. These include the U.K. Collaborative Trial of Ovarian Cancer Screening (UKCTOCS),[29] the European Randomized Trial of Ovarian Cancer Screening (ERTOCS),[29] and the NIH Prostate, Lung, Colon, Ovary (PLCO) trial in the U.S.[30,31]

The UKCTOCS is enrolling 200,000 postmenopausal women aged 50 to 74 recruited from community registers. These women are randomized in a 1:1:2 ratio to ultrasound screening, multimodal screening (sequential CA 125 tests followed by ultrasound in those testing positive), and a control group. Positive thresholds for CA 125 are calculated on the basis of age and level of change of CA 125 levels. Women will be tested annually 6 times, and followup will continue for 7 years using cancer registrations and postal questionnaires to obtain mortality outcomes. Additional endpoints include quality of life, health economics, morbidity, and compliance with screening.

The ERTOCS trial is recruiting women aged 50 to 64 from population registries or from breast cancer screening programs to total 30,000 in each intervention arm and 60,000 in the control group. The screening protocol includes transvaginal ultrasound at either 18- or 36-month intervals. Women are referred for repeat scans if ovarian volume is 3 or more multiples of the median for postmenopausal women or if a complicated or large ovarian cyst is present. The study may include a 10-year followup time using cancer registrations and death notifications for mortality outcomes.

The NIH PLCO trial has recruited women aged 55 to 74 by using primarily mass mailings for a total 38,000 women in each arm. The screening protocol includes transvaginal ultrasound annually for 4 years and CA 125 annually for 5 years. A control group receives usual care. A positive result on testing initiates a referral to the patients' own physicians for diagnosis.

2. How Well Do Screening Tests or Procedures Identify Women with Ovarian Cancer?

The HTA review identified 16 prospective cohort studies of screening in asymptomatic, average-risk women that reported data on sensitivity and specificity of tests for women who underwent diagnostic surgery.[13,32] Findings indicated that the sensitivity of annual ultrasound screening was approximately 100 percent, with a false-positive result rate of approximately 1.2 percent to 2.5 percent based on 5 studies.[20,22-24,33] The addition of color Doppler imaging to ultrasound screening reduced the false-positive rate to 0.3 percent from 0.7 percent; however, results of studies were inconsistent.[22,34] The sensitivity of annual CA 125-based multimodal screening was estimated at 80 percent, with false-positive rates of 0.1 percent to 0.6 percent based on 3 studies.[14,15,17] All these estimates were based on small numbers of cancers, and studies varied in length of followup, although most did not extend longer than 1 year. Not enough data are available to determine the sensitivity and specificity of successive screening rounds.

3. What Are the Harms of Screening?

Because of the low incidence of ovarian cancer in the general U.S. population, the positive predictive value (PPV) of screening is low. The HTA evidence review estimated that using annual ultrasound screening, only 0.6 percent of those recalled for abnormal results, and 3 percent undergoing surgery, have cancer.[13] The PPV for CA 125-based multimodal screening was estimated as 1 percent for initial recall and 15 percent for surgery. An estimated 3 percent to 12 percent of screened women will be recalled for further testing and assessment, resulting in potential distress and anxiety to otherwise healthy women.[32] Approximately 0.5 percent to 1 percent of women will suffer a significant complication because of surgery, based on reports from published studies.[13]

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Discussion

The HTA systematic review applied estimates from currently available studies to outcome tables to determine the potential benefits and harms of ovarian cancer screening. These calculations assumed an average annual incidence of ovarian cancer of 40 per 100,000 for women aged 50 to 64 and a 40 percent reduction in mortality with screening. Two approaches were evaluated: one using biannual transvaginal ultrasound (assuming 7 percent of women recalled for abnormal findings and 1.3 percent false-positive results at diagnostic surgery) and another using annual CA 125 (assuming 3 percent recall and 0.2 percent false-positive results). Results are illustrated in Table 1. A sensitivity analysis that considered higher risk women using bi-annual transvaginal ultrasounds indicated improved predictive value (Table 2).

Available evidence indicates that screening asymptomatic, average-risk women with ultrasound or with CA 125 tests followed by ultrasound, if levels are high, can detect ovarian cancer at an earlier stage than it would be detected in an unscreened population. The sensitivity of ultrasound screening after 1 year of followup approaches 100 percent and CA 125-based screening, 80 percent; however, these estimates are based on limited data. Although specificity for either strategy is high, the predictive value of a positive test is low because of the low prevalence of ovarian cancer in the general population. The studies in which these estimates are based were not RCTs of screening, did not report mortality outcomes, had short lengths of followup, reported few cancer cases, and often included self-selected volunteers. Important biases limit the interpretation of the results of these studies. Large RCTs of screening with mortality outcomes are currently in progress and will provide

more definitive evidence of the benefits and harms of ovarian cancer screening.

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References

1. U.S. Preventive Services Task Force. *Guide to Clinical Preventive Services*, 2nd ed. Washington, DC: Office of Disease Prevention and Health Promotion; 1996.

2. American Cancer Society. *Cancer Facts & Figures 2001*. Available at: http://www.cancer.org/downloads/STT/F&F2001.pdf. Accessed May 2004.

3. SEER. *Cancer incidence in the United States 2003*. Available at: http://seer.cancer.gov/faststats/html/inc_ovary.html. Accessed May 2004.

4. Whittemore AS, Harris R, Itnyre J. Characteristics relating to ovarian cancer risk: collaborative analysis of 12 US case-control studies. II. Invasive epithelial ovarian cancers in white women. Collaborative Ovarian Cancer Group. *Am J Epidemiol* 1992;136(10):1184-1203.

5. Kerlikowske K, Brown JS, Grady DG. Should women with familial ovarian cancer undergo prophylactic oophorectomy? *Obstet Gynecol* 1992;80(4):700-7.

6. Lacey JV Jr, Mink PJ, Lubin JH, et al. Menopausal hormone replacement therapy and risk of ovarian cancer. *JAMA* 2002;288(3):334-41.

7. Rodriguez C, Patel A, Calle E, Jacob E, Thun M. Estrogen replacement therapy and ovarian cancer mortality in a large prospective study of US women. *JAMA* 2001;285(11):1460-5.

8. Persson I, Yuen J, Bergkvist L, Schairer C. Cancer incidence and mortality in women receiving estrogen and estrogen-progestin replacement therapy-long-term followup of a Swedish cohort. *Int J Cancer* 1996;67(3):327-32.

9. Ford D, Easton DF. The genetics of breast and ovarian cancer. *Br J Cancer* 1995;72(4):805-12.

10. Fleischer AC, James A, Millis J, Julian C. Differential diagnosis of pelvic masses by gray scale sonography. *Am J Roentgenol* 1978;131:469-76.

11. Granberg S, Norstrom A, Wikland M. Tumors in the lower pelvis as imaged by sonography. *Gynecol Oncol* 1990;37:224-9.

12. Depriest PD, Varner E, Powell J, et al. The efficacy of a sonographic morphology index in identifying ovarian cancer: a multi-institutional investigation. *Gynecol Oncol* 1994;55:174-8.

13. Bell R, Petticrew M, Sheldon T. The performance of screening tests for ovarian cancer: results of a systematic review. *Brit J Obstet Gynaecol* 1998;105(11):1136-47.

14. Jacobs I, Stabile I, Bridges J, et al. Multimodal approach to screening for ovarian cancer. *Lancet* 1988;1 (8580):268-71.

15. 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.

16. Grover S, Quinn MA, Weideman P, et al. Screening for ovarian cancer using serum CA 125 and vaginal examination: report on 2550 females. *Int J Gynecol Cancer* 1995;5:291-5.

17. Adonakis GL, Paraskevaidis E, Tsiga S, Seferiadis K, Lolis DE. A combined approach for the early detection of ovarian cancer in asymptomatic women. *Eur J Obstet, Gynecol, & Reprod Biol* 1996;65(2):221-5.

18. Goswamy RK, Campbell S, Whitehead MI. Screening for ovarian cancer. *Clin Obstet Gynaecol—Supplement* 1983;10(3):621-43.

19. Millo R, Facca MC, Alberico S. Sonographic evaluation of ovarian volume in postmenopausal women: a screening test for ovarian cancer? Clin Exp *Obstet Gynecol* 1989;16(2-3):72-8.

20. Campbell S, Bhan V, Royston P, Whitehead MI, Collins WP. Transabdominal ultrasound screening for early ovarian cancer. *BMJ* 1989;299(6712):1363-7.

21. Tabor A, Jensen FR, Bock JE, Hogdall CK. Feasibility study of a randomised trial of ovarian cancer screening. *J Med Screen* 1994;1(4):215-9.

22. Vuento MH, Pirhonen JP, Makinen JI, Laippala PJ, Gronroos M, Salmi TA. Evaluation of ovarian findings in asymptomatic postmenopausal women with color Doppler ultrasound. *Cancer* 1995;76(7):1214-8.

23. Parkes CA, Smith D, Wald NJ, Bourne TH. Feasibility study of a randomised trial of ovarian cancer screening among the general population. *J Med Screen* 1994;1(4):209-14.

24. Schincaglia P, Brondelli L, Cicognani A, et al. A feasibility study of ovarian cancer screening: does fine-needle aspiration improve ultrasound specificity? *Tumori* 1994;80(3):181-7.

25. Holbert TR. Screening transvaginal ultrasonography of postmenopausal women in a private office setting. Am J *Obstet Gynecol* 1994;170(6):1699-1703; discussion 1703-4.

26. Sato S, Yokoyama Y, Sakamoto T, Futagami M, Saito Y. Usefulness of mass screening for ovarian carcinoma using transvaginal ultrasonography. *Cancer* 2000;89(3):582-8.

27. 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.

28. Jacobs IJ, Skates SJ, MacDonald N, et al. Screening for ovarian cancer: a pilot randomised controlled trial. *Lancet* 1999;353(9160):1207-10.

29. European randomized trial of ovarian cancer screening (protocol). London: Wolfson Institute of Preventive Medicine, Department of Environmental and Preventive Medicine; 1995.

30. Gohagan JK, Prorok PC, Hayes RB, Kramer BS; Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial Project Team. The Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial of the National Cancer Institute: history, organization, and status. *Control Clin Trials* 2000;21(6 Suppl):251S-272S.

31. 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.

32. Bell R, Petticrew M, Luengo S, Sheldon TA. Screening for ovarian cancer: a systematic review. *Health Technol Assess* 1998;2(2):i-iv, 1-84. Review.

33. van Nagell JR Jr, Gallion HH, Pavlik EJ, De Priest PD. Ovarian cancer screening. *Cancer* 1995;76(10 Suppl):2086-91.

34. Kurjak A, Shalan H, Kupesic S, et al. An attempt to screen asymptomatic women for ovarian and endometrial cancer with transvaginal color and pulsed Doppler sonography. *J Ultrasound Med* 1994;13(4):295-301.

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