Ovarian Cancer Screening: Are There Any Options?

Jennifer Tiffen, RN, MS, APN, and Suzanne M. Mahon, RN, DNSc, AOCN®, APNG

Ovarian cancer is the leading cause of death among cancers of the reproductive system (22,220 cases are estimated for 2005) and the fourth-leading cause of all cancer deaths among American women (16,210 estimated deaths in 2005) (American Cancer Society [ACS], 2005). In the general population, 1 in 70 women, or 1.5% of all women, will develop ovarian cancer. Although the rate is much lower in comparison to the 13.4% of women who will develop breast cancer, 5.5% who will develop colorectal cancer, and 2.6% who will develop uterine cancer, ovarian cancer’s five-year survival rate for all stages is a dismal 44% as compared to 88%, 84%, and 63% for these other cancers, respectively (Ries et al., 2004).

Despite advances in surgery and treatment modalities, the prognosis for most women with ovarian cancer continues to be poor. The five-year survival rate for women with advanced-stage disease (stage III–IV) is 29% in contrast to a 94% survival rate in women with early and localized disease. Only 19% of ovarian cancers are detected when confined to the ovary (ACS, 2005). Ovarian cancer usually is diagnosed in an advanced stage because it presents with few, if any, distinctive symptoms. Even when subtle symptoms such as abdominal bloating and discomfort, dyspepsia, and unexplained weight loss or gain occur, they usually happen after the extensive spread of ovarian cancer (Fishman & Bozorgi, 2002). Because of a lack of specific or early warning symptoms, the accurate and early detection of early-stage ovarian cancer is critical.

Figure 1 highlights risk factors for developing ovarian cancer. With the exception of women with known mutations for breast and ovarian cancer (BRCA1 and BRCA2) and hereditary nonpolyposis colorectal cancer (HNPCC), risk factor assessment is not particularly helpful in identifying women who might benefit from aggressive screening. For women with known BRCA1 and BRCA2 and HNPCC mutations, current screening modalities likely are inadequate, and such women should be counseled about the risks and benefits of prophylactic surgery between the ages of 35 and 45, when childbearing is complete.

Bimanual rectovaginal examination, ultrasound, and the cancer antigen-125 (CA-125) blood test are three modalities used to screen for ovarian cancer. However, according to several published screening guidelines, insufficient evidence exists to recommend population-based screening for ovarian cancer. Currently available methods have not been shown to be effective in reducing mortality and morbidity from the disease. Furthermore, costs associated with annual screening of women older than 45 in the general population using ultrasound and CA-125 was estimated 10 years ago to be more than $13 billion yearly (Gladstone, 1994). Because of these limitations, organizations such as the American Academy of Family Physicians and the U.S. Preventive Services Task Force do not recommend screening for ovarian cancer. Table 1 provides a comparison of screening guidelines from professional organizations (American Academy of Family Physicians, 2003; Gladstone; Institute for Clinical Systems Improvement, 2004; Scottish Intercollegiate Guidelines Network, 2003; Smith, Cokkinides, & Eyre, 2005; U.S. Preventive Services Task Force, 2004).

The potential benefit of a screening test for ovarian cancer is the ability to identify the disease in its early stages, when treatment is more likely to be effective. Such a test should have high sensitivity and specificity with an acceptable positive predictive value. Specificity is a major concern in ovarian cancer screening. A test with 98% specificity would result in 50 false positive results for every case of ovarian cancer detected in screening of postmenopausal women. This is unacceptable given that women would experience further expensive testing and possibly require exploratory surgery, a large expense not without risks. Most experts recommend that a screening test for ovarian cancer requires a 99.6% specificity to yield a positive predictive value of 10%. At a specificity of 99.6%, 1 of 10 patients taken to the operating room actually would have cancer (Fishman & Bozorgi, 2002).

At present, no such screening test exists for ovarian cancer.

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### Table 1. Comparison of Guidelines for Ovarian Cancer Screening

<table>
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<tr>
<th>Agency and Reference</th>
<th>Funding Source</th>
<th>Intended Users</th>
<th>Objective</th>
<th>Target Population</th>
<th>Outcomes Considered</th>
<th>Recommendations and Comments</th>
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<tbody>
<tr>
<td>American Cancer Society (Smith et al., 2005)</td>
<td>Private group: American Cancer Society</td>
<td>Physicians, nurses, and healthcare providers</td>
<td>To provide recommendations for the early detection of cancer in asymptomatic individuals</td>
<td>Healthy women older than age 20</td>
<td>Effectiveness of screening tests and morbidity and mortality associated with disease</td>
<td>During a periodic health examination, the cancer-related check-up should include examination for cancers of the ovary. Patients should receive counseling about diet, nutrition, and risk factors as part of the cancer-related check-up.</td>
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<td>American Academy of Family Physicians, 2003</td>
<td>Private group: American Academy of Family Physicians</td>
<td>Physicians</td>
<td>To give recommendations to provide guidance against interventions that should not be offered</td>
<td>Asymptomatic adults of average risk</td>
<td>Not stated</td>
<td>No recommendation was made regarding pelvic examination. The group recommended against the use of ultrasound of the pelvis and serum tumor markers.</td>
</tr>
<tr>
<td>U.S. Preventive Services Task Force (USPSTF)*, 2004</td>
<td>U.S. government</td>
<td>Advanced practice nurses, allied health personnel, healthcare providers, nurses, physician’s assistants, and physicians</td>
<td>To summarize the current USPSTF recommendations</td>
<td>Women seen in primary care settings</td>
<td>Accuracy and reliability of screening, effect of screening on incidence and mortality, adverse effects of screening tests, and cost-effectiveness</td>
<td>Pelvic examination was not recommended. Nor were cancer antigen-125 (CA-125) and ultrasound.</td>
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<tr>
<td>Institute for Clinical Systems Improvement*, 2004</td>
<td>Private nonprofit organization</td>
<td>Advanced practice nurses, allied health personnel, healthcare providers, health plans, hospitals, nurses, physician’s assistants, and physicians</td>
<td>To identify preventive services with good or fair evidence for inclusion in a periodic health evaluation</td>
<td>Low-risk, asymptomatic adults ages 19 and older</td>
<td>Effectiveness of screening, effectiveness of education, and predictive value of screening tests</td>
<td>No recommendation was made regarding pelvic examination. The institute recommended discontinuing pelvic ultrasound and CA-125 testing.</td>
</tr>
<tr>
<td>Scottish Intercollegiate Guidelines Network, 2003</td>
<td>National governmental agency</td>
<td>Advanced practice nurses, nurses, pharmacists, physician’s assistants, and physicians</td>
<td>To provide evidence-based recommendations for the screening, diagnosis, and management of people with epithelial ovarian cancer</td>
<td>Women with epithelial ovarian cancer</td>
<td>Accuracy of diagnostic tests, overall survival rates, response rates, progression-free survival, quality of life, and adverse effects of treatment</td>
<td>Screening for ovarian cancer should occur in high-risk groups only and in the context of a research study. Women with genetic mutations in <em>BRCA1</em> and <em>BRCA2</em> should be counseled regarding prophylactic oophorectomy. Screening programs should include mechanisms for emotional and psychological support.</td>
</tr>
<tr>
<td>Canadian Task Force on Preventative Health Care* (Gladstone, 1994)</td>
<td>National governmental agency</td>
<td>Physicians, nurses, and healthcare providers</td>
<td>To determine how the periodic health examination might enhance or protect the health of Canadians</td>
<td>Women seen in primary care settings</td>
<td>Accuracy and reliability of screening, cost effectiveness, and treatment efficacy</td>
<td>It is reasonable to examine the ovaries if a pelvic examination is being done for another reason, such as Pap test. The group recommended against the use of ultrasound or CA-125 for asymptomatic pre- and post-menopausal women. Insufficient evidence exists to recommend for or against screening in individuals with one or more first-degree relatives with ovarian cancer.</td>
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* Cost analysis was performed.
Physical Examination

Ovarian cancer occasionally is detected during bimanual rectovaginal examination, although the sensitivity and specificity of rectovaginal examination are estimated to be low in the detection of early-stage disease. In a study looking at the sensitivity and specificity of preoperative pelvic examination in women with known pelvic masses, the sensitivity and specificity of rectovaginal examination were 67% and 96%, respectively (Andolf & Jorgensen, 1988). Although the value of rectovaginal examination as a screening tool is unknown and presumed to be low, it is incorporated into most well-woman screening because of its tolerability and low cost. A Pap test may detect malignant ovarian cells but is not considered a valuable screening test for ovarian cancer because its sensitivity is estimated to be 10%–30% (Smith & Oi, 1984).

Cancer Antigen-125

CA-125 is a serum glycoprotein shed from the cell surfaces of the fallopian tubes, endometrium, endocervix, peritoneum, pleura, pericardium, and bronchus. Little, if any, CA-125 can be detected on normal ovarian epithelium. CA-125 is elevated (> 35 U/ml) in the blood of 80% of patients with advanced-stage epithelial ovarian cancer, yet it detects early-stage, asymptomatic ovarian cancer less than 50% of the time (Bast et al., 1983; Berek & Bast, 1995). The specificity of CA-125 is 98%–99% among healthy premenopausal women without gynecologic symptoms but is much lower among premenopausal women. Elevated levels have been found in women with benign gynecologic conditions such as pregnancy, pelvic inflammatory disease, endometriosis, fibroids, and menstruation (Berve & Evans, 1997). CA-125 blood tests also cost approximately $70 (Carroll, 1999), and because it does not have high sensitivity or specificity, it is not recommended as a screening test for women in the general population.

Transvaginal Ultrasound

Transvaginal or pelvic ultrasound has proven useful in detecting advanced-stage ovarian cancer in asymptomatic women with a reported 98.1% specificity and 100% sensitivity (van Nagell et al., 1990, 1991). Its value in detecting early-stage disease has not shown as much promise. Two studies found that among high-risk women, the sensitivity of ultrasound for detecting early-stage disease was 25% (Bell, Petticrew, & Sheldon, 1998) and 31% (van Nagell et al., 2000). The average cost of transvaginal ultrasound is approximately $250, which most insurance companies are unwilling to reimburse (Carroll, 1999).

A Multimodal Approach

The combined use of CA-125 and ultrasound has yielded higher specificity and positive predictive value as compared with strategies using CA-125 or ultrasound alone. Two studies found that ultrasound following elevated CA-125 screening had a positive predictive value of 21% (Jacobs et al., 1999) and 50% (Einhorn et al., 1992).

New Screening Methods

Recent research has identified several blood markers with the potential to assist in the identification of ovarian cancer at earlier stages. Table 2 highlights the markers. Although preliminary results have been promising, extensive research is needed before the markers can be applied in clinical settings.

Nursing Implications

Ovarian cancer, unlike breast, colon, and uterine cancers, is characterized by vague symptoms. No effective means currently exist for the early detection of the malignancy. Women often inquire about screening for ovarian cancer, and oncology nurses must be able to explain the strengths and limits of available screening tests. Nurses also should remain aware of changes in guidelines from professional groups and national agencies. This can be done easily with the National Guideline Clearinghouse, available at www.guideline.gov.

When women have known mutations in BRCA1, BRCA2, or HNPCC or a family history suggestive of risk, screening may be inadequate. Such women should be referred to healthcare providers with expertise in genetics who can counsel about prophylactic surgery. Nurses can assist in referring high-risk women to ovarian cancer screening programs and prevention and early detection research studies. The National Institutes of Health Clinical Trials Web site (http://clinicaltrials.gov) can be used as a resource to find ongoing studies. Also helpful are the ACS Web site (www.cancer.org) and specific ovarian cancer sites such as the National Ovarian Cancer Coalition (www.ovarian.org) and the Gynecologic Cancer Foundation (www.wcn.org).

A potential test not yet ready for clinical use often will be touted as the latest discovery, raising the hopes of many and causing confusion for those who desire to have the test performed. Nurses can become the voice of reason by providing information to patients and the public and by educating them on the rigorous research process. Nurses should not underestimate the importance of patient and public education regarding the current state of screening for ovarian cancer and the need for more research.

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References


### Table 2. Results from Preliminary Testing of New Ovarian Cancer Screening Markers

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<th>NEW SCREENING MARKER</th>
<th>PRELIMINARY RESULTS</th>
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<tr>
<td>Proteomics</td>
<td>100% sensitivity and specificity</td>
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<tr>
<td>Lyosphosphatic acid</td>
<td>95% sensitivity and 89% specificity</td>
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<tr>
<td>Osteopontin</td>
<td>80.4% specificity with a sensitivity of 80.4% in early-stage disease and 85.4% in later-stage disease</td>
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<tr>
<td>p110 ErbB1</td>
<td>Levels have been found to be significantly lower in women with all stages of ovarian cancer as compared to healthy women and in women with benign pelvic disease.</td>
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Note. Based on information from Baron et al., 2003; Kim et al., 2002; Lu et al., 2004; Petricoin et al., 2002; Schorge et al., 2004; Sutphen et al., 2004; Xu et al., 1998.


