

Sorting through the complexities of ovarian cancer

Every year approximately 24,000 new cases of ovarian carcinoma are diagnosed in the United States. Causing nearly 14,000 deaths per year, ovarian cancer is the most lethal of the gynecologic malignancies. It is the fifth most common cause of cancer among women in the United States.

These figures graphically illustrate the need for screening, early diagnosis, and prevention of this lethal disease. The National Institute of Health (NIH) Consensus Development Conference on Ovarian Cancer addressed these issues in a meeting held April 5 through 7, 1994. A panel of 14 experts convened, including epidemiologists, obstetricians/gynecologists, oncologists (gynecologic, medical, and radiation), as well as a consumer representative to address the following areas:

- current status of screening and prevention approaches in ovarian cancer;
- appropriate management of early-stage ovarian cancer as well as advanced epithelial ovarian cancer;
- appropriate follow-up with primary therapy; and
- direction of future research.

In part, because of media attention to ovarian cancer, the demand for early detection through screening has increased. Yet, no evidence exists that proves screening benefits asymptomatic women. And thus, most women with ovarian cancer have it first diagnosed when it has reached an advanced stage.

Among the screening tests currently used are bimanual rectovaginal pelvic examination, measurement of CA 125 serum antigen levels, and transvaginal ultrasonography. Alone, each of these tests has an inadequate sensitivity and specificity. With false-positive results, patient anxiety ensues. Similarly, the risks associated with any surgical procedures may outweigh the potential benefits.

Although the etiology of ovarian cancer remains unknown, certain risk factors have been

identified. These include advancing age; nulliparity; North American or Northern European heritage; a personal history of endometrial, colon, or breast cancer; or a family history of ovarian cancer. Specifically, the lifetime risk of ovarian cancer developing in women with two or more first-degree relatives is 7%. Of these 7%, approximately 3% of women have hereditary ovarian cancer syndrome. They should consult a gynecologic oncologist.

Hereditary ovarian cancer syndromes include breast/ovarian cancer syndrome, site-specific ovarian cancer syndrome, and hereditary nonpolyposis colorectal cancer. Patients with hereditary ovarian cancer syndrome have a 40% lifetime risk of having ovarian cancer develop. Such women would benefit from undergoing annual rectovaginal examinations, having CA 125 antigen levels measured, and undergoing transvaginal ultrasonography annually until childbearing is completed. At age 35, prophylactic bilateral oophorectomy should be considered. Even with prophylactic oophorectomy, a small risk remains of having peritoneal carcinomatosis develop.

Protective factors include one full-term pregnancy, oral contraceptive use of 5 years or more, breastfeeding, and (possibly) tubal ligation. Removal of ovaries at the time of hysterectomy for benign uterine disease will almost eliminate the risk of ovarian cancer. However, estrogen replacement therapy should be thoroughly discussed with the patient before such surgery.

In evaluating an adnexal mass, the first step is to perform a complete history and physical examination, including bimanual and rectovaginal examination. A transvaginal ultrasound examination can help to evaluate the mass. Determining the CA 125 serum antigen levels may also be useful, particularly in postmenopausal women. Once an adnexal mass has been documented, management will depend on a combination of many predictive

factors—patient's age and menopausal status, mass size, ultrasound findings, specific symptoms, CA 125 serum antigen levels, and whether the mass is unilateral or bilateral.

The patient's age is particularly important in asymptomatic premenopausal women whose simple cystic adnexal mass measures 6 cm to 10 cm in diameter. These patients can be managed with follow-up examinations and ultrasonography, because 70% of the masses in these women will resolve without therapy. However, most postmenopausal women with ovarian masses will require surgical intervention. The exception here may be patients with unilocular cysts that measure less than 5 cm in diameter and who have normal CA 125 serum antigen levels.

Approximately 25% of women with newly diagnosed ovarian cancer have stage I disease. Although the medical community has yet to agree on which patients would benefit most from adjuvant therapy, several recommendations were made at the NIH conference. They include all patients with grade 3 tumors; patients with clear-cell carcinoma; and many, but not all, patients with stage Ic disease.

A consensus has not been reached regarding the need for postoperative adjuvant therapy in other patients with stage I epithelial ovarian cancer either. Patients with stage Ia and most Ib tumors do not require adjuvant therapy. The most effective adjuvant therapy for many subsets of women with stage I tumors has not been established. Because a substantial likelihood exists for recurrence and mortality, these patients should be enrolled in clinical trials.

All women with ovarian cancer should undergo surgical staging. A total abdominal hysterectomy and a bilateral salpingo-oophorectomy is the therapy of choice for women with stage I ovarian cancer. If a woman of child-bearing age with a stage Ia tumor desires to maintain her reproductive capability after undergoing complete surgical staging, she can have her uterus and contralateral adnexa pre-

served. The uterus may be preserved in the same woman with stage Ib tumors.

Unusual histologic subtypes of ovarian cancer (low malignant tumors, germ-cell cancers, and sex cord stromal cancers) require additional review of the pathologic specimen. Current data indicate that only patients with germ-cell cancer of the ovary benefit from adjuvant therapy.

Anything other than stage I disease represents advanced ovarian cancer. As mentioned earlier, most patients (75%) have advanced-stage ovarian cancer when they are first diagnosed. In these patients, a thorough history and careful examination are also necessary. A chest x-ray film is routinely ordered before surgery. Magnetic resonance imaging films, a barium enema, and intravenous pyelograms rarely add valuable information. Ultrasonography is used to evaluate the pelvic mass and assess ascites. In 80% of patients with ovarian cancer, the CA 125 serum antigen level is elevated. As such, CA 125 levels can be used to evaluate disease status during and after therapy.

Hematologic, hepatic, and renal function should be assessed before surgery. Bowel cleansing should be done in case bowel resection is required. Complete surgical intervention by a gynecologic oncologist permits precise staging, accurate diagnosis, and optimal cytoreduction.

Postoperative systemic chemotherapy (cisplatin and paclitaxel) is a first-line treatment of advanced epithelial ovarian malignancy. Radiation therapy remains controversial.

Second-look laparotomy remains controversial and should not be used routinely. After surgical staging, asymptomatic patients should be followed up by complete history, physical examination, rectovaginal examination, and measurement of CA 125 serum antigen levels every 3 to 4 months for a least 2 years.

Currently available salvage therapy is not curative for patients with a recurrence of ovarian cancer. The patient's quality of life, then, becomes a major consideration when deter-

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mining treatment options. Currently, paclitaxel is the best salvage agent available. The physician and patient should discuss whether the patient desires vigorous treatment or no treatment. Whatever the patient decides, the physician should respect her wishes.

The physician should not give the patient unrealistic expectations. The patient's physiologic state—not chronologic age—should influence the physician's treatment suggestions. As such, appropriate psychologic support is an important component in the treatment regimen.

All women should have access to accurate and complete information regarding ovarian cancer. There must be no barriers to women's access to qualified specialists who can provide optimal therapy. ♦

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