TABLE 117-1 STAGING AND SURVIVAL IN GYNECOLOGIC MALIGNANCIES

Stage	Ovarian	5-Year Survival, %	Endometrial	5-Year Survival, %	Cervix	5-Year Survival, %
0	—		—		Carcinoma in situ	100
I	Confined to ovary	90–95	Confined to corpus	89	Confined to uterus	85
II	Confined to pelvis	70–80	Involves corpus and cervix	73	Invades beyond uterus but not to pelvic wall	65
III	Intraabdominal spread	20–50	Extends outside the uterus but not outside the true pelvis or to lymph nodes	52	Extends to pelvic wall and/or lower third of vagina, or hydronephrosis	35
IV	Spread outside abdomen	1–5	Extends outside the true pelvis or involves the bladder or rectum	17	Invades mucosa of bladder or rectum or extends beyond the true pelvis	7

these tumors tend to exfoliate throughout the peritoneal cavity and thus present with symptoms associated with disseminated intraperitoneal tumors. The most common symptoms at presentation include a multimonth period of progressive complaints that typically include some combination of heartburn, nausea, early satiety, indigestion, constipation, and abdominal pain. Signs include the rapid increase in abdominal girth due to the accumulation of ascites that typically alerts the patient and her physician that the concurrent gastrointestinal symptoms are likely associated with serious pathology. Radiologic evaluation typically demonstrates a complex adnexal mass and ascites. Laboratory evaluation usually demonstrates a markedly elevated CA-125, a shed mucin (Muc 16) associated with, but not specific for, ovarian cancer. Hematogenous and lymphatic spread are seen but are not the typical presentation. Ovarian cancers are divided into four stages, with stage I tumors confined to the ovary, stage II malignancies confined to the pelvis, and stage III tumors confined to the peritoneal cavity (Table 117-1). These three stages are subdivided, with the most common presentation, stage IIIC, defined as tumors with bulky intraperitoneal disease. About 60% of women present with stage IIIC disease. Stage IV disease includes women with parenchymal metastases (liver, lung, spleen) or, alternatively, abdominal wall or pleural disease. The 40% not presenting with stage IIIC disease are roughly evenly distributed among the other stages, although mucinous and clear cell tumors are overrepresented in stage I tumors.

Screening Ovarian cancer is the fifth most lethal malignancy in women in the United States. It is curable in early stages, but seldom curable in advanced stages; hence, the development of effective screening strategies is of considerable interest. Furthermore, the ovary is well visualized with a variety of imaging techniques, most notably transvaginal ultrasound. Early-stage tumors often produce proteins that can be measured in the blood such as CA-125 and HE-4. Nevertheless, the incidence of ovarian cancer in the middle-aged female population is low, with only approximately 1 in 2000 women between the ages of 50 and 60 carrying an asymptomatic and undetected tumor. Thus effective screening techniques must be sensitive but, more importantly, highly specific to minimize the number of false-positive results. Even a screening test with 98% specificity and 50% sensitivity would have a positive predictive value of only about 1%. A large randomized study of active screening versus usual standard care demonstrated that a screening program consisting of six annual CA-125 measurements and four annual transvaginal ultrasounds in a population of women age 55–74 was not effective at reducing death from ovarian cancer and was associated with significant morbidity in the screened arm due to complications associated with diagnostic testing in the screened group. Although ongoing studies are evaluating the utility of alternative screening strategies, currently screening of normal-risk women is not recommended outside of a clinical trial.

TREATMENT OVARIAN CANCER

In women presenting with a localized ovarian mass, the principal diagnostic and therapeutic maneuver is to determine if the tumor is benign or malignant and, in the event that the tumor is malignant, whether the tumor arises in the ovary or is a site of metastatic disease. Metastatic disease to the ovary can be seen from primary tumors of the colon, appendix, stomach (Krukenberg tumors), and breast. Typically women undergo a unilateral salpingo-oophorectomy, and if pathology reveals a primary ovarian malignancy, then the procedure is followed by a hysterectomy, removal of the remaining tube and ovary, omentectomy, and pelvic node sampling along with some random biopsies of the peritoneal cavity. This extensive surgical procedure is performed because approximately 30% of tumors that by visual inspection appear to be confined to the ovary have already disseminated to the peritoneal cavity and/or surrounding lymph nodes.

If there is evidence of bulky intraabdominal disease, a comprehensive attempt at maximal tumor cytoreduction is attempted even if it involves partial bowel resection, splenectomy, and in certain cases more extensive upper abdominal surgery. The ability to debulk metastatic ovarian cancer to minimal visible disease is associated with an improved prognosis compared with women left with visible disease. Patients without gross residual disease after resection have a median survival of 39 months, compared with 17 months for those left with macroscopic tumor. Once tumors have been surgically debulked, women receive therapy with a platinum agent, typically a taxane. Debate continues as to whether this therapy should be delivered intravenously or, alternatively, whether some of the therapy should be delivered directly into the peritoneal cavity via a catheter. Three randomized studies have demonstrated improved survival with intraperitoneal therapy, but this approach is still not widely accepted due to technical challenges associated with this delivery route and increased toxicity. In women who present with bulky intraabdominal disease, an alternative approach is to treat with platinum plus a taxane for several cycles before attempting a surgical debulking procedure (neoadjuvant therapy). Subsequent surgical procedures are more effective at leaving the patient without gross residual tumor and appear to be less morbid. Two studies have demonstrated that the neoadjuvant approach is associated with an overall survival that is comparable to the traditional approach of primary surgery followed by chemotherapy.

With optimal debulking surgery and platinum-based chemotherapy (usually carboplatin dosed to an area under the curve [AUC] of 6 plus paclitaxel 175 mg/m^2 by 3-h infusion in 21-day cycles), 70% of women who present with advanced-stage tumors respond, and 40–50% experience a complete remission with normalization of their CA-125, computed tomography (CT) scans, and physical examination. Unfortunately, a small proportion of women who obtain a complete response to therapy will remain in remission. Disease recurs within 1–4 years from the completion of their primary therapy in 75% of the complete responders. CA-125 levels often increase as a first sign of relapse; however, data are not clear that early intervention in relapsing patients influences survival. Recurrent disease is effectively managed, but not cured, with a variety of chemotherapeutic agents. Eventually all women with recurrent disease develop chemotherapy-refractory disease at which point refractory ascites, poor bowel motility, and obstruction or pseudoobstruction due to a