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Pathways in Cancer

Clinical insight and analysis
in advanced cancer care

Ovarian Cancer and the Role of Surgery in the Current Era

Kevin Elliott, MD

Ovarian cancer is the sixth most common cancer among women in the U.S. with approximately 22,000 new diagnoses annually. Prognosis and survival correlate with the stage of disease at diagnosis with advanced stage patients succumbing to their disease in over 85% of cases. However, for patients diagnosed with early stage disease, long term survival is enjoyed by 50-90% of women. There is an important role for surgery in the majority of patients with ovarian cancer, including accurate surgical staging, aggressive surgical debulking and palliative procedures for patients suffering from recurrent tumor. Below we will briefly review the role of the gynecologic oncologist in the surgical management of ovarian cancer.

Surgical Staging

Ovarian cancer is a surgically staged disease in which pathologic findings at diagnosis direct subsequent treatment and prognosis. The Federation Internationale of Gynecology and Obstetrics (FIGO) stage can be summarized as follows: stage I disease is confined to the ovaries, stage II includes patients with extra-ovarian tumor that remains anatomically confined to the pelvis, stage III includes patients with disease outside of the pelvis and those with retroperitoneal lymph node involvement, stage IV includes patients with solid organ involvement and those patients with disease outside of the peritoneal cavity.

Surgery for Early Stage Disease

Most patients with a diagnosis of ovarian cancer benefit from the addition of chemotherapy to their care. The exceptions include patients with FIGO stage I, grade 1 or 2 tumors. The role of surgery to accurately establish the correct surgical stage is paramount in these patients. As the presence of microscopic occult disease in peritoneal tissues or microscopic involvement of the retroperitoneal lymph nodes is necessary in establishing the accurate stage of disease, failure to gather these tissues at initial diagnosis can result in an error of "understaging" and subsequent inadequate treatment. In studies of women with apparent early stage disease, a subsequent rigorous staging increases the stage in 20% of women. And while adjuvant chemotherapy is obligatory for the majority of patients, the chemotherapeutic regimen is different for patients with early stage disease as compared to more advanced disease.

Surgery for Advanced Stage Disease

Ovarian cancer typically presents with abdominal carcinomatosis. Aggressive surgical resection of diffuse intraperitoneal spread of cancers is generally considered to be of dubious benefit. Surgical intervention in this setting is often with a goal towards palliation of symptoms such as pain, bleeding or bowel obstruction without attention to maximal resection. For ovarian cancer, however, there is good evidence that surgical "debulking" with the goal of maximal tumor resection has clinical utility and contributes to improved survival outcomes. The benefits of aggressive surgical efforts wane sharply as the residual tumor diameter after surgery (measured at one or many remaining tumor sites) increases beyond 1 cm.

As advanced ovarian cancer typically presents with involvement of the peritoneal surfaces diffusely, the surgical efforts aimed at resection can become quite radical, and the perils of aggressive retroperitoneal resection and removal of all or parts of other abdominal organs can undermine the goal of a timely recovery in the elderly patient. Adjuvant chemotherapy ideally should be initiated within six to eight weeks of the surgery, otherwise tumor progression may negate the surgeon's efforts. For those in whom an optimal tumor debulking will likely be unsafe or unsuccessful, a strategy of neoadjuvant chemotherapy may be employed with an interval surgical debulking effort, typically following the 3rd or 4th chemotherapy cycle. The surgical goals at such procedures remain the same, but very often enjoy a less radical complement of procedures than if her disease had been confronted primarily with surgery. Survival outcomes, however, are generally somewhat inferior.

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Ovarian Carcinoma in the Elderly

Luko Laptalo, MD

Ovarian carcinoma is one of the more common types of gynecologic malignancies in the elderly. Approximately 80% of women who present with ovarian cancer are advanced—stage III or IV. Of those, over 60% are over 65 years of age. Despite this finding, most patients in clinical trials are under 65 years of age. Compared to patients of younger age, the elderly have poorer survival outcomes.

To optimize cure and survival rates, two events need to occur. First is extensive debulking surgery. Most studies have shown that leaving less than 1 cm of residual tumor is associated with superior survival. Secondly, chemotherapy with a platinum and a taxane pre-operatively or postoperatively have shown improved survival. Oftentimes the difficulty with proceeding with debulking surgery is the increased perioperative complications with increasing age. With each year above 65 there have been reports of a 7.5% increase in risk of 30-day mortality. One option that has been proposed in the elderly is neoadjuvant chemotherapy. Recent studies have shown that in patients who have undergone neoadjuvant chemotherapy there were fewer perioperative complications. However comorbidities, age, disease burden and performance status need to be taken into account when considering neoadjuvant chemotherapy, with primary cytoreductive surgery (debulking).

As noted, most elderly patients with ovarian carcinoma have poorer survival outcomes as compared to their younger counterparts. One of the reasons is the reduced use of standard chemotherapy in women over the age of 65. Some reports have suggested only half of all women receive platinum-based chemotherapy and the likelihood of not having chemotherapy increases in age, despite the fact that with chemotherapy, overall survival improved by 38%. Poor tolerance to chemotherapy was related to advanced age, poor performance status, depression and stage IV status. Also the use of paclitaxel with advanced age was an independent factor for poor survival.

> "For those elderly patients who present with stage IV disease or relapse, there are possibilities for treatment."

The typical schedule for adjuvant chemotherapy is carboplatin and paclitaxel every three weeks. There have been smaller studies with elderly patients receiving weekly carboplatin and paclitaxel. One study had patients 70 or older and one to two comorbidities who received weekly carboplatin and paclitaxel for six cycles. Response rates were high, toxicity generally much less than an every three week regimen. Therefore weekly paclitaxel and carboplatin may be a good alternative for adjuvant chemotherapy.

Another chemotherapy option is cisplatin based intraperitoneal (IP) chemotherapy, which has shown a survival advantage over intravenous-only chemotherapy. Unfortunately, IP chemotherapy has more technical difficulties such as intraperitoneal catheter complications and increased toxicities. Despite age, studies have shown less than 50% of all women were able to complete four or more cycles. Smaller studies in the elderly have shown that with the elderly who have few comorbidities and good performance status, three cycles of modified IP chemotherapy may have similar benefits to the standard regimen. That said, there is still a protocol therapy in which less chemotherapy is given intraperitoneally and intravenously, but results are pending. Therefore with elderly patients who are in good health and with few other medical conditions, intraperitoneal chemotherapy may still be a possibility.

For those elderly patients who present with stage IV disease or relapse, there are possibilities for treatment. For those patients who relapse after six months of adjuvant therapy with platinum agents, repeat carboplatin and paclitaxel may be used. However in the elderly, there is a higher chance of myelosuppression and severe neuropathy with a paclitaxel. To avoid neuropathy, liposomal doxorubicin may be used first and may be better tolerated. In patients who are platinum refractory, liposomal doxorubicin and topotecan have better toxicity profiles in the elderly.

Given the clinical variability in the elderly, surgery and chemotherapy should be tailored to the extent of the disease and the patient's overall health and prognosis.

Image Guided Brachytherapy for Locally Advanced Cervical Cancer

Ellen Wiegner, MD

The standard treatment for women with locally advanced cervical cancer (disease that has spread beyond the cervix or to lymph nodes) is definitive radiation therapy with concurrent chemotherapy. Because high dose radiation is required to effectively treat cervical cancer, a combination of external beam radiation and internal radiation therapy (brachytherapy) are used. External beam radiation therapy delivers radiation to the entire pelvis including the primary tumor and pelvic lymph nodes. This is followed by brachytherapy, which delivers focused high dose internal radiation to the primary cervical tumor while minimizing exposure to adjacent normal tissues (Figure 1). Despite aggressive treatment with chemotherapy and radiation, local control remains an issue for patients with locally advanced disease.

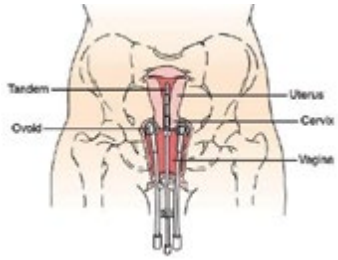

Figure 1

Image guided brachytherapy is a recent advance in radiation treatment for cervical cancer. Traditionally, brachytherapy treatments have been planned using 2D radiographs. However, it is difficult to precisely identify the tumor and normal adjacent organs on plain radiographs (Figure 2A). Therefore, radiation dose typically has been prescribed to a standard point A, and has not been individualized to the patient's tumor volume. Image guided brachytherapy utilizes MR and/or CT imaging for radiation planning where the cervical tumor can be accurately delineated, and radiation dose precisely prescribed to cover the entire tumor (Figure 2B). Additionally, radiation dose to normal adjacent tissues is accurately calculated, potentially reducing toxicity and possibly allowing safe delivery of higher radiation doses than traditionally possible.

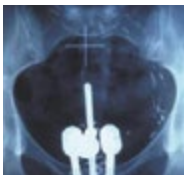

Figure 2A

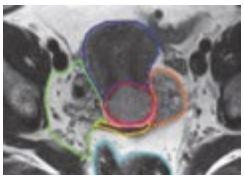

Figure 2B

Several retrospective studies suggest more favorable outcomes using image guided brachytherapy. In one study, the local control rate for patients with bulky cervical tumors was 90% if treated with image guided brachytherapy, compared to only 75% if treated with 2D brachytherapy technique. To verify these results, the EMBRACE clinical trial was initiated in Europe. This trial prospectively registered patients with newly diagnosed cervical cancer treated with external radiation and image guided brachytherapy and chemotherapy. Approximately 500 patients were registered on the trial and treated at radiation centers in Europe and Asia. The initial results were presented in June 2013. The investigators reported that image guided brachytherapy allowed high dose radiation to be safely and accurately delivered to the cervical tumor resulting in local control rates greater than 90%. These results compare favorably to historical series where local control is 50-80% (depending on stage) using traditional radiation planning methods.

In the United States, brachytherapy technique continues to evolve. Most radiation centers prescribe dose using the traditional point A method. Increasingly, though, radiation oncologists are utilizing MR and/or CT imaging for brachytherapy planning. At Mercy Cancer Center, we use 3D-imaging for all cervical cancer brachytherapy treatments to more accurately monitor dose to adjacent normal tissues and ensure that the cervical tumor is adequately covered using the point A prescription method. As we incorporate these advanced radiation techniques into practice, outcomes for women with locally advanced cervical cancer are likely to improve and therapy related toxicity minimized.

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Additional Issues

In the recurrent and palliative setting, surgical efforts are somewhat more nuanced and customized to the clinical situation. An extended discussion of these and other topics are beyond the scope of this summary, but these issues fall under the expertise of the board certified gynecologic oncologist and consultation with these specialists should be obtained whenever ovarian cancer is present or suspected.

Dignity Health
Mercy Cancer Institute
of Greater Sacramento

3400 Data Drive
Rancho Cordova, CA 95670

TUMOR BOARDS

Mercy Cancer Institute of Greater Sacramento's multidisciplinary approach to cancer care includes regularly scheduled Tumor Boards held throughout Sacramento, offering clinical review of patient cases for optimal treatment results. For each of our Tumor Boards, physicians are eligible for 1 CME credit. Lunch is also provided.

To present a case at an upcoming Tumor Board, please email or call contacts noted below. To present a case, please provide the patient's name, date of birth, disease site and where path and imaging can be found.

Mercy Cancer Center: Breast-focus

3rd Friday of each month at 12:30 p.m.
Location: 3301 C Street, Suite 550, Conference Room
Available via WebEx

Contact: Dawn Lenakakis, CTR
dawn.lenakakis@dignityhealth.org
916.537.5262 for access information

Mercy General Hospital

Wednesdays at 12:15 p.m.
Location: Greenhouse Conference Room
Available via WebEx

Contact: Dawn Lenakakis, CTR
dawn.lenakakis@dignityhealth.org
916.537.5262 for access information

Mercy Hospital of Folsom

4th Wednesday of every other month at Noon (September, November, January, March, May, July)
Location: CC1 and 2 or PCU conference room

Contact: Mansoor Javeed, MD
mansoor.javeed@dignityhealth.org
916.984.6230

Mercy San Juan Medical Center

Thursdays at 12:30 p.m.
Location: Conference Room 2
Available via WebEx

Contact: Dawn Lenakakis, CTR
dawn.lenakakis@dignityhealth.org
916.537.5262 for access information

Methodist Hospital of Sacramento

3rd Friday of each month at Noon
Location: Bistro Conference Room

Contact: Monica Zunker
monica.zunker@dignityhealth.org
916.683.9616

Sierra Nevada Memorial Hospital

Thursdays at 12:30 p.m.
Location: OPC 110-120

Contact: Debby Kirk,
debby.kirk@dignityhealth.org
530.274.6600

St. Joseph's Medical Center

Thursdays at Noon
Location: St. Joseph's Medical Center Auditorium

Contact: Cora Rios
cora.rios@dignityhealth.org
209.461.5104

Woodland Healthcare

Tuesdays at 12:15 p.m.
Location: DCR 5

Contact: Michelle Ing, PA
michelle.ing@dignityhealth.org
530.662.3961

Mark Twain Medical Center

4th Wednesday of each month at 12:30 p.m.
Location: Classroom 2

Contact: Deborah Peterson
deborah.peterson2@dignityhealth.org
209.754.9132