The Role of Surgery in the Management of Epithelial Ovarian Cancer

Ingrid Ramirez, MD, Hye Sook Chon, MD, and Sachin M. Apte, MD, MS

Background: Epithelial ovarian cancer is the most deadly gynecologic cancer in the United States. Multiple modalities of therapy are utilized in the management of the disease. The role of surgery remains important in the treatment of this disease and is described herein.

Methods: Medline and PubMed were utilized to search the English language medical literature up to March 2010. A broad range of studies and quality of data were analyzed, including prospective studies, case control analyses, and meta-analyses. When possible, the highest level of evidence was reviewed and presented.

Results: For the medically fit patient, optimal cytoreductive surgery positively impacts survival. For some highly selected patients, there is a role for a minimally invasive approach. In the recurrent setting, factors such as interval to recurrence and the distribution of disease will determine the utility of secondary cytoreductive surgery. A subgroup of patients may benefit from palliative surgical procedures in the recurrent setting.

Conclusions: Despite advances in the use of chemotherapy and biologic agents, surgery remains an important modality in the diagnosis and treatment of ovarian cancer.
and adjuvant chemotherapy. Primary cytoreduction refers to the initial surgical excision of tumor and tumor-involved organs prior to chemotherapy. According to the Gynecologic Oncology Group (GOG), optimal surgical cytoreduction is defined as residual tumor less than 1 cm. Interval cytoreduction is performed on patients who have previously received neoadjuvant chemotherapy. Secondary cytoreduction refers to the surgical management of recurrent ovarian cancer. Cytoreduction and debulking are terms that are used interchangeably. Neo-adjuvant chemotherapy is the administration of chemotherapy prior to cytoreductive surgery. This is reserved for those patients in whom optimal cytoreduction is not possible because of either the distribution of disease or poor performance status. Adjuvant chemotherapy is administered after surgery in appropriate patients. Patients usually receive 6 cycles of adjuvant platinum and taxane-based chemotherapy.

**Role of Surgery**

Surgical evaluation is indicated for most women with known or suspected EOC. Surgery is generally recommended, provided there are no medical contraindications and the distribution of disease is deemed resectable on preoperative evaluation. The goals of the initial surgery are to obtain a pathologic diagnosis, accurately determine the extent of disease and, when feasible, optimally cytoreduce the ovarian cancer. For patients with suspected EOC, the usual differential diagnosis includes uterine, fallopian tube, primary peritoneal, or metastatic cancers from the gastrointestinal tract or breast.

Accurate surgical staging is particularly important for apparent early-stage disease, ie, women with an ovarian cancer that appears grossly confined to the ovary. Approximately 25% to 30% of women with apparent early-stage disease will be upstaged upon thorough surgical staging. Treatment is often driven by the surgical stage, as expressed by the International Federation of Gynecology and Obstetrics (FIGO) staging system (Table). Precise surgical staging is critical for the patient in terms of both therapy and prognosis. Women with a true stage I, well-differentiated EOC may be observed; however, those with more advanced disease are generally treated with chemotherapy. Due to a lack of effective screening and insidious symptoms, the majority of women will present with advanced disease. In the setting of advanced disease, the goal of the initial surgical effort is to achieve optimal cytoreduction. Intraoperative chemotherapy is considered for some patients with advanced disease who have undergone optimal cytoreductive surgery. A careful preoperative assessment is mandatory to determine patient fitness for surgery. The surgeon must take

### Table. — Carcinoma of the Ovary: FIGO Nomenclature (Rio de Janeiro 1988)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Stage I</strong></td>
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<tr>
<td>IA</td>
<td>Growth limited to the ovaries.</td>
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<tr>
<td>IB</td>
<td>Extension and/or metastases to the uterus and/or tubes.</td>
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<tr>
<td>IC</td>
<td>Tumor either stage IA or IB, but with tumor on surface of one or both ovaries, or with capsule ruptured, or with ascites present containing malignant cells, or with positive peritoneal washings.</td>
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<th><strong>Stage II</strong></th>
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<tbody>
<tr>
<td>IIA</td>
<td>Growth involving one or both ovaries with pelvic extension.</td>
</tr>
<tr>
<td>IIB</td>
<td>Extension to other pelvic tissues.</td>
</tr>
<tr>
<td>IIC</td>
<td>Tumor either stage IIA or IIB, but with tumor on surface of one or both ovaries, or with capsule(s) ruptured, or with ascites present containing malignant cells, or with positive peritoneal washings.</td>
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<tr>
<th><strong>Stage III</strong></th>
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<tr>
<td>IIIA</td>
<td>Tumor involving one or both ovaries with histologically confirmed peritoneal implants outside the pelvis and/or positive retroperitoneal or inguinal nodes. Superficial liver metastases equals stage III. Tumor is limited to the true pelvis but with histologically proven malignant extension to small bowel or omentum.</td>
</tr>
<tr>
<td>IIIB</td>
<td>Tumor of one or both ovaries with histologically confirmed implants, peritoneal metastasis of abdominal peritoneal surfaces, none exceeding 2 cm in diameter; nodes are negative.</td>
</tr>
<tr>
<td>IIIC</td>
<td>Peritoneal metastasis beyond the pelvis &gt; 2 cm in diameter and/or positive retroperitoneal or inguinal nodes.</td>
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<th><strong>Stage IV</strong></th>
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<tr>
<td>IV</td>
<td>Growth involving one or both ovaries with distant metastases. If pleural effusion is present, there must be positive cytology to allot a case to stage IV. Parenchymal liver metastasis equals stage IV.</td>
</tr>
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* In order to evaluate the impact on prognosis of the different criteria for allotting cases to stage IC or IIC, it would be of value to know if rupture of the capsule was spontaneous, or caused by the surgeon; and if the source of malignant cells detected peritoneal washings, or ascites.

into consideration a variety of factors, such as performance status, nutrition, medical comorbidities, impending bowel obstruction, and patient age. The patient must undergo a careful and thorough consent process and must understand the risks, benefits, and radicality of the possible procedures involved.

**Staging Procedure**
The staging procedure is usually performed via a vertical incision, and a thorough exploration is performed to assess the extent of disease. All peritoneal surfaces and organs are palpated, including the diaphragm, liver, spleen, gall bladder, small and large intestine, and mesentery. The retroperitoneum is carefully evaluated for bulky adenopathy. A frozen section is obtained, usually of a portion of involved omentum or adnexa. An assessment is made regarding whether a patient can be debulked optimally. If so, attention should first be placed on the area of most concern so that it can be rendered free of disease. Also, potential sites of bowel obstruction must be carefully evaluated and addressed.

In the absence of gross extra-ovarian disease, multiple peritoneal biopsies are obtained, along with a pelvic and para-aortic lymphadenectomy. An omentectomy, hysterectomy, and bilateral salpingo-oophorectomy are also performed. For women with early-stage ovarian cancer, systematic lymphadenectomy is part of the complete staging procedure. Nearly one-fourth of patients with apparent early-stage ovarian cancer who undergo this procedure are upstaged to stage IICC due to the presence of node metastases. However, in patients with advanced-stage EOC, the role and benefit of systematic lymphadenectomy are unclear. In a study of 456 women with advanced stage III/IV ovarian cancer, no correlation between nodal status and survival was noted. In addition, nodal status was not a prognostic factor for optimally cytoreduced patients with advanced-stage EOC. In another trial, 427 women with stage III/IV ovarian cancer were randomized to either systemic lymphadenectomy vs resection of bulky nodes. No statistical difference in the 5-year overall survival rate (48.5% vs 47%, respectively) was noted. Systemic lymphadenectomy, however, was associated with increased progression-free survival compared to the no-lymphadenectomy arm: 31.2% vs 21.6%. Therefore, the recommendation is to resect bulky tumor-involved nodes in advanced-stage ovarian cancer.

**Primary Cytoreduction**
The cornerstones of the initial management of EOC are staging and surgical cytoreduction. For patients with advanced-stage ovarian cancer, the optimal cytoreductive rate has been shown to vary from 17% to 87%. To achieve an optimal surgery, a variety of procedures may need to be performed, such as splenectomy, diaphragm stripping, partial hepatic resection, partial bladder or ureteral resection, or bowel resection.

In the 1970s, Griffiths et al described an association between overall survival and cytoreduction of bulky disease. In a study of 102 patients with stage II and III EOC, residual disease > 1.5 cm was identified as a poor prognostic indicator. Hoskins et al also reported on the size of residual disease and overall survival in patients with stage III ovarian cancer. Patients with suboptimal cytoreduction (> 1 cm) but with smaller diameter residual disease (< 2 cm) still had an increased overall survival compared with those who had larger volume residual disease (> 2 cm). Since then, multiple studies have consistently shown that the volume of residual disease remaining after cytoreductive surgery inversely correlates with survival.

The term optimal cytoreduction has recently become a topic of controversy since the definition has now evolved to also include maximal cytoreductive efforts, with the end goal of complete resection of all visible disease. No residual disease at the completion of surgery has consistently been shown to result in improved overall survival and progression-free survival. Although studies have described optimal cytoreduction by different criteria, for example, < 2 cm or < 0.5 cm, to date, no prospective randomized control trials have defined the degree of residual disease that has the best clinical outcome.

Based on current retrospective studies, the recommendation for complete resection of all visible disease is becoming more widely accepted as it has been shown to improve overall survival. Chi et al reported that the amount of residual disease was recognized as a significant prognostic factor. In that study, 465 patients with stage IIC EOC who had undergone primary cytoreductive surgery were identified from a prospective database. The amount of residual disease was categorized into five distinct groups: no gross residual, gross ≤ 0.5 cm, 0.6–1.0 cm, 1–2 cm, and > 2 cm residual. The median overall survival rates in the five groups were as follows: 106 months for no gross, 66 months for gross ≤ 0.5 cm, 48 months for 0.6–1.0 cm, 33 months for 1–2 cm, and 34 months for > 2 cm. In a study of 3,126 patients, Bois et al also demonstrated improved overall and progression-free survival with complete resection. The patients with complete resection had a median survival of 99.1 months, whereas the median survival for patients with residual disease remaining after cytoreduction was 36.2 and 29.6 months, respectively.

The findings from the above studies reiterate the importance of optimal cytoreduction at the time of primary surgery for EOC. In addition, although the GOG defines optimal cytoreduction as residual disease of < 1 cm, data from more recent studies suggest that overall and progression-free survival are improved to a greater extent when maximal cytoreduction is achieved. These findings of increased overall survival with maximal cytoreduction have led many to advocate for complete
Adjuvant Chemotherapy
After primary cytoreductive surgery, adjuvant platinum and taxane-based chemotherapy is used in the majority of women with advanced ovarian cancer. Optimal debulking is thought to maximize the efficacy of chemotherapy. Chemotherapeutic drugs exert their maximum effects on small tumors that are well perfused and therefore mitotically active. Large tumor size is associated with poor perfusion, a greater chance of sublethal cellular damage, and the emergence of multidrug-resistant clones. Chemotherapy can be administered by intravenous or intraperitoneal routes. In EOC, the peritoneum is the focus of tumor metastasis. The intraperitoneal route allows for direct exposure to chemotherapeutic agents and has been shown to increase overall and progression-free survival in advanced ovarian cancer compared with intravenous chemotherapy.\(^{25-27}\) In a recent study by Armstrong et al,\(^{27}\) 429 optimally debulked patients were randomized to receive intravenous paclitaxel followed by either intravenous cisplatin on day 2 (intravenous group) or intraperitoneal cisplatin on day 2 and intraperitoneal paclitaxel on day 8 (intraperitoneal group). Among 415 eligible patients, the median progression-free survival and overall survival in the intraperitoneal group vs the intravenous group were 23.8 vs 18.3 months and 65.6 vs 49.7 months. However, intraperitoneal chemotherapy is associated with more side effects and thus has a higher discontinuation rate. Nonetheless, in this study, despite the discontinuation rate (only 42% of the patients in the intraperitoneal group completed the assigned six cycles), a survival benefit was shown. Most of the complications with intraperitoneal chemotherapy were catheter related, such as infection, leakage near the port, access difficulties, blocked catheter, and leakage of fluid through the vagina.\(^{28}\) Other adverse events included abdominal pain, nephrotoxicity, fatigue, hematologic disorders, and neuropathy. Despite these adverse effects, intraperitoneal chemotherapy should be considered for adjuvant chemotherapy in optimally cytoreduced patients with advanced-stage ovarian cancer, as it has consistently been shown to confer a clinical advantage with increased overall survival.

Suboptimal Debulking
Achieving optimal debulking is not always feasible. Limiting factors may include extensive upper abdominal or retroperitoneal disease, large tumor burden in bowel mesentery, or porta hepatitis. Selection criteria often used to determine which patients cannot be optimally cytoreduced include presence of stage IV disease, massive ascites, bulky omental disease with splenic involvement, and suprarenal lymphadenopathy. If optimal debulking is not possible, then the operation is generally limited to a bilateral salpingo-oophorectomy and/or omentectomy to prove the site of origin and to address potential sites of bowel obstruction.

Clinical models have been developed to try to identify those patients who will have a low probability of optimal cytoreductive surgery. Computed tomography (CT) scans have been evaluated to determine their predictive value in identifying unresectable disease. Nelson et al\(^{29}\) assessed the likelihood of resectability based on CT findings. The CT findings predictive of unresectability included the presence of an omental cake extending to the spleen, a diaphragm coated by tumor extending to the liver serosa, lesions > 2 cm in the suprarenal para-aortic lymph nodes and porta hepatitis, parenchymal liver disease, pulmonary metastases, and enlarged pericardial lymph nodes. With these criteria, the likelihood of resectability was accurately predicted in 23 of 24 patients. Bristow et al\(^{30}\) also used CT radiographic features for predicting the outcome of cytoreductive surgery in advanced ovarian cancer. The authors identified 13 radiographic features corresponding to certain anatomic locations that have traditionally made optimal cytoreductive surgery difficult, such as extensive upper abdominal disease. Forty-one patients with stage III/IV EOC who had undergone primary surgical cytoreduction were identified. Their preoperative CT scans were reviewed and, based on certain radiographic features and performance status, the patients were assigned a score. In this study, a Predictive Index score ≥ 4 was indicative of poor likelihood to undergo optimal cytoreduction. However, more recent studies have contradicted these findings.\(^{31}\) Axtell et al\(^{32}\) analyzed preoperative CT scans from 65 patients with stage III/IV ovarian cancer who had undergone primary cytoreduction. Fourteen radiologic criteria were chosen as possible pertinent predictors of suboptimal cytoreduction, including large-volume ascites, pleural effusion, diffuse peritoneal thickening, omental caking, omental extension to spleen or stomach, suprarenal lymph nodes > 1 cm, infrarenal or inguinal lymph nodes > 2 cm, and tumor implants > 2 cm (located on bowel mesentery, peritoneum, diaphragm, liver, or porta hepatitis). Only diaphragmatic disease > 2 cm and large bowel mesentery implants > 2 cm were noted to be statistically significant predictors of suboptimal cytoreductive outcome. However, the utility of this finding is limited because half of the patients with >
2-cm disease in the diaphragm and large bowel actually underwent optimal cytoreduction. In addition, when these criteria were applied to two previously published patient cohorts (patients who underwent primary cytoreduction at Johns Hopkins Medical Institute and the Mayo Clinic), the sensitivity, specificity, and accuracy of these positive predictors were all noted to decrease. CT scans should thus be used with caution when trying to identify those patients who are not likely to achieve optimal cytoreduction. Clinical judgment must be exercised when deciding whether to proceed with primary cytoreductive surgery, as no clinical model has yet accurately predicted disease resectability.

In addition, the above clinical models did not take into account the surgeon as an independent predictive factor of surgical outcome. In a study by Aletti et al., certain preoperative and intraoperative factors were analyzed to identify a correlation with optimal residual disease. The variables analyzed were patient age, performance status, CA-125 level, ascites volume, carcinomatosis, diaphragm, and mesentery involvement, and surgeon tendency. Only performance status, carcinomatosis, and surgeon tendency were independently associated with optimal cytoreduction. These findings were consistent with the belief that resectability of tumor is highly dependent on surgical skills. This study also demonstrated that any proposed model to preoperatively identify patients unlikely to have optimal cytoreduction must take into account surgeon tendency as a predictive factor.

Preoperative CA-125 level also has been evaluated as a predictor for primary optimal cytoreduction in patients with advanced ovarian cancer. Despite initial positive results from Chi et al. regarding the preoperative predictability of CA-125 for optimal cytoreduction, the same group recently reported that there was no threshold CA-125 level that accurately predicted cytoreductive outcome after their change in surgical paradigm that incorporated extensive upper abdominal procedures to attain optimal debulking. It is a general consensus that, currently, CA-125 level does not appear to be a significant predictor of tumor resectability.

In addition to cytoreduction and surgeon skill, a patient's specific tumor biology likely plays a role in resectability of disease and survival. The reasoning is that certain tumor cells have the ability to escape cell repair mechanisms, making them inherently more aggressive. For example, the “biological aggressiveness” of certain tumors may decrease long-term survival due to tumor characteristics, such as rapid development of chemoresistance, despite optimal cytoreduction. A study by Hacker et al. showed that large-volume ascites or large tumor burden (> 10 cm), despite cytoreduction, was a poor prognostic factor. Heintz et al. found that ascites, large tumor diameter, and peritoneal carcinomatosis were poor prognostic factors despite cytoreduction. The above studies support the idea that initial tumor burden may be in itself an indicator of tumor biological aggressiveness.

The majority of women will receive adjuvant chemotherapy after suboptimal debulking. Whether these women would benefit from another attempt at debulking is unclear. A report by van der Burg et al. described the findings of a European Organisation for Research and Treatment of Cancer (EORTC) study in which 278 evaluable patients with suboptimal tumor debulking (residual tumor > 1 cm) were randomly assigned, after three cycles of cyclophosphamide and cisplatin, to either undergo a secondary attempt at debulking or continue with another three cycles of chemotherapy. Those with progressive disease after neoadjuvant chemotherapy were excluded from the study. The secondary attempt at debulking was performed on 140 patients and was well tolerated: 65% of patients had residual disease > 1 cm after neoadjuvant chemotherapy, and optimal cytoreduction was achieved in 45% of patients in this group. Median survival time was 26 months for those undergoing a secondary attempt and 20 months for those in the non-secondary attempt group (P = .04). Overall, after adjustments were made for all other prognostic factors, surgery reduced the risk of death by 33% (95% confidence interval, 10% to 50%; P = .008). A second study showed results contradictory to the EORTC study. In GOG 152, Rose et al. reported on 425 patients with advanced EOC who had been suboptimally debulked (residual tumor > 1 cm) at primary surgery, received three cycles of paclitaxel and cisplatin chemotherapy, and then were randomized to secondary attempt at debulking or no surgery followed by chemotherapy in both groups. Patients receiving secondary attempt at debulking had a median survival time of 32 months compared with 33 months for those receiving chemotherapy alone. There was no difference in progression-free survival time (10.5 and 10.8 months, respectively). Unlike the EORTC trial, GOG 152 had inclusion criteria for a maximal surgical effort at the time of primary surgery. It is apparent that patients who have had a maximal but suboptimal primary cytoreductive surgical effort do not benefit from a secondary attempt at debulking. Therefore, women who have undergone an attempted cytoreduction by a surgeon trained in the aggressive management of this disease are unlikely to benefit from a secondary attempt for debulking surgery after chemotherapy.

Neoadjuvant Chemotherapy Followed by Interval Debulking Surgery

For patients with suspected advanced ovarian cancer, the general recommendation is for primary surgical cytoreduction followed by chemotherapy. However, when this is not advisable, patients are usually treated initially with neoadjuvant platinum and taxane-based chemotherapy prior to cytoreductive surgery. These patients may have significant pre-existing medical comorbidities or severe malnutrition and thus be at high risk for perioperative...
morbidity or mortality. Patient age, poor performance status, and complexity of surgery are associated with peri-operative morbidity. Stage of disease, volume of ascites, and serum albumin levels are also correlated with morbidity. In addition, the distribution of disease is an important determinant in choosing whether patients should be treated with neoadjuvant chemotherapy. Patients with massive ascites, large bilateral pleural effusions, extensive retroperitoneal lymphadenopathy, disease involving the porta hepatitis, or bulky intraparenchymal liver disease may benefit from neoadjuvant chemotherapy. Such patients should have a biopsy-proven diagnosis prior to chemotherapy. Provided that the patients have a favorable response to chemotherapy and their performance and nutritional status improves, they should generally be considered for interval debulking surgery.

Neoadjuvant chemotherapy has previously been considered for those who are believed to have extensive disease that precludes them from obtaining maximal cytoreductive surgery. Results from a GOG study on patients with stage IV EOC noted that, postoperatively, only 8% of patients had been cytoreduced to microscopic residual disease. In numerous retrospective and prospective case-control studies, neoadjuvant chemotherapy followed by interval debulking has been shown to be associated with decreased morbidity when compared to initial cytoreductive surgery in advanced ovarian cancer. Neoadjuvant chemotherapy also identifies those patients with chemosensitive disease who can then undergo optimal cytoreduction, while at the same time identifying those patients with chemoresistant disease who will have a poor outcome regardless of treatment, therefore avoiding the morbidity associated with cytoresection in this subset of patients. With regard to overall survival, it seems that when neoadjuvant chemotherapy followed by interval debulking is compared with initial cytoreductive surgery, the overall survival rates are similar.

In a retrospective trial of 172 patients with advanced EOC, 109 patients were treated with primary debulking surgery and 63 patients were treated with neoadjuvant chemotherapy. Interestingly, in this trial, an improved overall survival was noted in patients with stage IV disease who received neoadjuvant chemotherapy (31 months) compared with those who underwent primary debulking surgery (20 months). Nonetheless, the majority of data demonstrate similar overall survival rates.

Preliminary data from an EORTC trial (protocol 55971), a randomized study of neoadjuvant chemotherapy followed by interval cytoreduction vs primary cytoreduction in stage IIIIC/IV EOC patients, suggested that neoadjuvant chemotherapy is comparable to primary cytoreductive surgery. The overall survival rates were similar: 30 and 29 months, respectively. In addition, patients assigned to the neoadjuvant arm had decreased mortality and morbidity. Another randomized control study, Chemotherapy or Upfront Surgery (CHORUS), is currently underway in the United Kingdom. This trial will also be comparing neoadjuvant chemotherapy with primary cytoreductive surgery.

One theoretical disadvantage with neoadjuvant chemotherapy is the potential for developing chemoresistance, which in turn makes tumor cells less responsive to chemotherapy following interval debulking surgery. Although no specific number of cycles of chemotherapy has been identified as the ideal number in neoadjuvant chemotherapy, most patients receive an average of three to four cycles.

One limitation with neoadjuvant chemotherapy is that the data supporting its association with survival rates are based on retrospective reviews, meta-analyses, and uncontrolled prospective reviews. These data lack controls for patient population and compare different chemotherapy regimens, again without well-matched control groups. Because of a lack of good evidence and the small number of randomized controlled trials analyzing neoadjuvant chemotherapy, primary optimal cytoreductive surgery remains the recommendation for the management of advanced EOC.

**Use of Minimally Invasive Surgery**

Laparoscopic management of ovarian cancer is feasible, but it is not for routine clinical use and should be utilized judiciously. It can be utilized in the surgical management of apparent early-stage ovarian cancer, in assessing resectability of advanced disease prior to laparotomy, and also in second-look procedures.

Laparoscopic staging for EOC has been generally performed in young women who have had surgery for a suspected benign adnexal mass that is found to be malignant intraoperatively. Several studies suggest that laparoscopy is safe and feasible in the surgical management of apparent early-stage ovarian cancer. In a study comparing laparoscopic treatment of gynecologic malignancies with traditional laparotomy for early-stage ovarian cancer, Tozzi et al demonstrated acceptable survival rates with decreased morbidity and shorter hospitalization: 91.6% with disease-free survival and overall survival of 100% at 46 months. Staging was performed according to FIGO guidelines, including pelvic lymphadenectomy and infrarenal para-aortic lymphadenectomy. Because a diagnosis of early-stage ovarian cancer is less common, data comparing the overall survival rate associated with laparoscopy vs laparotomy are limited. The advantages of laparoscopy in patients with early-stage ovarian cancer also include faster recovery with early return of bowel function and a shorter hospital stay.

Laparoscopy can also be a useful tool when deciding whether to proceed with primary cytoreductive surgery or neoadjuvant chemotherapy in advanced EOC. In a study of 87 patients who underwent diagnostic laparoscopy, 53 were deemed resectable. Of these 53 patients, 96% were optimally cytoreduced. Laparoscopy seems
to be an acceptable method for assessing disease resectability. Operative time of 120 to 240 minutes has been reported with laparoscopic staging of ovarian cancer.\textsuperscript{59} Complications include vascular and gastrointestinal injuries, and another concern is the formation of port site metastases, particularly in the setting of carcinomatosis. The etiology and true incidence remain unclear.\textsuperscript{60}

Another concern in the laparoscopic management of ovarian cancer is that in many instances, the mass is ruptured while trying to remove it. Ovarian cyst rupture has been reported in 12% to 25% of patients undergoing laparoscopy,\textsuperscript{61,62} and rupture may cause intra-abdominal dissemination, thus worsening prognosis. Indeed, several studies have suggested that cyst rupture should be avoided as it may increase recurrence rate and worsen survival.\textsuperscript{63,64} The ovarian mass should be placed in a laparoscopic bag and retrieved through the umbilical port or through a colpotomy, while taking care to avoid any spillage.

**Second-Look Surgery**

Second-look surgery, via either laparotomy or laparoscopy, is a procedure to determine the disease status in an asymptomatic ovarian cancer patient who has no clinical evidence of disease and has completed the planned number of chemotherapy cycles. The procedure was used initially to determine the endpoint for chemotherapy, given the concerns for leukemogenic therapy. Second-look surgeries via laparoscopy are associated with decreased blood loss and shorter hospital stays.\textsuperscript{65,66} The value in laparoscopy lies mostly in its positive predictive value; if unresectable residual disease is identified, then a laparotomy can be avoided. However, its negative predictive value is limited because complete exploration is usually restricted by significant adhesions.\textsuperscript{67} Thus, after a negative second-look laparoscopy, some will proceed with laparotomy.

Second-look surgery involves a thorough evaluation of peritoneal surfaces and organs and mesentery, with liberal use of biopsy. In women with a history of advanced-stage disease with apparent complete response to therapy, > 50% will have microscopic residual disease on second look. Despite this information, it has not been demonstrated that women who receive additional therapy based on this pathologic confirmation survive longer than those who receive additional therapy that is based on clinical information. Clinical information may include cancer-related symptoms, physical findings, or recurrence seen on imaging. Although second-look surgery is the most accurate means of determining response to therapy, there is no clear survival benefit. Even with a negative second look, the patient has a 30% to 50% chance of recurrence. For these reasons, second-look procedures are generally not performed outside of a clinical trial setting.\textsuperscript{68,69}

**Secondary Cytoreduction Surgery**

Some women with recurrent ovarian cancer are candidates for secondary cytoreductive surgery. Due to a lack of large randomized trials, conclusive data are limited regarding the benefits of secondary cytoreductive surgery. A patient with a rapid, multifocal recurrence is unlikely to obtain any clinical benefit from surgery. Secondary cytoreduction should be considered for the subgroup of patients with progression-free interval of > 12 to 18 months from completion of adjuvant chemotherapy, localized recurrence amenable to complete cytoreduction, potentially chemosensitive disease, and good performance status.\textsuperscript{70-75} As with primary debulking, resection to no gross residual disease is the most important prognostic factor.\textsuperscript{76-78}

Patients with optimal secondary cytoreduction (< 1 cm) survived for 16 to 60 months, compared to 8 to 27 months for those patients with residual diseases ≥ 1 cm. However, the benefit of surgery, compared to chemotherapy alone, is unclear because of a lack of data. As with primary surgery, the biology of the cancer is certainly another confounding factor. Although data are limited, a subgroup of patients may be candidates for tertiary debulking, based on similar selection criteria used for secondary debulking.

**Surgery for Bowel Obstruction**

Some patients with recurrent ovarian cancer will develop small and/or large bowel obstruction. Palliative surgery in this setting is controversial and requires skilled patient selection. Patients are often end-stage and malnourished, with substantial chemoresistant tumor burden. The causes of obstruction are often multifactorial and include mechanical blockage, dense mesenteric infiltration, carcinomatosis, and adhesions. Possible palliative procedures include bowel resection, colostomy, or intestinal bypass. On occasion, the bowel and mesentery may be so heavily involved by cancer that only a gastrostomy tube can be used for decompression. Even with palliative methods to remove obstruction, the reobstruction rate is 10% to 50%.\textsuperscript{79} Despite these data, a subset of patients will benefit from palliative surgery. Jong et al\textsuperscript{80} noted factors associated with successful palliation, which included absence of the following: > 3 liters of ascites, multifocal obstruction, palpable bulky tumors, and preoperative weight loss > 9 kg. Others, however, have failed to elucidate specific factors predicting successful palliation.\textsuperscript{81} This likely shows the importance of individualizing the approach to a patient with a terminal bowel obstruction. In patients with a malignant bowel obstruction who are not surgical candidates, percutaneous gastrostomy, hydration, and hospice should be considered.

**Conclusions**

EOC remains the most deadly gynecologic cancer in the United States. Despite significant progress in chemotherapy and biologic therapy, surgery remains an important modality in the treatment of this disease. Despite the benefits of surgical intervention, the specific biology of a patient’s disease is central to her response to chemotherapy, duration of remission, and ultimate survival.
References


