Indications for Minimally Invasive Surgery for Ovarian Cancer

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Key Words
Ovarian cancer, laparoscopy, minimally invasive surgery

Abstract
Epithelial ovarian cancer is often diagnosed in advanced stages and typically managed with surgical debulking followed by chemotherapy. For patients with presumed early-stage ovarian cancer, comprehensive surgical staging is essential for management, because 31% are upstaged. Over the past 15 years, minimally invasive techniques have improved and are increasingly being used to treat patients with ovarian cancer. Currently, only retrospective data support laparoscopic staging of patients with a suspected adnexal mass or those surgically diagnosed with presumed early-stage ovarian cancer. Laparoscopy is also used in patients undergoing second-look procedures and to help evaluate whether patients should undergo optimal tumor debulking procedures or be initially managed with neoadjuvant chemotherapy. Randomized clinical studies are needed to further support the role of minimally invasive surgery in the treatment of ovarian cancer. (JNCCN 2011;9:126–132)

More than 21,000 women are estimated to be diagnosed with epithelial ovarian cancer in the United States in 2010, and an estimated 13,850 will die of the disease.1 Of all gynecologic cancers, ovarian cancer is the most common cause of death.1 Advanced-stage disease (stage III–IV) is diagnosed in 75% to 85% of patients, and standard management generally involves cytoreductive surgery and platinum/taxane-based chemotherapy.2 Novel strategies and technologies are desperately needed to diagnose ovarian cancer at earlier stages, because 5-year survival rates for stage I and II cancers are 90% and 80%, respectively.2

Surgical management of epithelial ovarian cancer typically involves a hysterectomy, bilateral salpingo-oophorectomy, omentectomy, pelvic and para-aortic lymph node dissection, and peritoneal biopsies and washings performed through a vertical midline incision.3–4 When evidence of a metastatic tumor is present within the abdominal/pelvic cavity, tumor debulking is performed with goal of maximal cytoreduction.

Minimally invasive surgery has evolved over the past several decades and is now commonly used for appendectomies and cholecystectomies. Minimally invasive surgery for gynecologic malignancies has been primarily focused on uterine and cervical cancers. Most studies involve nonrandomized retrospective reviews of institutional experiences. A recent phase III trial comparing laparoscopy to laparotomy for uterine cancer staging in 1682 patients reported that the laparoscopic approach was associated with fewer postoperative complications and shorter hospital stays but longer procedure times.5 A 26% conversion rate to laparotomy was also noted. Although survival data have not matured, laparoscopy may evolve as the primary means to manage uterine cancers. Minimally invasive approaches have also been used for cervical cancer and show similar benefits, although randomized phase III studies are lacking.6

The use of minimally invasive surgery for managing ovarian cancer has been slower to adopt, but has been reported for the treatment of early- and advanced-stage ovarian cancers, second-look surgeries, assessment of feasibility for tumor debulking, and management of recurrent ovarian cancer. Minimally invasive surgical techniques primarily involve laparoscopy, and newer
Minimally Invasive Surgery in the Management of Early Ovarian Cancer

Ovarian cancer staging is based on the International Federation of Gynecology and Obstetrics (FIGO) staging system that was revised in 1985. Early-stage ovarian cancer is confined to one or both ovaries (stage I) or limited to the pelvis (stage II). When patients are identified as having presumed early-stage ovarian cancer, comprehensive surgical staging is critical because up to 31% of patients are upstaged. In addition, the decision to administer adjuvant chemotherapy is determined based on comprehensive surgical staging. Patients with stage IA grade 1 to 2 and IB grade 1 to 2 cancers may undergo observation, whereas patients with stage I grade 3 or stage IC disease undergo adjuvant chemotherapy.

Laparoscopic approaches to comprehensive staging of ovarian cancer have been reported since 1994. Early feasibility studies showed that laparoscopic staging was possible for patients with presumed early-stage ovarian cancer or those diagnosed with ovarian cancer after surgery but were unstaged. Table 1 summarizes the various parameters used to evaluate laparoscopic staging. These studies showed that both intra- and postoperative complications from laparoscopy were low, and that upstaging of patients was similar to that expected with laparotomy staging (10%–42%). Although recurrences were generally low with favorable survival rates, these reports included a significant proportion of patients with non-epithelial ovarian cancers, with borderline tumors, and undergoing fertility-sparing procedures (Tables 1 and 2). Many of the studies also did not report whether intraoperative cyst rupture occurred. The studies included patients with a history of surgically removed pelvic masses, which may alter the length of surgery and recovery process.

Currently, 5 retrospective studies have compared laparoscopic and laparotomy approaches in the surgical staging of ovarian cancer (Table 3). Generally, laparoscopic staging was associated with longer operative times, but decreased blood loss, length of hospital stay, and surgical complications. The number of pelvic and para-aortic tissues removed was similar to that reported for laparotomy (Table 3). Because these studies are retrospective with limited sample sizes, whether survival rates were affected by the surgical approach is difficult to determine. All studies in which recurrences were reported seem to indicate similar recurrence rates, although Lecuru et al. noted a 15% recurrence rate in the laparotomy group compared with 5% in the laparoscopy group, but this difference was not statistically significant (Table 3). Although randomized clinical trials are needed, the logistics of performing a trial may be challenging because of concerns about obtaining a sufficient number of patients with early ovarian cancer and creating uniform standard surgical protocols.

Despite the potential advantages, several concerns regarding laparoscopy have been raised. First, the laparoscopic approach may limit the surgeon’s ability to thoroughly explore the abdominal/pelvic cavity, thereby missing small areas of disease that would upstage a patient and cause patients with an incomplete resection to be considered having no gross residual disease. In addition, the ability to resect para-aortic lymph nodes may be limited with laparoscopy. In the phase III trial of laparoscopy versus laparotomy for staging of uterine cancer, more patients undergoing laparotomy had a complete pelvic and para-aortic lymph node dissection than those undergoing laparoscopic staging. However, the authors recognize the limitations of cross-comparison with ovarian cancer and other potentially specific factors related to uterine cancer staging, which may account for this difference. Reports of laparoscopic staging have varied in terms of para-aortic lymph nodes obtained, with some studies reporting none taken and others reporting adequate dissection (Table 1). Secondly, concerns exist for port-site metastases when patients with ovarian cancer undergo laparoscopic surgery. Port-site metastasis rates for patients with early-stage disease seem to be low (Table 1). However, patients with advanced-stage disease undergoing diagnostic laparoscopy seem to have higher rates of port-site recurrence. Despite procedures such as resecting port sites to limit port-site metastases, standardized protocols have not been established. Third, concerns about intraoperative spillage during removal of pelvic masses have been reported. Intraoperative and preoperative spillage are believed to be associated with a worse prognosis.
### Table 1  Summary of Laparoscopic Staging for Presumed Early-Stage Ovarian Cancer

<table>
<thead>
<tr>
<th>Study</th>
<th>N (Number of Patients With EOC/FTC)</th>
<th>Prior Surgery for Mass, But Unstaged (n)</th>
<th>Fertility-Sparing Surgery (n)</th>
<th>EBL (mL)</th>
<th>OR Time (min)</th>
<th>Hospital Stay (d)</th>
<th>Pelvic LN (n)</th>
<th>PA LN (n)</th>
<th>Complications</th>
<th>% Upstaged</th>
<th>% Conversion to Laparotomy</th>
<th>Port-Site Met (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Querleu and LeBlanc(^a)</td>
<td>9</td>
<td>9</td>
<td>0</td>
<td>&lt; 300</td>
<td>227</td>
<td>2.8</td>
<td>NR</td>
<td>8.6</td>
<td>None</td>
<td>11.1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Childers et al.(^d)</td>
<td>14 (12)</td>
<td>5</td>
<td>0</td>
<td>NR</td>
<td>120–240</td>
<td>1.6</td>
<td>NR</td>
<td>NR</td>
<td>Vena cava injury, Ecchymosis</td>
<td>42.8</td>
<td>0</td>
<td>NR</td>
</tr>
<tr>
<td>Pomel et al.(^j)</td>
<td>10 (11)</td>
<td>10</td>
<td>0</td>
<td>NR</td>
<td>313</td>
<td>4.75</td>
<td>7.1</td>
<td>8.8</td>
<td>Hemoperitoneum, Pulmonary embolism</td>
<td>10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Tozzi et al.(^i)</td>
<td>24 (11)</td>
<td>11</td>
<td>10</td>
<td>NR</td>
<td>176</td>
<td>7</td>
<td>19.6</td>
<td>19.6</td>
<td>Chylous ascites, Vena cava injury</td>
<td>20.8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Leblanc et al.(^k)</td>
<td>42 (42)</td>
<td>42</td>
<td>9</td>
<td>NR</td>
<td>238</td>
<td>3.1</td>
<td>14</td>
<td>20</td>
<td>Hematoma, Lymphoceysts</td>
<td>19</td>
<td>2.4</td>
<td>0</td>
</tr>
<tr>
<td>Spirto et al.(^l)</td>
<td>75 (*)</td>
<td>NR</td>
<td>NR</td>
<td>171.9</td>
<td>187.9</td>
<td>3.35</td>
<td>18.6</td>
<td>10.3</td>
<td>Bowel injuries, Cystotomy, SBO, Fever, Venotomy, Excessive bleeding</td>
<td>10.8</td>
<td>22.7</td>
<td>NR</td>
</tr>
<tr>
<td>Colomer et al.(^n)</td>
<td>20 (11)</td>
<td>17</td>
<td>8</td>
<td>NR</td>
<td>223</td>
<td>3</td>
<td>18</td>
<td>11.3</td>
<td>Vein injury</td>
<td>20</td>
<td>5</td>
<td>0</td>
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<tr>
<td>Jung et al.(^o)</td>
<td>24 (16)</td>
<td>5</td>
<td>1</td>
<td>567</td>
<td>254</td>
<td>10.6</td>
<td>22.5</td>
<td>11</td>
<td>SBO</td>
<td>42</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Nezhat et al.(^p)</td>
<td>36 (17/3)</td>
<td>9</td>
<td>11</td>
<td>195</td>
<td>229</td>
<td>2.4</td>
<td>14.8</td>
<td>12.2</td>
<td>SBO, Pelvic lymphocysts, Lymphocele cyst</td>
<td>19.4</td>
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<td>0</td>
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<tr>
<td>Ghezzi et al.(^q)</td>
<td>26 (26)</td>
<td>0</td>
<td>2</td>
<td>250</td>
<td>348</td>
<td>4</td>
<td>24.5</td>
<td>9.8</td>
<td>Hematoma, Lymphocele cyst</td>
<td>23.1</td>
<td>0</td>
<td>NR</td>
</tr>
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</table>

Abbreviations: EBL, estimated blood loss; EOC, epithelial ovarian cancer; FTC, fallopian tube cancer; LN, lymph node; Met, metastasis; NR, not reported; OR, operating room; PA, para-aortic; SBO, small bowel obstruction.

\(^a\)Mixture of epithelial ovarian, fallopian tube, primary peritoneal, and uterine cancers with 58 laparoscopic and 17 laparotomy cases.
sues of cost and training of physicians to adequately perform comprehensive staging procedures for ovarian cancer have not been addressed.

**Minimally Invasive Surgery in the Management of Advanced Ovarian Cancer**

Cytoreductive surgery is an important aspect in managing patients with epithelial ovarian cancer. Bristow et al. reported in a meta-analysis that every 10% increase in maximal cytoreduction of tumor was associated with a 5.5% increase in median survival. Patients have been dichotomized to optimal (≤ 1 cm) and suboptimal (> 1 cm) debulking based on the residual disease remaining after surgery. Generally 17% to 87% of patients are able to undergo successful optimal debulking procedures, which is dependent on the skill and experience of the surgeon. To improve on this, investigators have tried to use various tools, such as imaging studies, CA-125, and ascites volume, to predict which patients may likely undergo optimal debulking procedure. Those that are not candidates for possible optimal tumor debulking surgery would then undergo neoadjuvant chemotherapy followed by interval debulking surgery if an appropriate response was noted.

Minimally invasive surgery has also been used to decide whether patients are candidates for successful cytoreductive surgery. Several studies have suggested that laparoscopic assessment of the abdominal/pelvic cavity improves the ability to determine which patients would be able to undergo an optimal tumor debulking. This has led to development of various scoring systems. However, these studies have primarily come from single institutions and have not been validated prospectively by different investigators. Access to centers with expert surgical care and variability among gynecologic oncologists to per-

### Table 2  Recurrence and Survival Data From Case Series in Laparoscopic Staging for Ovarian Cancer

<table>
<thead>
<tr>
<th>Author</th>
<th>n</th>
<th>Median Follow-up (mo)</th>
<th>Recurrence (n)</th>
<th>% Disease-Free Survival</th>
<th>% Overall Survival</th>
<th>Port-Site Metastasis</th>
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<tr>
<td>Pomel et al.</td>
<td>10</td>
<td>NR</td>
<td>1</td>
<td>90</td>
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<tr>
<td>Tozzi et al.</td>
<td>24</td>
<td>46</td>
<td>2</td>
<td>91.6</td>
<td>100</td>
<td>0</td>
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<tr>
<td>Leblanc et al.</td>
<td>42</td>
<td>54*</td>
<td>4</td>
<td>90.5</td>
<td>97.6</td>
<td>0</td>
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<tr>
<td>Colomer et al.</td>
<td>20</td>
<td>24.7</td>
<td>1</td>
<td>95</td>
<td>100</td>
<td>0</td>
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<td>Jung et al.</td>
<td>24</td>
<td>10</td>
<td>1</td>
<td>95.8</td>
<td>95.8</td>
<td>1</td>
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<tr>
<td>Nezhat et al.</td>
<td>36</td>
<td>55.9*</td>
<td>3</td>
<td>100</td>
<td>100</td>
<td>0</td>
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<tr>
<td>Ghezzi et al.</td>
<td>26</td>
<td>26.7</td>
<td>1</td>
<td>96.1</td>
<td>96.1</td>
<td>NR</td>
</tr>
</tbody>
</table>

Abbreviations: NR, not reported. *Study reported mean.

### Table 3  Retrospective Comparison of Laparotomy Versus Laparoscopic Staging of Ovarian Cancer

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Lap EBL (mL)</th>
<th>Lap OR Time (min)</th>
<th>Lap Pelvic LN (n)</th>
<th>Lap Para-aortic LN (n)</th>
<th>Lap LOS (d)</th>
<th>Complications (%)</th>
<th>Upstaged (%)</th>
<th>Intraoperative Cyst Rupture (%)</th>
<th>Follow-up (mo)</th>
<th>Recurrence (n)</th>
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</thead>
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<td>Chi et al.</td>
<td>30</td>
<td>367</td>
<td>276</td>
<td>14.7</td>
<td>9.2</td>
<td>5.8</td>
<td>2</td>
<td>10</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Lecuru et al.</td>
<td>20</td>
<td>235</td>
<td>321</td>
<td>12.3</td>
<td>6.7</td>
<td>3.1</td>
<td>0</td>
<td>10</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Lecuru et al.</td>
<td>114</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>16</td>
<td>41</td>
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<tr>
<td>Lecuru et al.</td>
<td>34</td>
<td>NR</td>
<td>NR</td>
<td>ND</td>
<td>ND</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>31</td>
<td>34</td>
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<tr>
<td>Ghezzi et al.</td>
<td>19</td>
<td>400</td>
<td>272</td>
<td>25.1</td>
<td>7</td>
<td>7</td>
<td>42.1</td>
<td>31.6</td>
<td>10.5</td>
<td>60</td>
<td>4</td>
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<tr>
<td>Ghezzi et al.</td>
<td>15</td>
<td>250</td>
<td>377</td>
<td>25.2</td>
<td>6.5</td>
<td>3</td>
<td>13.3</td>
<td>26.7</td>
<td>20</td>
<td>16</td>
<td>0</td>
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<tr>
<td>Park et al.</td>
<td>19</td>
<td>505.3</td>
<td>290.4</td>
<td>19.3</td>
<td>6.4</td>
<td>14.1</td>
<td>26.3</td>
<td>35.3</td>
<td>0</td>
<td>14</td>
<td>0</td>
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<tr>
<td>Park et al.</td>
<td>17</td>
<td>231.2</td>
<td>303.8</td>
<td>13.7</td>
<td>8.9</td>
<td>9.4</td>
<td>11.8</td>
<td>5.3</td>
<td>0</td>
<td>19</td>
<td>2</td>
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<tr>
<td>Park et al.</td>
<td>19</td>
<td>568.2</td>
<td>274.7</td>
<td>33.9</td>
<td>8.8</td>
<td>14.5</td>
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<td>21.2</td>
<td>12.1</td>
<td>23</td>
<td>0</td>
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<tr>
<td>Park et al.</td>
<td>19</td>
<td>240.0</td>
<td>220.7</td>
<td>27.2</td>
<td>6.6</td>
<td>8.9</td>
<td>10.5</td>
<td>21.1</td>
<td>10.5</td>
<td>17</td>
<td>0</td>
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</table>

Abbreviations: EBL, estimated blood loss; Lap, laparotomy; LN, lymph node; LOS, length of stay; Lsc, laparoscopic; ND, not done; NR, not reported; OR, operating room.
form” aggressive” surgical debulking make this issue even more challenging. Some investigators have also used laparoscopy to perform cytoreductive surgery. Fanning et al. published a case series of 11 patients who underwent a laparoscopic cytoreductive procedure for stage III/IV ovarian cancer. Of 11 patients, 9 were able to undergo laparoscopic cytoreduction without conversion to laparotomy. Interestingly, 45% of patients had no residual disease at the end of the procedure, and 7 had stage IIIC disease. The authors accomplished the cytoreductive procedure with a laparoscopic 5-mm Argon-Beam Coagulator with a median operative time of 2.5 hours, and the specimen was brought through a 6-cm periumbilical Maylard incision. Krivak et al. reported on a series of 25 patients, 6 of whom had initially known advanced-stage disease, who underwent surgical staging and debulking with hand-assisted laparoscopy. After staging, 13 were noted to have advanced-stage disease, with 3 cases requiring conversion to laparotomy to complete the surgical debulking. Although a laparoscopic approach to cytoreductive surgery was able to be accomplished, further studies are needed to establish the feasibility and whether surgical outcomes are comparable to those of patients undergoing laparotomy.

Minimally Invasive Surgery in Second-Look Surgery
Second-look procedures for ovarian cancers have been used to obtain prognostic information and evaluate the efficacy of chemotherapy. However, second-look procedures are not therapeutic. In fact, progression-free or overall survival does not improve in patients undergoing second-look procedures when compared with those who opt for clinical monitoring. Although second-look procedures are no longer recommended, they are being used under certain specific circumstances related to clinical research protocols. Generally, a generous vertical midline incision is made, but recently laparoscopic approaches have been used for second-look operations.

Husain et al. reported on their experience of 150 patients undergoing laparoscopic second-look operations. At initial surgery, 87% of patients had stage III or IV disease, with 54% undergoing optimal cytoreductive surgery. The authors found a 54% positive second-look rate with a 12% conversion rate to laparotomy. The overall major complication rate was 2.7%, with patients undergoing conversion to laparotomy for bowel injuries (n = 3) and bladder injury (n = 1). Littell et al. found that a negative second-look laparoscopy with negative biopsies and cytology is 91.5% predictive of a negative laparotomy. No significant intraoperative or postoperative complications were seen with laparoscopy. Laparoscopic approaches to second-look surgeries may be a reasonable option for patients under the appropriate clinical circumstances.

Minimally Invasive Surgery in Recurrent Ovarian Cancer
Few reports exist on the use of minimally invasive surgery in recurrent ovarian cancer. Most of the reports have centered on treating isolated splenic recurrences with laparoscopy or hand-assisted laparoscopy. Chi et al. reported on a series of 6 patients with presumed isolated splenic recurrence. Of these patients, 5 were able to undergo laparoscopic or hand-assisted laparoscopic splenectomy, with 1 dying 20 months after the procedure and 4 others having no evidence of disease for 2 to 84 months. No complications were noted. Trinh et al. reported on debulking of patients with recurrent ovarian cancer, but only those with elevated CA-125 and normal preoperative CT scans were selected for laparoscopic debulking. Whether patients with elevated CA-125 levels and no other clinical or imaging-based signs of disease gain any survival benefit from surgery or even chemotherapy is unclear.

Conclusions
Use of minimally invasive approaches to managing ovarian cancer is increasing. For the management of early-stage ovarian cancer, a laparoscopic approach to staging can be considered as an alternative to standard laparotomy, but should not be considered the new standard of care. Similarly, laparoscopic management of advanced-stage ovarian cancer to triage patients for primary or interval debulking surgery can be considered, but further research is needed to validate and establish clear protocols before its use becomes widespread among gynecologic oncologists. The use of minimally invasive surgery for treatment...
of recurrent ovarian cancer is still limited to specific circumstances (e.g., isolated splenic recurrences), and further studies are needed to establish feasibility for minimally invasive surgery in debulking patients with newly diagnosed or recurrent cancer. Despite the numerous benefits associated with decreased blood loss, fewer complications, and shorter hospital stays, randomized clinical trials are lacking to establish the minimally invasive approach as the standard of care.

References


