Four ovarian cancers diagnosed during laparoscopic management of 1011 women with adnexal masses

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OBJECTIVES: This study was conducted to assess the value of laparoscopic management of adnexal masses. Two concerns we wish to address are the failure to diagnose early ovarian cancer at laparoscopy and worsening the prognosis of stage I cancer by spilling fluid during surgery.  
STUDY DESIGN: The setting is a predominantly referral-based, private subspecialty practice. All operations were performed in the outpatient surgical suite of a large suburban hospital. After extensive patient screenings, which included history and physical examination, preoperative serum CA 125 levels (since 1988), and pelvic ultrasonography, 1209 adnexal masses were managed laparoscopically.  
RESULTS: Of 1011 patients with surgical management, ovarian cancer was discovered intraoperatively in four.  
CONCLUSIONS: Our findings indicate that with consistent use of frozen sections of all cyst walls and suspicious tissue, laparoscopic management did not alter the prognosis. Neither CA 125 level, pelvic ultrasonography, nor peritoneal cytologic testing had sufficient diagnostic specificity to predict malignancy. Experienced surgeons using intraoperative histologic sampling may safely evaluate adnexal mass laparoscopically. (Am J Obstet Gynecol 1992;167:790-6.)

Key words: Operative laparoscopy, ovarian cancer, adnexal mass

Operative laparoscopy has proved to be a safe and effective diagnostic and therapeutic tool in the hands of experienced laparoscopists. Laparoscopy can be used to evaluate an adnexal mass with minimal morbidity. Doubts remain, however, about the laparoscopist's ability to diagnose and properly manage early ovarian cancer when the adnexal mass in question is found to be malignant.1 Concern about 'worsening prognosis by spillage of a cancer confined to the ovary exists. Therefore we wish to report on our experience with four cases of ovarian cancer first diagnosed at the time of operative laparoscopy, initially performed to evaluate an adnexal mass.

Material and methods

Our practice is a busy, primarily referral private practice working in an outpatient surgical suite of a large suburban hospital. Two of the authors (C.N. and F.N.) performed all of the operative laparoscopies included in this study. From July 1985 to June 1990 we have surgically managed 1011 women clinically diagnosed to have an adnexal mass, which in some cases was accompanied by endometriosis and/or adhesions. According to our protocol, patients were evaluated clinically with a pelvic examination and vaginal ultrasonography. In addition, previous intraoperative records were reviewed. The diagnosis of endometriosis or adhesions was based on the patient's history and presenting symptoms. Simple (unilocular) cysts were initially managed with hormone suppressive therapy consisting of oral contraceptive pills containing 50 μg of estrogen, depot medroxyprogesterone acetate, or danazol. Since 1988, a serum CA 125 level has also been measured. Those patients who then underwent operative laparoscopy had adnexal masses varying in size from 2 to 25 cm. Masses that appeared cystic, complex, or solid before operation were included, because endometriomas, benign cystic teratomas, and intraligamentous myomas can produce these patterns on ultrasonography. No patients were excluded preoperatively on the basis of serum CA 125 levels or ultrasonographic findings. One case was excluded from the study early in our series because the mass extended above the umbilicus. A total of 1209 masses were managed laparoscopically.

Informed consent included a statement to the patient that laparoscopic diagnosis and treatment of an adnexal mass were not considered to be standard medical practice. The patients were further informed that if a cancer were found, intraoperative cancer cell spillage could occur and possibly influence the chance of survival. In
addition, the patients understood that a second surgery, specifically a laparotomy, might be required if the findings at laparoscopy could not be properly managed without laparotomy. All procedures were performed at an outpatient facility with patients under general endotracheal anesthesia and with multipuncture operative laparoscopy. This technique has been described before. For the past 2 years we have been using the Ultrapulse 5000L (Coherent, Palo Alto, Calif.), which utilizes carbon 13 rather than carbon 12. By use of a different carbon isotope, the laser beam stays focused as the power is increased. This in turn significantly reduces the power loss associated with other carbon dioxide lasers. Intraoperative management of all patients with masses was carefully standardized, including inspection of the pelvis, ovaries, upper abdomen, and diaphragmatic surfaces for any growths or other sign of malignancy. Peritoneal washings were obtained for cytologic testing. If a strong suspicion of malignancy based on intraoperative findings existed, an attempt was made to obtain frozen section biopsy specimens without rupturing the cyst. If that was not possible, the laparoscopic procedure was terminated, and the patient underwent laparotomy.

In addition to the four cases described here, four additional patients required laparotomy on the basis of the appearance of lesions at laparoscopy. Three were suspicious large ovarian cysts, which could not be sampled without rupture (one benign cystic teratoma, one mesothelioma, and one case with bilateral lesions—a serous cystadenoma on the right side and a benign cystic teratoma on the left side). The fourth patient had a large degenerated myoma that appeared highly suspicious. Laparotomy was done and revealed a benign myoma.

The management of a cystic mass itself incited aspiration of the fluid, which was sent for cytologic examination, followed by opening the cyst and inspecting the wall for excrences or irregular thickening. Frozen-section biopsy specimens were obtained if the surgeon thought any surfaces were suspicious. Finally, an ovarian cystectomy or oophorectomy (depending on the patient’s age and pertinent clinical history) was performed. This tissue was sent for permanent-section histologic examination. Tissue was removed from the abdominal cavity through the 5 or 10 mm trocar sleeves, through a posterior colpotomy, or in some cases by use of a small extension of the suprapubic abdominal incision. At times, we inserted a No. 8 surgical glove in the abdomen via the laparoscopic trocar as a bag for specimen removal. More recently, an Endopouch (Ethicon) has been used rather than a surgical glove. Copious amounts of irrigation were used to clean the incision.

After the cyst was removed, the abdominal and pelvic cavities were thoroughly washed with copious amounts of saline to prevent adhesions. Mucinous cystadenomas. It is imperative that the entire cyst and its contents be removed from the pelvic and abdominal cavity.

Before the procedure was terminated, any associated pelvic abnormality such as endometriosis or other adhesions was treated, and hemostasis was assured. No medical adjuvant therapies were used at the end of each procedure other than leaving 400 to 500 ml of lactated Ringer’s solution in the pelvic cavity. At 6 weeks and at 6 months after operation, patients with benign ovarian neoplasms (mucinous or serous cystadenomas or cystic teratomas) underwent follow-up with a bimanual pelvic examination and an ultrasonographic examination for possible recurrence.

Case summaries of four patients with ovarian cancer are presented here.

Case reports

Case 1. A 44-year-old woman, gravida 3, para 3-0-0-3, presented with pelvic pain. A 7 cm mass with cystic and solid components was diagnosed by ultrasonography. The patient wished to avoid laparotomy, if possible. Laparoscopy revealed bilateral ovarian masses with numerous pelvic adhesions. A biopsy was performed of the papillary growth found on the right ovarian surface. When frozen section revealed poorly differentiated adenocarcinoma and further laparoscopic evaluation demonstrated intraabdominal spread of disease, the procedure was terminated. The patient was informed of the findings and agreed to total abdominal hysterectomy, bilateral salpingo-oophorectomy, and staging laparotomy performed by a gynecologic oncologist 3 days later. The final surgical staging was IIIIC, poorly differentiated serous cystadenocarcinoma involving both ovaries, with extension to the pelvic wall, omentum, and uterine serosa. Cytologic examination of fluid taken at laparoscopy was negative for tumor cells, but fluid obtained at laparotomy was positive for tumor cells. The patient underwent three cycles of chemotherapy and refused further treatment. She died of intestinal obstruction 2 years and 5 months after the diagnosis of cancer.

Case 2. A 45-year-old woman, gravida 0, presented with pelvic pain and a desire to achieve pregnancy. She had a history of endometriosis diagnosed by laparoscopy 4 years earlier and had been treated briefly with danazol. The findings at our laparoscopy were multiple myomas, stage 1 IV endometriosis (revised American Fertility Society classification), and bilateral ovarian cysts. The right ovary contained a 5 cm cyst and the left ovary contained a 3 cm cyst, both of which were aspirated and contained “chocolate” material. Both cyst walls and part of the right ovary were removed. The pathology report revealed a hemorrhagic corpus luteum on the right and endometrioid adenocarcinoma without stromal invasion (endometrioid low malignant potential tumor) on the left. The patient underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy, and staging laparotomy 3 weeks later, with...
mor. She is without evidence of recurrence >3 years later.

Case 3. A 43-year-old woman, gravida 0, presented with a large adnexal mass for which she refused laparotomy. In 1983 she was found to have a left ovarian endometrioma at laparotomy. In 1985 a laparoscopy revealed persistent extensive endometriosis. In 1987 we performed operative laparoscopy and found stage IV endometriosis, including an 8 cm right ovarian mass, consistent with an endometrioma. The cyst was aspirated and "chocolate" material obtained; the cyst wall was removed and the ovary was saved. The pathology report revealed benign mucinous cystadenoma. In 1988 the patient presented with pain but continued to have a strong desire to preserve the pelvic organs. Repeat laparoscopy revealed a 4 cm right ovarian cyst, diagnosed as an endometrioma by frozen section and permanent histologic examination. In 1989 a right adnexal mass recurred, extending to the umbilicus, with cystic and solid components. When the patient refused laparotomy, an open laparoscopy was performed. Two cysts were noted on the right ovary. Frozen section of the larger cyst revealed an endometrioma. A smaller cyst on the right ovary was a benign mucinous cystadenoma. Cytologic examination of peritoneal washings gave negative results. The left ovary could not be visualized because of dense adhesions. The procedure was terminated, and total abdominal hysterectomy and bilateral salpingo-oophorectomy were suggested because of a recurring benign mucinous tumor on the right ovary and the inability to visualize the left adnexa.

The patient agreed to a laparotomy but chose to delay it for 2 months. A papillary mucinous cystadenocarcinoma, well differentiated, stage II (with extension to the right tube), and extensive pelvic adhesions were found. Peritoneal cytologic testing was not diagnostic, but the fluid contained atypical cells. She has undergone several courses of chemotherapy, a second-look laparotomy, and debulking, followed by five more courses of chemotherapy. She is doing well 16 months after the laparotomy.

Case 4. A 33-year-old woman, gravida 0, presented with a 5 to 6 cm mass that failed to resolve with danazol. A previous laparoscopy in 1985 revealed endometriosis. During that laparoscopic examination, minimal bladder and left ovarian endometriosis was found. At the current laparoscopy biopsy of a 2 cm left ovarian cyst was performed, and the cyst was found to be follicular. On the right, a 6 cm cystic structure was noted to be translucent, without surface excrescences. The cyst was aspirated and clear yellow fluid was obtained. The cyst was then opened and found to have papillary growths on the inside surface. Two frozen sections revealed necrotic tissue with atypical glands. The frozen-section report left some doubt about the diagnosis; therefore a right salpingo-oophorectomy was performed through the laparoscope. In addition, biopsies of the peritoneum and omentum were performed, and an appendectomy, retroperitoneal, paraaortic, and pelvic node evaluation were carried out because of our uncertainty regarding the pathologic classification of the lesions. Permanent sections revealed moderately differentiated clear cell carcinoma of the ovary, with no extension to the tube, omentum, or appendix. Results of peritoneal cytologic testing were negative. Three weeks later the patient underwent a total abdominal hysterectomy, left salpingo-oophorectomy, and staging laparotomy. The pathologic report of the remaining pelvic organs and omentum stated that they were free of any residual tumor. Biopsy specimens of peritoneal thickenings revealed fibrosis, connective tissue, and endometriosis. Peritoneal fluid contained atypical cells, of the reactive mesothelial type in origin. The patient remains well 1 year after surgery.

**Results**

From July 1985 until June 1990, 1011 operative laparoscopies were performed on patients with adnexal masses measuring from 2 to 25 cm. No major intraoperative complications were noted. All procedures were carried out endoscopically except for the intentional laparotomies mentioned. Minor complications included laceration of the inferior epigastric artery, postoperative nausea and vomiting, shoulder pain, incisional ecchymosis, urinary tract infection, and temporary urinary retention. All women were discharged...
from the hospital within 24 hours of surgery. No recurrence has been noted during follow-up pelvic and ultrasonographic evaluation in patients with organic cysts (excluding endometriomas) except in case 3. Ovarian cancer, including one case of borderline adenocarcinoma, accounted for 0.4% of the cases. Table I summarizes our findings of the 1011 patients who underwent follow-up. In Table II the four cases of cancer are analyzed for characteristics to determine whether any could be used to predict an increased probability of malignancy in advance. In Table III the cytologic results of the peritoneal washings taken at laparoscopy are compared with those taken at laparotomy in the four patients who had ovarian cancer. Frozen-section histologic examination and permanent section pathologic diagnoses were the only reliable indicators; patient's age, cyst size, serum CA 125 levels, ultrasonographic findings, and peritoneal cytologic results at laparoscopy did not distinguish these patients from the others in our series.

A total of 734 patients had CA 125 levels determined before the laparoscopic procedures (Table IV). Correlations of the preoperative CA 125 level with the type, size, and ultrasonographic characteristics of the adnexal cyst are recorded.

The majority of functional cysts clinically appeared to be endometriomas; however, this suspicion was not confirmed by pathologic examination. Thirty-seven patients had other pelvic abnormalities, including peritoneal cysts, one bowel cyst, loops of adherent bowel simulating a mass, and an abdominal wall hematoma 8 weeks after a Marshall-Marchetti-Krantz bladder suspension procedure. In one patient, in spite of pelvic and ultrasonographic evidence of a 7 cm right cystic adnexal mass, no abnormality was found.

**Comment**

Can an adnexal mass be safely evaluated and treated with operative laparoscopy? Different authors have reported their experience in the laparoscopic management of ovarian cysts. The patients included here represent a referral bias, in that the Fertility and Endoscopy Center in Atlanta has a predominance of referrals for benign conditions (frequently endometriosis), usually involving a premenopausal age group.

Of the four patients in whom ovarian cancer was found, we can make some important observations. The first case represents disseminated disease (surgical stage IIIC ovarian cancer). Finding the cancer was not difficult, considering the extent to which the tumor had spread.

The other three patients are of more particular interest, in that each one had a previous surgical diagnosis of endometriosis, either by laparotomy or by operative laparoscopy. Conditions such as endometriosis, which so frequently become a chronic problem, could cause the surgeon to be less thorough in evaluating a patient's pelvic findings than he/she should be. A high index of suspicion must always be maintained, with adherence to a protocol that emphasizes cytologic sampling and tissue biopsies. Even a documented history of endometriosis does not rule out the possibility of new problems. Case 2 illustrates the necessity for removing an entire cystic capsule to find the early carcinoma. Cases 2 and 4 emphasize the importance of tissue biopsies from any area that appears abnormal to the surgeon.
## Table IV. CA 125 levels correlated with type of adnexal cyst

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Cyst type</th>
<th>No. of cysts</th>
<th>Size of cyst (cm)</th>
<th>Age range (yr)</th>
<th>CA 125 level (U/ml)</th>
<th>Ultrasonographic characteristics of cysts</th>
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<td>Range</td>
<td>Mean</td>
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<tr>
<td>360</td>
<td>Endometrioma</td>
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<td></td>
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<td>219</td>
<td>Functional</td>
<td>172</td>
<td>2.5-6</td>
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<td>&lt;2-135</td>
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<td></td>
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<td>45</td>
<td>5-10</td>
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<td>&lt;2-53</td>
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<td></td>
<td></td>
<td>2</td>
<td>10-12</td>
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<td>6</td>
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<td>34</td>
<td>Simple</td>
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<td>2.5-6</td>
<td>23-47</td>
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Without careful intraoperative evaluation, errors could be made by missing significantly abnormal areas. These cases illustrate a "worst case" scenario, where an unsuspected malignancy is confined to the ovary and spillage could have occurred at surgery. The absence of any tumor cells by peritoneal cytologic testing or extensive histologic testing at subsequent surgery 3 weeks later is notable.

Case 3 is probably the most typical, as well as the most frustrating. This patient had one previous pelvic laparotomy and three previous laparoscopies, all for endometriosis. In 1987 a benign mucinous cystadenoma was found as part of an 8 cm right ovarian mass. In 1989 she had a recurrent cyst on the right ovary, which again was a benign mucinous tumor. Because of the recurrence and/or persistence of this benign tumor, laparotomy was recommended. A well-differentiated mucinous cystadenocarcinoma was found. In light of this patient's age and the recurrent nature of the mass, major surgery would be an appropriate management option. We do not recommend major surgery to remove the adnexa and/or uterus for each patient with a benign serous or mucinous ovarian cyst; however, if such lesions do persist and/or recur, then radical exirrative adnexal surgery may be advised.

The value of cytologic washings from the peritoneal cavity remains unclear, especially in cases of early stage disease. Patient 1, who had disseminated stage III ovarian cancer, had negative washings at laparoscopy, although positive washings were found at subsequent laparotomy. Parker and Berek conducted a pilot study in which 25 postmenopausal women with adnexal masses <10 cm underwent operative laparoscopy. Preoperative screening included the use of strict ultrasonographic criteria for the tumor CA 125 level (<35

had clearly positive cytologic results from the peritoneal cavity. The primary malignancy's size and location may explain the absence of exfoliated malignant cells in the peritoneal cavity in these three patients. Other authors have reported 20% to 30% positive cytologic findings in peritoneal cavity washings taken with the laparoscope. With only four of 1011 patients in this series exhibiting malignant cells, we cannot make any general statements about the place of cytologic washings, except to report that our group continues to routinely take such cytologic samples.

The use of CA 125 levels as a preoperative screening test has not been specific enough to detect the presence of ovarian cancer (Table IV). In all cases of ovarian cancer in which CA 125 levels were determined, normal levels were detected. Patients having endometriosis or benign serous cystadenomas tended to have slightly elevated CA 125 levels. The size of the adnexal mass was only occasionally correlated with the actual CA 125 level. Characteristics of the mass (e.g., solid, cystic, etc.) did not correlate with CA 125 levels. The patients in this series were premenopausal, an age group in which it is most difficult to establish an adequate specificity of CA 125 in the detection of ovarian cancer. In contrast, postmenopausal patients have an increased diagnostic specificity of CA 125.
U/ml) was used to rule out any possibility of malignancy. Intraoperative evaluation did not show any malignancy. However, it is not clear what number of patients were excluded preoperatively, on the basis of this screening, who indeed had benign disease and were not given the benefit of operative laparoscopy.

During the laparoscopic management of cystic masses in 481 women, Mage et al.\textsuperscript{5} claim to have been able to diagnose nine borderline tumors and ovarian cancers with 100\% sensitivity. Seven were diagnosed visually and two required incision and examination of the internal cyst wall. However, this diagnosis was based on visualization without biopsy, and their false-positive rate for malignancy was quite high (52.6\%). In our opinion, on the basis of extensive experience, all adnexal masses can first be explored laparoscopically, unless they are preoperatively shown to be cancer. Then, depending on the surgeon’s knowledge and skill, the mass can be managed laparoscopically or by laparotomy (through an appropriate transverse or vertical incision) without compromising the outcome of the procedure. It is our belief that even cases of early stage ovarian cancer can be managed laparoscopically if the operator is able to perform complicated procedures such as laparoscopically assisted vaginal hysterectomy and para-aortic and pelvic node dissection.\textsuperscript{14,15}

The risk of spillage during removal of a tumor, as in cases 2 and 4, is important at either laparotomy or laparoscopy. Whether spillage of tumor cells at laparotomy or laparoscopy influences the ultimate patient survival is unknown.\textsuperscript{15,16} Every attempt should be made to avoid spillage. Copious irrigation and washing of the abdominal and pelvic cavity with liters of lactated Ringer’s solution should be performed in cases of spillage. With dermoid cysts, >10 L may be required to cleanse the cavity of the cyst contents. Commercially available laparoscopic bags (Endopouch, Ethicon) can be used to contain and remove the cyst completely from the abdominal cavity. It has been reported that a tumor was found at a trocar puncture site as early as 3 weeks after laparoscopic biopsy.\textsuperscript{1,18} Such cases are likely ones in which the tumor was already disseminated before laparoscopy. Similar findings can be noted when nodules grow along a catheter track after paracentesis for drainage of malignant ascites.

Our experience with 1011 patients evaluated and treated by operative laparoscopy reveals that 99.6\% of the patients in our referral group with a known adnexal mass were found to have benign disease. This does not imply that the risk of finding cancer is so low as to be of no concern. Successful identification of cancer and referral to a gynecologic oncologist for treatment are possible when operative laparoscopy is used. New standards of medical care must evolve as available technology improves.

Mens is possible through the laparoscope when it is used by someone with proper training and experience. In our experience CA 125 levels, pelvic ultrasonographic, and peritoneal cytologic results alone have not had sufficient diagnostic specificity to adequately predict malignancy. Generous biopsy specimens must be obtained in all cases, including the most benign-appearing cysts. The laparoscopic surgeon must be competent to remove cyst walls and tumors through the laparoscope. We concur with others that simple aspiration of an ovarian cyst at laparoscopy is inadequate therapy. In those cases where tissue cannot be obtained or doubt exists about the possibility of cancer, operative laparoscopy is contraindicated and plans should be made for conventional laparotomy. For cases in which cancer has been encountered, a gynecologic oncologist can then be consulted for further management. Maintaining a high index of suspicion and obtaining generous tissue samples during all laparoscopic procedures will ensure the timely discovery and management of early, unsuspected ovarian cancers.\textsuperscript{14,16}

Finally, it must be emphasized that there is no technological substitute for sound clinical judgment. Surgeons should select the procedure or technique that they are most competent to perform. Operative laparoscopy is an excellent alternative to laparotomy. The surgeon’s eyes are within millimeters to centimeters from the tissue (via the video scope), so the operative field is well magnified. This allows the most tedious procedures to be performed microsurgically. However, the surgeon must be properly trained, then increase his skill level gradually to ensure that this method is used effectively and safely, without needless complications. Video endoscopic procedures lack the three-dimensional perspective present with laparotomy. Successful utilization of videolaparoscopy requires that the previously trained surgeon relearn his operating skills. The time necessary to acquire the ability to perform advanced operative laparoscopy is typically at least as long as that for laparotomy. A lack of training or inexperience will be revealed by an unacceptable complication rate. This will impede the advancement of therapeutic laparoscopy, as did the problems and injuries that occurred during the use of the electrocoagulator for tubal ligation. However, future generations of surgeons can be taught the technique of operative videolaparoscopy without ever having to learn laparotomy.

By combining careful patient selection with adequate physician training and experience, we believe that this new technology of operative laparoscopy can be safely extended to the evaluation of many adnexal masses. Risks of failure to diagnose cancer or improper management should thereby be minimized.

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REFERENCES


