

Operative Laparoscopy in the Management of Ovarian Cancer

D. Paul Amara, M.D., Camran Nezhat, M.D., Nelson N.H. Teng, M.D., Ph.D.,
Farr Nezhat, M.D., Ceana Nezhat, M.D., and Maurizio Rosati, M.D.

Summary: Advances in operative laparoscopic techniques have made possible the extension of this technology to the treatment of women with ovarian cancer. We present a detailed case series of eight patients with ovarian cancer who underwent a total of 11 operative laparoscopies for treatment of ovarian cancer ranging in stage from IA to IIIC. Three patients underwent initial laparoscopic staging and therapeutic debulking procedures. In three other cases that were incompletely staged via laparotomy, laparoscopy was used to complete the staging. Interval laparoscopic tumor debulking combined with second-look laparoscopy was performed in four cases. We describe our experience with these new applications of evolving techniques with particular regard to potential advantages, disadvantages, and complications. This detailed preliminary case series suggests the need for prospective clinical studies to establish the safety and efficacy of the approach. **Key Words:** Laparoscopy—Ovarian cancer.

In recent years, the development of advanced operative laparoscopic techniques has allowed selected cases of gynecologic malignancy to be approached laparoscopically. The use of laparoscopy in the management of adnexal masses that were subsequently proven to be malignant has been reported (1-5). Traditionally, gynecologic oncologists have been reluctant to use operative laparoscopy in cases of known or suspected malignancy, as the long-term results of such interventions have yet to be established. However, the adaptation of operative laparoscopy to the care of patients with ovarian cancer is being examined at centers where experienced laparoscopists work in concert with gynecologic oncologists. We report a series of eight pa-

tients with ovarian carcinoma in whom operative laparoscopy was used either for initial staging and debulking or for interval evaluation and debulking.

MATERIALS AND METHODS

Between September 1993 and April 1994, eight patients underwent operative laparoscopy for treatment at various stages of suspected or known ovarian carcinoma. All but one of these procedures were performed at the Stanford Center for Special Pelvic Surgery, a specialized referral-based laparoscopic surgical center. The remaining procedure was performed at the Center for Special Pelvic Surgery in Atlanta. The procedures were performed by an experienced laparoscopist and a board-certified gynecologic oncologist working as a team. Informed consent prior to surgery included counseling the patients that laparoscopic intervention is not, at present, the standard medical practice in treating ovarian cancer. A standard preoperative evaluation and bowel preparation were employed in all pa-

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From the Department of Gynecology and Obstetrics, Stanford University School of Medicine and Stanford University Hospital, Stanford, California (P.A., C.N., N.T., F.N., C.N.); and St. Elizabeth Hospital, (M.R.), Namur, Belgium.

Address correspondence to Dr. Nelson N.H. Teng, Department of Gynecology and Obstetrics, Stanford University Hospital, Stanford, California 94305-5317, U.S.A.

ents. General anesthesia was used. Pelvic and upper abdominal washings were obtained at the beginning of the laparoscopy. Operative management included, if not performed previously, the following: total hysterectomy with bilateral salpingo-oophorectomy (BSO), appendectomy, pelvic and para-aortic lymph node dissection, and omentectomy. Peritoneal biopsies were obtained. When indicated, laparoscopic tumor debulking was performed by excising or vaporizing lesions with the CO₂ laser and/or the Cavitation Ultrasonic Surgical Aspirator (CUSA, Valley Lab, Boulder, CO, U.S.A.). Our techniques for laparoscopic hysterectomy (4), oophorectomy (3), appendectomy (6) and pelvic and para-aortic lymph node dissection (7) have been previously described.

For omentectomy, the patient is taken out of Trendelenburg position and placed in a neutral position, allowing the omentum to descend. Infracolic omentectomy was performed using sutures, bipolar electrocoagulation, or a linear stapling device (Ethicon Endosurgery, Cincinnati, OH, U.S.A.). Laparoscopic endobags (Ethicon) were used to confine specimens for removal without contamination of the abdominal wall.

Case 1

A 77-year-old woman, para three, status post-total abdominal hysterectomy (TAH) in 1950 for benign disease, initially presented with a 6-cm cystic ovarian mass. A diagnosis of a grade 3 ovarian carcinoma was made by fine-needle aspiration (FNA). The patient initially refused any surgical intervention and underwent five cycles of chemotherapy with carboplatin and cyclophosphamide. Six months later, she was referred for operative laparoscopy. Laparoscopic BSO (bilateral salpingo-oophorectomy) and lymph node dissection were performed. A small focus of poorly differentiated ovarian carcinoma was noted on the right ovary. All lymph nodes were negative.

Consolidation chemotherapy with intraperitoneal cisplatin was followed by a recurrence 1 year later. After six cycles of Taxol, an 18 × 20-cm mass was noted on computed tomography (CT) scan. Exploratory laparotomy with omentectomy was performed for a large recurrence. Subsequent CT revealed recurrent disease, and she began tamoxifen.

Twenty-seven months after initial presentation, the patient became symptomatic with a partial large bowel obstruction and asked for intervention. At operative laparoscopy, a large abdominal mass was

found along the ascending colon. A pelvic mass adherent to the small bowel was also noted. Serosal surfaces showed a few isolated tumor implants. Multiple peritoneal biopsies were taken. Using a combination of the endoscopic CUSA and the CO₂ laser, adhesions were lysed and the tumor was debulked to residual disease measuring less than 5 mm. A small enterotomy was repaired laparoscopically with PDS 4.0 suture (5). An intraperitoneal infusion catheter was then placed under laparoscopic guidance. Surgical time was 3 h 40 min. The pathology report confirmed the frozen-section diagnosis of high-grade ovarian carcinoma in the abdominal and pelvic tumors as well as in the small bowel adhesions and peritoneal biopsies.

Postoperatively, the patient, who had a history of congestive heart failure, developed mild pulmonary edema, which responded to diuresis. An ileus resolved with conservative management, and the patient was discharged home on postoperative day 6.

The patient was readmitted the following month to rule out a large bowel obstruction. She responded to conservative management with a nasogastric tube. Three months later, she was readmitted with diagnoses of persistent ovarian cancer, anemia, and failure to thrive. After initial treatment with total parenteral nutrition, she declined all but comfort care and died on hospital day 26.

Case 2

A 68-year-old woman, gravida 0, with stage IIIA papillary serous carcinoma of the ovary, status postdebulking, surgery, and chemotherapy was referred after a positive second-look laparoscopy. This woman had undergone a diagnostic laparoscopy followed by exploratory laparotomy, TAH-BSO, partial omentectomy, and appendectomy. Findings were a stage IIIA papillary serous ovarian carcinoma involving both ovaries.

Following six cycles of carboplatin and cyclophosphamide, second-look laparoscopy with pelvic washings revealed microscopic disease. The patient was then referred to our institution.

The patient underwent operative laparoscopy with pelvic lymph node dissection and insertion of a peritoneal catheter. Small bowel adhesions were also lysed. Estimated blood loss was 35 ml. Duration of the operation was 2 h. The pathology report revealed nodes to be negative for carcinoma, but washings showed adenocarcinoma. The patient's course was uneventful, and she was discharged on postoperative day 1 with plans for follow-up chemotherapy.

Case 3

A 31-year-old woman, gravida 0, presented with several months of enlarging abdominal girth. Ultrasound revealed a 20-cm pelvic mass composed of mixed cystic and solid components. At time of exploratory laparotomy and left oophorectomy, frozen sections revealed degenerating teratoma. Permanent sections, however, revealed well-differentiated mucinous cystadenocarcinoma, teratoma, and negative pelvic washings.

The following month, the patient underwent operative laparoscopy with lymph node dissection, ovarian and multiple peritoneal biopsies, appendectomy, lysis of adhesions, omentectomy, sigmoidoscopy, and anal fistulotomy (for a long-standing fistula). The patient had no visible evidence of persistent disease. Estimated blood loss was 250 ml. Duration of the operation was 5 h 25 min. The final pathology report revealed the absence of carcinoma in all biopsies; however, one washing revealed metastatic adenocarcinoma.

The patient's course was remarkable only for a spontaneously resolving corneal abrasion. She was discharged on postoperative day 2. She continues to do well after three cycles of chemotherapy with carboplatin and cyclophosphamide.

Case 4

A 40-year-old woman, gravida 0, with an enlarging adnexal mass was referred for therapy. Physical exam revealed a 12- to 14-week-sized adnexal mass extending from the right to the left side. Following extensive counselling, the patient elected to undergo laparoscopic management of her condition.

She underwent laparoscopic tumor debulking and staging, including laparoscopic hysterectomy, BSO, omentectomy, pelvic lymph node sampling, multiple biopsies, ureterolysis, and cystoscopy. Operative findings revealed diffuse ovarian carcinoma consistent with stage IIIC. Duration of surgery was 6 h 10 min. Estimated blood loss was 800 ml. The patient received 2 units of packed red blood cells intraoperatively and two additional units postoperatively. The pathology report revealed bilateral ovarian papillary serous carcinoma, grade 3. Metastatic involvement of the omentum, bowel serosa, diaphragm, and pararectal area was noted. Lymph nodes and pelvic washings were negative. Postoperatively, she experienced antibiotic-associated diarrhea and was discharged on postoperative day 5.

The patient began chemotherapy with carboplatin on postoperative day 7. Four months later, she un-

derwent a second-look laparoscopy with additional tumor debulking. Scattered seedlings less than 1 cm in diameter were noted throughout the peritoneal cavity. However, multiple biopsies of pelvic sidewall, diaphragm, pelvic and abdominal adhesions, perirectal tissue, cul-de-sac lesions, and round ligament revealed only fibrous tissue with inflammation. The duration of the surgery was 2 h 25 min, and estimated blood loss was 100 ml. A peritoneal catheter was also placed at this time, and the patient received her first cycle of i.v. taxol, followed by i.p. cisplatin 2 days following the second-look laparoscopy.

After four cycles of chemotherapy, she underwent a third-look operative laparoscopy with extensive lysis of adhesions involving both large and small bowel as well as the perihepatic area. Multiple biopsies revealed no evidence of carcinoma. Operative time was 1:05 and estimated blood loss was less than 50 ml. She was discharged on postoperative day 1 and continues to do well on chemotherapy.

Case 5

A 47-year-old woman, para 2, with well-differentiated mucinous adenocarcinoma of the ovary presented for complete staging and laparoscopic lymph node dissection after incomplete staging at an outside institution. The patient first noticed a left abdominal mass, which was found by ultrasound to be a 12-cm-diameter cyst with septations. The patient underwent an exploratory laparotomy and TAH-BSO at an outside facility, where intraoperative frozen sections were read as benign mucinous cystadenoma. The final pathology report revealed a well-differentiated mucinous adenocarcinoma of the left ovary that was invasive into the left fallopian tube. The uterine serosa had invasive implants as well. Washings were negative. After extensive discussion with the patient, it was decided that she would benefit from a laparoscopic staging procedure, including lymph node dissection.

She underwent laparoscopic staging of her cancer, including omentectomy, appendectomy, cytologic washings, and pelvic and periaortic lymph node sampling. A permanent i.p. infusion catheter was also placed. Operative findings revealed no additional tumor burden. Estimated blood loss was 300 ml, and the duration of the procedure was 5 h 10 min. Pathology of all specimens was negative; surgical stage was IIA. On postoperative day 2, the patient began a chemotherapeutic regimen including i.v. taxol and i.p. cisplatin. Six month follow-up revealed no clinical evidence of disease.

Case 6

A 46-year-old woman, para 2, was noted on routine gynecologic exam to have a large pelvic mass. Ultrasound revealed a complex cyst of the left ovary. She was then referred for evaluation and treatment.

During laparoscopic surgery, frozen section revealed a possible low malignant potential (LMP) tumor. She underwent four-quadrant pelvic washing, laparoscopic hysterectomy, BSO, pelvic and para-aortic lymph node dissection, omentectomy, and appendectomy. Operative findings included an 11 × 8-cm cystic and solid left ovarian mass, multiple papillary excrescences on the surface of the right ovary, and normal fallopian tubes, bowel, bladder, and diaphragms. Operating time was 5 h 5 min, and estimated blood loss was 100 ml. The final pathology revealed left ovarian endometrioid adenofibroma with focal endometrioid tumor of LMP. The right ovary and all other biopsies and cytology were benign. The patient did well and was discharged home on postoperative day 2.

Case 7

A 52-year-old woman, para 2, with recurrent stage III ovarian cancer refractory to multiple chemotherapeutic regimens was referred for further treatment. Initially, a pelvic ultrasound revealed enlarged ovaries, and the patient underwent exploratory laparotomy with supracervical hysterectomy, BSO, and a staging procedure from which a diagnosis of bilateral poorly differentiated papillary serous adenocarcinoma stage IIIC grade 3 was made. Omental involvement was noted, but all lymph node specimens were negative. Following six cycles of carboplatin and cyclophosphamide chemotherapy, second-look laparoscopy showed persistent disease, and she began hexamethylmelamine.

After a rise in her CA-125, she began taxol. Despite six cycles, her CA-125 continued to rise and 2 months of tamoxifen was given with no response. VP-16 was tried, but her CA-125 continued to rise. Increasing ascites required paracenteses for symptomatic relief.

The patient was referred to our institution and underwent operative laparoscopy with fulguration of residual tumor, enterolysis, and insertion of an i.p. catheter. Operative findings included 1500 ml of ascites and multiple small (<5 mm) tumor nodules on the bowel and undersurface of the diaphragms. Estimated blood loss was 10 ml, and operative time

was 1 h 40 min. The patient began i.p. chemotherapy on postoperative day 3.

Case 8

A 41-year-old woman was referred following incomplete staging of an ovarian granulosa cell tumor at laparotomy. She presented to her gynecologist complaining of bloating, abdominal pain, and fainting episodes. A radioisotopic red cell scan revealed a leaking ovarian mass causing hemoperitoneum. At laparotomy, a general surgeon performed a TAH-BSO, appendectomy, and pelvic washings. Final pathology revealed a right ovarian granulosa cell tumor weighing 1,200 g and pelvic washings consistent with the tumor.

Operative laparoscopy was performed to complete the staging. Peritoneal washings, omental biopsies, and pelvic and para-aortic lymph node dissection were accomplished. Both operative findings and final pathology revealed no additional disease. She received a surgical stage IC. Operating time was 3 h 10 min, and estimated blood loss was 30 ml. The patient was discharged on postoperative day 1 and continues to do well.

ANALYSIS

This case series describes eight patients with known or suspected ovarian cancer who underwent operative laparoscopy in the treatment of their disease. Initial disease stages ranged from IA to IIIC. The average age of the patients was 47 years (range, 31-77). Mean operating time was 3 h 35 min (range, 1 h 5 min to 6 h 10 min). Mean postoperative hospital stay or days to commencement of chemotherapy was 2.5 days (range, 1-6 days). Table 1 summarizes the surgical interventions performed.

Three patients underwent initial laparoscopic staging and therapeutic debulking procedures. In case 1, performed initially at the Center for Special Surgery in Atlanta, a high-grade stage IC carcinoma spread despite chemotherapy, repeat laparotomy, and repeat debulking via laparoscopy, resulting in the patient's death 32 months after diagnosis. In case 4, a stage IIIC carcinoma was debulked laparoscopically at initial staging and again during chemotherapy. In case 6, a stage IA LMP tumor was completely staged and definitively treated, avoiding the morbidity of a laparotomy.

In three cases (cases 3, 5, and 8) in which frozen section at laparotomy was read as benign or the patients were not completely staged, laparoscopy

TABLE 1. Summary of cases

Case	Age (yr)	Onset (DX)	Initial surgery	Stage	Subsequent surgeries (interval in mo from previous surgery)	Follow-up
1	77	6/91	Laparoscopy with BSO and LND (Atlanta, 2/92) ^a	IC	Laparotomy with omentectomy (12 mo). Laparoscopy with redbulking (8 mo) i.p. catheter placed	Death at 32 mo s/p Dx
2	44	12/92	Diagnostic laparoscopy	IIIA	Laparotomy with debulking (same mo). Diagnostic laparoscopy (9 mo). Laparoscopy with pelvic LND (1 mo) i.p. catheter placed	A&W 7 mo
3	31	11/93	Laparotomy with left oophorectomy, not staged	I	Laparoscopy to Complete staging (1 mo) (LND, Bx's, apply LOA omentectomy)	A&W 4 mo
4	40	10/93	Laparoscopic debulking (LHBSO, LND, Bx's omentectomy)	IIIC	Laparoscopic redbulk (3 mo) i.p. catheter placed; laparoscopic redbulk (3 mo)	A&W 6 mo
5	47	12/93	Laparotomy with TAH-BSO, not staged	IIA	Laparoscopy to complete staging (LND, omentectomy, appy) (1 mo)	A&W 6 mo
6	46	1/94	Laparoscopic staging (LHBSO, LND appy, omentectomy)	IA	None	A&W 6 mo
7	52	1/92	Laparotomy with debulking	IIIC	Diagnostic laparoscopy (11 mo) Laparoscopy with debulking (13 mo)	A&W 2 mo
8	41	12/93	Laparotomy with TAH-BSO, not staged	IC	Laparoscopy to complete staging (4 mo)	A&W 1 mo

Dx, diagnosis; BSO, bilateral salpingo-oophorectomy; LND, lymph node dissection; s/p, status post; A&W, alive and well; Bx, biopsy; appy, appendectomy; TAH, total abdominal hysterectomy; LHBSO, laparoscopic hysterectomy bilateral salpingo-oophorectomy.
^a Underlined procedures represent operative laparoscopies.

was used to complete the staging, determining stages of IC, IIA, and IC malignancies. This management avoided a repeat laparotomy in these cases.

In four cases (cases 1, 2, 4, and 7), interval laparoscopic second look with tumor debulking was used. These patients had initial stages ranging from IC to IIIC, and all had undergone chemotherapy. In case 1, an attempt to provide symptomatic relief from refractory disease was made. In cases 2 and 7, persistent disease requiring additional chemotherapy was observed. In case 4, stage IIIC disease appeared to be responding to chemotherapy at both second and third looks.

DISCUSSION

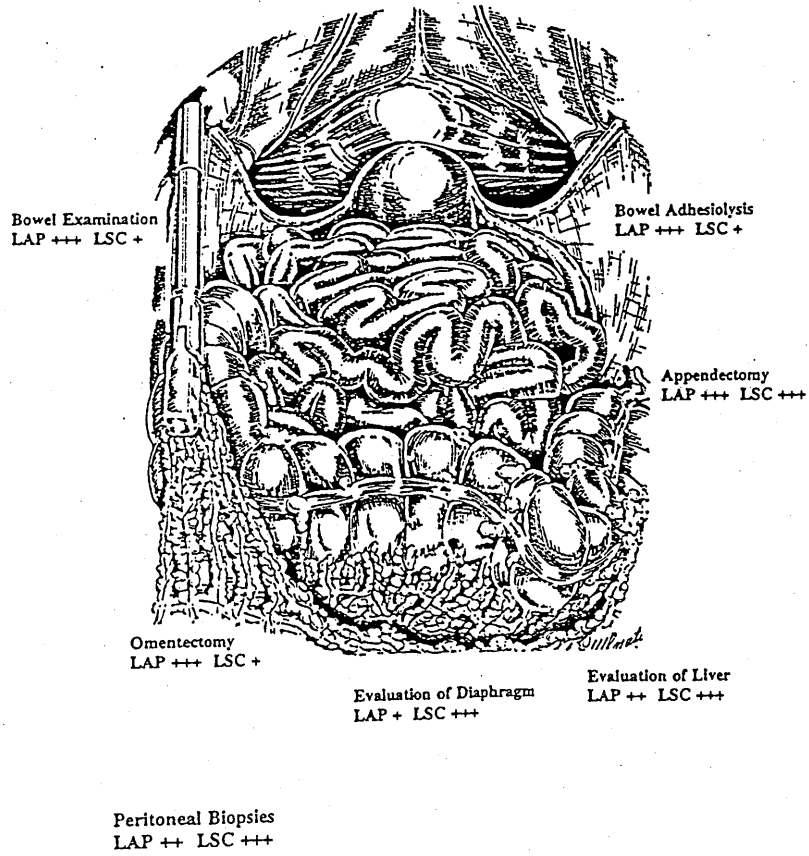
Initial experience with laparoscopy and ovarian cancer has involved the laparoscopic management of presumed benign adnexal masses. In one series of 1,011 patients with 1,209 adnexal masses, four patients were diagnosed intraoperatively with ovarian cancer, and subsequent staging laparotomies were performed by gynecologic oncologists (1). Subsequently, in the management of a borderline ovarian tumor, laparoscopically assisted vaginal

hysterectomy, bilateral salpingo-oophorectomy, and partial omentectomy have been described (4). Experience has also been gained with second-look laparoscopy in the monitoring of ovarian cancer (8-11).

Technologic advances and the development of surgical experience have enabled precise, safe treatment of disease. Following the description of laparoscopic pelvic lymphadenectomy (12,13), experience was gained with this technique in the treatment of cervical cancer (7,14). We have applied this technical experience to ovarian cancer as described in this case series. Additional technical advances include the development of laparoscopic bowel-running devices that allow better evaluation of abdominal spread of tumor. Some aspects of ovarian cancer staging are facilitated by the laparoscopic approach. Figures 1-3 summarize our experience and opinions regarding the relative accessibility of various ovarian cancer staging procedures via laparotomy versus via laparoscopy. One technical development that is needed is the development of a laparoscopic equivalent of an LDS device (U.S. surgical Corp, Norwalk, CT, U.S.A.) to facilitate omentectomy and other bowel surgery.

The potential advantages of operative laparoscopic

FIG. 1. Accessibility for ovarian cancer staging procedures: laparotomy (LAP) versus laparoscopy (LSC). Accessibility is graded on a scale from 1 to 3, with 3 indicating the most accessible. Access to bowel is shown.



Pelvic and Abdominal Washings
LAP ++ LSC +++

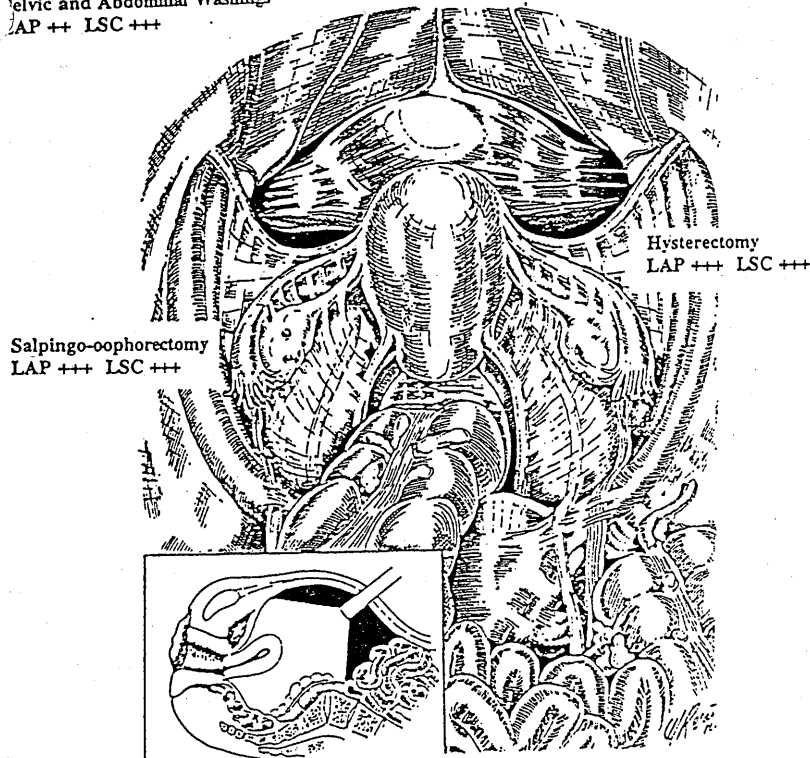


FIG. 2. Accessibility for ovarian cancer staging procedures: laparotomy (LAP) versus laparoscopy (LSC). Accessibility is graded on a scale from 1 to 3, with 3 indicating the most accessible. The pelvis and peritoneum are illustrated.

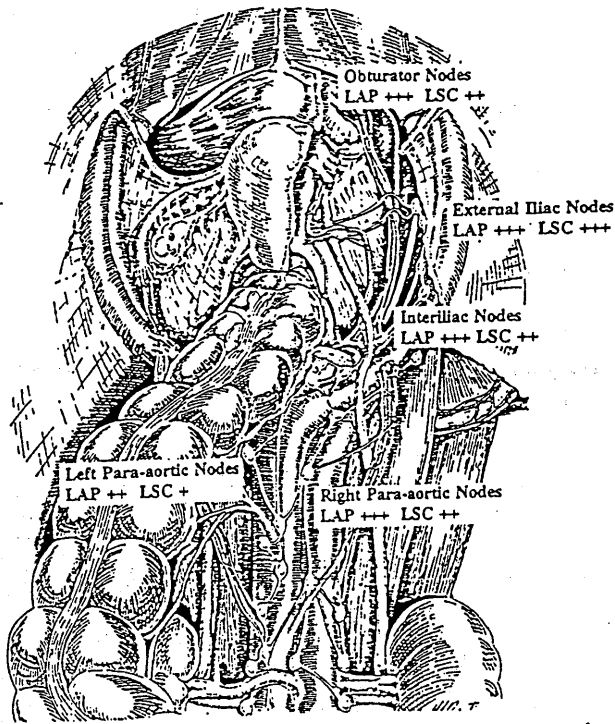


FIG. 3. Accessibility for ovarian cancer staging procedures: laparotomy (LAP) versus laparoscopy (LSC). Accessibility is graded on a scale from 1 to 3, with 3 indicating the most accessible. The retroperitoneum is shown.

py in the treatment of ovarian masses are many, including improved visualization by magnifying small peritoneal metastases and allowing better access to the upper abdomen, the surfaces of the liver and diaphragm, and the deep pelvis. Pneumoperitoneal pressure reduces intraoperative bleeding from small vessels and also distends the peritoneum, thus allowing better visualization. Furthermore, the avoidance of laparotomy could decrease recovery time and the incidence of wound infection and wound dehiscence. Early ambulation reduces the risk of deep venous thrombosis. In addition, faster recovery could allow early institution of chemotherapy.

Endoscopic second-look surgeries allow monitoring of the effectiveness of anticancer treatments such as chemotherapy or radiation therapy. The ability to biopsy residual or recurrent cancer at frequent intervals may allow the clinician to evaluate drug resistance by assessing the expression of the multi-drug-resistant gene or other markers of drug resistance. The combination of interval debulking with second-look laparoscopies as described in four of the patients in this case series may improve therapeutic outcomes.

Although minimizing disruption of the abdominal wall, operative laparoscopy is not without significant potential morbidity in the treatment of ovarian cancer. Cases of abdominal wall metastases at trocar sites have been reported (15,16). Case 1 in this series illustrates the risk of fluid overload with extensive dissection and i.p. irrigation. Concern is appropriately raised about the increased operating time in difficult cases and the steep learning curve necessary in acquiring additional technical skills for the laparoscopic approach.

The adaptation of operative laparoscopy to the treatment of patients with ovarian cancer is a recent development, and long-term results have yet to be determined. In the application of any new technology in the field of oncologic surgery, two fundamental principles must not be violated (7). First, the adequacy of the surgery must not be compromised by the new technology; that is, the specimen removal and the staging information must be as adequate as achievable with conventional surgery. Second, morbidity from a new technique must be no greater than that incurred with conventional therapy. This case series demonstrates the technical feasibility and flexibility of applying operative laparoscopy to the treatment of patients with ovarian cancer.

The potential risks and benefits of operative laparoscopic management of ovarian cancer can be analyzed using three separate outcomes: cost, morbidity, and mortality. Each of these variables needs to be studied in a prospective, randomized fashion. The role of laparoscopy in gynecologic oncology is still evolving. Exciting technical advances have made applications in this field feasible, and their contribution to improving both the quality of life and survival of selected women with ovarian cancer remains to be defined.

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