The Safety and Efficacy of Laparoscopic Surgical Staging and Debulking of Apparent Advanced Stage Ovarian, Fallopian Tube, and Primary Peritoneal Cancers

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ABSTRACT

Objectives: To describe our experience with laparoscopic primary or interval tumor debulking in patients with presumed advanced ovarian, fallopian tube, or peritoneal cancers.

Methods: This is a retrospective analysis of a prospective case series. Women with presumed advanced (FIGO stage IIC or greater) ovarian, fallopian tube, or primary peritoneal cancers deemed appropriate candidates for laparoscopic debulking by the primary surgeon(s) were recruited.

Results: The study comprised 32 patients who underwent laparoscopic evaluation. Seventeen underwent total laparoscopic primary or interval cytoreduction, with 88.2% optimal cytoreduction. Eleven underwent diagnostic laparoscopy and conversion to laparotomy for cytoreduction, with 72.7% optimal cytoreduction. Four patients had biopsies, limited cytoreduction, or both. In the laparoscopy group, 9 patients have no evidence of disease (NED), 6 are alive with disease (AWD), and 2 have died of disease (DOD), with mean follow-up time of 19.7 months. In the laparotomy group, 3 patients are NED, 5 are AWD, and 3 are DOD, with mean follow-up of 25.8 months. Estimated blood loss and length of hospital stay were less for the laparoscopy group (P=0.008 and P=0.03), while operating time and complication rates were not different. Median time to recurrence was 31.7 months for the laparoscopy group and 21.5 months for the laparotomy group (P=0.3).

Conclusions: Laparoscopy can be used for diagnosis, triage, and debulking of patients with advanced ovarian, fallopian tube, or primary peritoneal cancer and is technically feasible in a well-selected population.

Key Words: Laparoscopy, Ovarian Cancer, Cytoreduction.

INTRODUCTION

In the United States, ovarian cancer will affect approximately 21,550 women in 2009 with 14,600 estimated deaths.[1] Approximately 70% of patients are diagnosed with extraovarian disease. The traditional approach to manage patients with ovarian cancer involves midline laparotomy, hysterectomy, bilateral salpingo-oophorectomy (BSO), omentectomy, peritoneal biopsies, diaphragmatic scrapings, bilateral pelvic and para-aortic lymph node sampling, and maximal debulking effort with the intent of leaving "no visible disease," followed by chemotherapy. Optimal cytoreductive surgery has been consistently shown to have a significant survival benefit in the setting of primary advanced ovarian cancer.[2] In patients with disease thought not to be optimally resectable, the use of neoadjuvant chemotherapy to reduce tumor load can allow for interval surgical debulking.[3]

Advances in laparoscopic surgery have extended this minimally invasive surgical approach to managing ovarian cancer. In early stage ovarian cancer, multiple studies have demonstrated feasibility and efficacy of complete laparoscopic staging.[4-14] Laparoscopy offers several advantages to traditional open surgery: optical magnification of abdominal and pelvic anatomy, ease in visualization of

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DOI: 10.4293/108680810X12785289143990

the diaphragm and peritoneal surfaces, shorter postoperative recovery, and a decrease in length of hospital stay.[4] In advanced stage ovarian cancer, the role of laparoscopy has been described as a tool to triage for resectability and second-look evaluations, with limited studies on its role in cytoreductive procedures. The objective of this study was to describe our preliminary experience with laparoscopic total primary or interval cytoreduction in patients with advanced ovarian, fallopian, and primary peritoneal cancers.

MATERIALS AND METHODS

Patients

Select women with confirmed or suspected advanced ovarian cancer (≥FIGO stage IIC) presenting to authors (FN, HG, LC) from January 2005 to June 2009 at their affiliated medical centers underwent exploratory laparoscopy and biopsy, followed by subsequent primary or interval cytoreduction by laparoscopy or laparotomy following laparoscopic assessment. Women were recruited who were medically stable enough to undergo surgery and were judged by the primary surgeon(s) to be good candidates for laparoscopic debulking. Among those patients presenting with suspected primary advanced ovarian cancer, exploratory laparoscopy was offered to confirm the diagnosis and to assess the possibility of optimal laparoscopic or open cytoreductive surgery with a goal of no residual disease. All patients underwent preoperative evaluation including history, physical examination, medical assessment, and imaging of the chest, abdomen, and pelvis. All patients were counseled extensively preoperatively and appropriate informed consent was obtained. During the initial intraoperative assessment, the decision to proceed with a total laparoscopic approach was made by the treating physician. Factors influencing the surgical approach included extent of disease, location of tumor, and medical comorbidities. Only patients with gross extraovarian disease were included in this study. Patients were discharged from the hospital when they were medically stable and able to tolerate oral intake well. Intravenous or intraperitoneal standard chemotherapy was started as soon as the patients were able to tolerate it. All patients were followed every 3 months to 4 months with complete physical examination, measurement of tumor markers, and imaging studies as needed. Subsequent surgery and chemotherapies were initiated as standard practice.

Outcome variables analyzed included histology, stage, site of disease, extent of debulking, operative time, blood loss, length of hospital stay, complications, follow-up duration, and survival time. Pathology, operative reports, hospital and office charts were reviewed retrospectively upon approval by the institutional review board. Postoperative complications were defined as adverse events occurring within 30 days of surgery. Optimal cytoreduction was defined as residual disease <1 cm. Recurrence of disease was defined as recurrence after a period of at least 6 months with no evidence of disease. Statistical analysis was performed using Systat 12.0. The Kaplan-Meier estimator was used to estimate disease-free survival. The 2-sample *t* test and the Wilcoxon rank sum test were used for continuous variables, as appropriate. Results were considered significant if $P<0.05$.

Surgical Technique

All procedures were performed using a multiple puncture operative laparoscopy with the patient under general anesthesia.[15] Initial closed transumbilical or left upper quadrant (Palmer's point) entry using a Veress needle was utilized in most patients. Alternatively, periumbilical cutdown and balloon trocar was utilized. All patients received one dose of preoperative antibiotic therapy. The surgical principles used for staging and tumor debulking during laparotomy were followed. The procedure began with careful inspection of the abdomen and pelvis. If extraovarian disease was noted, that patient was included in this study. Following the initial survey of the abdomen and pelvis, aspiration of any pelvic ascites or peritoneal washings was performed and submitted for cytologic evaluation. If there was no preoperative diagnosis of ovarian, fallopian tube, or primary peritoneal carcinoma, appropriate biopsies were performed and sent for frozen section evaluation. Upon a diagnosis of primary ovarian, fallopian tube, or peritoneal carcinoma, staging and cytoreduction procedures were performed either laparoscopically or via laparotomy, depending on the treating physician's decision, the patient's medical condition, and the extent of disease. Staging and debulking consisted of hysterectomy, BSO, resection of bulky pelvic and para-aortic lymph nodes, and radical debulking of metastatic tumor, including bowel resection and diaphragm ablation with resection, with a goal of no visible disease.[16] Different laparoscopic instruments and techniques were used to achieve optimal cytoreduction, including sharp scissors, electrosurgery, CO_2 laser, PlasmaJet (Plasma Surgical Limited, Oxfordshire, UK), and argon beam coagulator.[15] Rectosigmoid colon resection, where necessary, was performed first by mobilizing the descending colon to the level of the splenic flexure. A low anterior rectosigmoid resection was performed proximally and distally utilizing a 60-mm GIA stapler. The mobilized proximal sigmoid colon was brought out through the vagina after the hysterectomy portion was completed, and an anvil was placed and secured by using a purse string suture. The anvil was then placed back into the peritoneal cavity, and the vagina closed laparoscopically. A 33-mm EEA stapler was passed into the rectum, and the spike was deployed, connected to the anvil and activated, creating an end-to-end anastomosis. Clamping the proximal colon with a bowel grasper, the anastomosis site was tested by filling the pelvis with lactated Ringer's solution and, under observation with the laparoscope, insufflating the rectum with air to check for leakage. The site was also tested by filling the rectum with indigo carmine and examining for leakage.[15]

All specimens were placed in endoscopic bags and removed vaginally or extracted from the abdomen prior to terminating the procedure. The port sites were irrigated and a full thickness closure was performed to possibly decrease trocar-site metastasis.

RESULTS

Included in this study were 32 patients who initially underwent laparoscopic evaluation. They were subsequently divided into 3 groups: (1) primary cytoreduction and interval debulking via laparoscopy, (2) diagnostic laparoscopy followed by primary cytoreduction and debulking via laparotomy, and (3) diagnostic laparoscopy and biopsies. Four patients underwent diagnostic laparoscopies and subsequent biopsies, limited surgical cytoreduction, or both of these. Two of these patients were diagnosed with gastrointestinal primary malignancies, and after diagnosis were excluded and referred to medical oncologists. The third patient in this group had primary peritoneal adenocarcinoma and underwent laparoscopy with pelvic washings, biopsies, and BSO. Because of her advanced age of 90 years and multiple medical comorbidities, the patient had preoperatively declined surgical debulking surgery. She underwent neoadjuvant chemotherapy and developed partial small bowel obstruction (SBO) 11 months later. She is alive with disease (AWD) at last follow-up. The fourth patient underwent laparoscopic-assisted vaginal hysterectomy (LAVH), BSO, and omentectomy and was diagnosed with benign disease, struma ovarii. None of these patients had intra- or postoperative complications.

Comparison of patient and tumor characteristics in the cytoreduction groups by laparoscopy and laparotomy shows no statistically significant differences in age, body mass index (BMI), or histologies **(Table 1)**.

Laparoscopic Primary Cytoreduction

Seventeen patients with abdominal, or pelvic masses, or both, suspicious for advanced ovarian cancer underwent total laparoscopic primary or interval cytoreduction **(Table 2)**. Overall extent of disease, assessed grossly, revealed 9 patients with upper abdominal disease and 8 patients with initial disease confined to the pelvis. All patients were surgically stage IIIA or greater, with 2 being stage IV.

Fifteen of the 17 patients were optimally cytoreduced to <0.5 cm of residual disease (88.2%), including 4 who were cytoreduced to microscopic disease. Four of the 15 patients who were optimally cytoreduced (#1, #9, #10, #13) had interval laparoscopic debulking, 2 patients to microscopic disease and 2 to <0.5 cm of residual disease. Two patients (#5, #15) were not optimally cytoreduced due to medical conditions. One patient was 85 years old with stage IV disease and bowel obstruction, and preoperatively declined aggressive surgical management. The other patient had multiple pulmonary embolisms diagnosed preoperatively and could not medically tolerate prolonged surgery. The operation was performed in this patient to confirm the diagnosis and remove a large symptomatic pelvic mass.

The operative procedures for each patient are listed in **Table 3**. The mean operative time (OR time) was 307.0

Table 1.
Patient Characteristics

Variables*	Group 1 Laparoscopy (n=17)	Group 2 Laparoscopy/ Laparotomy (n=11)	P Value*
Age (years)	60.9 ± 14.8	65.6 ± 11.4	NS
BMI (kg/m^2)	35.9 ± 17.9	30.6 ± 5.0	NS
Histologic type			NS
Serous	13 (76.5%)	7 (63.6%)	
Adenocarcinoma	2 (11.8%)	2 (18.2%)	
Endometrioid	1 (5.9%)	0	
Clear cell	1 (5.9%)	0	
Mixed	0	1 (9.1%)	
MMMT	0	1 (9.1%)	

*BMI=body mass index; MMMT=malignant mixed Müllerian tumor; NS = not significant.

Table 2.
Laparoscopy Group

Patient	Age	Stage, Grade, Pathology	Extent of Disease (Gross)	Extent of Debulking
1	46	IV grade 3 Adenocarcinoma ovarian	No gross disease	Optimal microscopic
2	44	IIIC Endometrioid adenocarcinoma ovarian	Pelvis	Optimal <0.5 cm
3	35	IIIC Papillary serous ovarian	Pelvis	Optimal <0.5 cm
4	63	IIIA Papillary serous ovarian	Pelvis	Optimal <0.5 cm
5	85	IV poorly differentiates Adenocarcinoma ovarian	Pelvis, Upper Abdomen	Suboptimal
6	76	IIIC Papillary serous primary peritoneal	Pelvis, Upper Abdomen	Optimal <0.5 cm
7	46	III grade 2 Papillary serous ovarian	Pelvis, Upper Abdomen	Optimal <0.5 cm
8	70	IIIC poorly differentiated Papillary serous ovarian	Pelvis, Upper Abdomen	Optimal <0.5 cm
9	80	IIIC Papillary serous ovarian fallopian tube	Pelvis	Optimal microscopic
10	60	IIIC Papillary serous, clear cell ovarian	Pelvis, Upper Abdomen	Optimal <0.5 cm
11	49	IIIC high grade Papillary serous ovarian	Pelvis, Upper Abdomen	Optimal <0.5 cm
12	72	IIIC grade 2 Papillary serous ovarian	Pelvis	Optimal <0.5 cm
13	79	IIIC poorly differentiated Papillary serous primary peritoneal	Pelvis, Upper Abdomen	Optimal <0.5 cm
14	67	IIIC Papillary serous ovarian Synchronous IB endometrial	Pelvis	Optimal <0.5 cm
15	49	IIIC Clear cell adenocarcinoma ovarian	Pelvis	Suboptimal
16	52	IIIC high grade Papillary serous ovarian	Pelvis, Upper Abdomen	Optimal microscopic
17	62	IIIC Papillary serous ovarian Synchronous IA endometrial	Pelvis, Upper Abdomen	Optimal microscopic

minutes with a range of 47 minutes to 510 minutes. Estimated blood loss (EBL) ranged from 10 mL to 500 mL with a mean of 247.6 mL. Overall mean hospital length of stay (LOS) was 6.1 days, with a range of 1 day to 24 days. Two patients had LOS of 16 days and 24 days. The prolonged LOS was secondary to other medical conditions and not due to the surgical procedures performed. One patient was septic preoperatively as a result of bowel obstruction from a tumor, and the other patient had pulmonary embolisms preoperatively that required medical therapy. With exclusion of these 2 patients in the assessment of LOS, the mean is 3.8 days, with a range of 1 day to 7 days.

One intraoperative complication occurred in patient #2 where the right ureter was transected. This patient had extensive endometriosis with distorted anatomy, limiting identification of the ureter. The injury was noted intraoperatively and repaired laparoscopically with a ureteroneocystotomy. Four patients had 6 postoperative complications. Patient #1 had symptomatic lymphocele that required paracentesis. Patients #8, #10, and #17 had postoperative ileuses that were managed conservatively. Patient #8 also had diverticular perforation 12 days after her initial operation and her first course of intravenous chemotherapy. She presented with rectal bleeding and had evidence of air and a pelvic collection on CT scan. Exploratory laparoscopy revealed perforated sigmoid diverticulum. The perforation and an incidental cystotomy were repaired, and a colostomy was placed.[15] She subsequently developed a vesicovagina fistula, which was repaired at the time of colostomy reversal 5 months later. Patient #17 had temporary urinary retention, which resolved with conservative prolonged bladder catheterization management.

In addition, there were 2 delayed postoperative complications that occurred more than 30 days after surgery, in patients #3 and #7. Patient #3 experienced vaginal cuff dehiscence with small bowel evisceration 4 months postoperatively, requiring immediate surgical repair. She had a subsequent recurrence at the vaginal cuff at 15 months postoperatively that was also surgically resected. She is AWD at 19-month follow-up. Patient #7 had a vesicovaginal fistula 3 months postoperatively that was successfully repaired laparoscopically after she completed intraperito-

Table 3.
Laparoscopy Group

Patient	Procedure	OR Time (min)	EBL (mL)	LOS (days)	Complications	Length of Follow-up (months)	Current Status*	Subsequent Surgeries
1	Washings, LAVH, LSO, omentectomy, PPALND, appendectomy, LOA, enterolysis	250	200	2	Lymphocele requiring paracentesis	26	DOD	Resection of brain metastasis at 12 months
	INTERVAL							
2	D+C hysteroscopy, washings, radical hysterectomy, BSO, PLND, omentectomy, treatment of endometriosis, ureteroneocystostomy, cystoscopy, sigmoidoscopy	510	300	4	Right ureteral transection repaired intraoperatively	23	NED	None
3	Radical hysterectomy, BSO, PLND, omentectomy	160	250	7	Vaginal cuff dehiscence (4 months postop)	22	AWD	None
4	Radical hysterectomy, BSO, PLDN, PALND biopsies, omentectomy, posterior culdectomy	205	300	2	None	45	NED	None
5	Laparoscopy, biopsies, infracolic omentectomy, minilaparotomy, transverse loop colostomy	47	50	16	None	1	DOD	None
	PALLIATIVE							
6	LAVH, BSO, omentectomy, tumor debulking, IP port placement	240	100	6	None	33	NED	Second look laparoscopy, appendectomy at 7 months
7	LAVH, RSO, tumor debulking, omentectomy, resection of distal left ureter, left ureteroneocystostomy, cystoscopy, IP port placement	420	250	5	Vesicovaginal fistula (3 months postop)	45	NED	Second look laparoscopy and repair of vesicovaginal fistula at 6 months, negative
8	Aspiration of ascites, radical hysterectomy, BSO, omentectomy, anterior and posterior culdectomy, debulking, cystoscopy with left ureteral stent, IP placement, sigmoidoscopy	420	400	7	Ileus	32	AWD	1. Laparoscopic evaluation of perforated sigmoid diverticula, colostomy, repair of incidental cystotomy
					Postoperative diverticular perforation			2. Laparotomy, reversal of colostomy, repair of rectovesical fistula at 17 months, disease positive

Table 3 continued on next page.

Table 3. (Continued)

Patient	Procedure	OR Time (min)	EBL (mL)	LOS (days)	Complications	Length of Follow-up (months)	Current Status*	Subsequent Surgeries
9	TLH, washings, bilateral PLND, LOA, colostomy reversal, omentectomy, cystoscopy	450	200	6	None	27	AWD	None
	INTERVAL							
10	Washings, LAVH, BSO, omentectomy, cystoscopy, sigmoidoscopy	450	500	6	Ileus	17	NED	None
	INTERVAL							
11	TLH, BSO, washings, anterior and posterior culdectomy, omentectomy, cystoscopy, sigmoidoscopy	385	300	3	None	10	AWD	Second look laparoscopy at 6 months, positive
12	Laparoscopy, washings, LOA, biopsies, infracolic omentectomy	139	10	1	None	13	NED	None
13	Laparoscopy, washings, LOA, biopsies, omentectomy, cystoscopy, sigmoidoscopy	265	100	1	None	5	AWD	None
	INTERVAL							
14	LAVH, BSO, PPALND, debulking, cystoscopy	135	150	3	None	10	NED	None
15	Laparoscopy, LSO, LOA, biopsies, cystoscopy	278	500	24	None	10	AWD	TAH, RSO, rectosigmoid resection, omentectomy, optimal cytoreduction at 4 months
16	Aspiration of ascites, biopsies, LAVH, BSO, LOA, CO2 laser debulking, omentectomy, cystoscopy, sigmoidoscopy	485	300	4	None	9	NED	None
17	D+C, radical LAVH, BSO, washings, low anterior rectosigmoid resection, LOA, biopsies, omentectomy, cystoscopy, sigmoidoscopy	410	300	5	Ileus Temporary urinary retention	7	NED	None

*LAVH=laparoscopic-assisted vaginal hysterectomy; TLH=total laparoscopic hysterectomy; D+C=dilatation and curettage; BSO=bilateral salpingo-oophorectomy; LOA=lysis of adhesions; PLND=pelvic lymph node dissection; PALND=paraaortic lymph node dissection; IP=intraperitoneal.

neal chemotherapy. At that time, the patient did not have any evidence of disease.

None of the patients had trocar complications including port-site metastases. Of these 17 patients, 9 are with no evidence of disease (NED), 6 are AWD, and 2 have died of disease (DOD). Mean follow-up time for these patients is 19.7 months, with a range of 1 month to 45 months.

Exploratory Laparoscopy and Open Primary Cytoreduction

Eleven patients were converted to laparotomy for cytoreduction after diagnostic laparoscopy due to the extent of disease at the discretion of the operating surgeon **(Table 4)**. Eight of these patients were optimally reduced to <1 cm of residual disease (72.7%). Specifically, 3 patients were reduced to between 5 mm and 1 cm, 4 to <0.5 cm, and 1 to microscopic disease. Patients #5, #6, and #7 had suboptimal debulking with BSO by laparotomy. Patients #5 and #7 received intravenous chemotherapy for 8 cycles and then underwent complete laparoscopic debulking at 8 months. Patient #5 underwent total laparoscopic hysterectomy (TLH), bilateral pelvic lymph node dissection, omentectomy, and colostomy reversal, and had no pathological disease. Patient #7 underwent TLH and right pelvic lymphadenectomy, and had microscopic disease. Patient #6 also received intravenous chemotherapy, and underwent secondary laparoscopic debulking including omentectomy for recurrence at 17 months.

Overall extent of disease for all patients revealed all but one patient with upper abdominal disease in addition to pelvic disease. All patients but one had IIIC disease; the other patient had IIIB. The operative procedures for each patient are listed in **Table 5**. Mean OR time was 241.3 minutes with a range of 142 minutes to 382 minutes. Estimated blood loss ranged from 300 mL to 1500 mL with a mean of 609 mL. Mean LOS was 8.2 days, with a range of 3 days to 14 days.

Two intraoperative complications occurred in this group. Cystotomy occurred in patient #5, which was repaired, with no further complications. Patient #11 had blood loss of 1.5L that required transfusion of 4 units PRBCs. Five patients had 7 postoperative complications. Patients #3, #5, and #7 had ileus, one managed with a nasogastric tube (NGT) and the other 2 with bowel rest. Patient #8 had a pleural effusion and a small wound separation. She was taken back to the operating room at an outside hospital 15 days postoperatively for suspected bowel perforation, after presenting to the emergency room with abdominal pain. Patients #5 and #9 had pulmonary emboli, with subsequent placement of an IVC filter in patient #9. None of the patients had trocar complications including port-site metastases. Of these 11 patients, 3 are NED, 5 are AWD, and 3 are DOD. Mean follow-up time for these patients is 25.8 months, with a range of 5 months to 50 months.

Comparison of the laparoscopic debulking group with the laparoscopy/laparotomy debulking group with respect to OR time, EBL, LOS, and complications shows statistically significant differences for EBL and LOS only, with the

Table 4.
Laparoscopy/Laparotomy Group

Patient	Age	Stage, Grade, Pathology*	Extent of Disease (Gross)	Extent of Debulking
1	65	IIIC Papillary serous ovarian	Pelvis, Upper Abdomen	Optimal <0.5 cm
2	51	IIIB Papillary serous ovarian	Pelvis, Upper Abdomen	Optimal <0.5 cm
3	70	IIIC Serous, mucinous, and endometrioid ovarian	Pelvis	Optimal microscopic
4	67	IIIC poorly differentiated Papillary serous ovarian	Pelvis, Upper Abdomen	Optimal <1 cm
5	85	IIIC Adenocarcinoma ovarian	Pelvis, Upper Abdomen	Suboptimal
6	54	IIIC Papillary serous ovarian	Pelvis, Upper Abdomen	Suboptimal
7	79	IIIC Papillary serous ovarian	Pelvis, Upper Abdomen	Suboptimal
8	71	IIIC grade 3 Serous and clear cell ovarian	Pelvis, Upper Abdomen	Optimal <1 cm
9	62	IIIC poorly differentiated Papillary serous ovarian	Pelvis, Upper Abdomen	Optimal <0.5 cm
10	48	IIIC high grade Papillary serous ovarian	Pelvis, Upper Abdomen	Optimal <0.5 cm
11	69	IIIC MMMT ovarian	Pelvis, Upper Abdomen	Suboptimal

*MMMT=malignant mixed Müllerian tumor.

Table 5.
Laparoscopy/Laparotomy Group

Patient	Procedure*	OR Time (min)	EBL* (mL)	LOS* (days)	Complications	Length of follow-up (months)	Current Status*	Subsequent Surgeries
1	D+C, diagnostic laparoscopy, aspiration of ascites, laparotomy, modified radical hysterectomy, BSO, anterior and posterior culdectomy, omentectomy, transverse colon resection and anastomosis, resection abdominal wall mass	325	500	9	None	27	DOD	Second-look laparoscopy positive at 9 months
2	Diagnostic laparoscopy, laparotomy, TAH, BSO, PPALND, resection diaphragm nodules	159	300	3	None	50	AWD	2 Laparotomies at other institution
3	Laparoscopy, washings, LOA, biopsies, laparotomy, TAH, BSO, PPALND, debulking, appendectomy, omentectomy, cholecystectomy, inguinal hernia repair, cystotomy repair	305	500	8	Ileus, managed with NGT	32	AWD	1. Laparoscopic secondary debulking at 24 months 2. Laparoscopic debulking, liver and colon resections at 32 months
4	Laparoscopy, biopsies, laparotomy, TAH, BSO, omentectomy, debulking, anterior culdectomy	146	700	10	None	34	AWD	1. Laparoscopic debulking at 6 months 2. Second look positive at 15 months 3. Third look positive at 25 months
5	Diagnostic laparoscopy, argon beam vaporization of peritoneal implants, laparotomy, LOA, biopsies, omentectomy, BSO, cystotomy repair, cystoscopy	244	300	9	Cystotomy Pulmonary embolism Ileus	30	AWD	1. Laparoscopic interval debulking at 8 months 2. Third look falsely negative at 20 months
6	Laparoscopy, hernia repair, biopsies, laparotomy, TAH, BSO, omentectomy	289	300	7	None	27	NED	Laparoscopic secondary debulking at 17 months
7	Laparoscopy, aspiration of ascites, biopsies, laparotomy, partial tumor debulking, BSO, omental biopsies, appendectomy, rectosigmoid resection, end-colostomy	170	300	10	Ileus	22	AWD	Laparoscopic interval debulking at 8 month, after neoadjuvant chemo

Table 5 continued on next page.

Table 5. (Continued)

Patient	Procedure*	OR Time (min)	EBL* (mL)	LOS* (days)	Complications	Length of follow-up (months)	Current Status*	Subsequent Surgeries
8	Laparoscopy, laparotomy, SCH, BSO, PLND, omentectomy, small bowel resection with side-to-side anastomosis	382	750	14	Pleural effusion, Small wound separation	5	DOD	Ex-Lap at 15 days at outside hospital for suspected bowel perforation
9	Laparoscopy, aspiration ascites, biopsies, laparotomy, SCH, BSO, omentectomy	180	400	10	Pulmonary embolism (IVC filter placed)	23	NED	None
10	D+C, laparoscopy, laparotomy, TAH, BSO, omentectomy, biopsies, cystoscopy	312	950	4	None	9	NED	None
11	Laparoscopy, aspiration ascites, laparotomy, TAH, BSO, omentectomy, supracolic omentectomy, radical debulking, posterior culdectomy, resection small and large bowel	142	1500	6	Intraoperative blood transfusion 4units	27	DOD	None

*TAH=total abdominal hysterectomy; SCH=supracervical hysterectomy; D+C=dilatation and curettage; BSO=bilateral salpingo-oophorectomy; LOA=lysis of adhesions; PLND=pelvic lymph node dissection; PALND=paraaortic lymph node dissection; PPALND=pelvic and paraaortic lymph node dissection

Table 6.
Surgical Outcomes

Variables	Group 1 Laparoscopy (n=17)	Group 2 Laparoscopy/Laparotomy (n=11)	P Value
Operative time (min)	307.0 ± 140.6	241.3 ± 85.3	NS
Estimated blood loss (mL)	247.6 ± 140.9	609.1 ± 31.1	.008
Hospital length of stay (days)			
All	6.1 ± 5.8	8.2 ± 3.1	.03
Excluding 2 from LSC* group	3.8 ± 2.5	8.2 ± 3.1	.003
Complications (%)			
Intraoperative	1 (5.9%)	2 (18.2%)	NS
Postoperative	6 (35.3%)	7 (63.6%)	NS

*LSC=Laparoscopy

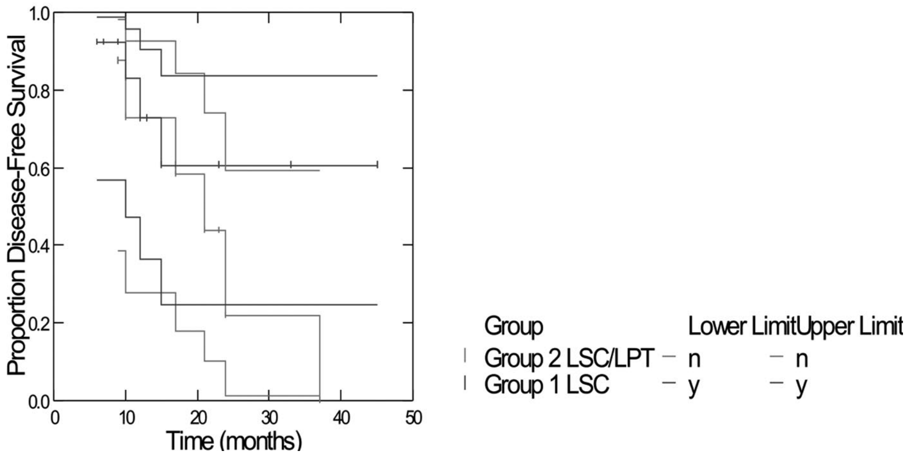

Figure 1. Recurrence

laparoscopy group having less EBL and LOS **(Table 6)**. Kaplan-Meier analysis of the median time to recurrence in the laparoscopy group was 31.7 months, and for the laparoscopy/laparotomy group 21.5 months **(Figure 1)**. Although not statistically significant (P=0.3), there appears to be a trend to greater time to recurrence in the laparoscopy group.

DISCUSSION

Applications of laparoscopy in advanced ovarian cancer have been described in triage for resectability, second-look assessment, and, in select cases, primary and secondary cytoreduction[b].[17,18] Thorough staging procedures, and optimal cytoreduction, provide both essential prognostic information and confer a survival benefit to those who have microscopic postoperative disease.[19,20] In situations where the ability to achieve an optimal cytoreduction is unlikely, neoadjuvant chemotherapy followed by interval cytoreduction may be appropriate.[3] Thus, laparoscopy offers a less morbid approach for determining which patients will likely have suboptimal cytoreduction at the time of primary surgery and hence benefit from neoadjuvant chemotherapy. Vergote et al[21] reported a series of 285 patients who underwent open laparoscopy to determine whether optimal debulking is possible. They found a 96% accuracy of prediction of tumor resectability. Fagotti[22] reported a subsequent study where patients underwent laparoscopy followed by immediate laparotomy to compare the intraoperative impression of resectability. They found that 87% of patients deemed resectable at laparoscopy were optimally debulked at laparotomy. Additionally, no cases of unresectable disease at laparoscopy were deemed resectable at subsequent laparotomy, yielding a negative predictive value of 100%. Angioli et al[23] reported a significant improvement in rate of optimal debulking from 61% to 96% with the use of open laparoscopy to determine suitability for cytoreductive surgery. The shorter recovery period associated with laparoscopic surgery compared with recovery for laparotomy also adds the benefit of a shorter interval to commencing chemotherapy. In fact, select patients may begin neoadjuvant chemotherapy the day after surgery.

Advances in laparoscopic instrumentation and technique have made a laparoscopic approach to surgical cytoreduction possible in select patients. The first report of successful laparoscopic cytoreduction in advanced ovarian cancer was described by Amara and Nezhat et al. [24] This case series included 5 patients who underwent successful total laparoscopic primary staging or secondary cytoreduction. All patients did well postoperatively. One patient subsequently expired due to recurrent disease, declining further intervention. The remaining literature on laparoscopic primary staging of advanced ovarian cancer involves the use of hand-assisted laparoscopic surgery (HALS). In this technique, a combination of operative laparoscopy and minilaparotomy is utilized. A hand is introduced intraperitoneally during laparoscopy to facilitate specimen extraction, tissue manipulation, and retention of tactile sensation. Krivak et al[18] reported the first case series of 25 patients who underwent HALS for the treatment of advanced ovarian cancer. They achieved optimal cytoreduction in 22/25 (88%) patients. Among the 9 with gross disease noted on initial inspection, 6 patients (3 stage II and 3 stage III) were successfully optimally debulked with hand-assisted laparoscopy. The remaining 3 patients required conversion to laparotomy: one had extensive upper abdominal disease, one required a modified posterior exenteration due to bulky pelvic disease, and the last had extensive abdominal adhesions. We report the largest case series utilizing laparoscopic surgery in assessing the resectability and its ability to debulk advanced ovarian, fallopian, and primary peritoneal cancers.

Laparoscopic debulking is feasible for upper abdominal diseases. This may include resection of bulky omental diseases and ablation of diaphragmatic implants. In our series of a primary laparoscopic cytoreduction group, 9 of 17 patients had upper abdominal disease in addition to pelvic involvement during laparoscopic evaluation. In the laparoscopy/laparotomy cytoreduction group, 10 of 11 patients had upper abdominal disease in addition to pelvic disease. In our series, other procedures including bowel resection, peritonectomy, diaphragm stripping, and ureteral resection were performed in addition to the standard staging/debulking surgery **(Tables 2 and 4)**. Despite the widespread extent of disease and radical nature of some procedures, the overall mean OR time of 307 minutes, length of hospitalization, and complication rate are comparable to those reported for open procedures.[25]

Several of our patients had intra- and postoperative complications that required surgical repair. These were performed laparoscopically, including a ureteroneocystostomy, repair of cystotomy, and repair of diverticular perforation. In addition, vaginal cuff dehiscence with small bowel evisceration at 4 months postoperatively in one of our patients was repaired laparoscopically. Nezhat et al[26] published in 1996 the first case series of 3 women with vaginal evisceration after total laparoscopic hysterectomy, 2 months to 5 months postoperatively. Two were repaired via the vaginal route, and the third laparoscopically. A vesicovaginal fistula in another patient was also successfully repaired laparoscopically. In 1994, a case report of laparoscopic repair of a vesicovaginal fistula was reported by Nezhat et al.[27]

In our series, we observed a longer recurrence-free interval in the group of patients who underwent laparoscopic debulking, 31.7 months versus 21.5 months **(Figure 1)**. Animal studies[28] have shown that surgery can promote metastasis and that invasiveness of the surgery is directly proportional to the degree of metastasis. Animal and human studies[29,30] have also shown that less postoperative immunosuppression occurs after laparoscopic surgery compared with laparotomy, and that immune homeostasis is restored earlier in patients who have undergone laparoscopic surgery. These immune factors, specifically cell-mediated immunity, are proposed to possibly influence cancer recurrence. This may explain the longer time to recurrence in our laparoscopy patients. In addition, the patients who had laparoscopic debulking were able to commence chemotherapy earlier than the patients who had laparotomy.

However, our study has its limitations. Our patients were not randomized to laparoscopic cytoreduction, but rather, selected for the procedure by the treating physician, which may account for the high rate of optimal debulking. Upon deciding that the patient was a candidate for cytoreductive surgery, the feasibility of laparoscopic cytoreduction was determined by the surgeon.

Additional concerns about the application of laparoscopy in advanced ovarian cancer include inadequate resection, carbon dioxide mediated dissemination, and port-site metastases. This series demonstrates that complete laparoscopic management of intestinal, ureteral,

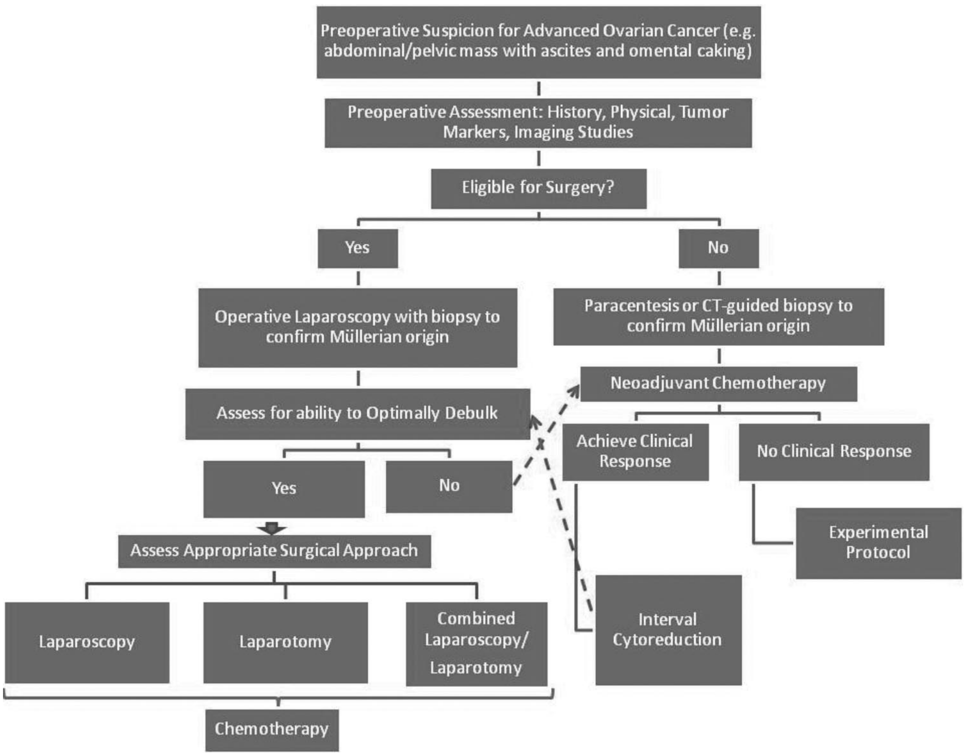

Figure 2. Clinical paradigm implemented in the present study.

or retroperitoneal involvement is possible with surgeons proficient in advanced laparoscopy, thus rendering the suggestion of inadequate resection moot. Carbon dioxide pneumoperitoneum has been suggested to lead to stimulation of ovarian cancer cell line growth. Smidt et al[31] reported that carbon dioxide promoted in vitro growth in the ovarian epithelial carcinoma cell line SKOV-3. However, few studies have examined the effect of carbon dioxide in humans. Abu-Rustum[32] compared the survival of 289 patients with persistent ovarian or primary peritoneal cancers who underwent second-look procedures either with laparoscopy or laparotomy. There were no differences in the overall survival. They concluded that carbon dioxide exerts no adverse effects on patient survival. In regards to the possibility of port-site metastases, such events have been reported in up to 16% of cases.[33] No port-site metastases have been noted in our patients to date. However, it has been suggested that a higher risk of port-site metastases occurs among patients with ascites.[34] Techniques that may lower the risk of port-site metastases include intact removal of the specimen in an endoscopic bag and layered closure of the trocar site.[33] These tactics were implemented into the surgical technique used in this study.

CONCLUSION

In summary, the role of laparoscopy in advanced ovarian, fallopian, and primary peritoneal cancers is (1) to rule out benign and non-Müllerian malignancies and (2) to assess the extent of resectability either by laparoscopy or laparotomy, and to assess the option for neoadjuvant chemotherapy followed by cytoreduction. Our cohort suggests that laparoscopic optimal cytoreduction in patients with advanced ovarian, fallopian, and primary peritoneal cancers is technically feasible with acceptable morbidity in a well-selected population either upfront or after neoadjuvant chemotherapy. Furthermore, there may be a greater time to recurrence in patients who have undergone laparoscopic cytoreduction. The clinical paradigm implemented in this study is illustrated in **Figure 2**. This algorithm may be used as a guide in future studies to evaluate the continuously expanding role of laparoscopy in patients with ovarian, fallopian, and primary peritoneal cancers.

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