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Laparoscopic technology for the treatment of endometrial cancer

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1. Introduction

Endometrial cancer remains the leading gynecologic cancer in the United States accounting for 32,800 new cases in 2004 with 5900 deaths [1]. Historically, treatment of endometrial cancer has consisted of surgery combined with radiation on chemotherapy for selected individuals with intermediate or high-risk disease based on surgical staging and histology. This has produced excellent outcomes, but may also result in significant patient morbidity. Laparoscopic techniques and equipment have matured over the last 15 years and are now widely used to treat many endometrial cancers and other gynecologic malignancies, thereby potentially reducing postoperative morbidity while producing outcomes equivalent to those of laparotomy. We will present an overview of the laparoscopic approach to endometrial cancer, focusing on outcomes, techniques and strategies to deal with some of the challenges encountered with this patient population.

2. Feasibility

Over 70% of new endometrial cancer cases are diagnosed in postmenopausal women. The disease is commonly associated with medical co-morbidities such as diabetes, hypertension and obesity [2]. As a result, many women affected by endometrial cancer are classified as high-risk surgical patients. For patients presenting with disease that appears to be confined to the uterus on initial examination, treatment consists of total hysterectomy, bilateral salpingo-oopherectomy, pelvic and para aortic lymphadenectomy.

The primary endpoints of studies on laparoscopic cancer staging are to demonstrate equivalence with laparotomy with respect to completeness of surgical staging while providing comparable survival rates. Table 1 lists the numerous published reports demonstrating the adequacy of laparoscopy for obtaining complete surgical staging specimens in comparison with laparotomy data, presented in Table 2. When compared to laparotomy, major advantages of the laparoscopic approach include faster healing, reduced postoperative ileus, less pain, fewer adhesions, less blood loss and a better view of upper abdominal organs, not to mention equal or better numbers of lymph nodes retrieved

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Table 1 Summary of publications on laparoscopy for endometrial cancer

	N	OR time	EBL	Nodes	Days	Convert
Boike et al. [27]	33	217	na	18.9	2.5	5.3%
Magrina et al. [28]	15	174	272	18.5	3.4	3.4%
Spirtos et al. [29]	13	na	na	28	2.4	0
Holub et al. [30]	11	153	130	na	4.7	na
Moore et al. [31]	80	170	223	20.1	2.5	1.3%
Gemignani et al. [25]	69	214	211	7	2.9	3.0%
Scribner et al. [26]	19	237	350	34	3.7	0
Eltabbakh et al. [16]	40	195	318	11.3	2.5	2.5%
Holub et al. [9]	177	163	211	16.8	3.9	3.4%
Langebrekke et al. [11]	27	143	na	6.8	4.3	3.7%
Eltabbakh [10]	100	na	200	13.5	2.0	1.0%
Litta et al. [32]	29	186	125	14.2	2.5	0
Occelli et al. [33]	69	165	na	15.8	4.0	1.2%
Kuoppala et al. [12]	40	145	171	11.1	2.7	0
Unweighted average		180.2		16.6	3.1	

and equal complication rates [3—5]. Lower morbidity leads to earlier recovery with shortened hospital stays.

The first laparoscopic staging study reported using the laparoscopically assisted vaginal hysterectomy technique with lymphadenectomy to treat clinical stage I endometrial cancer in 59 women [6]. They were unable to perform a laparoscopic lymphadenectomy in 6% of patients due to exposure or body habitus, and had a 5% complication rate. Many of the more recent studies show a progressive decrease in the complication rate and the percentage of patients unable to be staged laparoscopically (see Table 1).

There are three published prospective series comparing outcomes for laparoscopic versus staging via laparotomy for endometrial cancer, one of which is a prospective randomized clinical trial. In the randomized trial, 63 patients underwent laparoscopy and 59 patients underwent laparotomy for treatment [7]. Disease-free survival and overall survival were not significantly different in the two groups but the power of the study is relatively low due to the small size of the two treatment groups. In the two prospective series and in two additional case—control, retrospective series, disease-free survival is not statistically different for the laparoscopy versus laparotomy groups with 12—76 months of follow-up [8—12]. The patterns of recurrence are similar in all five reports and no port-site metastases were recorded. There is as yet no large, published, prospective, randomized trial comparing laparotomy with laparoscopy in the management of endometrial cancer. The Gynecologic Oncology Group is conducting an ongoing Phase III randomized trial comparing laparoscopic lymph node sampling with vaginal hysterectomy and bilateral salpingo-oopherectomy to laparotomy with lymph node sampling, abdominal hysterectomy and bilateral salpingo-oopherectomy in women with clinical stage I and stage IIA endometrial adenocarcinoma. The purpose of this study is to compare the incidence of surgical complications, morbidity and mortality, length of stay, quality of life and recur-

Table 2 Summary of publications on laparotomy for endometrial cancer

	N	OR time	EBL	Nodes	Days
Boike et al. [27]	37	194	na	18.7	5
Magrina et al. [28]	15	142	502	23.5	6.6
Spirtos et al. [29]	17	na	na	29	6.4
Holub et al. [30]	26	127	150	na	7.7
Moore et al. [31]	45	140	474	20.1	6.7
Gemignani et al. [25]	251	144	209	11.7	4.1
Scribner et al. [26]	17	157	344	6	6.7
Eltabbakh et al. [16]	86	na	250	30	5.2
Holub et al. [9]	44	115	255	10.5	5.0
Langebrekke et al. [11]	24	87	na	14.3	7.3
Eltabbakh [10]	40	na	303	5.3	6.5
Litta et al. [32]	30	152	153	13.4	6.4
Occelli et al. [33]	58	123	na	11.0	9.0
Kuoppala et al. [12]	40	96	238	7.3	7.6
Unweighted average		134.3		15.4	6.4

rence. This study is closed to accrual but the results will not be available for several years.

3. Management of comorbidities

Obesity is a common condition in women with endometrial cancer and this may complicate surgical treatment of the disease. Classifying obesity is most commonly done by calculating body mass index (BMI) and the severity of obesity is stratified according to the BMI. Obesity is commonly defined as a BMI of 30 or higher and extreme obesity as a BMI of 40 or higher. Table 3 demonstrates a classification system summarizing the guidelines published by the National Heart, Lung, and Blood Institute and the World Health Organization [13].

Waist circumference and waist/hip ratio (WHR) are newer methods for assessing the severity of a patient's obesity. Waist circumference has been positively correlated with abdominal fat content. However, when evaluating a patient for fat distribution the waist/hip ratio seems to be of greater relevance. A WHR of greater than 0.85 indicates android or abdominal obesity. These patients have adipose tissue that is mainly distributed over supraumbilical areas, trunk, and arms [14]. Use of the WHR is very helpful for planning laparoscopic surgery.

Induction, maintenance of sedation, and waking obese patients can be a challenge, not to mention post-operative risk of atelectasis, pneumonia, deep venous thrombosis, pulmonary embolus, ileus, and wound infection. These risks have also been shown to be increased with more extensive laparotomy procedures, often leading to slower return of bowel function, prolonged immobilization, and longer hospital stays [15].

Laparoscopy provides an alternative to laparotomy for a number of surgical procedures in obese patients that may result in fewer operative complications, shorter hospital stays, and more rapid recoveries. It has recently been shown that laparoscopy is feasible in the obese patient. Eltabbakh et al. reported on 42 women with clinical stage I endometrial cancer and a body mass index (BMI) of greater than 28.0 who were offered laparoscopic staging and compared to matched controls that underwent laparotomy [16]. The mean BMI was 35.8, but conversion to laparotomy occurred in only 7.5% of patients. There was no difference in surgical complications, total cost per case, postoperative pain perception or patient satisfaction. Women undergoing laparoscopy had a greater number of lymph nodes retrieved, less blood loss, decreased pain medication requirements, shorter hospital stays, but operative time was significantly longer.

Table 3 National heart, lung, and blood institute and the World Health organization classification system for obesity [13]

Description	Class	BMI
Normal weight		18.5–24.9
Overweight		25.0–29.9
Obesity	I	30.0–34.9
Obesity	II	35.0–39.9
Extreme obesity	III	≥40

Multiple studies suggest that laparoscopy in the elderly is also safe, feasible and has similar outcomes to the same procedures in a younger patient population. Scribner et al. evaluated elderly patients for their ability to withstand laparoscopic surgery in a retrospective study of 125 women with endometrial cancer [17]. 67 patients underwent planned laparoscopic staging and they were compared with 45 patients who underwent laparotomy and 13 patients who underwent vaginal hysterectomy. Of the patients who underwent laparoscopic staging, the procedure was completed in 77.6% of the patients but could not be performed in 10.4% secondary to obesity. When compared with the women who had staging at laparotomy, the elderly patients who underwent laparoscopy had significantly shorter hospital stays, fewer postoperative fevers, lower likelihood of postoperative ileus and fewer wound complications.

4. Other outcome measures

Quality of life outcome measures for obese patients were compared in a study of laparoscopic staging and laparotomy staging [16]. Patients in the two groups reported equal satisfaction. The laparoscopic staging group resumed full activities in 23 days on average, in comparison with 45 days for patients who underwent laparotomy. Return to work was correspondingly shorter in the laparoscopy group compared to the laparotomy group, with an average of 35 and 67 days, respectively.

The use of uterine manipulators during laparoscopic staging procedures has been postulated to increase the risk of positive intraperitoneal cytology by causing extrusion of endometrial tissue through patent Fallopian tubes. The incidence of this problem and the prognostic significance of positive peritoneal washings in this setting is not clear [18]. To address this concern, Eltabbakh et al. recently completed a prospective study that included 42 women undergoing laparoscopic surgery

for endometrial cancer. The authors found that intrauterine use of the Pelosi uterine manipulator did not increase the incidence of malignant peritoneal cytology among women with early stage endometrial cancer. No patients had positive washings after the insertion of the manipulator if the washings were initially negative [19]. Based on this single study, it is likely that laparoscopic surgery probably does not significantly increase the chance of positive peritoneal cytology. Until more data are available, it is prudent to seal the Fallopian tubes before the insertion of the uterine manipulator. This technique should minimize the risk of iatrogenic peritoneal spread.

5. Laparoscopic staging technique in endometrial cancer

Surgical approaches utilized in the laparoscopic staging of endometrial cancer include the laparoscopic-assisted vaginal hysterectomy (LAVH), total laparoscopic hysterectomy (TLH), and the use of robot-assisted laparoscopy using the daVinci® surgical system (Intuitive Surgical). The latter two approaches are favored at the author's institution. The patient is placed in the dorsal lithotomy position with arms tucked at the sides and using both padded stirrups and padded shoulder braces. Typically, four radial-dilating ports are placed. The radial dilating ports have an improved safety profile over older cutting-type ports [20]. After pneumoperitoneum is obtained, a uterine manipulator such as the ZUMI® (Cooper Surgical) is placed in conjunction with a Koh® colpotomy (Cooper Surgical) ring and a vaginal pneumo-occluder balloon. Peritoneal cytology is collected first. Performing the para-aortic node dissection early in the case is easiest because the bowel tends to be least likely to be distended with gas or to be edematous. Moreover, leaving the peritoneal attachment of the descending colon attached to the left pericolic gutter aids exposure of the para-aortic nodes. This attachment is divided later to expose the pelvic nodes, which would lessen the exposure of the para-aortic nodes if done first. Para-aortic and pelvic lymphadenectomy is performed utilizing a microprossessor-controlled, bipolar vessel sealer that can be used for grasping, traction, dissection, vessel sealing and cutting, thereby greatly reducing the number of times an instrument needs to be changed in order to complete the dissection. In the author's institution, we use the Gyrus Plasmakinetic System® cutting forceps for this function, although there are 3 commercial products available with similar features. These include the Gyrus product in addition to LigaSure (Valleylab) and EnSeal (SurgRx). All three are approved for sealing vessels up to 7 mm in diameter with burst strength exceeding 300 mm Hg and with 1—3 mm of lateral thermal spread. Once the lymphadenectomy is complete, the hysterectomy and bilateral salpingo-oophorectomy is completed laparoscopically using the microprocessor-controlled, bipolar vessel sealer to seal and divide the ovarian and uterine vessels. A colpotomy incision is made using a monopolar hook with electrosurgical cutting current onto the underlying colpotomy ring previously placed in the vagina. After the specimen is removed via the vagina, the vaginal cuff is sutured laparoscopically either with conventional suture or with a laparoscopic suturing device such as the Endo Stitch® (United States Surgical).

The daVinci® surgical system is an innovative technology that addresses many of the current limitations of laparoscopy, including development of a three-dimensional vision system for the surgeon, and laparoscopic instruments with a wrist-like mechanism allowing full replication of the range of motion of the surgeon's hand with an 8 mm instrument. The daVinci® surgical system was profiled in the lead article of this Surgery and Technology series and a recent publication from this institution demonstrated the feasibility of using robot-assisted laparoscopic staging for gynecologic malignancies [21,22].

6. Cost analysis and training

Laparoscopic staging procedures are complex and the time and effort necessary for a surgeon to master the necessary skills is substantial. A study evaluating the learning curve for laparoscopic endometrial cancer staging demonstrated that operating time and rate of complications fell as experience increased [23]. Moreover, the number of lymph nodes removed during the lymphadenectomy rose substantially as experience increased. Commitment on the part of surgeons and the health care systems in which they work

Table 4 Cost comparison for laparoscopy versus laparotomy for gynecologic cancer staging procedures

	Laparoscopy	Laparotomy
Spirtos et al. [24]	13,809	17,119
Gemignani et al. [25]	11,826	15,189
Scribner et al. [26]	5198	5331
Eltabbakh et al. [16]	13,003	11,878

Values expressed in US $.

is a necessary prelude to developing this expertise. As would be expected, treatment-related cost is increased early in the experience of a laparoscopic surgeon. Four authors have published data comparing cost for treatment of endometrial cancer by experienced surgeons [16,24—26]. In Table 4, data from the four series shows that laparoscopic staging was less expensive than laparotomy in three of the four studies. Given the need to optimize care within the budget constraints of health care systems around the world, careful, ongoing analysis of cost—benefit ratios including impact on quality of life and return to productive work will be necessary.

7. Conclusion

Laparoscopic staging of endometrial cancer has been shown to be feasible and safe. Multiple studies have demonstrated equivalence of laparoscopic staging in comparison to traditional laparotomy. A definitive, large, prospective, randomized clinical trial to confirm the smaller studies currently in the literature is in progress but results are likely to be several years in the future.

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