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Minimally Invasive Surgical Approaches for Patients with Endometrial Cancer

Michael Frumovitz, MD, MPH^{1,*}, Pedro Escobar, MD², and Pedro T. Ramirez, MD¹

¹Department of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, Houston, Texas

²Department of Obstetrics and Gynecology, The Cleveland Clinic, Cleveland, Ohio

Abstract

Over the past 10 years, multiple studies have shown that minimally invasive surgical approaches for the treatment of endometrial cancer reduce blood loss, length of hospital stay, and the incidence and severity of surgical complications compared to laparotomy. In addition, minimally invasive approaches result in better cosmesis and short-term patient quality of life. Although data from prospective studies have yet to mature, laparoscopic and open surgeries seem to be equivalent oncologically. In this article, we will review the current literature on traditional laparoscopy, robotically assisted laparoscopy, and single-port laparoscopy as surgical approaches for the treatment of endometrial cancer.

Keywords

endometrial cancer; robotics; minimally invasive; laparoscopy; hysterectomy; lymphadenectomy

Introduction

Although minimally invasive techniques have been adopted by virtually every surgical subspecialty, it was gynecologists who pioneered the laparoscopic approach to abdominal surgery, beginning in the 1960s. Although laparoscopy was originally used only as a diagnostic tool for direct visualization of pelvic anatomy, the 1970s brought improvement in optics and evolution of instrumentation such that minor pelvic procedures could be safely performed laparoscopically. Again, gynecologists were at the forefront of the expansion of laparoscopic approaches, performing bilateral tubal ligations and other limited pelvic surgeries with a minimally invasive approach. In the 1980s, urologists, not gynecologists, were the first to perform minimally invasive surgery for major oncologic procedures. In an effort to limit unnecessary laparotomies for patients with prostate and bladder cancers,

*Corresponding author: Michael Frumovitz, MD, MPH, Department of Gynecologic Oncology and Reproductive Medicine, CPB6.3244, Unit 1362, The University of Texas MD Anderson Cancer Center, 1155 Herman Pressler, Houston, TX 77030. Phone: (713) 592-9599. Fax: (713) 792-7586. mfrumovitz@mdanderson.org.

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urologists used the laparoscope to evaluate nodal and peritoneal spread prior to open exploration.

In the early 1990s, gynecologic oncologists further advanced laparoscopic techniques with reports in the literature of complex gynecologic oncology procedures, such as radical hysterectomy, performed laparoscopically. However, even though there were reports by individual surgeons of laparoscopic surgery for cervical, uterine, and ovarian cancer, gynecologic oncologists as a group were originally slow to integrate minimally invasive techniques into their surgical armamentarium, citing to explain the poor uptake of such techniques issues of increased operative time, concerns about whether open and laparoscopic surgery produced equivalent oncologic outcomes, and lack of technical skills, training, and equipment. By the late 2000s, however, with significant improvement in training and instrumentation and innovative adaptation of instruments and techniques, minimally invasive approaches for the treatment of women with all gynecologic malignancies had become ubiquitous in our field, and there were seemingly endless reports on laparoscopic surgery.

Although many of the recent adopters of minimally invasive surgery have adopted minimally invasive approaches because of the introduction of robotically assisted laparoscopic surgery at many centers, there are several good reasons for learning, mastering, and retaining the skills required to perform traditional or “straight stick” laparoscopic surgeries. First, an overwhelming majority of centers in both developed and developing countries lack robotic systems. Second, even at centers where robotic systems are available, the equipment may not be available until further into the future than we would like our patients with gynecologic cancers to wait, because surgeons from other services (in particular urology) have booked cases far in advance. In such circumstances, patients of gynecologic oncologists who rely solely on robotic technology to perform minimally invasive surgery might lose the opportunity for a minimally invasive approach. Finally, our role as gynecologic oncologists often requires us to assist colleagues who have patients with incidental findings of a gynecologic cancer or complex benign gynecologic pathology. Many times such cases were started with a traditional laparoscopic approach, and ideally we should be able to perform the necessary procedures without conversion to laparotomy.

Because robotic systems are a relatively recent addition and are available in only a minority of the hospitals worldwide, most of the literature on applications of minimally invasive surgical techniques to gynecologic malignancies involves traditional laparoscopy.

In this article, we will review the current literature regarding traditional laparoscopy, robotically assisted laparoscopy, and single-port laparoscopy for the treatment of endometrial cancer. Both retrospective and prospective studies show that laparoscopic surgery for the treatment of women with uterine cancers is technically feasible and early data from prospective studies suggest that such laparoscopic surgery is oncologically safe.

Traditional Laparoscopic Surgery

The introduction of minimally invasive surgery as a treatment option for women with endometrial cancer began in the early 1990s with multiple reports of laparoscopic-assisted vaginal hysterectomy and lymph node staging.¹ Even in its infancy, this approach was shown

both to be less expensive and to improve patient recovery compared to laparotomy.¹ As many women with endometrial cancer are overweight and as obesity is a known risk factor for intraoperative and postoperative morbidity, it was hypothesized that minimally invasive surgical approaches could reduce complications in women with endometrial cancer. In fact, in small prospective studies comparing laparoscopy to laparotomy in women with endometrial cancer, investigators noted that laparoscopy was associated with decreased blood loss and need for transfusions without an increase in the incidence of other intraoperative complications.² In addition, early and late postoperative complications were significantly more common for patients who underwent laparotomy than for those who underwent laparoscopy.³ Univariate analysis identified higher body mass index (BMI), comorbid medical conditions, older age, and surgical approach (laparotomy vs. laparoscopy) as significant risk factors for postoperative morbidity. On multivariate analysis, however, laparotomy was the only predictor of postoperative complications.³ As occurred in the evolution of laparoscopy for cervical cancer, however, widespread adoption of laparoscopy for uterine cancer did not become standard of care until after publication of studies establishing the oncologic safety of the procedure.

In 1996, the Gynecologic Oncology Group opened LAP2, a study designed and powered specifically to show non-inferiority of laparoscopy to laparotomy in terms of recurrence in patients with clinical stage I and IIA uterine cancer. Secondary endpoints were also included: perioperative adverse events, conversion to laparotomy, length of hospital stay, operative time, quality of life, sites of recurrence, and survival. A total of 2,616 patients were enrolled in this randomized controlled trial and assigned to laparoscopy or laparotomy in a 2:1 ratio. Upon completion of the study, 2,516 patients were evaluable.⁴ Disease-free and overall survival data have yet to mature; however, intraoperative and postoperative complications have been reported.

As expected, operative time was longer in the laparoscopy group (median, 204 minutes vs. 104 minutes), but length of hospital stay was shorter with laparoscopy (median, 3 days vs. 4 days). Only 52% of the patients who underwent laparoscopy stayed more than 2 days, compared to 94% of those who underwent laparotomy. There was no difference in the incidence of intraoperative complications between the two groups, although 26% of the patients in the laparoscopy group required conversion to laparotomy. In more than half (57%) of the patients requiring conversion, the reason for conversion was “poor exposure”. In an additional 16%, the reason was “cancer requiring laparotomy for resection”, and in another 11%, the reason was bleeding.⁴ Although higher BMI, older age, and presence of metastatic disease were significantly associated with conversion to laparotomy, no analysis of the “learning curve” was reported. This study began accrual in 1996 and closed in 2005, and we suspect that more conversions occurred in the early years of the study than in the later years of accrual. Grade 2 or more severe postoperative complications were significantly more common in the laparotomy group than in the laparoscopy group (21% vs. 14%). Overall, the laparoscopy patients had better quality of life than the laparotomy patients at 6 weeks after surgery; however, by 6 months, there was no statistically significant difference between the two groups.⁵

Two small randomized, controlled trials comparing laparoscopy to laparotomy in clinical stage I endometrial cancer have been published. The first included 122 patients,⁶ and the second included 78 patients.⁷ Because of the small numbers of patients, a meta-analysis of the two studies was performed.⁸ Laparoscopy had no significant effect on overall survival (odds ratio = 0.8, $p=0.7$) or disease-free survival (odds ratio = 0.76, $p=0.7$). However, as recurrence and death due to clinical stage I uterine cancer are exceedingly rare, data from these small studies, even when combined in a meta-analysis, cannot definitively answer the question whether laparoscopy is oncologically equivalent to traditional laparotomy in patients with clinical stage I disease.

One of the perceived limitations of laparoscopy for patients with endometrial cancer is that with laparoscopy it is difficult to adequately perform lymph node staging, particularly staging of the paraaortic nodes. In the LAP2 study, significantly fewer patients in the laparoscopy group than in the laparotomy group underwent paraaortic node dissection (94% vs. 97%, $p=0.002$).⁴ However, the previously mentioned meta-analysis of two studies in patients with clinical stage I endometrial cancer indicated that when paraaortic nodal dissections were undertaken, lymph node yields were equivalent for laparoscopy and laparotomy.⁸ Performing a transperitoneal paraaortic lymphadenectomy can be challenging, especially in obese endometrial cancer patients. Kohler et al.⁹ detailed their experience in 650 patients who underwent laparoscopic transperitoneal lymphadenectomy for gynecologic malignancies. Even these surgeons, who had exceptionally high surgical volume and extensive experience, reported that lymph node yields decreased as BMI increased (Table 1). Dowdy et al.¹⁰ used a laparoscopic extraperitoneal approach to lymphadenectomy in patients with uterine cancer. These authors found that they were actually able to remove more paraaortic nodes in morbidly obese women (BMI ≥ 35 kg/m²) with the laparoscopic approach than with open surgery (21.6 vs. 17.8).¹⁰ This finding is not surprising because with the laparoscopic extraperitoneal approach, the entire dissection is performed in the retroperitoneum, which eliminates the problem of obscuration of the aorta and vena cava by the bowel and omentum, a problem commonly encountered with the transperitoneal approach in obese and morbidly obese women.

Taken together, the studies published to date of traditional laparoscopic surgery for endometrial cancer indicate that this surgical approach is safe and feasible. Furthermore, it certainly reduces intraoperative complications, postoperative morbidity, and length of hospital stay while improving short-term quality of life. Although data from the LAP2 prospective study on oncologic equivalence has yet to mature, multiple retrospective studies and clinical experience strongly suggest that survival after the laparoscopic approach for endometrial cancer is similar to that of open surgery.

Robotically Assisted Laparoscopic Surgery

Robotically assisted laparoscopic surgery has been shown to provide benefits very similar to those of traditional laparoscopic surgery for standard simple hysterectomy, bilateral salpingo-oophorectomy, and disease staging. In the largest series to date of robotic surgery for endometrial cancer, Lowe et al.¹¹ retrospectively evaluated perioperative outcomes and learning-curve characteristics in a multiinstitutional experience with robotic hysterectomy

and surgical staging. Four hundred five patients were included; the mean age was 62.2 years, and the mean BMI was 32.4 kg/m². The mean operative time was 170.5 minutes, and the mean estimated blood loss was 87.5 mL. The mean lymph node count was 15.5, and the mean length of hospital stay for all patients was 1.8 days. An intraoperative complication occurred in 3.5% of the patients, and conversion to laparotomy occurred in 7%. The rate of postoperative complications was 14.6%.

Retrospective studies have compared the robotically assisted approach to traditional laparoscopy and laparotomy. Seamon et al.¹² compared 105 women who underwent robotic laparoscopic hysterectomy and lymphadenectomy for endometrial cancer to 76 women who underwent traditional laparoscopic hysterectomy and lymphadenectomy for endometrial cancer. The authors found that although the BMI was higher for the robotic-surgery group (34 kg/m² vs. 29 kg/m²), the patients treated with robotic surgery had less blood loss (100 vs. 250 ml), were less likely to require transfusions (3% of patients vs. 18%), and were less likely to require conversion to laparotomy (12% of patients vs. 26%). Boggess et al.¹³ compared the outcomes in women who underwent endometrial cancer staging by one of three surgical techniques. The study included 138 women who underwent laparotomy, 81 women who underwent traditional laparoscopy, and 103 women who underwent robotic surgery. The authors found that the robotic-surgery group had a higher BMI than the traditional laparoscopy group. The robotic-surgery group had the highest lymph node yield and the lowest length of hospital stay and estimated blood loss. Operative times were 213.4 minutes for the traditional laparoscopy group, 191.2 minutes for the robotic-surgery group, and 146.5 minutes for the laparotomy group. Postoperative complication rates were lower for patients treated with robotic surgery than for those treated with laparotomy (5.9% vs. 29.7%). Conversion rates for the robotic and traditional laparoscopic groups were similar. In both the Seamon et al. and Boggess et al. series, however, the authors were skilled in the performance of traditional laparoscopy before they performed their large series of robotically assisted cases. Whether the lower blood loss, fewer conversions to laparotomy, and faster operative times were a reflection of robotically assisted surgery or a manifestation of expert surgeons having already become experts in minimally invasive surgery via traditional laparoscopy prior to utilizing the robotic system cannot be determined from the data reported.

In an effort to synthesize the available literature on various surgical approaches for endometrial cancer, Gaia et al.¹⁴ performed a systematic review of all published comparative studies with at least 25 robotic-surgery cases. Their review included eight retrospective studies that included 589 robotic surgeries, 396 traditional laparoscopic surgeries, and 606 open surgeries. The authors found no differences in lymph node counts or the incidence of operative complications between the three approaches and no differences in rates of conversion to laparotomy between the two minimally invasive approaches. Operative times for the two minimally invasive approaches were similar; however, both types of minimally invasive surgery took longer than open surgery. The robotic approach was associated with less blood loss than traditional laparoscopy and laparotomy, but this did not translate into a difference in transfusion rates between the three approaches.¹⁴

One proposed advantage of robotically assisted laparoscopic surgery for endometrial cancer is that it may allow successful minimally invasive surgery in obese patients. Seamon et al.¹⁵ compared 109 patients with endometrial cancer with a mean BMI of 40 kg/m² who underwent robotic surgery to 191 similar patients who underwent laparotomy. The authors found no differences between robotic surgery and laparoscopy in the proportions of patients who underwent lymphadenectomy or the total lymph node count. Patients in the robotic-surgery group were less likely to require blood transfusions, had fewer complications and wound problems, and had a shorter length of hospital stay.¹⁵ The authors concluded that morbidly obese patients with endometrial cancer are good candidates for robotically assisted surgery.

The cost of the robotic system has continually been cited as a barrier adoption of this surgical approach. Robotic surgical systems have an initial cost of \$1.5–\$2 million with significant annual maintenance. In addition, robotic instruments have a finite number of uses (typically 10 cases) before they must be discarded and replaced. These cost concerns have led many to perform cost comparisons of robotic surgery to traditional laparoscopy and open surgery for endometrial cancer.

In 2008, Bell et al. compared laparotomy to traditional laparoscopy and robotically assisted surgery for the treatment of endometrial cancer.¹⁶ The authors found that laparotomy was more expensive than either minimally invasive approach largely due not to operating costs but rather increased hospital length of stay and longer return to normal activity. Although robotic surgery was \$672 more expensive than traditional laparoscopy, this amount did not reach statistical significance.¹⁶ Holtz et al.¹⁷ compared traditional laparoscopy to robotic surgery for women with endometrial cancer. They found robotically assisted surgery to be significantly more expensive than laparoscopy when assessing hospital costs (\$5084 vs. \$3615, $p=0.002$) and operative costs (\$3323 vs \$2029, $p<0.001$). This study did not assess cost of open surgery in these patients. Finally, Barnett et al.¹⁸ developed a decision model to compare costs of the three approaches. In their model, traditional laparoscopy was the least expensive with robotic surgery adding \$1300 to total cost and open surgery costing an additional \$2700 compared to traditional laparoscopy. The delayed return to normal activity was the main factor in the additional cost of laparotomy while the amount of disposable equipment (the 10 use robotic instruments) were the driving force for the added expense of robotic surgery.

In summary, for the treatment of endometrial cancer, traditional laparoscopy appears to be the most cost efficient. Although robotic surgery was more expensive than traditional laparoscopy, it was significantly less costly than open surgery. From a cost point of view, either of the minimally approaches would be preferred over laparotomy for these patients.

Single-Port Laparoscopic Surgery

Recently, an alternative to conventional laparoscopy or robotic surgery has been developed: single-port laparoscopic surgery, also known as laparoendoscopic single-site surgery (LESS). Single-port laparoscopy is an attempt to further enhance the cosmetic benefits of minimally invasive surgery while avoiding the potential morbidity associated with multiple incisions. While the single-port approach is innovative, it presents some unique challenges,

such as instrument crowding, loss of depth perception, and need for significant laparoscopic skills.

Single-port laparoscopy is not a new concept in gynecologic surgery. In the 1970s, Wheelless et al. reported on more than 3,600 women who underwent a rapid, inexpensive, and effective surgical sterilization performed with “single trocar laparoscopy”.¹⁹ Laparoscopic hysterectomy was first described in the early 1990’s. Despite these pioneer efforts, single-port laparoscopy did not become a standard surgical technique in gynecologic surgery. However, in the last decade, technology has advanced tremendously and surgeons have overcome some of the initial limitations of the single-port approach.

In 2009, Fader and Escobar²⁰ published the first report in the field of gynecologic oncology on a series of patients who underwent single-port surgery. This was a single-institution retrospective series of 13 women who underwent a variety of procedures performed with single-port surgery. The technique was feasible in this selected group of patients, and all procedures were successfully performed through a single incision with no postoperative complications. However, concerns were raised about the reproducibility of this new technique, about the learning curve for single-port surgery, and about applicability of the technique to more complex gynecologic oncology procedures such as radical hysterectomy and pelvic and paraaortic lymphadenectomy.

Limited data have been published to date about the clinical benefits of single-port surgery. Proposed advantages of single-port over conventional multi-port laparoscopy include better cosmesis because of a relatively hidden umbilical scar (scarless abdominal surgery) and improved postoperative pain. Recently, Kim et al.²¹ compared perioperative outcomes between single-port and conventional laparoscopic-assisted vaginal hysterectomy. The two surgical approaches were associated with similar operative times, estimated blood loss, drop in hemoglobin level between the preoperative level and postoperative day 1, and length of postoperative hospital stay. However, single-port laparoscopic-assisted vaginal hysterectomy was associated with reduced postoperative pain.

A growing body of literature in gynecologic oncology and other surgical specialties indicates that single-port laparoscopy is safe, effective, and may be an appropriate surgical modality for complex gynecologic oncology procedures. Fader et al. recently described their learning curve for single-port total laparoscopic hysterectomy and bilateral salpingo-oophorectomy.²² The mean time required to perform a Hasson open umbilical incision and single port insertion was 9.2 minutes for cases 1–10, 4.8 minutes for cases 11–20, and 4.3 minutes for cases 21–31 ($p<0.0001$). Operative times required for total laparoscopic hysterectomy and bilateral salpingo-oophorectomy decreased similarly for the 31 consecutive cases, although the most significant reductions in operative time were again observed between cases 1–10 (mean = 79.4 minutes) and cases 11–20 (mean = 56.8 minutes, $p=0.0002$). These preliminary results suggested a similar learning curve for conventional laparoscopy and single-port laparoscopy.²³

Lymphadenectomy (pelvic and paraaortic) is one of the cornerstone procedures in gynecologic oncology. Transumbilical transperitoneal laparoscopic lymphadenectomy

remains the most popular approach among gynecologic oncologists. The procedure and setup are essentially the same as for traditional laparoscopy and robotic surgery, although there is some variation in port placement depending on the intended level of aortic dissection. A recent report by Escobar et al.²⁴ described the technique and feasibility of single-port laparoscopic pelvic and paraaortic lymph node sampling or lymphadenectomy in gynecologic malignancies (endometrial, ovarian, and cervical cancer). The report included 21 patients; the median patient age was 58 years (range, 17–80 years), and the median patient BMI was 30 mg/kg² (range, 19–46 mg/kg²). Median overall operating time was 120 minutes (range, 60–185 minutes). Median pelvic and paraaortic lymph node counts were 14 (range, 7–19) and 6 (range, 2–14), respectively. In this preliminary report, the technique was feasible, and no morbidity was noted.

Whether single-port surgery or natural-orifice transluminal endoscopic surgery is the next revolution in minimally invasive surgery remains to be seen. The ability to detect disease at early stages will change not only indications for surgery but the approach to surgery. The goal of all gynecologic cancer surgeons should be to perform surgery in a way that minimizes disfigurement and psychological trauma and preserves function. Innovative instruments and methods, such as sentinel lymph node biopsy, single-port surgery, and robotic surgery, will continue to evolve as technology advances.

Currently, research and development in single-port robotics is ongoing. A single-port robotic platform may overcome technical limitations of nonrobotic single-site surgery (instrument crowding, lack of triangulation, and loss of depth perception/instability with current two-dimensional flexible optics); more importantly, it may play an essential role in the reproducibility and diffusion of the single-port approach. This new fusion technology of single-port laparoscopy and robotics may be the next step in the evolution of minimally invasive gynecologic oncology surgery.

Conclusions

Although prospective data on long-term oncologic outcomes of patients undergoing minimally invasive surgery for treatment of endometrial cancer have yet to mature, the vast majority of gynecologic oncologists believe that laparoscopic and open surgery are surgically equivalent. Multiple prospective and retrospective studies have shown that laparoscopic surgery is equal to open surgery in terms of adequacy of surgical resection and lymph node counts and have shown that laparoscopic surgery is associated with decreased risk of intraoperative and postoperative complications, which ultimately translates into improved short-term quality of life. As endometrial cancer patients are often morbidly obese, successful minimally invasive surgery will certainly reduce postoperative wound complications and most likely reduces other postoperative morbidities because of faster recovery and resumption of normal activities of daily living. For those reasons, we strongly advocate consideration of a minimally invasive approach for women with endometrial cancer.

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Table 1

Relationship between body mass index (BMI) and lymph node counts (from Kohler et al. [¹⁵])

BMI (kg/m ²)	No. of Patients	No. of Paraaortic Lymph Nodes Retrieved
<20	39	13.4
20–24.9	191	11.1
25–29.9	156	10.6
30	79	9.9

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