Role of Minimally Invasive Surgery in Gynecologic Cancers

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Abstract
The role of minimally invasive surgery in the management of gynecologic cancers continues to expand. Radical vaginal trachelectomy with laparoscopic pelvic lymphadenectomy has emerged as a safe, reasonable option for women with early-stage cervical cancer desiring fertility preservation. Similarly, laparoscopically assisted radical vaginal hysterectomy has been systematically described, is feasible, and can be offered to women with early-stage cervical cancer who do not desire future childbearing. In the treatment of early-stage endometrial cancer, the surgical approach of laparoscopic hysterectomy, peritoneal washings, and pelvic and para-aortic lymph node dissection, with or without an omentectomy, is being compared with the same surgery performed via laparotomy in the cooperative Gynecologic Oncology Group LAP 2 study, which has completed accrual, and appears to be a reasonable surgical option. In ovarian cancer, minimally invasive surgery has been incorporated to manage early-stage, advanced-stage, and recurrent disease, as well as second-look procedures. Hand-assisted laparoscopy has also recently been described in managing larger volume primary and recurrent gynecologic cancers. Extrapelvic laparoscopy for para-aortic and pelvic lymph node dissections has been shown to yield adequate nodal counts and to be safe and feasible in the management of gynecologic cancers. The Oncologist 2006;11:895–901

Introduction
Minimally invasive surgery has progressed in many surgical disciplines over the last three decades. In gynecologic oncology, the re-emergence of radical vaginal surgery and the ability to perform complete laparoscopic staging procedures have allowed minimally invasive surgery to serve a greater role in the treatment of women with gynecologic cancers.
Cervical Cancer

Dargent [1] was the first to report on the radical vaginal trachelectomy with pelvic lymphadenectomy in the treatment of early-stage cervical carcinoma with preservation of the uterus in order to maintain fertility. This procedure involves a laparoscopic pelvic lymph node dissection and then, via a vaginal approach, the surgical resection of the upper vagina, the affected cervix with an adequate margin, and the cardinal and uterosacral ligaments. This is then followed by an endocervical and endometrial sampling above the radical trachelectomy specimen with intraoperative pathologic evaluation of surgical margins.

Follow-up showed an acceptable rate of recurrence comparable with that of radical hysterectomy. Dargent et al. [2] reported on 96 patients, with a median follow-up of 76 months, and noted recurrence in four patients (4.1%). Plante et al. [3], who evaluated all published series, reported a recurrence rate of 4.2% of a total of 319 patients, with a median follow-up of 44 months. In the Dargent et al. [2] study, recurrence was more frequent with a cervical lesion >2 cm \( (p = .002) \) and with a depth of stromal invasion >10 mm \( (p = .001) \).

Guidelines have not been universally established in determining eligibility for radical vaginal trachelectomy [4]. At our institution, eligibility for radical vaginal trachelectomy requires the patient be of reproductive age, desires fertility, and preferably has a cervical lesion ≤2 cm. Lymphovascular space involvement and histology are not absolute contraindications to performing this procedure; however, all cases are presented at our weekly tumor board to ensure the suitability of the procedure for each patient.

Roy and colleagues [5] retrospectively analyzed their first 52 cases of patients undergoing laparoscopic pelvic lymphadenectomy to compare safety, efficacy, and the benefits of vaginal radical hysterectomy and abdominal radical hysterectomy. They identified 25 vaginal radical hysterectomy and 27 abdominal radical hysterectomy patients with a mean follow-up of 27 months. Estimated blood loss (EBL), operative time, incidence of blood transfusion, and postoperative stay were comparable between the two surgical approaches. The authors concluded that both procedures were equally safe and efficacious, with the main advantage of vaginal radical hysterectomy being learning the skills applicable to perform a radical vaginal trachelectomy to offer fertility preservation to patients with early-stage cervical cancer [5]. Recently, Plante et al. [6] reported on pregnancy outcomes for 72 patients who had a vaginal radical trachelectomy performed. Thirty-one women (43%) had a total of 50 pregnancies. Thirty-six of these pregnancies (72%) resulted in third-trimester deliveries. There were eight (16%) first-trimester miscarriages, two (4%) second-trimester miscarriages, and two (4%) therapeutic abortions. Two patients were pregnant at the time of publication [6].

With acceptable recurrence rates and multiple successful pregnancies reported, radical vaginal trachelectomy is emerging as an acceptable alternative for treating patients with early-stage cervical cancer who desire fertility preservation [7–11].

In 1990, Canis and colleagues [12] first described the laparoscopic radical hysterectomy. By 1996, Spirtos et al. [13] systematically outlined the technique for what was classified as the laparoscopic type III radical hysterectomy with aortic and pelvic lymphadenectomy. The technique begins with a laparoscopic bilateral aortic and pelvic lymphadenectomy. Paravesical and pararectal spaces are then created to facilitate ureteral dissection and ligation of the uterine artery at its origin. Careful development of the vesicouterine and rectovaginal spaces allows for parametrial resection and resection of the uterosacral ligaments. Finally, the upper vagina is resected to complete the procedure [13].

In 2002, Spirtos et al. [14] described 78 patients with early-stage cervical cancer who had undergone this procedure. Ninety-four percent of the procedures were completed laparoscopically. The average operative time was 205 minutes. The average EBL was 225 ml, with only one patient requiring a blood transfusion. There were three cystotomies and one ureterovaginal fistula noted. The average lymph node count was 34, with 11.5% of patients having positive nodes. Three patients had close or positive surgical margins, and 5.1% of patients recurred within at least a 3-year follow-up [14]. In a similar fashion, Pomel and colleagues [15] evaluated 50 patients with stage IA2 and IB1 cervical cancers treated by laparoscopic radical hysterectomy and noted a 96% 5-year survival rate.

Abu-Rustum et al. [16] compared patients undergoing laparoscopic radical hysterectomy with pelvic lymphadenectomy with patients with abdominal radical hysterectomy with pelvic lymph node dissection. The laparoscopic approach for radical hysterectomy was safe, feasible, and associated with low morbidity. Both patient groups had similar age, body mass index (BMI), stage, histology, and mean pelvic lymph node counts. However, the median operative time was longer for the laparoscopic approach, while the hospital stay and EBL were significantly less in the laparoscopic group [16].

Thus, while abdominal radical hysterectomy remains the standard of care for early-stage cervical cancer, laparoscopic radical hysterectomy appears to be a safe, reasonable alternative.
The issue of laparoscopy in the management of locally advanced cervical cancer has been addressed by several authors. In particular, researchers from Korea, Chung and colleagues [17], evaluated the feasibility and safety of pre-treatment laparoscopic surgical staging in the treatment of locally advanced cervical cancer. The authors contended that pretreatment laparoscopy is the best guideline for individualized concurrent chemoradiation. When compared with magnetic resonance imaging, laparoscopic surgical staging was superior in detecting microscopic lymph node metastases. The 2-year disease-free survival rate was 89.7%, and there were three patients (6.8%) who recurred [17].

Marnitz and collaborators [18] from Germany investigated 84 patients with locally advanced cervical cancer who were selected for laparoscopic staging for primary chemoradiation. In that study, they found that removal of more than five pelvic and/or more than five para-aortic lymph nodes was associated with significantly longer overall survival. The authors concluded that debulking of tumor-involved lymph nodes should be performed prior to primary chemoradiation in patients with locally advanced cervical cancer [18].

However, Kupets et al. [19], based on their statistical analysis, asserted that 1% of stage IB, 2% of stage IIB, and 4% of stage IIB patients would benefit from the debulking of pelvic lymph nodes. They also concluded that select patients with small central tumor burden and low-volume nodal involvement, but with tumors >2 cm would benefit from debulking [19].

Operative laparoscopy has also been used as a means of determining a patient’s eligibility for pelvic exenteration for recurrent cervical cancer. It has been proven to be a valuable step in the workup and management of patients with locally recurrent cervical cancer.

Plante and Roy [20] found that operative laparoscopy helps to prevent unnecessary laparotomies, can reduce morbidity, and leads to a shorter postoperative hospital stay. In their series, 9 of 12 patients with recurrent cervical cancer had positive para-aortic lymph nodes. Eight of the nine avoided an unnecessary exenterative procedure, and one patient had a palliative exenteration.

Kohler and colleagues [21] evaluated 41 consecutive patients undergoing exploratory laparoscopy to determine eligibility for exenteration. Almost half (48.7%) of the patients avoided unnecessary exenteration for unresectable disease or intra-abdominal spread of disease. Similarly, Dargent et al. [22] in an editorial suggested that laparoscopic pelvic lymphadenectomies can facilitate detecting patients who are the best candidates for pelvic exenteration.

**ENDOMETRIAL CANCER**

The Gynecologic Oncology Group (GOG) LAP 2 trial is a large, prospective, randomized trial designed to determine equivalency in early-stage endometrial cancer outcomes of laparoscopically assisted vaginal hysterectomy/bilateral salpingo-oophorectomy (LAVH/BSO) with surgical staging when compared with traditional laparotomy with a total abdominal hysterectomy (TAH)/BSO with surgical staging. The accrual goal was achieved in September 2005. While awaiting the results of this study, there are other studies that demonstrate that a minimally invasive approach in the management of early-stage endometrial cancer is safe, feasible, can result in lower hospital costs, and can yield results comparable with those of an abdominal approach.

The laparoscopic staging procedure includes a laparoscopically assisted or total vaginal hysterectomy with pelvic and para-aortic lymph node dissection, peritoneal washings, and an omentectomy in patients with serous malignancies of the endometrium. Childers and Surwit [23] and Abu-Rustum et al. [24] have described these procedures in the management of endometrial carcinoma. Gemignani et al. [25] looked at cost-effectiveness in comparing LAVH with TAH and showed that LAVH was associated with a shorter hospital stay, fewer complications, and lower overall hospital charges. Spirtos et al. [26] also noted lower hospital costs when patients with endometrial cancer were managed via a laparoscopic approach.

In other studies, the laparoscopic approach for endometrial cancer staging has been compared with exploratory laparotomy. In Germany, Malur and colleagues [27] prospectively compared 37 patients treated by a laparoscopic and vaginal approach with 33 patients who were treated by conventional laparotomy. Patients underwent pelvic and para-aortic lymph node dissection unless their tumor invaded less than one third of the myometrium and was well differentiated. There was no difference between the two groups with regard to the mean Quetelet index, number of lymph nodes, and mean operating time. The mean follow-up for the laparoscopy group was 16.5 months, compared with 21.6 months for the laparotomy group. The recurrence-free survival rate was not significantly different between the laparoscopy (97.3%) and laparotomy (93.3%) groups. Similarly, the overall survival rate was 83.9% in the laparoscopic group and 90.9% in the laparotomy group [27].

Tozzi et al. [28] were the first to report their survival outcomes from a randomized, prospective clinical trial analyzing laparoscopy versus laparotomy in endometrial cancer. At a median follow-up of 44 months, the authors reported that patients with an International Federation of Gynecology and Obstetrics stage I endometrial cancer had disease-free survival rates of 91.2% (in the laparoscopic group) and...
Ovarian Cancer
Minimally invasive surgery for patients with ovarian cancer can be incorporated in different ways depending on the stage of disease and surgical goals of the procedure. In advanced-stage disease, laparoscopy in general can be used to confirm diagnosis and determine resectability. In early-stage disease, patients can be comprehensively staged via the laparoscopic approach. The laparoscopic second-look procedure is a reasonable approach to assessing disease status at completion of adjuvant chemotherapy in selected patients.

Ben David et al. [31] evaluated 18 patients with advanced-stage ovarian cancer initially with laparoscopy. Seven of the patients (40%) were found to have unresectable disease, had a biopsy performed, and were spared a laparotomy. The 11 remaining patients had a complete tumor debulking procedure performed after laparoscopic evaluation.

Chi et al. [32] evaluated 20 patients undergoing laparoscopic staging and 30 patients having staging via laparotomy for apparent stage I ovarian or fallopian tube cancers. All patients were comprehensively staged with an LAVH or TAH, BSO, bilateral pelvic and para-aortic lymphadenectomy, omentectomy, and peritoneal washings and biopsies. There were no differences in patient age, BMI, omental size, and number of lymph nodes removed between the two groups. The EBL was lower and hospital stay was shorter in the laparoscopy group; however, operating time was longer. There were no conversions to laparotomy in the laparoscopic group. The authors concluded that patients with apparent stage I ovarian and fallopian tube cancers can safely and adequately undergo laparoscopic surgical staging [32].

Unfortunately, incompletely staged ovarian carcinoma is frequently encountered when gynecologists or general surgeons operate on a patient with an adnexal mass and histologic evaluation subsequently reveals an ovarian cancer. Leblanc and colleagues [33] reported their 10-year experience with laparoscopic staging of incompletely staged invasive adnexal tumors. Forty-two patients were restaged after their initial surgery. All procedures were completed laparoscopically, except for one, because of adhesions. The average hospital stay was 3.1 days, and the average operative time was 238 minutes. Eight patients (19%) were upstaged by laparoscopy and given chemotherapy. After a 54-month median follow-up, 3 of the 34 remaining patients diagnosed as stage IA, grade 1 and 2 (6.4%), recurred and died [33]. Husain and her colleagues [34] at the Memorial Sloan-Kettering Cancer Center reported their experience with second-look surgical assessment. They found it to be safe, accurate, and with a low incidence of complications, particularly in the group of patients who had already undergone prior abdominal surgery. They found that the rates of negative evaluations and recurrence rates were comparable between patients undergoing laparoscopy and those undergoing laparotomy [34].

Hand-Assisted Laparoscopic Surgery
Spannuth and colleagues [35] at the University of Alabama, Birmingham, described their initial experience in comparing hand-assisted laparoscopic surgery (HALS) with conventional laparotomy in evaluating pelvic masses. They analyzed 29 patients who were treated by HALS and 41 who were managed with exploratory laparotomy. The two groups had a similar age (48 versus 49 years, respectively), BMI (29.1 versus 29.8 kg/m², respectively), and pelvic mass size (11.0 versus 11.3 cm, respectively). HALS was associated with a lower EBL, shorter hospital stay, and fewer postoperative complications. In this preliminary study, the authors concluded that HALS was a safe and a feasible alternative in the surgical management of pelvic masses [35].
In terms of the management of ovarian cancer, Krivak et al. [36] evaluated 25 patients initially with HALS. Six patients were noted to have advanced-stage disease. Nineteen patients had apparent early-stage disease, five of whom were upstaged by nodal involvement, three of whom were upstaged by disease spread to other pelvic structures, and two of whom were upstaged with microscopic disease on the omentum. Twenty-two patients (88%) had their procedure completed by HALS. Three required laparotomy to complete their cytoreductive surgery. The mean hospital stay was 1.8 days for the patients undergoing HALS. The operating times were in the range of 81–365 minutes. Krivak et al. [36] concluded that HALS may be incorporated into the initial management of ovarian carcinoma.

HALS has also been used to facilitate the resection of recurrent disease in patients with ovarian carcinoma. The ideal surgical candidate for this procedure is a platinum-sensitive patient who has an isolated area of recurrence that appears surgically resectable on imaging studies. Chi et al. [37] described the technique of hand-assisted laparoscopic splenectomy in five patients in whom the spleen was the only site of recurrent disease; the procedures were safely performed without complications.

**Laparoscopic Extraperitoneal Lymphadenectomy**

The extraperitoneal laparoscopic approach for para-aortic lymph node dissection was first described by Vasilev and McGonigle [38]. Several authors have outlined their technique and assessed its safety and feasibility [39–41]. Generally, after the laparoscope is placed through the umbilicus and the abdomen is insufflated, an incision is made 2 cm medial to the anterior superior iliac spine along the McBurney line and carried down to the fascia. Blunt dissection is carried to the peritoneum. Once the retroperitoneum is identified and entered, dissection is performed to open the area above the psoas muscle [39]. A trocar is then placed in the retroperitoneum, CO2 gas is removed from the intraperitoneum, and the retroperitoneal space is insufflated to allow for para-aortic and common pelvic lymph node dissection.

Mehra et al. [39] found that this approach identifies those cervical and endometrial cancers requiring extended-field radiation as part of their adjuvant therapy and can be used efficaciously in staging early ovarian cancers to determine the need for adjuvant chemotherapy.

Burnett et al. [40] performed the procedure on 46 patients, with a median lymph node yield of 14 (range, 0–60). Only two patients had a disruption of their peritoneum such that transperitoneal lymphadenectomy had to be performed.

In the largest series, Sonoda et al. [41] identified 111 patients who underwent an infrarenal aortic and common iliac lymph node dissection for bulky or locally advanced cervical cancer. The mean node count was 19 (±12). The mean postoperative stay was 2 days. Preventive peritoneal marsupialization was performed in the final 37 patients to prevent lymphocele formation. The authors concluded that this procedure was feasible and helped to tailor patients to receive external radiation therapy [41].

**Important Considerations in Minimally Invasive Surgery**

The role of minimally invasive surgery continues to develop and provide less invasive treatment alternatives to patients with gynecologic cancers. Operating times intuitively have improved with greater surgical experience.

In addition, adequacy of the procedure being performed needs to be assured. Comparison of recurrence rates and survival provide some insight. Schlaerth et al. [42] evaluated women with cervical cancer undergoing laparoscopic retroperitoneal lymphadenectomy followed by immediate laparotomy to assess the adequacy of lymph node removal. In that study, the investigators reported that laparoscopic aortic lymph node sampling could be performed safely and adequately. Laparoscopic pelvic lymphadenectomy was noted at the time of laparotomy to have residual tissue lateral to the common iliac vessel and distal external iliac vessels in 15% of patients. Because none of the laparoscopic surgeons were aware of the presence of this residual tissue, awareness should allow for correction of this potential surgical shortcoming [42].

Also, there was concern that tumor implantation might be more commonly associated with laparoscopy. Abu-Rustum and colleagues [43] noted that s.c. tumor implantation is not limited to laparoscopy. In a 12-year period, 1,288 patients had 1,335 transperitoneal laparoscopies. Laparoscopy-related s.c. tumor implantation was noted to be rare (0.97%) in women undergoing transperitoneal laparoscopy with malignant disease. Patients with advanced intra-abdominal or pelvic metastatic disease and progressive carcinomatosis appeared at greatest risk. Abu-Rustum et al. [43] concluded that the risk for s.c. tumor implantation should not preclude laparoscopy in women with gynecologic malignancies managed by gynecologic oncologists.

Frequently, obesity can present a challenge in managing early endometrial cancer via a minimally invasive approach. Eltabkakh and colleagues [44] prospectively studied 42 obese women with clinical stage I endometrial cancer over a 2-year period. Forty patients were offered laparoscopic surgery. The procedure was converted to open laparotomy in three (7.5%) of the patients. Compared with
historical controls for laparotomy, obese women treated by a laparoscopic approach had more pelvic lymph nodes removed, had a smaller decrease in postoperative hematocrit, required less pain medication, and had a shorter hospital stay. From these results, Eltabbakh et al. [44] concluded that obese patients can be safely managed with a minimally invasive approach, with excellent surgical outcome.

Holub et al. [45] also reported on peri- and postoperative outcomes in obese versus nonobese patients using a minimally invasive surgical approach. They reported no statistical difference in operating time, lymph node counts, blood loss, or hospital stay. However, in a group of 33 obese and 32 nonobese patients, there was a higher number of major complications in obese patients than in nonobese patients (eight vs. five). In the obese subgroup, complications included pulmonary microembolism, injury to the epigastric artery, injury to the bladder, uncontrolled bleeding, and conversion to laparotomy. Holub et al. [45] concluded that the expected outcome should be balanced with risks, but emphasized that laparoscopic surgery in obese women, much like in non-obese women, is safe, feasible, and should be considered in patients with endometrial cancer.

Injuries to the bladder and epigastric artery, as reported by Holub et al. [45], highlight the difficulties of trocar placement in patients who are morbidly obese. Childers and colleagues [46] also found that, in patients with endometrial cancer, obesity was the limiting factor in performing lymphadenectomies. Eltabbakh and colleagues [44] were unable to perform para-aortic lymph node samplings in two patients because of poor visualization secondary to obesity. However, they did report higher pelvic lymph node yields laparoscopically when compared with laparotomy. Finally, assessment of complications and conversion rate need to be addressed as the role of minimally invasive surgery increases in the management of gynecologic cancers. In evaluating their initial 10-year experience with laparoscopy, Chi and colleagues [47] noted a low complication rate (2.5% grade 3–5) and a low conversion rate of 7%. They identified older age, malignancy, previous radiation, and previous abdominal surgery as significant risk factors for complications or conversion to laparotomy, which should help guide patient selection and surgical planning [47].

**CONCLUSION**

Minimally invasive surgery continues to develop and become a suitable alternative in the surgical management of gynecologic malignancies. Intuitively, patient satisfaction has helped to drive the discipline of minimally invasive surgery. Smaller incisions, less postoperative pain, and shorter hospital stays are welcomed by women suffering from gynecologic cancers. More importantly, though, the science has kept up with innovative minimally invasive techniques [42]. Minimally invasive surgery has been shown to be safe and feasible while treating patients with the same efficacy as traditional open procedures. This, above all else, will help guarantee minimally invasive surgery as an acceptable approach in treating gynecologic malignancies.

**DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST**

The authors indicate no potential conflicts of interest.

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