

The Role of Laparoscopy in Gynecologic Oncology

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ABSTRACT

Laparoscopy is a surgical procedure which has been used in gynecologic cancer since 1994. With technology progressing during years, there are so many kinds of minimally invasive surgeries in gynecologic malignancies. Regarding the importance of overall survival and progression of free survival in cancerous patients, we should consider this type of surgery very wisely not to compromise patient's prognosis. Considering all the points above, a review was performed to study the role of laparoscopy in gynecologic oncology including endometrial and cervical cancer. It can be concluded that laparoscopy is not safe in a disease with high risk of tumor spread. Also a good prognosis of cancer patients should not be jeopardized by doing incomplete laparoscopic surgery.

Keywords: Disease free survival, Laparoscopy, Prognosis

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Introduction

Laparoscopy was used for a second-look assessment in ovarian cancer patients back in the 1970s. However, it was only with the advent of new developments in equipment in the late 1980s and early 1990s, along with the vision of pioneers in laparoscopic surgery that made operative laparoscopy in gynecologic oncology feasible. Laparoscopy has multiple benefits in cancer patients, including:

1. Image magnification to visualize metastatic or recurrent disease in the deep pelvis, anterior abdominal wall and upper abdomen, improved dissection, and fewer injuries in challenging areas such as the retro peritoneum.
2. Decreased bleeding from small vessels due to the pressure from pneumoperitoneum, shorter hospital stay, and faster recovery.
3. Less postoperative complications such as ileus, small bowel obstruction, wound infection and separation, and thromboembolic events.
4. Postoperative chemotherapy or radiation can be initiated earlier and radiation complications from bowel adhesions are minimized.
5. No need for an incisional hernia repair.

However, in cancer patients regardless of smaller incision and less postoperative pain, long-term and optimal surgical outcomes about the overall survival and progression-free survival (PFS) should be considered as an important issue. Moreover, if laparoscopy surgery has

a comparable overall survival and PFS to laparotomy surgery, laparoscopy is a preferable technique.

Pitfalls of Laparoscopic Management in Gynecologic Cancers

There are three main pitfalls regarding laparoscopic management in gynecologic cancers, including port site metastasis, incomplete surgical staging, and more ovarian cyst/tumor rupture. In this study, we will discuss the role of laparoscopy in cervical and endometrial cancer.

Laparoscopy in Cervical Cancer

Laparoscopy has been used in the management of both early and advanced stages of cervical cancer in a number of different applications. In early cervical cancer, laparoscopy has been utilized to perform pelvic and para-aortic lymphadenectomy along with a laparoscopic-assisted radical vaginal hysterectomy or vaginal trachelectomy and total laparoscopic radical hysterectomy or a radical trachelectomy. In advanced stages, pretreatment surgical staging with pelvic and para-aortic lymphadenectomy has become a useful way to direct treatment. Although the data are limited in these clinical scenarios, laparoscopy has also been applied prior to a pelvic exenteration, laparoscopic ovarian transposition, and laparoscopically guided interstitial radiation implant placement (1).

To confirm the equivalency of laparoscopic radical hysterectomy to open radical hysterectomy in early stages

of cervical cancer regarding survival outcomes, Pedro Ramirez (2018) carried out a phase 3, prospective, and multicenter randomized clinical trial. A total of 33 centers from all around the world recruited patients from June 2008 to June 2017, and 631 patients were enrolled. Then, 319 patients were randomly assigned to minimally invasive surgery and 312 to open surgery. The study had been planned to be continued up to July 2020, but in June 2017, the data and safety monitoring committee recommended that randomization be temporarily suspended and additional follow-up sought owing to an imbalance in deaths between the two groups. On March 24, 2018, the first results were announced as follows:

1. Minimally invasive surgery was associated with a lower rate of disease-free survival (DFS) compared to open surgery (3-year rate was 91.2% vs. 97.1%; hazard ratio for disease recurrence or death from cervical cancer was 3.74; 95% CI, 1.63 to 8.58); a difference that remained after adjustment for age, body-mass index (BMI), stage of disease, lympho-vascular invasion, lymph-node involvement, and the Eastern Cooperative Oncology Group (ECOG) performance-status score.
2. Minimally invasive surgery was also associated with a lower rate of overall survival compared to open surgery (3-year rate was 93.8% vs. 99.0%; hazard ratio for death from any cause was 6.00; 95% CI, 1.77 to 20.30); a higher rate of death from cervical cancer (3-year rate of 4.4% vs. 0.6%; hazard ratio, 6.56; 95% CI, 1.48 to 29.00), and a higher rate of locoregional recurrence (3-year rate of locoregional recurrence-free survival of 94.3% vs. 98.3%; hazard ratio for locoregional recurrence was 4.26; 95% CI, 1.44 to 12.60) (2).

Following this research, Melamed A. *et al.* (2018) performed a cohort study involving women who underwent radical hysterectomy for stage IA2 or IB1 cervical cancer during the 2010–2013 period in the United States. They also conducted an interrupted time-series analysis involving women who underwent radical hysterectomy for cervical cancer during the 2000–2010 period, using the Surveillance, Epidemiology, and End Results (SEER) program. During the 2010–2013 period, 2461 women with data in the National Cancer Database underwent radical hysterectomy for stage IA2 or IB1 cervical carcinoma and met the inclusion criteria; of these women, 1225 (49.8%) underwent minimally invasive surgery. In addition, among the women who underwent minimally invasive surgery, 978 (79.8%) underwent robot-assisted laparoscopy. Their findings suggested that minimally invasive surgery was associated with a higher risk of death than open surgery among women who underwent radical hysterectomy for early-stage cervical cancer. This association was apparent regardless of laparoscopic approach (robot-assisted or traditional), tumor size, or histologic type. This finding was consistent across several analytic approaches and robust to multiple sensitivity analyses. Moreover, they observed that the adoption of minimally invasive surgery in the United States, starting in 2006, coincided with the beginning of a decline in 4-

year relative survival rates among women undergoing radical hysterectomy for cervical cancer (3).

Furthermore, Kim SI *et al.* (2019) retrospectively identified stage IB1-IIA2 cervical cancer patients who underwent either laparoscopic or open radical hysterectomy between 2000 and 2018. In total, 435 and 158 patients were assigned to two open surgery and minimally invasive surgery (MIS) groups, respectively. Multivariate analyses identified minimally invasive surgery as an independent poor prognostic factor for PFS (adjusted HR=2.883; 95% CI, 1.711–4.859; $P<0.001$). Consistent results were observed among 349 patients with stage IB1; minimally invasive surgery was associated with higher recurrence rates (adjusted HR=2.276; 95% CI, 1.039–4.986; $P=0.040$). However, minimally invasive surgery did not influence PFS of stage IB1 patients with cervical mass size ≤ 2 cm on pre-operative magnetic resonance imaging (MRI) (4).

In conclusion, the findings of studies regarding the survival rate of women with cervical cancer revealed that patients treated with minimal access approach had lower survival rates than those treated with open surgery. Although no clear reasons for higher recurrence rates and a greater risk of death by laparoscopy have been reported, the following issues might justify the case:

- ✓ Necessity for pneumoperitoneum
- ✓ Common practice of using a uterine manipulator
- ✓ Surgeon experience
- ✓ Method of colpotomy that might expose the cervix and corresponding tumor to the abdominal cavity. In this regard, the technique modified by Köhler *et al.* (transvaginal closure of vaginal cuff before laparoscopy radical hysterectomy) seems to have the biologic rationale and robust retrospective results with over 10 years of follow-up, that make it a worthwhile technique to be considered in future randomized controlled trials (RCTs) (5).

Taking what was mentioned into account, in 2019, the European Society of Gynaecological Oncology (ESGO) and the American Society of Clinical Oncology (ASCO) recommended to record prospectively all minimally invasive surgical procedures for cervical cancer, including tumor characteristics and technical details; in addition they suggested that all procedures be performed only in highly specialized centers by appropriately trained surgeons. If minimal access surgery is offered and accepted by the patient, every effort should be made to avoid spillage of tumor cells in the peritoneal cavity (e.g., avoiding crushing lymph nodes, banning vaginal or uterine manipulators, and closing the vaginal cuff in order to avoid any contact between tumor and peritoneal cavity). Patients must be informed about the available prospective and retrospective evidence on survival, complications, and quality of life relating to the surgical approach.

Laparoscopy in Endometrial Cancer

The most definitive study evaluating the role of laparoscopy in patients with endometrial cancer was the Gynecologic Oncology Group Study LAP2 published in 2012 (6). Additionally, Janda *et al.* compared total laparoscopic hysterectomy (TLH) with total abdominal hysterectomy (TAH) for stage I endometrial cancer (LACE Trial). The results showed that the quality of life (QoL) improves from baseline during early and later phases of recovery, and the adverse event profile, favor TLH compared with TAH for treatment of stage I endometrial cancer. (LACE trial) (7).

In 2012, a Cochrane database of systematic reviews was conducted by Galaal K. *et al.*, which included nine RCTs regarding the safety of laparoscopy in early stage of endometrial cancer. They concluded that laparoscopy comparing to laparotomy in early stages of endometrial cancer, has similar overall survival and disease free survival. Furthermore, laparoscopy is associated with reduced operative morbidity and hospital stay and there is no significant difference in severe postoperative morbidity between the two modalities (8).

Obesity is a serious risk factor in endometrial cancer. Increased blood loss, increased rate of wound infection and dehiscence, increased risks of thrombosis, and pulmonary embolism are associated with laparotomy; hence, the use of laparoscopic surgery is preferred in obese patients.

Limitations and challenges with accessing the pelvic organs and adequate lymphadenectomy perform in increased BMI patients are associated with a proportional increase in conversion rate to laparotomy. But with skilled surgeons and centralizing this type of surgeries, it is possible to decrease the conversion rate to laparotomy (9).

Conclusion

Considering what was mentioned, the following issues might be concluded:

1. Laparoscopy is not safe in a disease with high risk of tumor spread (cervical cancer and sarcoma) except in the early stage of endometroid endometrial adenocarcinoma.
2. A good prognosis of cancer patients should not be jeopardized by doing incomplete laparoscopic surgery.
3. Do not look for single center series reporting safety of a surgical method (endoscopy) and follow prospective RCTs.

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Conflict of Interest

Authors declared no conflict of interests.

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