

Laparoendoscopic Single-Site Surgery in Gynecologic Oncology

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ABSTRACT

Objective: To provide a review in the available literature in laparoendoscopic single site surgery in gynecological oncology, focusing on epidemiology of ovarian and endometrial cancer in reproductive age, role of minimally invasive surgery in the management of ovarian and endometrial cancer and laparoendoscopic single site surgery elective oophorectomy and risk-reducing oophorectomy. Finally, laparoendoscopic single-site surgery for ovarian and endometrial cancer.

Design: Literature survey.

Conclusion: Laparoscopy is a safe and effective approach for surgical staging and treatment of selected patients with endometrial and ovarian cancer. Further studies and analyses are required to determine if the use of robotics improves outcomes over standard laparoscopy and can extend the benefits of minimally invasive surgery to a larger proportion of patients with this common gynecologic malignancy.

Keywords: Single-port laparoscopy, Robotic surgery, Gynecologic oncology.

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INTRODUCTION

Minimally invasive surgery has become the gold standard treatment for many gynecologic diseases. In the past, numerous studies have demonstrated that laparoscopic surgery plays an important role in various gynecologic oncologies particularly for early-stage endometrial, ovarian and cervical cancers with shorter hospital stays, improved quality of life and comparable surgical and oncologic outcomes to laparotomy.¹ Recently, an even less invasive alternative to conventional laparoscopy has been developed: Laparoendoscopic single-site surgery (LESS) which is an attempt to further enhance the cosmetic benefits of minimally invasive surgery while minimizing the potential morbidity associated with multiple incisions. LESS is applied to urologic and gastrointestinal surgery firstly and demonstrates that the techniques are feasible.² In this review article, we review the available literature about role of LESS in management in gynecological malignancies, focusing on epidemiology of ovarian and endometrial cancer in reproductive age, role of minimally invasive surgery in the management of ovarian and endometrial cancer and LESS

elective oophorectomy and risk-reducing oophorectomy. Finally, LESS for ovarian and endometrial cancer.

EPIDEMIOLOGY OF OVARIAN CANCER IN REPRODUCTIVE AGE

In gynecologic oncology, ovarian cancer leads to more deaths than all other gynecologic malignancies. Each year about 204,000 women are diagnosed with ovarian cancer but only 125,000 women die from this disease.³ The incidence of ovarian cancer is about one in 78 American women (1.3%) that can develop ovarian cancer during her lifetime. But the incidence has been declining slowly since 1990. The epithelial ovarian carcinomas consider the most common one which represent about 90 to 95% of all cases. In general, the diagnosis of ovarian cancer is difficult because the symptoms of ovarian cancer are vague and related mainly to GIT system and there is no effective screening test for ovarian cancer, so most of the patients have advanced disease when they are diagnosed and need usually aggressive debulking surgery followed by chemotherapy which usually results in clinical remission, but about 80% of women will develop recurrence that leads to disease progression and death.

In 2007, there were 22,430 cases which estimated to develop in the United States. However, the early diagnosis is still strict only to a few cases, so the ovarian cancer is still the fifth leading cause of cancer-related death.⁴

Numerous risk factors are associated with the development of ovarian cancer including reproductive, environmental and genetic risk factors but the most important risk factor is a family history of ovarian cancer and breast cancer because there are about 5 to 10% of patients having an inherited genetic predisposition, but still 90 to 95% have no genetic link for ovarian cancer. Many risk factors are related to a pattern of ovarian cycles during the reproductive years, so repeated stimulation of the surface epithelium of the ovary will lead to malignant transformation later on. Also the parity of the female plays an important role in development of ovarian cancer because the nulliparity is usually associated with long periods of repetitive ovulation, and also women without children have double the risk of developing ovarian cancer.⁵ Women who have long period of infertility have a higher risk for ovarian cancer. Although the genetic link of ovarian cancer is very high but also the iatrogenic effect of the drugs used in

induction of ovulation increases the risk of ovarian cancer.⁶ The menstrual pattern of the female should be put in to consideration because early menarche and late menopause have been associated with an increased risk of ovarian cancer. On the other side, breast feeding has a protective effect as it prevent, the ovarian cancer, may be due to amenorrhea and an ovulation associated usually with lactation.⁷ The combined oral contraceptive also reduces the risk of ovarian cancer by 50% by its effect in inhibition of ovulation.⁸ In contrast, hormone replacement therapy by estrogen after the menopause elevate the risk.⁹ The racial and ethnic factors can give some explanation for development of ovarian cancer. The incidence of ovarian cancer among white women is higher than black women.

Although exact reasons are unknown, but gynecologic surgery may have a role. Tubal ligation and hysterectomy have been associated with reduction in the risk of developing ovarian cancer.¹⁰ The incidence of ovarian cancer rises with increasing age up to 70 years and then begins to decrease among women above 80 years.¹¹

EPIDEMIOLOGY OF ENDOMETRIAL CANCER IN REPRODUCTIVE AGE

The incidence of endometrial cancer is about one in 38 American women (2.6%) during their lifetime. In 2007, 39,080 new cases are estimated to be developed in the United States, but only 7,400 deaths are expected. The endometrial cancer is considered less dangerous than ovarian cancer because the early diagnosis is easy and so the cure rate is high. All over the world, the endometrial cancer is the fourth leading cancer in incidence but only the eighth leading cause of cancer deaths among women.

Numerous risk factors have been described for developing endometrial cancer but the most important risk factor is related to excessive estrogen state. Obesity is considered as the most common cause of overproduction of endogenous estrogen because the excessive adipose tissue increases peripheral conversion of androstenedione to estrone. The estrogen replacement therapy is the next most important factor in development of endometrial cancer, so combined estrogen plus progesterone hormonal therapy should be prescribed for postmenopausal women to reduce their risk of endometrial cancer.

The reproductive factors play an important role in development of endometrial cancer whenever anovulation is present in women with polycystic ovarian syndrome and thus have an increased risk of developing endometrial cancer,¹² and also menstrual pattern especially when the duration of uninterrupted menstrual cycles is prolonged, so early menarche and late menopause both increase the risk of endometrial cancer.¹³

Family history is also linked to endometrial cancer and they are many genetic syndromes, such as Lynch syndrome which also known as nonpolyposis colorectal cancer (HNPCC), in which the endometrial cancer is considered the most common extracolonic manifestation of this syndrome.¹⁴

Oral contraceptive use for at least 1 year decreases the risk of endometrial cancer by about 30 to 50% and risk reduction extends for 10 to 20 years.¹⁵ The medical conditions play an important role in development of endometrial cancer. Cancer corpus triad include obesity, diabetes mellitus and hypertension which are commonly associated with endometrial cancer.¹⁶

ROLE OF MINIMALLY INVASIVE SURGERY IN THE MANAGEMENT OF OVARIAN CANCER

Minimally invasive surgery for patients with ovarian cancer plays an important role in different ways depending on the stage in which the disease is discovered and also the surgical aim of the procedure.¹⁷

In early-stage of the disease, laparoscopy may be used in staging instead of surgical staging, and also the second-look operation is one of its use to assess the progress of the disease after the patient completes the course of adjuvant chemotherapy.

In advanced stage of ovarian malignancy the laparoscopy in general can be used to confirm diagnosis by visualization of internal organs and also give picture about nature of the tumor and its respectability. Frozen section biopsy can be taken during the operation for histological testing. However, when the ovarian cancer has been confirmed through frozen section biopsies, the laparoscopy procedure is usually converted into laparotomy that enables removing the tumor without contact with the abdominal wall as well as performing infracolic omentectomy for tumor staging.¹⁸

The use of minimal invasive surgery to evaluate ovarian masses began approximately 10 years ago but it was only considered as a diagnostic method because laparoscopy could facilitate tumor spreading in the cavity. In addition, the omentectomy, which needed to complete staging, is difficult to be done by laparoscopy but nowadays the risk of tumor dissemination during laparoscopy was reduced by using of the endobag which consist of sheath placed around removed adnexal mass to eliminate tumor dissemination.¹⁹

ROLE OF MINIMALLY INVASIVE SURGERY IN THE MANAGEMENT OF ENDOMETRIAL CANCER

Endometrial cancer is the most common gynecologic malignancy in the United States. Surgical staging plays an

essential role in the treatment of this disease.²⁰ Minimally invasive surgical techniques have been utilized with increasing frequency in the management of endometrial cancer, minimally invasive surgery have demonstrated the safety and feasibility of laparoscopy in performing hysterectomy, bilateral salpingo-oophorectomy, and pelvic and periaortic lymphadenectomy for surgical staging in endometrial cancer.²¹ The use of minimally invasive techniques does not appear to have an adverse impact on survival, and it improves quality of life in the postoperative period.

Some gynecologist find high incidence of positive peritoneal cytology for the endometrial cancer in patients after laparoscopy, this may be due to the retrograde dissemination of cancer cells into the peritoneal cavity during uterine manipulation, but the clinical significance of these findings is not clear yet. Many studies proved that obesity is not a contraindication to laparoscopic staging in endometrial cancer. This is an important consideration, as many patients with endometrial cancer are obese.²²

However, minimally invasive surgical techniques which are used in management of endometrial cancer include instrumentation, and technology have improved significantly. The application of these techniques in treatment of endometrial cancer is safe and effective alternative to laparotomy and appears to provide similar result and survival rates. Patient benefit is demonstrated by faster recovery, decreased pain and improved quality of life.

LESS ELECTIVE OOPHORECTOMY

Definition of the Concept

This is the mean removal of the ovaries with another indicated surgical operation, it is always removed to prevent morbidity or mortality, which can occur later on if the ovaries are left.

Elective oophorectomy has a great benefit because we presently lack the ability to routinely recognize ovarian cancer in a premalignant form or even when it is confined as early invasive cancer to the ovary itself,²³ as a result most ovarian cancers are present as advanced stage of the disease and the cure rates are low.

Indications of Elective Oophorectomy

A number of surgeons have suggested that elective bilateral salpingo-oophorectomies in women over age 40 should routinely undergo at the time of hysterectomy. If a prophylactic oophorectomy was performed in all women over age 40 years, 2,200 women may subsequently avoid ovarian cancer per year. This concept of bilateral salpingo-

oophorectomies of 99.75% women undergoing hysterectomies in order to avoid ovarian cancer in 0.25% need more further assessment.²⁴ However, there is a recent study in Japan, where the incidence of ovarian cancer is very low and failed to prove the significance of prophylactic oophorectomies to spare cancer ovary in all women over age 45 undergoing hysterectomy.²⁵

There is another study which suggests that women who undergo a hysterectomy are actually at low risk for development of ovarian cancer. So the indications of prophylactic oophorectomy may include postmenopausal women, nulliparous women, women with long history of infertility, women with past history of breast, colon and uterine cancer and women with a genetic predisposition to developing ovarian cancer. However, we must remove the ovaries of the patients with a past history of breast, colon or uterine cancer if abdominal surgery will be performed because the ovaries are common sites for metastasis.

LESS RISK-REDUCING OOPHORECTOMY

Definition of the Concept

Risk reducing bilateral salpingo-oophorectomy (rrBSO) is a method for decreasing the risk of ovarian cancer in women with a genetic disposition for this malignancy. This procedure is done because of the efficacy of current modalities is limited for early detection and there is high mortality rate associated with ovarian cancer.

Indications of Risk-reducing Oophorectomy

Before performing rrBSO, it is important to differentiate between women with possible familial ovarian cancer syndromes, which is rare syndrome, and other women who have no familial ovarian cancer syndromes and no one in there family having it. The familial ovarian cancer syndromes account for approximately 10% of cases of epithelial ovarian cancer. The key for diagnosis of these hereditary syndromes is the presence of ovarian cancer in a family member at any age, or appearance of breast cancer in premenopausal women and the occurrence of cancers in multiple members of two to four generations.²⁶

The familial cancer syndromes include:

- Site-specific ovarian cancer syndrome.
- Breast-ovarian cancer syndrome.
- Hereditary nonpolyposis colorectal cancer syndrome (HNPCC).

The first two groups are associated with gene mutations in the BRCA1 and BRCA2 genes but hereditary colon cancer syndrome (HNPCC) is associated with gene mutation in DNA mismatch repair (MMR) genes.

Most ovarian cancers associated with the BRCA mutations are diagnosed at a younger age and mostly are

serous carcinomas. Patients with a BRCA1 or BRCA2 mutation also have an increased risk of developing other rare gynecological cancer, like fallopian tube carcinoma. This indication leads to development of a risk reduction strategy that includes removal of the ovaries and tubes to prevent the development of carcinoma.

Many studies proved that prophylactic bilateral salpingo-oophorectomy reduces ovarian cancer risk in BRCA1 and BRCA2 mutation carriers by about 96%. Additionally, if the prophylactic bilateral salpingo-oophorectomy is done perimenopausally, the risk of development of cancer breast decrease up to 50 to 68%.²⁷

Another inherited mutation include mutation which occur in certain genes like MSH2, MLH1, PMS2 and MSH6 which called DNA MMR genes, this mutation leads to Lynch syndrome or HNPCC, in this syndrome the most common cancers which occur are colon, endometrial and ovarian cancer.²⁸

However, the decision to perform prophylactic risk-reducing oophorectomy should be based on several patient factors and choices not only on the age, women undergoing prophylactic bilateral salpingo-oophorectomy should be counseled about the risks and benefits of hormone replacement therapy before surgery. So for women with BRCA1 mutations, risk-reducing prophylactic bilateral salpingo-oophorectomy should be done after the complete the child-bearing period, but for individuals with a personal or family history of breast and ovarian cancer who have not had genetic testing or who have undergone these testing and no mutations in BRCA1 or BRCA2 gene is detected, the risks and benefits of prophylactic bilateral salpingo-oophorectomy is not proved yet. So these individuals are best managed by strict follow-up by gynecologists, oncologists, and geneticists to detect any risk for cancer.

So risk-reducing oophorectomy should be done to select women when:

1. The women have a positive BRCA1 or BRCA 2 genetic test.
2. There is a first-degree family history of ovarian cancer.
3. There are two or more second-degree relatives with history of ovarian cancer or breast cancer.
4. When women will use estrogen as adjuvant therapy in treatment of breast cancer.
5. Bilateral salpingo-oophorectomy should be done with hysterectomy in HNPCC syndrome.

LESS SURGERY FOR OVARIAN CANCER

Laparoscopic surgery has become the preferred surgical approach for a variety of gynecologic oncology; single-port laparoscopy is not a new method in mangement of various

gynecologic oncologies. Wheelless and Wheelless and Thompson reported in the 1960s that more than 4,000 women underwent rapid, inexpensive, effective surgical sterilization by using single-trocar laparoscopy. In 1991, Pelosi and Pelosi performed the first hysterectomy using a single-trocar technique.²⁹

The ovarian cancer is responsible for more deaths than all other gynecologic malignancies combined. Each year in the United States, 204,000 women are diagnosed, and 125,000 women die from this disease.³⁰ The epithelial ovarian carcinomas comprise 90 to 95% of all cases, including the more indolent low malignant potential (borderline) tumors.³

The treatment of ovarian cancer is dependable on many factors; however, the most important factors are age of the patient, the parity, and the stage of disease when discovered. In stage I ovarian cancer, the LESS is used mainly in staging which consider being a primary treatment. In those with advanced disease, laparoscopy is used in visualization of abdominal organ and it gives a picture about the respectability of the tumor, so all the required procedures could be proceeded safely by laparoscopy.³¹

The treatment of the early stage ovarian cancer is simple hysterectomy and bilateral salpingo-oophorectomy, then bilateral pelvic lymph node dissection should be done through an incision in the retroperitoneal space. All these procedures were successfully performed via LESS by a single 2 to 3 cm incision and there were no conversions to multiport laparoscopy or open surgery.³²

The epithelial ovarian cancers develop in about 10% in women younger than 40 years of age, so the fertility sparing surgery, which include unilateral adnexectomy, may be an option in selected patients when disease is present only in one ovary, this can be easily done by LESS.³³ Instrument crowding was noted in most cases done by LESS but if we use a laparoscope with a flexible tip (the 30° Viscera Endo Eye) or articulating instruments, this will be easy.

LESS gives better cosmesis due to hidden umbilical scar so it is psychologically more supportive due to good body image, and the risk of visceral and vascular injury during trocar placement is low, which decrease the morbidity rate and also there is decreased risk of postoperative wound infection, hernia formation, and also fewer incisions may result in faster recovery and so the administration of adjuvant therapies will be faster. Also, the use of LESS plays an important role in reduction of postoperative pain and narcotics use.

LESS SURGERY FOR ENDOMETRIAL CANCER

In the last years, many studies proved that laparoscopic approaches to various gynecologic oncology conditions

particularly for early-stage endometrial cancer where the tumor is limited to the uterus, become easy and feasible, also the patient will stay for short period in the hospital, so there is clear improvement in quality of life.³⁴

The surgical staging of endometrial cancer is very important because it gives picture about the method of the treatment and prognosis, but an alternative method of surgically staging is a LESS approach. In general, this approach is limited to a selected group of women with stage I disease. However, laparoscopic pelvic and para-aortic lymph node dissection may also be done in women who are incompletely staged at their primary surgery.³⁵

There is another minimally invasive alternative method for laparoscopy which is called robotic surgery, which is used nowadays in surgical treatment of endometrial cancer, the use of robotic procedures for treating gynecologic oncology diseases has increased alot nowadays as many studies have proved that.³⁶ This robotic surgery has great benefits, like improvement of surgeon movement, and allows 3-D optics. Recent reports demonstrate that endometrial cancer staging can be performed with a daVinci surgical system which is preferable over abdominal staging and also over the laparoscopic staging because it gives many advantages, like enhancement of lymph nod excision, decrease in the blood loss and decrease in operative time.³⁷

However, the surgeons can nowadays perform easily hysterectomy easily with bilateral salpingo-oophorectomy to treat the endometrial cancer laparoscopically by LESS surgery via a single-site incision. This will be done by utilizing the newest generation of port systems that allow several laparoscopic instruments to be used in the same time through a single-operating trocar.

Absolute contraindications to the performance of LESS include cancer patients with evidence of metastatic disease, also patients with poor pulmonary function who cannot stay in the positioning required for LESS, but relative contraindications are dependent on surgeon experience and skillful level in LESS. Trials of the operations done by LESS in gynecology are given in the Table 1.

DISCUSSION

The treatment of gynecological oncology diseases has been developed nowadays. The old concept for treatment of gynecological tumors is radical surgery by laparotomy to give a good field to manipulate the tumor as in endometrial cancer or ovarian cancer but nowadays this method has been changed as minimally invasive surgery for patients with gynecologic malignancies has progressively increase.

Numerous studies have proved that laparoscopic approaches to various gynecologic oncology conditions

Table 1: Summary of trials of the operations done by LESS in gynecology

References (years)	Type of study	No. of patient	Type of operation	Duration of the surgery (min)	Blood loss (CC)	Hospital stay (day)	Complications rate (%)	Conversion to other method (%)
Ghezzi, Cromi et al (2005)	Prospective	10	SPL salpingectomy	27	-	1	0	0
Kim, Lee et al (2008)	Prospective	24	SPA-LAVH	199	400	3	-	3
Lim, Kim et al (2009)	-	12	Adnexectomy	73	10	1	0	0
Fader and Escobar (2009)	-	13	Adnexectomy	65	-	1	0	0
Kim, Lee et al (2009)	Prospective	24	Salpingo-oophorectomy	70	10	1	0	12
Yoon, Park et al (2009)	Prospective	20	SPL salpingectomy	55	Minimal	2	2	0
Yoon, Kim et al (2009)	Prospective	7	Hysterectomy	157	200	4	0	0
Langebrette and Qvigstad (2009)	-	1	Total laparoscopic hysterectomy with single-port access without vaginal surgery	60	Minimal	5 hrs	0	0
Fader and Escobar (2009)	Retrospective	30	Endometrial ovarian cancer staging hysterectomy/ bilateral salpingo-oophorectomy	65	Minimal	1	0	0
Escobar, Bedaiwy et al (2010)	Cohort	7	LESS surgery for benign adnexal disease	-	75	>24 hrs	0	14

particularly for early stage endometrial, cervical cancers and select pelvic masses is feasible and results in shorter hospital stays, improved quality of life and gives the same result in comparison to surgical approach.

The surgeon preferred LESS surgery because it gives better cosmesis and decrease the morbidity of the patient and also it decreases risk of postoperative wound infection, hernia formation. LESS in gynecological oncology has many advantages, the staging which has very important role in treatment of the tumor and need laparotomy to be done, nowadays can be done easily by LESS. Hysterectomy with bilateral salpingo-oophorectomy, which is the main management of most of gynecological oncology diseases, become feasible to be done by LESS by utilizing the newest generation of port systems that allow several laparoscopic instruments to be used in the same time through a single-operating trocar.

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