Laparoscope minimally invasive surgery in gynecologic oncology and controversies: a review

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Abstract

Laparoscope minimally invasive surgery has gradually become one of the options for the treatment of early gynecologic malignancies for that it is superior to open surgery in perioperative efficacy and has no disadvantage in oncological outcomes. Nevertheless, the Laparoscopic Surgical Pathway for Cervical Cancer study has shown that early-stage cervical cancer patients owns higher recurrence rates and shorter overall survival with laparoscopic surgery compared to open surgery. In this review, we discuss the current status and controversies regarding the use of minimally invasive surgery in common gynecologic malignancies.

Introduction

In 1990, laparoscopy began to be used for gynecological oncology surgery. Reich et al. performed laparoscopic ovarian cancer staging surgery on a patient who refused open surgery[1]. In 1992, laparoscopic surgery was applied to the treatment of cervical cancer [2]. And Childers et al. firstly reported the application of laparoscopic staging surgery for patients with endometrial cancer in the same year [3]. After the 20th century, minimally invasive surgery (MIS) has gradually become one of the options for the treatment of early gynecologic malignancies for that it is superior to open surgery in perioperative efficacy and has no disadvantage in oncologic outcomes. Until 2018, a well-known phase III randomized controlled clinical trial of the Laparoscopic Surgical Pathway for Cervical Cancer (LACC) study on patients with early-stage cervical cancer revealed higher recurrence rates and shorter overall survival (OS) with laparoscopic surgery compared to open surgery [4]. This study will raise the issue of the appropriateness of MIS in other gynecologic oncologic settings and review the current status and controversies regarding the use of MIS in common gynecologic malignancies.

Conventional multiport laparoscopy

Cervical cancer

Back to the history of cervical cancer surgery in 1992, Dargent in France reported laparoscopic pelvic lymph node dissection laparoscopic-assisted transvaginal extensive hysterectomy, while Nezhat et al. in the United States recommended laparoscopic extensive hysterectomy with pelvic lymph node dissection [2 5]. Since then, laparoscopy has become increasingly used in surgery for early-stage cervical cancer. However, two clinical studies published in N Engl J Med on October 31, 2018, compared the efficacy of open surgery and minimally invasive radical hysterectomy for early-stage cervical cancer, and concluded that MIS was inferior to open surgery in terms of disease free survival (DFS) and OS [4 6]. Although it is simple

to abandon laparoscopy and return to open surgery, it is unscientific to dismiss the role and value of laparoscopic surgery in early-stage cervical cancer only based on the results of these two studies. The debate of the treatment of cervical cancer should not be limited to the laparoscopic versus open surgery, but should be used to find the causes, improve the approaches, and conduct high-level evidence-based clinical studies.

After the publication of the LACC study, many scholars have explored the reasons for the poor prognosis in the MIS group. Thereinto, the understanding and implementation of intraoperative tumor-free principles and the choice of surgical indications have attracted our attention. Recent improvements in the surgical approach in different studies have focused on avoiding the use of uterine lifters and improving vaginal dissection approaches. Of all the laparoscopic operative steps for cervical cancer, one of the most suspected to affect prognosis is the use of the uterine lift. Among these various lifts, the use of the cup lift cup has been the most questioned [7]. However, there is no direct evidence indicates that the uterine lift promotes cancer metastasis. For caution's sake, laparoscopic uterine suspension is recommended. The exact method of suspension varies from person to person. Sutures can be used to suspend bilateral fundus and uterine horn, and that ligation of the lower segment of the uterine body can also be considered. The final stage of vaginal dissection is also a crucial step. To avoid tumor rupture and implantation in the incision or pelvic and abdominal cavity, it is recommended that the uterus should be removed preferably without pneumoperitoneum by incision of the vaginal mucosa. Laparoscopic vaginal closure with vaginal ligation ring followed by distal vaginal dissociation to remove the uterus may also be considered.

Another aspect of reflection on the LACC study is the choice of surgical indications. Since the LACC study was insufficient for subgroup analysis in low-risk patients, namely patients those with tumor diameter <2 cm, depth of infiltration <10 mm, and no interstitial infiltration of the vasculature and lymph node metastasis.

Therefore, the safety of laparoscopic surgery cannot yet be completely denied in this group of patients. Dimitrios et al. systematically analyzed data on stage A cervical cancer patients from the National Cancer Database from 2010 to 2015. Results suggested that there was no difference in survival between laparoscopic and open surgery[8]. Kim et al. reported that there was no significant difference in progression free survival and OS between the MIS group and the open group for patients whose tumor diameter <2 cm as indicated by preoperative MRI at stage B1[9]. However, a recent meta-analysis found that the progression free survival of the open group was significantly better than that of the MIS group when the tumor length diameter <2 cm [10]. Therefore, for patients with tumor diameter <2cm, invasion depth <10mm, no vascular interstitial invasion and lymph node metastasis, it is urgent to provide guidance for the results of well-designed prospective studies.

For the treatment of malignant tumor, the therapeutic effect and the clinical prognosis of tumor are very important. For the surgical treatment of cervical cancer, the concept and principle of tumor-free surgery are very important. Although it is suspected that the high survival rate in the open LACC group and the high recurrence rate in the MIS group may be related to surgeons and surgical techniques, the insufficiency of laparoscopic surgical techniques in the treatment of cervical cancer still needs to be reconsidered. In addition, the positive effect of LACC results on clinical guidance should be fully recognized[11 12]. Most importantly, it is a huge challenge to identify the cause, refine surgical procedures, and conduct high-level evidence-based clinical trials to demonstrate that improved MIS can be used equally well for the treatment of selective early cervical cancer.

Endometrial cancer

Childers et al. first reported laparoscopic staging surgery for endometrial cancer in 1992. Since then, the use of laparoscopy for endometrial cancer has attracted the attention of global physicians [3]. Studies have shown that laparoscopic surgery and

open surgery have no significant difference in the prognosis of endometrial cancer, and that laparoscopic surgery has become the standard operation for endometrial cancer. However, the LACC study raises questions about the appropriateness of MIS in endometrial cancer.

Laparoscopic surgery is the first choice for early, low-risk endometrial cancer due to its safety and reliability. A prospective randomized controlled study titled Gynecological Oncology Group 2222 found no statistical differences in 3-year cumulative recurrence rates and 5-year cumulative recurrence rates between the laparoscopic and open surgery groups, and the 5-year overall survival rates were the same between the two groups[13]. Another prominent clinical study named the Laparoscopic Approach to Cancer of the Endometrium showed no statistically significant differences in 4.5-year of recurrence, mortality, or DFS between the laparoscopic and open surgery groups[14]. To date, there have been six prospective randomized controlled studies of laparoscopic surgery in individuals with low-risk endometrial cancer [13-18]. Although these studies were conducted at different times by different institutions, DFS rates did not differ significantly. Patients with high-risk pathological endometrial cancer have a poor prognosis due to low tumor differentiation. Unfortunately, there is no data available from prospective randomized controlled studies on the safety of MIS in high-risk pathological types of endometrial cancer. One large retrospective study of the National Cancer Database showed similar survival outcomes after the two surgical approaches in almost all pathological subtypes [19]. Collectively, MIS also appears to be safe for high-risk types of endometrial cancer. However, the pathologic types of high-risk tumors are more aggressive, and the principle of tumor-free during surgery is critical. More prospective studies are required to confirm the safety of laparoscopic surgery. With the advent of the molecular era, molecular staging of endometrial cancer is gradually gaining clinical applicability. The Cancer Genome Atlas research network comprehensively revealed the molecular genetic map of endometrial cancer in 2013,

grading the risk of endometrial cancer at the molecular level and complementing the clinicopathological dimension. The safety of laparoscopic surgery in different molecular subtypes has also been explored at the molecular level. Dai et al. discovered that the endometrial cancer molecular features have a link with survival rates by different surgical approaches. MIS has a better clinical prognosis in patients with POLEmt, MSI-H, while open surgery should be recommended in patients with TP53 mutation [20 21]. As tumourgenesis and treatment are further explored, the molecular characteristics of tumors will play a crucial part in influencing tumor treatment modalities.

Laparoscopic surgery has traditionally been considered a safe procedure for endometrial cancer. However, data from the LACC trial led us to reconsider its safety in endometrial cancer. The concept of tumor-free operation should be maintained throughout the treatment of endometrial carcinoma MIS. First, the fallopian tubes should be blocked during surgery. Before surgery, both fallopian tubes can be closed at the isthmus of the fallopian tube to avoid tumor cells reflux through the fallopian tube. Second, pay attention to the use of uterus lifting apparatus to avoid intraoperative uterine perforation. Third, for patients with cervical involvement, vaginal separation is also a key step. When the vagina is severed, the operation method of cervical cancer can be referred to. Fourth, the specimen should be bagged immediately after resection to reduce the possibility of tumor implantation. Fifth, for patients with large lesions or difficult uterus removal, the specimen can be put into the removal bag or small abdominal incision to remove the specimen. Sixth, pay attention to the influence of laparoscopic pneumoperitoneum to avoid frequent changes in intraoperative abdominal pressure. Air should be deflated before removing the puncture trocar after operation to reduce the smoke impact. Seventh, the pelvic cavity, abdominal cavity and abdominal wall perforation should be fully cleaned with plenty of distilled water before the end of the operation. Eighth, after the operation, check the uterus and other specimens, while ensuring the integrity of the specimen [22].

As for endometrial cancer, the current findings have completely confirmed the status of laparoscopic surgery in the treatment of early low-risk endometrial patients, but more data are still needed to verify the safety of high-risk types of endometrial cancer. Therefore, we should strictly grasp the surgical indications, strengthen the concept of tumor-free, effectively perform the tumor-free techniques, and standardize the whole management of endometrial cancer patients. In this way, we can achieve the perfect combination of MIS and tumor treatment.

Ovarian cancer

In 1990, Reich et al. reported the first full staging laparoscopic surgery for stage I ovarian cancer [1]. Since then, numerous studies have explored the feasibility, efficacy, and safety of laparoscopic techniques for the treatment of ovarian cancer. There are generally consistent results from various clinical studies represent that experienced gynecologic oncologists and laparoscopists performing laparoscopic full-stage surgery for appropriate stage I and II ovarian cancer can achieve the same oncologic outcomes as open surgery, along with less trauma, less bleeding, faster postoperative recovery, shorter hospital stay, and no delay in follow-up treatment [23 24]. The National Comprehensive Cancer Network guidelines also endorse laparoscopic surgery for ovarian cancer performed by experienced gynecologic oncologists [25].

The use of laparoscopic surgery in advanced ovarian cancer is controversial. Most patients with advanced ovarian cancer have extensive metastasis and attachment to vital organs such as the bowel, omentum, ileocecum area, hepatocolonic ligament, and splenocolonic ligament. All of these metastases are mostly dense adhesions, making them extremely difficult to eliminate. In addition, when the tumor is large, laparoscopic surgery often causes the tumor to rupture, and improves staging. However, laparoscopic surgery for ovarian cancer reduction is still being explored. Neoadjuvant chemotherapy should be considered when optimal cytoreduction is failing in advanced ovarian cancer. Neoadjuvant chemotherapy combined with

interval debulking surgery in the treatment of advanced ovarian cancer deserves further study and promotion[26]. Despite the increasing acceptance of minimally invasive interstitial tumor cell reduction for ovarian cancer, there are no strong studies to prove that this surgical approach does not affect survival outcomes in cancer patients. There is consensus on the importance of optimal (R0) cell reduction in recurrent tumors. Reduction of R0 cells is considered useful in patients with platinum-sensitive recurrent or multiple lesions [27 28]. However, there is no consensus on the choice of laparoscopic or open secondary tumor cytoreductive surgery [29]. Laparoscopic ovarian tumor cell reduction is more challenging and its clinical application still remains controversial.

The principle of anaplasia is a key factor in minimizing local recurrence and improving the prognosis in the surgical treatment of malignant tumors. Preventing tumor extrusion and rupture, thorough resection of tumor tissue, and removal of large pieces of tumor tissue are the challenges of laparoscopic surgery for ovarian cancer using the tumor-free principle. Operation precautions are as follows. First, the operation should be gentle, to avoid squeezing the tumor, to avoid tumor rupture when separating or removing the tumor. Second, put the removed tissue into the bag in time and pull it to the puncture point for complete removal. Third, blunt tearing should be avoided in the operation of malignant tumor, and sharp anatomy should be emphasized. Fourth, for ovarian cancer with complete capsule, surgery emphasizes a certain distance from the tumor, and the whole tumor focus is completely removed. Fifth, in order to prevent tumor blood spread caused by surgery, the blood supply should be coagulated and cut off before the tissue around the tumor is separated. Pelvic and abdominal lymph nodes adjacent to blood vessels should be removed intraoperatively to reduce tumor spread along lymphatic vessels. Lymph nodes should be removed proximal to the vessel and from the distal end of the tumor. Sixth, the pelvic cavity and abdominal cavity should be rinsed with distilled water after surgery to further reduce the chance of tumor implantation[30].

Existing studies have not demonstrated that MIS for ovarian cancer has significantly adverse effect on patient survival. However, with the exception of randomized controlled studies of the role of laparoscopy in preoperative assessment of ovarian cancer cell reduction, other studies are methodologically flawed to a greater or lesser extent, and these data should be treated with caution. Scientific prediction method is the key to the best treatment and success. Therefore, more high-quality clinical studies are needed to confirm the application of MIS in ovarian cancer.

Single-port laparoscopic technique

Single port laparoscopic technique is the direction of MIS. Laparoscopy single site surgery (LESS) and natural endoscopic surgery (NOTES) have emerged in order to achieve both aesthetic and minimally invasive purposes. In 2009, Fader et al. first described the treatment of 13 gynecological tumor patients with LESS, including 9 cases undergoing laparoscopic surgery and 4 cases undergoing robotic surgery. The procedures included endometrial cancer stage (1 case), ovarian cancer stage (1 case), retroperitoneal pelvic lymph node dissection (1 case), and low-risk extrafascial hysterectomy/bilateral salpingo-oophorectomy (BSO, 2 cases) [31]. In 2012, Fogatti et al. reported the results of a multicenter clinical study on surgical pathological staging of endometrial cancer by LESS [32]. In the same year, the first successful extensive resection of cervical cancer was reported by Garrett et al [33]. In 2018, Yoo et al. reported that robot-assisted LESS performed a comprehensive staging operation for a patient with early-stage ovarian cancer, including greater omentum resection at the lower margin of the transverse mesenteric membrane and lymph node resection in the region below the inferior mesenteric artery, which was successful [34]. Now, a number of units have reported using LESS for more complex gynecological tumor surgery. However, it should be emphasized that these reports are from units and doctors with rich multiport laparoscopy experience, so more objective conclusions about LESS

need to be further confirmed by large sample studies on the application of LESS in surgery for various gynecological malignant tumors. In general, the advantages of LESS surgery over conventional laparoscopic surgery are mainly in terms of the reduced postoperative pain and incision-related complications, as well as a more aesthetic appearance after the union[35]. While the biggest challenge in the treatment of gynecologic malignancies should be the doctor to the challenge of self. Despite the basic laparoscopic technique used in LESS, various problems are faced involving different surgical approaches, different views, and different instruments, which undoubtedly poses a new requirement to the surgeon's creativity and perseverance. Especially in the operation of gynecological malignant tumor, the anatomical relationship is relatively complex, involving more organs, the change of approach, field of vision and instruments will bring more difficulties to the operation [36].

In 2014, Lee et al. reported the first global clinical data of vNOTES for gynecological malignancies, and the author successfully completed total hysterectomy and pelvic lymph node resection for 3 cases of stage I A endometrial carcinoma [34]. Yannick Hurni et al. first described vNOTES for staging surgery in 2 patients with ovarian cancer in 2022 [37]. However, due to the technical difficulty and the complexity of the disease, as well as the results of LACC studies, vNOTES has not been used in the clinical practice of cervical cancer. Some retrospective studies have summarized the advantages of vNOTES over traditional laparoscopic surgery, but nearly all of them were performed for benign gynecological diseases, such as vNOTES hysterectomy or vNOTES adnexectomy.[38] The most significant difference of vNOTES compared to LESS is the different way where the surgical access is established, which means that intraoperative attention should be paid to the successful establishment of surgical. In addition, the field of vision for vNOTES surgery is the exact opposite of traditional laparoscopy, with the patient looking from the gluteal side to the cephalic side, requiring a re-establishment of the surgical anatomy. This

difficulty can be conquered by identifying important anatomical markers before performing surgical procedures [39].

Both LESS and NOTES are still faced with inherent contradictions such as a lack of surgical triangle and insufficient space for the movement of surgical instrument. At present, it is considered that the key to solve this problem is how to cooperate with both hands in a narrow space. In the process of surgical exploration, the First Affiliated Hospital of Third Military summed up the "chopstick method" operation technology [40]. Two equal-length instruments are adopted for two-handed operation: the left hand holds the tissue with the grasping forceps and maintain a certain tension before fixing it; the right hand is responsible for the main surgical operation with the energy instruments; the tips of the instruments hold in two hands are opposite to each other, and the surgical operation is completed under the cooperation of left and right hands. Two instruments of equal length are used for two-handed operation: the left hand holds the gripper, holds the tissue, and holds it fixed after maintaining a certain tension; The right hand holds the energy instrument and is responsible for major surgical operations. The tips of left hand and right hand instruments are opposite, and the left hand and right hand cooperate to complete the operation. However, due to the narrow operation space and difficulty of operation, the application of this method in gynecological tumor surgery, especially malignant tumor surgery, still has great limitations.

Conclusion

For gynecological oncologists, while developing, selecting and implementing laparoscopic surgery, it should still be based on the principles of standardized tumor treatment. We advocate the concept of MIS, but do not deliberately pursue all MIS. A mature surgeon will choose the most appropriate surgical procedure according to the patient, disease and individual technical characteristics to achieve the perfect combination of efficacy and safety.

Disclosure of interests

None declared. Completed disclosure of interests form available to view online as supporting information.

Contribution to authorship

ML completed the initial draft, with several general ideas for the direction of the manuscript provided. CC made major contributions to revising the manuscript. PY provided critical expertise on gynaecological malignancies.

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