

# Minimally Invasive Surgery: A New Approach for Uterine Cervical Cancer

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## Abstract

Initially used for diagnostic, laparoscopy has become a method of treatment in the field of gynecological surgery, but also in many other fields. The results of laparoscopic surgery are now comparable with those obtained by laparotomy in benign and malignant pathologies. Laparoscopy provides improved results in the short term and at least equivalent results in terms of long-term recurrence when compared with open surgery. Robotic-assisted laparoscopy was performed to prevent the disadvantages of conventional laparoscopy. It emerged as a revolutionary technology and has spread in less than a decade in many surgical fields, including urology, cardiothoracic surgery, pediatric surgery and general surgery. Minimally invasive techniques provide a lower rate of complications during surgery as compared to open surgery, which is appropriate tissue due to handling and better anatomical views. Laparoscopic treatment of cervical cancer provides benefits on increasing comfort with decreased convalescence time, but these cases should be reserved for surgeons with extensive experience in laparoscopic procedures. One of the most important advantages of minimally invasive surgical techniques is the short duration of hospitalization.

**Keywords:** Cervical cancer; Laparoscopic radical hysterectomy; Robotic surgery hysterectomy

## Introduction

In the early 1990s, the laparoscopic approach in uterine cervical cancer has started to become quite popular among oncologist surgeons in order to minimize postoperative morbidity. When a new surgical technique is taken into consideration or suggested, it is compared with the standard therapy hitherto. Important issues to be taken into account include the feasibility and applicability of the new technique, intraoperative and postoperative complications and in oncological cases, survival and risk of recurrence.

Gold standard for uterine cervical cancer in the early stages was abdominal radical hysterectomy with pelvic lymphadenectomy for more than 100 years. This technique, described for the first time Wertheim, Meigs subsequently underwent some changes. The first laparoscopic hysterectomy was performed and published in 1989 [1], but the first laparoscopic radical hysterectomy with pelvic and para-aortic lymphadenectomy in a patient with cervical cancer stage IA2 was performed by Nezha et al. in June 1989 and reported in 1992 [2]. Since then, it has been reported in the literature over 1000 cases [3].

## Laparoscopic Surgery versus Open Surgery in Uterine Cervical Cancer

Initially used for diagnostic, laparoscopy has become a method of treatment in the field of gynecological surgery, but also in many other field. The results of laparoscopic surgery are now comparable with those obtained by laparotomy in benign and malignant pathologies. The most important advantages of the laparoscopic technique include more pleasing cosmetic appearance, or minimum parietal infectious complications, low incidence of adhesion formation, low cost associated with hospitalization and recovery period smaller resumption of daily activities in a shorter period [4]. In a study comparing the two surgical techniques, the results show an average of operating time with significant differences statistically 231.7 minutes for cases treated laparoscopically and 207 minutes to classical surgery, which can be explained by the fact that laparoscopic hysterectomies implemented quite recently requires a learning curve. The surgeons will become more familiar with laparoscopic procedure; the operative time is

expected to become shorter. Intraoperative blood loss was lower in the laparoscopy (161.1 ml) compared with the traditional method (394.4 ml), with blood transfusions in 3 patients. Postoperative complications, represented mostly wound infections were recorded only in the group that received radical abdominal hysterectomy. The hospital stay was less in laparoscopic interventions (mean=2.9 days) compared with the second procedure (mean=5.5 days) [5].

Perino et al. reported similar results for the same parameters for laparoscopic hysterectomies: less hospitalization period (mean=2.4 days versus 6.2 days), minimal intraoperative bleeding (140.0 ml vs 406.0 ml) [6].

A randomized, multicenter study including 116 patients demonstrated that laparoscopic assisted vaginal hysterectomy can be performed in a similar operating time classic surgery with intraoperative blood loss less and a relatively shorter period of hospitalization ( $p < 0.01$ ). Postoperative pain, another important parameter discussed, is lower for the first 3 days of laparoscopy versus open surgery ( $p < 0.5$ ) [7].

In 2010, Naik et al. published a randomized trial comparing laparoscopic-assisted vaginal radical hysterectomy with abdominal radical hysterectomy in a group of 13 patients (7 patients receiving laparoscopic technique, 6 patients classical intervention) diagnosed with cervical cancer in stage IB1 with a follow-up period of 20 months. The results from minimally invasive and traditional method are statistically significant for the following parameters: catheter maintenance, 4 days versus 21 days, intraoperative blood loss of 400 ml versus 1000 ml, length of stay, less need for analgesics lower. Vaginal

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resection and the resection of utero-sacral ligaments is in each case less (1.26 cm, respectively 1.47 cm) than as compared to the classic approach (2.16 cm, respectively 4.68 cm), which suggests that the laparoscopic hysterectomy is less radical, noting that patients should be carefully selected [8].

Studies show that obesity is associated with a higher incidence of comorbidities and an increased risk of perioperative complications. The main cause of conversion of laparoscopy to laparotomy represents obesity. Many surgeons believe that obesity surgery prevents radical resection limiting parameters of the vagina and the number of lymph-nodes, which influence survival. In this regard, Park et al. conducted a study including 166 patients diagnosed with cervical cancer stages IA2-IIA2 and body mass index (BMI) of at least 30 receiving laparoscopic hysterectomy with pelvic lymphadenectomy (n=54) and classic method surgery (n=112). The authors suggest that the minimal invasive technique is preferred in the case of obese patients due to superior results in the resumption of bowel habits, length of hospitalization, post-operative complications and intra-operative blood loss [9].

Radicality of laparoscopic surgery in patients with cervical cancer can be compared with the classical method. Therefore, surgical excision parts were analyzed in a study by Ghezii et al. Results reported parameters resection was the same in class II radical hysterectomies performed laparoscopically or classic (2.4 cm vs. 2.3 cm), and in the case of class III hysterectomy no statistically significant differences (resection parameters 3.8 cm vs. 3.4 cm) [10]. For cases of cervical cancer in the early stages, IA2-IB1, Malzoni et al. published the results of a study conducted on a group of patients who received laparoscopic radical hysterectomy class II or III with lymphadenectomy. The results were similar to those in the literature, and namely, short hospitalization, no need for blood transfusion, negative resection margins [11].

Laparoscopic approach for cervical cancer has better results compared to open surgery. Laparoscopy provides improved results in the short term and at least equivalent results in terms of long-term recurrence when compared with open surgery. Spirtos et al. reported in a study conducted on a group of 78 patients with cervical cancer in stages IA2 and IB who received laparoscopic radical hysterectomy class III with pelvic and para-aortic lymphadenectomy mean operative time of 205 minutes, with the presence of 3 intraoperative cystotomies and one ureteral injury that required stenting. The average number of lymph nodes removed was 34. Recurrence rate at 3 years was 5.1% [12].

A study comparing the same parameters between the two methods reports that there were no differences in the histologic examination of the tissue resection of parameters, the vaginal resection and negative margins achieved. Postoperative morbidity was present in a larger number of patients for radical abdominal hysterectomy (53% vs 18%) [13].

One topic discussed in laparoscopic surgery for gynecological malignancies remains recurrence rate. Besides learning curve, laparoscopic radical intervention, pelvic and para-aortic lymphadenectomy are particularly important in oncological surgery. Yan et al. performed a study including 240 patients with cervical cancer stages IA2-IIB receiving laparoscopic radical hysterectomy and lymphadenectomy, with a conversion rate of 1.25%. The survival rate at 5 years was for IA2, IB1, IB2, IIA 100%, 82%, 66% and 60% respectively. The author suggests that in IA2-IB1 stages, laparoscopic intervention can be performed without compromising long-term survival. For locally advanced stages, laparoscopic technique requires more investigation [14].

### Laparoscopic and Robotic Learning Curve Technique in Gynecologic Pathology

Regarding the learning curve of the technique, Siren et al.

describes the first 100 laparoscopic hysterectomies performed for both benign and malignant pathology with an operating time from 45 minutes to 245 minutes with an average of 109 minutes. For the first 10 interventions, the average operative time was 180 minutes, for the last 20 hysterectomies it reach to 75 minutes, which emphasizes the importance of the learning curve [15]. Reade et al. concluded in a study that after a laparoscopy training in gynecological oncology, the learning curve is improving after only 23 cases, with reduced operative time, intraoperative blood loss decreases and the number of resected lymph nodes higher [16].

Another study compares the evolution of the parameters that help technique being feasible and safe for cancer cases (operating time, intra-and postoperative complications, length of hospital stay, number of lymph nodes removed, the rate of transfusion). In this regard were grouped top 50 and next 50 hysterectomies. Authors concluded that all of the aforementioned parameters were improved in group 2 [17]. Similar results were published by Hwang et al. for uterine cervical cancer in the early stages who received laparoscopic radical hysterectomy with lymphadenectomy. 35 patients were compared with the following 35 intervention. Operating time, the number of complications (9 vs 1) was significantly higher in the first group, no significant difference statistically in terms of the number of nodes excised, resection, parametrectomy, lymphovascular space invasion. The authors suggest that the learning curve reaching time from 40 cases [18].

The same reports are available in literature about robotic assisted laparoscopic hysterectomies, with decreased operative time after 20-30 intervention of this type [19]. Yim et al. performed a study of 65 cases of cervical cancer in the early stages that radical hysterectomy with pelvic lymphadenectomy was assisted robotic. Operative time was lower after the first 28 interventions with improved track parameters authors: reduce the bleeding, low rate of postoperative complications [20]. However, Schreuder et al. suggest that the 14 cases is sufficient to reduce the operating time with 48% [21].

### The Risk of Metastasis at Incision Trocars / Port-site Metastases

Another concern that arises when laparoscopic techniques are performed for the treatment of gynecologic malignancies is the incidence of metastases at incision trocars. Although this complication is recognized in ovarian cancer, it is very rare in cervical and endometrial cancer. To clarify the rarity of these metastases, Zivanovic et al. identify two cases of 1694 patients operated for gynecologic malignancies compared with 15 cases of ovarian cancer in the same batch. Specifically, in patients in whom recurrence of the incisions for trocars within less than 7 months after the original surgery, the overall survival rate is lower when compared with patients whose recurrence occurs more than 7 months [22]. Moreover, Chen et al. presents a prospective study that included 295 patients with cervical cancer, one patient with metastasis at the trocar incision [23]. As reported by Imachi et al. the incidence of port site metastases from squamous cell carcinoma of the cervix is 0.9% and 5.8% in cases of adenocarcinomas. Moreover, the risk of port-site metastasis in laparoscopic hysterectomy is 6-fold increase for the cases of advanced uterine cervical cancer [24].

Regarding laparoscopic radical hysterectomy for cervical neoplasia, the theory that is mentioned in the literature on the occurrence of metastases at incision trocars is based on the leak, remove carbon dioxide along trocars, phenomenon called "chimney effect" [25].

A systematic evaluation of the literature on this topic was conducted, and the results were presented in an article that included 1216 laparoscopic procedures performed for cervical cancer and endometrial cancer (921, 295 procedures, respectively). The incidence

of metastases to the incision site of the trocars was 0.43%, 0.33%, respectively [26].

One case of port-site metastasis following a robotic-assisted laparoscopic radical hysterectomy with bilateral pelvic lymph node dissection for a cervical adenocarcinoma has been described [27].

### Types of Laparoscopic Hysterectomies

Single Incision Laparoscopic Surgery (SILS), Natural orifice transluminal endoscopic surgery (NOTES) and is Robotic-assisted laparoscopic surgery (RALS) are the latest technique used in minimally invasive surgery.

Nomenclature LESS (Laparoendoscopic single-site surgery) was controversial and varied. It has been called single access/port/site/incision/trocar surgery, OPUS (one port umbilical surgery), and embryonic natural orifice transluminal endoscopic surgery (eNOTES).

The fundamental idea is to have all of the laparoscopic working ports entering the abdominal wall through the same incision. Single-incision laparoscopic surgery is an alternative to conventional multiport laparoscopy. The advantages of single-access laparoscopic surgery may include less bleeding, infection, and hernia formation and better cosmetic outcome and less pain. The disadvantages and limitations include longer surgery time, difficulty in learning the technique, and the need for specialized instrument [28].

Hysterectomy is one of the most common surgical procedures performed in women. In the United States it is estimated that one third of women undergoing hysterectomy by age 60 years [29]. Use of a single incision for laparoscopic hysterectomy was described in the early 1992. Reducing the number of punctures might potentially reduce morbidity from bleeding, port-site hernias, and internal organ damage and have cosmetic benefits [30].

In surgery field, there has been a continued push toward decreasing the complications associated with large surgical incision sites and its other associated disadvantages. With the advent of laparoscopic surgery, it can now minimize the size of the incision. The Laparoscopic Robot has accorded the benefit of mobility with each of the Robot arms having seven degrees of mobility and great visualization with the high definition 3D (dimensional) laparoscopic camera. The single port laparoscopic system allows several ports to be introduced into the abdomen via one central incision. The size of the port is about 4 cm and fits through a 2 cm incision. Once healed, the scar is virtually unnoticeable [31].

A study by Fader et al. included 13 patients with various gynecological malignancies that surgery (laparoscopic or robotic) was performed through a single incision, LESS. Median operating time was 65 min. All procedures were successfully performed via a single incision and no post-operative complications occurred. The majority of patients required no narcotics post-operatively [32].

Tergas et al. reported the case of a patient diagnosed with stage IB1 cervical cancer who received radical hysterectomy type LESS, bilateral ovariectomy and lymphadenectomy through an umbilical incision 2 cm. Operative time was 251 minutes without intra- or postoperative complications. Tissue parameters and the 16 lymph nodes resected showed no tumor aspects [33].

In a multicenter retrospective study conducted on a group of 46 patients with uterine cervical cancer stages IA2-IB1/IIA1, of which 19 patients received radical hysterectomy through a single incision, and 27 laparoscopic technique (in addition to umbilical trocar were placed 3 other trocars), the results were significant in terms of operating time (270 minutes versus 180 minutes). There were no differences between the two groups in relation to the type of radical hysterectomy, number

of lymph nodes resected or perioperative complications. The percentage of patients in first group who were discharged on day 2 postoperative was 57.9% versus 25.0% ( $p=0.030$ ) [34].

### Robotic Surgery for Uterine Cervical Cancer

Robotic-assisted laparoscopy was performed to prevent the disadvantages of conventional laparoscopy. It emerged as a revolutionary technology and has spread in less than a decade in many surgical fields, including urology, cardiothoracic surgery, pediatric surgery and general surgery. The first robotic procedure in gynecologic surgery was performed in 1998 [35]. The da Vinci System has been approved by the Food and Drug Administration for gynecologic surgery in 2005 [36].

This technology has advantages such as a relatively short learning curve, eliminating tremor, increased surgical dexterity and handling of the wrists, 3D visualization, digital zoom, camera stability, motion scaling, 7 degrees of freedom, ergonomic advantages for the surgeon, fulcrum effect, telesurgery and remote surgical education. However, robotic surgery has some disadvantages: loss of feeling of the surgeon, the high cost of equipment for increased assembly and disassembly of the robot.

Using robotic surgery is considered to be associated with low operative time, increased accuracy, improved dexterity, faster suture, fewer errors compared to open surgery or laparoscopic method. However, there is debate on two issues: oncological outcomes and safety intervention. A systematic evaluation of the literature regarding surgical treatment of cervical cancer in the early stages has been completed and the results were presented in an article that included 1339 patients who received laparoscopic radical hysterectomy, 1552 patients with abdominal radical hysterectomy and 327 patients who underwent robotic-assisted radical hysterectomy. Data were collected from international databases (MEDLINE, EMBASE, BioMed Central, Cochrane Database of Systematic Reviews (CDSR) and were finally selected 320 articles relevant to the topic proposed. Average loss was significantly greater in abdominal radical hysterectomies compared with laparoscopic and robotic techniques ( $p<0001$ ). As is the oncologic outcomes, the average number of nodes removed in the three types of procedures was similar. A single resection margin was positive in a study that belonged robotic surgery. Postoperative morbidity was significantly higher in open surgery compared to the other two techniques regarding wound infection. The number of cystotomies and vessel damage is slightly higher than the laparoscopic method for the two techniques [37].

Minimally invasive surgery is used in locally advanced cervical cancer without notable adverse effects reported prognosis and overall survival. A study by Vizza et al. on this topic, including patients with neoadjuvant chemotherapy for locally advanced cervical cancer (IB2-IIb) and robotic radical hysterectomy is practiced. It was reported one intraoperative and 19 postoperative complications. At a follow-up of 28 months, 83% of patients had no recurrence [38].

Minimally invasive techniques provide a lower rate of complications during surgery as compared to open surgery, which is appropriate tissue due to handling and better anatomical views. Sert and Eraker reported for robotic radical hysterectomies to 25 patients, 3 cases of bladder injury, which was repaired everything about robotics [39].

A review comparing hysterectomy vs. radical robotic laparoscopic radical hysterectomy for cervical cancer in the early stages identifies a 6% rate of intraoperative complications, with low urinary vascular lesions where robotic surgery [40]. Estap et al. report a single cystotomy in a patient who has had three previous cesarean section and two cystotomies in the laparoscopic group [41]. Ko et al. compare with conventional radical hysterectomy hysterectomy 32 cases with 16

robotic radical hysterectomy: there was no complication in the robotic group, while in open surgery group was reported section of the ureter, requiring surgical repair [42]. Magrini et al. report the results of a study conducted on a group of 27 patients with robotic radical hysterectomy compared with laparoscopic and open techniques, results showing a similar operative time for robotic surgery and classical method. Blood loss, length of hospital stay was the same for laparoscopy and robotics, and significantly lower compared with conventional surgery [43].

With the new classification of radical hysterectomy proposed by Querleu in 2008, the literature shows the results of nerve-sparing technique in robotic surgery in cervical cancer. Gil-Ibanez et al. reported three robotic radical hysterectomies interventions types B1 and C1. The average operating time was 260 minutes. During postoperative follow (mean=13.7 months), 3 patients reported anorectal dysfunction. No patient had recurrence. The authors suggest that nerve-sparing technique is attractive in robotics because it allows a good quality visualization of blood vessels and autonomic (sympathetic and parasympathetic branches) of the bladder and rectum, allowing the procedure to be feasible and safe in view of oncology [44].

Parametrectomy, another important element for the assessment of surgical radicality in cervical cancer, was studied by Ramirez et al. who reported 5 cases of robotic parametrectomy and pelvic lymphadenectomy, with one intraoperative complication and two postoperative complications in the same patient (vesico-vaginal fistula and lymphocele). Surgical excision specimen was not infiltrated the tumor [45].

## Discussion

Minimally Invasive Gynecologic Oncology Surgery lasted many years to practice acceptance, largely because of the lack of results in terms of distance recurrence in cancer, but also because of the need to conduct training for advanced laparoscopic techniques.

Laparoscopic treatment of cervical cancer provides benefits on increasing comfort with decreased convalescence time, but these cases should be reserved for oncologic surgical oncologist with extensive experience in laparoscopic procedures.

One of the most important advantages of minimally invasive surgical techniques is the short duration of hospitalization. According to the literature, robotic surgery offers other advantages, such as intra-and postoperative complications with a low rate of occurrence, minimal postoperative pain. All of this positively affects quality of life, with rapid reintegration daily activities, which provides medical benefit, socially and economically. However, the cost of the machine DaVinci is a limiting factor for the development of robotic surgery, however, indirect costs related to the reduction in the duration of hospitalization, and complications must be taken into account.

## Conflict of interests

The authors have no conflicts of interest to declare.

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