Endoscopic Surgical Procedures for Cervical Cancer Treatment: A Literature Review

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1 Introduction

Cervical cancer is the second most common cancer in women worldwide and is a leading cause of cancer-related death in women in underdeveloped countries. Worldwide, approximately 500,000 cases of cervical cancer are diagnosed each year: approximately 13,000 cases of invasive cervical cancer and in the USA 50,000 cases of cervical carcinoma in situ (i.e., localized cancer) are diagnosed yearly. In developed countries, over the last 40 years, cervical cancer death rate has decreased by more than 70% because pre-invasive lesions and cervical cancers were detected at an earlier stage (Tinelli *et al*., 2009b).

Cervical cancer is always associated with a HPV infection, since a carcinogenic human papillomavirus (HPV) infection is necessary for the development of cervical cancer (Tinelli *et al*., 2007). Cervical cancer risk seems to be influenced by other variables too, like smoking and immunodeficiency. Infection with other sexually transmitted viruses seems to act as a cofactor in the development of cervical cancer (Tinelli *et al*., 2009a).

We will focus on fertility-sparing techniques such as radical trachelectomy and on the area of minimally invasive treatment of cervical cancer, since this tumor can be safely and feasibly managed from minimally invasive endoscopic radical operations, such as hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy for surgical treatment.

2 Cervical Cancer Staging and Radical Hysterectomy Classification

Correct staging of advanced cervical cancer is essential to optimize its oncological treatment. However, the new FIGO classification is limited to clinical findings and does not include complex imaging. The rationale is to provide a template allowing both resource-rich and resource-poor countries to compare data by stage so as to standardize management of the disease. It can be difficult to accurately assess parametrial and sidewall invasion, as well as metastases to lymph nodes, using clinical staging alone. These are the limitations of FIGO clinical staging.

The purpose of the staging system is to provide uniform terminology for better communication among health professionals and to provide appropriate prognosis for the patients resulting in treatment improvement (Pecorelli *et al*., 2009). This is a constantly evolving process as new therapeutic modalities are being developed and new imaging and surgical approaches are applied. In those countries where medical research and more prognostic information has become available, in recent years, new knowledge has boomed.

A constantly evolving process is also being applied in surgery techniques. The term “radical” or “extended” hysterectomy encompasses various types of surgery. Since the first publications of large series of surgeries for cervical cancer by Wertheim in Austria (Wertheim, 1912) and later by Okabayashi in Japan (Okabayashi, 1921) and Meigs in the USA (Meigs, 1944), many radical procedures according with different degrees of radicality have been described and performed.

The problem with all these procedures is that they name the same anatomical structures differently and define these structures according to different anatomic interpretations. In this scenario, the Piver–Rutledge–Smith classification published in 1974 has achieved substantial popularity (Piver *et al*., 1974). It describes five classes of radical hysterectomy (Symmonds, 1975) including a class I category, which is not radical hysterectomy, and a class V category, which is no longer used. The rationale and anatomic definitions for differentiation between class III and IV are unclear. Surgeons frequently need to define

intermediate classes inbetween classes II and III (eg, II-III or II-and-a-half). The original paper does not refer to clear anatomical landmarks or international anatomical definitions. The vaginal extent of resection is systematically attached to the pericervical extent; vaginal resection is excessive—from a third to three-quarters of the vagina.

The classification by Piver *et al*. (1974) does not take into account the idea of nerve preservation that was introduced in the 1950s (Kobayashi, 1961) and subsequently refined by Japanese surgeons (Fujii *et al*., 2007; Sakuragi *et al*., 2005) and adopted by European surgeons (Raspagliesi *et al*., 2004; Trimbos *et al*., 2001). The Piver–Rutledge–Smith classification applies to open surgery only. Querleu & Morrow (2008) recently published a new radical hysterectomy classification, based, for simplification's sake, on only the lateral extent of uterine resection.

Only four types of radical hysterectomy are described, adding a few subtypes when necessary. Instead of the classification by Piver *et al*. (1974), stable anatomical landmarks are used to define the limits of resection. To make a clear distinction with the Piver–Rutledge–Smith, in the Querleu and Morrow classification (Querleu *et al*., 2008) letters are used rather than numbers to define classes. Simple hysterectomy is not included in the classification. Lymph-node dissection, an essential part of surgical cervical cancer management, is considered separately. For lymph-node dissections, the limit between level 1 and level 2 is the bifurcation of the common iliac artery; the limit between level 2 and level 3 the bifurcation of the aorta; and the limit between level 3 and level 4 the inferior mesenteric artery.

3 History and Evolution of Surgery in Cervical Cancer

The ancient Egyptians used bamboo knives and in ancient India volcanic glass, obsidian, was used to operate on patients. Over 1,000 years later until now, steel scalpels have been used to perform surgery. Only 200 years ago, in 1809, the first documented laparotomy was performed for a gynaecological tumour by Ephraim McDowell, who removed an ovarian cyst.

Since the late nineteenth century until now, surgery, and in particular radical surgery, has taken an astonishingly conservative approach. The same technique for radical cervical surgery surgery as introduced by Wertheim in 1896 (Wertheim, 1912) is still being used today, and gynaecological oncological surgeons are very reluctant to change even minor details of this operation. Essentially, radical gynaecological surgery has remained fairly standard and unchanged. Although a first attempt at laparoscopy, on his dog, was made by Georg Kelling in 1901, it took until the 1970s for laparoscopy to be introduced into gynaecological surgery. In the beginning, it was only used for diagnostic purposes and sterilizations. As recently as 1989, the first series of 'laparoscopically assisted vaginal hysterectomy' were reported by Harry Reich (Reich & DeCaprio, 1989).

Two years earlier, Dargent (1987) had described the use of laparoscopy as 'presurgical retroperitoneal pelviscopy for Schauta's operation' in preparation for the vaginal approach for cervical cancer. In 1992, Nezhat (1992) performed the first laparoscopic radical hysterectomy with pelvic and para-aortic lymph node dissection. In 2000, Dargent *et al.* (2000) reported successful laparoscopic vaginal radical trachelectomy and pelvic lymphadenectomy for young women with cervical cancer, who wanted to preserve their fertility. In 2000, Possover *et al.* (2000) reported modified laparoscopic nerve sparing type III radical hysterectomy for cervical cancer and found that this procedure decreased postoperative bladder dysfunction incidence subsequently Pomel *et al.* (2003) evaluated, in a series of 50 consecutive patients,

the feasibility, morbidity, and survival outcome of laparoscopic radical hysterectomy for carcinoma of the uterine cervix.

With technical advances and emerging devices, as well as accumulating experience in laparoscopic surgery, some surgical procedures that are difficult to carry out even by traditional open procedures can be performed successfully by laparoscopy. The major advantages associated with minimally invasive laparoscopy are, amongst others, lower intraoperative bleeding rates, less post-operative pain, a shorter recovery time and a shorter hospital stay.

In addition, the optical devices used for laparoscopic surgery feature a 10 to 15 times magnification and, therefore, provide an excellent view of pelvis anatomy.

During the past decade some reports, on a limited number of patients, have shown the feasibility of radical resection by laparoscopic surgery and have documented an equivalent number of pelvic nodes harvested by laparoscopy and open surgery (Canis *et al*., 1995; Hsieh *et al*., 1998; Kim *et al*., 1998; Krause *et al*., 1995; Pomel *et al*., 1997; Sedlacek *et al*., 1994; Spirtos *et al*., 1996). Nevertheless, few long-term data on the morbidity and survival after laparoscopic radical hysterectomy are available. In gynecological oncology laparoscopic surgery does not substantially reduce tissue trauma, which makes it possible for extensive and complex operative procedures to be performed through small incisions, reducing intra-operative blood loss and impact on the body as well as common surgical complications. In addition, laparoscopic surgery is superior to conventional surgery with regard to postoperative mental rehabilitation in gynecological oncology patients.

From the original publications on this radical hysterectomy surgery, surgical technique has aimed at a re-classification including a variety of techniques via laparotomy (Averette *et al*., 1993; Magrina *et al*., 1999), then via laparoscopy, resulting in reasonable morbidity with similar surgical outcomes (Abu-Rustum *et al*., 2003; Magrina, 2005). However, longer operating times, steep learning curves, and lack of training have prevented laparoscopic treatment from becoming a widely adopted surgical approach to radical hysterectomy (Boggess, 2007; Ramirez *et al*., 2006). Although open radical hysterectomy is still considered the gold standard for the treatment of early cervical cancer (Abu-Rustum *et al*., 2001), laparoscopic radical (LRH) and laparoscopy-assisted radical vaginal hysterectomy (LARH) are evolving as potential surgical alternatives. The principles are: to resect tumor and its surrounding tissues en bloc, to use tumor-free techniques when manipulating tumors, to preserve sufficiently incised margins, and to perform complete pelvic lymphadenectomy. Lymph node status is the most important prognostic factor in gynecologic tumor and surgical removal of the pelvic. Para-aortic lymph nodes for histological assessment are part of gynecologic malignancies staging. Hence, laparoscopic surgery is consistent with the concept of minimally invasive surgery, i.e., smaller trauma, milder pain or analgesia, better homeostasis, more accurate operative outcomes, shorter hospital stay and better psychological effects than current standard open surgery. As a technical innovation, laparoscopic techniques for gynecological oncology do not change gynecological oncological surgery fundamentally, but they have improved surgical techniques for gynecological oncology in many aspects, and enhanced the efficacy of surgical cervical cancer treatment.

Additionally, removal of bulky lymph nodes may have therapeutic benefit. According to the requirement by established FIGO classification systems, a different range of lymphadenectomy will be performed depending on the different type of tumor present. The range of lymphadenectomy, consistent with that of open abdominal surgery, depends on cervical cancer disease. Lymph nodes, para-aortic and iliac vessels are resected within the vessel sheath. Obturator and deep inguinal lymph nodes, including lymph nodes below the obturator nerve, must be resected radically.

The indication for laparoscopic surgery was similar to open surgery in cervical cancer patients. According to literature and our experience, the indication for laparoscopic radical hysterectomy (type III) and pelvic lymphadenectomy was earlier than the FIGO stage IIa in cervical cancer (Malzoni *et al*., 2004). The indication for this surgical procedure is mainly influenced by the experience of the surgeon (Lecuru *et al*., 1998). More recently, it was reported that stage IIb or more advanced cervical cancer may be treated with type IV radical hysterectomy under laparoscopy (Chen *et al*., 2008; Possover *et al*., 1998; Querleu *et al*., 2008), as the aim of surgery is to stage and radically resect the tumor (including metastases). For certain patients, prolong survival is the objective of tumor treatment.

4 Laparoscopic and Robotic-assisted Approaches in Gynaecological Malignancies

The goal of laparoscopic surgery is to duplicate traditional open procedures via small incisions in the skin with surgical outcomes equivalent or superior to a traditional surgical approach. Laparoscopy offers multiple advantages in the management of malignancy, including smaller incisions, shorter hospital stay, quicker recovery, improved visualization, less need for postoperative analgesics, and a lower risk of complications, such as blood loss, wound infection, herniation, and ileus. These characteristics may prove particularly important in the setting of oncology where a shorter recovery period may facilitate a shorter interval to postoperative treatments such as chemotherapy or radiation. Laparoscopy also has its limitations. Disadvantages include a long learning curve, counterintuitive motions, and limited depth perception as imaging is limited to 2-dimensional views.

In an effort to overcome these limitations, multiple innovations have evolved over the last decade. Laparoscopic instrumentation has expanded to include several different vessel sealing devices with integrated cutting capabilities, endoscopic staplers, articulating instrument tips, 3-dimensional capabilities, and computer-enhanced technology in the form of robotics. Therefore, robotic surgical systems seem to be the future in gynecologic surgery, since robotic technology can improve accuracy, enhance dexterity, and provide for faster suturing and a lower training curve than laparoscopy. All of this makes gynecologic surgeons tend to perform a greater number of gynecologic procedures by robotic approach, when available. In the last five years, a large number of robotic surgery related papers have been published, both for benign and oncological cases, which is proof of the rapid spread and high acceptance of this new technology.

Gynecological oncology probably presents the optimal forum for application of robotics, given the complexity of surgical steps involved in performing radical hysterectomies for cervical cancer and lymph node sampling for endometrial cancer. Radical hysterectomy was one of the first indications for robot-assisted laparoscopy, as this made it possible to perform a complex and long procedure laparoscopically. Studies comparing the results of robot-assisted and conventional laparoscopic surgery yielded slightly different but conflicting results. Boggess *et al.* (2008) found a rate of 7.8 % for major complications after robotic surgery, compared with 16.3 % after conventional laparoscopic surgery, whereas Kruidenberg *et al.* (2011) found just the opposite, with 9.6 % and 5.5 %, respectively (statistically significant differences in both studies). Survival after both modalities seems to be similar.

5 The History of Laparoscopy in Cervical Cancer

In 1989, Querleu *et al.* (1989) performed the first laparoscopic pelvic lymphadenectomy for cervical cancer, then, in 1990, Canis *et al*. (1990) described a totally laparoscopic radical hysterectomy. In 1991, Querleu *et al.* (1991) reported laparoscopic pelvic lymphadenectomy and vaginal assistant radical hysterectomy for early cervical cancer. In 1992 and in 1993, Nezhat *et al.* (1992; 1993) reported the first case of cervical cancer treated with laparoscopic radical hysterectomy and pelvic lymphadenectomy. Since then, the techniques have been applied clinically and achieved satisfactory clinical outcomes, Vaginal radical trachelectomy and laparoscopic pelvic lymphadenectomy were done by Dargent *et al.* (1996).

In 2000, Possover *et al.* (2000) reported modified laparoscopic nerve sparing type III radical hysterectomy for the treatment of cervical cancer, and found that this procedure decreased the incidence of postoperative bladder dysfunction. In 2003, Pomel *et al.* (2003) reported the feasibility, morbidity, and survival outcome of the laparoscopic radical hysterectomy for carcinoma of the uterine cervix, operated between 1993 and 2001 at two cancer centers. Thirty-one patients had prior brachy therapy. The median overall operative time was 258 min. The mean number of harvested pelvic external iliac nodes was 13.22 per patient. The median postoperative hospital stay was 7.5 days. Two patients had major urinary complications; one had a bladder fistula and one ureteral stenosis. Median follow-up was 44 months. Overall 5-year survival rate of FIGO stage Ia2 and Ib1 patients was 96%. Their results demonstrated that radical hysterectomy can be performed by laparoscopy in stage IB1 or less advanced node negative cervical cancer patients without compromising survival; moreover, prior brachytherapy did not affect the feasibility of this radical procedure.

With technical advances and emerging devices, as well as accumulating experience in laparoscopic surgery, some surgical procedures that are difficult to carry out even by traditional open procedures can be performed successfully by laparoscopy. During the past decade some reports, on a limited number of patients, have shown the feasibility of a radical resection by laparoscopic surgery and have documented an equivalent number of pelvic nodes harvested by laparoscopy and open surgery (Gil-Ibáñez *et al*., 2013; Kho *et al*., 2009; Krause *et al*., 1995; Pomel *et al*., 1997; 2003; Sedlacek *et al*., 1994). Nevertheless, few long-term data on the morbidity and survival after laparoscopic radical hysterectomy are available. Although open radical hysterectomy is still considered the gold standard for the treatment of early cervical cancer (Spirtos *et al*., 1996), laparoscopic radical (LRH) and laparoscopy assisted radical vaginal hysterectomy (LARH) are evolving as potential surgical alternatives.

LRH or LARH have been established as standard procedures routinely performed as first line therapy for the treatment of early cervical cancer at specialized centers (Hatch, 1996; Kohler *et al*., 2004; Obermair *et al*., 2003; Pomel *et al*., 2003). The major advantages associated with minimally invasive laparoscopy are, amongst others, lower intraoperative bleeding rates, less post-operative pain, a shorter recovery time and a shorter hospital stay. In addition the optical devices used for laparoscopic surgery feature a 10 to 15 times magnification and, therefore, provide an excellent view of pelvis anatomy. Since Liang *et al.* reported their initial experience with 57 LRH; they have continuously improved and standardized the technique (Liang *et al*., 2006; Querleu, 1990). The indication for laparoscopic surgery was similar to the indication for open surgery in cervical cancer patients. According to literature and experience, the indication for laparoscopic radical hysterectomy (type III) and pelvic lymphadenectomy was earlier than the FIGO stage IIa in cervical cancer (Liang *et al*., 2006). However, initially, laparoscopic technique treatment of cervical cancer is associated with a high complication rate so the indication must be carefully assessed, and patients have to be counseled extensively prior to surgery. Apart from the size

and stage of the tumor, the indication for this surgical procedure is mainly influenced by the experience of the surgeon (Malzoni *et al*., 2004).

More recently, it was reported that stage IIb or more advanced cervical cancer may be treated with type IV radical hysterectomy under laparoscopy (Chen *et al*., 2008; Lecuru *et al*., 1998; Querleu & Morrow, 2008), as the aim of surgery is to stage and radically resect the tumor (including metastases). For certain patients, prolonged survival is the objective of tumor treatment. Through laparoscopic exploration, the feasibility and thoroughness of surgery can be evaluated, and the relative benefits of surgery for the patient can be weighed. However, it is still controversial what types or what stages of cervical cancer should be adopted for laparoscopic surgical treatment.

Another minimally invasive surgical option used for cervical cancer is laparoscopically assisted vaginal radical hysterectomy (LAVRH) or Coelio-Schauta procedure. The Coelio-Schauta procedure consists of 2 major steps, 1 laparoscopic and 1 transvaginal. Four trocars are inserted, 1 transumbilical, 2 lateral to the inferior epigastric vessels, and 1 in the right lower abdomen. Traditionally, laparoscopy has been used to develop the paravesical and pararectal spaces and to perform lymphadenectomy of iliac vessels. In the transvaginal step, the urinary bladder is dissected from the cervix, the posterior cul-de-sac is opened, and the ureters are identified before their insertion into the bladder pilar; then the uterine arteries are ligated, and the cardinal ligaments are transected 3 cm from the cervix. Ligation of the utero-ovarian ligaments (or the infudibulopelvic ligaments if ovarian preservation is not mandated) is then performed, the round ligament is resected, and the specimen is extracted (Schneider *et al*., 1996).

A recent review of Pergialiotis *et al* (2013) on LAVRH on Medline (1966-2013) and Scopus (2004-2013), as well as on reference lists from all included studies, retrived 10 studies: including 6 retrospective cohort studies, 2 prospective cohort studies, 1 retrospective randomized trial, and a phase II randomized control trial.LAVRH provided equal recurrence-free rates when performed in patients with tumors not exceeding 2 cm in greatest diameter. Its main advantages seem to be less intraoperative blood loss and more radical pelvic lymphadenectomy. The primary disadvantages of the technique are a higher rate of disease-positive surgical margins, resulting in the need for adjuvant therapy, and the slow learning curve required for a surgeon to gain expertise.

6 Total Laparoscopic Radical Hysterectomy for Cervical Cancer

Laparoscopy can be safely and adequately used in the treatment of endometrial, ovarian and cervical cancer (Possover *et al*., 1998). In the setting of gynecologic oncology, laparoscopic approaches have been implemented in radical hysterectomy. For gynecological oncology laparoscopic surgery is an important step forward combining scientific, technological and surgical techniques, which not only enhance the efficacy of surgical treatment of gynecological oncology, but are also superior to conventional open surgery with regard to postoperative mental rehabilitation in gynecological oncology patients. The first total laparoscopic radical hysterectomy with lymphadenectomy was reported in June 1989 by Nezhat *et al.* (1992). Since then, more than 600 cases of total laparoscopic radical hysterectomy have been reported. A recent prospective case-control series compared total laparoscopic radical hysterectomy with abdominal radical hysterectomy and found shorter hospital stays and lower blood loss as well as a statistically significantly higher nodal yield among total laparoscopic radical hysterectomy cases (Zakashansky et al., 2007).

Spirtos *et al.* (2002) described 78 patients with early-stage cervical cancer undergoing laparoscopic radical hysterectomy. In that series, 94% of the procedures were completed laparoscopical.Mean fol-

low-up time was 67 months. Mean operative time was 205 min, and mean blood loss was 225 mL. One patient required a blood transfusion, three patients had unintended cystotomies, two patients required laparotomy to control bleeding, and one patient suffered an ureterovaginal fistula. Three patients had microscopically positive or close margins. The authors reported a cervical cancer recurrence rate of 5%.

Pomel *et al.* (2003) reported 50 patients with stage IA1–IB1 cervical cancer who underwent total laparoscopic radical hysterectomy. The median operating time was 258 min, and the mean number of lymph nodes harvested was 13. No conversions to laparotomy were reported. Median hospital stay was 7.5 days. The authors reported that 10 patients had early complications (within 2 months of surgery) and that three of those patients required reoperation. They also reported three patients had late complications (more than 2 months after surgery) two of them requiring reoperation. Three patients experienced recurrence with a median follow-up time of 44 months.

Frumovitz *et al.* (2007) compared 35 patients undergoing total laparoscopic radical hysterectomy with 54 undergoing total abdominal radical hysterectomy. Mean estimated blood loss was significantly lower in the laparoscopic-surgery group than in the open-surgery group (319 vs. 548 mL; p=0.009). Mean operative time was significantly longer with laparoscopic surgery (344 vs. 307 min; p=0.03), but median hospital stay was significantly shorter (2.0 vs. 5.0 days, pb0.001). Postoperative infections were much less common after laparoscopic surgery (18% vs. 53%; p=0.001). Notwithstanding the obvious advantages of conventional laparoscopy, recent surveys of practicing gynecologic oncologist revealed that most respondents believed minimally invasive surgery by conventional laparoscopy had only a minimal role in the management of cervical cancer (Fastrez *et al*., 2009).

Puntambekar *et al.* (2007) reported a retrospective review of 248 patients with FIGO stage Ia2 (n=32) and Ib1 (n=216) cervical cancer who underwent a TLRH (type III) with bilateral pelvic lymphadenectomy, which is the largest single-institution study. The operation was performed entirely by laparoscopy in all patients and by the same surgical team. Median operative time was 92 min. Median number of resected pelvic nodes was 18. Median blood loss was 165 ml. Median duration of hospital stay was 3 days. None of the patients required conversion to laparotomy. Seventeen patients had complications within 2 months of surgery. Seven patients had recurrences after a median 36-month follow-up. They concluded that TLRH can be performed safely, reduces morbidity associated with ARH and is an easily replicable technique.

Colombo *et al.* (2009) evaluated surgical outcome and oncologic results of total laparoscopic radical hysterectomy (TLRH) after neoadjuvant chemoradiation therapy (CRT) for locally advanced cervical carcinoma. All patients who underwent TLRH after CRT for stages IIB–IIA and bulky IB diseases were reviewed. The control group for this analysis was a cohort of patients treated with abdominal radical hysterectomy (ARH) after CRT for the same stage cancers. They reviewed 102 patients operated on between 2000 and 2008 (46 TLRH and 56 ARH). Mean age at diagnosis was 44 years, and mean B.M.I was 22.1. There was no difference in tumor characteristics between the two groups. Seven patients in the laparoscopic group required conversion to laparotomy (15%). Mean estimated blood loss (200 vs. 400 mL, pb0.01) and the median duration of hospital stay (5 vs. 8 days, p<0.01) were significantly lower in the laparoscopic group. Morbidity rates and urinary complications were reduced in the laparoscopic group (p=0.04). Local recurrence rates, disease-free and overall survival were comparable in the two groups. Best survival was observed for patients with pathological complete response or microscopic residual disease compared to patients with macroscopic residues (pb0.01). Authors concluded that radical hysterectomy after CRT, with significant morbidity rates, is known to be difficult and remains controversial in comparison to exclusive CRT. TLRH after preoperative CRT is feasible in 85% of the cases for patients

with locally advanced cervical cancer. For these patients, TLRH compared with ARH was associated with favorable surgical outcome with comparable oncological results.

Although laparoscopic surgery has many advantages, it is also associated with a number of potential drawbacks, including limited range of intra-abdominal motion (only 4° of freedom), counterintuitive movements, amplification of tremors in prolonged cases due to the length and rigidity of the instrumentation, and reduced depth perception secondary to a two-dimensional view. Naturally, total laparoscopic radical hysterectomy is not without its risks and complications.

There are still several new challenges to be met regarding theory and enhancement of surgical skils (Persson *et al*., 2008). Firstly, to form a laparoscopic surgical team, a lot of special requirements relating to both the team members and the equipment have to be met, thus restricting the popularization of laparoscopic radical hysterectomy. Secondly, every detail should be taken into careful consideration, risks should be balanced and benefits ascertained before performing laparoscopic procedures. Moreover, it is likely that well-known barriers to the implementation of advanced minimally invasive procedures such as association with a long learning curve, lack of training, complexity of the operations, limitation of technology and instrumentation, and the necessity of an expert assistant were responsible for this sentiment. For these reasons, only a few surgeons have adopted a laparoscopic approach to type III cervical cancer radical. There are issues with the length of the procedure, as type III laparoscopic hysterectomies take significantly longer than open cases. Furthermore, intraoperative complications of the urinary tract (for example as a result of thermal injuries) tend to be much more common in laparoscopic than in open cases (Xu *et al*., 2007).

A recent experience of Malzoni *et al.* (2009) on 71 patients treated by total laparoscopic radical hysterectomy (type II, III) with lymphadenectomy was done between January 2000 and March 2008. The authors concluded that total laparoscopic radical hysterectomy can be considered a safe and effective therapeutic procedure for the management of early stage cervical cancer with a low morbidity, offering an alternative option for patients undergoing radical hysterectomy, although multicenter studies and long-term follow-up are required to evaluate the oncologic outcomes of this procedure.

A literature review on laparoscopic radical hysterectomy demonstrates the procedure is also safe and feasible, but is associated with an operative time range of 205 min–371 min, an estimated blood loss of 200 cc–445 cc, a nodal yield ranging from 13–25, a hospital stay ranging from 1–7.5 days, and an overall complication rate of 11%–20%, as sorted by the referenced papers who provide a good cross section of the data (Abu-Rustum *et al*., 2003; Magrina, 2007; Pomel *et al*., 2003; Ramirez *et al*., 2006; Spirtos *et al*., 1996; 2002).

7 Contra-indications to Laparoscopic Surgery for Gynecological Oncology

As previously noted, there are very few absolute contra-indications. However, with increased anesthesia ability, some of these may not be considered as absolute. Severe cardiac diseases could be a problem, since some patients may not tolerate the operation due to the deep Trendelenburg positions necessary during most operative laparoscopy in order to maintain an adequate pneumoperitoneum. Severe patient liver/renal/respiratory dysfunction, which cannot be corrected preoperatively, is also considered to be an absolute contraindication.

Surgeons may refuse laparoscopy for advanced or late stage gynecological tumor in patients with stage III or above cervical carcinoma, lymph node metastases of cervical cancer which inter-fuse and encapsulate vital vessels, and/or extensive infiltration of adjacent tissues. On the other hand, there are few relative contra-indications to laparoscopy for cervical cancer patients; for example, severe abdominal adhesions or morbid obesity and so on.

8 Total Robotic-assisted Laparoscopic Radical Hysterectomies

Today there is only one U.S. Food and Drug Administration approved device for surgical robotics. This current robotic platform is known as the "da Vinci" surgical system, developed by Intuitive Surgical, Inc. (Intuitive Surgical, Mountain View, CA, USA). The da Vinci surgical system is equipped with a 3-dimensional vision system in which double endoscopes generate two images resulting in perception of a 3D image. In addition, with the development of endowrist, it reproduces the range of motion and dexterity of the surgeon hand, providing high precision, flexibility and the ability to rotate instruments 360 degrees. Thus, the learning curve of achievement for the surgeons using the da Vinci surgical system was shortened. In 2001, a more advanced da Vinci surgical system with four robotic arms gained US FDA approval and is now being used in many surgical procedures throughout the world.

Recently, FDA-approved robotic surgery has become an option in the definitive surgical management of early stage cervical cancers. Several case series about robotic-assisted radical hysterectomies for cervical cancer have now been published (Boggess, 2007; Kim *et al*., 2008; Magrina *et al*., 2008; Magrina, 2007; Malzoni *et al*., 2004; 2009).

The initial experience and the first publications on robot assistance in gynecological oncology date from recent years. In February, 2006, Boggess (2005) performed the first live telecast, demonstrating a technique for performing robotic-assisted radical hysterectomy and subsequently presented data for a series of 13 radical hysterectomies at the Society of Gynecologic Oncologists annual meeting in March of the same year. Since this initial demonstration of feasibility and technique, the interest in robotic-assisted gynecologic oncology procedures has spread rapidly.

Recently, Nezhat *et al.* (2008) prospectively compared the outcomes of 13 total robotic-assisted laparoscopic radical hysterectomies to 30 cases of traditional total laparoscopic radical hysterectomy with pelvic lymphadenectomy in patients with stage IB to IIA cervical cancer. There was no difference in operative time, hospital stay, blood loss, complications, or number of nodes retrieved. This study suggests that robotic radical hysterectomy may be a feasible alternative to total laparoscopic radical hysterectomy (unpublished data). However, there were no advantages of robotic-assisted procedures compared to traditional total laparoscopic radical hysterectomy when performed by an experienced laparoscopic gynecologic oncologist.

Fanning *et al.* (2008) reported the first series of robotic radical hysterectomy on 20 women with stage IB–IIA cervical carcinoma. Median operative time was 6.5 hours, and median blood loss was 300 mL.No complications were encountered, and all patients were discharged home on the first postoperative day. A retrospective cohort study of robotic vs. open radical hysterectomy found that the mean blood loss was significantly lower for the robotic group (81.9 vs. 665 mL, $p<0.0001$), but operative time was longer (4.5 vs. 3.39 hours, $p=0.0002$). The mean number of lymph nodes resected did not differ, and no complications were reported in the robotic assisted group (Ko *et al*., 2008). Furthermore, laparoscopic radical hysterectomy studies, although variable, report an operating times from 92 to 350 minutes, an estimated

blood loss of 165 ml, and a length of stay of three days, whereas for robotic surgery comparable figures are 190-370 minutes, 140 ml, and two days (Decloedt & Vergote, 1999; Li *et al*., 2007; Possover *et al*., 1998; Zakashansky *et al*., 2007).

The first radical hysterectomy in cervical cancer with robot assistance was described by Sert and Abeler (2006). They concluded that radical dissection could be performed much more precisely than with conventional laparoscopy. In 2007, they described 15 women with early-stage cervical cancer as a pilot case–control study and compared robotic-assisted laparoscopic radical hysterectomy with conventional total laparoscopic radical hysterectomy. There was a significant difference in mean operating time (241 minutes in the robot group and 300 minutes in the conventional group). No difference in the number of lymph nodes and size of parametrial tissue was found. In the robot group, there was significant less bleeding and shorter hospital stay.

Kim *et al.* (2008) performed robotic radical hysterectomy and pelvic lymphadenectomy in ten cases and found a mean operating time of 207 minutes. The mean docking time was 26 minutes, but this was reduced significantly with experience (from 35 to 10 minutes). These small series, however, do not report the outcome of surgery in terms of lymph node yield and radicality and also lack sufficient oncological follow up.

Boggess *et al*. (2008) found no difference in the operating time (242 versus 240 minutes). He performed 13 robot-assisted radical hysterectomies and compared them with 48 open radical hysterectomies. Significantly more lymph nodes were collected in the robot group (33 versus 22). All the robotic patients were discharged within 24 hours. He also describes how to set up a robotic program in gynaecological oncology.

Recently, a study of Lowe *et al.* (2009) reported a multi-institutional experience with robotic-assisted radical hysterectomy in patients with early stage cervical cancer with respect to peri-operative outcomes. In their investigation, a multi-institutional robotic surgical consortium consisting of five board-certified gynecologist oncologists in distinct geographical regions of the United States was created, in order to evaluate the utility of robotics for gynecologic surgery (benign and malignant). Between April 2003 and August 2008, a total of 835 patients underwent robotic surgery for benign gynecologic disorders and/or gynecologic malignancies by a surgeon in the consortium. For the purpose of the study, a multi-institutional HIPPA compliant database was then created for all patients. In the results, from a database of 835 patients who underwent robotic surgery by a gynecologic oncologist they identified, a total of 42 patients who underwent a robotic-assisted type II (n=10) or type III (n=32) radical hysterectomy for early stage cervical cancer. With regard to stage, seven patients (17%) were Stage IA2, twenty-eight patients (67%) were Stage IB1 and six patients (14%) were Stage IB2. There was a single patient with Stage IA1 cervical cancer with vascular space invasion who underwent type II radical hysterectomy. Overall median operative time was 215 min. Overall median estimated blood loss was 50 cc. No patient received a blood transfusion. Median lymph node count was 25. Median hospital stay was 1 day. Positive lymph nodes were detected in 12% of the patients. Pelvic radiotherapy or chemo-radiation was given to 14% of the patients based on final surgical pathology. Intraoperative complications occurred in 4.8% of the patients and included one conversion to laparotomy (2.4%) and one ureteral injury (2.4%). Postoperative complications were reported in 12% of patients and included a DVT (2.4%), infection (7.2%), and bladder/urinary tract complication (2.4%) Conversion rate to laparotomy was 2.4%. In their conclusions, Lowe *et al*. reported that robotic-assisted radical hysterectomy is associated with minimal blood loss, a shortened hospital stay, and few operative complications. Operative time and lymph node yields are ac-

ceptable. This data suggests that robotic-assisted radical hysterectomy may offer an alternative to traditional radical hysterectomy.

Persson *et al.* (2009) reported their experience in 80 robot-assisted laparoscopic radical hysterectomies to evaluate its feasibility and morbidity, from December 2005 to September 2008. They used a prospective protocol, and an active investigation policy to define adverse events, perioperative, and short and long term data. Also in their conclusions, authors showed that robot- assisted laparoscopic radical hysterectomy could be a feasible alternative to conventional laparoscopy and open surgery, even if efforts should be made to ensure proper closure of the vaginal cuff, trocar sites and to develop nerve sparing techniques.

Cantrell *et al.* (2010) assessed progression-free and overall survival for women with cervical cancer who underwent type III robotic radical hysterectomy, in a retrospective analysis of women who underwent RRH from 2005 to 2008. They were compared to a group of historical open radical hysterectomies. They analyzed seventy-one women who had undergone attempted RRH during the study period. Eight were excluded from analysis: 4 for non-cervical primary and 4 cases were aborted due to the extent of the disease. Squamous was the most common histology (62%) followed by adenocarcinoma (32%). Median patient age was 43 years. There was one intraoperative complication (asystole after induction) and two postoperative complications (ICU admission to rule out myocardial infarction and reoperation for cuff dehiscence). Of the patients who underwent RRH, 32% received whole-pelvis radiation with chemo sensitization. Median follow-up was 12.2 months (range 0.2–36.3 months). Kaplan–Meier survival analysis demonstrated 94% PFS and OS at 36 months due to recurrence and the death of one patient. As compared with a historical cohort at our institution, there was no statistically significant difference in PFS (P=0.27) or OS (P=0.47). In the conclusions, Cantrell *et al*. reported that RRH is safe and feasible and has been shown to be associated with improved operative measures. This study showed that at 3 years, RRH appears to have PFS and OS equivalent to that of traditional laparotomy. While the 5-year data are not yet available for the cohort of patients treated with robotic surgery, the 94% survival upon 3 years of performing RRH is comparable to other surgical methods and radiation.

9 The problem of Lymph-node in Endoscopic Lymphadenectomy

The limitations of FIGO clinical staging involve the possibility to detect metastases to lymph nodes, using clinical staging alone. This leads to under staging of some patients (Lagasse *et al*., 1980; LaPolla *et al*., 1986). Failure to detect metastasis to para-aortic nodes in patients with locally advanced cervical cancer leads to suboptimal treatment. One option consists of evaluating lymph node invasion using imaging techniques. However, as reported recently, false negative rates as high as 11% have been reported when comparing PET to lymphadenectomy in advanced cervical cancer (Mortier *et al*., 2008). Ramirez *et al.* compared positron emission tomography (PET)/computed tomography (CT) with laparoscopic extraperitoneal staging in the evaluation of para-aortic lymph nodes. The sensitivity and specificity of PET/CT in detecting positive para-aortic nodes when nodes were negative on CT or MRI were 36% and 96%, respectively. The PPV and NPV of PET/CT for para-aortic metastasis were 71% and 83%, respectively. For the subset of patients with positive pelvic lymph nodes on preoperative PET/CT, the sensitivity of PET/CT for identifying para-aortic lymph node metastases was 45%, the specificity was 91%, the PPV was 71%, and the NPV was 78% (Pecorelli *et al*., 2009). Therefore, another option is to perform surgical staging (Kohler *et al*., 2004; Marnitz *et al*., 2005; Possover *et al*., 1998).

Laparoscopic para-aortic node sampling has been shown to be feasible in gynecological malignancies. In addition, it is associated with lower morbidity than staging using laparotomy (Dargent *et al*., 2000; Denschlag *et al*., 2005; Querleu *et al*., 1993; 2000; Spiritos *et al*., 1995; Vergote *et al*., 2002). Its only technical limitation occurs in obese patients. However, using the classical laparoscopic approach, the surgeon is limited in the degrees of his movements. By assisted-robotic surgery, this problem could be solved. The feasibility of a robotically assisted retroperitoneal approach, to dissect lower lumbo-aortic lymph nodes, was reported recently. Simultaneously to Vergote *et al.* (2008), Fastrez *et al.* (2009), evaluated the feasibility and safety of a robot-assisted laparoscopic transperitoneal approach of the para-aortic lymph node dissection on 8 patients with advanced cervical carcinoma who were eligible for primary pelvic radiotherapy combined with concurrent cisplatin chemotherapy or pelvic exenteration and who underwent a pre-treatment robot assisted transperitoneal laparoscopic para-aortic lymphadenectomy. Authors isolated from 1 to 38 para-aortic nodes per patient and had one para-aortic node positive patient who was treated with extended doses of pelvic radiotherapy. We did not encounter any major complications and post-operative morbidity was low. In the conclusions, Fastrez reported that robot assisted transperitoneal laparoscopic para-aortic lymphadenectomy is feasible and provides the surgeon with greater precision than classical laparoscopy, even if larger prospective multicentre trials are needed to validate the generalized usefulness of this technique.

The technique of the robotic retroperitoneal para-aortic lymphadenectomy has been described by Vergote *et al.* (2008), who reported the feasibility of robot-assisted laparoscopic retroperitoneal para-aortic lymphadenectomy in five patients.

In 2008 Ramirez *et al.* (2008) described a series of patients diagnosed with invasive cervical cancer after undergoing simple hysterectomy who subsequently underwent robotic radical parametrectomy and bilateral pelvic lymphadenectomy. In their results, authors included 5 patients in analysis, with invasive squamous cell carcinoma of the cervix. There were no conversions to laparotomy. There was 1 intraoperative complication—cystotomy. No patient required blood transfusion. The mean duration of hospital stay was 1 day (range, 1 to 2). One patient experienced two postoperative complications, a vesicovaginal fistula and a lymphocyst. No patient had a residual tumor in the parametrectomy specimen, and no patient underwent adjuvant therapy. Median number of pelvic lymph nodes removed was 14 (range, 6 to 16). Median follow-up for all patients was 7.5 months (range, 1.3 to 13.8), without recurrences. In conclusion, Ramirez assessed that robotic radical parametrectomy and bilateral pelvic lymphadenectomy is feasible and safe and can be performed with an acceptable complication rate.

Robotic assistance with the Da Vinci system provides the surgeon with more precise dissection conditions, thanks to the three-dimensional visualization, instrumentation with articulating tips, that allows the surgeon's hands more mobility and decreases tremor movements. This increased precision in procedure as compared with classical laparoscopy is particularly important in the para-aortic region and may enhance safety and decrease intraoperative morbidity.

10 Fertility-sparing Surgery in Cervical Cancer

The incidences of cervical cancer are increasing in young women and women are delaying their childbearing. Available literature shows that there are interesting fertility-sparing treatment alternatives to the “golden standard” for the management of early cervical cancer in young women. So, the fertility-sparing surgery becomes an option for young women affected by cervical cancer. Fertility-sparing sur-

gery can be offered to carefully selected patients with cervical cancer for the management of early-stage (IA or IB1) disease who wish to preserve fertility (Lange *et al*., 2013). Simple trachelectomy (cervicectomy) and radical trachelectomy (resection of parametrial tissue with cervix) are being used in women with early stage disease. Cervical conization used in preinvasive cancer as investigative biopsy could also become a therapy. Randomized controlled trials of fertility-preserving surgery are impractical and unfeasible; however, radical trachelectomy has been retrospectively shown to have similar oncologic outcomes to radical hysterectomy in select patients with stage IB1 cervical cancer. In patients with stage IA1 cervical cancer, conization is a valid alternative. Patients with stage IA2-IB1 disease can be conservatively treated by radical trachelectomy. This is as well-established conservative approach and appears to be safe and effective in allowing a high chance of conception (Lange *et al*., 1986).

Prematurity is the most serious issue in pregnancies following trachelectomy. Less invasive options such as simple trachelectomy or conization seem to be feasible for stages IA2-IB1, but more and better evidence is needed. Neoadjuvant therapy might allow conservative surgery to be performed, also in patients with more extensive lesions. Ovarian transposition is important when adjuvant radiation is needed (Noyes *et al*., 2011).

Trachelectomy has been adopted by many oncological centers all over the world with good oncological and obstetric results. The selection of patients by adequate preoperative evaluation is an important process before a decision regarding conservative treatment is taken. Lesionextent is of great importance; the tumor should be small in size and confined to the cervix without parametrial invasion or spread to the uterine corpus. A 19% recurrence rate has been reported for patients with lesions >2 cm and 25% for those with lesions >2 cm and depth of invasion > 1 cm (Lambaudie *et al*., 2010 Ramirez *et al*., 2008).

Radical trachelectomy is performed in select patients diagnosed with early-stage cervical cancer who wish to preserve their fertility. Since the procedure was first described by Dargent *et al.* (1994), numerous reports have documented the safety and feasibility of the vaginal approach (Beiner *et al*., 2008; Dursun *et al*., 2007; Hertel *et al*., 2006; Plante, 2008; Ungar *et al*., 2005). Alternatively, the procedure may also be performed successfully via the abdominal approach. Several groups have published works on the success rate and feasibility of the abdominal approach (Geisler *et al*., 2008; Pergialiotis *et al*., 2013).

The first to report on robotic radical trachelectomy were Geisler *et al.* (2008), who reported on a patient with stage IB1 cervix adenosarcoma. In this case, total operative timewas 172 min, and the estimated blood loss was 100 ml. No residual tumor was found in the surgical specimen, and all lymph nodes were negative for any evidence of disease .

Persson *et al.* (2008) published on 2 patients who underwent robotic radical trachelectomy. One patient was diagnosed with a stage IB1 cervix adenocarcinoma and the other with a stage IA2 squamous cervix carcinoma. This group of investigators was the first to publish on robotic radical trachelectomy in conjunction with lymphatic mapping and sentinel node identification. In that study, console time was 387 min for the first patient and 359 min for the second. Estimated blood loss was 150 ml for the first patient and 100 ml for the second. The authors reported no intraoperative complications. Neither patient had residual cancer or evidence of lymph node disease.

Chuang *et al.* (2008) described a robotic radical trachelectomy in a young woman with cervical cancer who desired preservation of fertility; the patient had previously undergone a cervical conization procedure, with negative margins. Findings at positron emission tomography and computed tomography were normal, and there was no evidence of metastasis before surgery. The operation lasted 345 minutes, with 200 mL blood loss. Final pathologic analysis showed no evidence of residual cancer. All reported

cases were completed successfully and highlight robotic-assisted laparoscopy as a useful approach to trachelectomy in appropriate patients.

As one could argue that parametrectomy is not necessary for small tumours, it is relevant that this approach allows one to tailor the extent of parametrectomy according to the size of the tumour. Potentially, this minimally invasive approach may also overcome a severe disadvantage of abdominal trachelectomy, namely that pregnancy rate is much lower than after vaginal radical trachelectomy, but series are as yet too small to assess this potential benefit.

The robotic approach also seems safe in cases where surgery follows neoadjuvant chemotherapy for locoregional extensive tumours. In a study comparing robot-assisted laparoscopy, conventional laparoscopy and laparotomy groups, there was no difference in the recurrence rate (27.3 %, 29.4 % and 30 %, respectively) (Burnett *et al*., 2009; Dargent *et al*., 1994).

Ramirez *et al.* (2010) described their surgical technique in a retrospective review on 4 patients who underwent robotic radical trachelectomy and bilateral pelvic lymphadenectomy from October 2008 to May 2009. Their analysis included 4 patients with early-stage squamous cell carcinoma of the cervix. The median body mass index was 27.1 kg/m2 (range, 22.7 to 39.1). Three patients had stage IA2 adenocarcinoma; 1 patient had stage IA1 adenocarcinoma with lymph-vascular space invasion. Median operative time was 339.5 min (range, 245 to 416). Median console time was 282.5 min (range, 217 to 338). Median estimated blood loss was 62.5 ml (range, 50 to 75). There were no conversions to laparotomy. There were no intraoperative complications. No patient required blood transfusion. The mean duration of hospital stay was 1.5 days (range, 1 to 2). One patient experienced a postoperative complication, transient left lower extremity sensory neuropathy. No patient had residual tumor in the trachelectomy specimen, and no patient underwent adjuvant therapy. The median number of pelvic lymph nodes removed was 20 (range, 18 to 27). The median time to a successful voiding trial was 8 days (range, 7 to 9). The median follow-up was 105 days (range, 82 to 217). There were no recurrences. Ramirez *et al*. concluded that robotic radical trachelectomy and bilateral pelvic lymphadenectomy is feasible and safe and should be considered for patients desiring fertility-sparing surgery.

There is increasing evidence in literature that not only is radical trachelectomy feasible and safe but the oncologic outcomes are similar to those of equivalent patients undergoing radical hysterectomy. In a recent article, Diaz *et al.* (2008) compared the outcomes of 40 patients with stage IB1 cervical cancer who underwent radical trachelectomy and 110 patients with stage IB1 cervical cancer who underwent radical hysterectomy. The median follow-up time was 44 months. The 5-year recurrence-free survival rate was 96% for the radical trachelectomy group compared to 86% for the radical hysterectomy group (p=NS). The authors concluded that for select patients with stage IB1 cervical cancer, fertility-sparing radical trachelectomy appears to produce oncologic outcomes similar to those after radical hysterectomy.

Recently, many studies analysed the reproductive outcome after fertility-sparing radical trachelectomy. One of these studies was performed by Kim *et al.* (2012) on 105 patients who underwent RT. 77 (73%) did not require a conversion to radical hysterectomy or postoperative treatment. Median age was 32 (range, 25-38 years). Most patients (75%) had stage IB1 disease. Sixty-six patients (63%) were nulliparous. Thirty-five women were actively attempting conception 6 months after surgery, and 23 (66%) women were successful in conceiving: there were 20 live births, 3 elective terminations, and 4 spontaneous miscarriages. Four patients had 2 pregnancies each; all delivered their second pregnancy between 32 and 36 weeks. Cerclage erosion through the vaginal wall occurred in 6 cases and was treated by transvaginal removal of protruding suture material. One of these patients experienced a second trimester miscar-

riage. In conclusion: the majority of women who attempted to conceive after radical trachelectomy were successful, and most of their pregnancies resulted in full-term births.

Finally, even more intriguing, recent studies have suggested that even more conservative techniques such as cervical conization, with or without pelvic lymphadenectomy, may be applicable in treatment of early-stage cervical cancer including stage IB1 (Maneo *et al*., 2011). If the surgical community accepts the findings of these early reports, minimally invasive techniques including simple conization or trachelectomy plus lymphadenectomy may need to either become more challenging, with cases with more advanced presurgical staging, or totally lose ground as treatment alternatives. Assisted reproduction played an important role in select women. Cerclage likely contributed to a post-trachelectomy uterine ability to carry a pregnancy to the third trimester. The second post-trachelectomy pregnancy appears to be at higher risk for preterm delivery than the first pregnancy. In term of histopatological outcomes there is no evidence.

11 Comparison between Laparoscopy and Robotic in Radical Hysterectomy

There is a growing trend to practice less aggressive surgery in order to preserve fertility in young women and avoid an excess of treatment in some selected patients and nerve-sparing techniques can help to improve the quality of life. Laparoscopic robotic-assisted radical hysterectomy with nerve sparing technique is an attractive surgical approach for early invasive cervical cancer. Robotic technology allows a stereoscopic visualization of blood vessels and autonomic nerve supplies (sympathetic and parasympathetic branches) to the bladder and rectum making nerve sparing a safe and feasible procedure (Gil-Ibáñez *et al*., 2013).

Magrina *et al*. (2008) recently presented the first prospective study comparing the perioperative results of patients undergoing radical hysterectomy and lymph node dissection by robotics, laparoscopy and laparotomy. Mean operating time for a robotic, laparoscopic and radical hysterectomy per laparotomy was 190, 220 and 167 min, respectively; mean blood loss was 133, 208 and 444 mL respectively; mean number of removed lymph nodes was 26, 26 and 28, respectively, and mean hospital stay was 1.7, 2.4 and 3.6 days, respectively. There were no significant differences in intra- or postoperative complications among the three groups and no conversions in the robotics or laparoscopic groups. At a mean follow up of 31 months, none of the patients with cervical cancer experienced a recurrence. The authors concluded that laparoscopy and robotics are preferable to laparotomy for patients requiring radical hysterectomy, with advantages like significantly shorter operating times noted for robotics over laparoscopy. Their results are in accordance with other groups, although some reported the feasibility of a more radical lymph node dissection with the robotic system when compared to conventional laparoscopy (Boggess, 2007; Kim *et al*., 2008). Several case reports suggest that debulking surgery is a further potential application for robotics surgery in gynaecological oncology (Chavin, 2008; van Dam *et al*., 2007).

In a recent paper, Cho and Nezhat (2009) compared robotic and laparoscopy in gynecological oncology. The objectives of their article were to review the published scientific literature about robotics and its application to gynecologic oncology to date and to summarize findings of this advanced computer enhanced laparoscopic technique. Relevant sources were identified by a search of PUBMED from January 1950 to January 2009 using the key words Robot or Robotics and Cervical cancer, Endometrial cancer, Gynecologic oncology, and Ovarian cancer. Appropriate case reports, case series, retrospective studies,

prospective trials, and review articles were selected. A total of 38 articles were identified on the subject, and 27 were included in the study. The data for gynecologic cancer show comparable results between robotic and laparoscopic surgery for estimated blood loss, operative time, length of hospital stay, and complications. Overall, there were more wound complications with the laparotomy approach compared with laparoscopy and robotic-assisted laparoscopy. There were more lymphocysts, lymphoceles, and lymphedema in the robotic-assisted laparoscopic group compared with the laparoscopy and laparotomy groups in patients with cervical cancer. Overall, 126 robotic-assisted laparoscopies, 68 laparoscopies, and 136 laparotomies were performed in the cohort studies of cervical cancer, each with varying intraoperative and postoperative issues. In the robotic-assisted laparoscopy group, there were 24 complications, with lymphocysts or lymphoceles, infections, and vaginal cuff complications most commonly reported. In the traditional laparoscopy group, there were 16 complications, with lymphocysts or lymphoceles and infections most commonly reported. In the laparotomy group, there were 24 complications, with adverse wound and gastrointestinal sequelae most commonly reported.

Computer-enhanced technology may enable more surgeons to convert laparotomies to laparoscopic surgery with its associated benefits. It seems that in the hands of experienced laparoscopic surgeons, final outcomes are the same with or without use of the robot (Cho & Nezhat, 2009).

Lambaudie *et al.* (2010) compared the feasibility and efficacy of 22 robot-assisted laparoscopies with 20 traditional laparotomy and 16 conventional laparoscopy in a series of patients with locally advanced cervical cancer managed in two institutions. In the results, there was no significant difference between the three groups in terms of body mass index, FIGO stage, or tumor histology. Complication rate was similar in the three groups of patients, although there was a trend towards more lymphatic complications in the robot-assisted subgroup managed medically. There was no significant difference in the recurrence rate between the robot-assisted laparoscopy, conventional laparoscopy and laparotomy groups (27.3%, 29.4% and 30%, respectively). Authors concluded that robot-assisted laparoscopy is feasible after concurrent chemoradiation and brachytherapy in cases of locally advanced cervical cancer, reduces hospital stay, and seems to result in less severe complications than conventional laparotomy without modifying the oncological outcome.

12 Complications of Endoscopy in Cervical Cancer

Robotics, like any novel technology, has its advantages, disadvantages and reported complications. In the modern era of minimally invasive techniques, current developments in surgical robotics represent only the initial attempts to simplify complex laparoscopic procedures, providing precision in dexterity and perfection of repetitive tasks such as suturing. The current evidence shows that minimally invasive surgery is associated with less morbidity compared with open surgery and can be considered as an alternate option for surgical management of cervical cancer without compromising the oncologic outcome. There are several studies in literature, which compared laparoscopic or robotic surgeries with open method. In a majority of the studies, the operating time for laparoscopy was higher compared with the open method (Li *et al*., 2007; Malzoni *et al*., 2009).

In comparative studies, laparoscopic and robotic methods were associated with shorter hospital stay when compared to the open method. Mean blood loss and transfusion rates were more for the open method. In a comparative study between laparoscopic and robotic radical hysterectomy, Nezhat *et al.* (2008) showed that there is no difference between operating time, hospital stay, mean pelvic lymph node

yield or intraoperative or postoperative complications between the robotic and laparoscopic method. The complication rates of robotic radical hysterectomy are lower compared to our historical cohort of radical hysterectomy by standard laparotomy.

Many authors and surgeons affirm that some complications may be associated with robotic or laparoscopic surgery per se. The frequent reported complications are on vaginal cuff (dehiscence, lymphatic leaking, infection, hematoma, vault prolapse, short vagina), on the lymphatic system (proximal lymphedema, mild distal lymphedema, severe distal lymphedema, lymphocyst), on the neural peripheral system (genitofemoral nerve injury, partial obturator nerve palsy), on the abdominal wall (port site hernia, port site muscle rupture, hematoma, port site metastases) and the vascular system (postop hemoglobin and/or transfusion, ovarian vein thrombosis and pulmonary embolism).

Symptomatic postoperative lymphocysts (SPOLs) and lower-limb lymphedema (LLL) are probably underestimated complications of lymphadenectomy for gynecologic malignancies. Adjuvant radiotherapy was significantly associated with the development of lymphedema in women who had undergone radical surgery with lymphadenectomy for FIGO stage I to stage IIA cervical cancer (odds ratio, 3.47; 95% confidence interval, 2.086-5.788; P = 0.000) (Kim *et al*., 2012). Moreover, there are also risks of infection by pneumonia, with pyelonephritis and/or fever of unknown origin, a risk of ureter stenosis and of uncorrected positioning, with arm/shoulder/leg pain.

In the Piver study, there were 2 deaths (one from pneumonia and one from pelvic abscess), 2 pulmonary emboli, one ureterovaginal fistula and one ureteral stricture and a total of 15 complications in 55 patients who underwent type III open radical hysterectomy (27%). Moreover, Piver *et al*. (1974) showed a 5-year disease-free interval of 87.5–100% in women with cervical cancers less than 3 cm treated by type III radical hysterectomy.

About the incidence of port site hernia and/or dehiscence after laparoscopic surgery and robotic assisted surgery in oncology, literature has recent evidences. The incidence of port site hernia and/or dehiscence using bladeless trocars is 0-1.2%. Robotic surgery uses additional port sites and increases manipulation of instruments, raising the concern for more complications. Authors reviewed Robotically-assisted (RA) 842 procedures performed for suspected gynecologic malignancy between 1/2006 and 12/2011. Bladeless 12mm and 8mm robotic trocars were used. Fascial closure was not routinely performed except after specimen removal through the port site. The decision to close the fascia remained at the discretion of the surgeon. RA-total laparoscopic hysterectomy (TLH)±unilateral or bilateral salpingo-oophorectomy (BSO)±lymphadenectomy (LND) accounted for 91.6% of procedures. Final pathology confirmed malignancy in 58.6% of cases, primarily endometrial cancer. In 35 cases, the specimen was removed through the port site; fascia was closed in 54.3% of them and no port site hernias or dehiscences occurred. In the study conclusion, authors affirmed that port site hernias and dehiscences are rare in RA gynecologic oncology procedures. When bladeless dilating trocars are used, routine closure of even up to a 12mm port site is unnecessary, even in cases requiring removal of the specimen through the trocar sites (Boone *et al*., 2013).

13 Literature Drawbacks Concerning Robotic Surgery in Gynaecological Oncology

In recent years, robotic surgery or robot assisted surgery has been developed to support a range of surgical procedures. Robotic surgery in cervical and endometrial cancer is one of the fastest growing areas.

Robotic surgical systems have been used to perform surgery for endometrial, cervical cancer and ovarian cancer. There is mounting evidence which demonstrates the feasibility and safety of robotic surgery for gynaecological oncology.

Cochrane Gynaecological Cancer Group evaluated in 2012 all randomised controlled trials (RCTs) comparing robotic assisted surgery for gynaecological cancer to laparoscopic or open surgical procedures as well as RCTs comparing different types of robotic assistants. To review authors independently screened studies for inclusion and no RCTs were identified (Lu *et al*., 2012). The robotic approach was explored in a study by Lambaudie *et al* (2010); it seemed safe in cases where surgery follows neoadjuvant chemotherapy for locoregional extensive tumours. In a study comparing robot-assisted laparoscopy, conventional laparoscopy and laparotomy groups, there was no difference in the recurrence rate (27.3 %, 29.4 % and 30 %, respectively). Although already known to be commoner after laparoscopic hysterectomy than after laparotomy (Chan *et al*., 2012), a particularly striking finding is a relative high number, up to 20 %, of patients with vaginal dehiscence after robot-assisted laparoscopic surgery (Persson *et al*., 2009). This may be explained by the initial use of extensive cautery or tight suturing, causing necrosis. Although some authors reported a significant decrease in vaginal cuff dehiscence when closing the vagina vaginally instead of laparoscopically (Uccella *et al*., 2011), others did not find a difference between the methods of closure (Hwang *et al*., 2011).

In recent series, this complication seems to occur less prominently than in the past, maybe due to caution with cautery and the use of self-locking sutures. Published experience has suggested that the outcomes with Robotic Radical Hysterectomy (RRH) are similar to that for patients undergoing a traditional radical hysterectomy via an exploratory laparotomy (Cantrell *et al*., 2010; Estape *et al*., 2009; Maggioni *et al*., 2009). These primarily single institution series have compared primarily surgical outcomes of patients undergoing RRH with Laparoscopic RH and/or Abdominal RH. Secondary to the relatively recent introduction of roboticassisted radical hysterectomies, limited information regarding oncologic outcomes specifically in terms of survival is available. Overall, these studies have suggested that robotic surgery is generally longer, with less estimated blood loss and similar nodal yield.

Lowe *et al.* (2009) reported their multi-institutional experience in a group of 42 patients undergoing Type II or III RRH. Overall 42 patients underwent either a Type II or III RRH with operative outcomes similar to other series and an overall low complication rate of 4.8%. Many authors affirmed that robotic total laparoscopic radical hysterectomy with pelvic and para-aortic lymphadenectomy is feasible and may be preferable over laparoscopic or radical abdominal hysterectomy. They reported advantages to both minimally invasive approaches, with decreased average estimated blood loss, length of stay, number of catheter days, days on pain medication, and a faster return to work in both the robotic and laparoscopic groups when compared to laparotomy.

Even with increased visualization and surgical precision, complications still may occur. A large review from Kho *et al.* (2009) at the Scottsdale Arizona Mayo Clinic of >500 patients undergoing various robotic-assisted surgical procedures noted a 4.1% (95% CI 2.3–5.8%) vaginal cuff dehiscence rate. Of these 21 patients, 9 (43%) had a pre-operative diagnosis of cancer including 3 with cervical carcinoma. This rate is similar to the 7.5% incidence seen in the cervical cancer series from Italy by Maggioni *et al.* (2009), although as they note in their follow-up letter to the editor, following a modification in surgical technique, the incidence in their patients has decreased to 1% (Sert, 2010). Although unlikely, based on the size of the predicted fascial defect, herniation of small bowel through an 8-mm robotic trocar has been reported (Seamon *et al*., 2008).

The published data comparing different surgical approaches to radical hysterectomy, including traditional laparoscopy or laparotomy show that the robotic approach produces more favorable perioperative outcomes, such as less blood loss, abbreviated hospitalizations, and equivalent or lower rates of intraoperative and postoperative complications. While these series are relatively small and non-randomized, they consistently demonstrate safety and efficacy with respect to complications, blood loss, operative time and patient convalescence comparing robotic assisted surgery with laparoscopy (Estape *et al*., 2009; Magrina *et al*., 2008; Nezhat, 2008; Symmonds, 1975). Despite that these findings are consistently reproducible in larger and multi-institutional studies, there are no prospective data to resolve these unequivocal comparisons in cervical cancer patients. We hope that the prospective randomized controlled trial that is currently ongoing will provide further insight. Although robotic-assisted technology is supposedly an enhancement of conventional laparoscopy, several studies have reported conversion of the robotic approach to laparotomy, not laparoscopy. There were 6 conversions from robotic-assisted laparoscopy to laparotomy in 2 studies (Boggess *et al*., 2008).

14 Pro and Contra of Robotic Assisted Surgery

In 2005, the first feasibility studies in both Europe and the United States were published, since robotic-assisted procedures provide several advantages. Binocular vision and 3-dimensional views permit improved depth perception, which may facilitate advanced laparoscopic procedures, such as intracorporeal suturing. The console is located away from the patient and permits the surgeon to operate in a comfortable, seated position, thus making operator positioning more ergonomic.

Tremor filtration is another benefit of robotic-assisted surgery, as the video laparoscope is no longer in a human hand, which may tire or move, but rather is fixed in position by the robotic arm. This feature permits finer surgical movements with more precise dissections. The articulating instrument tips that are utilized in traditional laparoscopy are taken to a new level with not only rotational capabilities but an independent 90-degree articulation of the tip. These features make robotic surgery more intuitive, with a shorter learning curve. Additional robotic arms have been introduced to further minimize the need for surgical assistants in institutions that may have limited staff.

Robotic-assisted procedures are not, however, without their limitations. The equipment is still very large, bulky, and expensive. The staff must be trained specifically on draping and docking the apparatus to maintain efficient operative times. Functional limitations include lack of haptic feedback, limited vaginal access, limited instrumentation, and larger port incisions requiring fascial closure. In terms of haptic feedback, visual cues become imperative to ensure that tissue manipulation is not performed with undue force. Intracorporeal knots must be tied carefully such that the suture is not avulsed by the strength imposed by the robotic arm. Limited vaginal access can be problematic in gynecologic surgery as frequent uterine or vaginal manipulation is necessary, particularly in extirpative procedures. Once the robot has ascended into place, access to the vagina becomes markedly limited. Robotic accessory trocars are 8 mm in size with a 12 mm laparoscope. These incision sizes are larger than the 5 mm accessories that are frequently used in traditional laparoscopy and also require fascial closure, with higher risks of herniation.

The robot is also limited in its instrumentation. Exchanging instruments becomes more cumbersome and requires a surgical assistant to change the instruments. Additionally, the current robotic instruments do not include endoscopic staplers or vessel sealing devices. Moreover, the trocars required for robotic procedures are larger than those used for traditional laparoscopy. In radical hysterectomy, the dis-

section of the uterine arteries, ureteral tunneling, and vaginal cuff closure are among the most useful indications for robotic-assisted procedures. The greater range of motion afforded by the robotic instruments permits easier maneuverability for these dissections.

These multiple optional of robotic-assisted surgery had been evaluated by literature. A recent paper on robotics has definitely been shown that robotic surgeries are more costly than regular laparoscopic approaches (Shah *et al*., 2011). Nevertheless, one study found an additional $3000 in operative case per robot-assisted vs laparoscopic hysterectomy (Jonsdottir *et al*., 2011). This cost differential may change with a decrease as other robotic systems come on line in the future. Moreover, another blinded, prospective randomized controlled trial comparing operative time and intra- and postoperative complications between total laparoscopic hysterectomy and robotic-assisted total laparoscopic hysterectomy, concluded that, although laparoscopic and robotic-assisted hysterectomies are safe approaches to hysterectomy, robotic-assisted hysterectomy requires a significantly longer operative time. The lengthier times in the robot group are likely due to operating room set up, docking time, troubleshooting of technical aspects that may be faulty with the robot (e.g., collision of arms, malfunctioning instrumentation), and less efficient electrosurgical vessel-sealing instrumentation for robot-assisted surgery during the time that this trial was undertaken (Paraiso *et al*., 2013).

A recent investigation show that robotic-assisted laparoscopy is safe, effective, and successful in obese and morbidly obese patients who undergo hysterectomy for malignancy which further decreases the incidence of laparotomy in the future (Leitao *et al*., 2012) and an American study on 1000 cases on robotic surgery (RS) in oncology from May 2006 through December 2009, analyzed patient characteristics and outcomes on a total of 377 women undergoing RS for endometrial cancer staging (ECS), compared with the historical data of 131 undergoing open ECS. Authors concluded that RS is associated with favorable morbidity and conversion rates in an unselected cohort. Compared to laparotomy, robotic ECS results in improved outcomes (Paley *et al*., 2011). Thus, after data revision, robot-assisted hysterectomy does not confer any perioperative patient benefits over laparoscopic hysterectomy in the hands of experienced conventional laparoscopic surgeons, except in gynecological oncology, where robotics have advantages (Rodriguez, 2013).

15 Conclusions

The robotic-assisted surgery has emerged as an invaluable minimally invasive approach to comprehensive surgical staging and the treatment of cervical cancer. There is good evidence that robotic surgery facilitates laparoscopic surgery, with equivalent if not better operative time and comparable surgical outcomes, shorter hospital stay, and fewer major complications than with surgeries using the laparotomy approach. And the role of robotic-assisted surgery is still expanding (Krill & Bristow, 2013). In addition to radical hysterectomy, gynecologic oncologists are applying robotic technology to ovarian transposition, lymphadenectomy, and even tumor debulking. Some future directions that will further the scope of robotic-assisted surgery include incorporation of the robotic system in the operating room facility to permit better accessibility to the patient during the procedure as well as expansion in instrumentation. Total laparoscopic radical hysterectomy is a feasible and safe procedure that is associated with fewer intraoperative and postoperative complications than abdominal radical hysterectomy. Longer follow-up is needed, but early data are supportive of at least equivalent oncologic outcomes compared with other surgical modalities. The role of robotic-assisted surgery is continuing to expand and new promising approaches with

added benefits are emerging, such as the one of the ALF-X system. Surgeons await results from additional series of radical hysterectomy performed by robo-endoscopic assisted surgery and from International prospective randomized trial evaluating outcomes in patients randomly assigned to either open or laparoscopic/robotic radical hysterectomy.

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