Abstract

Endometrial cancer is the most common gynecological malignancy, most are diagnosed at an early stage, and in most cases the curative management is surgical. In the treatment of early stage endometrial cancer, minimally invasive approach, laparoscopic or robotic, has been shown to be safe and feasible, and preferable to laparotomy. Certainly it will become increasingly offered to patients as training programs evolve to teach its trainees laparoscopic and robotic skills.

In this chapter, the history, risks and benefits of minimally invasive approach will be presented and compared to traditional laparotomy.

Introduction

First laparoscopic assisted vaginal hysterectomy was performed in 1989 [1]. In the same year, Dargent et al. used the laparoscope to perform limited pelvic lymphadenectomy on women with cervical cancer [2]. Laparoscopic pelvic and para-aortic lymph node dissection for endometrial cancer was described by Childers et al. in 1992 [3].

Since then, laparoscopy evolved slowly for the treatment of endometrial cancer. However, since the advent of the robotic technology it has experienced a rapid growth. A recent survey of the Society of Gynecologic Oncologists has indicated that most of its members believe in the benefits of laparoscopy for their patients [4].
Conventional Laparoscopy

Laparoscopic surgery for endometrial cancer started with laparoscopic assisted vaginal hysterectomy (LAVH) and progressed to total laparoscopic hysterectomy (TLH) and staging, with many proven advantages compared to laparotomy.

Obermair et al. did a retrospective review comparing TLH to open hysterectomy. Recurrence, disease-free, and overall survivals were similar. No port site metastases were noted in the TLH group [5].

Magrina et al. retrospectively reviewed 56 patients with clinical Stage I endometrial cancer treated laparoscopically. The mean follow-up was 6.4 years. Laparoscopic approach provided 5-year survival and recurrence rates similar to those previously attained by laparotomy in the same institution [6].

Magrina et al. reported a review of pertinent studies comparing laparoscopy to laparotomy for surgically manageable endometrial cancer. Similar results for recurrence and survival rates were noted for patients treated by laparoscopy and laparotomy, while laparoscopy patients had lower blood loss and shorter hospital stay. A similar or reduced cost was also noted for the laparoscopic approach [7].

In a small randomized trial, comparing LAVH to TLH in endometrial cancer with pelvic node dissection. The TLH had a shorter operative time and less operative complications, with no difference in port site metastasis [8].

The largest randomized trial comparing laparoscopic management of endometrial cancer to traditional open surgery was GOG LAP-2 trial. A total of 2616 patients with clinical stage I/IIA uterine cancer were randomized to laparotomy, or laparoscopy. There was a 23% conversion to laparotomy in the laparoscopy group. The laparoscopy group had a shorter hospital stay by average of one day, while the operating time was longer by one hour on average. Quality-of-Life (QoL) ratings were higher for the laparoscopy group at 6 weeks postoperatively. However, no differences were noted at 6 months. [9].

LACE was a two-stage randomized controlled trial, comparing TLH with total abdominal hysterectomy (TAH) for stage I endometrial cancer. The primary objective of the first stage of the study was to assess whether TLH resulted in equivalent or improved QoL up to 6 months after surgery compared with TAH. Three hundred sixty one participants were enrolled in the QoL study at 19 centers; 332 completed the QoL analysis. Results showed QoL improvements from baseline during early and later phases of recovery, and the adverse event profile favored TLH compared with TAH for treatment of stage I endometrial cancer. Stage 2 results are still pending [10].

Robotic-Assisted Laparoscopy

The surgical robot is a computer-controlled device that can be programmed to help in manipulating surgical instruments. The prototype was originally designed for use by the military to provide immediate operative care on the battlefield from a remote surgical station. Robotic telepresence technology became commercially available in 2000 (da Vinci® Surgical System, Intuitive Surgical inc., Sunnyvale, CA, USA). The system was developed by the
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Stanford Research Institute, National Aeronautics and Space Administration [11]. The surgical robot is mainly used for laparoscopy instead of open procedures.

Surgical robotics were first used in 1985 in neurosurgery; application soon followed in urology and orthopedics [11,12]. In 1998, the first robotic assisted laparoscopic tubal anastomosis in live porcine was performed [13]. Diaz-Arrastia et al. published the first 10 case series reporting the use of a computer-enhanced surgical robot for performing hysterectomy in humans in 2002 [14].

Reynolds et al. attempted 7 robot-assisted laparoscopic staging procedures in gynecologic malignancies with no conversions to laparotomy. He concluded that robot-assisted laparoscopic staging is a feasible technique that may overcome the surgical limitations of conventional laparoscopy [15]. Bandera and Magrina et al. did a review of case series and concluded that robotic surgery is a minimally invasive alternative to laparoscopy for the surgical treatment of endometrial and cervical cancer [16]. Veljovich et al reported their first year experience in 1,188 patients, comparing robotic surgery to laparotomy in endometrial cancer staging, and concluded that robotic surgery is feasible in gynecologic oncology and facilitated a dramatic expansion in their minimally invasive surgical practice [17]. Boggess et al. compared the outcomes in women who underwent endometrial cancer staging by different surgical techniques. Three hundred twenty two women were included: 138 had laparotomy (TAH); 81 had laparoscopy (TLH) and 103 had robotic technique (TRH). They reported that TRH with staging is feasible and preferable over TAH and may be preferable over TLH in women with endometrial cancer [18]. Magrina et al. evaluated the results of robotic surgery for the primary treatment of endometrial cancer patients and compared them to a matched group of patients treated by laparoscopy, laparotomy, and vaginal- laparoscopy. Robotic, laparoscopy, and vaginal-laparoscopy techniques were preferable to laparotomy. Robotic was preferable to laparoscopy due to a shorter hospital stay and lower conversion rate, it was preferable to vaginal/laparoscopy due to a reduced hospitalization [19]. Paley et al. analyzed their first 1,000 robotic cases in gynecological oncology and found that robotic surgery is associated with favorable morbidity, conversion rates and outcome in an unselected cohort compared to laparotomy [20].

Lim et al. analyzed the learning curve and outcome for robotic assisted hysterectomy with lymphadenectomy in patients with endometrial cancer and compared it to laparoscopy. He observed that Robotic hysterectomy with lymphadenectomy had a faster learning curve in comparison to laparoscopy. The adequacy of surgical staging was comparable between the two surgical methods. The robotic surgery was associated with shorter hospitalization, less blood loss, less intraoperative and major complications, and lower rate of conversion to open procedure [21,22]. Seamon et al. studied the number of cases required in the learning curve for performing robotic hysterectomy with pelvic-aortic lymphadenectomy for endometrial cancer. The authors concluded that proficiency for robotic hysterectomy with pelvic-aortic lymphadenectomy for endometrial cancer was achieved after 20 cases; however, the number of procedures to gain efficiency varies for each portion of the case and continues to improve over time [23].

Barnett et al. did a cost comparison analysis between robotic, laparoscopic, and open hysterectomy for endometrial cancer. He found that laparoscopy is the least expensive surgical approach for the treatment of endometrial cancer. Robotics is less costly than abdominal hysterectomy when the societal costs associated with recovery time are accounted for and is most economically attractive if disposable equipment costs can be minimized [24].
Holtz et al. compared the cost of robotics vs. laparoscopy in endometrial cancer surgery in 33 patients. Robotic surgery costs were significantly higher than traditional laparoscopy costs for staging of endometrial cancer in a small cohort of patients [25]. Martino et al. compared the cost analysis of postoperative management for endometrial cancer between the robot and laparoscopy in 215 patients. Patients in the robotic surgery arm experienced less initial postoperative pain and had fewer drug interventions. The costs associated for their pain management represented a savings of greater than 50%, indicating the value of robotic surgery in regards to postoperative pain management by delivering higher quality care at a lower cost [26]. Bell et al. compared the outcome and cost of endometrial cancer surgery via laparotomy, robotics and laparoscopy. Robotic hysterectomy provided comparable node retrieval to laparotomy and laparoscopy in the case of an experienced laparoscopic surgeon. While robotic hysterectomy took longer to perform than via laparotomy, it was equivalent to laparoscopic approach and provided the patient with a faster return to normal activity and reduced post-operative morbidity. The average cost for hysterectomy and staging was highest for laparotomy, followed by robotic, and lowest for standard laparoscopy [27].

**Minimally Invasive Surgery in the Elderly**

The risk of gynecologic malignancy increases with age, 45% of endometrial cancers are diagnosed in women age 65 years or older [28]. With traditional open surgery, elderly patients are prone to have higher rate of postoperative cardiac, respiratory and thromboembolic complications, longer length of hospital stay, and greater risk for loss of independence after surgery [29].

Scribner et al. reported on the laparoscopic management of endometrial cancer in patients > 65 years. In their series of 67 patients, a shorter length of stay, less postoperative fever, less postoperative ileus and fewer wound complications were noticed in the laparoscopic group compared to laparotomy [29].

Vacnin et al. prospectively evaluated the perioperative data and postoperative quality-of-life survey of the first hundred robotic surgeries for endometrial cancer. Patients were divided in 2 groups based on age, 41 patients age ≥ 70 years and 59 patients age < 70 years. Elderly women had similar operative time, mean blood loss and perioperative complications compared with the younger group.

Median hospital stay tended to be longer in the elderly women (2 vs. 1 days), but it was not statistically significant. Quality-of-life was high in both groups. Robotics was safe and conferred an excellent quality-of-life for elderly patients [30]. Frey et al. compared the surgical outcome of elderly and younger patients undergoing laparoscopic or robotic surgical staging for endometrial cancer.

Sixty patients were > 65 years of age, and 69 patients were < 65 years of age. Among the 109 patients who underwent laparoscopic or robotic staging, there were no differences in estimated blood loss, lymph node count, surgical time, complications, rate of blood transfusion, conversion to laparotomy, and mean of postoperative stay between elderly and younger patients [31].
Minimally Invasive Surgery in the Obese Patient

Obesity is defined as a body mass index (BMI) $\geq 30 \text{ kg/m}^2$. Obese women have a higher risk of developing uterine and ovarian cancer [32]. According to the women’s health initiative study, obese women who needed a hysterectomy were at a higher risk of having metabolic syndrome (hypertension, diabetes, hypercholesterolemia) and lower physical activity compared to women who did not have hysterectomy, with subsequent higher risks for cardiovascular events and mortality [33]. Therefore, it is important to be able to provide such women with a low risk surgical treatment. Laparoscopy in gynecologic surgery has consistently been demonstrated to improve the outcome over laparotomy for women regardless of BMI [34].

Eltabbakh et al. prospectively collected data on women with BMI 28-60 who underwent laparoscopy and compared their outcome to a controlled group of women who had a laparotomy 2 years prior. Laparoscopic surgery was successfully completed in 88% of patients. The laparoscopic group had a longer operative time. However surgeons were able to retrieve more pelvic lymph nodes in spite of less blood loss, less postoperative pain, and shorter hospital stay [35]. Scribner et al. compared the outcome of laparoscopic pelvic and para-aortic lymph node dissection to a historical control arm of obese patients who underwent laparotomy. Laparoscopy was successfully completed in 64% of patients. The laparoscopic group had a significantly shorter hospital stay, with similar blood loss and transfusion rates [36]. Eisenhauer et al. reported a higher node count in obese women with uterine cancer undergoing laparoscopy compared to laparotomy [37]. Gehrig et al. reported the outcome of robotic endometrial cancer staging in 36 obese and 13 morbidly obese patients and compared it to a matched group of laparoscopic patients. For both obese and morbidly obese patients, robotic surgery was associated with significantly shorter operative times, less blood loss, increased lymph node count, and shorter hospital stay [38].

Seamon et al. compared the outcome of 109 obese patients with a BMI $\geq 30$ who underwent robotic staging for endometrial cancer to 162 matched laparotomy patients. Both groups had similar lymph node counts. The robotic group had statistically significant lower rates of complications, blood transfusion, and shorter hospital stay [39]. Subramaniam et al. reported a similar study comparing robotic staging in obese patients with endometrial cancer to a laparotomy group and reached similar conclusions. Robotic surgery is safe, efficient and feasible for obese women when compared to laparoscopy and laparotomy [40].

Complications

Incision Hernia

The American Association of Gynecologic Laparoscopists reported in their survey that the incidence of hernia was 21 per 100,000 laparoscopic procedures, 18% of these hernias occurred despite fascial closure [45]. The incidence of hernia in another study of 3,560 laparoscopic cases was 0.17%, with the greater risk in the extra-umbilical sites of $\geq 12 \text{ mm}$ trocar (3.1%) than with a 10 mm trocar (0.23%) [46,47].
Vaginal Dehiscence

Hur et al. did an observational study of 7,039 hysterectomies done by different approaches. Laparoscopic hysterectomy had a significantly higher risk of vaginal dehiscence of 4.93% compared to vaginal hysterectomy of 0.29% and abdominal hysterectomy of 0.12% [52]. Kho et al. reviewed 510 post robotic hysterectomy cases. The incidence of vaginal cuff dehiscence was 4.1%. Coitus triggered 50% of vaginal deshiscences. Patients most commonly presented with vaginal bleeding or a sudden gush of watery vaginal discharge. Bowel evisceration was noted in only 28% of patients [53]. Nick et al. retrospectively studied 417 patients with laparoscopic or robotic hysterectomy for benign and malignant causes, 57 of those had radical hysterectomy. The overall risk of vaginal cuff complication was 1.7%. Radical hysterectomy was associated with a 9-fold increase in vaginal cuff complications [54].

Port Site Metastasis

It is very uncommon to have port site metastasis (PSM) post minimally invasive surgery for endometrial cancer. Nagarsheth et al. reviewed their own experience in 87 laparoscopic procedures in gynecological cancer, 39 of those patients had endometrial cancer. The rate of PSM was 2.3% (2 of 87 procedures); both were in advanced ovarian and peritoneal cancer patients.

There were no PSM in endometrial cancer patients [55]. Ramirez et al. did a midline search for laparoscopic PSM in gynecologic malignancy, 31 articles were found with a total of 58 patients. Majority of patients had an advanced ovarian cancer, 4 of 58 had endometrial cancer with a median age of 63 years, and a median time to diagnosis of 13.5 months. In three of the four patients, the PSM was not an isolated recurrence, at the time of re-exploration; evidence of disease was found at other sites [56].

Zivanovic et al. analyzed 2251 patients post laparoscopic procedure in women with underlying malignancy. Subdivided in two groups, 1694 patients underwent laparoscopic procedures for malignant intraabdominal condition, 505 were breast cancer patients undergoing risk-reducing, diagnostic or therapeutic laparoscopic procedures without intraabdominal disease. Port site metastases were documented in 20 of 1694 patients (1.18%) who underwent laparoscopic procedures for a malignant intraabdominal condition only. Of these, 15 patients had a diagnosis of epithelial ovarian or fallopian tube carcinoma, 2 had breast cancer, 2 had cervical cancer, and 1 had uterine cancer (0.05%). Nineteen of 20 patients (95%) had simultaneous carcinomatosis or metastases to other sites at the time of PSM [57].

Martínez et al. published a review of their own experience in PSM after laparoscopic procedures for cervical and uterine cancer. During the study period, 921 patients underwent laparoscopic staging for cervical cancer and 295 for endometrial cancer. The incidence of PSM after laparoscopy for cervical and endometrial cancer was 0.43% and 0.33%, respectively. The incidence of isolated PSM was 0%. They concluded that PSM is a rare complication of laparoscopic staging for endometrial and cervical cancer [58].
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