Advances in Minimal Access Surgery in the Surgical Staging of Carcinoma Endometrium

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ABSTRACT

The concept of minimal access surgery for gynecologic malignancies has gone from a perceived near impossibility to a fully recognized option for many patients over the past 10 years. This article reviews the different minimal access techniques used for surgical staging of carcinoma endometrium, their outcome, feasibility and safety in comparison to conventional staging laparotomy. After review of literature, it is concluded that laparoscopic and robotic-assisted procedures are acceptable and safer alternatives to traditional laparotomy in the staging of carcinoma endometrium, especially in obese women. Long-term outcome reports for robotic surgery is awaited.

Keywords: Carcinoma endometrium, Laparoscopy, Robotic surgery, Surgical staging.

INTRODUCTION

Endometrial carcinoma is one of the most common gynecological malignancies in women. It is expected to become more common as the prevalence of obesity, one of the major risk factors of endometrial carcinoma increases worldwide.1

Surgical management is the mainstay of initial treatment for most patients and is usually curative. Comprehensive surgical staging includes total hysterectomy, bilateral salpingo-oophorectomy, pelvic and para aortic lymphadenectomy and pelvic cytology. This has been shown to define the biology of disease and guides the use of postoperative adjuvant therapy.2

Regarding the therapeutic role of lymphadenectomy in women with disease that clinically seems to be confined to the uterus, there has been much debate. Although lymphadenectomy forms part of the International Federation of Gynecology and Obstetrics (FIGO) surgical staging system,3 evidence from a large randomized controlled trial. A study in the treatment of endometrial cancer (ASTEC) showed that this approach does not provide therapeutic benefit.4 Inspite of debates, surgical treatment and staging are performed according to the FIGO5 staging system and American Joint Committee on Cancer.6

Comprehensive surgical staging is technically difficult in obese patients with comorbidities which is the usual clinical picture in endometrial cancer. Limiting surgical morbidity while maintaining staging adequacy is a primary concern in patients with uterine malignancy. Hence, research directed to improve surgical techniques to appropriately manage these patients is important.7

Surgical staging of carcinoma endometrium was primarily by laparotomy. Childers and Surwit first proposed laparoscopy as an option for apparently early stage endometrial cancer (1993). Since April 2005, the role of robotic-assisted surgery in gynecologic oncology was identified. Several studies are published comparing the surgical, pathologic and quality of life and survival outcomes for conventional laparotomy and the two minimally invasive treatment modalities for endometrial cancer—laparoscopy and robotics. This article compares the different modalities of surgical staging in carcinoma endometrium, the advances in minimal access surgery in this context, its relevance and safety.

OBJECTIVES

The objective of this article is to review the advances in minimal access surgery in the surgical staging of carcinoma endometrium and to compare the outcome of the different modalities of surgical treatment in patients with carcinoma endometrium.

MATERIALS AND METHODS

Articles published regarding the methods of surgical staging in carcinoma endometrium for a period of 10 years from January 2001 to date were reviewed. The extensive electronic search included Medline, PubMed, Cochrane library, HighWire press, SAGES website, Google search engine, Yahoo search engine and SpringerLink Journal Electronic Library.

REVIEW OF LITERATURE

Regardless of preoperative grade, our management goal in endometrial cancer is comprehensive staging, to include pelvic washings, hysterectomy, bilateral salpingo-oophorectomy and pelvic cytology. The boundaries of the pelvic and para-aortic lymph node dissection include up to the duodenum on the right side and to the inferior mesenteric artery on the left.8

Historically, comprehensive surgical staging in endometrial cancer has been accomplished via open laparotomy.9 The decade of the 1990s brought the use of minimally invasive surgery to replicate the traditional goals of comprehensive surgical staging of endometrial cancer. Dargent and Querleu et al in France and
Childers et al and Spirtos et al in the United States demonstrated the adequacy and safety in small single-institution studies. There are isolated reports of surgical staging with micro-laparoscopy also.

Inspite of its advantages, the limitations of laparoscopy which includes counterintuitive motion, nonwristed instrumentation and heavy reliance on skilled surgical assistance contributed to a difficult and long learning curve. Comprehensive laparoscopic surgical staging is more difficult in the morbidly obese and with other patient factors, such as associated comorbidities, adhesive disease, large uteri, fatty mesentery. Since, the da Vinci surgical system was approved for gynecology in April 2005, the role of robotic-assisted surgery in gynecologic oncology continues to evolve.

The main concerns with the advent of minimal access surgery in surgical staging were adequacy of lymphadenectomy, intraoperative and postoperative complications, long-term survival, quality of life, feasibility in elderly and obese, learning curve and cost involved.

**Adequacy of Surgical Staging and Operative Complications**

A large randomized control trial comparing laparotomy and laparoscopy in surgical staging of carcinoma endometrium was done by gynecologic oncology study group (LAP 2 study). A total of 1,682 laparoscopy patients and 909 laparotomy patients were included in the analysis of short-term surgical outcomes. Laparoscopy was completed without conversion in 1,248 patients (74.2%). Conversion from laparoscopy to laparotomy was secondary to poor visibility in 246 patients (14.6%), metastatic cancer in 69 patients (4.1%), bleeding in 49 patients (2.9%) and other causes in 70 patients (4.2%). Laparoscopy had fewer, moderate to severe postoperative adverse events than laparotomy (14 vs 21% respectively; p < 0.0001) but similar rates of intraoperative complications, despite having a significantly longer operative time (median, 204 vs 130 minutes, respectively; p < 0.001). Hospitalization of more than 2 days was significantly lower in laparoscopy versus laparotomy patients (52 vs 94% respectively; p < 0.0001). Pelvic and para-aortic nodes were not removed in 8% of laparoscopy patients and 4% of laparotomy patients (p < 0.0001). No difference in overall detection of advanced stage (stage IIIA, IIIC or IVB) was seen (17% of laparoscopy patients and 18.2% in the laparoscopic group; p > 0.05). Pelvic lymph node metastases were detected in 7.7% of the patients in the laparoscopy group and 15.4% in the laparotomy group and the difference was not significant. Operative morbidity was higher in the laparotomy group mainly because of postoperative wound infection and the patients in the laparotomy group had a longer hospital stay. They concluded that the lymph node detection rates do not differ.

A retrospective cohort study compares the adverse event rates between laparoscopic versus open surgery. A total of 107, who underwent surgical staging for endometrial cancer were compared to 269 age and body mass index matched women. Laparotomies had higher rates of cellulitis (16 vs 7%; p = 0.018) and open wound infection (9 vs 2%; p = 0.02). Laparoscopy group had significantly higher sensory peripheral nerve deficit (5 vs 0%; p = 0.008) and lymphedema (7 vs 1%; p = 0.003).

After analyzing four randomized control trials, Suzanna Granado et al from Spain have concluded that the short-term results of laparoscopic surgery are better than laparotomy and long-term results are comparable.

Robotic surgical staging of carcinoma endometrium was started from 2003 onward. Several studies are published to date assessing the surgical adequacy and complications of robotic-assisted staging as well as it is compared with laparoscopic staging and conventional laparotomy. Lowe et al have published a multi-institutional data of all patients who underwent robotic staging for endometrial carcinoma. A total of 405 patients who underwent surgery in the period from April 2003 to January 2009 were included. Mean BMI was 32.4. A total of 55% had prior abdominal surgery. Mean operating time was 170.5 minutes. Mean estimated blood loss was 87.5 ml. Mean lymph node count was 15.5. Mean hospital stay was 1.8 days. Conversion to laparotomy was done in 6.7% of patients. Postoperative complications were reported in 14.6%.

A prospective analysis of 80 patients who underwent robotic staging is reported from European Institute of Oncology, Milan, Italy. They concluded that for endometrial cancer, open surgical procedures decreased from 78 to 35% and their preliminary data confirm that surgical robotic staging for early-stage endometrial cancer is feasible and safe. Age, obesity and previous surgery do not seem to be contraindications.

Dan SA et al have reported a prospective case-control study comparing robotic surgery with laparotomy. A total of 118 patients underwent robotic staging and were compared with 131 patients who had laparotomy and staging. Lymph node yield was comparable (p = 0.11). Blood loss was significantly more in the laparotomy group (66.6 and 197.6 ml, p < 0.001). Length of hospital stay was significantly longer in the
laparotomy group. Operating time was significantly more for the robotic group. (283 minutes vs 139 minutes, p < 0.001).21

Akhila Subrahmanian et al have also compared robotic surgery and laparotomy in a retrospective cohort study and has concluded that robotic management of obese women with endometrial cancer yields acceptable staging results and improved surgical outcomes. Although operating time is longer, hospital time is shorter. Robotic surgery may be an ideal approach for these patients.22

From University of Pennsylvania, Joel cardinas et al have conducted a retrospective chart review of cases of women undergoing minimally invasive total hysterectomy and pelvic and para-aortic lymphadenectomy by a robotic-assisted approach or traditional laparoscopic approach. A total of 275 cases were identified—102 patients with robotic-assisted staging and 173 patients with traditional laparoscopic staging. There was no significant difference in the rate of major complications between groups (p = 0.13). The mean operative time was longer in cases of robotic-assisted staging (237 minutes vs 178 minutes, p = 0.0001); however, blood loss was significantly lower (109 vs 187 ml, p < 0.0001). The mean number of lymph nodes retrieved were similar between groups (p = 0.32). There were no significant differences in the time to discharge, re-admission or reoperation rates between the two groups.23

Seamon et al have done a prospective cohort study of surgically staged carcinoma endometrium. A total of 105 patients underwent robotic staging from 2006 to 2008. Patients (n = 76), who underwent laparoscopic staging by the same surgeon from 1998 to 2005, were taken as the other cohort. Mean BMI was 34 in the robotic group, whereas mean BMI was 29 in the laparoscopy group. The estimated blood loss, transfusion rate, laparotomy conversion rate and length of stay were lower in the robotic group. The odds ratio for conversion to laparotomy based on BMI for robotics to laparoscopy is 0.2% (95% CI 0.08-0.56, p = 0.002). Mean skin to skin time was 242 minutes in robotic cohort, whereas it is 287 minutes in laparoscopic cohort, (p < 0.001). They concluded that robotic hysterectomy and lymphadenectomy can be achieved in heavier patients successfully.24

John FA Boggess et al have done a comparative study of three surgical methods for hysterectomy with staging for endometrial cancer: Robotic assistance, laparoscopy, laparotomy.

A total of 322 women underwent endometrial cancer staging: 138 by laparotomy (TAH); 81 by laparoscopy (TLH) and 103 by robotic technique (TRH).

The TRH cohort had a higher body mass index than the TLH cohort (p = 0.0008). Lymph node yield was highest for TRH (p < 0.0001); hospital stay (p < 0.0001) and estimated blood loss (p < 0.0001) were lowest for this cohort. Operative time was longest for TLH (213.4 minutes) followed by TRH (191.2 minutes) and TAH (146.5 minutes; p < 0.0001). Postoperative complication rates were lower for TRH, compared with TAH (5.9 vs 29.7%; p < 0.0001). Conversion rates for the robotic and laparoscopic groups were similar.

They concluded that TRH with staging is feasible and preferable over TAH and may be preferable over TLH in women with endometrial cancer. Further study is necessary to determine long-term oncologic outcomes.25

Long-term Oncologic Outcome

One of the most important concerns when any new modality of treatment is introduced in oncology is its long-term outcome. There are now several reassuring reports on the long-term outcome of minimal access surgery in the staging of carcinoma endometrium especially laparoscopic approach as it is now more than a decade older than robotics.

Nezhat et al have done a retrospective cohort study to assess the effect of laparoscopic surgery on the survival of women in early stage endometrial carcinoma from Jan 1993 to June 2003. A total of 67 women were treated by laparoscopy and 127 by laparotomy. Two and 5-year recurrence-free survival were 93 and 91.7% respectively. Overall 5-year survival rate was 100 and 97% respectively. They concluded that laparoscopic surgery resulted in similar survival rates as laparotomy.26

Another long-term data on this issue is published in 2009. Randomized control trial comparing laparoscopy (n = 40) and laparotomy (n = 38) with a follow-up period of 78 months. The cumulative recurrence rates were 8/40 and 7/38 respectively (p = 0.860). Death reported were 7/40 and 6/38 (p = 0.839), overall survival and disease-free survival were comparable (p = 0.535 and p = 0.515 respectively).27

Ghezzi et al report another comparative study supporting the same observations. A total of 117 patients of laparoscopy cohort were compared with 122 patients of laparotomy cohort with a median follow-up period of 52 months and 80 months respectively. Three-year recurrence-free survival and overall survival were comparable. Multivariate analysis showed that advanced surgical stage, unfavorable histology and patient age > 65 years significantly affect survival, regardless of the surgical approach used.28

Due to the recent incorporation of robotics in staging long-term survival data are not available. Prospective randomized trials are awaited.

Quality of Life

The first 802 eligible patients (laparoscopy, n = 535, laparotomy, n = 267) participated in the QoL study in a gynecologic oncology group (GOG) randomized trial of laparoscopy versus laparotomy (GOG 2222). Patients completed QoL assessments at baseline; at 1, 3 and 6 weeks; and at 6 months postsurgery. Laparoscopy patients reported significantly higher functional assessment of cancer therapy-general (FACT-G) scores (p < 0.001), better physical functioning (p < 0.006), better body image (BI; p < 0.001), less pain (p < 0.001) and its interference with QoL (p < 0.001), and an earlier resumption of normal activities.
with management. Women who underwent laparoscopy had a patients’ recall of postoperative pain and patients’ satisfaction procedures was converted to laparotomy in 3 (7.5%) patients. Forty out of 42 obese women had laparoscopic surgery. The characteristics, surgical outcome, cost and hospital stay and interviewed regarding time to recovery, recall of postoperative pain control, and overall satisfaction with their management. Forty out of 42 obese women had laparoscopic surgery. The procedure was converted to laparotomy in 3 (7.5%) patients. Laparoscopic surgery was thus successful in 88.1% of all obese women. There was no significant difference between women who underwent laparoscopy and those who underwent laparotomy in patient characteristics, proportion of women who underwent lymphadenectomy, complications, total cost, patients’ recall of postoperative pain and patients’ satisfaction with management. Women who underwent laparoscopy had a significantly longer operative time, more pelvic lymph nodes removed, a smaller drop in postoperative hematocrit, less pain medication, and a shorter hospital stay (194.8 vs 137.7 minutes, p < 0.001; 11.3 vs 5.3, p < 0.001; 3.9 vs 5.4, p = 0.029; 32.3 vs 124.1 mg, p < 0.001; and 2.5 vs 5.6 days, p < 0.001 respectively). There was a trend toward earlier resumption of full activity and return to work among women who underwent laparoscopy (23.2 vs 45.0 days, p = 0.073, and 35.3 vs 67.0 days, p = 0.055 respectively).

They concluded that most obese women with early stage endometrial cancer can be safely managed through laparoscopy with excellent surgical outcome, shorter hospitalization and less postoperative pain than those managed through laparotomy. Seamon et al have done a case-control study comparing robotic surgery and laparotomy in obese women. A total of 109 patients underwent surgery with the intent of robotic staging and were matched to 191 laparotomy patients. The mean BMI was 40 for each group. The robotic conversion rate was 15.6% [95% confidence interval (CI) 9.5-24.2%]. Ninety-two completed robotic patients were compared with 162 matched laparotomy patients. The two groups were comparable regarding total lymph node count (25 ± 13 compared with 24 ± 12, p = 0.45) and the percentage of patients undergoing adequate lymphadenectomy (85% compared with 91%, p = 0.16) and adequate pelvic (90% compared with 95%, p = 0.16) and aortic lymphadenectomy (76% compared with 79%, p = 0.70) for robotic and laparotomy patients respectively, but there was limited power to detect this difference. The blood transfusion rate [2% compared with 9%, odds ratio (OR) 0.22, 95% CI 0.05-0.97, p = 0.046], the number of nights in the hospital (1 compared with 3, p < 0.001), complications (11% compared with 27%, OR 0.39, 95% CI 0.13-0.65, p = 0.003), and wound problems (2% compared with 17%, OR 0.10, 95% CI 0.02-0.43, p = 0.002) were reduced for robotic surgery. In obese women with endometrial cancer, robotic comprehensive surgical staging is feasible. Importantly, obesity may not compromise the ability to adequately stage patients robotically.

Laparoscopic and robotic-assisted staging seem to be promising in the management of obese and elderly women with carcinoma endometrium.

**Feasibility in Elderly and Obese**

Melissa KF et al have done a retrospective analysis on 60 patients aged above 65 years and 69 patients less than 65 years who underwent surgical staging of carcinoma endometrium by laparoscopic and robotic hysterectomy. They concluded that minimal access surgery is feasible and safe in elderly women. Sribner et al have reported that age is not a contraindication for laparoscopic surgery. Transvaginal hysterectomy remains a proven option for women with serious comorbidities.

A review article published from North Carolina School of Medicine, Obesity–Physiologic Changes and Challenges in Laparoscopy concludes that with thorough preparation and careful preoperative evaluation, laparoscopy can be performed safely and is the preferred surgical method in obese patients.

Gamal H et al compared laparoscopy and laparotomy in a cohort of obese women with carcinoma endometrium. Prospective study over 2 years applying laparoscopic surgery to all women with clinical stage I endometrial cancer and body mass indices (BMIs) between 28.0 and 60.0 who can tolerate such surgery. Controls were women with clinical stage I endometrial cancer and similar BMIs who underwent laparotomy in the previous 2 years. Both groups were compared in their characteristics, surgical outcome, cost and hospital stay and interviewed regarding time to recovery, recall of postoperative pain control, and overall satisfaction with their management. Forty out of 42 obese women had laparoscopic surgery. The procedure was converted to laparotomy in 3 (7.5%) patients. Laparoscopic surgery was thus successful in 88.1% of all obese women. There was no significant difference between women who underwent laparoscopy and those who underwent laparotomy in patient characteristics, proportion of women who underwent lymphadenectomy, complications, total cost, patients’ recall of postoperative pain and patients’ satisfaction with management. Women who underwent laparoscopy had a...
Lowe et al report that the learning curve for robotic hysterectomy with pelvic and aortic node dissection lies between 9 and 20 cases.\textsuperscript{19}

**Cost Analysis**

With regard to costs, there has been one article to date comparing robotic, open and laparoscopic procedures to surgically stage endometrial cancer. In that report, the cost of the robotic system was included in the cost analysis for robotic surgery. Interestingly, there was no statistically significant difference in costs between robotic and laparoscopic approach (p < 0.06). Both minimally invasive approaches cost significantly less than an open approach (p < 0.001). However, robotics was associated with less perioperative morbidity and quicker return to normal activity.\textsuperscript{38}

**Uterine Manipulation**

Regarding uterine manipulation in laparoscopic hysterectomy, there are conflicting reports.

Querleu et al reported three patients with stage I, noninvasive or superficially invasive endometrial cancer with vaginal cuff recurrence within 9 months of treatment. They raised the concern that the obligatory use of a vaginal manipulator at the time of surgery may lead to antegrade and retrograde dispersal of tumor cells with subsequent vaginal cuff and peritoneal metastasis. No evidence exists to link vaginal recurrence with the use of uterine manipulators or with the omission of tubal occlusion.\textsuperscript{39}

Sonoda et al showed that the treatment of low-risk endometrial cancer by laparoscopy is associated with a significantly higher incidence of positive peritoneal cytology when compared with patients operated by laparotomy. The use of an intrauterine manipulator is not necessarily required to perform an adequate laparoscopic-assisted procedure and could prevent the retrograde dissemination of cancer cells into the peritoneal cavity during uterine manipulation.\textsuperscript{40}

Gamal H Eltabakh et al in a prospective study of laparoscopic surgical staging of clinical stage 1 endometroid endometrial carcinoma using Pelosi uterine manipulator have reported that it does not increase the incidence of positive peritoneal cytology.\textsuperscript{41}

**Portsie Metastasis**

The incidence of portsite metastasis treated by total laparoscopic hysterectomy is low. Andreas Obermair et al have reported that on a median follow-up of 29.4 months, no portsite metastasis was seen in 215 patients treated with laparoscopy. The disease-free survival was statistically comparable to 284 laparotomy treated controls.\textsuperscript{42}

**Microlaparoscopy in Surgical Staging of Carcinoma Endometrium**

Consecutive patients undergoing surgical staging of endometrial cancer using exclusively 3 mm working ports and a 3 or 5 mm laparoscope at the umbilicus (microlaparoscopy group; N = 23) were compared with historical controls selected from consecutive women who had staging with conventional laparoscopy (N = 80).

No difference was found in demographics and preoperative variables between the two groups. Conversion from microlaparoscopy to a conventional laparoscopic technique occurred in two cases (9.7%), while there was no conversion to open surgical staging in either group. There were no significant differences between the microlaparoscopy group and the control group with regard to estimated blood loss [100 (10-400) vs 100 (10-400), p = 0.09], number of pelvic lymph nodes (19.2 ± 7.4 vs 18.6 ± 7.2, p = 0.79) and complication rate (intraoperative: 0 vs 2.5%, p = 1.0; postoperative: 8.7 vs 13.7%, p = 0.73). Operative time was similar between groups when analysis was restricted to the last 20 conventional procedures performed period prior to beginning of the microlaparoscopy trial [155 (110-300) vs 160 (115-295), p = 0.17]. The median length of hospital stay was 2 (1-10) days for women undergoing microlaparoscopic procedures compared to 3 (1-15) days for those undergoing conventional laparoscopy (p = 0.001).

These preliminary results suggest that microlaparoscopy is a safe and adequate surgical option for endometrial cancer staging with the potential to further decrease invasiveness of the conventional laparoscopic approach.\textsuperscript{43}

**DISCUSSION**

The role of minimally invasive surgical staging in the management of patients with apparent early endometrial cancer continues to evolve. From the above-mentioned review of literature, it is evident that comprehensive surgical staging of endometrial cancer can be performed using laparoscopy without increased intraoperative injuries, with fewer postoperative complications, and with shorter hospital stay. This makes attempting laparoscopy, when assumed to be feasible, worth the extraoperative time and surgeon training. The long-term results comparing recurrence-free survival, overall survival and quality of life are also promising. With the advent of robotic surgery, the limitations of the laparoscopic approach is presumed to be overcome.

The conversion rate to laparotomy is less frequent for those patients undergoing the robotic approach when compared to laparoscopy, despite a significantly higher BMI. In addition, the operating room times, length of hospital stay, blood loss and transfusion rates were significantly reduced in the robotic cohort. Therefore, it appears that the robotics platform may offer significant advantages over laparoscopy in the comprehensive surgical management of endometrial cancer. The three-dimensional, magnified images combined with wristed instrumentation, tremor filtration and motion scaling allow the surgeon to recapitulate open surgery. The counterintuitive motions encountered in conventional laparoscopy are eliminated and these advantages are readily apparent even to the advanced laparoscopic gynecologic oncologist. The robotics platform is associated with a shorter learning curve.
While a skilled robotic bedside assistant is essential, the robotic surgeon has the additional advantages of a stable camera and direct control of endoscope movement. Robotics also reduces the poor ergonomics associated with laparoscopy, which leads to surgeon discomfort and risk of chronic musculoskeletal occupational injury, particularly during longer procedures. Although robotics offers many potential advantages for endometrial staging procedures, there are many unknown entities surrounding this new technology. Robotic surgery for gynecology was approved only in April 2005, thus, limited published data exists of long-term survival advantage.

**CONCLUSION**

In conclusion, the data reported in this review article establishes the role of minimal access surgical staging by laparoscopy and robotics for the treatment of endometrial cancer. This is even more applicable for the obese, elderly women with comorbidities who form a major subset of women with carcinoma endometrium. Robotics has the potential to dramatically expand the minimal access surgical option for women undergoing surgery for endometrial cancer. Although robotics represents a technologic leap over traditional laparoscopy, long-term follow-up data are yet to be published.

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