ZKTB

ORIGINAL RESEARCH

Perioperative and Postoperative Outcomes of Laparoscopy and Open Method for Surgical Staging of Endometrial Cancer

Endometrium Kanseri Evrelemesinde Laparoskopik Yöntem ile Laparotomik Yöntemin Perioperatif ve Postoperatif Karşılaştırılması

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ABSTRACT

Objective: *The aim of the study was to compare the safety of the laparoscopic and open method for endometrial cancer staging.*

Material and Methods: *Between January 2015 and August 2017, we reviewed 121 women with endometrial cancer treated by open (n=81) or laparoscopic (n=40) approach, retrospectively. Two groups were compared in terms of operating times, intraoperative and postoperative complications, perioperative and postoperative features such as hemoglobin values, the lengths of hospital stay, and adjuvant therapy. All of the patients underwent a hysterectomy and bilateral salpingo-oophorectomy; and when indicated, omentectomy and lymphadenectomy were performed.*

Results: *There were no significant differences between the two groups with regard to the number of parities, body mass index, menopausal status, age, the American Society of Anesthesiologists (ASA) scores, the requirement of lymphadenectomy, and hospital stay. There were significant statistical differences between groups in terms of operation time and difference of hemoglobin ($p<0.001$, $p=0.013$; respectively). Laparoscopic surgery had a longer operative time than laparotomy, and difference of hemoglobin in the laparotomy group is more than the laparoscopy group. Patients who underwent staging with laparotomy had bowel injury (1.2%), wound infection (13.6%), and postop ileus (8.6%) while in the laparoscopy group patients had wound infection (2.5%) and postop ileus (5%). There were no statistically significant differences between the two groups in terms of the intraoperative ($p=1$) and postoperative complications ($p=0.101$ for wound infection, $p=0.716$ for postop ileus). The groups were similar in terms of the histological grade, FIGO stage, histologic subtype, the rate of lymphovascular invasion, the depth of myometrial invasion, the total number of lymph nodes resected in lymph node dissections, the rate of lymph node metastasis, the location of the tumor, cervical stromal invasion, and the adjuvant therapy such as chemotherapy and brachytherapy. None of the patients in both groups had a recurrence and long-term lymphatic complication such as lymphocyst, lymphedema.*

Conclusion: *Our current data demonstrated that the laparoscopic approach can be performed without loss of safety with similar complication rates in patients with endometrium cancer. Additionally, the laparoscopy was not inferior to the laparotomy in terms of efficacy.*

Keywords: *endometrial carcinoma, laparoscopy, laparotomy, surgical staging*

ÖZET

Amaç: *Endometrium kanserinin evreleme cerrahisinde laparoskopik yaklaşımın güvenirliğini laparotomi ile karşılaştırmak.*

Gereçler ve Yöntem: *Ocak 2015 ile Ağustos 2017 tarihleri arasında laparoskopik (n=40) ve laparotomik (n=81) yöntemle tedavi edilen 121 endometrium kanserli hastanın bilgileri geriye dönük olarak değerlendirildi. İki grup operasyon süreleri, intraoperatif ve postoperatif komplikasyonlar, hemoglobin değerleri, hastanede kalış süreleri ve postoperatif ek tedavi gibi preoperatif ve postoperatif özellikleri açısından karşılaştırıldı. Bütün hastalara histerektomi ve bilateral salpingo-ooferektomi uygulandı ve gereklilik halinde lenf nodu diseksiyonu ve omentektomi yapıldı.*

Bulgular: *Gruplar yaş, doğum sayısı, vücut kütle indeksi, menopozal durum, ASA (the American Society of Anesthesiologists) skoru, lenfadenektomi gerekliliği ve hastanede kalış süreleri açısından benzerdi. Preoperatif ve postoperatif hemoglobin değişim değerleri ($p=0.013$) ve operasyon süreleri ($p<0.001$) arasında istatistiksel olarak anlamlı fark vardı. Laparoskopi yapılan gruptaki hastaların operasyon süreleri daha fazla bulunurken, hemoglobin değişim değerleri daha az bulundu. Laparotomi yapılan grupta barsak hasarı (%1,2), yara yeri infeksiyonu (%13,6) ve postop ileus (%8,6) gelişirken, laparoskopi yapılan grupta yara yeri infeksiyonu (%2,5) ve postop ileus (%5) gelişti. Gruplar arasında intraoperatif ($p=1$) ve postoperatif komplikasyonlar açısından (yara yeri infeksiyonu için $p=0.101$; postop ileus için $p=0.716$) anlamlı fark yoktu. Gruplar histolojik grade, FIGO evresi, histolojik alt tip, lenfovasküler alan invazyon oranları, myometrial invazyon, çıkarılan lenf nodu miktarı, nodal metastaz oranları, tümör yerleşimi, servikal stromal invazyon ve kemoterapi ya da radyoterapi gibi ek tedavi uygulanmaları açısından benzerdi. Hiçbir hastada lenfokist ya da lenfödem gibi uzun dönem komplikasyonlar ve rekkürens gelişmedi.*

Sonuç: *Çalışmamız laparoskopik yaklaşımın endometrium kanserli hastaların evrelemesinde laparotomiye benzer komplikasyon oranlarıyla güvenli bir şekilde uygulanabileceğini gösterdi. Ayrıca laparoskopi endometrium kanserinin evrelemesinde ve tedavisinde laparotomi kadar etkin bulunmuştur.*

Anahtar Kelimeler: *endometrium kanseri, cerrahi evreleme, laparoskopi, laparotomi*

INTRODUCTION

Endometrial cancer (EC) is the most frequently diagnosed female genital malignancy with an incidence of 12 per 100,000 women (1). This incidence is on the rise due to increasing rates of elevated body mass index, diabetes, and metabolic syndrome which are known risk factors for the disease.

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The most common presenting symptom is abnormal uterine bleeding and the mean 5-year-survival rate is 90% for patients with early stage disease. EC is managed with hysterectomy and bilateral salpingo-oophorectomy, with pelvic and para-aortic lymphadenectomy being performed in accordance with staging guidelines when indicated. Surgical technique and radicality should always be adapted to the patient's general status and individual risk factors.

Surgical staging for EC had been generally performed through laparotomy. In recent years, minimally invasive surgery has become an attractive alternative to the classic open approach. Both techniques offer similar recurrence-free and overall survival rates with laparoscopy being associated with less surgical morbidity, faster recovery and improved quality of life (2-4). Laparoscopic management of early EC has therefore become the new standard of care. The aim of this study was to compare the peri- and post-operative outcomes as well as cancer recurrence rates between laparotomy and laparoscopy in the management of early EC.

MATERIALS AND METHODS

Patients

The study was approved by the local ethical committee. We retrospectively reviewed the files of 121 patients diagnosed with EC between January 2015 and August 2017 who were managed with either conventional laparotomy (n=81) or laparoscopy (n=40). Women diagnosed with uterine sarcomas were excluded. Patient characteristics included age, parity, menopausal status, and body mass index (BMI). We compared operative times, intra- and post-operative complications, pre- and post-operative hemoglobin values, lengths of hospital stay, and the use of adjuvant chemotherapy and radiotherapy when indicated. A complete gynecologic examination, pelvic ultrasound and magnetic resonance imaging, preoperative endometrial sampling and cervical cytology were obtained for all patients. Low molecular weight heparin and compression stockings were used for thrombophylaxis in all cases.

Surgical Technique

All patients underwent a hysterectomy with bilateral salpingo-oophorectomy. Lymph node dissection was performed when indicated in accordance with the Mayo criteria for endometroid tumors (tumor size ≤ 2cm, grade 1 or 2 tumors, and depth of invasion ≤ 50% on imaging or intra-operative examination) and systematically with other epithelial subtypes histologies (clear cell and serous carcinomas).

Pelvic lymphadenectomy was defined as removing all lymphatic tissue around the obturator nerve and the iliac vessels. Para-aortic lymphadenectomy was defined as removing all lymphatic tissue around the aorta and vena cava up to the renal vein. Infracolic omentectomy was performed for all non-endometroid carcinomas. The laparotomy was always a midline incision. All surgeries were performed by one gynecological oncologist.

Statistical Analysis

Data was analyzed with SPSS (Version 20.0. 2011, IBM SPSS Statistics for Windows; IBM Corp. Armonk, NY, USA). Histograms, normality plots and the Shapiro-Wilk normality test were used to analyze data distribution. Median, mean, standard deviation, frequency and ratio were used for descriptive statistics. The Mann-Whitney U test was used to analyze quantitative data. The $\chi 2$ test or Fisher's exact test were used to analyze qualitative data. A p-value < 0.05 was considered statistically significant.

RESULTS

One hundred and twenty-one women with endometrial carcinoma met the inclusion criteria. Eighty-one patients underwent laparotomy for their disease while 40 were managed laparoscopically. All surgeries were completed laparoscopically in the laparoscopy group with the exception of one patient for which conversion to laparotomy because of acute bleeding was necessary. This patient was subsequently included in the laparotomy group for analysis. Demographic characteristics, intra- and post-operative parameters, and intra- and post-operative complications for all patients are presented in Table 1.

Table 1: Demographics and operative features of the patients.

	Staging with laparotomy (n=81)	**Staging with laparoscopy (n=40)**	**p**
Age	60.05 ± 11.46	58.45 ± 4.08	0.289
Parity	2 (0-8)	2 (0-5)	0.128
Body mass index (kg/m²)	31.29 (18-39)	28.33 (22-35)	0.944
Menopausal status			
Premenopausal	12 (14.8%)	5 (12.5%)	0.730
Postmenopausal	69 (85.2%)	35 (87.5%)	
American Society of Anesthesiologists (ASA) score	2 (1-3)	3 (1-3)	0.066
Lymphadenectomy	55 (67.9%)	31 (77.5%)	0.273
Operation time (min)	157	218	
Without lymphadenectomy	132	172	**<0.001**
With lymphadenectomy	169	251	
Hospital stay (day)	4 (2-15)	3 (2-8)	0.737
Difference of hemoglobin (g/dl)	1.43 ± 0.75	1.19 ± 0.91	**0.013**
Intraoperative complications			
Bowel injury	1 (1.2%)	0 (0%)	1
Postoperative complications			
Wound infection	11 (13.6%)	1 (2.5%)	0.101
Ileus	7 (8.6%)	2 (5%)	0.716

Table 2: Histopathological features of the patients.

	Staging with laparotomy (n=81)	Staging with laparoscopy (n=40)	p
Histological grade			
G1	27 (33.3%)	20 (50%)	0.153
G2	47 (58%)	16 (40%)	
G3	7 (8.6%)	4 (10%)	
FIGO stage			
1	62 (76.5%)	35 (87.5%)	0.157
2	11 (13.6%)	3 (7.5%)	
3	8 (9.9%)	2 (5%)	
4	0 (0%)	0 (0%)	
Histologic subtype			
Endometrioid	73 (90.1%)	40(100%)	0.051
Others	8 (9.9%)	0 (0%)	
Myometrial invasion			
< ½ thickness	48 (59.3%)	29 (72.5%)	0.154
≥ ½ thickness	33 (40.7%)	11 (27.5%)	
Lymphovascular space invasion			
No	56 (69.1%)	34 (85%)	0.06
Yes	25 (30.9%)	6 (15%)	
Tumor size (cm)	4.59 ± 2.72	2.81 ± 1.95	**<0.01**
Lymph nodes	21.82 ± 10.67	21.65 ± 12.87	0.558
Lymph node metastasis (n)	8 (9.9%)	2 (5%)	0.494
Cervical stromal invasion			
No	66 (81.5%)	37 (92.5%)	0.109
Yes	15 (18.5%)	3 (7.5%)	
Tumor location			
Fundus	26 (32.1%)	16 (40%)	
Corpus	34 (42%)	21 (52.5%)	0.083
Isthmus	4 (4.9%)	0 (0%)	
Diffuse	17 (21%)	3 (7.5%)	
Brachytherapy			
No	50 (61.7%)	29 (72.5%)	0.242
Yes	31 (38.3%)	11 (27.5%)	
Chemotherapy			
No	67 (82.7%)	38 (95%)	0.061
Yes	14 (17.3%)	2 (5%)	

The two groups were similar in age, parity, body mass index, menopausal status, ASA scores, lymphadenectomy rates and length of hospital stay (Table 1). There were statistically significant differences in operative time and blood loss as estimated by pre – and post-operative hemoglobin values ($p<0.001$, $p=0.013$ respectively), it was associated with less hemoglobin loss. There was a trend towards more bowel injury (1.2% vs 0%), wound infection (13.6% vs 2.5%) and post-operative ileus (8.6% vs 5%) in the laparotomy group but this difference was not statistically significant (Table 1). The two groups have similar distributions of EC histologic subtypes, histological grade and FIGO disease stage. They had comparable myometrial invasion depths but tumors managed laparoscopically tended to have lower LVSI rates (15% vs 30.9%) without reaching statistical significance ($p=0.06$). Other pathological data such as the total number of removed lymph nodes and the ratio of lymph node metastasis as well as tumor location and cervical stromal invasion were similar in both populations. There was no difference in adjuvant chemotherapy and brachytherapy rates. Tumors managed laparoscopically were smaller as the final tumor size on pathology reports was 4.59±2.72 cm in the laparotomy group compared with 2.81±1.95 cm in the laparoscopy group ($p<0.01$) (Table 2). None of the 121 patients in this study had recurrence of their disease clinically or on imaging and no long-term lymphatic complications such as lymphocyst formation or lymphedema were reported up to 20 months postoperatively.

DISCUSSION

Our study adds to existing evidence suggesting that laparoscopy is a safe and acceptable alternative to conventional laparotomy in the staging and management of EC (5-8). Minimally invasive surgery rates are gradually increasing and could soon surpass those of conventional laparotomy as experienced gynecologic oncologists become more efficient at laparoscopic procedures while maintaining equal safety profiles. In addition, laparoscopy offers the benefit of less pain and increased comfort for patients which improves quality of life and satisfaction scores.

Laparoscopic surgery required almost one hour more to complete when compared to laparotomy. These findings are in accordance with the LAP2 study and other previous studies (2, 9, 10). Interestingly, Boosz et al reported there was no statistically significant difference between the two groups with regard to operation times in their population. However, the procedures were performed by 5 different gynecologic oncologists and lymphadenectomy rates in the laparotomy group were significantly higher which might have increased the duration of surgery (29% vs 22.6%, $p<0.001$) (11).

Most of the studies reported lower blood loss in the laparoscopy group (9, 12-14). In our study, the difference between pre-operative and post-operative hemoglobin values was higher in the laparotomy group and was similar to published data. No women required blood transfusion during surgery or in the post-operative period.

The mean tumor size was lower in the laparoscopy group because surgeons might have opted for laparotomy in patients with large tumors on pre-operative clinical or radiological evaluation.

A mean of 21.65 lymph nodes and 21.82 lymph nodes in the laparoscopy and laparotomy groups was removed respectively, which is in accordance with the number of nodes recommended for staging of EC (15). In previous studies, the range of removed lymph nodes was not always adequate (8.2 to 27.1 nodes), which might affect the rates of post-operative events related to lymph node dissection (8, 16, 17). In fact, lymphocyst formation is a long-term complication which negatively impacts the quality of life of EC survivors. The risk factors for the development of this entity are injury to lymphatic vessels or their insufficient closure, pelvic radiotherapy, and the presence of lymph node metastases (18, 19). A number of studies reported higher lymphocyst formation rates after laparotomy (6, 20). This complication was not reported in any group in our study.

Muntz et al. reported port-site recurrence following laparoscopy in patients with endometrial cancer (21). This rate is variable according to published literature. No port-site metastasis occurred in the laparoscopy group of this study up to 20 month post-operatively.

The LAP2 study reported a higher rate of conversion to laparotomy (25%) (2) while other studies reported conversion rates of 0-36.4% (20, 22). In our study, only one laparoscopic procedure was converted to laparotomy because of acute bleeding and was subsequently included in the laparotomy group for the statistical analysis.

There were no significant differences between the two groups with regard to intraoperative and postoperative complications. Mourits et al. had also demonstrated similar complication rates between laparoscopy and laparotomy (14.6%, 14.9%, respectively) (7). Walker et al. however reported more postoperative complications in the laparotomy group (23). We noted a trend toward more post-operative wound infections in the laparotomy group. Interestingly, most of the repeat operations performed by Boosz et al. were due to wound healing complications when a traditional midline incision was performed for the staging of EC (11).

Most of the previous studies reported significantly shorter hospital stays with laparoscopy (9, 13, 24). We found that both groups were similar in terms of hospitalization. This phenomenon could be attributed to the belief that it is safer for patients diagnosed with cancer to have extended hospital stays after surgery for fear of complication or death regardless of surgical technique, despite evidence to the contrary.

This study did not report increased rate of disease recurrence at 20 months in the laparoscopy group compared with the laparotomy group. Chu et al. had previously declared no significant difference in the recurrence rates between the two groups after 5 years of follow-up (9). The survival data was limited in our population, however, because of the small number of patients and the relatively short follow-up period. The limitations of the present study also included the retrospective approach and a single-institution trial.

CONCLUSION

Despite the limitations of this retrospective study, our current data further underlines the role of minimally invasive techniques in the management of endometrial cancer staging. Laparoscopy in this setting can be performed without loss of safety with similar complication rates to a conventional open technique. Patients with endometrial cancer could therefore benefit from laparoscopic surgery when it is available and feasible.

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