

Mini-laparoscopy versus conventional laparoscopy for the management of endometrial cancer

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ABSTRACT

OBJECTIVE: We aimed to evaluate the feasibility of a mini-laparoscopic surgical approach versus standard laparoscopy.

METHODS: 75 patients with endometrial cancer treated by mini-laparoscopic (n=25) or conventional laparoscopic surgery (n=50) at a tertiary-care university-based teaching hospital and academic affiliated private hospital were included.

RESULTS: There was no significant difference between the mini-laparoscopy and the conventional laparoscopy group regarding surgical procedures. The mean operation time and the median estimated blood loss were similar (p=0.671 and p=0.158, respectively). No difference was found in terms of the number of lymph nodes removed. No intraoperative complications were observed in both groups. Return to daily routine and the rate of additional analgesia requirement were similar in the groups. The mean duration of hospitalization was 3.6±1.2 days in the mini-laparoscopy group and 4.9±3.6 days in the conventional laparoscopy group (p=0.025).

CONCLUSION: We demonstrated that mini-laparoscopic staging could be a competent technique performed regardless of harm by talented surgeons using state-of-the-art instruments. Mini-laparoscopic surgery appears to be a further possibility to minimize surgical trauma by reducing the size of the ports without decreasing the extent and effectiveness of the procedures.

Keywords: Endometrial cancer; laparoscopy; mini-laparoscopy; staging.

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Endometrial cancer (EC) is the most common gynecologic malignancy globally, with an incidence of 12 cases per 100,000 susceptible people [1]. Approximately 80% of endometrial carcinoma have been found to harbor a couple of risk factors, including high body mass index (BMI), diabetes, and metabolic syndrome. Patients with early-stage EC have been

shown to have a better five-year survival rate, around 90%, compared to those with advanced stages. Standard surgery (total hysterectomy and bilateral salpingo-oophorectomy), whether lymphadenectomy or not, due to risk factors leading to decreased survival and treatment resistance, has also been demonstrated in several studies.

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As per current literature, the safety and effectiveness of the laparoscopic approach for malignant procedures have been proven in different settings, particularly in gynecological cancers [2–6]. It is associated with rapid recovery, less pain, and improved quality of life judged against open surgery. Standard laparoscopic surgery is performed using 5-mm and 10-mm diameter instruments along with 10-mm optics. On the contrary, mini-laparoscopic surgery is a procedure that leverages below 5-mm diameter instruments (≤ 3.5 mm) concomitant with either 5-mm or 3.5-mm optics. Recently, the mini-laparoscopic approach has gained tremendous popularity in the era of gynecological surgery [7, 8]. Several studies have reported astonishing results favoring mini-laparoscopy for benign and malignant conditions without detrimental surgical quality [9–11]. Today, myomectomy, radical hysterectomy, and lymphadenectomy can be carried out using mini-laparoscopy with minimal surgical trauma and better cosmetic outcome [11–13]. Furthermore, mini-laparoscopy is associated with low pain scores, diminished wound complication rates, de-escalated port-site hernia cases, and improved beautifying consequences compared to standard laparoscopy [10]. Notably, 5-mm laparoscopes are not routinely preferred due to their lack of resolution and image quality.

Using propensity-matched comparison, we sought to evaluate the feasibility of a mini-laparoscopic surgical approach (5-mm scope and 3-mm/5-mm instruments) versus standard laparoscopy (10-mm scope and 5-mm instruments).

MATERIALS AND METHODS

Study Population

Patients with EC treated at a university hospital by mini-laparoscopic ($n=25$, Group A) or conventional laparoscopic ($n=50$, Group B) surgery were enrolled in this study. All operations were performed by gynecologic oncology surgeons with equal expertise in minimally invasive surgical approaches in the field. Informed consent was obtained before surgery after a discussion of the surgical risks in obedience to the declaration of Helsinki. Gynecologic examination, pelvic ultrasonography, cervical cytology, pre-operative endometrial sampling, adjacent and distant organ metastasis screening (abdominal magnetic resonance imaging, computerized tomography of thorax), and blood sampling were performed on all participants. Groups were compared in terms of age, menopausal status, gravida, parity, BMI, previous

Highlight key points

- Endometrial cancer (EC) is the most common gynecologic malignancy globally.
- Mini-laparoscopic surgery is a procedure for leverages below 5-mm diameter instruments (≤ 3.5 mm) concomitant.
- Today, myomectomy, hysterectomy, and lymphadenectomy can be carried out using mini-laparoscopy with minimal surgical trauma.
- Mini-laparoscopy is associated with low pain, diminished wound complication, de-escalated port-site hernia, and improved cosmetic consequences compared to standard laparoscopy.

abdominal surgery, American Society of Anesthesiology (ASA) score, surgical procedure, operating time, estimated blood loss, complications, analgesia requirement, hospitalization, return to daily routine, and final pathology report. Low molecular weight heparin and compression stocking were applied to prevent thromboembolic complications. The study was approved by the Koc University Ethical Committee (approval date: 24.04.2020 approval number: 2020.159.IRB2.049).

Data Collection

Data was extracted from the institution-based electronic medical records, including preoperative examination notes, operative reports, discharge summaries, pathology documents, and outpatient follow-up charts. In addition, clinical research associate team members jotted down a customized gynecologic oncology worksheet. Baseline characteristics, including age, BMI (kg/m^2), parity, previous history of abdominal surgery, and menopausal status, were recorded. Operative time and intra-operative complications were re-reviewed by observing full-length video of all operations. Total operative time was the interval between the start of abdominal insufflation and skin closure.

Surgical Technique

All procedures were performed under general anesthesia in the dorsal lithotomy position. First, the abdominal cavity was insufflated with carbon dioxide, and pneumoperitoneum (12 mm/Hg) was achieved, then the visualization was obtained with a 30° high-definition scope. Surgical technique was performed using an optical trans-umbilical 5-mm or 10-mm trocar and 5-mm ancillary trocars in the conventional laparoscopy group. An optical trans-umbilical 5-mm and 3.5-mm ancillary trocar on the left side and 3.5-mm and 5-mm ancillary trocars (just one 5 mm

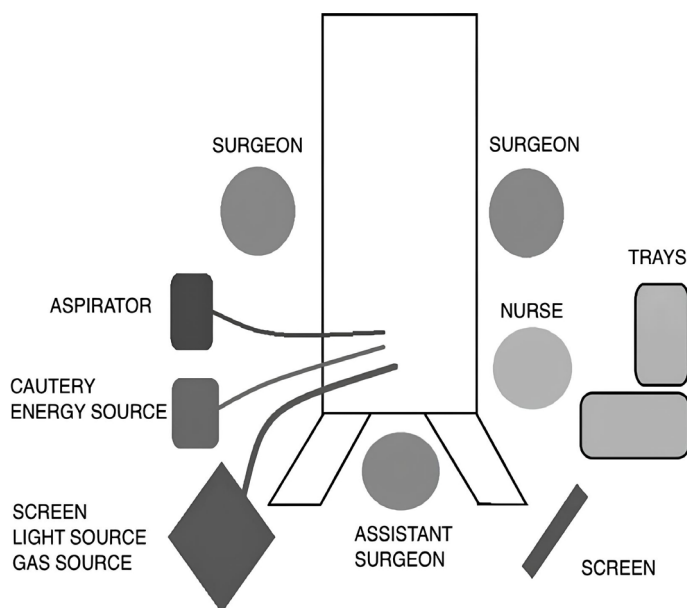


FIGURE 1. Schematic representation of the operating room.

to use an energy device) on the right side were used in the mini-laparoscopy group (Karl Storz, GmbH & Co. KG., Tuttlingen, Germany) [8]. A 5 mm trocar to use a cutting and coagulation device was inserted at the right lower abdominal wall near the anterior superior iliac spine in the mini-laparoscopy group. Figure 1 shows the schematic representation of the operating room [14]. For all procedures, a uterine manipulator was used to make uterine manipulation easier. All of the patients underwent a hysterectomy and bilateral salpingo-oophorectomy. Lymph node evaluation was performed based on the risk factors. In our institution, the sentinel lymph node (SLN) mapping technique with indocyanine green (ICG) has been widely used since 2014. The standard technique is to inject 4 ml of ICG diluted in aqueous solvent into the uterine cervix at the 3 and 9 o'clock positions, submucosally and deep of the cervix, and the Pinpoint® Endoscopic Fluorescence Imaging System (Pinpoint®, Novadaq Technologies, Bonita Springs, FL, USA) was opted out intraoperatively to locate the SLN. Pelvic lymphadenectomy was defined as removing lymphatic tissue around the obturator nerve accompanied by common, external, internal iliac arteries and veins. Para-aortic lymphadenectomy was defined as removing lymphatic tissue around the aorta and vena cava up to the inferior mesenteric artery or renal vein. The vaginal vault was closed with the V-Loc™ wound closure device. The 3.5-mm and 5-mm ancillary incisions were approximated using strips without suturing, while 10-mm incisions were closed with su-

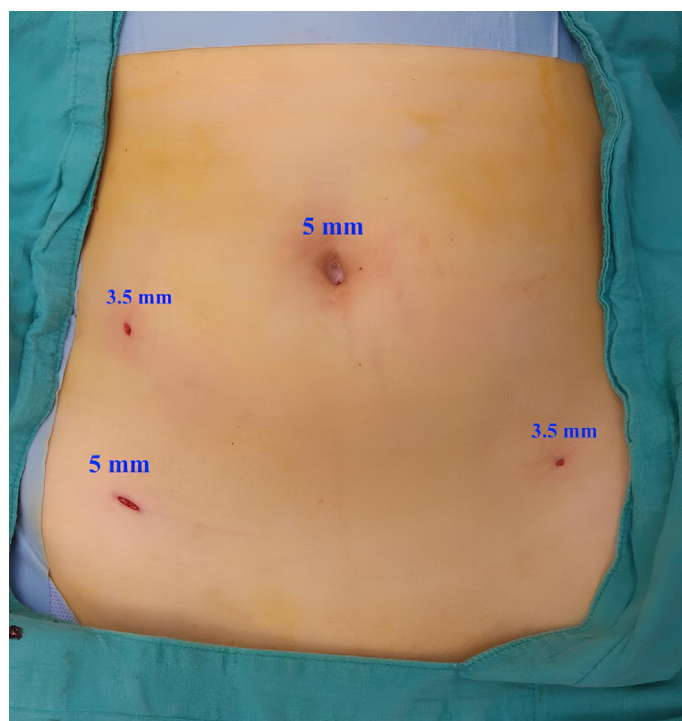


FIGURE 2. Postoperative incisional scars.

tures instead. Postoperative incisional scars are shown in Figure 2. For postoperative analgesia, patients were given ibuprofen (400 mg), paracetamol (1 gr), and tramadol (1 mg/kg) approximately 30 minutes before the skin closure. In the first 24 hours, postoperative pain was relieved with diclofenac potassium (50 mg) administered orally every 8 hours.

Statistical Analysis

Data was analyzed by SPSS (Version 26.0. 2011, IBM SPSS Statistics for Windows; IBM Corp. Armonk, NY, USA). Since this is a retrospective comparison between two groups, we adopted a propensity-matched comparison to reduce the covariate imbalance in measured baseline patient characteristics between surgical groups. Patients who underwent mini-laparoscopic surgery were matched 1:2 to a group of patients who underwent conventional laparoscopic surgery. Median, mean, standard deviation, frequency, and ratio values were used for descriptive statistics. The variables were investigated using Kolmogorov-Smirnov/Shapiro-Wilk's test to determine whether or not they are normally distributed. The χ^2 or Fisher's exact test was used to analyze categorical variables. The Student's *t*-test and Mann-Whitney *U* test were used to analyze continuous variables. A *p*-value <0.05 was used as the cutoff for significance.

TABLE 1. Baseline characteristics of the patients who underwent mini-laparoscopy and conventional laparoscopy^a

	Mini-laparoscopy (n=25)	Conventional laparoscopy (n=50)	p
Age, years	62.2±9.9	60.9±13.2	0.645
Menopausal status			0.189
Premenopausal	4 (16%)	15 (30%)	
Postmenopausal	21 (84%)	35 (70%)	
Gravida	2 (0–7)	2 (0–8)	0.670
Parity	2 (0–6)	2 (0–8)	0.632
BMI ^b , kg/m ²	28±4.6	29.2±4.5	0.855
Previous abdominal surgery	17 (68%)	42 (84%)	0.111
ASAc score	2 (1–3)	2 (1–3)	0.317

a: Data are presented as number (%), mea±SD or median (range); b: BMI, body mass index; c: ASA, American Society of Anesthesiologists.

RESULTS

Records of 25 patients with EC who underwent mini-laparoscopy and 50 patients with EC who underwent conventional laparoscopy were analyzed. The median age was 61 years (range, 37–87 years), the mean BMI was 29 kg/m² (range, 21–39.8 kg/m²), the median gravida was 2 (range, 0–8), the median parity was 2 (range, 0–8), 59 of 75 patients (78.7%) had a history of previous abdominal surgery, and the median ASA score was 2 (range, 1–3) without significant difference between the groups (Table 1). There was no significant difference between the mini-laparoscopy and the conventional laparoscopy group regarding surgical procedures (Table 2). The mean operation time and the median estimated blood loss were similar ($p=0.671$ and $p=0.158$, respectively) (Table 2). Tumor characteristics in the two groups were reported in Table 3. No difference was found in mean uterine diameter, mean tumor diameter, tumor histology, grading, staging, the number of lymph nodes removed, and lymph node involvement (Table 3). No intraoperative complications were observed in both groups. As a postoperative complication, umbilical wound infection was seen in one patient in both groups, and ileus was observed in one patient in the mini-laparoscopy group. Umbilical wound infections of the patients were superficial and treated with oral antibiotic agents. Postoperative ileus occurred at postoperative day 3 and resolved with conservative treatment at postoperative day 5. Return to daily routine and the rate of additional analgesia requirement were similar in the groups. The mean duration of hospitalization was 3.6 ± 1.2 days in the mini-laparoscopy group and 4.9 ± 3.6

days in the conventional laparoscopy group ($p=0.025$). Five patients (20%) received adjuvant therapy in the mini-laparoscopy group, while 7 (14%) received adjuvant therapy in the conventional laparoscopy group. The median follow-up was 29.1 months (15–52 months) for the mini-laparoscopy group and 46.7 months (14–107 months) for the conventional laparoscopy group. Recurrence was detected in 2 patients in the conventional laparoscopy group. No death was detected in either group.

DISCUSSION

In the last decade, mini-laparoscopic surgical approaches have drawn remarkable popularity in gynecological and non-gynecological surgery [15, 16]. The industry has provided a wide range of mini-laparoscopic instruments for laparoscopic surgeons to enhance their utilization of those cutting-edge technologies [17]. Of course, technological advances have facilitated the application of minimally invasive techniques in gynecological cancer treatment. For instance, decreasing wound size was found to be potentially associated with abatement of incisional hernias as well as other wound complications. Moreover, the smaller trocars do not require vigorous force to penetrate through the abdominal wall, resulting in a dropped rate of injuries to vessels and visceral organs.

To the best of our knowledge, limited studies investigated the safety and feasibility of mini-laparoscopy in EC staging [18–21]. Our study indicates that staging of EC could be performed using mini-laparoscopic instruments without mischievous outcomes similar to conventional laparoscopy. There was no significant difference between

TABLE 2. Surgery related parameters of the patients^a

	Mini-laparoscopy (n=25)	Conventional laparoscopy (n=50)	p
Surgical procedures ^b			0.154
TLH + BSO	1 (4%)	9 (18%)	
TLH + BSO + SLNB	0 (0%)	1 (2%)	
TLH + BSO + BPLND	0 (0%)	6 (12%)	
TLH + BSO + BPLND + SLNB	16 (64%)	23 (46%)	
TLH + BSO + BPPALND	1 (4%)	3 (6%)	
TLH + BSO + BPPALND + SLNB	7 (28%)	7 (14%)	
Radical hysterectomy + BPLND + SLNB	0 (0%)	1 (2%)	
Mean operation time (min) ^b			
TLH + BSO	110	150±49	0.456
TLH + BSO + BPLND	183±58	177±58	0.771
TLH + BSO + BPPALND	266±52	305±87	0.284
Radical hysterectomy + BPLND	–	220	–
Estimated blood loss (ml) (median, range)	60 (20–200)	80 (30–400)	0.158
Intraoperative complications	–	–	
Port site-related complications			
Umbilical wound infection	1 (4%)	1 (2%)	1
Postoperative complications			
Ileus	1 (4%)	–	0.333
Additional analgesia requirement	4 (16%)	10 (20%)	0.763
Mean duration of hospitalization (day)	3.6±1.2	4.9±3.6	0.025
Return back to daily activity (day)	7.8±3.1	8.9±3.7	0.205
Rehospitalization	–	–	–
Adjuvant treatment ^c			0.101
None	20 (80%)	43 (86%)	
BrT	1 (4%)	5 (10%)	
ERT	4 (16%)	1 (2%)	
Chemoradiotherapy	0 (0%)	1 (2%)	

a: Data are expressed as number (%) or mean±SD; b: BPLND, bilateral pelvic lymph node dissection; BPPALND, bilateral pelvic-paraaortic lymph node dissection; BSO, bilateral salpingoophorectomy; SLNB, sentinel lymph node biopsy; TLH, total laparoscopic hysterectomy; c: BrT, brachytherapy; ERT, external radiotherapy.

the groups regarding baseline characteristics and history of previous abdominal surgery. Seventeen out of 25 patients (68%) and 42 out of 50 patients (84%) had a history of previous abdominal surgery in the mini-laparoscopy and conventional laparoscopy groups, respectively. Cianci et al. [22] reported 46 EC cases, which were done using mini-laparoscopic instruments. It is worth mentioning that half of the patients had a history of previous abdominal surgery in their study. Consequently, mini-laparoscopic surgery seems suitable for patients with previous surgery.

This study found no difference between the groups regarding the surgical procedures and the mean operation times. The management of EC staging, including bilateral pelvic-paraaortic lymphadenectomy (BPPALA), was performed successfully in all patients. No conversions were needed from mini-laparoscopy to open surgery as bilateral pelvic-paraaortic lymphadenectomy was indicated. Ghezzi et al. [19] encountered no technical difficulties with the smaller instruments during lymphadenectomy in patients with endometrium cancer and indicated that bleeding was controllable even with the small diameter coagulation devices.

TABLE 3. Final pathological findings of the patients who underwent mini-laparoscopy and conventional laparoscopy^a

	Mini-laparoscopy (n=25)	Conventional laparoscopy (n=50)	p
Mean uterine diameter (mm)	71±13.7	73.4±17.7	0.524
Mean tumor diameter (mm)	23.6±19.8	21.1±15.6	0.550
Histology			0.659
Endometrioid	24 (96%)	46 (92%)	
Non-endometrioid	1 (4%)	4 (8%)	
Grade			0.816
G1	12 / 25 (48%)	26 / 50 (52%)	
G2	10 / 25 (40%)	18 / 50 (36%)	
G3	3 / 25 (12%)	6 / 50 (12%)	
Stage ^b			0.793
I A	19 (76%)	41 (82%)	
I B	5 (20%)	8 (16%)	
II	1 (4%)	0 (0%)	
III C1	0 (0%)	1 (2%)	
Number of removed lymph nodes ^c			0.082
TLH + BSO + SLNB	–	3	
TLH + BSO + BPLND	–	18.8±8.8	
TLH + BSO + BPLND + SLNB	22±14.1	17±11.6	
TLH + BSO + BPPALND	78	39.3±18.8	
TLH + BSO + BPPALND + SLNB	31.3±7.1	41.14±15.3	
Radical hysterectomy + BPLND + SLNB	–	21	
Lymph node involvement	0 (0%)	1 (2%)	1

a: Data are expressed as number (%) or mean±SD; b: According to the FIGO 2009 classification; c: BPLND, bilateral pelvic lymph node dissection; BPPALND: Bilateral pelvic-paraaortic lymph node dissection; BSO: Bilateral salpingoophorectomy; SLNB: Sentinel lymph node biopsy; TLH: Total laparoscopic hysterectomy.

SLN mapping, in conjunction with minimally invasive techniques, has been accelerated in the management of endometrial cancer. Accordingly, SLN mapping was performed successfully in both groups. In a study conducted on 38 patients with early-stage endometrium cancer, Uccella et al. [23] obtained bilateral sentinel node detection in 11 patients out of 15 using a mini-laparoscopic approach without complication.

None of the patients were converted to laparotomy or required blood transfusion in both groups. There was no statistical difference between the groups regarding port site-related or postoperative complications. Our data and the findings of trials comparing mini-laparoscopy and conventional laparoscopy are alike, which means no statistically significant difference has been reported related to intraoperative or early postoperative complications [18, 20].

There is clear evidence that mini-laparoscopic surgery is associated with less postoperative pain, better cosmetic outcomes, and less hospitalization than conventional laparoscopy [24, 25]. In this study, the rates of additional analgesia requirement were sequentially found to be 13% and 17% in the mini-laparoscopy group and the conventional laparoscopy group. A previous randomized study indicated that the necessity for postoperative analgesics was lower when laparoscopy is performed with 3-mm instead of 5-mm ancillary ports [24].

Acton et al. [18] found no difference in length of hospital stay between 5-mm and 10-mm laparoscopic surgery. The mean time of return to daily routine was similar between the groups, while the mean duration of hospitalization was lower in the mini-laparoscopy group than in the conventional laparoscopy group.

As we know, the use of smaller instruments has not limited the ability of gynecologic surgeons to perform staging surgery. Therefore, the mini-laparoscopic route does not compel a learning curve for trained conventional laparoscopic surgeons. Overall, our promising results demonstrate the feasibility and reliability of mini-laparoscopic surgery in EC staging.

Study Limitations

The present study has some limitations which must be pointed out. Our study is limited by its relatively small sample size. Retrospective design can also be criticized; however, we strongly believe that our sample size handicap has been adjusted by propensity matching comparison. As a result, it reduces the covariate imbalance in measured baseline patient characteristics between surgical groups. Another strength of this study is our highly experienced surgeons. Given that, there was no potential bias in the practices of different surgeons.

Conclusion

We demonstrated that mini-laparoscopic endometrial cancer staging could be a competent technique that is performed regardless of harm by talented surgeons using state-of-the-art instruments. Mini-laparoscopic surgery, of note, appears as a further possibility to minimize surgical trauma by reducing the ports' size without decreasing the procedures' extent and effectiveness. Undoubtedly, additional prospective studies are necessary to get external and internal validation of our findings.

Ethics Committee Approval: The Koc University Clinical Research Ethics Committee granted approval for this study (date: 24.04.2020, number: 2020.159.IRB2.049).

Informed Consent: Written informed consents were obtained from patients who participated in this study.

Conflict of Interest: No conflict of interest was declared by the authors.

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