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## Laparoscopic versus open hysterectomy in type I endometrial cancer – a tertiary referral center experience

Porównanie histerektomii laparoskopowej i drogą laparotomii w leczeniu raka endometrium typu I – doświadczenia ośrodka o trzecim stopniu referencyjności

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### Abstract

**Background:** Surgery has been considered the cornerstone in the management of endometrial cancer, especially in its early stages. The use of minimally invasive surgeries in patients with endometrial cancers has been widely adopted worldwide. In this study, we discuss the outcomes of type I endometrial cancer patients who underwent laparoscopic hysterectomy at our center. **Results:** The patients were categorized into two groups: open surgery group (59 patients) and laparoscopy group (60 patients). There was no significant difference between both groups as regards the epidemiologic and clinicopathologic parameters. There was no statistical difference between the two groups in the FIGO stage (International Federation of Gynecology and Obstetrics). Operative time was significantly longer in the laparoscopy group compared to the open surgery group ( $p < 0.0001$ ). No significant difference was found between both groups as regards the type of operation and blood loss. The rate of intraoperative complications was nearly similar in both groups. There was no significant statistical difference between the numbers of lymph node yield in both groups. **Conclusion:** The results in this study support the use of laparoscopy in early stage type I endometrial cancers without compromising the oncological outcomes regarding the disease-free and overall survival. We encourage further prospective multicenter randomized trials to consolidate these results.

**Keywords:** endometrial cancer, laparoscopy, open surgery

### Streszczenie

**Wstęp:** Chirurgia stanowi podstawę leczenia raka endometrium, zwłaszcza we wczesnych stadiach choroby. Na całym świecie u pacjentek z rakiem błony śluzowej trzonu macicy powszechnie stosuje się małoinwazyjne zabiegi chirurgiczne. Autorzy pracy omawiają wyniki leczenia chorych z rakiem endometrium typu I, które poddano zabiegowi histerektomii laparoskopowej w ośrodku autorów. **Wyniki:** Pacjentki podzielono na dwie grupy: grupę leczoną metodą chirurgii otwartej (59 osób) i grupę leczoną metodą laparoskopową (60 pacjentek). Nie stwierdzono istotnej różnicy między obiema grupami w zakresie parametrów epidemiologicznych i kliniczno-patologicznych. Nie odnotowano również statystycznej różnicy między badanymi grupami w odniesieniu do stopnia zaawansowania choroby wg FIGO (International Federation of Gynecology and Obstetrics). Czas trwania operacji był istotnie dłuższy w grupie leczonej laparoskopowo w porównaniu z grupą leczoną metodą otwartą ( $p < 0,0001$ ). Obie grupy nie różniły się istotnie pod względem rodzaju operacji i utraty krwi. Częstość występowania powikłań śródoperacyjnych była zbliżona w obu grupach. Nie stwierdzono też istotnej statystycznie różnicy między liczbą pobranych węzłów chłonnych. **Wnioski:** Wyniki badania potwierdzają słuszność stosowania laparoskopii we wczesnym stadium raka endometrium typu I bez ryzyka niekorzystnego wpływu na wyniki onkologiczne pacjentek w zakresie przeżycia wolnego od choroby i przeżycia całkowitego. Przeprowadzone powinny być prospektywne, wieloośrodkowe badania z randomizacją w celu skonsolidowania przedstawionych wyników.

**Słowa kluczowe:** rak endometrium, laparoscopia, chirurgia drogą laparotomii

## INTRODUCTION

Surgery has been considered the cornerstone in the management of endometrial cancer, especially in early stages<sup>(1)</sup>. The use of minimally invasive surgeries in patients with endometrial cancers has been widely adopted worldwide. Minimally invasive surgery provides many advantages compared to open surgery in the management of endometrial cancer patients as regards perioperative complications, blood loss and shorter hospital stay<sup>(2,3)</sup>. Since most endometrial cancer patients are elderly and suffer from obesity, minimally invasive surgery is usually a very convenient approach for such patients<sup>(4-6)</sup>. Several studies have documented the oncologic safety of minimally invasive approaches in endometrial cancer patients; however, most of these studies were confined to low risk endometrial cancers<sup>(3,7,8)</sup>.

Endometrial cancers are usually classified into two types: type I, which is hormonal dependent and has a better prognosis, including grade 1–2 endometrioid adenocarcinomas, and type II, which is usually more aggressive with worse prognosis, including high-grade serous carcinoma, clear cell carcinoma, carcinosarcomas and high grade endometrioid adenocarcinomas<sup>(9-14)</sup>.

Type II endometrial carcinomas are usually characterized by *p53* and *PIK3CA* overexpression, while type I tumors are characterized by *PTEN* mutations<sup>(15)</sup>. Also, type II endometrial carcinomas compared to type I showed significant DFF40 and *BCL2* underexpression as reported by Banas et al.<sup>(16)</sup>.

Minimally invasive surgery has been widely accepted to be used as the preferred approach in type I endometrial cancers and in selected cases of type II endometrial cancer<sup>(3,7,17,18)</sup>.

In this study, we discuss the outcomes of type I endometrial cancer patients who underwent laparoscopic hysterectomy at our center.

## MATERIALS AND METHODS

### Patient cohort and study design

This was a retrospective cohort study in type I endometrial cancer patients surgically treated in Oncology Center Mansoura University (OCMU) in the period from January 2014 till January 2019. The basic epidemiologic and clinicopathologic data were collected, thereafter the patients were arranged into two arms according to the surgical approach used (open or laparoscopic). The two arms were compared regarding epidemiologic, clinicopathologic criteria, and outcomes (surgical and oncological).

### Statistical analysis

The data of these patients were analyzed, and statistical values were obtained using SPSS version 22 (Inc, Chicago, IL). Distribution of continuous variables was evaluated using a histogram and the Shapiro–Wilk test. Normally distributed variables (parametric) were presented as mean and standard

deviation and non-parametric variables were presented as median and interquartile range. Categorical variables are presented as proportions. Bivariate analysis was done using the Chi-square test and Fischer's exact test. Survival analysis was done using the Kaplan–Meier curve and the significance was determined by log rank test. A *p* value <0.05 was considered significant.

## RESULTS

A total of 119 patients were retrieved. The patients were categorized into two groups: open surgery group (59 patients) and laparoscopy group (60 patients). There was no significant difference between both groups as regards the epidemiologic and clinicopathologic parameters (Tab. 1). Vaginal bleeding was the main complaint in both groups. Only 2 cases in the open surgery group had complaints other than bleeding that were discovered accidentally during a pelviabdominal ultrasound. There was no statistical difference between the two groups in the stage of tumor according to FIGO (International Federation of Gynecology and Obstetrics).

As regards the perioperative data (Tab. 2), the operative time was significantly longer in the laparoscopy group compared to the open surgery group (*p* < 0.0001). No significant difference was found between both groups as regards the type of operation or blood loss. The rate of intraoperative complications was nearly similar in both groups; 5.08% in open surgery group and 6.67% in laparoscopy group, with no statistically significant difference (*p* = 0.731). In the total study population, 7 patients developed intraoperative complications (3 in the open surgery group and 4 in the laparoscopy group). These included bladder injury in 2 patients, ureteric injury in 1 patient, intestinal injury in 1 patient, injury to the obturator nerve in 1 patient and injury to the external iliac vein during lymphadenectomy in 2 patients. All intraoperative complications were managed successfully during the surgery.

Parameter	Open surgery	Laparoscopy	<i>p</i> value
Number	59	60	
Age: • median (IQR)	62.5 (57–69)	59 (52.5–63.5)	0.034
BMI: • median (IQR)	38.2 (36–45.8)	38 (34.2–46)	0.546
Comorbidity: • no • yes	15 (25.42%) 44 (74.57%)	21 (53.01%) 39 (64.99%)	0.323
Complaint: • bleeding • abdominal or GI • accidental	57 (96.6%) 1 (1.7%) 1 (1.7%)	60 (100%)	0.355
FIGO staging: • IA • IB • II • IIIA • IIIC1 • IIIC2 • IV	33 (55.93%) 11 (18.64%) 4 (6.77%) 6 (10.16%) 3 (5.08%) 1 (1.69%) 1 (1.69%)	32 (53.33%) 17 (28.33%) 3 (5.00%) 4 (6.66%) 1 (1.66%) 2 (3.33%) 1 (1.66%)	0.783

Tab. 1. Epidemiologic and clinicopathologic features of both groups

Sixteen patients in the laparoscopy group were converted to open surgery (26.6%); 6 patients due to increased peak inspiratory pressure and decreased oxygen saturation because of increased intraabdominal pressure from pneumoperitoneum, 2 patients due to laparoscopically uncontrollable bleeding, 4 patients due to large size of the specimen that was not suitable for delivery through the vagina, 2 patients for iliac lymphadenectomy as surgeon preference and 1 patient due to bladder injury.

As regards the hospital stay, no significant difference was documented between both groups.

Postoperative complication rate was higher in the open surgery group, with 11 patients versus only 4 patients in the laparoscopy group; however, this difference was not statistically significant. From the 11 patients in the open surgery group, 8 patients had a wound gap and infection that were managed conservatively, one patient had an intestinal leak that needed exploration, one patient had a deep venous thrombosis (DVT) and 1 patient developed postoperative bleeding requiring re-exploration.

There were 4 patients with postoperative complications in the laparoscopy group; one patient developed latent vesicovaginal fistula after bladder injury, 2 patients had pelvic collections that were managed conservatively and 1 patient presented with DVT.

There was no significant statistical difference between the numbers of lymph node yield in both groups.

A total of 60 patients needed adjuvant therapy after the operation: 31 in the open surgery group and 29 in the laparoscopy group. The median duration of follow-up in months was  $19.78 \pm 14.25$  in the open surgery group and  $21.36 \pm 14$  in the laparoscopy group. Recurrence was documented in 5 patients in the open surgery group and 2 patients in the laparoscopy group. The disease-free survival and overall survival were nearly similar in both groups without a significant statistical difference (Tab. 3).

## DISCUSSION

Laparoscopic hysterectomy has been widely adopted in the management of early stage endometrial cancers worldwide. In Egypt, our developing country, and at our center we started using laparoscopy for the treatment of early stage endometrial cancer patients with endometrioid pathology in 2013. Recently, endometrial carcinomas have been molecularly classified into four subtypes: POLE (ultra-mutated) (7%), microsatellite instability (MSI)/hypermutated (28%), copy number low/microsatellite stable (39%), and serous-like/copy number high (26%)<sup>(19)</sup>. Since this recent classification has not been yet integrated in our pathological departments in Egypt, we still use the old classification which stratifies endometrial carcinomas to type I tumors, which include grade 1–2 endometrial carcinomas, and type II tumors, which include the high-grade serous carcinoma, clear cell carcinomas, carcinosarcomas and the high grade endometrioid adenocarcinomas<sup>(9,10)</sup>.

In this study, we present several outcomes of type I endometrial cancer patients who underwent laparoscopic hysterectomy at our center in comparison to conventional open hysterectomy.

Postmenopausal bleeding was the most common complaint recorded in our study for endometrial cancer patients, with nearly 98.3% of affected females. Most of our patients were obese or morbidly obese as the rate of obesity is very high in our country<sup>(20)</sup>.

The operative time was reported by several studies in literature to be nearly similar in minimally invasive approach and open approach<sup>(21–23)</sup>. However, in our study, the operative time was significantly longer in the laparoscopic group than the open group, which is in line with other published trials reporting longer operating times associated with minimally invasive surgery<sup>(8,24–27)</sup>. As this is anticipated generally in laparoscopy, the heterogeneity in the surgeons performing the operations at our center

Parameter	Open surgery	Laparoscopy	p value
Laparoscopy converted	-	16	
Surgery:			0.253
• TH+BSO	32 (55.17)	32 (53.33)	
• TH+BSO and LND	20 (34.48)	26 (43.33)	
• TH+BSO and LND and omentectomy	6 (10.34)	2 (3.33)	
Operative times median (IQR)	120 (110–180)	180 (150–240)	<0.0001
Blood loss median (IQR)	100 (100–150)	120 (100–200)	0.154
Hospital stay median (IQR)	3 (2–4)	3 (2–3)	0.126
Intraoperative complications:			0.731
• no	56 (94.91%)	56 (93.33%)	
• yes	3 (5.08%)	4 (6.67%)	
Postoperative complications:			0.058
• no	48 (81.36%)	56 (93.33%)	
• yes	11 (18.64%)	4 (6.67%)	
Total number of LN	5 (0–13)	5 (0–11)	0.951

TH+BSO – total hysterectomy and bilateral salpingo-oophorectomy; LND – lymphadenectomy.

Tab. 2. Perioperative data

Parameter	Open surgery	Laparoscopy	p value
Adjuvant therapy:			
• no	21 (40.38%)	29 (50%)	
• yes	31 (59.62%)	29 (50%)	
Type of adjuvant therapy:			0.866
• RT	4 (11.76%)	4 (13.33%)	
• CT	7 (20.59%)	5 (16.67%)	
• CRT	9 (26.47%)	6 (20%)	
• BT	10 (29.41%)	12 (40%)	
• CRT+BT	3 (8.82%)	3 (10%)	
• hormonal	1 (2.94%)	0	
Recurrence:			0.422
• no	32 (86.49%)	29 (93.55%)	
• yes	5 (13.51%)	2 (6.45%)	
Recurrence:			0.321
• bone	1	0	
• local + peritoneal	0	1	
• nodal	1	0	
• pelvic	1	0	
• sigmoid	0	1	
• stump	1	1	
Follow-up in months	19.78 ± 14.25	21.36 ± 14	0.571
DFS	18.36 ± 14.56	22.11 ± 12.9	0.367
OS	20.18 ± 14.9	23.88 ± 12.9	0.358
<b>RT</b> – radiotherapy; <b>CT</b> – chemotherapy; <b>CRT</b> – chemoradiotherapy; <b>BT</b> – brachytherapy alone; <b>CRT+BT</b> – chemoradiotherapy + brachytherapy; <b>DFS</b> – disease-free survival; <b>OS</b> – overall survival.			

Tab. 3. Adjuvant therapy and follow-up data

and the presence of many surgeons at the beginning of their learning curve also had an impact on the operating time.

The rate of perioperative complications was in favor of minimally invasive approach compared to open surgery in several studies<sup>(8,21,23,24)</sup>. As regards the perioperative complications, we found no significant difference between the laparoscopy vs. open group in the intra-operative or post-operative complications. Liu et al., Holub et al. reported similar complication rates in both study groups comparing minimally invasive and open techniques for hysterectomy<sup>(22,25)</sup>. Also, Mourits et al., Walker et al., and Janda et al. reported no statistically significant difference between laparoscopy and laparotomy groups as regards postoperative complications<sup>(7,8,27)</sup>.

The rate of conversion from minimally invasive surgery to open surgery varied widely across studies ranging from 0 to 27%<sup>(21,23,24,28–30)</sup>. In our study, we observed a high rate of conversion, approaching nearly 26.6%. This high conversion rate may be attributed to the learning curve at our center and the high BMI in most of our patients. We started performing laparoscopic hysterectomy in 2013 and not all of our surgeons were well-trained in such procedures. We had a higher conversion rate in the first years of performing laparoscopy, which of course had its impact on the total rate of conversion. Also, we have a very high rate of overweight in our country with mean BMI in our study of nearly 40 in both study groups. Thus we reported conversion to the open approach in 16 patients of whom 6 were converted to an open surgery due to high BMI that increased the peak inspiratory pressure in Trendelenburg position, thus forcing conversion.

A large number of studies reported significantly shorter hospital stay in minimally invasive groups than conventional open groups<sup>(21,23,25–28,30,31)</sup>. In our study, we reported a median hospital stay of 3 days in the laparoscopy group, which is in concordance with several other studies<sup>(7,8,21,22,26,27,30,32)</sup>; however, there was no statistically significant difference between the laparoscopy and open group as the median duration of hospital stay was also 3 days in the open group, which is shorter than that reported in most previous studies.

In our study, no statistically significant differences in recurrence rates, disease-free survival, and overall survival were found between both groups, and these results support a large body of previously published data regarding the oncologic safety of minimally invasive techniques in early stage endometrial cancer patients<sup>(3,7,8,22,24–27,30,31)</sup>.

Our study had some limitations. The retrospective design may have some selection and information bias as usually surgeons preferred laparoscopic technique in patients with better performance status. The relatively small sample size, a short follow-up, as well as the heterogeneity of surgeons' preference and experience level in laparoscopy may have affected the treatment outcomes.

## CONCLUSION

The results in this study support the use of laparoscopy in early stage type I endometrial cancers without compromising the oncological outcomes regarding the disease-free and overall survival. We encourage further prospective multi-center randomized trials to consolidate these results.

## Ethics

We conducted this study in compliance with the principles of the Declaration of Helsinki. The study protocol was approved by Faculty of Medicine, Mansoura University institutional review board (IRB). The IRB number is R.21.01.1140.

Informed consent is not needed in retrospective studies.

## Conflict of interest

The authors declare that they have no competing interests.

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