Comparison of the Oncologic Outcomes between Exploratory Laparotomy and Laparoscopic Surgery for Endometrial Cancer: Siriraj Experience

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ABSTRACT

Objective: This study was undertaken to evaluate surgical and oncologic outcomes for patients with endometrial cancer, compared between exploratory laparotomy and laparoscopic surgery.

Method: In total, 324 patients who diagnosed with endometrial cancer during January 2007 to December 2016 were enrolled. The comprehensive surgical staging procedures, including total hysterectomy, bilateral salpingo-oophorectomy (BSO), pelvic lymphadenectomy (PL), and/or para-aortic lymphadenectomy (PAL) were undergone. Demographic, clinical, treatment, operative, outcome, and survival outcome were recorded and evaluated.

Results: 81 patients performed laparoscopy without conversion. No significant difference in baseline characteristics and pathological characteristics between two groups was observed. When compared with laparotomy group, the laparoscopy group had longer operative time, shorter hospital stays, and lower blood loss. Two-year overall survival (OS) was 97.9% and 95.1% in the laparotomy and laparoscopy groups, respectively (p=0.263). In addition, 2-year disease-free survival (DFS) between both groups was equal (93.7% versus 88.6%, respectively; p=0.309).

Conclusion: Laparoscopic surgery is an efficacious, achievable and safe technique for patients with endometrial cancer. Good surgical skills and proper surgical techniques are required to effectuate optimal outcomes.

Keywords: Endometrial cancer; oncologic outcomes; laparoscopic surgery (Siriraj Med J 2020; 72: 195-201)

INTRODUCTION

Currently, endometrial cancer is the cancer that commonly found Thailand. The surgical procedures that can be employed to determine the stage of disease in endometrial cancer includes total hysterectomy, bilateral salpingo-oophorectomy (BSO), pelvic lymphadenectomy (PL) and para-aortic lymphadenectomy (PAL). Traditionally, these procedures are performed by exploratory laparotomy approach. However, during the last decade, laparoscopic surgery has played an important role in comprehensive surgical staging in gynecologic cancer. Laparoscopic surgery not only reduces postoperative pain, wound complication, length of hospital stay, and postoperative adhesion, but it also improves patient quality of life. The result of all these benefits is that patients can receive their adjuvant treatment earlier.

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In early stage endometrial cancer, several studies found the same postoperative complications, and survival outcome between exploratory laparotomy and laparoscopic surgery.[1-9] We performed the first total laparoscopic hysterectomy (TLH) at our center in 2004, and we subsequently introduced the Siriraj TLH technique (SiTLH) in 2006.[10] This meticulous technique, has allowed us to safely perform PL and PAL since 2007. Thus, comparison of the outcomes between laparoscopic surgery and exploratory laparotomy in endometrial cancer at Siriraj Hospital was the objective of our present study.

MATERIALS AND METHODS

The study design was a retrospective cohort study. Medical records were retrieved from the database of the Department of Obstetrics and Gynaecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand during 5th January 2007 to 27th December 2016 study period. All patients were histologically confirmed as endometrial cancer and primary surgery was scheduled. The histological subtypes included endometrioid adenocarcinoma, papillary serous carcinoma, clear cell carcinoma, and mixed carcinoma. Patients with incomplete medical records were excluded. Informed consent was not required due to the retrospective nature of the study. This study was reviewed and approved by the Ethics Committee of the Faculty of Medicine Siriraj Hospital, Mahidol University before the study initiated (Si 005/2018).

The sample size was calculated using non-inferiority, based on data of previous study[9] that reported 90% survival rate. Calculated sample size using a power of 80% (type II error = 0.20), ratio between two groups was 3.0. Our sample size calculation revealed that a minimum sample size of 300 patients, 225 in exploratory laparotomy group and 75 in laparoscopic surgery group, would be required to achieve a 90% confidence level.

A total of 324 patients who met our criteria were enrolled. Two hundred and forty-three patients underwent exploratory laparotomy, while the others performed surgical staging by laparoscopic surgery. Surgical procedures included total hysterectomy, BSO, PL, and PAL. PL and PAL is indicated in patients with high risk for lymph node metastasis (non-endometrioid histologic subtype, extra-uterine involvement, grade 3 with myometrial invasion of greater than 50%) and can be considered in patients with intermediate risk (invasion of more than half of the myometrium or grade 3 with less than 50% myometrial invasion). However, some patients did not undergo this kind of surgery due to inadequate exposure, morbid obesity, and/or patient comorbidity.

Data collection included preoperative patient characteristics. The duration from skin incision to wound closure labeled as operative time. Major complications were defined as mortality, visceral organ injury, vascular injury, massive blood loss, conversion from laparoscopic surgery to exploratory laparotomy, venous thromboembolic events and wound morbidity. Patients who died within 30 days of surgery classified as mortality. Organ injuries were defined as those requiring surgical correction. Massive blood loss was defined as total blood loss >1,000 ml. Deep vein thrombosis or pulmonary embolism categorized as venous thromboembolic events. Wound morbidity meant wound dehiscence or a deep wound surgical site infection of fascial or muscle layers that required readmission or surgical intervention. Patients with a temperature of greater than 38°C, after the first day of the postoperative period, measured on two separate occasions at least 12 hours apart, labeled as postoperative fever. Minor complications included superficial surgical site infections (skin and subcutaneous infection), urinary tract infections and fever. Loss of blood was calculated from the estimation of blood volume on swabs and the difference between the volume of fluid used during surgery and blood volume in suction containers. After the treatment, all patients received disease surveillance for at least 2 years. The period from the start of treatment to the date of death or the date of the last follow up defined as overall survival (OS). Whereas, the length of time from the start of treatment to the date of recurrence referred as disease-free survival (DFS). Response rate (RR) was defined as the percentage of patients whose cancer shrank or disappeared after treatment.

Comparison of the oncologic outcomes (OS, DFS, RR) between the laparoscopic surgery and exploratory laparotomy was the primary outcome. Surgical outcomes between groups, such as operative time, blood loss, major complications, and length of hospital stay, were also compared.

Laparoscopic surgery technique for surgical staging in endometrial cancer

We developed and introduced the SiTLH technique in 2006.[10] The principles of this technique include early identification of both ureters at the beginning of surgery, dissection at the retroperitoneal space and then restoration of the pelvic anatomy from adhesion-free area to the adhesion area. This technique, allow us to dissect the vital organs safely, and to perform transperitoneal lymphadenectomy.

All patients were placed on the table in the lithotomy position after general anesthesia was performed. A uterine manipulator was placed depending on surgeon discretion. A 10-mm laparoscopic trocar was inserted at the umbilical or supraumbilical area for the optic, and three or four 5-mm trocars were inserted at the iliac, suprapubic, and left paraumbilical regions for ancillary instruments. The 10-step SiTLH BSO was routinely performed. The anatomic boundaries for PL included common iliac bifurcation superiorly, deep circumflex vein inferiorly, iliopsoas muscle laterally, obliterated umbilical artery medially and obturator nerve inferiorly.

Transperitoneal PAL was performed by cutting the peritoneum along the right common iliac artery and aorta. The retroperitoneal space was exposed by hanging the cut peritoneum from the upper abdominal wall. The surgery was performed to at least the level of the inferior mesenteric artery (IMA).

Statistical analysis

SPSS for Windows version 18.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Descriptive statistics were analyzed using chi-square test and Fisher's exact test. Data are shown as number and percentage, mean ± standard deviation, or median and range. All calculated *P*-values were two-sided, and a *P*-value < 0.05 was considered statistically significant. DFS and OS were calculated using Kaplan-Meier method. Differences between survival curves were analyzed using log-rank test.

RESULTS

During the study period, a total of 324 patients underwent surgical staging for endometrial cancer. Of those, 243 patients underwent exploratory laparotomy, and 81 patients underwent laparoscopic surgery. Conversion rate was zero percent. Baseline characteristics and pathological characteristics are shown in Table 1 and Table 2. Those characteristics between groups were the same. Endometrioid adenocarcinoma was the most common histological subtype (91.7%), followed by clear cell carcinoma (4.0%). The most common FIGO stage was stage IA in both groups (57.2% and 60.5% in the laparotomy and laparoscopy group, respectively).

Patients who undertook laparotomy had more estimated blood loss and longer hospital stay, whereas patients who undertook laparoscopy had a longer operative time (Table 3). PAL which is a lengthy operative procedure, was more often performed in the laparoscopy group (77.8% versus 53.9%). However, the numbers of para-aortic lymph node retrieved between both groups were the same (Table 3). The major complication rate seemed to be lower in laparoscopy group (8.2% versus 2.5%, p=0.074). The most common complication was superficial wound infection, (a minor complication), as shown in Table 4.

With the clinical complete response rate of 98.8% in the laparoscopy group (Table 5), the 2-year OS was 95.1% which was not significantly different from that of the laparotomy group (Fig 1). DFS in the laparotomy and laparoscopy groups was 93.7% and 88.6%, respectively (Fig 2).

DISCUSSION

The 2-year OS in the laparoscopy group in the present study was 95.1%, which was not different from the 2-year OS in the laparotomy group. Terao, *et al.*[8] reported a 2-year survival rate of 94.6%, which is comparable to the rate observed in our study. The Gynecologic Oncology Group (GOG) do a study about laparoscopic surgery in endometrial cancer, LAP2 study[5], confirmed laparoscopic surgical staging for uterine cancer to be feasible and safe, with fewer complications. These benefits of laparoscopy also found in our study.

Palomba et al. showed that laparoscopic surgery in early stage endometrial cancer is safe and effective.[6] The long-term data showed no significant difference in OS, DFS or recurrence when compared between exploratory laparotomy and laparoscopic surgery.[7] Furthermore, a prospective analysis in 2012 reported a 5-year survival rate of 89.8%.[11]

No significant difference in DFS between laparoscopic surgery and laparotomy was reported by several studies. In 2012, GOG LAP2 study[11] reported recurrence and survival, the 3-year estimated cumulative incidence of recurrence in the laparoscopy group was 11.39%. Tozzi, *et al.*[4] reported a 2-year DFS of 87.4% in the laparoscopy group versus 91.6% in the laparotomy group - both of which are comparable to our study. However, surgical techniques to prevent tumor spillage during surgery were not used in all cases in our study. Those techniques included no uterine manipulator insertion through the uterine cavity, vaginal vault closure before surgery began, ligation of both fallopian tubes before surgery started, and the use of a specimen retrieval bag during tissue extraction. We expect that DFS will increase even further if these protective techniques can be used in all cases.

Due to the principle of the SiTLH technique, the laparoscopy group had lower blood loss. Early reduction of uterine blood supply at the beginning of the procedure not only reduce blood loss, but also reduces the rate of

TABLE 1. Baseline demographic and clinical characteristics (N=324).

Characteristics	Values[a]		*P* value
	Laparotomy group (n=243)	Laparoscopy group (n=81)	
Age, y	57.51+10.55	56.98+10.10	0.692
Body mass index[b]	26.82+5.49	26.74+5.84	0.908
Parity			0.702
0	89 (36.6)	30 (37)	
>1	154 (63.4)	51 (63)	
Menopause status			0.438
Pre-menopause	74 (30.5)	21 (25.9)	
Post-menopause	169 (69.5)	60 (74.1)	
History of hormone replacement therapy	3 (1.2)	1 (1.2)	1.000
ECOG performance status			0.530
0	219 (90.1)	71 (87.7)	
1	24 (9.9)	10 (12.3)	

[a] Values are given as mean + standard deviation or number (percentage).
[b] Calculated as weight in kilograms divided by the square of height in meters.

TABLE 2. Pathological characteristics (N=324).

Characteristics	Values[a]		*P*-value
	Laparotomy group (n=243)	Laparoscopy group (n=81)	
Histologic subtype			0.650
Endometrioid adenocarcinoma	224(92.2)	73(90.1)	
Serous carcinoma	1(0.4)	0(0)	
Clear cell carcinoma	10(4.1)	3(3.7)	
Mixed	8(3.3)	4(6.2)	
Histologic grading			0.752
1	127(52.3)	39(48.1)	
2	73(30.0)	25(30.9)	
3	43(17.7)	17(21.0)	
Presence of LVSI[b]	46(18.9)	16(19.8)	0.870
Positive for peritoneal fluid cytology	8(3.3)	4(4.9)	0.503
Isolated pelvic lymph node metastasis	16(6.6)	5(6.2)	0.869
Isolated para-aortic lymph node metastasis	1(0.4)	1(1.2)	0.438
Pelvic and para-aortic lymph node metastasis	10(4.1)	3(3.7)	1.000
FIGO[c] stage			0.969
IA	139(57.2)	49(60.5)	
IB	49(20.2)	14(17.3)	
II	18(7.4)	6(7.4)	
IIIA	9(3.7)	2(2.5)	
IIIB	1(0.4)	1(1.2)	
IIIC1	16(6.6)	5(6.2)	
IIIC2	11(4.5)	4(4.9)	

[a] Values are given as number (percentage)., [b] LVSI, lymphovascular space invasion., [c] FIGO, International Federation of Gynecology and Obstetrics.

TABLE 3. Surgical outcomes (N=324).

Outcomes	Values[a]		*P*-value
	Laparotomy group (n=243)	Laparoscopy group (n=81)	
Estimated blood loss, ml	306.7	128.6	<0.001
Duration of operation, min	177.8+52.9	259.2+73.8	<0.001
Length of hospital stay, d	6(5,8)	5(4,6)	<0.001
Pelvic lymphadenectomy	239(98.4)	80(98.8)	1.000
Para-aortic lymphadenectomy	131(53.9)	63(77.8)	<0.001
Number of lymph node			
Pelvic lymph node[b]	14(10,20)	14(9,20)	0.593
Para-aortic lymph node[b]	3(2,5)	3(2,6)	0.390
Residual tumour			0.483
no	237(97.5)	80(98.8)	
<1 cm	2(0.8)	1(1.2)	
>1 cm	4(1.6)	0(0)	
Major complication	20(8.2)	2(2.5)	0.074
Adjuvant treatment	141(58.3)	40(49.4)	0.163

[a] Values are given as mean + standard deviation, number (percentage), or median (interquartile range).,
[b] calculated only in patients who performed pelvic and para-aortic lymphadenectomy.

TABLE 4. Intraoperative complications and postoperative adverse events.

Complication rate	Values[a]		*P*-value
	Laparotomy group (n=243)	Laparoscopy group (n=81)	
Major complications			
Bowel injury[b]	2(0.8)	0(0)	1.000
Bladder injury[b]	1(0.4)	0(0)	1.000
Bowel obstruction[b]	1(0.4)	0(0)	1.000
Wound dehiscence[b]	8(3.3)	1(1.2)	0.458
Blood transfusuion[b]	10(4.1)	1(1.2)	0.303
Minor complications			
Fever[b]	1(0.4)	2(2.5)	0.160
Urinary tract infection[b]	2(0.8)	0(0)	1.000
Bowel ileus[b]	1(0.4)	0(0)	1.000
Superficial wound infection[b]	18(7.4)	8(9.9)	0.498

[a] Values are given as number (percentage)., [b] Calculated as number of events divided by total number of patients.

TABLE 5. Response of treatment.

Response rate	Values[a]	
	Laparotomy group (n=243)	Laparoscopy group (n=81)
Complete response	234(97.9)	80(98.8)
Partial response	1(0.4)	1(1.2)
Stable disease	1(0.4)	0(0)
progression	3(1.3)	0(0)

[a] Values are given as number (percentage).

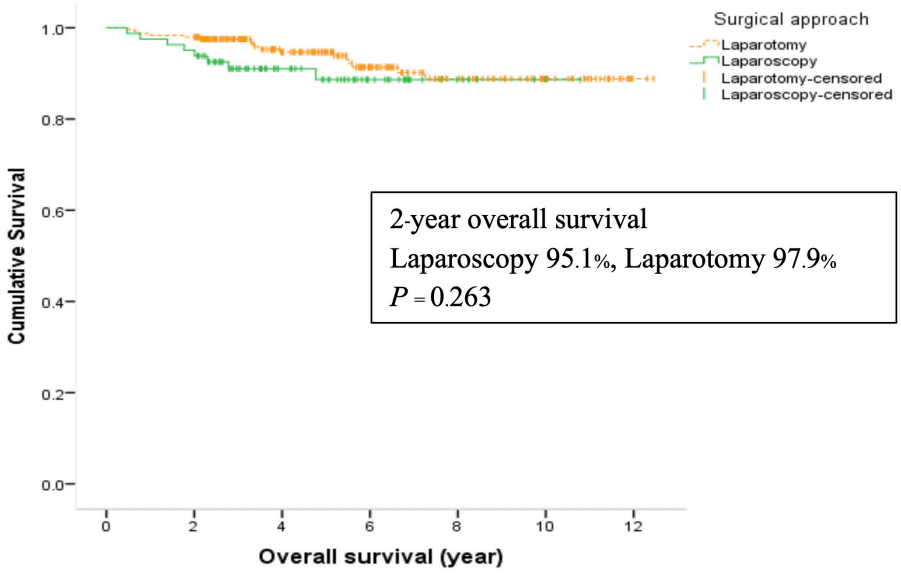

Fig 1. Overall survival in 324 endometrial cancer patients stratified by surgical approach (laparoscopy vs. laparotomy)

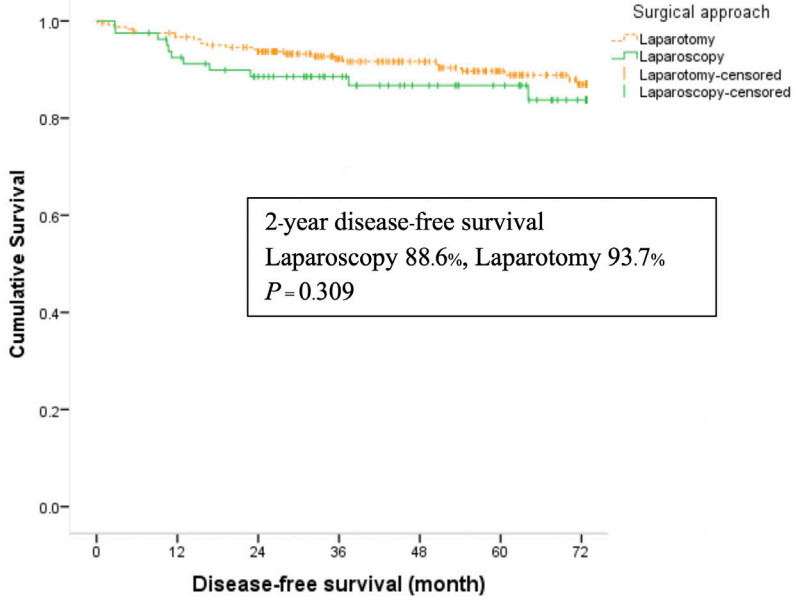

Fig 2. Disease-free survival in 324 endometrial cancer patients stratified by surgical approach (laparoscopy vs. laparotomy)

visceral organ injury.[10] This protective feature can be explained by the fact that unnecessary blood loss can obscure surgical field visibility, which leads to increased risk of visceral organ injury and massive blood loss during PL.

The result of our study revealed that PAL was performed more often in the laparoscopy group. This may be due to the fact that laparoscopy provides better visualization and an ability to access the retroperitoneal space, especially in obese patients. Surgeon experience and surgical skill are also the important factors that affect para-aortic lymph node retrieval.

In the present study, there was no statistically significant difference in the number of para-aortic lymph node retrieval between two groups. However, the median number of para-aortic lymph node retrieval was lower than the other studies.[5,9,12-13] We did not perform systematic PAL in all cases. Only para-aortic lymph node sampling was performed in some patients, and limited at the level below IMA. So, this may be causing the lower number of para-aortic lymph node in our study. During the last 2 years, systematic PAL was initiated in our center because surgeons had more experience in this kind of surgery and advanced bipolar electrosurgery was commonly used. The further study which included those patients may provide more information about benefit of systematic PAL in endometrial cancer.

Strengths and limitations

A large sample size and the fact that we include all histologic subtypes were the strengths of this study. The limitation of our study included it retrospective design, and the fact that we included data from a single center. Another limitation is the type of surgical method used was determined at the discretion of each surgeon. Last, the surgical procedure in each surgical technique varies by surgeon, and these variations could have adversely influenced our finding. Importantly, the findings of this study suggest laparoscopic surgery as feasible and safe treatment alternative to laparotomy.

CONCLUSION

Laparoscopic surgery is an efficacious, achievable and safe technique to treat patients with endometrial cancer. Good surgical skills and proper surgical technique are required to effectuate optimal outcomes.

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