

COMPARISON OF LAPAROSCOPY AND OPEN SURGERY FOR WOMEN WITH EARLY STAGE IN LOW GRADE ENDOMETRIAL CANCER

Joko Winarno^{1*}, Chamim², Sarah Miriam Ratna Pratamasari³

^{1*,2} Gynecological Oncology Consultant, Department of Obstetrics and Gynecology, Fatmawati Hospital, Jakarta, Indonesia

³ Recident of Obstetrics and Gynecology, Faculty of Medicine, University of Indonesia, Indonesia

Email: obgyn.rsufatmawati@gmail.com

Abstract

Endometrial cancer is a type of gynecological cancer that becomes a burden to the healthcare system. Laparotomy and laparoscopic surgical techniques are currently the two most common surgical methods for endometrial cancer. The laparoscopic approach was found to be associated with reduced operative morbidity. This study evaluated oncologic outcomes of laparoscopy and laparotomy surgery in the management in early stage of low-grade endometrial cancer. We conducted an observational study of women diagnosed with International Federation of Gynecology and Obstetrics (FIGO-2018) early-stage endometrial cancer who underwent surgery at the Fatmawati Hospital, Jakarta, Indonesia from 2021-2022. The histopathological types are endometrial cell, well differentiated, no evidence of invasion to the cervical/other organ (low grade). A total of 92 patients were treated for stage I endometrial cancer during the study period. Thirty-nine patients (42.4%) underwent laparoscopic surgery and 53 patients (57.6%) underwent laparotomy surgery. The average age of the laparoscopic group was younger than that of the laparotomy group. Comparison of laparotomy and laparoscopy in mean length of operation and amount of blood loss showed no statistically significant difference. The length of stay data showed mean length of stay in laparoscopic group was 3.67 days whereas in the laparotomy group was 5.14 days with significant results statistically. The mean survival of patients one year after the procedure is 49.49 weeks, with the average survival of 1 year in the laparoscopic group was 50.83 weeks and 47.98 weeks in laparotomy group with no statistically significant difference. Laparoscopic has several advantages especially, less blood loss, complication during operation, shorter hospital stay, 1 year survival rate but not significant statistically in this research.

Keywords: Endometrial cancer, Laparotomy, Laparoscopic

How to cite:	Joko Winarno, Chamim, Sarah Miriam Ratna Pratamasari (2022) Comparison of Laparoscopy and Open Surgery for Women with Early Stage in low grade Endometrial Cancer, (7) 09. Doi: 10.36418/syntax-literate.v7i9.14076
E-ISSN:	2548-1398
Published by:	Ridwan Institute

Introduction

The most common gynecological malignancy in women is corpus uteri cancer, which 83% cases were endometrial cancer (EC). It counts for more than 60,000 new cases per year and 11,000 deaths in America.(Mahdy H, Casey MJ, 2023) EC primarily affects 90% of perimenopausal women and 25% of premenopausal women. However, EC was found to occur in 4% of women aged less than 40 years with the majority being nulliparous (70%).(Trojano et al., 2019) The endometrioid subtype is the most usual histological type of EC with a good prognosis. Most women are diagnosed with stage 1 disease, in which the tumor is confined to the body of the uterus.(Burger, 2001)

Hysterectomy with bilateral salpingo-oophorectomy is the mainstay of EC management, especially at early stage.(Burger, 2001) The minimally invasive surgical method, laparoscopic procedure, plays important role in the field of gynecological oncology surgery. Laparoscopic surgery is superior to laparotomy in terms of lower morbidity rates, need of transfusion, shorter hospital stays, less pain, and faster recovery (Cakmak et al., 2020).

The aim of this study is to evaluate oncologic outcomes of laparoscopy and laparotomy surgery in the management in early stage of low-grade endometrial cancer.

Method

For this observational study, we reviewed 92 patients diagnosed with International Federation of Gynecology and Obstetrics (FIGO-2018) early-stage endometrial cancer who underwent surgery at the Fatmawati Hospital, Jakarta, Indonesia from 2021-2022. According to histopathologic evaluation, patients with endometrial cell, well differentiated, no evidence invasion to the cervical/other organ (low grade) were enrolled in this study.

Our data included patients' demographic characteristics in terms of age, stage, blood transfusion and complications during surgery. The main outcomes studied including length of operation, blood loss and length of stay, and 1 year survival rate between two groups. Data analyses was done using SPSS by the Mann Whitney *U* Test with statistically significance result was *P* values <0.05.

Results and Discussion

A. Characteristics of Research Subjects

This study collected 92 endometrial cancer patients who met the inclusion criteria. In this study, 39 patients (42.4%) underwent laparoscopic surgery and 53 patients (57.6%) underwent laparotomy surgery.

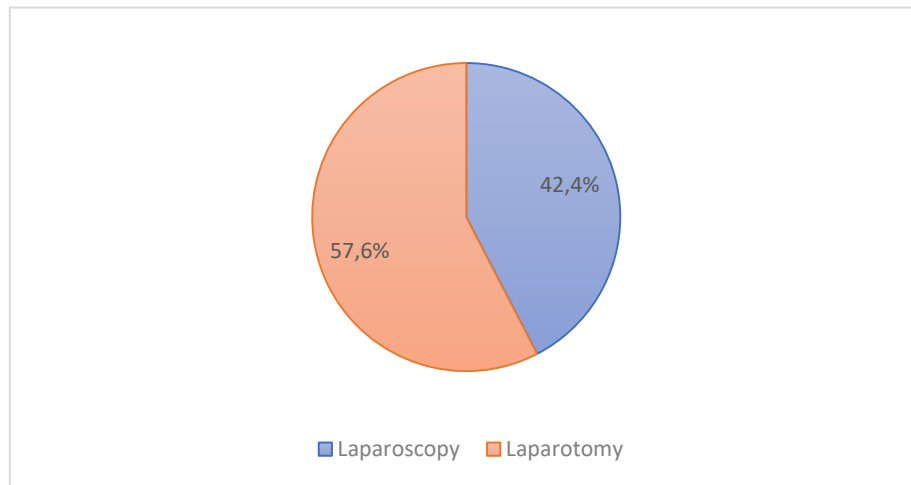


Figure 1. Surgery Proportions

In general the patient characteristics are shown in Table. 1. The mean age of endometrial cancer patients in this study was 55.71 years, with the youngest age was 28 years and the oldest was 78 years. The majority with stage IA cancer was 43 people (46.7%), stage IB was 23 people (25%), the majority of patients received blood transfusions 55 people (59.8%) and didn't have complications during surgery 87 people (94.6 %).

Table 1.
Patients' Characteristics

Variables	Patient n = 92
Age (years)	
Mean	55.71 years
Median	57.50 years
Minimum	28 years
Maximum	78 years
SD	10.52 years
SE	1.10 years
Stage (n=90)*	
IA	43 (46.7%)
IB	23 (25%)
II	6 (6.5%)
III	11 (12.0%)
Advanced	7 (7.6%)
n/a	2 (2.2%)
Blood transfusion (n =92)	
No	35 (38.0%)
Yes	55 (59.8%)

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n/a	2 (2.2%)
Complications during surgery (n=90)*	
No	87 (94.6%)
Yes	5 (5.4%)

B. Patient Characteristics Based on Surgery

This section is a comparison of patient characteristics in terms of age, stage, blood transfusion and complications during surgery between laparoscopy and laparotomy. For the age variable, an independent t-test was carried out while for the stage, the presence or absence of blood transfusions and complications during surgery variables, the chi square test was carried out.

Table 2
Patient Characteristics based on Surgery

Variables	Laparoscopy	Laparotomy	<i>P-value</i>
Age (years) (n=92)			
Mean	54.28 (50.44-58.13)	56.75 (54.16-59.35)	
Median	57.00	58.00	
Minimum	28.00	33	0.033**
Maximum	78.00	78	
SD	11.86	9.40	
SE	1.90	1.29	
Stage (n=90)*			
IA	26 (66.7%)	17 (33.3%)	
IB	10 (25.6%)	13 (25.5%)	0.003**
II	2 (5.1%)	4 (7.8%)	
III	1 (2.6%)	10 (19.6%)	
Advanced	0 (0.0%)	7 (13.7%)	
Blood transfusion (n =92)			
No	20 (51.3%)	15 (29.4%)	0.059
Yes	19 (48.7%)	36 (70.6%)	
Complications during surgery (n=90)*			
No	38 (97.4%)	49 (92.5%)	0.391
Yes	1 (2.6%)	4 (7.5%)	

Note: * there are two data not available

** P value \leq 0.05 is statistically significant

Table 2 shows that in the laparoscopic group the mean age of the patients was 54.28 years (50.44-58.13 years) with the median was 57 years. The youngest was 28 years old and the oldest was 78 years old. Whereas in the laparotomy group the mean

age was 56.75 years (54.16-59.35 years) and the median was 58 years. The youngest was 33 years old and the oldest was 78 years old. The results of the statistical test showed *p-value* was 0.033, which means that there was a significant difference in the average age of the patients who underwent laparoscopic and laparotomy procedures. It can be seen that the average age of the laparoscopic group was younger than that of the laparotomy group.

Based on the cancer stage, the data showed that the majority of the laparoscopic group consisted of 26 patients with stage IA (66.7%), followed by stage IB with 10 people (25.6%) and stage III with 1 person (2.6%). Whereas in the stage IA laparotomy group there were 17 people (33.3%), IB was 13 people (25.5%), III was 10 people (19.6%), advanced stage was 7 people (13.7%) and stage II was 4 people (7.8%). The results of the statistical test showed *p-value* was 0.003 which means there was a difference in stage between the laparoscopy and laparotomy groups. Patients with more advanced stages of cancer tend to undergo laparotomy surgery.

The data showed that in the laparoscopy group, 19 patients (48.7%) received blood transfusions, while in the laparotomy group, there were 36 patients (70.6%). The statistical test results found that the *p-value* was 0.059 which means there is no significant difference regarding blood transfusion between the laparoscopic and laparotomy groups.

Data on complications during surgery showed that in the laparoscopic group, 1 person (2.6%) had complications during surgery, while the laparotomy group had 4 people (7.5%). The results of the statistical test showed that *the p-value* was 0.391, which means that there was no significant difference based on surgical complications between the laparoscopic and laparotomy groups.

C. Comparison of Length of Operation, Blood Loss and Length of Stay between Laparotomy and Laparoscopy in Stage I Endometrial Cancer Patients

From a total of 92 patients, 66 patients with stage I will be analyzed by comparing the length of surgery, the estimated blood lose and the length of stay between patients who underwent laparotomy and laparoscopy surgery so that the data below is obtained:

Table 3
Comparison of the duration of surgery, blood loss and length of stay in patients with stage I endometrial cancer

Variables	Laparoscopy (n = 36)	Laparotomy (n = 30)	<i>P-value</i>
Operating time (minutes)	175.42 (156.67-194.16)	124.00 (102.52-145.48)	
Mean (CI: 95%)	165.00	115.00	0.876
Median	60 - 300	60-330	
Min – max	55,40	57,51	
SD	9,23	10.5	

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SE			
Blood loss (ml)			
Mean (CI: 95%)	156.67 (101.00-212.33)	217.33 (147.53-287.14)	
Median	100.00	200	0.600
Min – max	15 - 1000	20 - 950	
SD	164.51	186.93	
SE	27,42	34,13	
Length of stay (days)			
Mean (CI: 95%)	3.67	5,14	
Median	3	4.63	<
Min – max	2 – 6	3 – 10	0.001*
SD	0.93	2,14	
SE	0.15	0.39	

Note: *independent t-test* * P value ≤ 0.05 statistically significant

Table 3 shows that in the group of patients with laparoscopy the average length of operation was 175.42 minutes and the median was 165 minutes. The shortest operating time was 60 minutes and the longest was 300 minutes. Whereas in the laparotomy group the average length of operation was 115.00 minutes with a median was 115 minutes. The shortest operating time was 60 minutes and the longest operating time was 330 minutes. Data shows that the average duration of surgery with a laparoscopic procedure is longer than that of a laparotomy. However, when tested statistically, we get a p-value = 0.876, which means that there is no statistically significant difference based on the length of operation between laparoscopy and laparotomy surgery.

Data on the amount of blood loss during surgery found that the average amount of blood loss in the laparoscopy group was 156.67 ml and the median was 100 ml. The least amount of blood loss was 15 ml and the highest amount of blood loss was 1000 ml. Whereas in the group of patients who received a laparotomy, the average amount of blood loss was 217.33 ml and the median was 200 ml. The least blood loss was 20 ml and the most blood lost is 950 ml. The average amount of blood loss in the laparoscopic group of stage I patients was less than that of the laparotomy group. However, the results of the statistical test obtained a p-value was 0.600, which means that statistically there was no difference in the mean amount of blood loss between the laparoscopic and laparotomy groups in stage I endometrial cancer patients.

The length of stay data shows that in the laparoscopic group the mean length of stay was 3.67 days and the median was 3 days. The shortest length of treatment is 2 days and the longest treatment is 6 days. Whereas in the laparotomy group the average length of stay was 5.14 days and the median was 4.63 days. The shortest length of treatment was 3 days and the longest treatment was 10 days. It can be seen that the average length of stay in the laparoscopic group was shorter than the laparotomy group. The statistical test results showed that the p-value < 0.001 which mean there is

a significant difference between the means of long treatment between the laparoscopy and laparotomy groups.

Based on these data it can be concluded that in stage I endometrial cancer patients, laparoscopic procedures have advantages in terms of length of surgical treatment.

D. 1-Year Survival after Laparotomy and Laparoscopy in Stage I Endometrial Cancer Patients

The survival of research subjects with endometrial cancer was generally analyzed from research subjects with stage I endometrial cancer after laparotomy or laparoscopic surgery for up to the first year. Time to death was assessed by postoperative for 52 weeks (1 year). Of the 66 patients in the study, survival in one year after surgery was as follows:

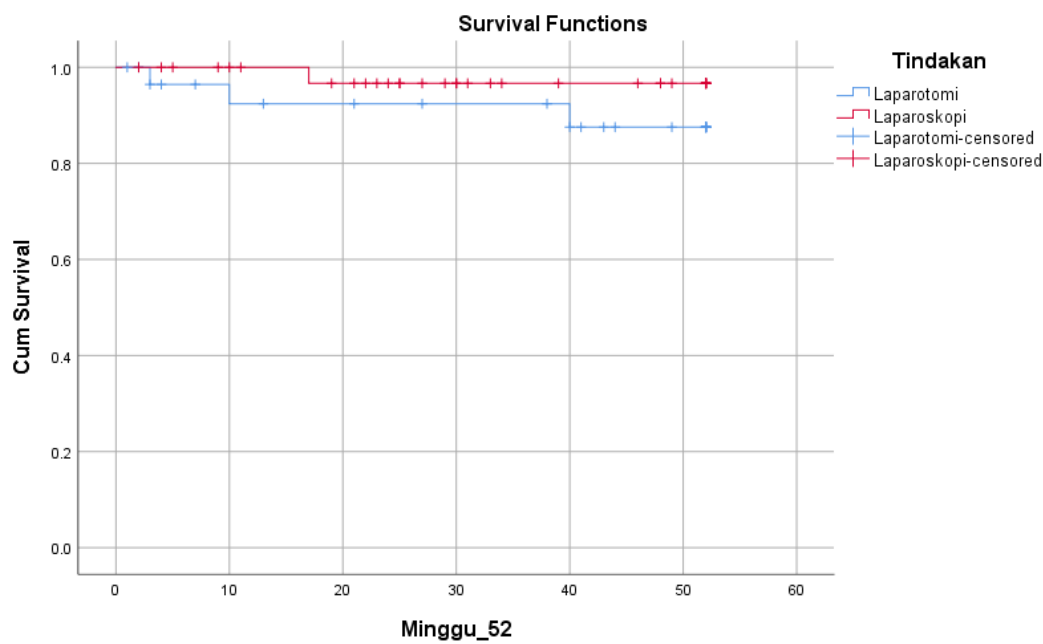
Table 4
One Year Postoperative Mortality

1 Year Post Operation	Laparoscopy (n = 48)	Laparotomy (n = 32)
Die	1 (2.8%)	3 (10.0%)
Alive/ <i>Censored</i>	35 (97.2%)	27 (90.0%)

In this study, out of 66 stage I endometrial cancer patients who were followed for 1 year, it was found that 1 (2.8%) died in patients who underwent laparoscopic procedures and 3 (10.0%) in the laparotomy group.

To assess whether there was a difference in the average incidence of recurrence between the laparoscopic and laparotomy groups, the log rank (LR) test was used or by looking at the Kaplan Meier graph. If the Kaplan Meier graphs do not intersect between groups and the log rank value was ≤ 0.05 , there is a difference in the incidence of death between the groups. To see the difference in survival, the Breslow test was used, if the Breslow test ≤ 0.05 then there was a difference in survival between the variable groups. The bivariate test of mortality and mean survival for 1 year is as follows:

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Graph 1. One-Year Survival of Endometrial Cancer Patients after Laparotomy/Laparoscopy

Table 5
Average Survival of Postoperative Stage I Endometrioid Patients

Action	Average (in week)	SE	LR	Breslow
Laparoscopic	50.83 (48.59 – 53.08)	2.38		
Laparotomy	47.98 (43.32 – 52.64)	1.15	0.254	0.254
All	49.49 (47.02 – 51.96)	1.26		

Data Table 5 shows that the mean survival of patients one year after the procedure is 49.49 weeks, with the average survival of 1 year in the laparoscopic group was 50.83 weeks and in the laparotomy group was 47.98 weeks. Based on the Log Rank and Breslow tests, it was found that *the p-value* was > 0.05 , so there was no statistically significant difference between the incidence of death and the average survival of stage I endometrial cancer patients between the laparoscopy and laparotomy groups. However, descriptively, the mortality in the laparoscopic group was lower than that in the laparotomy group and the average survival rate in the laparoscopic group was also higher.

E. 1-Year Survival after Laparotomy and Laparoscopy in All Stage Endometrial Cancer Patients

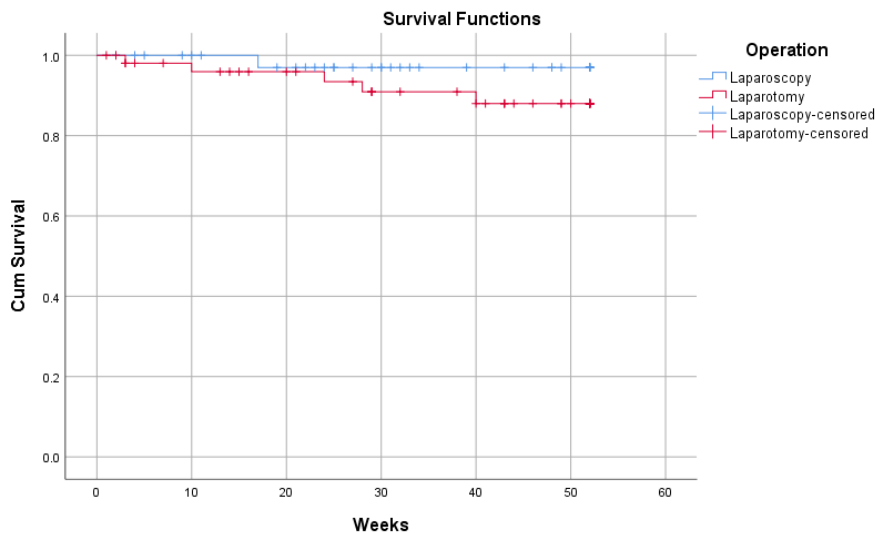
The survival of research subjects with endometrial cancer was generally analyzed from research subjects after laparotomy or laparoscopic surgery for up to the first year. We followed up the subjects after surgery for 52 weeks (1 year). Of the 92 patients in the study, survival in one year after surgery was as follows:

Table 6
One Year Postoperative Mortality

1 Year Post Operation	Laparoscopy (n = 48)	Laparotomy (n = 32)
Die	1 (2.6%)	5 (9.4%)
Alive/ <i>Censored</i>	38 (97.4%)	48 (90.6%)

Table 6 showed that endometrial cancer patients who were followed for 1 year, it was found that 1 (2.6%) died in patients who underwent laparoscopic procedures and 5 (9.4%) in the laparotomy group. More deaths occurred in the laparotomy group.

Graph 2 below shows that the laparoscopic group was better able to survive in one year after surgery. This is shown from the graph of the laparoscopic group which is above the laparotomy group.



Graph 2. One-Year Survival of Endometrial Cancer Patients After Laparotomy/Laparoscopy

Table 7
Average Survival of Postoperative in Endometrioid Cancer Patients

Action	Average (in week)	SE	LR	Breslow
Laparoscopic	50.94 (48.89 – 52.99)	1.04		
Laparotomy	48.50 (45.44 – 51.55)	1.56	0.225	0.244
All	49.46 (47.45 – 51.48)	1.03		

Data Table 7 shows that the mean survival of patients one year after the procedure is 49.46 weeks, with the average survival of 1 year in the laparoscopic group was 50.94 weeks and in the laparotomy group was 48.50 weeks. Based on the Log

Rank and Breslow tests, it was found that *the p -value* was > 0.05 , so there was no statistically significant difference between the incidence of death and the average survival of endometrial cancer patients between the laparoscopy and laparotomy groups. However, descriptively, the mortality in the laparoscopic group was lower than that in the laparotomy group and the average survival rate in the laparoscopic group was also higher.

Discussion

Our study showed the average age of the laparoscopic group was 54.28 years and 56.75 years in laparotomy group. The average age of the laparoscopic group was younger than that of the laparotomy group. This result is similar with a study by Zorlu, *et al.*, where the average age of laparotomy and laparoscopy group was 54.9 (range from 36 to 77) and 56.6 (range from 40 to 72) respectively. There was no significant difference between laparoscopic and laparotomy group based on age. (Zorlu et al., 2005)

Based on the cancer stage, more advanced stages of cancer tend to undergo laparotomy surgery with statistically significance result. The laparoscopic technique is able to execute almost all procedures performed by laparotomy in gynecological practice these days. Laparoscopic-assisted surgical staging (LASS) of early-stage endometrial cancer success rate is as good as laparotomic staging. (Zorlu et al., 2005) Based on the Gynecologic Oncology Group (GOG) trial, several factors associated with the conversion of laparoscopy to laparotomy include metastases, bleeding, and visual fields. Weight factors and disease stage also affect the conversion to laparotomy. Women with overweight and advanced endometrial carcinoma showed a laparoscopic conversion rate of 13.2%. (Arab et al., 2018)

A study that compared 465 patients with endometrial cancer showed no significant differences in intra-operative or post-operative complications in both the laparoscopic and laparotomy groups. (Arab et al., 2018) However, when performed by an experienced operator, laparoscopically assisted surgical staging of endometrial cancer can achieve success and safety with minimal morbidity as laparotomy. Some of the advantages of the laparoscopic method include reduced pain, quicker return to normal activities, improved quality of life, less blood loss and need for blood transfusion, and brief hospitalization time. However, for the duration of surgery, laparotomy shows a shorter operating time than laparoscopic surgery. (Zorlu et al., 2005) (Arab et al., 2018) (Lin et al., 2021)

Our study found that average duration of surgery with a laparoscopic procedure (175.42 minutes) is longer than that of a laparotomy (115.00 minutes). These finding are similar to research by Zorlu, *et al.*, which operative time of laparoscopy are longer laparotomy (155 vs 144 minutes, $P > 0.05$). As well as some studies, a significant longer operation duration was found in the laparoscopy group (237 vs 157 minutes in Scribner's study and 214 vs 144 minutes in Gemignani's study (Zorlu et al., 2005), 278.5 versus 220.0 minutes, $p < 0.001$ in Lin's study (Lin et al., 2021), 136.2 vs 101.9 minutes, $p < 0.05$ ranging from 70 to 215 minutes with median was 150 minutes in Fram's study (Fram, 2002)). A retrospective study by Anwar *et al.*, involved 41 laparoscopic hysterectomy

patients and 32 laparotomy hysterectomy patients. It was found that the operating time for the laparoscopic group was longer (276.8 ± 32.5) than the laparotomy group (213.6 ± 42.3) with significantly significant results ($P < 0.05$). (Anwar et al., 2022) The achievement of shorter operation duration is influenced by the learning curve and experience. Laparoscopic for endometrial cancer is influenced by experience. A surgeon needs to have some experience performing laparoscopic lymphadenectomy surgery in order to achieve independence and shorter operating times. Studies showed that perioperative complications tend to decrease after a person has treated about 30 cases. (Arab et al., 2018)

This study revealed the average amount of blood loss in the laparoscopic group was less than that of the laparotomy group with no statistically significant difference. A study in Bangkok found that patients who underwent laparotomy had more estimated blood loss, which is accordance with our result. (Srichaikul et al., 2020) Cakmak, et al., also support that laparoscopic associated with less blood loss compared to laparotomy. (Cakmak et al., 2020) Similar to a meta-analysis of three RCTs, evaluating 313 women with early-stage of EC, showed that laparoscopy was associated with less blood loss compared to laparotomy with a statistically significant result (MD=106.82 mL, 95% CI = 141.59–72.06). (Galaal et al., 2018) A retrospective study in Taiwan involving 177 (69.4%) underwent open laparotomy and 78 (30.6%) underwent laparoscopy. It revealed that laparoscopic surgery is associated with less blood loss (150.0 versus 180.0 cc) with significant result ($p = 0.015$). (Lin et al., 2021) Study by Fram, *et al.*, found blood loss ranging from 100-250 ml and median was 150 ml with significant result statistically ($p < 0.05$) 145.5 ml in laparoscopic group and 501.6 ml in laparotomy group. Two patients in laparotomy group and one patient in laparoscopic group needed blood transfusion. (Fram, 2002) Likewise, study by Santi, *et al.*, which involved 240 patients with 120 patients in each of the laparoscopic and laparotomy groups demonstrated that the laparotomy group had significantly greater intraoperative blood loss with seven patients requiring transfusion compared to laparoscopy. (Santi et al., 2010) Research showed that patients in the laparotomy group required higher blood transfusions than the laparoscopic group (14.5% and 10.7% respectively). The rate of blood transfusion needed was found to be higher for laparotomy group. (Arab et al., 2018)

The length of stay data showed mean length of stay in laparoscopic group was 3.67 days whereas in the laparotomy group was 5.14 days with significant result statistically. This result is in line with study by Cakmak, which laparoscopic is related to earlier hospital discharge of the patients. (Cakmak et al., 2020) A study by Arab, *et al.*, showed that the laparoscopic group had a lower length of stay of more than 2 days compared to the laparotomy (52% and 94% respectively). (Arab et al., 2018) Likewise, the average hospital stay in the laparotomy group (26.54 ± 6.2 days) was higher than that in the laparoscopy group (18.65 ± 7.4 days) significantly (p -value < 0.05) in Anwar's study, (Anwar et al., 2022) 8.0 days in laparotomy vs 7.0 days in laparoscopic ($p < 0.001$) in Lin's study), (Lin et al., 2021) 5.5 days in laparotomy and 2.3 days in the laparoscopy group ($p < 0.05$) ranging from 1 to 3 days, with median was 2 days. (Fram, 2002) The

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mean hospital stay was found to be shorter in the laparoscopy group when compared to the laparotomy group. This may be related to several factors, such as in the laparoscopic group found lower postoperative complications ($p=0.01$), lower postoperative pain ($p<0.05$), and shorter average time to resume activities ($p<0.001$) compared to the laparotomy group with statistically significant results.(Haddad et al., 2021)

We found that the average survival of 1 year in the laparoscopic and laparotomy group is similar, 50.83 weeks and 47.98 weeks, respectively. Research by Shui, *et al.*, showed similar result, which the 5-year overall survival (OS) rate was 69.1% in laparotomy group (95% CI: 58.8%-77.4%) similar as laparoscopy group, 60.8% (95% CI: 52.0%-68.5%).(Shui et al., 2022) A meta-analysis of six RCTs with total of 3993 women with EC, revealed that risk of death between laparoscopy and laparotomy group has no significant difference (HR 1.04, 95% CI 0.86 to 1.25).(Galaal et al., 2018)

Conclusion

Laparoscopic is safe and feasible for women with early-stage endometrial cancer. It has view advantages especially, less blood loss, complication during operation, shorter hospital stay, 1 year survival rate compared to laparotomy but not significant statistically in this research.

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