Original Research Article

Evaluation of clinical outcome of laparoscopic hysterectomy versus open abdominal hysterectomy with pelvic lymphadenectomy in endometrial carcinoma early stage

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ABSTRACT

Background: the aim of this study was to compare the operative, post-operative, and the oncological short-term outcomes of laparoscopic hysterectomy with lymphadenectomy and open abdominal hysterectomy with lymphadenectomy for early-stage endometrial cancer.
Methods: 80 patients with clinical stage I endometrial cancer were enrolled in this trial; they were divided according to their selection of the method of intervention after counselling into two groups: total laparoscopic hysterectomy with pelvic lymphadenectomy group and total abdominal hysterectomy with pelvic lymphadenectomy group.
Results: The mean operative time in the TLH group was 140.85 ± 10.033 minutes and was 118.45 ± 12.713 minutes in the TAH group (p<0.001). The mean blood loss in the TLH group was 127.5 ± 42.9 ml and 220.5 ± 84.82 ml in TAH group (p<0.001). The mean duration of postoperative ileus was 12.8 ± 5.022 hours in the TLH group, and it was 22.3 ± 5.573 hours in the TAH group (p<0.001). The mean time of hospital stay in the TLH group was 26.7 ± 5.667 hours and in the TAH group was 116.4 ± 17.31 hours (p<0.001).
Conclusions: Complete surgical staging of endometrial cancer can be performed using laparoscopy as an alternative to routine open method with similar efficacy about nodal retrieval and complication rate, and better operative and postoperative compliance in means of blood loss, ileus and hospital stay which may have an implication on cost saving in the medical service. Lymphadenectomy can be omitted in low-risk cases of endometrial cancer.

Keywords: Laparoscopic hysterectomy, Open abdominal hysterectomy, Lymphadenectomy

INTRODUCTION

Endometrial carcinoma (EC) is the most commonly diagnosed gynecologic malignancy. It is the fourth most common malignancy in women, and the eighth most common cause of cancer death.[1] Endometrial carcinoma occurs most often in the sixth and seventh decades of life, with an average age at onset of 60 years. It is estimated that 75% to 85% of the cases occur in patients 50 years old and older, and 95% occur in patients over 40 years of age.[2,3]

Endometrial cancer is commonly confined to the uterus at diagnosis. Data from the National cancer institute's surveillance, epidemiology, and end results (SEER) program demonstrated that stage I disease was found in 73% of patients, and 10% had stage II disease.[4] The 26th annual report of the international federation of gynecology and obstetrics (FIGO) on 9,386 endometrial cancer patients demonstrated that 83% of patients were stage I-II.[5] With the favourable disease distribution at presentation, it is not surprising that most patients have a favourable prognosis. Results from FIGO show that 85%

to 91% of stage I patients are alive at 5 years, and patients in the SEER database with localized disease have 96% 5 year survival. Despite the favourable characteristics for most patients, those with high-risk factors including increased age, higher tumor grade, aggressive histology, and advanced stage face real challenges.[4,5] Current clinical controversies center on the extent of nodal surgery and the changing roles of radiation therapy and chemotherapy. Increased use of surgical staging has translated to less frequent use of radiation therapy and to changes away from pelvic radiation.[6]

Aim

Aim of current investigation was to compare the operative, post-operative, and the oncological short-term outcomes of laparoscopic hysterectomy with lymphadenectomy and open abdominal hysterectomy with lymphadenectomy for early-stage endometrial cancer.

METHODS

The study was conducted in the laparoscopy unit of Zeint Elhyah private center, in the period between September 2018 and June 2020. Current clinical trial included 80 patients with clinical stage I endometrial cancer equally divided into two groups: Group A; underwent total laparoscopic hysterectomy with pelvic lymphadenectomy and Group B: underwent total abdominal hysterectomy with pelvic lymphadenectomy.

It should be mentioned that the study in its beginning was designed to include cases with early stages endometrial cancer which was meaning according to FIGO 1988 classification stages I (uterine corpus), and IIA (endocervical glandular involvement only). Now these stages became all involved in stage I according to FIGO 2009. Method of intervention was adopted according to patient desire. Appropriate informed consent was obtained from the patient after a thorough explanation of the planned operation, its potential risks and benefits, and the possibility of laparotomy in group A patients.

All cases had an established endometrial carcinoma proved by histopathology of endometrial biopsy. Full history taking, gynecologic and rectal examination, ultrasonographic assessment to confirm being stage I. Chest X-ray, and MRI and/ or CT scan to exclude the suspicion of metastatic disease. Routine preoperative tests including a complete blood count with differential, serum electrolytes, bleeding time, and urine analysis, thrombin time, partial thrombin time, and electrocardiography (ECG) were done.

Surgical techniques

Group A; four ports entry was initiated. A 10 mm trocar that incorporates the zero-degree laparoscope (Karl Storz, Tuttlingen, Germany) was inserted through a subumbilical vertical incision. Three suprapubic ancillary trocars were used: one 10 mm trocar was inserted in the midline 5 cm under the umbilicus, and one in each iliac fossa (5 mm each) lateral to inferior epigastric vessels. A uterine manipulator was inserted through the cervix. In this study, transperitoneal bilateral pelvic lymphadenectomy was initiated before proceeding to hysterectomy for all the patients.

Pelvic lymphadenectomy

Current study adopted the technique described by Nezhat et al.[7,8] Lymphadenectomy was initiated by identification of the lateral umbilical ligament. Incision of the lateral peritoneum by incising the round ligament, identification of the paravesical and pararectal fossae. The paravesical and pararectal spaces are important anatomic landmarks. When developed, they provide an opportunity for thorough exploration of the intervening base of the broad ligament. The broad ligament is then dissected in a cephalad fashion lateral and parallel to the infundibulopelvic ligament.

Lateral and intermediate external iliac lymph nodes were addressed by the dissection of the external iliac vessels. Dissection was initiated laterally over the psoas muscle and proceeded medially. It was done along the adventitia of the external iliac vessels, the external nodal chain above the external iliac artery was dissected then the internal surface, followed by the superior surface of the external iliac vein. Dissection was continued caudally from common iliac vessels to the level of the deep circumflex iliac vein seen crossing over the distal portion of the external iliac artery. Caution was taken to avoid injury of the genitofemoral nerve.

Medial external iliac lymph nodes were addressed. The internal and inferior surfaces of the external iliac vein were dissected. This dissection was pursued to the pelvic wall. The obturator space was entered by reflecting the external iliac vessels medially away from the psoas muscle and freeing the areolar tissue that lies directly between these vessels and the lateral pelvic wall with blunt dissection. Once the space has been entered, the artery and vein were released and gently retracted laterally, and the obturator space was clearly exposed. The lymphatic and areolar tissue were dissected from the obturator space to the region of the pelvic floor, with care to avoid trauma to the obturator nerve and vessels.

The dissection was continued by removing all of the nodes below the bifurcation of the iliac vessels, including the hypogastric nodes and the nodes in the obturator fossa. The hypogastric artery was dissected with identification of the visceral branches of the anterior trunk. The anterior division of the hypogastric artery continues along the paravesical fossa to become the obliterated lateral umbilical ligament beneath the anterior abdominal wall. The uterine artery was ligated at its

origin from the hypogastric artery. Sometimes the anterior division of the hypogastric artery was ligated just distal to the point of origin of its posterior division rather than ligating the uterine artery individually.

The lymph node chain was retracted posteriorly, their anterior attachments were divided after the use of Ligasure$^@$ for lymphostasis and avoiding lymphocyst formation. Finally, the tissues harboring the nodal chains were extracted using the spoon extractor through the midline subumbilical port.

Total laparoscopic hysterectomy

The ureter along its whole pelvic course crossing over the bifurcation of common iliac artery till piercing the cardinal ligament and passing through the ureteric canal should be clearly identified. It lies on the medial peritoneal leaf of broad ligament.

After bilateral completion of pelvic lymphadenectomy, laparoscopic hysterectomy was initiated. The broad and round ligaments were already dissected, the infundibulopelvic ligaments were sealed and dissected bilaterally using the Ligasure$^@$ (Vallylab TM, Tyco Healthcare UK ltd). A uterine manipulator placed inside the uterus vaginally was helpful in retracting the uterus in the opposite direction, facilitating the stretch on the infundibulopelvic ligament.

The uterovesical peritoneum was identified, grasped, and elevated with forceps while scissors were used to dissect the bladder off the cervix. The bladder was dissected from the uterus by pushing downward with the tip of a blunt probe or a piece of sponge on grasper along the vesico-cervical plane until the anterior cul-de-sac is exposed completely.

The uterine vessels were identified and desiccated. Dissection done during lymphadenectomy, was easily identifiable by following the obliterated umbilical artery till its origin from the hypogastric artery. It was sometimes sealed and cut flushing to the uterus and others at its origin from the anterior division of hypogastric artery. In some cases, the anterior division of hypogastric artery was also sealed.

Using contralateral retraction of the uterus, the cardinal ligament was dissected to identify tissue planes, vessels, and the ureter. Once the ureter was displaced laterally, the cardinal ligament tissue closest to the cervix was coagulated and transected using the LigaSure$^@$. Anterior and posterior culdotomy was done over (KOH colpotomizer, cooper surgical) or over a piece of sponge in the fornices in some cases. Once completely freed, removal of the specimen was done through the vagina.

Pneumoperitoneum was retained by putting a glove filled with cotton inside the vagina. The cuff was closed either by continuous suturing or two midline mattress sutures.

The pelvic and abdominal cavities were evaluated laparoscopically, irrigated, and cleared of blood clots and debris. Intra-abdominal pressure was reduced, and the pedicles were reinspected to confirm hemostasis. A tube drain was routinely introduced through one of the side ports, and fascial repair was done to the other ports after removal of trocars with delayed absorbable sutures.

Group B; Midline vertical incision was the routine approach. The abdomen was kept open by a self-retaining retractor, and the bowel was kept in place with warm, wet pads. The abdominal viscera were thoroughly examined, including the liver, gallbladder, stomach, kidneys, and aortic lymph nodes.

Pelvic lymphadenectomy

Transperitoneal pelvic lymphadenectomy was initiated. Node dissection was begun by separating the lymph nodes overlying the external iliac artery from the vessel by entering the plane of dissection between the adventitia of the artery and the areolar tissue. Dissection was carried out caudally down to the inguinal ligament and proximally up to the iliac bifurcation. The external iliac vessels were retracted medially, and the dissection was carried between the vessels and the psoas staying on its fascia. Near the iliac bifurcation, the obturator nerve was easily identified emerging from under the psoas muscle. The specimen was detached from the medial aspect of the external iliac artery and vein along the adventitial plane. The artery and vein were separated to remove the lymph nodes located between them. The lymphatic tissue was detached from the inferior aspect of the external iliac vein. With blunt dissection, the entire obturator nerve was freed from the lymphatic pad. The specimen was isolated from the surrounding vessels and nerve, the caudal border was dissected at the femoral ring, and the cranial end was carefully detached from the anterior aspect of the hypogastric artery and vein. These nodes are called the superficial obturators and include nodes called obturator, interiliac, hypo gastric and medial external iliac nodes.

Total hysterectomy

After completion of pelvic lymphadenectomy, total hysterectomy was started. The round ligament was cut between the clamps, then the vesico-peritoneal fold was elevated, and the bladder was gently separated from the corpus and cervix and mobilized inferiorly by sharp or blunt dissection. Securing the infundibulo-pelvic ligament by double ligation was done. Then the uterine arteries were skeletonized, triply clamped, cut and suture ligated. The upper portions of the cardinal ligaments were cut, and the uterosacral ligaments were clamped close to the cervix. The vagina was cut free from the cervix and the free edges of the vagina were grasped with long Allis clamps. The vaginal angles were secured with figure-of-eight suture ligatures, and then closure of the vaginal vault was completed.

Statistical analysis

Statistical analysis was performed using the statistical package for social science for windows (SPSS, Inc., Chicago, IL) version 14.

RESULTS

Patients in both groups were similar as regards age and BMI (Table 1). The mean operative time was 140.85±10.033 and 118.45±12.713 minutes in group A and B respectively. The difference was statistically significant. The mean amount of blood loss was 127.5±42.9 ml and 220.5±84.82 ml in group A and B respectively. The difference was also statistically significant. The mean number of the pelvic lymph nodes retrieved was 13.6±3.43 and 14.55±2.28 nodes in group A and B respectively. The difference between the two groups was statistically insignificant (Table 2). Regarding the postoperative details, hemoglobin decline 24 hours after surgery was (0.88±0.538 gm/dl) and (1.52±0.530 gm/dl) in group A and B respectively. The difference was statistically significant. The mean duration of postoperative ileus was 16.75±3.31and 23.05±5.17 hours in group A and B respectively. The difference between the two groups was statistically significant. Duration of hospital stay was 26.7±5.667 hours and 116.4±17.31 hours in group A and B respectively, the difference was statistically significant (Table 3). Complications encountered in this study were: lymphorrhea in four cases in group A and only one case had this complaint in group B. Fever more than 38°C was documented in one case in the group A and in two cases in group B. Only one case of postoperative hip pain and limitation of movement in the group A and this was attributed to faulty or prolonged positioning during operation. Blood transfusion was needed for only 2 cases in group A and for 5 cases in the group B. The difference was statistically insignificant (Table 4).

Table 1: Age and BMI of study groups.

Variables (n=40)	Group A Mean±SD	Group B Mean±SD	P value	Sig.
Age	62.6±6.2	60.5±4.5	0.263	NS
BMI	30.16±2.74	31.85±4.04	0.132	NS

Table 2: Operative details in the study groups.

Variables (n=40)	Group A Mean±SD	Group B Mean±SD	P value	Sig.
Op. time (mins.)	140.85±10.1	118.45±12.7	<0.001	HS
Blood loss (ml)	127.5±42.9	220.5±84.82	<0.001	HS
LN count	13.6±3.43	14.55±2.28	0.31	NS

The total number of cases proved to have positive nodes was 4 cases, only one case in stage IA (1/33 cases 3%),

two cases stage IB (1/6 cases 16%), and one stage IIIA (Table 5). Both study groups were comparable regarding histology type, grading, tumor stage and lymph node status (Table 5).

Table 3: Postoperative details in the study groups.

Variables (n=40)	Group A Mean±SD	Group B Mean±SD	P value	Sig.
Hb% decline (gm/dl)	0.88±0.538	1.52±0.53	<0.001	HS
Ileus duration (h)	16.75±3.31	23.05±5.17	<0.001	HS
Hospital stay (h)	26.7±5.667	116.4±17.31	<0.001	HS

Table 4: Complications occurred in both study groups.

Variables (n=40)	Group A	Group B	P value	Sig.
Intraoperative				
Bowel injury	0	0	-	
Bladder injury	0	0	-	
Vascular injury	0	0	-	
Transfusion	4	10	0.4	NS
Postoperative				
Haemorrhage	0	0	-	
Fever	2	4	0.65	NS
Lymphorrhea	8	2	0.65	NS
Locomotor	2	0	1.0	NS
Intraoperative				
Bowel injury	0	0	-	

Table 5: Histopathological results in the study groups.

Variables (n=40)	Group A N (%)	Group B N (%)	P value	Sig.
Grade				
I	10 (25)	8 (20)	1.0	NS
II	26 (65)	24 (60)	0.74	NS
III	4 (10)	8 (20)	0.65	NS
Stage				
IA	32 (80)	34 (85)	1.0	NS
IB	6 (15)	6 (15)	1.0	NS
II	0 (0)	0 (0)	1.0	NS
IIIA	2 (5)	0 (0)	1.0	NS
Histology				
Endometrioid	32 (80)	32 (80)	1.0	NS
Papillary serous	6 (15)	4 (10)	1.0	NS
Clear cell	2 (5)	4 (10)	1.0	NS

DISCUSSION

The surgical management for early-stage endometrial cancer is variable and is currently under investigation. The application of laparoscopy in the management of gynecologic malignancy has received much attention during the past few years.[7]

The laparoscopic approach is advantageous particularly in shortening hospital stay and decreased total hospital charges. The overall postoperative morbidity and complications inherent in both techniques are nearly the same.[8]

In current study, the mean operative time in group A (140.85±10.1) was significantly higher than that of group B (118.45±12.7). Perhaps the considerably longer time in laparoscopy group in comparison to laparotomy group is one of few points not in favor of laparoscopic approach, but the better postoperative convalescence nullifies the significance of this prolongation. Also, operative time showed considerable improvement with repetition of cases and progression in learning curve, starting by 190 minutes duration in the first cases and declining to reach 120 minutes in the last cases.

The operative time of the laparoscopy group showed a wide variation among different authors. It was similar to that reported by Eisenkop et al 139.5 min and Malzoni et al 136±31 min. On the other hand, it was shorter than that reported by Cho et al 154.9 (55-478) min., Lim et al 186.8±59.8 min., Scribner et al 237 (185-360) min., Frigerio et al 220 min and Soliman et al 296.8 (230-360) min.[9-16] The shorter duration of laparoscopic group of this study in relation to other studies could be explained by the use of LigaSure vascular sealing system which preserved considerable time in comparison to the traditional ligation of the pedicles and vessels in some of previous studies and limiting lymphadenectomy to pelvic nodes only without para-aortic nodal dissection being performed for cases with early-stage endometrial cancer.[15,16]

The mean amount of blood loss in group A was significantly lower than that of group B. This significant reduction in blood loss was also reported in most of studies on this literature (155.2 vs. 284.7 ml, 109 vs. 207 ml, 177 vs. 285 ml and 50 vs. 145 ml.[17-20] This was explained by the smaller incision size, limited abdominal wall dissection, less bleeding due to pneumoperitoneum compressing microcirculation, better visualization and magnification of smaller vessels added to the usage of LigaSure vascular sealing system.

As a consequence of reduced blood loss, the mean hemoglobin decline 24 hours after surgery was significantly lower in the group A compared to the group B. This was confirmed in many other studies.[9] The mean number of the pelvic lymph nodes retrieved was comparable between both groups. The relative similarity in the number of lymph nodes retrieved by each group suggests that the laparoscopic lymphadenectomy has similar efficacy as open lymphadenectomy. This was also suggested by other studies.[10]

The number of lymph nodes that must be removed for proper surgical staging is a controversial point. Lutman et al. found that pelvic lymph node count ≥12 is an independent prognostic factor for both overall and progression-free survival in patients with FIGO stage I and II with high-risk histology.[19] Another study by Cragun et al confirmed that patients with grade 3 endometrial cancers having more than 11 pelvic nodes removed had improved overall survival and progression-free survival compared with patients with 11 or fewer nodes removed.[20] Chan et al have shown a correlation between the increasing number of lymph nodes removed and number of nodal metastasis. They concluded that the removal of 21 to 25 nodes was considered to significantly increase the probability of detecting at least one lymph node metastasis.[11]

The routine performance of pelvic lymphadenectomy despite a good portion of study cases can be classified as low risk for nodal metastasis can be a matter of criticism towards this study. There is a controversy among routine, selective, and no lymphadenectomy for cases of early endometrial cancer. Currently, preoperative and intraoperative prediction of who will and who will not benefit from a lymphadenectomy is inaccurate and unreliable. Preoperative grade is not indicative of postoperative grade with 15-25% of preoperative grade 1 endometrial cancers upgraded on final pathology.[12] Pelvic systematic lymphadenectomy doesn't change the natural history of the disease as can be inferred from the pattern of disease recurrence, which was similar between the two groups. However, pelvic lymphadenectomy did allow for an accurate prognosis on the basis of a pathological lymph node assessment. It is an important marker of tumor aggressiveness that only partly overlaps with other well-known prognostic factors, such as depth of myometrial invasion and tumor grading.[13]

Although lymphadenectomy does not affect survival in this group it may identify patients with advanced disease and assist in tailoring adjuvant therapy for those with adverse risk factors.[14,15] The mean duration of postoperative ileus in group A was significantly lower than in group B. That significant difference could be explained by less intestinal manipulation, less exposure to dryness and less electrolyte disturbance secondary to wide incisions and more tissue trauma.

The mean time of hospital stay in the group A was significantly lower than in group B. Although that significant difference was reported in almost all studies in literature Volpi et al (3.18 vs. 4.59 days), Cho et al (9.5 vs. 14.3 days), more recent Kondo et al (3 vs. 6 days), Eisenkop et al (3.2 vs. 7.9 days), Malzoni et al (2.1 vs. 5.1 days).[16] It can be noticed that patients of the previous

studies stayed for days in hospital even patients of group A. It was a trend in this study to discharge patients of group A in the next day following surgery after being sure of wellbeing. This has resulted in dramatic reduction in hospital stay from days to just hours. As can be seen from complication rate, there were no major acute postoperative complications, which gives impression of safety of this strategy. This was ascertained by Gien et al who confirmed in their study that same-day discharge for laparoscopic gynecologic oncology surgery is feasible, with low morbidity and few readmissions within three weeks of surgery. No doubt that reduced hospital stay has its implications on the cost savings to medical systems.[17]

The total number of cases proved to have nodes positive was 4, one case in stage IA (1/33 cases, 3%), two cases stage IB (1/6 cases, 16%), and one stage IIIA. This gives impression that the discrepancy between the pre-treatment and postoperative diagnosis was limited. Also, this is going with the common knowledge that stage IA has low tendency for node metastasis and simple hysterectomy bilateral salpingo-oophorectomy without lymphadenectomy is sufficient to this patient group. Mariani and colleagues previously reported an institutional algorithm for determining who should undergo lymphadenectomy based on intraoperative grade, distance of invasion, and tumor size. The authors concluded that patients with "low risk" disease did not benefit from lymphadenectomy.[18]

The study results support the validity of Mayo algorithm. Although a small number of patients with advanced stage disease may be missed when applying the Mayo criteria, there is no apparent survival benefit to lymphadenectomy for patients satisfying this algorithm.[19] Out of 40 cases 32 cases proved to be endometrioid type adenocarcinoma (80%) going with most studies.[20] Fortunately, the complications in this study were very limited in both groups. There were no cases of bowel, bladder or vascular injury or cases of massive postoperative haemorrhage necessitating intervention. There were 4 cases of lymphorrhea in the group A and only one case in the group B. All cases spontaneously improved within one month of follow up. One case in the group A and two cases in the group B complained of fever more than 38°C, improved by fluids and simple antipyretics added to antibiotic therapy. Only one case of postoperative hip pain and limitation of movement in the group A was attributed to positioning during surgery. Exclusion of signs suggesting nerve injury was done and she was sent to physiotherapy and showed gradual improvement. There was no significant difference between the two groups in these complications. Only 2 cases in the group A needed blood transfusion, and 5 cases in the group B. This difference was statistically insignificant.

CONCLUSION

Complete surgical staging of endometrial cancer can be performed using laparoscopy as an alternative to routine open method with similar efficacy regarding nodal retrieval and complication rate, and better operative and postoperative compliance in means of blood loss, ileus and hospital stay which may have an implication on cost saving in the medical service. Having risk of lymph node metastasis approaching zero percent, lymphadenectomy can be omitted in low-risk cases and total hysterectomy without lymphadenectomy may be sufficient.

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