Laparoscopic versus laparotomic approach to endometrial cancer

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Summary

Objective: The aim of our study was to compare the feasibility, morbidity, long-term safety, disease-free survival, and overall survival of the laparoscopic (LPS) approach to early-stage endometrial cancer (EC) compared to the traditional laparotomic approach. *Methods:* We reviewed retrospective data of patients who underwent primary surgery from 1997 to 2009. We recorded clinical parameters, surgical stage, histological type, operative and peri-operative complications, time to resumption of normal functions, conversion to laparotomy, overall survival, and disease-free survival. *Results:* LPS, did not increase operative risk and peri-operative complications even in obese and older women. The number of pelvic lymph and aortic nodes removed was similar for the two groups. One hundred and eight patients had a follow-up of 60 months. The two groups were similar for disease-free survival and overall survival. *Conclusions:* Laparoscopic approach to EC provides a reduction in postoperative complications and hospital stay compared to the laparotomic approach.

Key words: Endometrial cancer; Laparoscopy; Laparotomy; Hysterectomy.

Introduction

Endometrial cancer (EC) is the third most common cancer in women worldwide [1, 2]. It is estimated that 70% of patients affected by endometrial tumors had a high body mass index (BMI > 25) and 50% had comorbidity such as diabetes or cardiovascular disease [3].

For patients with early stage EC, FIGO recommends total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH+BSO) with or without lymph node dissection through a laparotomic vertical midline incision [4]. The laparoscopic approach to EC is not a standard surgical procedure. In the last decade several retrospective and prospective studies have demonstrated that the laparoscopic approach is an effective and safe alternative to the open procedure allowing for significant reduction of treatment related morbidities, shorter hospital stay, less pain, and quicker return to daily activities. These advantages are even more pronounced in obese and older patients [5-8].

On this basis the laparoscopic approach has been used in EC. Laparoscopy in early-stage EC represents a minimally invasive technique compared to the laparotomic approach and in many countries this latter approach is being increasingly replaced by laparoscopy [9]. Like laparotomy, operative laparoscopy can accomplish full surgical procedures including complete intraperitoneal surveys, peritoneal washings, removal of adnexae, and performance of pelvic and paraaortic lymphadenectomy and total hysterectomy [10].

In this study we retrospectively reviewed the clinical records of hysterectomy and lymphadenectomy for EC performed by the authors. The aim of our analysis was to compare feasibility, morbidity, long-term safety, and survival rate of the laparoscopic (LPS) approach in early stage EC compared to the traditional laparotomic (LPT) approach.

Materials and Methods

Study design

We retrospectively reviewed the data of all patients who underwent primary surgical management (laparotomic or laparoscopic access) for EC from 1997 to 2009.

It is our policy to propose pelvic lymphadenectomy in patients with EC except histological type I, Stage IA (staging of the patients was carried out according to the FIGO 1988 staging system). Since there is no consensus on the need for a comprehensive staging procedure including systematic paraaortic lymphadenectomy, we performed paraaortic node dissection in selected cases such as in patients with poorly differentiated tumors with myometrial invasion greater than 50% (ICG3), and non-endometrioid carcinomas. Infracolic omentectomy was performed for papillary serous, clear cell carcinoma, and adenosquamous carcinoma in all cases. Vaginal cuff brachytherapy alone was prescribed for patients with FIGO Stages IB G2-G3, IA G3 and in combination with radiotherapy in patients with FIGO Stage IC, II disease. Chemotherapy in some cases in combination with radiotherapy was offered to patients with FIGO Stage III-IV.

Patient demographic and clinical characteristics

Clinical parameters, FIGO surgical stage, histological type, tumor grade, cytological grade, number and status of lymph nodes obtained, operative time, estimated blood loss, perioperative blood transfusions, length of hospital stay, time to resumption of normal bladder and bowel function, perioperative complications, overall survival, and disease-free survival were recorded.

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Inclusion criteria were clinical Stage I to IIA uterine cancer according to FIGO 1988 rules.

Exclusion criteria were previous malignancy, previous hysterectomy, EC histological type I and Stage IA, intra-operative findings of ovarian lesions, metastasis beyond the uterus, and procedures performed by surgeons in training. We also excluded patients undergoing laparotomy because of contraindications to LPS such as increased uterine volume (bulky > 12 week), history of cardiac failure, myocardial infarction, unstable angina or pulmonary obstructive disease, and poorly controlled or contraindicating prolonged Trendelenburg position. Prior abdominal surgery was not considered a contraindication for the LPS approach.

Operative time was calculated from first skin incision to last incision closure. Intraoperative blood loss hemorrhage was calculated as the difference between pre- and postoperative hemoglobin values. [11]. Active bleeding with symptomatic anemia and hemoglobin less than 8 g/dl were considered criteria for blood transfusion. Hospital stay was counted from the first postoperative day until discharge.

Postoperative morbidities recorded were fever (defined as a temperature of 38°C or higher on two occasions over 48 hours), urinary tract infection, respiratory tract infection, wound infection, pelvic lymphocyst with or without abscess, intestinal or ureteric fistula, need to return to operating theatre within 14 days following the primary surgery, deep venous thrombosis, and pulmonary venous embolism. Diagnosis of deep-vein thrombosis and pulmonary embolism was confirmed by venous ultrasound (US) and helical computed tomography (CT) or ventilation-perfusion scan, respectively.

Overall survival period, disease-free survival period, disease recurrence, port-site disease, and any long-term complications were retrieved from hospital records and direct patient reports. We confirmed information and patient status by direct telephone interview and clinical follow-up.

Surgical technique

The typical operative management of a patient is described as follows: routine preoperative investigations such as clinical examination, pelvic US, and hysteroscopy/uterine revision with biopsy were performed in all patients referred to our Institute. Pelviabdominal CT scan and colonoscopy are optional studies required if clinical metastasis is suspected.

Routine bowel preparation, thromboprophylaxis and antibioticprophylaxis were provided.

Patients were given a general anesthetic and placed in a modified lithotomy position using Allen's stirrups, and a urinary catheter was inserted.

In all cases (LPT and LPS) surgical staging began with an inspection of the entire abdominopelvic cavity. A sample of peritoneal fluid was obtained for cytologic analysis.

Since 2001 most patients have been screened via the sentinel lymph node procedure [12]. The time required for this procedure was subtracted from the total surgical time.

Laparotomic route

Abdominal access was performed through a vertical midline skin incision and the hysterectomy consisted of an extrafascial total hysterectomy. To minimize the risk of tumor spread we routinely grasped the fallopian tubes bilaterally before starting the laparotomic procedure.

Laparoscopic route

A laparoscopic spoon or a colpotomizer was placed within the uterus for manipulation. Abdominal entry was established via an umbilical 10-mm port for the laparoscope (directly or with open technique [13], two 5-mm ports on either side of the abdominal wall and one 12-mm port suprapubically were positioned (additional trocars may be used in accordance with surgical need). The vaginal cuff was sutured by laparoscopy in all total laparoscopic hysterectomies. To minimize the risk of tumor spread during manipulation of the uterus we routinely coagulated the fallopian tubes bilaterally before starting the laparoscopic procedure.

Both in laparotomic and laparoscopic access cytology were obtained on entry into the peritoneal cavity.

Limits of lymphadenectomy were lateral genitofemoral nerve, medial hypogastric artery, posterior obturator nerve, caudal circumflex iliac vein, and inferior mesenteric artery as the cranial limit when performing paraaortic lymphadenectomy.

Statistical analysis

All continuous data is expressed in terms of mean and standard deviation of the mean and range. The unpaired t-test was performed to investigate differences of continuous variables between the groups. Pearson's chi square test, calculated by the Montecarlo method, was performed to investigate the relationships between group variables. For all tests $p < 0.05$ was considered significant. Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS) software version 9.0 (SPSS Inc., Chicago, IL, USA).

Results

From 312 patients whose data were reviewed, 210 were considered eligible for the study; 115 in the LPS group and 95 in the LPT group. Table 1 lists the demographic and clinical characteristics of women with EC on the basis of the surgical approach used. The two groups were homogeneous for age, body mass index (BMI), menopausal age, comorbidities, histological type, preoperative stage and surgical risk (previous abdominal surgery, general health).

Conversion from LPS to LPT

Conversion to laparotomy was necessary in six (5%) of the 115 cases managed by laparoscopy. Poor tissue exposure and anesthesia problems (high saturation in CO2) in five patients; one case, for evidence of intraperitoneal tumor dissemination. In no patient was conversion to laparotomy due to obesity or adhesions.

Operative and postoperative results

Surgical time was 280 ± 80 vs 222 ± 82 minutes in the LPS and LTP groups, respectively ($p < 0.0005$).

The median hemoglobin decline was 2.2+1.0 g/dl (range 2.0-2.4) in the LPS group and 2.1+1.4 g/dl (range 1.8-2.4) in the LPT group. Drainage was positioned in 76 patients (80%) and in 63 patients (56%) of the LPS and LPT groups, respectively ($p = 0.001$).

The mean time of postoperative ileus was 2.0 ± 0.9 days in the LPS group and 3.5 ± 2.1 days in the LPT group ($p < 0.0005$). We routinely removed the urinary catheter the day following the surgical procedure in both groups and all patients were voiding spontaneously without any difficulty.

Table 1. — *Population characteristics in the two groups of patients*.

	LPS	LPT	*p*
Study patients (no.)	115	95	
Age, years (mean ± SD)	65.1 ± 10.8	66.6 ± 10.6	ns
BMI, Kg/m^2 (mean ± SD)	28.7 ± 6.0	28.6 ± 5.2	ns
Patients in menopausal status, no. (%)	87 (82)	76 (93)	ns
Menopausal age, years (mean ± SD)	50.8 ± 4.7	51.6 ± 3.5	ns
Histological Type I, no. (%)	83 (81)	82 (86.6)	ns
Histological Type II, no. (%)	32 (19)	13 (13.4)	ns
Stage I, no. (%)	83 (88)	86 (90)	ns
Stage II, no. (%)	32 (12)	9 (10)	ns
ASA I/II, no. (%)	104 (91)	86 (90)	ns
ASA III/IV, no. (%)	11 (9)	9 (10)	ns

Table 2. — *Surgical stage and tumor type after surgical staging in the two groups of patients*.

Surgical stage (FIGO 1988)	LPS No. of patients	%	LPT No. of patients	%	*p*
I	88	76	74	78	ns
II	13	11	11	12	ns
III	12	10	8	8	ns
IV	2	2	2	2	ns
Unstages	0	0	0	0	ns
Tumor type					
Type I	91	79	66	69	ns
Type II	24	21	29	31	ns

Table 3. — *Intraoperative and postoperative complications in the two groups of patients*.

	LPS No. of patients	%	LPT No. of patients	%	*p*
Intraoperative complications					
Bowel	0	0	1	1	ns
Vein	0	0	0	0	ns
Artery	1	1	0	0	ns
Bladder	1	1	1	1	ns
Ureter	1	1	1	1	ns
Nerve	1	1	0	0	ns
Postoperative complications					
Urinary tract infection	5	4	4	4	ns
Fever	33	29	60	63	$p < 0.005$
Lymphorrea	12	10	13	14	ns
Venous thrombophlebitis	1	1	2	2	ns
Bowel obstruction	3	3	2	2	ns
Urinary infection	7	6	4	4	ns
Wound infection	4	4	12	13	$p < 0.005$
Subfascial hematoma	0	0	1	1	ns
Urinary fistula	1	1	1	1	ns
Bowel fistula	1	1	0	0	ns
Arhythmia	3	3	2	2	ns
Blood transfusion	6	5	4	4	ns
Antibiotics	22	19	26	27	ns
Re-admission	4	4	5	5	ns
Re-operation	2	2	1	1	ns

ns: non significant.

The mean length of hospital stay was 3.1 ± 1.5 in the LPS group and 5.6 ± 1.5 days in the LPT group ($p < 0.005$).

Table 4. — *Operative results in patients with BMI < 30 and BMI ≥ 30*.

LPS	BMI < 30	BMI ≥ 30	*p*
No. of patients	72	43	
Age, years (mean ± SD)	65. ± 12.0	65.4 ± 8.5	ns
BMI, Kg/m^2 (mean ± SD)	25.0 ± 2.8	35.2 ± 4.3	$p < 0.005$
Surgical time, minutes (mean ± SD)	284.0 ± 78.3	269.4 ± 86.8	ns
% difference in Hb (mean ± SD)	2.1 ± 1.3	2.1 ± 1.9	ns
Lymph Node removed, no. (mean ± SD)	18.5 ± 9.7	14.9 ± 11.3	ns
Conversion to laparotomy	4 (5%)	2 (5%)	ns
Hospitalization stay, days (mean ± SD)	3.7 ± 1.7	3.4 ± 1.1	ns

Table 5. — *Operative results in patients aged < 70 and aged ≥ 70*.

LPS	age < 70	age ≥ 70	*p*
No. of patients	71	45	
Age, years (means ± SD)	58.9 ± 7.9	76.7 ± 4.0	$p < 0.005$
BMI, Kg/m^2 (mean ± SD)	29.2 ± 6.5	28.2 ± 5.4	ns
Surgical Time, minutes (mean ± SD)	285.8 ± 84	266.9 ± 78.8	ns
% difference in Hb (mean ± SD)	2.0 ± 1.5	2.2 ± 1.6	ns
Lymph Node removed, N (mean ± SD)	18.6 ± 10.3	15.2 ± 10.2	ns
Conversion to laparotomy	4 (5%)	2 (5%)	ns
Hospitalization stay, days (mean ± SD)	3.6 ± 1.6	3.5 ± 1.4	ns

Surgical staging

In Table 2 we report postsurgical staging in both groups. Staging of lymph nodes were histologically documented from the pelvis in both laparoscopic and laparotomic route patients. The number of pelvic lymph nodes removed was similar for the two groups: 18.0 ± 9.6 vs 14.9 ± 7.9 mean + SD in the LPS and LPT groups, respectively. Paraaortic lymphadenectomy was performed in 25 (22%) cases in the LPS group and in 21 (22%) cases in the LPT group. The mean number of resectioned aortic lymph nodes was 9.8 ± 3.1 in the LPS group compared to 8.9 ± 2.5 in the LPTs group (n.s.). Lymph node metastases were found in 10% of participants and were similar in both groups.

Intraoperative complications

Intraoperative complications were not statistically different between the two groups (Table 3).

In the LPS group we had one case of ureterovescical fold incision that was sutured laparoscopically. There was one case of obturator nerve injury during obturator pelvic node lymphadenectomy. The nerve was quickly sutured by LPS and the patient was submitted to rehabilitation therapy, and after one year no further problem was observed. One case of ureter damage due to accidental bipolar coagulation required anastomosis. No long-term problem was observed. One case of small aortic injury was sutured with a metallic clip.

In the LPT group one patient had a bowel perforation

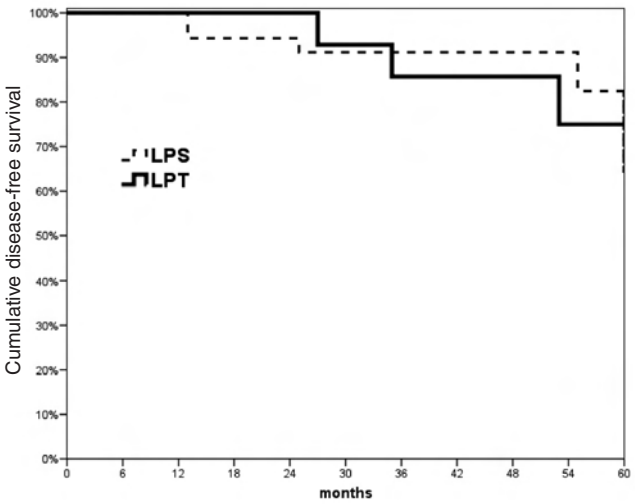

Figure 1. — Disease-free survival showing no significant difference between the two groups of patients.

due to dense adhesions of the uterus which was diagnosed during the surgical procedure and resolved with a bowel resection and latero-to-end anastomosis, one case of bladder injury was resolved quickly with a suture of the bladder and there was one case of ureter injury.

Postoperative complications

Postoperative complications are shown in Table 3. Fever and wound infections were significantly more common in the LPT group. Other complications were not significantly different between the two groups.

Adjuvant treatment

There was no significant difference between the two groups with respect to adjuvant treatment. In the LPS group, 61 (53%) patients underwent radiotherapy (RT) and seven (7%) underwent chemotherapy (two patients underwent both). In the LPT group, 59 (51%) patients underwent RT and 12 (13%) underwent chemotherapy (one patient underwent both).

BMI and age

The LPS group data was considered on the basis of BMI and age; no significant statistical differences were observed (Tables 4 and 5) in any parameters such as surgical length, hemoglobin decrease, and number of lymph nodes removed. No difference in intraoperative and postoperative complications or adverse events was observed.

Follow-up

One hundred and eight patients had a follow-up of 60 months. The total recurrence rate of the entire sample was 14% (n = 29 patients); eight (13%) of 62 patients in the LPS group had a recurrence versus seven (15%) of 46 patients of the LPT group. In the LPS group, metastases were detected in the vaginal cuff in two patients and distant metastases were found in six patients (lung, liver, bowel and skin). In the LPT group, metastases were located in the vaginal cuff in two patients and five distant metastases (brain, bowel, and aortic node) were detected in five patients. There were no port-site recurrences noted in the LPS group. Disease-free survival showed no significant difference between the two groups (Figure 1). No significant difference was found between the two groups when the recurrence rate was compared. At the time of last follow-up, six patients (10%) and four (8.6%) patients died of disease or correlated disease in the LPS and LPT groups, respectively.

Discussion

Our analysis confirms that total laparoscopic access represents a feasible and safe therapeutic procedure for the management of early-stage EC. The LPS approach to EC compared to the LPT approach allows for the reduction of postoperative complications and hospital stay. There were no significant differences in intraoperative complications, surgical performance, postoperative complications, and disease-free survival between the two approaches, even when considering obese and older patients.

In general, one of the principal problems for the surgeon is to choose the most appropriate surgical access approach to perform the operation. The choice must guarantee the patient the lowest possibility of complications and, in the case of oncologic surgery, the greatest oncologic profundity. In a LAP 2 study around a quarter of patients scheduled for laparoscopy only completed the operation after conversion to laparotomy. One of the most frequent reasons for conversion is that obesity has made laparoscopy difficult. This data could lead to the thinking that a large number of patients affected by EC are not candidates for laparoscopy as a high percentage of them are obese. In reality our data, as that of other studies [14], show a low percentage of conversion to laparotomy and in those few cases of conversion the reason was not patient obesity but more than anything, in our opinion, was due to the longer laparoscopic surgical time which encourages the absorption of CO_2 through the tissue and therefore an increase of the gas in the blood with the consequent risk of metabolic acidosis. In our experience this problem can be resolved by working towards maintaining low CO_2 pressure, not superior to 12 mmhg, from the beginning of surgery.

Our data showed that morbidly in obese patients (BMI > 30) treated with LPS was similar to that of non obese patients (BMI < 30) (Table 4). In obese patients, LPS presents some advantages versus LPT, being faster resumption of normal intestinal function, lower risk of wound infection and dehiscence of suture, shorter hospital stay without compromising surgical staging, and no increase in conversion rate. Other authors described the same advantages of LPS versus LPT in obese women [15, 16]. We found, in accordance with other authors, [17] the same results in older patients (Table 5), in that age does not increase perioperative complications and conversion rate. Obesity and age was not a contraindication to LPS

in EC patients. It is most important, when deciding the surgical approach for these patients, to evaluate the overall health including such things as renal function, respiratory, and cardiovascular conditions [18].

As in previous studies in the literature, we did not record differences between LPS and LPT approaches in terms of intra-operative complications [17-21]. Only data on blood loss was discordant. In a LAP 2 study [7] a slightly higher arterial bleeding was reported and in other studies there was a significant reduction in intraoperative blood loss [22] due to magnification of small blood vessels provided by the current optical systems [23, 24]. In our patients the percentage of hemoglobin decrease was similar in the two groups; no patients required intraoperative transfusion and the number of postoperative transfusions was similar in the two groups.

On the other hand significant advantages of LPS over LPT were obtained in terms of postoperative complications (fever, ileus, and wound infections) and shorter mean length of hospital stay. In contrast, as reported by other authors, laparoscopy was associated with a significantly longer operative time [17-24].

Although data is accumulating which shows that the laparoscopic approach represents a convenient alternative to the laparotomic surgery for EC, various questions remain unanswered, particularly related to oncologic safety. Some authors questioned that the use of a colpotomizer increases the risk of vaginal cuff recurrences [22, 23], positive cytology, and the possibility of port-site metastasis (PSM).

As described in the literature, we found no differences in surgical staging in the two groups. We had one vaginal cuff recurrence in both the LPS and LPT groups. The vaginal cuff recurrence in the LPS group was compatible with histological type (type II) and Stage II in both groups. No increase in positive cytology was observed. After five years post surgical staging we had generated information on 62 patients.

During five years of follow-up, PSM was not found in any patient. Data on the relative risk of parietal metastases in open incisions versus laparoscopy remains controversial [24, 25]. Recently Querleu *et al*. reported, in a series of 1,216 laparoscopies for uterine cancer, only five PSM (four in cervical cancer and one in an EC). All PSM patients had concomitant metastasis (peritoneal carcinomatosis, vaginal recurrence, and lymph node progression). The authors concluded that PSM represents a rare complication in patients with uterine cancer and cannot be used as an argument against laparoscopic staging in these patients [26].

Several postoperative studies showed that patients treated by LPS had a superior quality of life compared to patients treated by LPT [19, 27-29], however few studies have reported long-term results and oncological findings [21, 22-30]. An important aspect of our study is the length of follow-up (five years). Our data suggest that the surgical approach does not influence disease-free survival (Figure 1) and overall survival. The scientific world advocates new studies on this subject. Awaiting the long-term outcome data from the GOG-LAP2 and the LACE [7-30] trials, which are designed to answer the final questions relating to cancer-free survival following LPS, it is important to collect this information from the experience of the various centres.

The limits of this study were the difficulties in data collection in that all data was retrospective and that four different surgeons performed the operations. However we consider these problems to be insignificant because we carefully examined the standard parameters not subject to personal evaluation and, because the surgeons (experienced in both laparoscopy and laparotomy) performed the operations using the same techniques. We therefore consider our retrospective data to be reliable.

In conclusion, our study describes surgical experience in EC patients confirming and reinforcing previous preliminary reports suggesting feasibility, safety and advantages of the LPS approach to EC treatment. Obesity and age do not compromise LPS performance and these patients can benefit from a minimally invasive technique which leads to superior quality of life without compromising oncological security and survival.

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