Laparoscopic Pelvic Lymphadenectomy in the Surgical Treatment of Endometrial Cancer: Results of a Multicenter Study

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ABSTRACT

Objective: To analyze the results and determine the contribution of laparoscopic pelvic lymphadenectomy in the surgical treatment of women with endometrial cancer and compare with the open technique.

Methods: A prospective multicenter study was carried out on 120 women who underwent laparoscopic surgery (96 women) and open procedures (24 women) for endometrial cancer between April 1996 and March 2000.

Results: Four patients whose laparoscopic surgery was completed by laparotomy were excluded from the study. The other 92 laparoscopic procedures were successfully completed. Laparoscopically assisted surgical staging (LASS) was performed based on the grade of the tumor and the depth of myometrial invasion. Sixty-seven of the patients underwent hysterectomy, bilateral salpingo-oophorectomy (BSO), and pelvic lymphadenectomy, and 25 women also had para-aortic lymph node sampling dissection. Eleven of these patients had positive pelvic or para-aortic nodes. The mean operating time for the laparoscopic procedure was significantly longer (173.8 min, P < 0.0001) than the time for the open procedure (135.0 min). The rate of complications was similar in both groups. The recovery time was significantly reduced (P < 0.0001).

Conclusion: The laparoscopic approach to hysterectomy and lymphadenectomy for early stage endometrial carcinoma is an attractive alternative to the abdominal surgical approach. The advantages of laparoscopically assisted surgical staging are patient related. Because the abdominal incision is avoided, the recovery time is reduced. Laparoscopic pelvic lymph node dissection is a procedure that is appropriate, when applicable.

Key Words: Laparoscopic lymphadenectomy, Endometrial cancer.

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INTRODUCTION

Endometrial cancer is the most common gynecological cancer, with an incidence in the Czech Republic of about 30 cases per 100,000 women per year. Surgical treatment was traditionally performed by laparotomy; the laparoscopic approach, however, has gained wider acceptance by gynecologic oncologists. Several reports of laparoscopic staging of pelvic malignancy have been reported.[1-4]

The Gynaecologic Oncology Group (GOG) initiated 2 prospective feasibility trials at 6 institutions with a specific interest in laparoscopic surgery.[5] The Gynaecologic Oncology Group studies laparoscopic retroperitoneal lymph node sampling followed by laparoscopically assisted vaginal hysterectomy (LAVH) and bilateral salpingo-oophorectomy (BSO) in women with early stage endometrial cancer. Operating time, blood loss, duration of hospital stay, return to normal activity, and complications are evaluated. Node count, video recordings, and pathology review evaluate the adequacy of the procedure.

Based on the above criteria, the Czech multicenter prospective trial (CZEMPT) began in 1996, and the preliminary results of our study have been reported.[6] The primary aim of the study is to report the perioperative and postoperative outcomes of laparoscopic transperitoneal lymphadenectomy in a major group of patients with endometrial cancer. The second aim is to assess the contribution of pelvic lymphadenectomy to laparoscopically assisted surgical staging (LASS).

MATERIALS AND METHODS

This study was conducted at 3 oncolaparoscopic centers in the Czech Republic. We identified 192 patients who underwent surgery for early-stage endometrial cancer between April 1996 and March 2000. Only 120 women who had undergone laparoscopic (96 women) or abdominal (24 women) lymphadenectomy and hysterectomy with bilateral salpingo-oophorectomy (BSO) were included in the study. Seventy-two patients who underwent only laparoscopic, vaginal, or abdominal hysterectomy with BSO were excluded. A group of 24 patients, who underwent abdominal hysterectomy, salpingo-oophorectomy, and retroperitoneal lymph node dissection, was used as a control (open) group.

Selection criteria for the laparoscopic approach included clinician suspicion of early stage endometrial cancer, regardless of grade or histo-pathology and myoinvasion, as well a mobile uterus amenable to a laparovaginal approach for hysterectomy. The decision concerning the extent of laparoscopic surgery was based on the guidelines suggested by Childers et al[1] and included in the CZEMPT protocol.[6] The study protocol was approved by the Regional Committee on Human Research at the Hospital Kladno, and the participants gave informed consent at enrollment. The study was supported by the Grant Fund of the Health Ministry.

The patients who underwent abdominally assisted surgical staging (ASSS) had a standard open procedure with a vertical midline incision, total hysterectomy, bilateral salpingo-oophorectomy, peritoneal washing, pelvic lymph node dissection, and, in the presence of selected high-risk factors para-aortic sampling as well. For the open procedure, patients were selected who were not suitable for laparoscopic surgery because of the following reasons: concurrent illness that does not allow the use of the Trendelenburg position, high anesthesiology risk according to the classification of ASA (American Society of Anesthesiologists) III, and an enlarged myomatous uterus, in which the necessity for morcellation can be a prerequisite, and a history of repeated laparotomies for peritonitis.

A complete history was taken preoperatively of all the patients with clinical stage I carcinoma of the endometrium. All the patients underwent endometrial biopsy, ultrasound, and computerized tomography (CT) or magnetic resonance imaging (MRI).

All the procedures were carried out by 1 of 3 experienced oncogynecological surgeons. A video recording was taken of each patient. A case record form was completed that contained patient identification data, preoperative staging results (ultrasound, CT, MRI, and biopsy), surgical/pathological information (grading, myometrial invasion, typing, and cytology), and the definitive staging was completed. The types of surgery and characteristics of the women are shown in **Table 1**.

Laparoscopic Operating Technique

Laparoscopy, with the use of video monitoring equipment, was carried out with the patient in the lithotomy position. The telescope was inserted at the subumbilical site and one 10-mm port of entry was made suprapubically and medially. Finally, two or three 5-mm ports were placed in each of the lower quadrants at the lateral edge of the rectus muscle. Bipolar and monopolar electrocauterers (Karl Storz Endoscope, Tuttlingen, Germany) were used in most cases, whereas a Harmonic scalpel and LaparoSonic coagulating shears (LCS-K5), (UltraCision, Ethicon Endo Surgery, Johnson & Johnson Ltd, Cincinnati, Ohio, USA) were applied in some cases at 1 center only (Hospital Kladno).

Table 1.
Types of Surgery and Patient Characteristics.

	Laparoscopy	Control Group	Totals
Type of Surgery			
HYE, BSO, PLN	67	21	88
HYE, BSO, PLN, PALN	25	3	28
Totals	92	24	116
Patient Characteristics			*P* value
BMI	27.1	26. 7	NS
Range	18. 7-43.1	18. 7-32. 9	
Age (years)	59. 4	59. 5	NS
Range	42-76	47-79	

Values are means and ranges; HYE=hysterectomy; BSO=bilateral salpingo-oophorectomy; PLN=pelvic lymph node dissection; PALN=para-aortic lymph node dissection; NS=not significant; BMI=body mass index.

Laparoscopically assisted surgical staging required a complete inspection of the whole peritoneal cavity. Intraperitoneal fluid was aspirated in each of 4 quadrants for cytological investigation. A second look laparoscopy was then performed to secure or confirm hemostasis, and an intraperitoneal drain was left in situ until the next day. All patients received thrombosis prophylaxis in a form of low molecular heparin and also perioperative prophylactic antibiotics.

Transperitoneal Pelvic Lymph Node Dissection

The dissection was begun by opening the broad ligament and lateral pelvic peritoneum between the round ligament and the infundibulopelvic ligament. The lymph nodes bearing the adipose tissue were excised from the obturator fossa after mobilization of the external and internal iliac vessels and obturator nerve and vessels as well. We dissected the lymph nodes up to the level of bifurcation of the iliac vessels superiorly and to the femoral canal inferiorly. The paravesical and pararectal spaces were opened with blunt and sharp dissection. The ureter was visualized along the medial leaf of the peritoneum at the level of the bifurcation of the common iliac artery.

Transperitoneal Para-Aortic Lymph Node Dissection (PALN) or Sampling (PALS)

The para-aortic lymph node dissection was initiated by incising the peritoneum, which lies over the right common iliac artery, extending the incision cranially along the aorta up to the level of the inferior mesenteric artery. Only the lymph node sampling was performed from the para-aortic fields between the level of the inferior mesenteric artery and the level of the renal artery. Para-aortic lymph node dissection was done after the pelvic lymph node dissection. The nodal package was removed from the operative field through the upper 10-mm trocar.

Laparoscopy-Assisted Vaginal Hysterectomy with Vaginal Colpotomy (LAVH-VC)

The hysterectomy was begun with laparoscopy. The following steps were performed during the laparoscopic phase: severing of the round ligament, dissection of the upper portion of the broad ligament, severing of the infundibulopelvic ligament, preparation of the bladder flap, and severing of the bladder pillars. These steps

were finalized vaginally severing the uterine vessels, cardinal uterosacral ligament, performance of anterior and posterior culdotomy, and closure of the vaginal cuff.

The anterior peritoneum of the broad ligament was dissected towards the bladder. After the dissection of the bladder from the lower uterine segment, an inspection was carried out on each side to visualize the ureter and uterine artery.

Laparoscopy-Assisted Vaginal Hysterectomy with Laparoscopic Colpotomy (LAVH-LC)

All steps, including dissection of a uterine artery origin from the hypogastric artery, were performed laparoscopically, except severing of vaginal branches of the uterine vessels and closure of the vaginal cuff, which were completed vaginally. Koh's cup was placed over the cervix in LAVH-LC patients only. The cup was used alone with a uterine manipulator or as part of a new system described by Koh in 1998.[7] Principally, this system consists of lifting the neck and straining the vaginal vault with a plastic vaginal cuff manipulator. Distancing of uterine vessels from the ureter and safe dissection of uterine vessels and vaginal vaults were subsequently performed.

Statistical Analysis

We evaluated and compared differences in the perioperative and postoperative outcomes of the 2 groups (laparoscopy and open) of patients with different surgery techniques of endometrial cancer staging. Data regarding the duration of the surgery, the number of lymph nodes, the blood loss, and the length of hospital stay were collected. The differences between the 2 groups were determined by the unpaired t test by an independent biometrician. A P-value of less than 0.05 was considered significant.

RESULTS

The results are summarized in **Tables 2-5**. The laparoscopic procedure was completed successfully in 92 women (95.8%). The electrosurgery procedure of laparoscopy was carried out in 77 patients, and ultrasonic operative techniques with a Harmonic scalpel and shears were used in 1 center only (15 women). We were unable to perform prompt and thorough hemostasis in 1 obese patient due to ineffective post-LaparoSonic coagulation of venous varices on v. ovarica. Bipolar cautery

Table 2.
Outcomes and Length of Hospital Stay.

Outcome	Laparoscopy	Control Group	t test
Duration of surgery (min)	173.8	135.0	P < 0.0001
(range)	(120-220)	(95-180)	
Number of nodes recovered	19.0	17.0	NS
(range)	(3-34)	(6-26)	
Estimated blood loss (mL)	201.2	225.7	NS
Hospital stay (days)	4.1	7.7	P < 0.0001
(range)	(2-16)	(5-16)	

Table 3.
Results of Histological Examination.

Histological Finding	Laparoscopy	Control Group
Adenocarcinoma	83	20
Adenoacanthomas	2	1
Papillary carcinoma	2	1
Adenosquamous carcinoma	3	1
Clear-cell carcinoma	1	1
Carcinosarcoma	1	0

Table 4.
Surgical Staging.

Stage	Laparoscopy	Control Group
Stage Ia (no myoinvasion)	20	4
Stage Ib (to 50%)	38	8
Stage Ic (over 50%)	19	7
Stage IIa	0	1
Stage IIb	1	1
Stage IIIa	3	0
Stage IIIc	11	3
Lymph node positive (cases)	11	3
Pelvic lymph node	7	3
Para-aortic lymph node	1	0
Both lymph nodes positive	3	1
Grade 1	23	5
Grade 2	36	10
Grade 3	33	9

between groups was not substantial, mean BMI 27.1 in the laparoscopic group versus BMI 26.7 in the open group. The heaviest woman (BMI 43.1) successfully underwent laparoscopically assisted vaginal hysterectomy, and pelvic and para-aortic lymph node dissection. More than half of the patients in the laparoscopic group (52.1%) weighed more than 81.7kg/180 pounds.

Adenocarcinoma was the most common histology found in both groups **(Table 3)**. The frequency of poorly differentiated lesions (Grade 2, 3), (laparoscopy group 75.0% vs open group 79.1%) and lesions invading up to 50% of the myometrium was similar in both groups. Of the 92 patients who underwent laparoscopic lymphadenectomy, 25 patients also had para-aortic lymph node dissection or sampling with 4 positive results for metastases. We found malignant changes in lymph nodes in 11 women (11.9%) in the laparoscopic group versus 3 women (12.5%) in the control group. The average numbers of removed lymph nodes in our groups were comparable (19 LPSC group vs 17 open group).

was effective in this case, however. Electrosurgery was effective in all cases. We converted to laparotomy in 4 patients: 1 woman had uncontrolled bleeding from a branch of the iliac vein, 1 patient had oxygen hypoventilation during anesthesia, and 2 others sustained an injury to the epigastric artery and had extensive fibrotic adhesions and uncontrolled bleeding. These patients were removed from data analysis, but they remained in the laparoscopic group for analysis of complications only. An overview of pre- and postoperative complications is shown in **Table 5**.

The mean age and range of age distribution were similar in the 2 groups **(Table 1)**. The mean age in the laparoscopic group was 59.4 years, compared with 59.5 years in the open group. The difference in body mass index (BMI)

Table 5.
Complications.

Type of Complications	Laparoscopy	Control Group
Fever over 38°C	6	2
Hematoma	2	0
Wound abscess	1	2
Vaginal discharge	2	0
Phlebothrombosis	1	1
Pulmonary artery embolism	1	0
Injury to a. epigastrica	3	0
Injury to bladder	2	1
Neuritis n. obturatorii	1	0
Conversion	4*	0
Totals	23	6

* Results of anesthetic and uncontrolled bleeding problems

The blood loss was minimal and only 3 units were required for transfusion in the 3 patients with conversion for uncontrolled intraoperative bleeding. Preoperative blood loss was comparable in both groups (201.2 mL vs 225.7 mL in the laparoscopic and open group, respectively) without any significant consecutive changes in the serum hemoglobin value.

Although the length of operating time for a laparoscopic hysterectomy and lymphadenectomy was significantly longer than the time for the laparotomy procedure (173.8 min vs. 135.0 min, $P < 0.0001$), the laparoscopic group patients were discharged from hospital much earlier, at 4.1 days (range 2 to 16) after the laparoscopic procedure, compared with 7.7 days (range 5 to 16) after the abdominal procedure ($P < 0.0001$).

The patients who underwent operation at 1 particular center had the longest average duration of hospital stay (8.6 days). This center also had the longest operating time (220 min), the highest number of excised lymph nodes (26), and the most severe complications. All the patients, regardless of the surgical approach chosen, were treated postoperatively on the same clinical treatment pathways. The median follow-up in the laparoscopic group was 21 months (range 3 to 48). One case

of adenocarcinoma of the sigmoideum was found (second malignancy or recurrence) during surgical stage I. The median follow-up in the control group was 23 months (range 2 to 46), without any recurrence during surgical stage I and with 1 death during clinical stage I.

DISCUSSION

Endometrial cancer is now a surgically staged malignancy. The pilot study by Creasman et al[8] and subsequent reports of the GOG studies have been instrumental in this change. These reports document the significance of lymph node involvement. This study has recorded the spread to pelvic and para-aortic lymph nodes in 6% to 9% of cases where only the corpus is involved, and overall, a 22% incidence of extrauterine spread. Benedetti-Panici et al[9] analyzed the patterns of lymphatic spread in 91 endometrial cancer patients [surgical Federation International of Obstetrics and Gynecology (FIGO) stage I-IV] who underwent systematic pelvic and aortic lymphadenectomy. If regional lymph node sampling is done, some degree of additional morbidity is incurred. Several authors have retrospectively evaluated the morbidity and mortality of lymphadenectomy done by the open procedure of staging laparotomy.[10,11] Barakat and Benjamin[12] noted a statistically significant increase in perioperative parameters (mean operating time, blood loss, and duration of hospital stay).

Childers et al[1] reported on a series of 59 patients considered candidates for laparoscopically assisted surgical staging (LASS) for management of their clinical stage I adeno-carcinoma of the endometrium. These authors carried out pelvic and para-aortic lymph-adenectomy on 23 patients and were unable to perform laparoscopic common and para-aortic lymphadenectomy in 2 other patients because of obesity. Several authors concluded that removal of both pelvic and para-aortic lymph nodes can be accomplished laparoscopically even in obese patients.[13-16] However, at present, no agreement exists about indications and extent with regard to lymphadenectomy. Even in the presence of other pelvic pathology, obesity does not seem to limit the pelvic lymphadenectomy, allowing these women with endometrial and cervical cancer to be candidates for the procedures.[13] In addition, primary removal of aortic nodes is not warranted in most women with endometrial cancer and should be restricted to pelvic lymph nodes.[13,14] In our previous study, we assessed differences in duration

of surgery, number of excised lymph nodes, blood loss, and hospital stay after LASS in 2 groups of women of different weight with endometrial cancer.[16] It was surprising that the duration of surgery was shorter by 6 minutes in obese than in nonobese patients; the mean operating time was 166 and 172 minutes, respectively.

The results of our study shows that laparoscopy and the open procedure were similar in terms of perioperative outcomes in blood loss and the number of nodes recovered. The great effectiveness and reliability of the electrosurgical and ultrasonic operational techniques used were confirmed. Furthermore, electrosurgery was demonstrated to be superior to the Harmonic scalpel in cases of venous bleeding on v. ovarica during the salpingo-oophorectomy phase. The advantages of the LaparoSonic technique include less charring and plume, better visualization, and less thermal injury, particularly in respect to the important surrounding pelvic structures during lymph node dissection.[17] The rate of major and moderate complications was higher in the control group (25.0% vs. 23.0%). In 4 cases, the laparoscopic procedure was converted to laparotomy. In 1 patient of the 3 cases of uncontrolled bleeding from an injured branch of the iliac vein, laparoscopy was followed by laparotomy and multiple complications were induced (wound abscess, resuture, and pulmonary artery microembolism). In 1 patient in the laparoscopy group, the nervus obturatorius was irritated during the pelvic lymph node dissection done by the ultrasonic scissors. We suppose that the higher complication rate at 1 particular center is related to the greater radicalism of the surgery and the higher para-aortic lymphadenectomy rate.

Outcomes of the surgical treatment and follow-up were similar in both groups. Although the length of the operative time for laparoscopic procedure was significantly longer ($P < 0.0001$) than the time for the open procedure, the laparoscopic group patients were discharged from the hospital significantly earlier ($P < 0.0001$).

Among the 69 patients in the laparoscopic group with higher stage grading and deep myometrial invasion, only PLN was carried out in 44, and both PLN and PALN were also done in 25. In this group, the malignant changes in lymph nodes were confirmed in 10 women (14.5%) and in only 1 patient in the group of 23 women with low grading and myoinvasion less than 50%. The total number of women with pathologic lymph node and positive peritoneal cytology was 14 (15.2%). In these cases, clini-

cal evaluation alone may lead to understaging. Metastasis was found in 12.5% of the patients in the control group. In the above mentioned recent study of Benedetti-Panici et al,[9] nodal involvement was found in 16 cases (18%), but lymph node metastasis was the only site of occult extrauterine spread in 5 patients (6.6%). In a retrospective chart review of 320 patients with early-stage endometrial cancer treated by laparoscopic assisted vaginal hysterectomy (LAVH) or total abdominal hysterectomy (TAH) described by Gemignani et al,[18] no significant difference existed between either method in mean lymph node yield. Grade 1 tumors were the majority of the tumors in both groups, and the number of the patients with lymph node positivity was not specified.

We found only 1 case of positive aortic node without involvement of pelvic nodes, which is in accordance with reports of others.[9,13] Pelvic node metastasis is a better criterion for aortic lymphadenectomy than is myometrial invasion.[19] According to findings of Bendetti-Panici et al[9] in the pelvic area, the superficial obturator nodes were the frequently involved group. Evaluation of these nodes alone identified 71% of patients with positive nodes. On the other hand, when the external iliac and superficial common iliac nodes were evaluated together with the superficial obturator group, all patients having pelvic metastases were identified. According to recommendations of the FIGO Committee on Gynecologic Oncology,[20] indications for aortic node sampling would include suspicious aortic or common iliac nodes, grossly positive adnexa, and any grade of tumor showing the outer half of myometrial invasion. Patients with clear cell papillary serous or carcinosarcoma histologic subtypes are also candidates for aortic node sampling. Although mandated through the staging system, lymphadenectomy of the pelvis and para-aortic areas remains controversial, with most individuals using selective node sampling and reserving complete lymphadenectomy for cases with certain high-risk features. In clinical practice guidelines from FIGO, the open approach to surgery for endometrial cancer is generally recommended. It was recently stated[20] that laparoscopically assisted vaginal hysterectomy and laparoscopic lymphadenectomy are procedures that are appropriate, when applicable. Kadar[14] suggests using the 2-stage approach to aortic lymphadenectomy in obese or high-risk patients. In our opinion, laparoscopic pelvic lymphadenectomy has a significant role in surgical staging in patients with endometrial cancer. Prolongation of the operation time from 60 to 80 minutes on average increasing the risk of serious adverse events is acceptable

when the advantages of para-aortic lymph node dissection are compared. The follow-up result is another reason for inclusion of the pelvic lymphadenectomy as a firm part of surgical staging of patients with high-risk endometrial carcinoma. No deaths or port site metastases were observed during the follow-up period in the group of patients with surgical stage I endometrial carcinoma. Adenocarcinoma of the sigmoideum was found in 1 patient with negative pelvic nodes 3 months after hysterectomy with lymphadenectomy (recurrence rate 98.5%).

CONCLUSION

The laparoscopic approach to pelvic lymphadenectomy for early stage endometrial cancer is an attractive alternative to the open surgical approach. The advantages of laparoscopically assisted surgical staging are patient related. The laparoscope affords a surgeon the ability to avoid abdominal incision wound infection in these patients. The women who underwent the laparoscopic procedure had a short postoperative stay in the hospital. This approach also allows women to have all the benefits of minimally invasive surgery, such as less pain, less scarring, and a shorter recovery time.

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