

## Editorial Articles

# The role of laparoscopy in the surgical treatment of endometrial cancer

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### Summary

**Objectives:** Endometrial cancer is the most common gynaecological cancer. Surgical treatment has traditionally been done by laparotomy, however the laparoscopic approach has gained wider acceptance by gynecologic surgeons. Whether in combination with laparoscopic-assisted or laparoscopic hysterectomy, laparoscopic staging, including lymph-node dissection, is a major component in the treatment of patients with early endometrial cancer. It remains to be proven if these techniques are associated with the greatest benefit.

**Methods:** Substantial recent studies on the topic of surgical laparoscopic treatment of endometrial cancer were identified from Medline.

**Results and discussion:** Laparoscopically assisted surgical staging (LASS) has been reported in several case series totaling more than 600 cases.

**Conclusion:** The report illustrates that laparoscopically assisted surgical staging of endometrial cancer is safe as an open procedure. The laparoscopic approach may also be considered for endometrial malignancy which typically occurs in obese and elderly high-risk women.

**Key words:** Endometrial cancer; Laparoscopy; Hysterectomy; Lymphadenectomy; Survival.

### Introduction

Endometrial cancer (EC) is the most common gynaecological cancer with an incidence of 45.0 cases per 100,000 women in the U.S., 30.0/100,000 in the Czech Republic and 1.7/100,000 in Japan [1, 2]. Surgical treatment was traditionally done by laparotomy, however the laparoscopic approach has gained wider acceptance by gynecologic surgeons. Since the report by Childers *et al.* [3] on laparoscopically assisted surgical staging (LASS) several reports of case series of patients have followed [4-10].

#### *Early endometrial cancer*

Whether in combination with vaginal laparoscopically assisted or laparoscopic hysterectomy, laparoscopic staging, including lymphadenectomy, is a major component in the treatment

of patients with early endometrial cancer. It remains to be proven which of these techniques is associated with the greatest benefits [11]. The standard approach to the surgical management of early stage endometrial carcinoma has been to perform the primary surgery via an open technique [10]. Peritoneal washings are obtained for cytology, a thorough exploratory laparotomy is performed, and an extrafascial hysterectomy and bilateral salpingo-oophorectomy are carried out. Pelvic and para-aortic lymph-node dissection are done to complete surgical staging.

## Laparoscopic lymphadenectomy

The number of reports on the use of laparoscopy in lymph-node dissection in endometrial cancer remains surprisingly scant. Childers *et al.* [3] reported on a series of 59 patients considered candidates for LASS for management of their clinical Stage 1 adenocarcinoma of the endometrium. These authors carried out pelvic and para-aortic lymphadenectomy on 23 patients and were unable to perform by laparoscopy the common iliac and para-aortic lymphadenectomy in two 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 [5, 12, 13]. 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 pelvic lymphadenectomy, thus allowing these women with endometrial cancer to be candidates for the laparoscopic procedure [5]. In addition, primary removal of the aortic nodes is not warranted in most women with endometrial cancer and should be restricted to the pelvic lymph nodes [14].

Holub *et al.* [15] reported the findings of a Czech group study. Among the 69 patients in the laparoscopic group with higher stage grading and deep myometrial invasion, only pelvic lymph node dissection was carried out in 44, and both pelvic and para-aortic lymphadenectomy were also done in 25. In this group the malignant changes in lymph nodes were confirmed in ten women (14.5%) and in one patient in the group of 23 women with low grading and myometrial invasion less than 50%. The total number of women with pathologic lymph nodes and positive peritoneal cytology was 14 (15.2%). In these cases clinical evaluation alone may lead to understaging. Metastasis was found in 12.5% of the patients in the open procedure control group. In a recent study of Benedetti-Panici *et al.* [16] nodal involvement was found in 16 cases (18%), but lymph-node metastasis was the only site of occult extrauterine spread in five patients (6.6%). In a retrospective chart review of 320 patients with early stage endometrial cancer treated by laparoscopic-assisted vaginal hysterectomy or total abdominal hysterectomy described by Gemignani *et al.* [7], no significant difference existed between either method in mean lymph node yield. Pelvic node metastasis is a better criterion for aortic lymphadenectomy than is myometrial invasion [17]. According to the findings of Benedetti-Panici *et al.* [16] the superficial obturator nodes in the pelvic area were frequently involved. 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 with metastases were identified. According to recommendations of the FIGO Committee on Gynecologic Oncology [20], indications for aortic lymph-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 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.

## Sentinel node dissection

The presence of lymph-node metastases has a major impact on the prognosis of women with EC. One of the cornerstones of gynecologic cancer surgery is the assessment and removal of the regional lymph nodes. However, the most appropriate and reliable technique for assessing regional pelvic and para-aortic node remains uncertain [18]. The sentinel node (SN) is the first lymph node to receive cancer cell metastasis from the primary tumor. Sentinel lymph node dissection (SLND) and intraoperative lymphatic mapping were, therefore, designed as a less invasive alternative to the routine elective lymph-node dissection in patients with early-stage cutaneous melanoma [19].

Only two reports of cases of sentinel lymph-node dissection in endometrial cancer have been published up to today. Burke and colleagues [18] demonstrated an open technique of intra-abdominal mapping in endometrial cancer. The authors explored the possibility of using open intra-abdominal mapping as a method to visualize the lymphatic drainage of the uterus. A deposition of isosulfan blue dye into at least one the lymph nodes was only observed in 67% of cases. A report on the pilot study of laparoscopically assisted sentinel dissections has been published by Holub *et al.* (20). The authors report the results of a

continuing study comparing the two operative procedures for lymphatic mapping and sentinel dissection in surgically staged patients with early-stage endometrial cancer. An intraoperative combination of cervico-subserosal myometrium (SSM) application of the blue dye allows successful detection (83.3%) of sentinel lymph nodes in patients with EC. Comparing the subserosal myometrium application technique and the SSM technique, respectively, a statistically significant difference was found in the dye-colored lymph nodes/lymph-node rate and mean number of sentinel lymph nodes ( $p = 0.03$ ,  $p = 0.05$ , respectively). Judging from the outcome of the aforementioned study on women with endometrial cancer, it appears that further extensive prospective studies need to be carried out. The role of the molecular lymphatic mapping (MLP) of the sentinel lymph node in solid tumors such as melanoma and breast carcinoma was assessed by Taback *et al.* [21]. The MLM procedure was validated in a rat breast-tumor model with lymph-node metastasis. The procedure was successful in permanently labeling and identifying by polymerase chain reaction both frozen and paraffin-embedded SLN. MLM in conjunction with a conventional mapping agent can be a valuable asset for molecular assessment of the SN and retrospective analysis of paraffin-embedded specimens.

### *Surgical technique of hysterectomy*

Vaginal hysterectomy has long been viewed as an acceptable alternative for some women with endometrial carcinoma in whom total abdominal hysterectomy might be difficult or risky [22]. However, it may be difficult or impossible to inspect the peritoneal cavity, obtain peritoneal cytology, and perform salpingo-oophorectomy and lymph-node dissection through a vaginal approach. Recently, the shortcomings of the pure vaginal approach have been circumvented through laparoscopy [9]. Laparoscopic-assisted vaginal hysterectomy (LAVH) combined with laparoscopic lymphadenectomy in the management of EC has been reported in several series totaling over 600 patients [3-9, 23, 24]. Most of the gynecologic surgeons performing laparovaginal hysterectomy, particularly LAVH, find it safer and shorter than a purely laparoscopic approach [7, 12, 23].

Although various techniques of total laparoscopic hysterectomy (TLH) have been reported [25, 26], no series have described it for the management of endometrial cancer in peer-reviewed journals. Manolitsas and McCartney [26] compared total laparoscopic hysterectomy with open hysterectomy in the management of EC. The authors developed a safe and efficient technique for performing TLH using a specially designed silicone, transvaginal tube. However, other surgical approaches are able to achieve the standard recommendations for the management of early endometrial cancer. Fagotti *et al.* [27] suggest that mini-laparotomy is a feasible alternative to the standard treatment in endometrial cancer patients as it offers the patient a cost-effective procedure that avoids many of the potential complications of standard therapy.

### *Cost analysis*

Scribner *et al.* [28] reported the outcome of a retrospective analysis on a series of 36 women with presumed early stage endometrial cancer treated between 5/96 and 1/99 at a single institution. The patients were grouped according to the surgical approach utilized. The first group consisted of 19 patients who underwent complete laparoscopic surgical staging. The second group consisted of 17 patients who underwent abdominal surgical staging. The two groups were compared with a two-tailed Student's t-test. The cost analysis was divided into room and board, pharmacy, ancillary services, operating room equipment, operating room services, and anesthesia. The authors concluded that the laparoscopic surgical management of early stage endometrial cancer is feasible with minimal morbidity. The cost savings of early hospital discharge is offset by longer surgical time and higher anesthetic costs. The total costs for each surgical approach are not statistically different. The presumed advantages of less pain, early resumption of normal activities, and overall improvement of quality of life await further investigation.

### *Port-site metastases (PSM)*

The finding of tumor growth at the site of a previous laparoscopic trocar placement, commonly known as a port-site metastasis, is one of the most feared complications of a laparoscopic procedure in gynecologic

cancer treatment. It is likely that there is under-reporting of this complication in the literature, thus making an accurate estimate of incidence difficult to establish [29]. Port-site recurrence (PCR) has been reported in association with endometrial cancers managed laparoscopically; however, the mechanism of development is not fully understood [30]. In most cases they occur in association with advanced stage disease [31, 32], but there is at least one report of a port-site metastasis in low-risk, early stage disease [33]. On the contrary, in two recent major studies reported by Malur *et al.* [23] and Holub *et al.* [34], the authors did not observe metastasis in any incision in a total of 214 laparoscopically treated patients. Muntz *et al.* [33] reported successfully treating a case of PSM after laparoscopic surgery for EC. In an animal study, Wilkinson *et al.* [35] concluded that laparoscopic PSR can be reproduced using the transplantable VX-2 rabbit carcinoma model. In the VX-2 model, trocar recurrence was the result of direct contamination via surgical instrumentation of viable tumor cells. The effect of the pneumoperitoneum or intraperitoneal cytological spillage (indirect contamination) did not have any effect on trocar recurrence. The outcomes of studies regarding the impact of the pneumoperitoneum on tumor growth are controversial [36, 37]. Watson *et al.* [38] suggest that the excision of port-site wounds following laparoscopy for cancer in an experimental model does not prevent the subsequent development of port-site tumors.

Port-site metastasis is discussed as a problem of laparoscopic surgery in patients with uterine malignancy [33, 39, 40], but is also associated with open surgery. Hertel *et al.* [40] presented a case of a 66-year-old woman with endometrial cancer who was diagnosed with an umbilical tumor after LAVH and adnexectomy. The interval between LAVH and diagnosis of the umbilical tumor was 13 months. The tumor was excised and metastasis of EC was histologically confirmed. Review of computer tomograms taken before surgery showed a tumor in the umbilical area that had not been recognized before therapy. Therefore, tumor manifestation at the abdominal wall after laparoscopic surgery should not automatically be considered the result of iatrogenic spreading.

### Long term results

Several studies (Table 1) have evaluated the feasibility of laparoscopic surgery in women with endometrial cancer, but in only four of these studies are survival data reported. In a retrospective study of Gemignani *et al.* [7], 69 patients treated by LAVH had significantly shorter hospitalization and fewer complications, resulting in less overall hospital charges when compared to 251 patients treated by laparotomy. Long-term outcome was similar. In another retrospective study early recurrences and survival rates appear to be similar to those reported for laparotomy patients [24]. The 3-year recurrence rate for 45 patients with surgical Stage I endometrial cancer treated by laparoscopy and vaginal or laparoscopy hysterectomy was 2.5%. In a previous study from the Mayo Clinic involving 577 patients with Stage I cancer (1971 FIGO staging) treated by laparotomy, there were 52 recurrences, for a recurrence rate of a 9% [11]. Malur *et al.* [23] reported in a prospective randomized study ( $n = 70$ ) no significant differences in disease recurrence and long-term survival between the laparoscopy and laparotomy groups (97.3 % vs 93.3 % and 83.9% vs 90.9%, respectively). In seven patients death was related to cardiac or pulmonary disorders and in two patients it was tumor associated. In the Czech prospective multicentric study [34] no significant differences in tumor recurrence or long-term survival were found between laparoscopy and open surgery ( $p = 0.99$  and  $p = 0.86$ , respectively).

Table 1. — Review of reports regarding laparoscopic surgery in women with endometrial cancer.

Reference	No. of patients	Follow-up (months)	MNLN	Conversion (%)	Complications (%)
Childers <i>et al.</i>	59	—	—	13.6	5.1
Gemignani <i>et al.</i>	59	18	7.0	4.3	5.8
Eltabbakh <i>et al.</i>	86	17	10.8	5.8	10.5
Magrina <i>et al.</i>	56	28	19.4	4.3	23.2
Malur <i>et al.</i>	37	16.5	16.1	0	29.7
Scribner <i>et al.</i>	95	—	23.2	29.1	19.6
Holub <i>et al.</i>	177	34	16.8	3.4	15.2

MNLN= mean number of lymph nodes

### *Surgical staging after unexpected endometrial cancer in a hysterectomy specimen*

Laparoscopy is useful for the completion of disease treatment and surgical staging in patients found to have an unexpected endometrial cancer after hysterectomy performed for other reasons [11]. In a series of 13 patients in that situation, the mean interval from hysterectomy to laparoscopy was six weeks [41]. At laparoscopy, three patients (23%) had extrauterine disease, one had positive cytologic results and two had positive pelvic nodes.

### *Recurrent endometrial cancer*

As with recurrent cervical cancer, laparoscopic evaluation was beneficial before extenteration for recurrent endometrial cancer. Magrina [11] found in two patients with recurrent endometrial cancer after irradiation the following findings: Laparoscopic exploration in one revealed the presence of unresectable tumor fixed to the common iliac vessels and sacral promontory and in the other peritoneal invasion by the tumor.

In patients with apparently isolated vaginal-cuff recurrences, surgical evaluation by laparotomy has demonstrated additional metastatic sites in 37.5% of them [42]. Laparoscopic exploration may provide similar information, but with lower morbidity rates [11].

## **Conclusion**

The presented paper illustrates that laparoscopically assisted surgical staging of endometrial cancer is as safe as an open procedure. The laparoscopic approach may also be considered for endometrial malignancy which typically occurs in obese, elderly, high-risk women [5, 12, 13]. Laparoscopy affords a surgeon the ability to avoid abdominal incision wound infections in these patients. This approach also allows the women to have all the benefits of laparoscopic minimally invasive surgery, such as less pain, less scarring, and shorter recovery time.

Notwithstanding the current controversies regarding the optimal role of surgical staging in the management of endometrial cancer, laparoscopic surgical staging of endometrial cancer is likely to find increasing acceptance by gynecologic oncologists, pending the results of a Gynecologic Oncology Group trial that is presently accruing patients [29].

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