

The laparoscopic-assisted vaginal approach to early endometrial cancer

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Abstract

Introduction For the surgical treatment of endometrial cancer laparotomy still is regarded as the gold standard. Over the past decade, the laparoscopic approach has gained equivalence in FIGO stage I carcinomas.

Results Laparoscopic-assisted vaginal hysterectomy and bilateral salpingo-oophorectomy plus pelvic/paraortic lymphadenectomy have shown short-term advantages such as reduced blood loss and shorter hospitalization without reducing oncological safety or outcome. This has already been confirmed by numerous smaller studies and recent randomized controlled trials with sufficient numbers of patients are being published.

Conclusion Further acceptance of the technique is necessary to enable every gynecological oncologist to individualize treatment by offering minimal access options.

Keywords Endometrial cancer · Laparoscopic-assisted vaginal hysterectomy · Laparoscopy · Laparoscopic pelvic and paraortic lymphadenectomy · Laparoscopic staging

Introduction

Adenocarcinoma of the uterine corpus is the most common malignancy of the female pelvis. It takes fourth place

amongst all cancers in women [1, 2]. In Germany and in the United States, estimated incidences of approximately 12,000 and 42,000, respectively, have been published [3, 4]. The mean age at diagnosis is 61–68 years [1, 3].

Treatment has changed somewhat over the last 30 years. Surgical treatment alone or combined with adjuvant radiation therapy has become state-of-the-art. Primary radiation therapy is only indicated if the patient is not operable due to comorbidity. Endocrine and antineoplastic chemotherapy is taken into account for palliative treatment or fertility sparing therapies or as an adjuvant therapy after surgery in high risk cases [2, 5, 6].

Median laparotomy with hysterectomy, salpingo-oophorectomy plus pelvic and paraortic lymphadenectomy (LAE) depending on stage and risk factors is the gold standard in the surgical treatment of endometrial carcinomas [1, 5–7]. Looking at these risk factors and the epidemiology of the typical (type I) carcinoma, morbidity is often increased by multiple factors like older age, obesity, hypertension, diabetes and others [1, 5, 8, 9]. Avoiding the laparotomy in early cases (FIGO stage I) is, therefore, an ideal method to improve morbidity in such operations. Although this seems to be accomplished by a mere vaginal approach [10–14], it cannot be recommended as an oncologically safe alternative except for medically compromised patients. Vaginal inspection of the abdominal cavity is insufficient. In a Gynecologic Oncology Group (GOG) study by Creasman et al. [15], there were 6% extrauterine metastases found in clinically FIGO stage I patients. Furthermore, pelvic and paraortic lymph nodes cannot, if indicated, be assessed nor removed. In addition, since morcellation of the uterus has to be avoided, the size of the organ and vaginal space are limiting factors.

Therefore, a combined approach in form of a laparoscopic-assisted vaginal procedure is today the only

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guideline-approved alternative to laparotomy in FIGO stage I endometrial carcinoma. Initially used to ensure a vaginal hysterectomy in patients with adhesions, severe endometriosis, nulliparity or very big uteri, laparoscopy today is in experienced hands a procedure for systematic pelvic and paraaortic LAE, making a complete surgical staging in these early cases possible [5–7, 16].

Laparoscopic approach to endometrial carcinoma in literature

A systematic online search of the literature (PubMed) shows a first case report of the laparoscopic-assisted vaginal hysterectomy (LAVH) with LAE in 1992 [17]. Since then technical feasibility, safety and effectiveness have been described in numerous publications (Tables 1, 2). Clearly, the surgically new technique here was not so much the LAVH but rather the laparoscopic LAE. Here authors

described a considerable learning curve [18, 19]. Nevertheless, the procedure was mostly regarded as an attractive alternative in the treatment of endometrial cancer [20–24].

Further studies were dedicated to comparing the open to the laparoscopic approach. These studies are shown for a better overview in Table 1. On the whole, reduced intraoperative blood loss, shorter hospitalization and convalescence and less postoperative morbidity were favorable for the LAVH $\pm$ LAE [25–41]. The disadvantage of longer operating times lead to further investigation as to the cost of laparoscopy versus laparotomy. While the overall reduced costs of LAVH were presented in one study [27], other authors have even found increased charges [32]—and still others have found no difference [27]. Remarkably, in a recent comparison between costs of laparotomy, laparoscopy and robotic laparoscopy, the standard laparoscopy was the most cost effective procedure [42].

Still, the main criterion for the treatment of malignant tumors is survival. Reviewing the literature since 1992, all

Table 1 Laparoscopic-assisted vaginal hysterectomy (LAVH) $\pm$ lymphadenectomy (LAE) versus laparotomy $\pm$ LAE in the treatment of early endometrial cancer

References	n (laparoscopy/laparotomy)	Results and author's conclusions
Spirtos et al. [27]	13/17	Significant cost savings, improved quality of life
Hidlebaugh and Orr [28]	29/64	Fewer complications, shortened hospital stay
Gemignani et al. [29]	69/251	Fewer complications, shortened hospital stay
Scibner et al. [30]	19/17	Less pain, improved quality of life, total costs statistically not different
Holub et al. [31]	65/65	LAVH in early endometrial cancer feasible, also in obese patients
Eltabbakh et al. [32]	86/57	Shorter hospitalization, earlier recovery, higher financial costs
Scribner et al. [33]	67/45	Increased OR time, shorter stay
Holub et al. [34]	96/24	Attractive alternative, shorter recovery time
Malur et al. [26]	52/46	Reduced blood loss, shorter hospital stay
Holub [25]	600	Review article, laparoscopic-assisted surgical staging as safe as open procedure
Obermair et al. [35]	226/284	Eleven conversions, similar clinical course, similar recurrence rates
Obermair et al. [36]	47/31	Morbidly obese patients (mean weight 119 kg), five conversions, significantly fewer wound infections in laparoscopy group
Tozzi et al. [37]	63/59	Fewer postoperative complications in LAVH group—especially in patients with comorbidity
Volpi et al. [38]	41/36	Longer duration of surgery, but shorter hospital stay
Kim et al. [39]	74/168	Higher number of lymph nodes, fewer postoperative complications and shorter hospital stay for LAVH
Zapico et al. [40]	38/37	More postoperative complications in laparotomy group, shorter hospital stay in LAVH group
Wong et al. [41]	20/36	Longer operating time, less blood loss and shorter hospital stay for LAVH
Zullo et al. [75]	42/42	Focus on quality of life: laparoscopic approach provides significant benefits compared with laparotomy
Tollund et al. [76]	28/58	Less complications and shorter hospital stay for laparoscopy
Kalogiannidis et al. [77]	69/100	Significant longer operating time, lower blood loss and shorter hospitalization in laparoscopy group
Santi et al. [78]	120/120	No difference in mean operating time, but less blood loss and shorter hospital stay in laparoscopy group

Table 2 Follow-up, recurrence and survival after LAVH $\pm$ LAE compared with laparotomy $\pm$ LAE for early endometrial cancer

References	n (laparoscopy/laparotomy)	Results and author's conclusions
Magrina et al. [79]	56	Three-year survival and recurrence rates similar to abdominal approach
Holub et al. [80]	221/45	No difference with regard to recurrence or survival between groups (median follow-up 33.6 months)
Eltabbakh [81]	100/86	Similar 2-year and 5-year estimated recurrence-free survival rates as well as overall survival rates
Malur et al. [26]	52/46	No difference in overall and recurrence-free survival between laparotomy and LAVH (follow-up 0–67 months)
Chu et al. [67]	3	Case reports on vaginal cuff recurrences after LAVH
Magrina and Weaver [82]	47/31	Five-year survival rate similar
Obermair et al. [35]	226/284	Patterns of recurrence similar in both groups (median follow-up 29.4 months)
Tozzi et al. [83]	63/59	Disease-free and overall survival similar in both groups (median follow-up 44 months)
Volpi et al. [38]	41/36	Retrospective study, no differences in recurrence and survival rates
Kim et al. [39]	74/168	Three-year recurrence-free survival rates were similar
Seracchioli et al. [62]	19/94	No significant difference for disease-free and overall survival
Zapico et al. [40]	38/37	No significant difference in disease recurrence between the two groups
Sobiczewski et al. [84]	45/136	No statistically significant differences in disease-free survival and recurrence rate between the groups
Kalogiannidis et al. [77]	69/100	Surgical technique did not influence recurrence rate, disease-free and overall survival
Zullo et al. [85]	40/38	Randomized controlled trial (follow-up 78 months): no difference in recurrence rate, disease-free and overall survival

the studies investigating this issue could show no difference between classic open procedure and laparoscopy in respect to disease-free and overall survival (Table 2).

Amongst these many publications, there were two quite recent meta-analyses of randomized controlled trials (RCT) by Lin et al. [43] (4 RCTs; 331 patients) and Palomba et al. [44]. The latter was updated only recently [45] after the 2009 publication of a new randomized investigation by Malzoni et al. [46]. Altogether the Italian meta-analysis is now based on an sample of 359 patients (5 RCTs) and confirmed oncological safety (no significant difference in lymph node yield, disease-free and overall survival) plus equivalence next to the above mentioned short-term positive effects (e.g., reduced blood loss, shorter hospitalization or fewer postoperative complications) [45].

Further studies in this respect are on the way, the largest one being the Gynecologic Oncology Group (GOG) Lap 2 study [47–49]: a multicenter, randomized trial enrolling 2,616 patients with endometrial cancer. This study was conducted from 1996 until 2005. As expected, laparoscopy resulted in fewer postoperative moderate or severe adverse events, a shorter hospital stay, and a longer operative time. The number of harvested lymph nodes was similar in both groups, but the para-aortic node yield was quite low (6 and 7, respectively). Survival figures have yet to be published and there was an obviously quite high conversion rate of 26%. Failure to

complete laparoscopy successfully seemed to be related to increasing age and body mass index. In their editorial to the recent publications, Vergote et al. [50] suggest laparoscopic treatment to be more often successful in centers of excellence in laparoscopy, since reports from single institutions show lower conversion rates [8, 36].

A second awaited study is the 2007 started Australian LACE-trial (Laparoscopic Approach to Cancer of the Endometrium) [51]. Expected study end is 2010. In contrast to the other studies, here the total laparoscopic hysterectomy (TLH) will be investigated. The same goes for another study in the Netherlands expected to publish results by the end of 2009 [52].

With growing laparoscopic experience and improved equipment more and more surgeons are preferring the TLH. Two studies—one of them a randomized controlled trial—directly compared LAVH with TLH. No difference in disease-free survival or overall survival was found. However, LAVH showed longer operating time and higher blood loss when compared to TLH [53]. Obese patients seemed to benefit more from TLH than from LAVH in terms of shorter operating time [54]. Publications comparing TLH to laparotomy in the treatment of endometrial cancer found basically the same advantages and disadvantages plus oncological safety like the ones previously shown for LAVH in comparison to laparotomy [46].

Surgical technique of laparoscopic staging and treatment of endometrial cancer

The procedure of LAVH combined with LAE was in older publications restricted to presumed FIGO stage I. Laparoscopic treatment of stage IIB is today also feasible since performing a radical hysterectomy is no longer restricted to open surgery [55–57]. Although the necessity of a radical hysterectomy in general is not profoundly based on randomized controlled investigations [58, 59], existing guidelines and textbooks recommend it, not excluding laparoscopic approaches [1, 5, 60].

At first, the feasibility of a vaginal hysterectomy should be checked via pelvic examination under anesthesia. During laparoscopy, both the parietal and the visceral peritoneal surfaces, the liver, the diaphragm, and the pelvic lymph node regions are thoroughly inspected, and the uterine size is assessed again. If there are no peritoneal manifestations of the disease, and if the indication for the LAE is already clear at this point, the surgeon may want to start with the systematic removal of the pelvic and paraaortic lymph nodes (see below). However, the first step should be the bipolar coagulation of the fallopian tubes in order to prevent potential retrograde dissemination of tumor cells. For the laparoscopic part of the hysterectomy, the round ligaments are coagulated and cut, and the retroperitoneal space opened. The ureter is identified and the infundibulopelvic ligaments coagulated and cut while the adnexa remain connected to the uterus. Some authors prefer the laparoscopic mobilization of the uterus down to level of the ascending branch of the uterine artery including the dissection of the vesicocervical and rectovaginal septum; others even like to coagulate or clip the uterine artery at its origin from the internal iliac artery; and still others would at the point mentioned above proceed with the vaginal part of the operation. It seems to be important to stress that the uterine fundus should not be grasped with tenacula while being removed vaginally in order to leave it intact [61]. An alternative to this procedure would be the above mentioned and increasingly used TLH [35, 36, 52–54, 62]. Here the closure of the vagina can be performed laparoscopically or vaginally.

The laparoscopic pelvic and paraaortic LAE has been well standardized by a number of groups, and the authors would like to refer to the scientific literature [16, 63]. According to the latest Guidelines for the Management of Endometrial Cancer by the Task Force “Uterus” of the Gynecologic Oncology Study Group (AGO) of the German Society of Obstetrics and Gynecology [5, 6] the indications for the systematic pelvic and paraaortic LAE are as follows. With the exception of tumor stages pT1a and pT1b, grading 1–2 where the LAE is considered optional, the LAE is to be performed at all other stages of endometrioid adenocarcinoma. For the serous and clear cell forms of endometrial cancer, the LAE plus omentectomy is indicated at all stages

as these histological forms are considered “high grade” by definition, having a more aggressive malignant potential.

If the indication for LAE is only clear after the definite histologic examination, i.e., if the tumor is being upstaged on definite histology, the LAE should be performed during a second session [24]. Likewise, if endometrial cancer is found incidentally after a hysterectomy for another reason, the secondary laparoscopic LAE is a good procedure.

Special concerns regarding the use of laparoscopy in endometrial cancer

There are two special concerns throughout the literature dealing with laparoscopy in cancer surgery: port-site and vaginal cuff recurrences.

Amongst the many publications concerning port-site recurrences in gynecologic malignancies, those reported for stage I endometrial cancer after laparoscopic treatment are rare [64, 65]. Until now, the pathophysiology of these metastases is not clear. Because of this low incidence in early stages, it seems reasonable to assume that laparoscopic management does not worsen the prognosis of the patient [35]. Nevertheless it will be of special interest if the increasing number of studies with longer follow-up data will show a real need for concern. Meanwhile, since tumor cell spillage via the fallopian tubes or by laceration of the uterus itself is accused of upstaging the cancer by positive peritoneal cytology, the uterus must not be harmed during the operation and the fallopian tubes should be coagulated at the beginning of hysterectomy as mentioned above. It should be kept in mind that the causality of positive peritoneal cytology with recurrence rates (especially in port-sites via the so-called “chimney effect”) is not evidence based [66].

Special attention should be given to the use of harmful intrauterine manipulators for the TLH [43]. Chu et al. [67] reported on three cases of vaginal cuff recurrence and suggested that these may have been caused by intrauterine manipulators. Interestingly here, manipulators were used in LAVH, were the authors would usually not use any. This would be more of concern for the TLH, where manipulators are necessary. Looking back at all the above mentioned studies investigating disease-free survival or recurrences between laparoscopic and open approach, the cuff recurrence does not seem to be a specific problem of the LAVH or TLH, but rather of the cancer itself.

New developments in the surgical treatment of endometrial cancer

In the last few years, the development of robotic surgery has been in focus of surgical research. Since there were already

few differences between laparotomy and laparoscopy in the treatment of endometrial cancer, the comparison of laparoscopy with robotic surgery does not yield tremendous further advantages nor disadvantages [68–70]. Again parameters like blood loss or hospitalization were lower. But most importantly, robotic surgeries biggest achievement could be, that it is easier to learn by more closely resembling conventional open surgery than laparoscopy [71].

The sentinel node concept has been investigated in all gynecologic malignancies since its successful application in the treatment of breast cancer. First feasibility studies for the use with endometrial cancer were published in 2002 [72, 73]. Until today, the mode of tracer application (uterine subserosal, cervical or endometrial via hysteroscopy) and the tracer itself (radiolabeled technetium or/and blue dye) is not clear between researchers and application must be restricted to ongoing studies [74]. These should result in evidence about sensitivity and false-negative rates.

Conclusion

Compared with the conventional laparotomy, reduced blood loss and hospital stay can be stated as the advantage of the laparoscopic-assisted approach. Particularly obese patients profit from the decreased postoperative morbidity. In terms of oncological safety, measured through recurrence rate or survival, published studies have proven equivalence between laparoscopy and laparotomy. For laparoscopic LAE, the considerable learning curve must be taken into account, but—once learned—the surgeon gains a tool which gives him with the same lymph node yield as laparotomy does.

Although over the last years some randomized controlled trials were published and LAVH $\pm$ LAE has in some institutions become “a second standard procedure” next to the gold standard laparotomy, the long-term results of ongoing big multicenter trials (e.g., GOG LAP2) are awaited and needed.

Contraindications should remain other than endometrioid histology, due to the lack of experience in the outcome and the increased likelihood of intraoperative upstaging because of abdominal spreading of the tumor. Clearly any uterus requiring morcellation, would not be adequately treated laparoscopically.

Further spreading of the technique is necessary to enable every gynecological oncologist to individualize treatment by offering all the available treatment options. Thus, short-term morbidity will be reduced and quality of life improved, without changing expected oncological outcomes.

Conflict of interest statement None.

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