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## Laparoscopic staging in advanced cervical cancer: the pros and cons of an oncological concept

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**Abstract** In this paper, the concept of laparoscopic pretreatment staging in women with advanced cervical cancer is surveyed. While a number of authors have demonstrated the potential advantages of surgical staging for optimum individual treatment planning, clear definition of the radiation field, and potential avoidance of radical hysterectomy, an additional operation including para-aortic lymphadenectomy with considerable learning curve must also be considered. In one study, the negative effect of surgical staging on the survival of patients with cervical cancer has been reported. A positive effect of surgical staging on the prognosis of patients with advanced cervical cancer has not yet been shown. In conclusion, this concept must be further evaluated in specialized centers until a clear recommendation can be made.

**Keywords** Cervical cancer · Surgical staging · Laparoscopy

### Introduction

Cancer of the uterine cervix is the third most common gynecologic malignancy, with an incidence of about 7000 new cases per year in Germany [1]. While regular gynecologic check-up including colposcopy and PAP smear, and perhaps detection of human papilloma virus, is highly recommended in order to reduce the number of patients presenting with advanced disease, reality shows that there is still a high percentage of patients presenting with advanced tumors (FIGO stages IB2 and higher). Although FIGO stages IB2 through IIB, in general, are operable, they require adjuvant treatment, and the

question as to the best treatment for these stages remains unanswered while the following concepts are currently being investigated (Table 1).

If tumor-positive para-aortic lymph nodes are present, most centers consider the disease as surgically incurable, and radiochemotherapy including a para-aortic field will be initiated [1]. Exact pretreatment knowledge as to the spread of the disease would be most helpful in these cases [1–3]. However, the clinical pretreatment staging on which the therapeutic decision is based on is limited. In this paper, the concept of laparoscopic pretreatment staging in women with advanced cancer of the cervix is described.

### Clinical versus surgical staging

Aside from rectovaginal pelvic examination, computed tomography (CT), magnetic resonance imaging (MRI), sonography, cystoscopy and rectoscopy are employed for clinical staging (FIGO). As primary radiotherapy, or radiochemotherapy is performed internationally in most centers for FIGO stage II, there will be no exact pTNM staging possibly resulting in either up- or down-staging of the disease. Both clinical pelvic exam and imaging techniques (CT, MRI) lack precision. This consideration is especially important for the precise pretherapeutic assessment of pelvic and para-aortic lymph node involvement.

The assessment of the parametrial tissue by pelvic examination is difficult shortly after conization, or if additional endometriosis of the rectovaginal (i.e. utero-sacral) ligaments is present. This can most likely be differentiated upon laparoscopic inspection. In addition, bowel and bladder infiltration is not necessarily visible on rectoscopy or cystoscopy, respectively, if the infiltration does not involve the mucosa (which is defined as FIGO stage IVA) [4]. The therapeutic consequences, however, would be the same if the tumor infiltration involves the muscular layer of the bowel or the bladder which may go unrecognized by intraluminal

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**Table 1** Current concepts for the treatment of operable, bulky cancer of the cervix FIGO IB2–IIB

Radical hysterectomy followed by adjuvant platin-based simultaneous radiochemotherapy
Primary, simultaneous platin-based radiochemotherapy
Neoadjuvant chemotherapy followed by radical hysterectomy
Neoadjuvant radiochemotherapy followed by radical hysterectomy

endoscopy whereas laparoscopic inspection, dissection and biopsy would certainly discover this type of infiltration.

Lymph node involvement is one of the most important prognostic factors in cervical cancer. CT and MRI prediction of pelvic and para-aortic lymph node involvement is limited in regard to both sensitivity and specificity which has been shown in several studies [5–8], Table 2. For example, in a recent investigation, 18% of patients without suspicion of para-aortic lymph node metastases on CT scan had para-aortic involvement discovered by surgical staging [9]. Therefore, para-aortic lymphadenectomy is recommended during staging laparoscopy.

In a study from the University of Jena, specificity and sensitivity of para-aortic lymph node dissection of potentially involved nodes were 92.3% compared with the histologic result [10]. Also, in inoperable cases and in cases that are usually not surgically treated (FIGO stages III) the para-aortic lymph node status is important as in cases with negative para-aortic nodes a para-aortic radiation field will be unnecessary sparing those patients significant gastrointestinal morbidity associated with radiation therapy. In such cases, the additional information provided by the staging laparoscopy including para-aortic lymph node dissection may result in a modification of the primary therapeutic decision [7, 10].

Although intraperitoneal dissemination is very rare in cervical cancer, there are cases with peritoneal carcinosis [11]. While a miliary peritoneal carcinosis can easily go unrecognized by both CT and MRI, the laparoscopic inspection plus biopsy are likely to lead to the diagnosis. As peritoneal dissemination indicates generalization of the disease, a para-aortic lymphadenectomy is, of course, not justified for those patients. The same is true for localized manifestations in the upper quadrants of

the abdomen. Benedetti-Panici et al. [11] have found peritoneal dissemination in 27% in their series of 56 patients with locally advanced cancer of the cervix.

## Review of the literature

Several groups have reported their experience with surgical staging in women with advanced cervical cancer. In summary, the authors stress the feasibility of laparoscopic para-aortic lymphadenectomy, the low morbidity of the procedure, and, more importantly, the additional valuable information as to the lymph node status resulting in potential modification of treatment planning. Most of the investigators also agree that surgical staging is superior to CT and MRI in regard to the pelvic and para-aortic lymph node status [8, 9, 12–17] (Table 3).

One study has presented the detrimental effects of surgical staging in locally advanced cervical cancer upon survival [18]. In this prospective trial, 61 patients with locally advanced cancer of the cervix were randomized to either undergo clinical or surgical staging prior to treatment. In the surgical staging group, patients were again randomized and allocated to either the extraperitoneal, or the laparoscopic approach. Surprisingly, an interim analysis showed that patients with surgical staging had a significantly worse progression-free interval prompting termination of recruitment. A later follow-up showed a difference in overall survival in favor of the clinically staged patients [18].

From our perspective, the surgical staging in advanced cervical cancer is reserved for high risk patients. Potential indications are as follows: bulky disease (FIGO stage I tumors > 5 cm), FIGO stages II through IV, further risk factors such as lymphovascular space involvement (L1, V1), rare histological types such as clear cell carcinoma, suspicious pelvic and para-aortic lymph nodes on imaging, poor differentiation (G3), and age under 35 years. These factors, however, are not generally accepted. The individual risk of a patient increases with the number of factors present. More importantly, a surgical staging only seems to make sense if a modification of the planned treatment is a potential

**Table 2** Imaging techniques compared to laparoscopy/histology to assess lymph node involvement in advanced cervical cancer

Author [Reference]	Number of patients	Findings/conclusions
Matsukuma et al. [5]	70	CT diagnosis was true-positive in 71.4% for para-aortic lymph node metastases and true-positive in 45.5% for pelvic lymph node metastases
Oellinger et al. [6]	32	MRI provided accuracy of 69% for the detection of infiltrated lymph nodes
Odunsi et al. [7]	51	Preoperative CT when compared with histologic findings showed sensitivity and positive predictive value of 39%, and specificity and negative predictive value of 88% for pelvic and para-aortic lymph node metastases
Hertel et al. [8]	109	CT shows negative predictive value for the evaluation of positive pelvic lymph nodes of 73%

**Table 3** Surgical staging in advanced cervical cancer: experience

Author [Reference]	Number of patients	Findings/conclusions
Childers et al. [12]	10	Complete surgical staging including para-aortic lymphadenectomy prior to radiation therapy is feasible
Recio et al. [13]	12	Staging laparoscopy including para-aortic lymph node dissection prior to radiation therapy is associated with minimal morbidity and adds valuable information regarding treatment planning
Goff et al. [14]	86	Staging was performed retroperitoneally in 61 patients, laparoscopically in 18 patients, and by laparotomy in 7. Surgical staging resulted in modification of the standard pelvic radiation field for 43% of the patients
Chu et al. [15]	67	Laparoscopic pelvic and para-aortic lymphadenectomy is an efficient and feasible pretreatment staging procedure
Vidaurreta et al. [16]	84	Out of 49 pelvic CT scans, 38 were reported to be normal but 18 of these 38 had positive nodes which were detected laparoscopically. In summary: feasible method
Querleu et al. [17]	53	Extraperitoneal endosurgical aortic and common iliac dissection: tool to identify lymph node positive patients requiring extended field radiation therapy
Hertel et al. [8]	109	Laparoscopic staging is accurate, associated with low morbidity and provides information for treatment adjustment
Vergote et al. [9]	42	Feasible method with low morbidity. 18% of patients without suspicion of para-aortic metastases on CT were found to have para-aortic metastases

option [19–21]. After all, para-aortic lymph node metastases are present in 2–9% of FIGO stage IB tumors, in 11% of FIGO stage IIA tumors and in 20–28% of stage IIB tumors [22, 23]. The likelihood increases as additional unfavorable prognostic factors are present. The rate of positive para-aortic lymph nodes goes up to even 30–40% in FIGO stages III and IV [22, 23]. These figures may illustrate the potential benefit of pretreatment para-aortic lymph node dissection.

### Surgical management

Before performing surgical staging in a patient with advanced cervical cancer, distant metastases (liver, lung) should be ruled out. In patients with a very high risk of distant metastases, a scalenus muscle biopsy may be considered.

Upon laparoscopy, the whole abdominal cavity will be thoroughly inspected. If intraperitoneal spread or local intraabdominal metastases are visible a biopsy is taken and the procedure stopped as the disease is already generalized (FIGO stage IVB). In the absence of intraperitoneal dissemination, the vesicouterine and rectovaginal septa are inspected and—if there is any suspicion of infiltration—dissected, and biopsied. The pelvic side walls are also inspected and suspicious pelvic lymph nodes removed. Finally, a para-aortic lymphadenectomy is performed as described in detail in the literature [12, 17, 24, 25].

### Discussion and conclusion

As with any new concept in medicine, the surgical staging in advanced cancer of the cervix is controversially discussed. The potential advantages for optimum, individualized clinical management (i.e. adjustment of

treatment according to disease extent) are presented in detail in this paper. The only valid criterion for the assessment of oncologic concepts, however, is their potential impact upon survival. Care should be taken if other groups report observations similar to those of Lai et al. [18]. The reasons for their results can only be speculated on. First, the total number of patients per group is rather small (29 versus 32), with the latter group that underwent surgical staging again being randomly allocated to either extraperitoneal or laparoscopic access resulting in subgroups of 17 and 15 patients, respectively. Second, there were more adenocarcinomas in the group with surgical staging which may in part explain the differences regarding survival. Nevertheless, this study must be borne in mind when following the concept of surgical staging in cervical cancer. So far, a positive effect of surgical staging on the prognosis of patients with advanced cervical cancer has not been shown [26]. In short, it remains to be seen if the clinical outcome will be improved by this concept.

Most clinicians employing surgical staging in advanced cervical cancer favor the transperitoneal laparoscopy as this technique enables the inspection of the whole abdominal cavity. As far as lymph node dissection is concerned, the retroperitoneal laparoscopic approach [17] or the open retroperitoneal approach provide equal results [7, 27]. In a Gynecologic Oncology Group study, a lower rate of intestinal complications of radiotherapy has been reported for patients who underwent pre-radiation extraperitoneal lymphadenectomy for staging compared to patients staged transperitoneally [28]. Finally, some authors employ an explorative laparoscopy before planned exenterative surgery for relapsed, or primary FIGO stage IVA cervical cancer in order to evaluate patients who are potential candidates for this radical operation [29].

In summary, if the pros and cons are weighed up, there are optimum individual treatment planning, clear

definition of the radiation field, and potential avoidance of radical hysterectomy on the one hand, and additional, potentially risky operations (that is, para-aortic lymphadenectomy) with a considerable learning curve on the other. As a result, this concept should further be evaluated in specialized centers until a clear recommendation can be made.

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## References

1. Beckmann MW (ed) (2004) Interdisciplinary guideline for diagnostics and treatment of cervical cancer (in German). W. Zuckschwerdt, Munich
2. Waggoner SE (2003) Cervical cancer. *Lancet* 361:2217–2225
3. Schneider A, Köhler C, Klemm P, Hertel H, Dürst M, Kaufmann AM (2004) New aspects in the treatment of cervical cancer (in German). *Gynaekologe* 37:886–892
4. Wittekind C, Meyer HJ, Bootz F (2002) Tumor classification according to TNM and FIGO. TNM classification of malignant tumors (in German). Springer, Berlin Heidelberg New York
5. Matsukuma K, Tsukamoto N, Matsuyama T, Ono M, Nakano H (1989) Preoperative CT study of lymph nodes in cervical cancer—its correlation with histological findings. *Gynecol Oncol* 33:168–171
6. Oellinger JJ, Blohmer JU, Michniewicz K, Siewert C, Wust P, Gutberlet M, Lichtenegger W, Felix R (2000) Präoperatives Staging des Zervixkarzinoms: Vergleich von Magnetresonanztomographie (MRT) und Computertomographie (CT) mit histologischen Ergebnissen. *Zentralbl Gynäkol* 122:82–91
7. Odunsi KO, Lele S, Ghamande S, Seago P, Driscoll DL (2001) The impact of pre-therapy extraperitoneal surgical staging on the evaluation and treatment of patients with locally advanced cervical cancer. *Eur J Gynaecol Oncol* 22:325–330
8. Hertel H, Köhler C, Elhawary T, Michels W, Possover M, Schneider A (2002) Laparoscopic staging compared with imaging techniques in the staging of advanced cervical cancer. *Gynecol Oncol* 87:46–71
9. Vergote I, Amant F, Berteloot P, van Gramberen M (2002) Laparoscopic lower para-aortic lymphadenectomy in stage IB2, II, and III cervical cancer. *Int J Gynecol Cancer* 12:22–26
10. Possover M, Krause N, Kühne-Heid R, Schneider A (1998) Value of laparoscopic evaluation of para-aortic and pelvic lymph nodes for treatment of cervical cancer. *Am J Obstet Gynecol* 178:806–810
11. Benedetti-Panici P, Maneschi F, Cutillo G, Congiu M, Franchi M, Amoroso M, Greggi S, Mancuso S (1999) Laparoscopic abdominal staging in locally advanced cervical cancer. *Int J Gynecol Cancer* 9:194–197
12. Childers JM, Hatch K, Surwit EA (1992) The role of laparoscopic lymphadenectomy in the management of cervical carcinoma. *Gynecol Oncol* 47:38–43
13. Recio FO, Piver MS, Hempling RE (1996) Pretreatment transperitoneal laparoscopic staging pelvic and para-aortic lymphadenectomy in large (> or = 5 cm) stage IB2 cervical carcinoma: report of a pilot study. *Gynecol Oncol* 63:333–336
14. Goff BA, Muntz HG, Paley PJ, Tamimi HK, Koh WJ, Greer BE (1999) Impact of surgical staging in women with locally advanced cervical cancer. *Gynecol Oncol* 74:436–424
15. Chu KK, Chang SD, Chen FP, Soong YK (1997) Laparoscopic surgical staging in cervical cancer—preliminary experience among Chinese. *Gynecol Oncol* 64:49–53
16. Vidaurreta J, Bermudez A, di Paola G, Sardi J (1999) Laparoscopic staging in locally advanced cervical carcinoma: a new possible philosophy? *Gynecol Oncol* 75:366–371
17. Querleu D, Dargent D, Ansquer Y, Leblanc E, Narducci F (2000) Extraperitoneal endosurgical aortic and common iliac dissection in the staging of bulky or advanced cervical carcinomas. *Cancer* 88:1883–1891
18. Lai CH, Huang KG, Hong JH, Lee CL, Chou HH, Chang TC, Hsueh S, Huang HJ, Ng KK, Tsai CS (2003) Randomized trial of surgical staging (extraperitoneal or laparoscopic) versus clinical staging in locally advanced cervical cancer. *Gynecol Oncol* 89:160–167
19. Eifel PJ, Morris M (1995) Irradiation alone or combined with surgery in carcinoma of the cervix: when will we know the answer? *Int J Radiat Oncol Biol Phys* 31:1007–1008
20. Eifel PJ, Winter K, Morris M, Levenback C, Grisby PW, Cooper J, Rotman M, Gershenson D, Mutch DG (2004) Pelvic irradiation with concurrent chemotherapy versus pelvic and para-aortic irradiation for high-risk cervical cancer: an update of radiation therapy oncology group trial (RTOG). *J Clin Oncol* 22:872–880
21. Hänsgen G, Souchon R (2004) To choose the right option: operation, radio-, chemo-, or combination therapy for cervical cancer (in German). *Klinikarzt* 33:43–50
22. Levenback C, Morris M (2000) Cervical cancer. In: Barakat RR, Bevers MW, Gershenson DM, Hoskins WJ (ed) *Handbook of gynecologic oncology*. Martin Dunitz, London, pp 225–241
23. Schmidt-Matthiesen H, Bastert G, Wallwiener D (2000) Gynecologic oncology. Diagnostics, treatment and follow-up of malignant genital tumors and breast cancer, 6th edn. Schattauer, Stuttgart, pp 53–65
24. Possover M, Krause N, Plaul K, Kühne-Heid R, Schneider A (1998) Laparoscopic para-aortic and pelvic lymphadenectomy: experience with 150 patients and review of the literature. *Gynecol Oncol* 71:19–28
25. Schneider A, Possover M, Kühne-Heid R, Krause N (1997) Laparoscopic para-aortic and pelvic lymph node dissection (in German). *Gynaekologe* 30:483–499
26. Höckel M (2003) Surgical treatment of locally advanced and recurrent cervical carcinoma: overview on current standard and new developments. *Onkologie* 26:452–455
27. Massi G, Susini T, Amunni G (2000) Extraperitoneal pelvic lymphadenectomy to compliment vaginal operations for cervical and endometrial cancer. *Int J Gynecol Oncol* 69:27–35
28. Weiser EB, Bundy BN, Hoskins WJ, Heller PB, Whittington RR, DiSaia PJ, Curry SL, Schlaerth J, Thigpen JT (1989) Extraperitoneal versus transperitoneal selective para-aortic lymphadenectomy in the pretreatment surgical staging of advanced cervical carcinoma (a Gynecologic Oncology Group study). *Gynecol Oncol* 33:283–289
29. Köhler C, Tozzi R, Possover M, Schneider A (2002) Explorative laparoscopy prior to exenterative surgery. *Gynecol Oncol* 86:311–315