The Perioperative Morbidity of Laparoscopic Pelvic Lymph Node Staging in Patients with Advanced Cervical Cancer

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Abstract. *Background: Laparoscopic pelvic lymph node staging is widely used in patients with cervical cancer prior to the initiation of primary chemoradiation therapy. Data on the morbidity of this procedure are sparse. Patients and Methods: Between 1995 and 2007, 71 patients with locally advanced cervical cancer (FIGO stage IB2-IIIB) underwent laparoscopic pelvic lymph node staging prior to primary chemoradiation therapy. Surgical outcome and perioperative morbidity were evaluated. Results: The median operation time, number of resected lymph nodes and time between surgery and the initiation of chemoradiation therapy was 100 minutes, 15 lymph nodes and 18 days, respectively. Intraoperatively, one laceration of the obturatoric artery and one bladder injury occurred. One procedure was converted to a laparotomy. Three short-term postoperative complications including one hematoma in the port side area, one umbilical suture insufficiency requiring a hernia reposition, and one postoperative bleeding that required re-hospitalization were noted. Two patients with intra-abdominal abscesses required repeat laparoscopy. Of note, three patients developed port site metastases during follow-up. Conclusion: Although patients experienced perioperative morbidity, the present study provides further evidence that, overall, laparoscopic pelvic lymph node staging is a relatively safe procedure for patients with cervical cancer.*

According to the guidelines of the Fédération Internationale de Gynécologie et d'Obstétrique (FIGO) cervical cancer staging is performed clinically. However, pelvic lymph node status is the most important prognostic parameter in all stages of the disease (1).

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A number of different diagnostic approaches have been used in order to identify possible lymph node metastases. Imaging modalities such as computed tomography (CT) scans and magnetic resonance imaging (MRI) as well as fluorodeoxyglucose-positron emission tomography (FDG-PET) have been shown to provide valuable preoperative information of macroscopic lymph node involvement, but fall short of detecting microinvasive lymph nodes (2-6). Therefore, these techniques have not been implemented into clinical practice yet.

Surgical assessment of the pelvic lymph node status by laparoscopy or laparotomy has been recently introduced into standard clinical routine. This procedure allows tailored treatment planning of the primary radiation field (pelvic *vs.* pelvic plus paraaortal) with a subsequent reduced morbidity or increased efficacy as discussed in recent studies (7-9). Furthermore, a possible therapeutical benefit has been shown for resecting bulky lymph nodes in patients with advanced disease (7, 10-12).

The aim of the present study was to contribute further data on the morbidity and outcome of surgically staged patients with advanced cervical cancer.

Patients and Methods

Between 1995 and 2007, 71 patients with advanced cervical cancer (FIGO stage IB2-IIIB) underwent pretherapeutic transperitoneal laparoscopic pelvic lymph node staging prior to the initiation of chemoradiation therapy at the Department of Obstetrics and Gynecology at the Medical University of Vienna, Austria.

Prior to surgery, all patients underwent bimanual examination under general anesthesia. A perioperative single shot antibiotic prophylaxis was applied. The staging procedure began with the insertion of transumbilical port and a diagnostic laparoscopy in order to inspect the whole peritoneal cavity following the insertion of three additional ports. After macroscopic intraperitoneal disease was excluded, a transperitoneal pelvic lymphadenectomy was performed including the bilateral resection of external iliacal, obturator and common iliacal lymph nodes.

Subsequent chemoradiation therapy was tailored according to the results of the staging procedure. Patients without metastatic pelvic lymph nodes were managed with external beam radiotherapy to the

pelvis at a dose of 45 Gy, followed by an intracavitary brachytherapy at a dose of 20 Gy. An extended-field external beam radiotherapy of the paraaortic region was chosen for patients with metastatic pelvic lymph nodes. Five cycles of concomitant cisplatinum chemotherapy (40 mg/m^2 body surface) were given.

Patients were scheduled for the first follow-up visit three months after completion of therapy. For the subsequent three years, patients were followed up every three months, in the 4th and 5th year biannually, and yearly from the 6th to the 10th year after primary therapy at our Outpatient Department. If any clinically suspicious and/or tumor marker elevation was detected, CT was performed. Following standard clinical guidelines, recurrent disease was either diagnosed clinically, with a biopsy, or suspected radiologically. Documentation of death and causes of death was performed using autopsy test results.

Values were given as means (standard deviation [SD]) or medians (range) where appropriate. Groups were compared using t-test, Mann-Whitney *U*-test, or chi-square test, odds ratios (OR) with 95% confidence interval (CI) were reported accordingly. Survival probabilities were calculated by the product limit method of Kaplan and Meier. The results were analyzed for the endpoint of disease-free and overall survival. Survival times of patients disease-free or still alive were censored with the last follow-up date. Univariate and multivariate Cox regression models for disease-free and overall survival were performed, comprising tumor stage, lymph node involvement (negative *vs.* positive), histological grade (G1 *vs.* G2 *vs.* G3), patients' age, and histopathological type (squamous cell carcinoma *vs.* adenocarcinoma). *P*-values of <0.05 were considered statistically significant. The statistical software SPSS 11.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

Results

A total of 71 transperitoneal laparoscopic pelvic lymph node staging procedures were evaluated. The median operation time was 100 (35-230) minutes. The median number of resected lymph nodes was 15 (range 1-51). The median time between surgery and the initiation of chemoradiation therapy was 18 (range 2-67) days.

Two patients (2.8%) experienced intraoperative complications including one laceration of the left obturatoric artery that was managed laparoscopically using surgical clips and one intraoperative bladder injury that was sutured laparoscopically. One procedure (1.4%) had to be converted to a laparotomy due to the presence of bulky lymph nodes, adhesive to the iliacal vessels.

As a standard operating procedure at our Department, patients remained hospitalized for at least 4 days. Therefore, the median length of postoperative hospital stay was long, *i.e.* 7 (range 2-17) days. Two patients (2.8%) received two erythrocyte concentrates postoperatively. One patient (1.4%) reported two days of postoperative fever >38˚C. Further complications included one hematoma of the port site area, one umbilical suture insufficiency requiring a hernia reposition and one postoperative bleeding that required re-hospitalization.

Four (5.6%) and two (2.8%) patients developed postoperative lymphcysts and abscesses, respectively. While all patients with asymptomatic lymphcysts were managed conservatively, both patients with intra-abdominal abscesses required repeat laparoscopy. Of note, three patients (4.2%) developed port site metastases.

A Kaplan-Meier curve regarding the association between pelvic lymph node involvement and overall survival is shown in Figure 1. The risk of intraoperative (*i.e.* bladder injury, vascular lesion, conversion to laparotomy) and postoperative complications (*i.e.* postoperative bleeding, lymphcysts, abscesses, hernia) did not correlate with pelvic lymph node status ($p=1.0$ and $p=0.6$, respectively).

Discussion

The present study provides further data on the clinical value and the risks associated with transperitoneal laparoscopic pelvic lymph node staging procedures prior to chemo-radiation therapy. It has been hypothesized that information regarding lymph node status allows for tailoring the extent of the radiation field leading to a better treatment response and a reduced morbidity (8, 9). Other studies, however, showed possible disadvantages of this treatment approach, including increased peri- and postoperative morbidity, as well as a diminished prognosis due to port site metastases (13, 14).

Although practised in many gynecological oncology centers, pelvic lymph node staging has not been integrated into standard clinical routine. The results of the present study confirm those of previously published studies that pretreatment laparoscopic lymph node staging is a safe and feasible procedure for patients with cervical cancer (7-10). In our series, only two intraoperative complications, namely one lesion of the left obturatoric artery managed laparoscopically using surgical clips and one intraoperative injury of the bladder sutured laparoscopically, were seen. In both patients, the operation was finished laparoscopically. More bothersome are the conversion to laparotomy, the occurrence of two abscesses with the subsequent need for surgical intervention, as well as the three cases of port site metastasis diagnosed during follow-up.

The present study does not allow a definite recommendation for or against pelvic lymph node staging in patients with advanced cervical cancer. Our data show a reasonably low perioperative morbidity which was not associated with the presence/absence of metastatic lymph nodes. Our results show that an upstaging of affected patients was necessary in 39.4% of cases, being comparable to a different study by LeBlanc *et al.* (8). A survival advantage for patients undergoing pelvic lymph node staging as a diagnostic or therapeutic procedure, *i.e.* resection of bulky lymph nodes, has not been shown to date (8, 13). A common

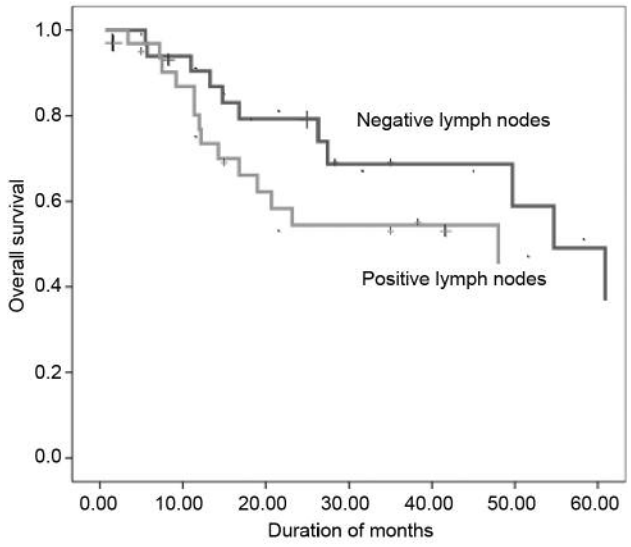

Figure 1. *Kaplan-Meier analysis of overall survival in patients with cervical cancer broken down by pelvic lymph node status.*

refutation against surgical lymph node staging is the topic of therapy delay. Our data showed a median time of 18 days between surgery and the initiation of chemoradiation, which can be regarded as negligible bearing in mind the pathogenesis of cervical cancer.

Some patients experienced significant perioperative morbidity. Overall, however, the present study provides further evidence that laparoscopic pelvic lymph node staging is a relatively safe procedure. Randomized trials should be performed in order to evaluate the therapeutic value and the impact on prognosis for these patients.

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