



Para-aortic lymph node metastases in locally advanced cervical cancer: Comparison between surgical staging and imaging



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HIGHLIGHTS

- Monocentric retrospective study of 336 patients with cervical cancer FIGO stage IB2-IVA
- 204 patients with normal or not overtly malignant para-aortic lymph nodes on imaging underwent surgical para-aortic lymph node staging
- Despite negative imaging para-aortic lymph node metastases were present in 8% of the patients with surgical para-aortic staging.

ARTICLE INFO

Article history:

Received 12 February 2015

Accepted 16 May 2015

Available online 23 May 2015

Keywords:

Cervical cancer

Staging

Para-aortic lymphadenectomy

PET/CT

ABSTRACT

Objective. Compare surgical staging with imaging (PET-CT, PET or CT) of the para-aortic lymph nodes (PAOLN) in locally advanced cervical cancer (LACC).

Methods. Monocentric retrospective study of 336 patients with cervical cancer FIGO stage IB2-IVA. All patients underwent staging of the PAOLN using imaging by PET-CT, PET or CT. Two hundred and four patients with normal or not overtly malignant PAOLN on imaging underwent surgical PAOLN staging up to the inferior mesenteric artery (189 endoscopy and 15 laparotomy).

Results. The patients were divided into 4 groups: 16 with positive surgical staging and negative PAOLN imaging (sPAOLN+), 172 negative surgical staging (sPAOLN−), 20 positive imaging without surgical staging (iPAOLN+) and 128 negative imaging without surgical staging (iPAOLN−). Median operative time of staging was 70 (40–160) min and median number of removed PAOLN was 5 (0–24). Operative complications were 10 peroperative bleedings, 2 ureteral traumas, 1 carbon dioxide retention and 1 retroperitoneal abscess. The median follow-up was 31 (1–218) months. Overall survival at 2 years was for sPAOLN+, sPAOLN−, iPAOLN+, and iPAOLN− 40%, 83%, 58%, and 69%, respectively ($p < 0.001$ for sPAOLN+ and iPAOLN+ versus sPAOLN− and iPAOLN−). The most frequent site of recurrence was distant LN metastases (outside the pelvic and PAO area) (36%) for sPAOLN+. For sPAOLN−, iPAOLN+, and iPAOLN− the most frequent site of recurrence was the cervix (27%, 66% and 26%, respectively).

Conclusion. Despite negative imaging, PAOLN metastases were present in 8% at surgical staging. Overall survival is significantly influenced by the presence of PAOLN metastases.

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1. Introduction

The presence of PAOLN metastases at the time of the diagnosis in locally advanced cervical cancer (LACC), FIGO IB2-IVA, is an important prognostic factor and a decisive factor in choosing the most appropriate therapy [1–5]. Detection of PAOLN metastases can be performed by

imaging and/or surgical staging of the para-aortic region. Recent studies have shown that PET-CT (positron emission tomography-computed tomography) has the highest sensitivity among currently used imaging techniques for the detection of lymph node metastases. The specificity is equal for PET-CT, CT and MRI (magnetic resonance imaging) [6–10]. With an incidence of PAOLN metastases in 10%–25% of FIGO stage IB2-IVA cervical cancer, surgical staging with para-aortic lymphadenectomy has shown to be a good method of diagnosing PAOLN metastases [11].

In this retrospective study we evaluated the results of staging of the para-aortic region with imaging (PET-CT, CT or PET) and surgical staging up to the inferior mesenteric artery. We only performed a lower

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para-aortic sampling because of the rare incidence of isolated supramesenteric lymph node metastases [12,13]. We investigated the value of endoscopic lower para-aortic lymphadenectomy, in combination with imaging through PET-CT, CT or PET as staging procedures in cervical cancer.

2. Methods

This is a retrospective study performed at the University Hospitals of Leuven with patients diagnosed with cervical cancer in the period between December 1994 and August 2013. In this study we included patients of previous reports [1,2]. Inclusion criteria for this study were a new diagnosis of cervical cancer FIGO (International Federation of Gynaecology and Obstetrics) stage IB2–IVA. In our earlier papers the different surgical techniques used to perform para-aortic lymphadenectomy were reported in a smaller number of patients. In this study we evaluated all consecutive patients with cervical cancer stage IB2–IVA treated in our institution over a longer time period, including those without surgical staging. The earlier papers included a maximum of 90 patients while we now report on 336 patients.

All patients had imaging (PET-CT, CT or PET) of PAOLN at the time of diagnosis. Because this analysis spans over a long period there are also patients included from the period before we performed a PET-CT routinely. Patients were excluded if there was no follow-up (19 patients), if simultaneously another malignancy (13 patients) was diagnosed. Approval of the ethical committee of the University Hospital Leuven was obtained.

Lower para-aortic lymphadenectomy was performed when imaging was normal or suspicious (but not reported to be metastatic) for PAOLN metastases. We performed a para-aortic lymphadenectomy independent of the result of the pelvic lymph nodes on imaging. We did not perform a para-aortic lymph node sampling or biopsy if imaging was reported to be positive for PAOLN metastases or if there were contraindications for this surgery as shown in Table 1. The group of patients with comorbidity as shown in Table 1 was a heterogeneous group with respiratory, cardiac, renal or cognitive impairment or poor general condition. The surgical staging was performed at the time of pelvic examination with cystoscopy under general anesthesia. In 189 patients the procedure was performed endoscopically. The endoscopic procedures used were as described in earlier reports [2,14,15]. In 15 selected cases the para-aortic lymphadenectomy was done at the time of a laparotomy for another reason (radical hysterectomy or exploratory laparotomy). During surgery the lymph nodes were sent for pathological examination and the operation was abandoned if the frozen section showed a para-aortic metastases. The pelvic nodes (including the common iliac nodes) were not sampled at the time of endoscopic staging.

Table 1
Exclusion from surgical staging (n = 132).

Imaging in another hospital	17 (13%)
Comorbidity	46 (34%)
Extensive invasion ^a	8 (6%)
Clinical stage < Ib2 ^b	28 (21%)
Positive PAOLN imaging	20 (15%)
Palliative setting	2 (2%)
Suspected endometrial cancer ^c	7 (5%)
Anticoagulation	1 (1%)
Severe cervical bleeding	2 (2%)
No patient consent	1 (1%)

PAOLN: para-aortic lymph nodes.

^a Of the surrounding organs, operation technically not possible.

^b Pre-operative staging < Ib2, upstaged during examination under anesthesia.

^c Pre-operative suspected endometrial cancer, post-operative diagnosis of cervical cancer.

The patients were divided into 4 groups: positive surgical staging with negative PAOLN imaging (sPAOLN +), negative surgical staging (sPAOLN –), positive imaging without surgical staging (iPAOLN +) and negative imaging without surgical staging (iPAOLN –).

2.1. Statistics

For the descriptive data the differences between group proportions were based on the Fisher exact test. Overall survival (OS) was defined as time from diagnosis to death from any cause. Progression-free survival (PFS) was defined as time from diagnosis to recurrence or disease progression or death. Survival curves were based on Kaplan–Meier estimates and Log rank test was used for the comparison of survival curves of different groups. All statistical tests were two-sided and a 5% significance level was assumed for all tests. All analyses have been performed using SAS software, version 9.3 of the SAS System for Windows (SAS Institute Inc., Cary, NC, USA).

3. Results

The patient characteristics of all included patients are shown in Table 2. Overall 34% of the patients had PET-CT, 20% PET (and a separate CT) and 46% CT (without PET). Of the 336 included patients 306 had a negative, 20 a positive and 10 a suspicious (i.e. when the radiologist or nuclear medicine physician reported that the lymph node was suspicious but not overtly metastatic) result on imaging of the PAOLN. Of 306 patients with negative PAOLN on imaging, 165 had no PAOLN metastases at surgical staging, 13 had metastatic PAOLN at surgical staging, 16 had no PAOLN removed, and 112 did not undergo surgical staging (the contra-indications for surgical staging are presented in Table 1). The last 2 groups are the 128 patients who are in iPAOLN –. In the group of 10 patients with suspicious but not overtly malignant PAOLN on imaging (4 on PET-CT, 5 on CT and 1 on PET), there were 3 with and 7 without metastatic PAOLN at surgical staging and they are categorized in sPAOLN + and sPAOLN – respectively. The 20 patients with metastases without any doubt on imaging (14/115 (12%) on PET-CT, 4/154 (3%) on CT and 2/67 (3%) on PET) did not undergo surgical staging.

In total 16 out of 204 (8%) patients without obvious metastases at imaging had PAOLN metastases at surgical staging. More specifically,

Table 2
Patient characteristics (n = 336).

<i>Age at diagnosis</i>	
Median	52.0
Range	22.0; 91.0
<i>FIGO stage</i>	
I B2	46 (14%)
II A	71 (21%)
II B	139 (41%)
III A	8 (2%)
III B	54 (16%)
IV A	17 (5%)
Not recorded	1 (0.2%)
<i>Differentiation</i>	
Well	30 (9%)
Moderately	148 (44%)
Poorly	111 (33%)
Unknown	47 (14%)
<i>Tumor type</i>	
Squamous-cell carcinoma	280 (83%)
Adenocarcinoma	26 (8%)
Adenosquamous carcinoma	21 (6%)
Clear cell carcinoma	4 (1%)
Small cell carcinoma	4 (1%)
Mesonephric carcinoma	1 (0.3%)

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