

Extracapsular extension of pelvic lymph node metastases is of prognostic value in carcinoma of the cervix uteri

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Abstract

Objectives. Pelvic lymph node involvement is a well-recognized prognostic factor in cervical carcinoma (CX). Limited knowledge exists about extranodal extension of the tumor outside the lymph node capsule, i.e. extracapsular spread (ECS).

Methods. Two hundred fifty-six cases of surgically treated CX (FIGO stage IB1 to IIB) with pelvic lymph node involvement were evaluated regarding the occurrence of extranodal spread of the metastatic deposits outside the lymph node capsule (ECS), determined on standardized handled lymphadenectomy specimens, regarding their impact of recurrent disease and overall survival during a median follow-up time of 62 months (95% CI 51–73 months).

Results. ECS was seen in 30.9% (79/256) of the cases. The occurrence of ECS showed a significant correlation to advanced stage disease ($p=0.02$), the number of involved nodes ($p<0.001$) and the size of metastatic deposits ($p<0.01$). The 5-year recurrence-free survival rate in patients with ECS was significant lower compared to patients without ECS (59.7% [95% CI: 46.3%–73.2%] versus 67.2% [95% CI: 58.9%–75.5%]; ($p=0.04$).

The 5-year overall survival rate was significant lower in patients with ECS (33.5% [95% CI: 20.6%–46.3%] vs. 60.5% [95% CI: 52.3%–68.6%]; $p<0.001$). In multivariate analysis, tumor stage, number of involved pelvic nodes, tumor differentiation and ECS were independent prognostic factors.

Conclusions. The results indicate that extracapsular spread (ECS) of pelvic lymph node metastases is of prognostic impact in cervical carcinomas. A revised FIGO/TNM classification system for pelvic lymph node disease is recommended: ECS 0=lymph node involvement without extranodal spread of the metastatic deposits and ECS 1=lymph node involvement with extranodal spread of the metastatic deposits.

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Introduction

Studies overwhelming indicate that the presence of lymph node metastases is an independent prognostic factor for overall and disease-specific survival, local recurrence and disease-free interval in carcinoma of the cervix uteri (CX; [1]). Other parameters related to lymph node status are also mentioned in the literature as prognostic factors. These parameters include the number of metastatic involved nodes, the size of the metastatic deposits and the localization of the metastatic nodes in the pelvis [2–4].

Previous studies of non-gynecological carcinomas as well as in those patients affected by breast or vulvar cancer have been shown that extranodal extension of the tumor outside the lymph node capsule, i.e. extracapsular spread (ECS), is another significant predictor of adverse outcome in node-positive patients [5–9]. But, there are only limited number of studies dealing with ECS in patients with CX, covering a small number of patients with inconsistent results [4,10–12].

The aim of the present study was to determine the prognostic impact of ECS in patients with surgically treated cervical carcinoma.

Materials and methods

Data from patients with CX and histologically confirmed pelvic lymph node involvement, staged FIGO IB to IIB were obtained from the files of our so-called

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Table 1
Patients characteristics

Median age	42 years (range 23–74 years)
Stage distribution	
pT1b	101 (39.5%)
pT2	142 (55.5%)
Unknown	13 (5.1%)
Tumor type	
Squamous cell carcinoma	243 (94.9%)
Adenocarcinoma	13 (5.1%)
Lymphovascular space involvement	
No	47 (18.4%)
Yes	209 (81.6%)
Tumor grade	
G1	100 (39.1%)
G2	88 (34.4%)
G3	68 (26.5%)
Laterality of pelvic lymph node involvement	
Unilateral	151 (59.0%)
Bilateral	104 (40.6%)
Unknown	1 (0.4%)
Extracapsular spread in nodal-positive cases	
No	177 (69.1%)
Yes	79 (30.9%)
Number of involved pelvic nodes	
<3	193 (75.4%)
>3	63 (24.6%)
Size of metastatic deposits in pelvic lymph nodes	
<5 mm	115 (44.9%)
>5 mm	140 (54.7%)
Unknown	1 (0.4%)
Recurrent disease	
No	175 (68.4%)
Yes	72 (28.1%)
Unknown	9 (3.5%)

Wertheim-Archive [13]. Patients who received neoadjuvant therapy, those with incomplete local tumor resection (R1- or R2-resection) and tumors of other histologic type as squamous cell and adenocarcinomas of the cervix uteri were excluded from the study. All women were treated with radical abdominal hysterectomy Piver type III [14] with systematic pelvic lymphadenectomy, but without para-aortic lymph node dissection. All patients with parametrial involvement and/or pelvic lymph node disease received adjuvant combined radiation therapy.

The pathological examination of the radical hysterectomy specimen was made in a standardized manner [15,16].

The pelvic lymph nodes were processed completely up to the size of 0.5 cm. Larger nodes were bivalved longitudinally and processed completely as well. From all blocks containing lymph nodes, three step sections were performed for routine histologic workup. The occurrence of any extranodal extension of the metastatic deposits outside the lymph node capsule, regardless of its extension, was recognized as extracapsular spread (ECS). The size of the extension of ECS into the perinodal fatty tissue was not determined.

All tumors were staged and classified according to the most recent WHO and TNM classifications [17,18].

Follow-up data regarding recurrent disease and death were obtained from the clinical files. There was a written informed consent was obtained from the patient for the use of the data.

Overall survival and recurrence-free survival were analysed using Kaplan–Meier curves and log-rank test. Five years overall and recurrence-free survival rates with 95% confidence intervals (CI) are given. Categorical data were analyzed by χ^2 -test. Mann–Whitney *U* test were used for comparisons of continuous data. *p*-values less than 0.05 were considered as statistically significant. To assess the independent impact of extracapsular spread on overall survival a cox regression model was fitted. Lymphovascular space involvement, tumor grade, laterality of pelvic lymph node involvement, size of metastatic deposits in the pelvic lymph nodes, number of involved nodes and tumor stage were included in the model to adjust for. Relative risks (RR) with 95% confidence intervals (95% CI) are given. All statistical analyses were performed using the software package SPSS for Windows®, release 11.5.1 (SPSS GmbH Munich, Germany).

Results

Two hundred fifty-six patients were obtained from our files fulfilling the above mentioned criteria. Their characteristics are given in Table 1. The median follow-up time was 62 months (95% confidence interval 51 to 73 months).

Seventy-nine of the patients (30.9%) with pelvic lymph node involvement showed extracapsular extension of the metastatic deposits (ECS; Fig. 1).

Stage pT2 tumors showed a significant increase of ECS when compared with tumors confined to the cervix uteri (35.2% in stage pT2 versus 21.8% in pT1b; $p=0.024$). There was a significant association between the size of pelvic lymph node metastases and the occurrence of ECS (Fig. 2). The median size of metastatic deposits without ECS was 5 mm (min=1; max=32) compared to 12 mm (min=2; max=50) in cases with ECS ($p<0.001$). Additionally, there was a significant difference in the number of involved nodes for patients with and without ECS (Fig. 3).

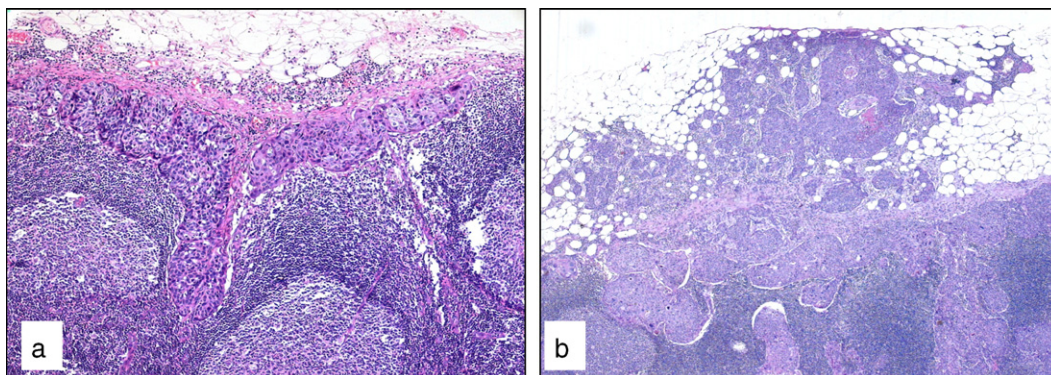


Fig. 1. Pelvic lymph node metastasis: Subcapsular localization of metastasis of squamous cell carcinoma of the cervix uteri without (a) and with (b) extracapsular spread (H&E staining, 214 \times and 109 \times).

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