

Patients with tumors > 2cm on the clinical examination had a 3.39-times higher hazard of death after relapse (HR, 3.39; 95% CI, 1.52- 7.53) and the distant/both location of relapse had 2.23- times higher hazard of death (HR, 2.23; 95% CI, 1.14- 4.36)

The 2-years survival rates after relapse were 76% for tumors <2cm, 50.0% tumors >2cm on the clinical examination, 76% for local relapse and 47% for distant/both location relapse.

Conclusion* The tumor size on clinical examination, the location of relapse, the histologic subtype and the treatment with Bevacizumab, modify the risks of death after relapse on patients with cervical cancer IB1. Tumor >2cm on clinical examination and distant recurrences have a shorter survival time after relapse

601 TRANSITION FROM FIGO-2009 TO FIGO-2018 IN WOMEN WITH EARLY-STAGE CERVICAL CANCER; DOES THE REVISED STAGING CORRECTLY REFLECT RISK GROUPS?

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10.1136/ijgc-2021-ESGO.47

Introduction/Background* The International Federation of Gynaecology and Obstetrics (FIGO) revised cervical cancer staging in 2018. We aimed to evaluate risk factors associated with lymph node macro- and micrometastases in women with early-stage cervical cancer, focusing on the revised FIGO-2018 staging system. The overall purpose was to evaluate if the stage migration related to the implementation of FIGO-2018 correctly reflects risk groups as indicated by the presence of lymph node metastases.

Methodology Using data from a national prospective cohort study on sentinel lymph node (SLN) mapping in 245 women with early-stage cervical cancer, we reallocated women from FIGO-2009 to FIGO-2018 stages. We used binary and multiple regression models to investigate the risk ratio of FIGO-2018 stages and tumour characteristics associated with nodal metastases.

Result(s)* Stage migration occurred in 80.4% (197/245), due to tumour size or depth of invasion in 75.1% (148/197), nodal metastases in 19.3% (38/197), and imaging in 4.5% (11/245). Downstaging to FIGO-2018 IA stages occurred in 36.7% (90/245). Six (5.7%) women with stage IA tumour characteristics were upstaged to IIIC1 due to the findings of nodal metastases. The depth of invasion ranged from 4-5 mm and the tumour size from 9-22 mm; all six metastases were SLNs. For the whole population, risk factors significantly associated with nodal metastases were FIGO-2018 \geq IB2 ($p <$

0.001), parametrial invasion ($p < 0.001$), and lymphovascular space invasion (LVSI) ($p < 0.001$). All three remained significantly associated with nodal metastases in a multivariate analysis.

Conclusion* The FIGO-2018 revised staging system causes stage migration for a large proportion of women with early-stage cervical cancer. The attention on depth of invasion rather than horizontal dimension seems to reflect the risk of nodal metastases correctly. The use of sentinel node mapping in stage IA FIGO-2018 appears to be justified.

604 ROUTINE USE OF CYTOKERATIN IMMUNOHISTOCHEMISTRY IMPROVES THE DETECTION OF LOW VOLUME DISEASE IN EARLY-STAGE CERVICAL CANCER BUT IS COSTLY

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10.1136/ijgc-2021-ESGO.48

Introduction/Background* In cervical cancer, the sentinel lymph nodes (SLNs) are processed according to the pathological ultrastaging protocol. As part of this protocol immunohistochemistry with cytokeratin AE1/AE3 is performed in addition to standard hematoxylin and eosin (H&E) staining, aiding the detection of low volume disease (i.e. micrometastases and isolated tumour cells (ITC)). Current guidelines advise routine use of cytokeratin immunohistochemistry. We studied the pathological yield, in terms of detecting low volume disease, and cost-effectiveness of this routine immunohistochemistry use.

Methodology We retrospectively included all FIGO stage IA-IIA1 cervical cancer patients who had undergone SLN procedures at our institution between 2007 and 2020. Pathological data were collected from every patient including the number of SLNs stained with cytokeratin immunohistochemistry. Data were analysed using descriptive statistics and McNemar test.

Result(s)* In total 232 cervical cancer patients had undergone a successful SLN procedure harvesting a total of 647 SLNs. Of these nodes, 540 SLNs from 215 patients were routinely processed with cytokeratin immunohistochemistry. Immunohistochemistry identified low volume disease in 25 SLNs from 22 patients: 14 with micrometastases (11 patients) and 11 with ITC (11 patients). Four nodes with micrometastases (three patients) and six nodes with ITC (six patients) would have been missed without the routine use of immunohistochemistry. Overall, 54 SLNs needed to be immunohistochemically stained to detect one additional SLN with low volume disease, 135 for micrometastases and 90 for ITC, leading to an expenditure of € 5920 to identify one additional low volume diseased SLN: € 14800 for micrometastases and € 9867 for ITC. Compared to H&E staining, routine immunohistochemistry significantly increased the rate of patients with low volume disease from 18 (8.4%) to 26 patients (12.1%) ($p=0.02$). When only micrometastases were considered as tumour positive, routine immunohistochemistry increased the rate of patients with positive sentinel lymph nodes from 12 (5.6%) to 15 patients (7.0%) ($p=0.25$).

Conclusion* The routine use of cytokeratin immunohistochemistry improves the detection of low volume disease in early-stage cervical cancer, though predominantly ITC, but is expensive.

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PROGNOSTIC SIGNIFICANCE OF HPV DNA PRESENCE IN LYMPH NODES IN CERVICAL CANCER PATIENTS – A LONG TERM FOLLOW-UP

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10.1136/ijgc-2021-ESGO.49

Introduction/Background* Metastatic involvement of lymph nodes (LNs) represents one of the most important prognostic parameter in cervical cancer patients. According to the stage it shortens the 5years survival rate by 25-60 %. Moreover, even in low risk group without any risk factor, a part of radically treated patients suffer from relapse of the disease. Presence of HPV DNA in LNs had been therefore studied as a potential marker of unrecognized metastatic involvement.

Methodology Detected were 13 genotypes of high-risk HPV in the lymphatic tissue harvested from patients who underwent radical hysterectomy with sentinel node biopsy and pelvic lymphadenectomy or paraaortic LN staging. The cytobrush technique was used for perioperative sample collection from the tumour and fresh lymphatic tissue. Only patients with HPV positive tumours who finished their treatment were included and followed.

Result(s)* Out of 119 patients who were included in the study, 93 had available data from their follow-up; 68 underwent radical surgery and 25 were treated by primary definitive radiotherapy. All 19 patients with metastatically involved LNs also had HPV in LNs. Another 23 patients had HPV in uninvolved LNs. After a mean follow up of 147 months 19 patients (5 early and 14 locally advanced stages) recurred and died. The majority of them (13/19) had HPV DNA in their LNs, but only 7 had metastases in the LNs at the same time. Only 6 patients (6.5%) without HPV DNA in LNs recurred – 2 early and 4 locally advanced stages. Negative predictive value for recurrence in cases with HPV negative LNs reached 87.8% in the whole cohort and 95% in early stages.

Conclusion* Our pilot study shows that the presence of HPV DNA in LNs is a promising marker of occult metastatic involvement. Its prognostic value should be confirmed in a prospective trial.

Abstract 606 Table 1 Correlation between HPV positivity/negativity and presence/absence of metastases in LNs

		HPV in LNs		
		Negative	Positive	Together
Metastases in LNs	Negative	49 (66.2%)	25 (33.8%)	74 (100%)
	Positive	0	19 (100%)	19 (100%)
	Together	49 (52.7%)	44 (47.3%)	93 (100%)

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SENTINEL LYMPH NODE MAPPING IN EARLY-STAGE CERVICAL CANCER – A NATIONAL PROSPECTIVE MULTICENTRE STUDY (SENTIREC TRIAL)

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10.1136/ijgc-2021-ESGO.50

Introduction/Background* Sentinel lymph node (SLN) mapping is routinely used in many centres to evaluate the lymph node status of women with cervical cancer and small volume disease. However, there is limited evidence regarding the accuracy of SLN mapping for larger cervical tumours. In a national multicentre setting, we evaluated the SLN detection rate and incidence of nodal disease in women with early-stage cervical cancer and investigated the accuracy of SLN mapping and FDG-PET/CT in tumours >20 mm.

Methodology We prospectively included women with early-stage cervical cancer from March 2017-January 2021 to undergo SLN mapping. Women with tumours >20 mm underwent completion pelvic lymphadenectomy and removal of FDG-PET/CT positive nodes. We followed an SLN algorithm with ultrastaging of all SLNs, removal of clinically suspicious lymph nodes and hemi- or full pelvic lymphadenectomy in cases of failed SLN mapping. We determined SLN detection rates, incidence of nodal disease, sensitivity and negative predictive value (NPV) of SLN mapping, and the sensitivity, specificity, NPV, and positive predictive value (PPV) of FDG-PET/CT.

Result(s)* We included 245 women, and 38 (15.5%) had nodal metastasis. The SLN detection rate was 96.3% (236/245), with 82.0% (201/245) bilateral detection. In a stratified analysis of 103 women with tumours >20 mm, 27 (26.2%) had nodal metastases. The sensitivity of SLN mapping adhering to the algorithm was 96.3% (95% CI 81.0-99.9%) and the NPV 98.7% (95% CI 93.0-100%). For FDG-PET/CT imaging the sensitivity was 14.8% (95% CI 4.2-33.7%), the specificity 85.5% (95% CI 75.6-92.5%), the NPV 73.9% (95% CI 63.4-82.7%), and the PPV 26.7% (95% CI 7.8-55.1%).

Conclusion* Our results suggest that SLN mapping is a reliable method in women with early-stage cervical cancer when adhering to an SLN algorithm. However, until the oncological safety is established, we recommend completion pelvic lymphadenectomy in women with tumours >20 mm. The use of FDG-PET/CT for nodal staging in women with early-stage cervical cancer should be re-evaluated.