Ann Surg Oncol (2016) 23:2383–2384
DOI 10.1245/s10434-016-5157-8

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

EDITORIAL – GYNECOLOGIC ONCOLOGY

The Risk of Contralateral Nonsentinel Metastasis in Patients with Primary Vulvar Cancer and Unilaterally Positive Sentinel Node

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Treatment of early-stage vulvar cancer has undergone major modifications during the last decades. The majority of these modifications aimed to reduce treatment-related morbidity, without compromising survival rates. In 2008 the results of GROINSS-V, the GROningen INternational Study on Sentinel node in Vulvar cancer, were reported.[1] This multicenter observational study investigated the safety of omitting inguinofemoral lymphadenectomy in patients with a negative sentinel node. Patients with unifocal squamous cell carcinomas smaller than 4 cm and no suspicious groin nodes on palpation were eligible for the sentinel node procedure. GROINSS-V showed that the groin recurrence rate after a negative sentinel node in these selected patients is low (2.3 %) and survival excellent. Treatment-related morbidity was significantly lower in patients who had undergone sentinel node biopsy only, with a reduction in frequency of lymphedema of the legs from 25.2 to 1.9 % and recurrent erysipelas from 16.2 to 0.4 %. With respect diagnostic accuracy, Levenback et al. showed similar results for the same group of patients in a study with a different design. In women with tumors smaller than 4 cm, the false-negative predictive value was 2.0 %.[2] A recent analysis of the long-term follow-up of GROINSS-V showed a 10-year survival for sentinel node negative patients of 91 %.[3] Since the publication of these papers, the sentinel node procedure has been widely accepted as standard of care in early-stage vulvar cancer patients. However, some controversies remain, such as the treatment of the contralateral groin in case of unilateral metastatic sentinel node. Opinions differ whether bilateral inguinofemoral lymphadenectomy should be performed in case of unilateral sentinel node involvement. Gynecologic oncologists who prefer bilateral lymphadenectomy largely base their opinion on historical data of which some indicate an increased risk of contralateral lymph node metastases in cases where one groin is proven to have metastatic disease, also in patients with lateralized tumors. One of the more recent papers on this subject shows that in patients with lateralized tumors (>1 cm from the midline) ≤2 cm and a depth of invasion ≤5 mm the risk of contralateral groin involvement is zero and that the risk of contralateral groin involvement in tumors >2 cm in diameter is 5 %.[4] However, these data all arise from studies in which no sentinel node procedure was performed and therefore do not take into account the extra information acquired with the sentinel node procedure, such as the negative predictive value of either an absent or negative contralateral sentinel node in case of a lateralized tumor.

In the current issue of *Annals of Surgical Oncology*, Woelber et al. present the results of their analysis on the risk of contralateral nonsentinel node metastasis in cases with only unilateral sentinel node involvement. In this retrospective analysis 33 patients with a unilateral metastatic sentinel node were analyzed.[5] Of 33 patients, 28 had a negative sentinel node in the contralateral groin, but nevertheless underwent bilateral inguinofemoral lymphadenectomy. No contralateral nonsentinel node metastases were found. The other five patients underwent ipsilateral inguinofemoral lymphadenectomy. No groin recurrences in the contralateral groin were observed in these patients, but three of the five received postoperative radiotherapy to the groins, which may have sterilized microscopic disease.

Woelber et al. provide the first data on the question whether or not to perform a bilateral inguinofemoral lymphadenectomy in case of unilateral sentinel node metastases. Of course, numbers are low, but their data

First Received: 19 January 2016;
Published Online: 30 March 2016

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support the omission of inguinofemoral lymphadenectomy in case of a metastatic unilateral sentinel node and a negative sentinel node in the contralateral groin. In general, considering an inguinofemoral lymphadenectomy in a groin with a negative sentinel node in a patient with a simultaneous metastatic sentinel node in the other groin should be based on data that indicate that the negative predictive value of a negative sentinel node is lower in these patients. Although numbers are low, the data of Woelber et al. and other available data do not indicate a lower negative predictive value. Also, on theoretical grounds there are no arguments for a less accurate sentinel node procedure in this situation. With the sentinel node procedure two different types of information are obtained: (1) on the draining pattern of the tumor and in case of drainage (2) the pathology of the sentinel node. Again, there are no data that indicate that the negative predictive value of either no drainage or a negative sentinel node is decreased in patients with a unilateral metastatic sentinel node. The data of Woelber et al. support this theory. For the patients with unilateral sentinel node metastases and no sentinel node detected in the other groin, this answer cannot be answered because of the low number of patients (only 5), of whom the majority also received radiotherapy.

In their study, Woelber et al. did not make a distinction between lateralized and midline lesions. Where in lateralized lesions it is considered safe to accept unilateral sentinel node detection, in midline lesions bilateral sentinel node identification is advised. In tumors involving the midline, an inguinofemoral lymphadenectomy is advised in case the sentinel node is found in only one groin, independent of the pathological status of that sentinel node. Data from GOG-173 showed that in vulvar tumors involving the midline, lack of bilateral lymph drainage with the sentinel node procedure should not be accepted because of the increased risk of lymph node metastases in the nondraining groin. For patients with lateralized lesions and lesions within 1 cm of the midline, but not involving the midline, they concluded that these patients can safely undergo a unilateral sentinel node procedure.[6]

Observations in larger groups of patients are needed to be able to answer the question on the difference between lateralized and midline lesions.

We congratulate Dr. Woelber and her colleagues with this publication. Although number are low, the results of their study support the theory that the sentinel node accurately predicts the pathological status of a groin. In case of an ipsilateral metastatic sentinel node and a negative sentinel node in the other groin, unilateral inguinofemoral lymphadenectomy should be sufficient and patients can be spared the morbidity of bilateral inguinofemoral lymphadenectomy.

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