Gynecologic Oncology 131 (2013) 113–117

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

The role of preoperative ultrasound evaluation of inguinal lymph nodes in patients with vulvar malignancy

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HIGHLIGHTS

- We looked how well ultrasonography could identify positive nodes in vulvar cancer patients.
- Despite good results, this method is not good enough to spare the patient a surgical staging.

ARTICLE INFO

Article history:
Received 13 June 2013
Accepted 24 July 2013
Available online 7 August 2013

Keywords:
Vulvar cancer
Inguinal lymph nodes
Sentinel lymph node biopsy
Inguinal ultrasound

ABSTRACT

Objectives. Inguinal lymphadenectomy in vulvar malignancies is associated with significant morbidity, especially in patients over 70 years old. Under certain conditions, surgical guidelines recommend biopsy and evaluation of the sentinel node in early vulvar cancer. The purpose of our study is to evaluate ultrasonography as a predictor of inguinal lymph node involvement.

Methods. A retrospective study was performed with 60 patients who had vulvar malignancies (92% of which were squamous cell carcinomas) and who were treated at our hospital between 2002 and 2012. The patients ranged in age from 35 to 89 years, with a median age of 76 years. In total, 118 groin scans were retrospectively evaluated for sonographic evidence of lymph node involvement (i.e., absence of fatty hilum, irregular shape, cortical region diameter and vascularization pattern). The results were then compared with histopathologically confirmed lymph node status.

Results. Histopathologically confirmed lymph node status was available for 107 of the inguinal nodes examined by ultrasound, and lymph node metastases were found in 38 (35.5%) cases. The presence or absence of inguinal lymph node metastases was correctly identified by sonography in 92 (86.0%) of the scanned areas. Sensitivity was 76.3%, specificity was 91.3%, and positive and negative predictive values were 82.9% and 87.5%, respectively.

Conclusions. Ultrasonography of the inguinal lymph nodes showed a relatively high sensitivity and specificity for predicting inguinal tumor metastases. However, our results indicate that surgical lymph node staging is still needed to precisely determine inguinal lymph node status in vulvar cancer, especially because a missed lymph node-metastasis is often fatal.

Introduction

In treating vulvar cancer, it is currently unclear whether sentinel node biopsy is a sufficient substitute to prevent the morbidity linked with complete removal of the inguinal nodes. Standard treatment involves wide radical excision of the primary tumor and inguinal lymphadenectomy. Even with contemporary surgical techniques, half of treated patients suffer from post-surgical complications, such as impaired wound healing or acute infections [1]. These complications are predominantly short term; however, lymphedema caused by lymphadenectomy can be a lifelong issue. Nevertheless, because nodal involvement is negatively correlated with survival, lymph node status remains the most important predictor of overall prognosis [2]. Fifty-three percent of all recurrences develop in the groin, with a 5-year-survival rate of only 27%; in the case of a locoregional relapse, the 5-year-survival rate is 60% [3]. While little progress has been made in the treatment of lymphedema, the modern sentinel lymph node biopsy (SLNB) procedure is intended to prevent lymphedema by reducing the number of patients subjected to a full lymphadenectomy.

The SLNB procedure was proposed by Morton et al. [4] as an alternative to observation or elective regional lymphadenectomy in women

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http://dx.doi.org/10.1016/j.ygyno.2013.07.103

with early cutaneous melanoma. This technique provides the opportunity for early intervention in women with SLN metastases and spares women without SLN metastases the morbidity of unnecessary regional lymphadenectomy. As with melanoma and breast cancer, vulvar cancer is in an excellent anatomic position for the SLN procedure. The tumor is easily reached for tracer injection, and the lymph drainage is limited to either groin. The Gynecologic Oncology Group (GOG) has studied various surgical and radiotherapy techniques for women with vulvar cancer. Consequently, the SLN procedure is only recommended for women with clinically negative lymph nodes [5]. As in breast cancer, palpation is one method of determining clinical lymph node status. Another method is ultrasonography. The aim of this study is to evaluate whether inguinal ultrasonography is a useful diagnostic tool to predict lymph node involvement in vulvar cancer patients. Accordingly, we retrospectively assessed ultrasound images obtained before surgery and compared the results to the corresponding histopathologically confirmed lymph node status.

Methods

In total, 60 patients with early vulvar malignancy treated from January 2002 to December 2012 at the Department of Gynecology and Obstetrics in Ulm were included in this study. Patients with tumor stage FIGO 1a, which is a negative predictor for nodal involvement, were excluded [6,7]. However, three patients with histologically proven pT1a were included, as in preoperative clinical examination a higher stage was assumed.

Patients who presented with suspected vulvar malignancy were referred to the ultrasound department for a presurgical inguinal scan. Neither the patients nor the health care providers had pay for the additional ultrasound, which was offered on a voluntary basis to all patients studied. Ultrasonography was performed using GE 730 Expert and Voluson E8 ultrasound devices (GE Healthcare, Solingen, Germany). Both devices are equipped with linear probes at 12 MHz. Greyscale and color Doppler imaging were performed with the linear probes. Images were stored in the ViewPoint Software System (GE Healthcare, Solingen, Germany) and reviewed by three investigators according to the recommendations for axillary lymph nodes (i.e., the absence of fatty hilum, irregular shape, cortical region diameter ≥4 mm and peripheral vascularization) (Fig. 1 and Fig. 2) [8,9]. In the few cases in which the initial assessment of the three investigators differed, a consensus was reached after visually cross checking the images. Overall, ultrasound scans were available for 118 inguinal areas; for two of the 60 patients, ultrasonography was only performed on the right groin.

Surgery was performed by 4 experienced surgeons. Following national guidelines, technetium-99 m was applied one day prior to the procedure, and blue dye was given intraoperatively to tag the sentinel node. If the tumor was unilaterally localized, the procedure was only performed on the ipsilateral groin. All stained and/or radionuclide-marked nodes were identified visually and with gamma probe, surgically removed and then subjected to a frozen section procedure. If a neoplasia was detected, a complete inguinofemoral lymphadenectomy was performed.

In 39 patients, a successful sentinel node biopsy was performed for both inguinal areas, and in 8 patients, sentinel node biopsy was performed for one side only, resulting in a total of 86 sentinel node biopsies. Histopathologically confirmed lymph node status was obtained for both inguinal areas in 47 patients, while for the remaining 13 patients, histopathology was available only for one of the two inguinal areas (due to the tumor being unilaterally localized as described above). Thus, histopathologically confirmed lymph node status was available for 107 of the 118 scanned groins. In 3 cases (4.8%), lymph node metastases that were later confirmed by histopathological analysis had been missed on assessment of the fresh frozen sections.

Statistical analyses were performed using the appropriate non-parametric tests. Comparisons regarding continuous non-normally distributed data were conducted using the Mann–Whitney-U test, while categorical data were analyzed using the Chi-square test or Fisher's exact test. When investigating the predictive factors for lymph node involvement, patients were excluded from the analysis if they had histopathologically confirmed negative lymph node status for one inguinal area but no histopathologically confirmed lymph node status for the other inguinal area, because we could not be certain about the lymph node status of the other side. To evaluate ultrasonography as a predictor of inguinal lymph node involvement, the scan of each inguinal area was treated as an independent event. All statistical tests reported here were two-sided, and a test result was regarded as statistically significant if $p < 0.05$. All statistical analyses were performed using IBM Statistical Package for the Social Sciences (SPSS) version 19.

Results

Patient characteristics

Patient characteristics for the 60 patients are shown in Table 1. The majority of patients had squamous cell carcinoma, the most common tumor size was pT1b, and histological grade was mostly grade 2. Invasion depth (data available for 46 patients) ranged from 1 to 22 mm with a median of 4 mm.

Sentinel node biopsy revealed positive nodes in 22 (25.6%) of the 86 cases. Histopathologically confirmed lymph node metastases were found in 38 (35.5%) of the 107 inguinal areas studied. A median of 3 nodes were dissected if the nodes were negative (range 1–19, $n = 69$), and a median of 7 nodes were dissected if the nodes were histopathologically positive (range 1–15, $n = 38$); the difference was statistically significant (Mann–Whitney-U-test, $z = 4.48$, $p < 0.001$). No significant difference was found in the number of nodes that were dissected between the left and right groins (Mann–Whitney-U-test, $z = 1.21$, $p = 0.23$).

Predictive factors for lymph node involvement

No significant difference in age was found between patients with and without positive nodes (Mann–Whitney U-test, $z = 0.5$, $p = 0.62$). However, the tumors of patients with lymph node metastases had a significantly higher invasion depth (median 10 mm, range 2–22 mm) than the tumors of patients without lymph node metastases (median 3 mm,

Table 1
Patient characteristics ($n = 60$).

Age in years	Mean	70.1
	Median	76
	Range	35–89
Body Mass Index ($n = 59$)	Mean	26.7
	Median	25.4
	Range	19.0–48.9
Invasion depth in mm ($n = 46$)	Mean	6.1
	Median	4.0
	Range	1–22
Histological type	Squamous cell carcinomas	55 (91.7%)
	Melanomas	3 (5.0%)
	Bowen-carcinoma	1 (1.7%)
	Basalioma	1 (1.7%)
pT	pT1a	3 (5.0%)
	pT1b	33 (55.0%)
	pT2	17 (28.3%)
	pT3	5 (8.3%)
	n/a	2 (3.3%)
pN	pN0	31 (51.7%)
	pN1	16 (26.7%)
	pN2	8 (13.3%)
	pN3	5 (8.3%)
Histological grading	G1	10 (16.7%)
	G2	42 (70.0%)
	G3	4 (6.7%)
	n/a	4 (6.7%)