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Long-term follow-up of vulvar cancer patients evaluated with sentinel lymph node biopsy alone

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HIGHLIGHTS

- Vulvar cancer patients that undergo SLN dissection have similar groin recurrence rates to superficial inguinal lymph node dissection.
- SLN dissection in vulvar cancer is associated with few groin complications.

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ABSTRACT

Objective. The objective of this study was to examine SLN evaluation alone in women with squamous cell carcinoma (SCC) of the vulva and evaluate the inguinal recurrence and complication rates.

Methods. An IRB approved prospective study enrolled patients with SCC of the vulva. Peritumoral injection of Tc-99 sulfur colloid and blue dye was used to identify SLNs intraoperatively. Patients with negative SLN for metastasis were followed clinically without further treatment. Patients with metastasis to a SLN underwent full groin node dissection followed by standard treatment protocols.

Results. A total of 73 women were enrolled onto protocol with 69 patients undergoing SLN dissection. Mean age was 66.9 years (range: 29–91) with 47 stage I, 12 stage II, 9 stage III, 2 stage IV and 3 unstaged patients. SLN dissections were successful in 63 patients. Of the 111 groins evaluated with a SLN dissection 93% had a SLN identified with an average of 2 SLN per groin. There were 92 groins with negative SLN and 11 groins with positive SLN. 57 patients had negative SLN and underwent conservative management with the median follow-up of 58.3 months. Three patients experienced groin recurrences (2 unilateral, 1 bilateral) for a recurrence rate of 5.2% (3/57). The complication rate for the inguinal incisions was 17.5% (1 cellulitis, 1 abscess, 2 lymphoceles, 5 lymphedema and leg pain).

Conclusions. Isolated SLN dissection alone has a low inguinal recurrence rate with decreased complications and should be considered as an option for women with SCC of the vulva.

Introduction

Vulvar cancer is a relatively rare gynecologic malignancy with a projection of 4700 new cases and 990 deaths in 2013 [1]. The classical approach for the surgical management of vulvar cancer was a radical vulvectomy with en-bloc inguinofemoral lymphadenectomy. These surgeries were plagued with exceedingly high morbidity rates [2]. In recent years, the triple incision technique has been the standard of care and most recently the use of sentinel lymph node (SLN) mapping has been evaluated. The feasibility of performing a SLN dissection has been demonstrated in multiple studies [3–9], including a recent meta-analysis by Hassanzade et al. [10]. The majority of these studies combined a sentinel node dissection followed by a complete groin node dissection to determine the predictive value of the sentinel node [11].

In contrast, the GROningen INternational Study on Sentinel nodes in Vulvar cancer (GROINSS-V) was a prospective multicenter observational study, in which sentinel node biopsy was performed in patients with unifocal vulvar squamous cell carcinoma less than 4 cm [12]. In this study, patients with a negative sentinel node at pathologic ultra-staging had close follow-up, whereas patients with a positive sentinel node underwent inguinofemoral lymphadenectomy. They demonstrated that in patients with early stage disease and

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negative lymph nodes, the groin recurrence was low, survival was excellent and morbidity from surgery was minimal [12].

We published our interim experience with sentinel node biopsy alone in 35 vulvar cancer patients and similar to the trial by Van der Zeen et al., our initial data also showed that in patients with negative sentinel lymph nodes, groin recurrence and morbidity were low and survival was not affected [13]. The objective of this study was to examine SLN evaluation alone in women with SCC of the vulva and evaluate the inguinal recurrence rates as well as complication rates.

Materials and methods

This was a prospective observational cohort study approved by the institutional review board and registered with the National Institute of Health clinical trials protocol registration system (Protocol Registration #2006-04-13). Patients were enrolled through the Program in Women's Oncology over a 10 year period from 2002 until 2012. Patients diagnosed with a biopsy proven clinical stage I or II squamous cell carcinoma of the vulva with greater than 1 mm depth of invasion were eligible for the study. Patients with suspicious inguinal lymph nodes either by palpation or on radiologic evaluation were ineligible.

After informed consent was obtained patients underwent surgery, consisting of a radical wide local excision or radical vulvectomy plus a unilateral or bilateral inguinal sentinel node dissection. Patients with lesions within 1 cm from the midline had bilateral inguinal node evaluation either by sentinel lymph node dissection or complete inguinal node dissection if a sentinel lymph node was not detected. Patients with lesions greater than 1 cm from the midline underwent unilateral sentinel lymph node dissection or a unilateral complete groin dissection if a sentinel lymph node could not be detected. In addition, a sentinel node dissection was performed on all groins, regardless of primary tumor location, if there was an uptake of Tc-99m sulfur colloid detected by preoperative lymphoscintigraphy or by preoperative examination with a handheld gamma counter. If a sentinel was unable to be detected in a groin that required evaluation either due to primary tumor location or preoperative evidence of a sentinel lymph node, a complete groin dissection was performed.

The sentinel lymph node protocol as described in prior publications was followed [8,13,14]. Each patient underwent two intradermal peritumoral injections on both the medial and lateral edges of the tumor with a total of 2 mCi of unfiltered technetium-99m sulfur colloid (Tc-99m) in a volume of 1 cc, 90 to 180 min prior to surgery. Lymphoscintigraphy was performed to detect the presence of a sentinel node preoperatively. Intraoperatively, 3 cc of methylene blue dye was injected at the peritumoral edge in a manner and location similar to the Tc-99m sulfur colloid injection. Prior to groin node dissection, a handheld collimated gamma counter was used to identify the sentinel node and the area was marked with ink. An inguinal sentinel node dissection was then performed through a 2 to 3 cm groin incision prior to excision of the vulvar tumor. Sentinel nodes that had taken up blue dye only were labeled as cold sentinel nodes. Sentinel nodes that had taken up Tc-99m sulfur colloid alone were labeled as hot sentinel nodes and sentinel nodes containing both blue dye and Tc-99m sulfur colloid were labeled as hot and blue. Radiolabeled lymph nodes with a 10 s gamma count of at least 10% of the hottest sentinel node were considered hot with increased activity, defined as a count greater than 5% of that at the injection site. Upon completion of the groin node dissection, the lymphatic beds were rescanned to ensure that all sentinel nodes had been removed and the background of the nodal basin was less than 10% of the gamma count of the hottest sentinel node.

A sentinel node ultra-staging protocol was used to evaluate each sentinel node as described in prior publications [14]. On pathologic examination, each sentinel lymph node was cut at 2-mm intervals parallel to the long axis of the node. These 2-mm thick sections were submitted for histologic evaluation in one or more blocks. From each block, five levels were cut at 100-micrometer intervals with a 5-micrometer section cut at each level and stained with hematoxylin and eosin (H&E).

Patients with sentinel nodes containing metastatic disease subsequently underwent a complete groin node dissection followed by radiation therapy if clinically indicated. These patients were not followed on protocol after their complete groin dissection. All patients with sentinel nodes that were negative for metastatic disease did not undergo a complete groin dissection and were followed postoperatively every 3 months for the first 2 years and then every 6 months. If there was evidence of a vulvar or groin recurrence, a biopsy was performed for pathologic diagnosis. In addition, all patients were evaluated for surgical complications including wound cellulitis, wound breakdown, lymphocyte, seroma formation and lymphedema.

Results

A total of 73 women were enrolled onto the trial with 69 patients undergoing a SLN dissection. One patient did not undergo a sentinel node dissection secondary to the technetium-99 injected in an incorrect location with respect to the primary tumor. This patient underwent a complete groin node dissection. There were three patients that did not undergo surgery after enrollment. The average age of the study group was 66.9 years old (range 29 to 91). Forty-seven patients were diagnosed with surgical stage I disease, 12 with stage II disease, 9 with stage III disease, 2 with stage IV disease and 3 patients that were unstaged (Table 1).

Of the 69 patients that underwent SLN dissection, 63 patients had successful SLN dissection and six had unsuccessful SLN dissections. Three patients had a unilateral SLN but a contralateral SLN was not identified and therefore a complete inguinal node dissection was performed. The other 3 patients had unsuccessful SLN dissections and underwent a complete inguinal node dissection. Of the 111 groins evaluated with a SLN dissection 103 (93%) had a SLN identified. Of the sentinel lymph nodes obtained, 81 were hot only, 23 were blue only and 109 were both hot and blue (Table 2). Of the 111 groin dissections 95 had a SLN detected with Tc-99m and 75 had a SLN detected with blue dye. Of the 103 groins with a SLN detected 92 groins were negative for metastatic disease and 11 groins had a positive SLN for metastatic disease giving a SLN metastatic rate of 10.7%. There was no correlation with tumor size and the number of SLN obtained per dissection.

Table 1
Patient demographics and tumor characteristics ($n = 73$).

	Average (SD)	Median (range)
Age (years)	66.9 (15.6)	70 (29–91)
Pathologic lesion size (mm) *(n = 70)*[a]	19.3 (13.0)	18 (0–65)
Depth of invasion (mm) *(n = 70)*[a]	4.0 (2.9)	3 [1–13]
	n	%
Tumor location *(n = 69)*[b]		
Midline (<1 cm)	33	47.8
Lateral (>1 cm from midline)	36	52.2
Pathologic stage		
Stage 1	47	64.4
Stage 2	12	16.4
Stage 3	9	12.3
Stage 4	2	2.7
Unstaged	3	4.1
Clinical stage		
Stage 1	36	49.3
Stage 2	23	31.5
Stage 3	10	13.7
Stage 4	1	1.4
Unstaged	3	4.1

[a] 3 patients did not undergo surgery.
[b] 3 patients did not undergo surgery and one did not have tumor location documented.