Sentinel Lymph Node in Vulvar Cancer

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BACKGROUND. The aim of the study was to assess the feasibility, efficacy, and accuracy of the sentinel lymph node (SLN) procedure in vulvar cancer.

METHODS. From April 2004 to September 2006, all patients with vulvar cancer, clinical stages I and II, underwent SLN detection, followed by a complete inguinofemoral lymphadenectomy. Demographic, surgical, and pathologic data on all patients were prospectively entered in a database.

RESULTS. Forty-two patients underwent the SLN procedure. One patient was excluded from further analysis due to metastases to the vulva. The detection rate for at least 1 SLN per patient was 95%, with bilateral SLNs detected in 46% of patients. There was a trend toward improved ability to detect bilateral SLNs and proximity of the cancer to the midline ($r = 0.996$; $P = .057$). No contralateral SLNs were identified in patients with lateral vulvar lesions (>1 cm from the midline). For 'close-to-midline' (≤1 cm from the midline) lesions, SLNs were detected in 93% of ipsilateral groins and bilateral SLNs were found in 46% of patients, whereas lesions abutting the midline had unilateral and bilateral SLN detected in 100% and 93%, respectively. Sixteen of 41 patients (39%) and 18 of 68 groins (26%) revealed metastatic disease in the lymph nodes; all were correctly identified by the SLN procedure. There were no false-negative SLN results.

CONCLUSIONS. SLN dissection is feasible and safe to perform in vulvar cancer. The ability to identify bilateral sentinel inguinal lymph nodes appears to be related to the proximity of the vulvar cancer to the midline. ***Cancer* 2007;110:1015–22.** © *2007 American Cancer Society.*

KEYWORDS: sentinel lymph node, dissection, vulvar cancer, proximity to midline.

Over the last several decades, the surgical treatment of vulvar cancer has become more conservative, primarily based on the fact that tumor margins are more important rather than the actual removal of an organ.[1] For most vulvar cancers, separate incisions are made for the primary cancer and the inguinal lymph node dissection.

Overall, 30% of vulvar cancer patients have metastatic disease in their lymph nodes. The incidence of positive lymph node findings is related to the clinical stage and the depth of invasion.[2] Lymph node status is the single most important prognostic factor for survival in vulvar cancer.[3] Survival is correlated with the number of positive lymph nodes as well as the presence or absence of bilateral lymph node metastases.[3] In contrast to some other disease sites, such as breast cancer, patients with recurrence in inguinal lymph nodes are rarely salvaged,[4] making it imperative that lymph node metastases are correctly identified and removed at the time of primary surgery. Independent risk factors for inguinal lymph node metastases are clinical lymph node status, tumor grade, lymph vascular space invasion, depth of invasion, and age.[3] Lymph node-negative patients with a tumor measuring ≤2 cm and with a tumor-free

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margin >8 mm have an excellent prognosis (5-year survival rate of 98%[3]), and no adjuvant therapy is warranted.

Different techniques have been tested for their reliability in assessing lymph node status. Although clinically involved lymph nodes are reported to be an independent prognostic factor for survival,[3] clinical examination is an unreliable predictor of lymph node status and is considered inaccurate in 25% to 30% of cases.[3,5] Ultrasound, computed tomography (CT) scan, magnetic resonance imaging (MRI), and positron emission tomography (PET) scan have all been evaluated in vulvar cancer. CT, MRI, and PET scan have not been proven to add improved accuracy over and above clinical examination.[6–10] Similar results were found in a study combining ultrasound with fine-needle aspirate cytology.[7]

The morbidity of inguinal lymph node dissections through separate incisions is less than with the classic 'butterfly' incision, but lymph edema, infection, and wound breakdown are still common complications in 25% to 35%, 40% to 60%, and 15% to 25% of cases, respectively.[11–14] While trying to maintain the sensitivity of detecting lymph node metastases, gynecologic oncologists have attempted to reduce morbidity from complete inguinofemoral groin dissections by performing sentinel lymph node (SLN) procedures in patients with vulvar cancer.[15–22] Because lymph edema can be a lifelong complication of inguinofemoral groin dissections,[11] the purpose of SLN procedures is to minimize the extent of the lymphadenectomy, thereby reducing resultant complications, without jeopardizing detection rates of metastatic lymph nodes. Studies in other diseases such as melanoma[23] and breast cancer[24] have shown that SLN procedures are associated with low false-negative rates when performed in experienced hands. SLN procedures, if proven to be as accurate in vulvar cancer, could drastically reduce morbidity. Smaller groin incisions should result in less wound breakdown and, by selectively removing the SLNs only, the likelihood of development of lymph edema should be reduced significantly.

Morbidity and quality of life assessment studies in breast cancer have shown that axillary SLN procedures reduce the relative risks of lymph edema and sensory loss[24] (5% vs 13%; relative risk [RR], 0.37) versus standard lymphadenectomy. Drain usage, length of hospital stay, and time to resumption of normal day-to-day activities after surgery were statistically significantly lower in the SLN biopsy group (all $P < .001$), and axillary operative time was reduced ($P = .055$). Overall patient-recorded quality of life and arm functioning scores were statistically significantly better in the SLN biopsy group. ($P \leq .003$). These benefits were observed with no increase in anxiety levels in the SLN biopsy group ($P > .05$). In an observational study by van der Zee et al.,[25] a lower incidence of wound breakdown/cellulitis (11% vs 33%) and lymph edema (5.9% vs 26.1%) was noted in patients who underwent SLN dissection only. The mean hospital stay was significantly shorter in patients who did not require full inguinofemoral lymph node dissection (7 days vs 10 days, respectively).

Currently, only a limited number of studies have been reported, and false-negative rates vary. Minimizing false-negatives in SLN procedures is essential because groin recurrences are nearly always fatal.

The aim of our study was to assess the feasibility, efficacy, and accuracy in the SLN procedure in vulvar cancer, and to compare it to the results reported by others. We also investigated the reliability of SLN procedures in relation to the proximity to the midline of primary vulvar cancers.

MATERIALS AND METHODS

Since the introduction of SLN biopsies on our service in April 2004 until September 2006, all patients with surgically managed vulvar cancer of clinical stages T1 and T2 [International Federation of Gynecology and Obstetrics (FIGO) staging] underwent SLN detection, followed by a complete inguinofemoral lymphadenectomy. The presence of clinically suspicious, palpable lymph nodes was a contraindication to performing the SLN procedure. In lymph nodes completely replaced by cancer, the SLN procedure has been shown to be less reliable, possibly due to obstruction of the lymphatic channels by tumor cells. The injected dye can bypass the SLN, which will lead to false-negative findings.

For the primary tumor, the distance to the midline was estimated both preoperatively and intraoperatively. An imaginary line was drawn from the clitoris, through the urethra to the anus. The distance to this imaginary line was estimated and categorized into midline lesion (abutting the midline), close-to-midline lesion (margin of the lesion does not abut on the midline, but approaches within 1 cm of the midline), or lateralized lesion (the medial margin of the lesion is >1 cm from the imaginary midline). For lesions that appeared to be 1 cm from the midline, the distance was measured with a ruler. For all patients with midline or close-to-midline lesions, bilateral groins were explored. Patients with lateralized lesions underwent ipsilateral inguinal exploration. Demographic, surgical, and pathologic data on all patients were prospectively entered in a database.

SLN Procedure

SLN were detected with technetium sulfur colloid and/or lymphazurin. Approximately 2–4 hours preoperatively, 0.1–0.2 mci of filtered sulfur colloid technetium was injected intradermally in 2–4 injection sites around the vulvar lesion. Early on in the study, both technetium and lymphazurin blue dye were used in all patients. Later on, and only if no lymph nodes were identified with technetium, up to 4 mL of lymphazurin blue dye was injected intradermal at the leading edge(s) of the lesion at the beginning of surgery. Intraoperatively, SLN were detected with a handheld gamma probe (Navigator GPS; Tyco Healthcare, Mansfield, Mass). Lymph nodes were considered 'hot' on the basis of their radioactive count (>5× background) with the gamma probe. Inguinal lymph node basins, defined by the inguinal ligament superiorly, the edge of the adductor longus muscle medially, and the sartorius muscle laterally, were scanned and hotspots were identified by gamma probe and/or with visualization of the blue lymph channels and blue lymph nodes. Hot lymph nodes (and/or blue lymph nodes) were selectively removed and sent to pathology for intraoperative review. After removal of the SLNs, the inguinofemoral lymph node basin was rescanned and considered negative if no further hot spots were identified. For the duration of the study all patients underwent a classic inguinofemoral lymphadenectomy after the SLNs were removed.

Histopathology

Intraoperative pathologic examination was performed according to a specific protocol. The SLN was cut perpendicular to the longest axis with an interval of 2 to 3 mm. If the lymph node was too small (2–3 mm) it was submitted either intact or divided in half for frozen section. The specimen was cut at 5-μm intervals and 1 section stained by hematoxylin and eosin (H & E) and evaluated at the time of frozen section. The tissue was then fixed in 10% formalin for permanent section processing. Additional sections, each 5-μm thickness, were obtained from paraffin-embedded frozen tissue. The depth of each level was tissue-dependent and ranged from 10 μm to 40 μm. The first 2 sections were stained by H & E and examined for routine reporting. The other 5-μm sections were cut next to the second level (for immunohistochemical evaluation). In cases with a diagnosis of squamous cell carcinoma, the section was stained by pan cytokeratin cocktail AE1/AE3 (Dako-Canada, Ontario) immunoperoxidase stain. S-100 and HMB-45 (Dako-Canada) and Melan-A (Zymed Laboratories, San Francisco, Calif) immunohistochemical (IHC) stains were used for the detection of malignant melanoma in the SLNs. The last section was used as a negative immunoperoxidase control.

All patients, regardless of the outcome of the intraoperative pathology report, underwent complete inguinofemoral lymphadenectomy for the duration of the study. The remaining non-SLNs were fixed in 10% formalin. After fixation, each lymph node was cut perpendicular to the longest axis with 2-mm to 3-mm intervals and completely submitted for permanent sections. Small uncut lymph nodes with a maximum of 5 were grouped in 1 cassette. Then 1 section of 5-μm thickness was obtained from the paraffin-fixed tissue and stained by H & E.

Statistical Analysis

Descriptive statistics were used. The correlation between the proximity of the cancer to the midline of the vulva and the identification of bilateral SLNs was analyzed using Pearson correlation (2-tailed analysis) (SPSS Inc, Chicago, Ill).

RESULTS

Forty-two patients underwent the SLN procedure. One patient was excluded from further analysis because she was diagnosed with a metastatic adenocarcinoma from a primary ovarian carcinoma. The patient and tumor characteristics of the remaining 41 patients are summarized in Table 1. The average age at diagnosis was 65 years (range, 34–92 years). The majority of the patients underwent wide local excision of the primary vulvar cancer (31 of 41 patients, 76%), 8 patients underwent a radical vulvectomy, and 2 patients underwent a lymphadenectomy only with primary radiation of the primary lesion.

Squamous cell carcinoma accounted for the majority of tumors (95%). Two patients (5%) had vulvar melanoma. The combination of technetium and blue dye was used in 30 patients (73%), technetium alone was used in 11 patients (27%), and no patients had blue dye only (Table 2).

Lymphoscintigram was not routinely performed in all patients during this study. In 39 patients (95%), an SLN was found (Table 3). Bilateral SLNs were observed in 19 patients (46%). We categorized vulvar lesions according to their proximity to the midline through review of the surgical report. In 27 patients (67%) the vulvar lesion was either close to the midline (defined as within 1 cm of the midline) (13 patients) or involving the midline (14 patients). Identification of bilateral SLN occurred in 6 of 13 (46%) 'close-to-midline' lesions, and in 13 of 14 (93%) of lesions abutting the midline. For 12 of 13 (92%) 'close to the midline' lesions the SLN was correctly identified in the ipsilateral groin. In 14 patients

TABLE 1
Clinical Characteristics of 42 Patients With Vulvar Cancer Undergoing a Sentinel Lymph Node Procedure

Variable	No.
No. of patients	41
Mean age (range), y	65 (34–92)
Tumor size	
T1 (<2 cm)	22 (54%)
T2 (>2 cm)	19 (46%)
Depth of invasion (squamous cell carcinomas), mm	n = 39
<3	10 (26%)
3–5	6 (15%)
>5	23 (59%)
Histology	
Squamous cell carcinoma	39 (95%)
Melanoma	2 (5%)
Grade (squamous cell carcinomas)	n = 39
1	18 (46%)
2	17 (44%)
3	4 (10%)
LVSI present	10 (24%)
Procedure	
Wide local excision + LN	31 (76%)
Radical vulvectomy + LN	8 (20%)
LN + radiation to the vulvar primary	2 (5%)

LVSI indicates lymph vascular space involvement; LN, lymph nodes.

TABLE 2
Sentinel Lymph Node Detection

Variable	No. of patients
Technetium + blue dye	30 (73%)
Technetium only	11 (27%)
Blue dye only	0 (0%)
Sentinel LN	
Ipsilateral	39 (95%)
Bilateral	19 (46%)

LN indicates lymph node.

(34%), the lesion was defined as lateralized (>1 cm from the midline), and 13 of 14 patients (93%) had an SLN detected in the ipsilateral groin. In none of 14 lateral lesions did we identify a contralateral or bilateral SLN. There was a trend toward an improved ability to detect bilateral SLNs and the proximity of the cancer to the midline ($r = 0.996$; $P = .057$).

With 27 midline lesions (54 groins) and 14 lateral lesions (14 groins), we explored a total of 68 groins. SLNs were identified in 58 of 68 groins (85% detection rate per groin). The average number of SLNs was 2.5 lymph nodes per basin. Full inguinal lymphadenectomy including the SLNs yielded an average of 8.3 lymph nodes per groin. In 16 of 41 patients (39%) and 18 of 68 groins (26%) metastatic lymph nodes were found. For 11 groins the SLNs were the only lymph nodes that contained metastatic disease. In 15 patients (94%) the metastases were correctly identified by the SLN at frozen section during surgery. In 2 patients with close-to-midline lesions, a positive lymph node was found in the contralateral groin in the absence of metastatic disease in the ipsilateral groin. In 1 patient, 3 SLNs were identified and found to be negative on initial frozen section pathology, but the final cytokeratin stain correctly detected micrometastases in 1 of the SLNs. In this patient, 2 non-SLNs were found to contain metastatic cancer as well. No false-negative results were encountered in our series.

In 2 patients no SLN was detected. The first patient had a lateralized lesion and ipsilateral inguinofemoral groin dissection did not reveal any metastatic lymph nodes. The other patient had a lesion close to the clitoris and bilateral inguinofemoral lymph node dissection revealed that 1 of 7 lymph nodes from 1 groin contained metastases and no lymph nodes in the other groin were metastatic.

Including the ultrastaging and cytokeratin IHC on final pathology, the SLN procedure had a sensitivity, specificity, and positive and negative predictive values of 100% in our series. In 5% of patients and 15% of groins, however, an SLN could not be identified. The false-negative rate was 0 of 16 (90% confidence interval [90% CI], 0–13%). Intraoperative analysis of SLNs by frozen section had a sensitivity, specificity, and positive predictive and negative predictive values of 94%, 100%, 100%, and 96%, respectively.

DISCUSSION

Several groups have reported their findings regarding SLNs in vulvar cancer.[15,17,20,26–33] In what to our knowledge is 1 of the earliest studies concerning SLN for vulvar cancer, Ansink et al.[30] reported their experience using blue dye only in 51 patients. In contrast to our results (39 of 41 patients, 95%) using the combined technique, they identified an SLN in 42 of 51 patients (82%). The overall detection rate from the current literature is 95% (range, 82–100%) to detect at least 1 SLN per patient and 80% (range, 56–100%) to detect at least 1 lymph node per groin lymph node basin. In the current series, we found similar detection rates (95% per patient and 85% per groin, respectively).

In the current study, lymphoscintigrams were not routinely performed preoperatively because all patients underwent full inguinal lymph node dissection

TABLE 3
SLN Detection According to Side and Proximity to the Midline of the Primary Lesion

Detection	Overall n = 41	Midline lesion n = 14	Close to midline lesion* n = 13	Lateralized lesion n = 14
At least 1 SLN	39/41 (95%)	14/14 (100%)	12/13 (92%)	13/14 (93%)
Ipsilateral SLN	—	—	12/13 (92%)	13/14 (93%)
Contralateral SLN	—	—	6/13 (46%)	0/14 (0%)
Bilateral SLN	19/41 (46%)	13/14 (93%)†	6/13 (46%)†	0/14 (0%)†

SLN indicates sentinel lymph node.

* Defined as <1 cm from the midline.

† Pearson correlation coefficient: $r = 0.996$ (2-tailed $P = .057$).

regardless of the results of SLN or lymphoscintigram. Performing routine lymphoscintigrams may have some benefits including the detection of lymph nodes outside of the groin basin, identifying which patients require lymphazurin, and providing feedback to the nuclear medicine physician who performs the injections of technetium preoperatively. It is important to note, however, that lymphoscintigrams are not used to decide whether unilateral or bilateral groins should be explored. Proximity of the cancer to the midline will select which patients undergo unilateral versus bilateral groin exploration.

In 2 of our study patients the SLN was not detected after injection with technetium and blue dye. Both patients underwent complete inguinofemoral lymph node dissection. One patient was found to have microscopic deposits in 1 of the lymph nodes of the completion of inguinal lymph node dissection. We interpreted this event as a failure of the SLN procedure and not as a false-negative finding because the absence of an SLN warrants a full lymph node dissection. If the SLN detection fails to identify an SLN, one should resort to the standard procedure (ie, a complete inguinofemoral lymphadenectomy). In patients with midline or close-to-midline lesions, we expect to find bilateral SLNs. Failure to detect an SLN bilaterally should result in a full inguinofemoral lymphadenectomy on the side(s) that failed to demonstrate an SLN.

In another patient, the frozen section pathologic examination did not correctly identify the micrometastases in the lymph node. However, on final pathology with further staining, a small metastatic focus was observed in that SLN. This finding is a failure of the frozen section diagnosis, which has been previously described in the literature, and should not be interpreted as a false-negative SLN procedure.

The main goal of the SLN procedure is to reduce the morbidity of a full inguinofemoral lymph node dissection. In addition to reducing morbidity, SLN procedures may be associated with improvements in efficacy. SLN may be associated with a higher detection rate of microscopic metastases in lymph nodes and may shorten operating times. We found metastases in the inguinal lymph nodes in 39% of patients. This is higher than the overall rate of 30% described in the literature,[2] particularly given our selected population. Because our protocol excluded all patients with clinically positive lymph nodes, we would expect the incidence of inguinal lymph node metastases to be <30%. In our study protocol, all SLNs underwent ultrastaging, which may lead to higher detection rates. Van der Zee et al.[25] reported a 32% metastatic rate in groins by using the SLN technique in an observation study for SLN procedures in vulvar cancer. Knopp et al.[34] performed ultrastaging on 421 lymph nodes retrieved from 75 patients with vulvar cancer. All lymph nodes were found to be negative on routine H & E microscopic examination. After recutting the paraffin-embedded lymph nodes at 150-μm intervals, positive cytokeratin stains were found in 25 of 421 lymph nodes (6%), confirming occult metastases in 17 of 75 patients (25%). Similarly, in a multicenter study of lymph node-negative breast cancer patients, Weaver et al.[35] demonstrated that for 214 patients who had negative lymph nodes on routine histologic examination, 22 of 214 (10.3%) had occult lymph node metastases detected by ultrastaging. In 20 of 498 (4.3%) of SLNs and in 11 of 3182 (0.35%) non-SLNs previously reported as negative on routine histology, micrometastases were found.

Whether IHC improves the detection of microscopic metastases in inguinal lymph nodes compared with standard H & E staining is not clear.[19,36] The majority of studies are based on the result of axillary lymph node dissection in breast cancer patients. IHC evaluation initially examined lymph nodes with standard sections and H & E staining without ultrastaging. This method increased the detection rate of metastatic disease by 10% to 30%.[37] Application of IHC staining and serial sectioning to the evaluation of the SLNs increased the detection of metastasis to 10% to 15%.[37–39] Several studies in patients with

squamous cell carcinoma of vulva who had undergone an inguinal SLN dissection failed to demonstrate undetected micrometastasis by additional IHC.[27,36,40] However, some authors found additional sectioning and IHC increases the detection rate of occult metastasis.[19] In other organs, all metastatic deposits identified by IHC were either micrometastasis (0.2–2.0 mm) or isolated tumor cells (<0.2 mm); nonetheless, the clinical significance of micrometastasis in inguinal SLNs in patients with vulvar cancer is unclear.

It has been long established that lymph flow from the vulva is mainly ipsilateral for lesions that are more lateralized.[41,42] The areas around the clitoris and perineum drain lymph bilaterally.[41,42] To maximize the detection rate for lesions close to the midline, injections of technetium and/or lymphazurin blue dye should be done at the leading edges to the groins around the tumor. For lateralized lesions, 1 or 2 injections at the border of the primary lesion should suffice.

Our surgical protocol required all patients with midline or close-to-midline lesions to undergo bilateral lymph node exploration. For these 'central' vulvar lesions, each groin should be regarded as a separate basin. If an SLN cannot be detected in either groin, a complete inguinofemoral lymphadectomy should be performed on that side. In the current study, 27 patients had a primary vulvar lesion that was 'close-to' midline or involving the midline. In 19 of these patients (70%), SLNs were detected bilaterally and the remaining 8 patients had unilateral SLNs. In other words, 46 of 54 groins demonstrated SLNs (detection rate of 85%).

Interestingly, for 14 patients with lateralized vulvar lesions, the detection rate was 93%. All SLNs were detected in the ipsilateral groin; none of 14 patients with a lateralized lesion were found to have bilateral SLNs. Fourteen patients with lesions involving the midline had a detection rate of 100%, with 13 of 14 (93%) SLNs detected bilaterally. In the remaining 13 patients with lesions close to the midline (<1 cm) the detection rate for an SLN on the ipsilateral side was 92% (12 of 13 patients), but only in 6 patients (46%) was an SLN detected on the contralateral side. This is in contrast with the 93% bilateral detection rate of lesions encroaching on the midline. Hence, it appears that the further the lesion is localized from the midline the less likely an SLN will be identified in the contralateral groin. To our knowledge, our study is the first to report this finding.

For the SLN procedure, to be representative of the inguinal lymph node status, one would prefer to identify SLNs in 100% of groins. As reported, the SLN detection rate is high (85–95%), but is limited when the SLN procedure is used without full groin dissection to 5 to 15% of patients. It is clinically significant, however, that when an SLN can be identified, it is a very sensitive and reliable predictor of inguinal lymph node status. When a test fails to produce a result, it can obviously not be representative (ie, whenever the SLN procedure fails to detect an SLN, it is not reflective of the inguinal lymph node status and it is of the utmost importance to revert to full inguinal lymph node dissection).

A study specifically addressing SLN in midline vulvar lesions reported limited bilateral findings for lesions located close to or in the midline.[21] In that study, SLNs were only identified in 21 of 34 groins (62%). In midline lesions, SLN should not replace the common practice of exploring bilateral groins. In the current study, 2 patients with close-to-midline lesions had metastatic disease in the opposite groin in the absence of ipsilateral metastases, highlighting the importance of bilateral inguinal investigation for lesions close to the midline.

Currently, to our knowledge, no data are available on the management of positive findings with SLNs. Our current approach is to perform a full inguinofemoral lymphadenectomy on the ipsilateral and contralateral groin when positive lymph nodes are identified. Adjuvant radiotherapy is often administered to the groin areas and the pelvis when positive lymph nodes are encountered[43] and the benefit of adjuvant radiation is most likely greatest in patients with >1 positive lymph node or extracapsular disease.[44,45]

An article published by Gannon et al.[46] regarding SLNs in melanoma patients demonstrated that patients who undergo an excision of the primary tumor before the SLN procedure have the same detection rate as patients with an intact primary lesion, but the disruption of the lymph channels by previous surgery resulted in more SLN basins. Similarly in patients with breast cancer, an excisional biopsy performed before the SLN procedures does not significantly alter the detection rate. In our study, 7 patients had no residual disease detected in the resected vulvar specimen. Three lesions were lateral, 2 were midline, and 2 were close to the midline. In all 7 patients, an SLN was detected. Although the numbers are small, prior excision of the primary lesion does not appear to influence the SLN detection rate.

In the combined literature, SLNs were detected in 95% of patients (Table 4). We combined data on 370 patients who underwent 569 inguinal lymph node dissections. The detection rate of at least 1 SLN per groin is 80% (Table 4). The detection rates are lower in studies using blue dye only (85% per patient and 65% per groin) compared with technetium, with

TABLE 4
Combined Literature Review of SLN Detection

Reference	Year	No. of patients	Detection method	Detection rate (per person)*	Detection rate (per groin) †	Positive patients	Positive groins	False-negative results
Ansink et al.[30]	1999	51	BD	42/51 (82%)	52/93 (56%)	9	14	2
Levenback et al.[20]	2001	52	BD	46/52 (88%)	57/76 (75%)	—	12	0
DeCesare et al.[32]	1997	10	T + BD	10/10 (100%)	20/20 (100%)	3	4	0
Bowles et al.[31]	1999	6	T	6/6 (100%)	7/11 (64%)	—	—	0
de Hullu et al.[17]	2000	59	T + BD	59/59 (100%)	95/107 (89%)	20	27	0
De Cicco et al.[33]	2000	37	T	37/37 (100%)	50/55 (91%)	8	8	0
Sliutz et al.[27]	2002	26	T + BD	26/26 (100%)	32/40 (80%)	9	9	0
Moore et al.[29]	2003	21	T + BD	21/21 (100%)	31/31 (100%)	—	9	0
Puig-Tintore et al.[28]	2003	26	T + BD	25/26 (96%)	31/37(84%)	8	9	0
Merisio et al.[15]	2005	20	T	20/20 (100%)	21/31 (71%)	2	2	1
Terada et al.[26]	2006	21	T + BD	21/21 (100%)	NA	3	–	0
Current study	2007	41	T + BD	39/41 (95%)	58/68 (85%)	16	18	0
Blue dye only		103		88/103 (85%)	109/169 (65%)	9	26/169 (20%)	2 (9%)
Technetium (+/− blue dye)		267		264/267 (99%)	345/400 (86%)	69/246 (28%)	86/400 (21%)	1 (1%)
Total all studies		370		352/370 (95%)	454/569 (80%)	78/291 (27%)	112/537 (21%)	3 (4%)

SLN indicates sentinel lymph node; BD, blue dye; T, technetium; NA, not available.

* At least 1 SLN was identified in that patient.

† At least 1 SLN identified per groin.

or without blue dye (99% per patient and 86% per groin). Combining all currently available studies (Table 4), only 3 false-negative findings have been reported for 569 groins (0.5%). Two false-negative lymph nodes were described by Ansink et al.[30] using blue dye only. Furthermore, in this study, neither IHC nor ultrastaging was performed on the SLN. Moore et al.[29] used a combination of technetium and blue dye, without any false-negative findings, but calculated that if only blue dye would have been used in their study they would have had a much higher false-negativity rate. Taking into account that 2 of these false-negative results were encountered in a study[30] that used blue dye only and the third false-negative finding occurred in a study that used technetium only,[15] we hypothesize that with a combination of radiolabeled technetium and blue dye (if required), plus the requirement for full inguinofemoral dissection if no SLN is detected, the false-negative rate should be very low.

Conclusions

The findings of the current study demonstrate that the SLN procedure is feasible in patients with vulvar cancer. Midline lesions have a very high detection rate for SLN in both groins and lateral lesions have a very high detection rate in the ipsilateral groin. For lesions close to the midline, the detection of SLN in the contralateral groin is limited. Taking certain guidelines into account, the SLN procedure is safe to perform in vulvar cancer patients and should reduce the morbidity when compared with full inguinofemoral dissection. Further large studies using uniform methodology are needed to elucidate the role of SLNs in vulvar cancer.

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