

Contemporary Management of Groin Lymph Nodes in Early Vulvar Cancer: Diagnosis and Treatment

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Introduction

The presence of lymph node metastasis is the most important prognostic factor in vulvar carcinoma [1-5]. Lymph node dissection is the single most important factor in reducing early recurrence and mortality [6]. In early vulvar cancer only 20% to 25% of patients have pathologically positive nodes, while the surgical procedure of inguinofemoral lymphadenectomy is associated with considerable morbidity. Significant morbidity such as wound infection, wound dehiscence, chronic lymphedema, lymphocysts, venous thrombosis, and lymphangitis has been reported in >50% of patients so treated [7, 8]. To decrease associated morbidities and improve the patient's quality of life, surgical modifications to the traditional radical resection have been described in the past ten years. These modifications are now possible because of a clear understanding of the regional anatomy, the mechanism of lymphatic spread, and the incidence of nodal metastasis. Modifications in lymph node management include deletion of lymphadenectomy in selective patients, separate groin incisions, and unilateral lymphadenectomy for lateral lesions [9-12]. It is now generally accepted that when the inguinal nodes are free of metastatic disease, the pelvic nodes are never involved, and pelvic lymphadenectomy in patients without inguinal metastases is therefore considered unnecessary [1, 10-12].

A randomized GOG study [13] showed that in patients with positive groin nodes after radical vulvectomy and bilateral groin node dissection, postoperative external groin and pelvic radiation therapy resulted in better survival and progression-free intervals compared with pelvic lymphadenectomy. Therefore, in patients with more than one positive inguinal node, or with the presence of extranodal growth, radiotherapy has replaced pelvic lymphadenectomy to a large extent [1, 4, 6].

Tumor diameter and depth of invasion have been identified to correlate with lymph node state. For example, a lesion < 2 cm in diameter with < 1 mm depth of invasion has a negligible incidence of groin metastasis, thus there is no need to perform groin dissection [1, 3, 14]. If the depth of invasion is > 1 mm, the incidence of lymphatic metastasis increases from approximately 7% to as much as 40% in lesions with > 5 mm of invasion. Therefore the International Society for the Study of Vulvar Diseases has defined a microinvasive stage for vulvar carcinomas that are < 2 cm in diameter with stromal invasion < 1 mm [1, 7]. These patients can be saved from inguinal lymphadenectomy.

The management of inguino-femoral lymph nodes remains problematic. Clinically nonsuspicious groin nodes proved to be positive in 25% of cases [1, 6, 7, 10-14]. Attempts have been made to reduce the surgical aggressiveness in the groin, sometimes resulting in an increased recurrence rate. Sentinel lymph node detection is an investigational and attractive technique that could ascertain the single node most likely to harbor subclinical disease.

Sentinel node in vulvar carcinoma

The sentinel node (SN) is defined as the first draining lymph node of an anatomical region, and histological examination of the sentinel node should be representative of all other lymph nodes in this region. In 1977,

Cabanas detected the first lymph node draining from a penile carcinoma and found a lower mortality rate among patients in whom this node was tumor-free [15]. In the 1970s, gynecologists were attempting to develop strategies to reduce the morbidity of radical vulvectomy and bilateral inguinal femoral lymphadenectomy, which was the standard treatment for cancer of the vulva [16, 17]. In an effort to apply the concepts of Cabanas to this problem, DiSaia *et al.* [18] designated the eight to ten superficial inguinal lymph nodes as the sentinel nodes of the vulva. These investigators reported that if these sentinel nodes were negative for metastatic disease, then the femoral nodes were always negative. DiSaia *et al.* stated that femoral lymphadenectomy could be omitted, thus reducing the risk of wound breakdown and lymphedema. This group did not attempt to replicate the lymphatic mapping strategy of Cabanas [15] to identify a single sentinel node directly draining the primary tumor. In 1992, Morton *et al.* [19, 20] applied the SN concept with cutaneous melanoma, injecting isosulfan blue inside the lesion before surgery to map the lymphatic drainage and visually identify the first coloured lymph node. They defined the SN as the lymph node closest to the site of the primary tumor, on the direct drainage pathway, and demonstrated that early metastases of melanoma are localized in the SN. If the SN does not show the presence of metastases, other regional nodes are also clear.

Diagnosis and Treatment

There are basically two techniques to identify sentinel nodes:

1. The blue dye technique
2. Lymphoscintigraphy and gamma detector method

Blue Dye Technique

This technique is performed intraoperatively under general anesthesia, thereby avoiding the need for painful perilesional injection. Isosulfan Blue is vital blue dye used mostly [21-23]. After induction of anesthesia and complete skin preparation and draping, 1 to 4 ml of isosulfan blue is injected with a 25-gauge needle into the dermis adjacent to the primary. The injection is made at the leading edge of the tumor closest to the groin. In patients with midline tumors, defined as tumors that come within 2 cm of a midline structure, bilateral injections are done. The injection site is massaged to help disperse the dye. Approximately 5 min after injection of blue dye, a groin incision is made and carried down to the level of Camper’s fascia. The afferent lymphatic channel is identified and followed to a blue node or nodes, which are designated as sentinel lymph nodes.

In 1994, Levenback *et al.* [21] applied the blue dye technique in early vulvar carcinoma. They expanded their first study and published the results in 2001 [23]. They indicated that lymphatic mapping with blue dye

Advantages and disadvantages of sentinel node (SN) identification techniques

Blue Dye

Advantages
Inexpensive
Visible in nodes and lymphatic channels
Rapid SN identification
Intraoperative complications are rare

Disadvantages
No preoperative phase
Rapid pass-through, can miss SN
Misses SN outside usual nodal basin
May lengthen learning curve
May reduce SN identification
Rare dramatic allergic reactions

Lymphoscintigraphy

Advantages
Preoperative determination of number and location of SNs
Quantitative measurement possible
Detects SN outside usual nodal basin. May shorten learning curve
May improve SN identification

Disadvantages
Cost of equipment
Cost of nuclear medicine study
More coordination of care (“hassle factor”)
Radiation safety concerns
Difficult to detect SN close to primary tumor due to “shine through”
Painful local injection

alone, when performed by experienced physicians, permits identification of the sentinel node in 90% of carefully selected patients with vulvar cancer. However, the blue dye technique has shown low sensitivity in identifying the SN in other studies [24-29]. In these studies, the SN was identified in one or both groins in 82.5% of patients with early vulvar cancer. Data from other studies conflict with Levenback's study that blue dye alone can be used to identify the sentinel node in a large proportion of patients with vulvar cancer. In the study of Ansink *et al.* [27], a similar mapping procedure was performed in 51 patients with vulvar cancer. However, these investigators identified a sentinel lymph node in just 56% of the 93 dissected groins in their study. In addition, two patients had false-negative sentinel lymph nodes. These two factors led the authors to suggest that the blue dye technique alone is insufficient for mapping in patients with vulvar cancer. However, Levenback's study differed from that of Ansink *et al.* in that theirs was a single-institution study. In the study of Ansink *et al.*, 80% of the patients came from two centers, and there were three centers with six or fewer patients. The impact of the learning curve on the outcome of the study was not described.

Lymphoscintigraphy

Lymphoscintigraphy associated with gamma-probe guided surgery has been proposed as a more suitable technique than the blue dye method to remove the SN in melanoma and breast cancer patients during surgery [30, 31]. Lymphoscintigraphy involves the peritumoral injection of a radionuclide, which is taken up by the sentinel node in a manner similar to that in which the node takes up blue dye. The sentinel node can be identified preoperatively in the nuclear medicine suit using scanning technology and in the operating room using a handheld gamma counter. The preoperative study is of great importance in cases of ambiguous lymphatic drainage, such as melanomas of the head and neck or trunk, which have multiple potential sites of lymphatic drainage. Preoperative lymphoscintigraphy also helps identify unusual anatomic variations, such as nonaxillary sentinel nodes in breast cancer patients; this occurs in 6% of patients [32].

Lymphoscintigraphy has been used by other investigators [33-37] to identify sentinel lymph nodes in patients with vulvar cancer. De Cicco *et al.* [34] used preoperative and intraoperative lymphoscintigraphy alone to successfully identify at least one sentinel node in each of the 37 patients in their series. There were no false-negative sentinel nodes. If lymphoscintigraphy did not identify a sentinel node in a groin, no metastases were found at surgery. The authors suggested that preoperative lymphoscintigraphy can help select patients who require unilateral vs bilateral lymph node evaluation [34].

De Hullu *et al.* [25] used a combination of preoperative lymphoscintigraphy, intraoperative lymphoscintigraphy, and blue dye in 59 patients with T1 and T2 vulvar cancer. Sentinel nodes were identified in all patients with at least one of the techniques and in 95 (89%) of a total of 107 groin dissections. These authors stated that they relied primarily on the gamma probe to identify sentinel nodes and that blue dye was visible in only 60% of sentinel nodes (Table 1).

Conclusion

The ideal technique for sentinel node identification in patients with early vulvar carcinoma is also still coming into focus. Shortening the learning curve is a high priority for gynecologic oncologists since vulvar cancer is so rare. From this point of view, lymphoscintigraphy is to be encouraged, as most investigators believe that it will shorten the learning period.

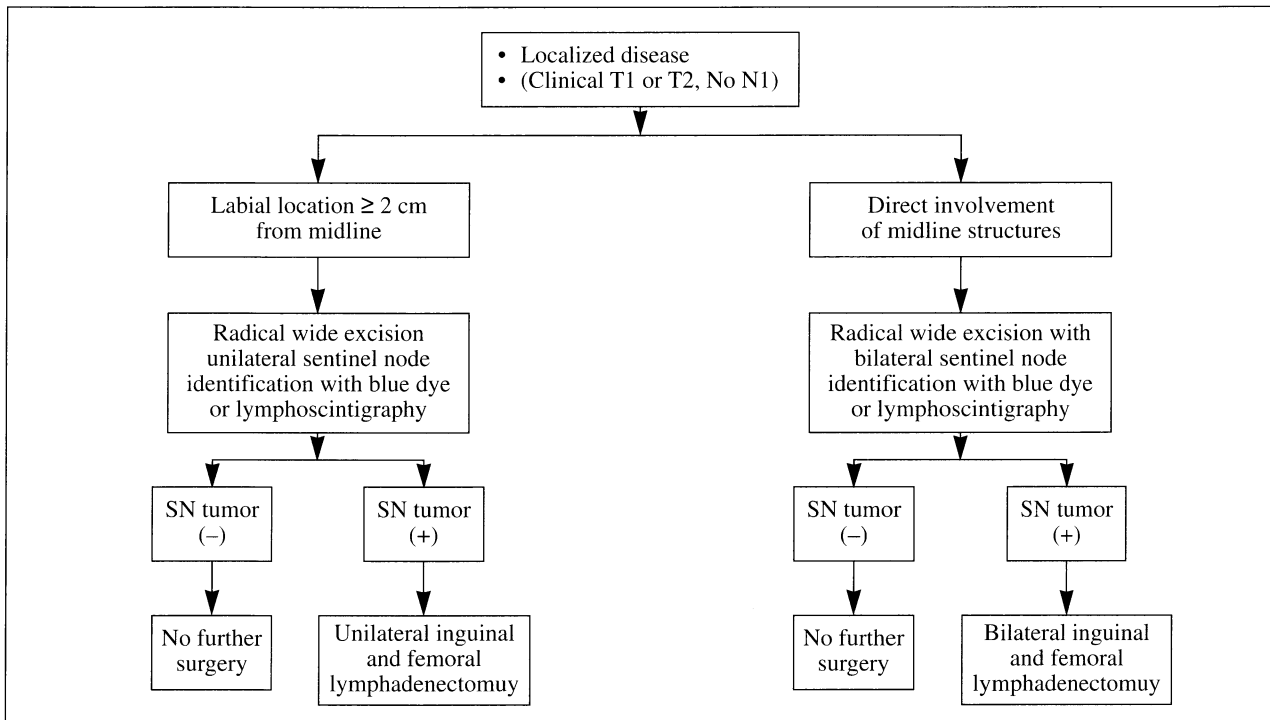
Preoperative lymphoscintigraphy is of great value in identifying sentinel nodes in cases of tumors with ambiguous lymphatic drainage, such as tumors of the medial third of the breast and melanomas of the trunk, and head and neck region [23]. As Levenback *et al.*

Table 1. — *Lymphatic mapping of the vulva: Published series.*

	Blue Dye	LS	Number of patients	Identification/SN%
Barton [38]		X	10	90
DeCasare [33]		X	10	100
Terada [28]	X	X	9	100
De Cicco [34]		X	37	100
Ansink [27]	X		51	82
De Hullu [25]	X		10	70
Rodier [26]	X		6	66
Sideri [35]		X	44	100
Molpus [36]	X	X	11	91
Tavares [37]		X	18	100
Levenback [23]	X		52	88
Sliutz [39]		X	26	100
De Hullu [24]		X	59	100
Rodier [26]		X	7	100

LS: lymphoscintigraphy; SN: sentinel node

Management of groin lymph node in early vulvar cancer



[23] said that “does the vulva have a region with ambiguous lymphatic drainage”? It seems that patients with lateral lesions far from the midline have predictable ipsilateral lymphatic drainage and that patients with tumors involving the midline have predictable bilateral lymphatic drainage. Routine lymphoscintigraphy would help determine if there is a region with ambiguous drainage and would help define it.

Both techniques have advantages and disadvantages [23]. Therefore it is difficult to justify lymphoscintigraphy for all patients when the MD Anderson Cancer Center’s data show that with sufficient training and careful patient selection, blue dye alone permits identification of a sentinel node in a very high proportion of patients. According to the advantages or disadvantages of both procedures and the clinical skills, gynecologic oncologists should decide what to do, and should perform intraoperative lymphatic mapping on all patients with early vulvar cancer.

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