

# Sentinel node dissection in the treatment of early stages of vulvar cancer

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## Summary

**Objectives:** To assess the results of sentinel lymph node (SLN) detection in the initial stages of vulvar cancer and the recurrences that may appear. **Study design:** 76 patients with vulvar carcinoma, Stage I and II. Between 2000 and 2010, identification of the SLN was performed with a perilesional injection of Tc99m and vital dye. Ninety sentinel lymph nodes were found. They were removed separately, and lymphadenectomy was performed depending on the involved areas. Vulvar tumour was also removed. **Results:** 76 patients were included in the study; 20 (22.22%) out of 90 SLNs presented metastases and 70 (77.77%) did not. There were no false negatives, and the sensitivity and negative predictive value reached 100%. Thirty-six months after treatment, one patient presented recurrence with a negative SLN, and two with positive SLNs. **Conclusion:** Biopsy of the SLN is a reasonable alternative to lymphadenectomy in patients with vulvar cancer Stage I and II.

**Key words:** Vulvar cancer; Sentinel lymph node; SLN biopsy.

## Introduction

Vulvar cancer is not one of the most common tumours in women [1]. However, if we take into account the characteristics of the patients, in which the age of appearance is usually between the seventh and eighth decades of life, together with the associated medical procedures and the aggressiveness of the surgical treatments that are performed, as well as the complications derived from them, we can observe that there is a high morbidity associated to these types of patients [2]. Prognostic factors for vulvar cancer have been established, not only in order to know the possible evolution of the oncologic process, but also in order to individualise treatment [3]. One of the most important factors in the prognosis of vulvar cancer is lymph node involvement, which leads to large lymphadenectomies being performed in surgery, in order to remove any affected inguinal lymph nodes, because the survival of the patient is determined by the presence or absence of affected unilateral or bilateral lymph nodes [4]. This factor accounts for the fact that morbidity after treatment for conventional vulvar cancer reaches rates of 85%; 69% of the patients can present chronic lymphedema. Identification of the sentinel lymph node (SLN) may reduce the aggressiveness of the surgical treatment, because it is defined as the first node that receives lymphatic drainage in a specific area (the vulva, in this case) [5]. Several techniques (US, CT, NMR), together with puncture cytology [6] have been used to identify the inguinal lymph nodes that have been infiltrated by the tumour.

Identification of the SLN in the treatment of vulvar cancer, together with conservative surgery, represents an advance in the reduction of morbidity and mortality in the treatment of patients affected by this condition [7]. Identification of lymph node metastases and micrometastases, on the other hand, is a useful tool for the application of complementary treatments. The introduction of procedures for identification of the SLN represents one of the latest advances in the surgical management of the initial stages of vulvar cancer [8].

The objective of our study was to assess the results of SLN identification in the initial stages of vulvar cancer and the recurrences that may appear in patients that have been treated with this technique.

## Material and Methods

We present a retrospective, observational, multicenter study in which 76 patients with initial stages of vulvar cancer were assessed. Histologically, they presented squamous cell carcinomas and melanomas with a maximum diameter of less than 4 cm. The data collection period started in the year 2000, and it ended in 2010 with the control stage. All data were sent to the Department of Gynaecology of the University Hospital of Salamanca, which is considered as a reference centre for the treatment of these processes.

Vulvar cancer was diagnosed with a vulvoscopy and a punch biopsy together with the corresponding imaging tests to assess the extension of the disease, according to current protocols. The study was completed with a preoperative assessment.

All patients were informed about the procedure and treatment they were being subjected to, and the corresponding informed consents were signed. Then, the protocol for the location of the SLN was programmed together with the Department of Nuclear Medicine.

**Procedure:** Early in the morning on the day of the operation,

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in the Department of Nuclear Medicine, the radiotracer, 2-3 mCi (71-111 Mbq) Tc99m-colloid rhenium sulphide (nanocis), was injected intradermally in the area of the tumour. Afterwards, anterior and lateral planar images were taken with an Elscint monohead gamma camera (model Apex SP -4HR), and the projection of the SLNs that had been observed were marked on the skin. Then, isosulfan blue or methylene blue vital dye was injected intradermally around the tumour.

When the surgical operation started, the SLN was explored with a small incision on the area that had been previously marked. Detection of the sentinel node was carried out with a gamma detection device model Europrobe, so that the SLN could be identified and subsequently extracted. The location of the SLN was found due to the increase in radiation count with regard to basal levels, and to the blue dye. The SLN was removed separately and it was labelled for the histopathological study. In cases in which the unilateral or bilateral SLN showed a positive result, a lymphadenectomy with separate incisions was performed. The incisions were parallel to the inguinal ligament, and the anatomical margins of the incision were limited by the inguinal ligament, the abductor muscle and the inferolateral sartorius muscle. After the incision, the fascia cribrosa was opened, releasing the femoral vein. The treatment of the vulvar lesion consisted of a radical vulvectomy with margins of 2 cm. Adjuvant radiation therapy was applied in cases of lymph node metastases, according to the protocol of the Department of Radiation Therapy. Inguinal recurrence was monitored, and the operation site was verified in later protocol-guided controls up to 36 months after the operation.

**Histopathology:** Lymph nodes that were identified as SLNs were sent unfixed to the laboratory. There they were macroscopically assessed, and some of the sections were studied with hematoxylin and eosin (HE). The samples were also subjected to immunohistochemical study.

The statistical study was performed with PASW for PC version 18.

## Results

An observational study in T1 and T2 stages was performed. It included 76 patients who presented vulvar cancer, with ages between 65 and 88 years. Of the patients 11.84% were 70 years old or younger, and 88.15% of the patients were over 70 years old. The average age was 76 years (Table 1). The primary tumour was 2cm in diameter or smaller in 36 patients (47.36%), and it was bigger in 40 patients (52.53%). Tumour invasion was less than 3 mm in 13 patients (17.10%), between 3 and 4 mm in 53.94% of the patients, and more than 4 mm in 22 patients (28.93%). The most common location of the tumour was the labia majora, with lateral location in 50 patients (65.58%). The most common central location was the periclitoral region in 26 patients (34.21%). In five patients (6.57%), the tumour was multifocal, and in 71 patients (93.42%), it was unifocal. The histologic study identified 65 tumours as squamous cell carcinoma (85.52%), and 11 lesions (14.47%) were identified as melanomas.

Identification of the SLN was positive and unilateral in 52 patients (68.42%), and it was bilateral in 24 patients (31.57%). The treatment was hemivulvectomy in 11 patients (14.47%), vulvectomy in 62 patients (81.57%)

Table 1. — *Patient characteristics.*

	N° patients	Percentage (%)
<i>Age</i>		
≤ 70 years	9	11.84
> 70 years	67	88.15
<i>Tumor size</i>		
≤ 2 cm	36	47.36
> 2 cm	40	52.53
<i>Stromal invasion</i>		
< 3 mm	13	17.10
3-4 mm	41	53.94
> 4 mm	22	28.93
<i>Lesión type</i>		
Multifocal	5	6.57
Isolated	71	93.42
<i>Primary local Treatment</i>		
Hemivulvectomy	11	14.47
Vulvectomy	62	81.57
Radical vulvectomy	3	3.94
<i>Midline tumor</i>		
No	50	65.58
Yes	26	34.21
<i>Histology</i>		
Squamous cell carcinoma	65	85.52
Vulvar melanoma	11	14.47
<i>Positives lymph nodes</i>		
Unilateral	52	68.42
Bilateral	24	31.57

Table 2. — *Technique of sentinel lymph node detection.*

Technique	No. of patients	Percentage (%)
Tc-99m + methylene blue	61	80.26
Tc-99m (no dye)	15	19.73
Methylene blue	0	0
Identified lymph nodes	90	100

and radical vulvectomy in three patients (3.94%). The SLN was identified with Tc99m and blue dye in 61 patients (80.26%), and with Tc99m alone in 15 patients (19.73%). None of the patients had their SLNs identified with dye alone. The total number of identified SLNs was 90 in the 76 patients of the study, including unilateral and bilateral nodes (Table 2).

In the group of lymph nodes that were identified as SLNs, 20 (22.22%) showed a metastasis of the primitive carcinoma, and the remaining 70 SLNs were negative for metastasis (77.77%). There were no false negatives identified, which means that sensitivity was 100% and the negative predictive value (NPV) was also 100 (Table 3).

The distribution of patients for T1 and T2 groups was 24 (31.57%) and 52 (68.42%), respectively. Controlled recurrences after 36 months were observed in three patients. One of them (1.31%) was in the T2 group. She showed a negative SLN and she did not undergo lymphadenectomy. The remaining two patients (2.63%) were also in the T2 group, and they presented metastatic positive SLNs with histology results of melanoma in both cases. The rest of the patients did not show any local or inguinal recurrence (Table 4).

Table 3. — Sentinel lymph node biopsy.

Sentinel lymph node biopsy	No. of patients	Percentage (%)
Metastatic sentinel node	20	22.22
No metastatic sentinel node	70	77.77
False negative	0	0
Sensitivity	—	100
Negative predictive value (NPV)	—	100

Table 4. — Recurrence data. Follow-up: 36 months.

	No. of patients T1 (%)	No. of patients T2 (%)	All patients (%)
Sentinel node detection	24 (31.57%)	52 (68.42%)	76
SN (-) + Recurrence	0	1	1 (1.31%)
SN (+) + Recurrence	0	2	2 (2.63%)

SN = Sentinel node.

## Discussion

The use of non-invasive or microinvasive techniques in the treatment of vulvar cancer has led to an evident improvement in the morbidity rate of patients, compared with the conventional block exeresis of the vulva and the lymph nodes. In these last cases, complications after surgery were common, and they included surgical wound dehiscence, the presence of cellulitis, lymphedema of the lower extremities and prolonged hospital stays as a consequence of radical treatments, plus the appearance of possible complications of medical conditions that were already affecting the patient prior to surgery [9]. For these reasons, biopsy of the SLN is currently a rational method in the treatment of vulvar cancer and vulvar melanoma, because it reduces the aggressiveness of lymphadenectomy. Biopsy of the SLN show lower rates of the previously mentioned complications. Thus, surgical wound dehiscence and lymphedema become rare, and they significantly reduce hospital stays [10].

The characteristics of inguinal lymph nodes in vulvar cancer are considered as the best prognostic factor and as a crucial element for adjuvant therapy [11], due to their histological assessment and identification during the clinical and surgical management [12].

The location of the tumour is particularly valuable when identifying the SLN because bilateral lymph drainage of the vulva needs be taken into account, as it involves the existence of a SLN in both inguinal regions.

The use of Tc99m-colloid is considered as the most accurate technique for the detection of the SLN in breast cancer, vulvar cancer and vulvar melanoma [13]. Tc99m has been combined with a dye (isosulfan blue or methylene blue) with good results that reached global percentages between 95% and 100%, according to Brunner [14], Hampl [15] and Moore *et al.* [13], among others. The radioactive technique seems to be more effective than the vital dye, with an identification rate of the SLN of 100% vs 82.5%. de Hullu [16] detected that 56% of all SLNs that had been identified with Tc99m had been dyed with the vital stain. Nevertheless, when the tumour is next to the inguinal region, the combination of Tc99m

and blue dye may be useful because the isolated use of the radiotracer can be compromised by the proximity between the tumour and the bladder, even though the stain is not considered as a fundamental element in the detection of the SLN and it is only recommended when preoperative lymphoscintigraphy shows any difficulty. Isolated use of the vital dye would significantly reduce the identification rate of the SLN [17]. In any case, the sensitivity and NPV are next to 100% [15, 18]. In spite of the good results described, false negatives have been observed in women with vulvar carcinoma [19]. Blocked lymph canals due to a metastasis in the SLN are a factor that might hinder the identification of said SLN [20]. The use of a histopathological technique, together with immunohistochemical techniques, makes it possible to identify micrometastases that might go unnoticed [21], and that should be clinically assessed due to the risk of metastasis.

The significant increase in the number of melanomas of the female genital tract, and particularly of the vulva, has made it possible to achieve significant advances in the diagnosis, staging, surgical treatment, and adjuvant therapies. The initial treatment of choice in vulvar melanoma is surgery. Recent results show that resections are less radical, as well as lymphadenectomies. The study of the SLN for the assessment of lymph nodes, together with immunohistochemical studies are especially important factors in the treatment of vulvar melanoma [22].

The results that have been established for the control of recurrences have been determined by the rate of false negatives. Brunner *et al.* [14] and Hampl *et al.* [15] described three false negatives in each of the studied series, with a sensitivity of 90% and 92%, respectively. The NPV was 97% in both cases. These parameters establish the reliability of this technique. However, both the sensitivity and the predictive values show a very small variability among studies, and they reach 100% in some cases [4, 23].

The prevalence rate of inguinal recurrences is highly variable, and depends on the retrospective studies that have been performed, reaching values that range between 0% and 5.8% in patients with negative nodes [24]. The months that pass until the monitoring control is verified are an important variable because recurrences usually take place between 24 and 36 months after treatment. Some control studies have been done with patients with a negative lymph node that did not go through lymphadenectomy, and no recurrences were found [25], whereas other references registered a recurrence rate of 14.3% [7]. Some authors also said that the size of the vulvar lesion can influence the appearance of recurrences, and that a smaller lesion means a lower risk of lymph node recurrence. Like in any other line of research, more observations and controls are needed to assess the recurrence rates in longer periods than what have been studied so far. Currently, and according to the results published by the International Sentinel Node Society, the biopsy of the SLN is a reasonable alternative to total inguinal lymphadenectomy in patients with vulvar cancer Stage I and II [26].

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