

# Isolated groin recurrence in vulval squamous cell cancer (VSCC). The importance of node count

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## Summary

**Objective:** To determine whether there is a node count which can define an adequate inguinofemoral lymphadenectomy (IFL) in primary VSCC. **Methods:** A retrospective and prospective review of patients with node negative VSCC who had a full staging IFL. Detection of isolated groin recurrences (IGR) would allow groins with higher risk of groin recurrence to be identified. **Results:** The median node count of 228 IFLs in 139 patients was eight (0-24). There were six IGR (4.3%). Increased rate of IGR was present in patients with increased age, tumour diameter and depth of invasion, lymphovascular space invasion, unilateral IFL, and moderate/poor tumour grade. In the 138 groins with node counts of eight or greater there were no IGRs compared to six in the patients with either undissected groins or groin node counts less than eight ( $p = 0.030$ ). Interval to IGR was significantly shorter than other sites of recurrence. Both disease-specific and overall survival were significantly reduced in IGR. **Conclusions:** An inadequate IFL is a nodal count of less than eight per groin; both these groins and undissected groins are at increased risk of IGR and should have close surveillance.

**Key words:** Vulval Cancer; Node count; Lymphadenectomy.

## Introduction

Vulval squamous cell cancer (VSCC) is a rare tumour of the female genital tract and most studies have involved small numbers of patients. There have been no studies to address in detail the prognostic importance of the number of nodes removed from the groins. The goals of surgery in VSCC are to resect the primary tumour and to remove the regional lymph nodes that may harbour metastatic disease. The standard management of VSCC is a tailored radical wide local excision of the vulval tumour and inguinofemoral lymphadenectomy (IFL) usually through separate incisions [1]. Alternative management of the lymph nodes includes in selected cases sentinel lymph node biopsies, high resolution ultrasound with fine needle aspiration, and inguino-femoral radiation without IFL [2-4]. Superficial lymphadenectomy is not safe because of the risk of involved lymph nodes being missed by the dissection and the poor prognosis of progressive undetected groin node disease [5].

### *Prognostic value of the number of nodes removed*

The extent of metastatic disease in the groin lymph nodes is an important prognostic factor and determines the need for adjunctive treatment [6, 7]. In some tumour sites (e.g., colorectal, pancreas, breast, and bladder) the number of lymph nodes excised has been shown to have prognostic importance as a low nodal harvest may indicate residual lymph nodes with an unknown disease status [8-11]. There have been limited studies to determine the adequacy of IFL in VSCC, and previous reports

include patients who had LNM and received radiotherapy [12]. We set out to determine whether groin node count is of clinical relevance in VSCC.

Low nodal counts following IFL may be because: (1) There are few nodes in the groin; (2) The lymphadenectomy was inadequate leaving residual nodes that may contain metastases [5]. The histopathological count of the lymph nodes was incomplete. A low node count would only be relevant to management and prognosis if the unresected nodes did contain tumour.

Approximately a third of patients with VSCC will have groin node metastases at the time of diagnosis and these will usually, but not always, receive adjuvant radiotherapy. In a series of 40 patients, Homesley showed that those with a single node involved without extracapsular spread did not derive a significant survival benefit from radiotherapy and were adequately treated with surgery alone [13]. It has subsequently been common practice not to offer radiotherapy to these women. A residual groin node containing disease may present later as a recurrence in the groin, or pelvis.

Previous studies assessing the adequacy of lymphadenectomy have used the total count of lymph nodes regardless of whether a unilateral or bilateral lymphadenectomy was performed; whether debulking or full lymphadenectomy was the objective; or whether adjuvant radiotherapy was given. It is important therefore to study women who have undergone a full lymphadenectomy and who have not had radiotherapy. The end point used in these studies was either death or recurrence but this would include patients with local recurrence and those whose death was not related to groin node disease. A more appropriate end point is groin recurrence. Groin recurrence may present in isolation or in combination

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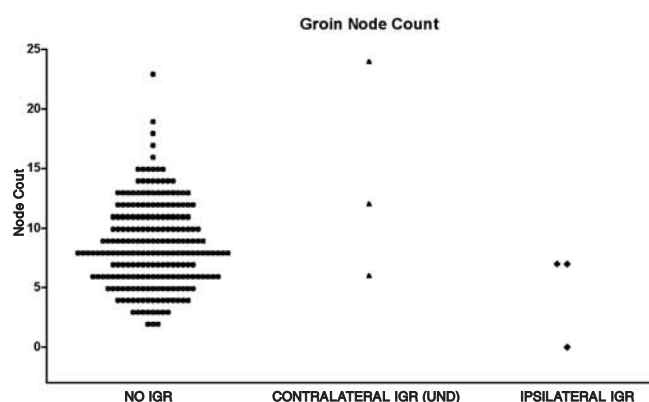


Figure 1. — Groin node count.

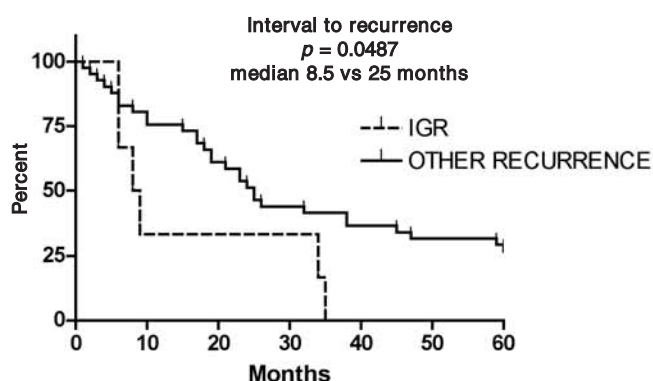


Figure 2. — Interval to recurrence.

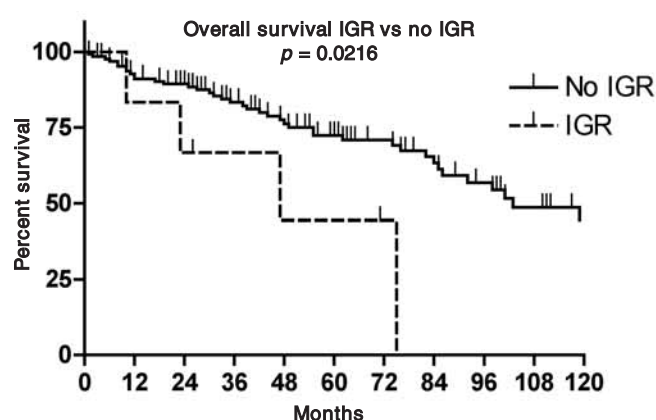
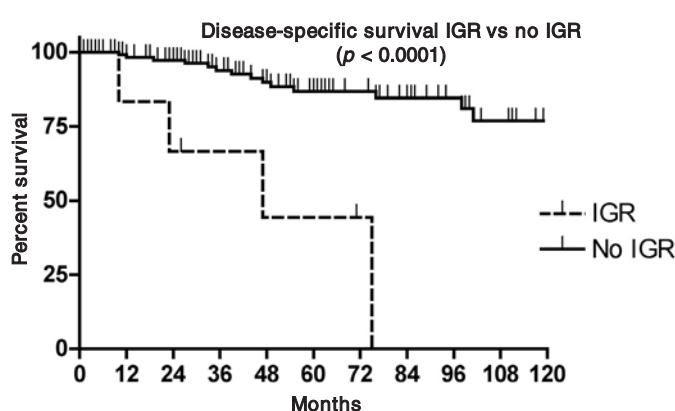
Figure 3. — Overall survival.  
IGR = Isolated groin recurrence.

Figure 4. — Disease-specific survival.

with recurrence on the vulva. In the latter case, the groin node disease may be previously undetected tumour in an unresected node; new metastasis to the groin from the vulval recurrence; or tumour growth in the connective tissue of the resected nodal basin. For that reason, it is essential to consider separately isolated groin recurrences and those that occur in conjunction with recurrence in the vulva.

### Aims

This study seeks to determine the rates of isolated groin recurrence (IGR) in the dissected and undissected groins of a low-risk group of vulval cancer patients. Assessment of node count will help determine whether there is a nodal count that can be considered to represent an adequate staging lymphadenectomy,

### Patients and Methods

All patients who were managed for primary or recurrent VSCC from 1980 to 2008 in three London gynaecological cancer centres were identified and a clinicopathological database was constructed retrospectively and prospectively. Histopathology records were retrieved and follow-up data obtained. Patients who had a full IFL were identified. Patients were excluded if they had lymph node metastases; if they

received adjunctive groin radiotherapy; if the procedure was palliative; if full central pathology review was not available; or if follow up data were not available. Assessment of nodal disease was performed using standard haematoxylin and eosin staining and microscopy by gynaecological oncology pathologists. Tumour depth of invasion, grade, and diameter were recorded. At follow-up, the site and interval to recurrence was recorded and, in those with groin recurrence, whether there was co-existent or previous local recurrence.

The end point of the study was cytologically confirmed isolated groin recurrence, VSCC recurrence (local, groin, or distant), VSCC death, death from other causes and overall survival. Local recurrence was defined as biopsy confirmed recurrence on the vulva, and suspected groin recurrences were confirmed by cytology or histology. Survival was compared using Kaplan Meier survival curves and Fisher's exact test for recurrence groups. Statistical analysis was performed using GraphPad Prism version 5.01 for Windows (GraphPad Software, San Diego CA, USA, [www.graphpad.com](http://www.graphpad.com)).

### Results

In the study period (1980-2008) 139 patients with primary VSCC met the criteria for analysis. Age at diagnosis ranged from 26 to 95 years (mean 67, median 71), and follow-up from three to 209 months (mean 54 months, median 44 months).

In the 139 patients there were 266 IFLs (89 bilateral IFLs and 50 unilateral IFLs). In the 133 patients with no IGR there were 219 IFLs (47 unilateral IFL, 86 bilateral IFL) the negative node count ranged from two to 23 (mean = 8.7, median = 8). First recurrence was IGR in six patients, and other sites in 41 patients. Three IGRs were in contralateral undissected groins of patients who had lateral tumours and a unilateral IFL, and three patients recurred in dissected groins where initial node counts were 0, 7 and 7 (Figure 1).

Four of the IGR patients died of recurrent disease, and two are alive with disease. There were 18 deaths of recurrent disease in other sites and 31 of other causes.

Rates of IGR per patient increased with age greater than 70 ( $p = 0.209$ ), tumour diameter greater than 20 mm ( $p = 0.230$ ), presence of lymphovascular space invasion ( $p = 0.079$ ), unilateral IFL ( $p = 0.667$ ), moderate/poor tumour grade ( $p = 0.663$ ), however only depth of invasion greater than 5 mm was significant ( $p = 0.007$ ).

IGR rates were increased in groins with no IFL (6%) compared to any IFL (1.3%) regardless of node count ( $p = 0.074$ ). In the 138 groins with node counts of eight or greater there were no isolated groin recurrences compared to six in the patients with either undissected groins or groin node counts less than eight ( $p = 0.030$ ) (Table 1).

The median interval to recurrence for IGR was 8.5 months (6 to 35 months) compared to 25 months for other sites of recurrence ( $p = 0.0487$ ) (Figure 2). Overall and disease specific survival were significantly lower in the IGR vs non IGR patients ( $p = 0.0216$ ,  $p < 0.0001$ ) (Figures 3 and 4).

## Discussion

Patients who develop an isolated groin recurrence may be considered to have had an inadequate initial lymphadenectomy at which nodal disease was not resected. Although this is a rare outcome rates have been observed between from 0 to 8.7% [5, 14–16] and our rate of 4.3% is consistent with previous studies.

In the absence of lymph node metastases there were no isolated groin recurrences where eight or greater lymph nodes were resected. It would therefore seem reasonable to define an inadequate lymphadenectomy as less than eight nodes per groin. It would not necessarily follow that an adequate lymphadenectomy is a node count of eight or greater as in the study period the 23 patients with single nodal metastases had groin node counts ranging from two to 16. Of these groins 43% had a nodal harvest of greater than eight and contained a solitary nodal metastasis that may have been missed if the node count was only eight. Furthermore previous studies have shown a range of node counts from IFL ranging from one to 36, therefore a count alone is unlikely to determine a full IFL. Interestingly, one of our patients recurred in a groin where no nodes were identified on histology despite dissection to the femoral vessels. Despite radiotherapy the patient developed widespread metastatic disease.

In the 50 patients where a unilateral lymphadenectomy

Table 1. — Risk factors for groin node recurrence.

Risk factors (per patient)	Isolated groin recurrence	
<i>Age (years)</i>		
≤ 70	1/68 (1.5%)	<i>p</i> = 0.209
> 70	5/71 (7.0%)	
<i>Unilateral/bilateral IFL</i>		
Unilateral	3/50 (6%)	<i>p</i> = 0.667
Bilateral	3/89 (3.5%)	
<i>Tumour diameter (mm)</i>		
≤ 20	1/61 (1.6%)	<i>p</i> = 0.230
> 20	5/78 (6.4%)	
<i>Grade</i>		
Well differentiated	1/46 (2.2%)	<i>p</i> = 0.663
Moderate/poor	5/93 (5.4%)	
<i>Depth of invasion (mm)</i>		
< 5	0/69 (0%)	<i>p</i> = 0.007
> 5	6/54 (11.1%)	
Unknown	0/16 (0%)	
<i>LVSI</i>		
Yes	3/26 (11.5%)	<i>p</i> = 0.079
No	3/113 (2.7%)	
Risk factors (per groin)	Isolated groin recurrence	
<i>IFL</i>		
Yes	3/228 (1.3%)	<i>p</i> = 0.074
No	3/50 (6%)	
<i>Node count</i>		
< 8 or No IFL	6/140 (4.3%)	<i>p</i> = 0.030
> 8	0/138 (0%)	

was performed, there were three (6%) isolated groin node recurrences in the undissected side where metastatic disease may have been resected and identified if a bilateral IFL had been performed. There were no isolated groin recurrences in the dissected side if the nodes were negative. This increased risk of node failure questions the safety of unilateral lymphadenectomy for lateral tumours and the need for close groin node surveillance of undissected groins.

It is unlikely that clinical examination alone is adequate to detect early nodal progression or recurrence which may be amenable to curative treatment. High resolution ultrasound combined with fine needle aspiration has been shown to be successful in the detection of early nodal disease and this would have a useful role in the surveillance of this high-risk group of patients [4]. Close follow up of the groin should probably continue for at least 36 months as isolated groin node metastases without local recurrence are unlikely after this time period.

## Conclusion

Isolated groin recurrence after primary treatment for node negative VSCC is a rare and usually fatal event. We have shown rates to be increased in groins where either less than eight nodes were dissected or no IFL was performed due to contralateral tumours. Our data therefore suggests an inadequate IFL if the node count is less than eight.

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