

Current Management of Early Vulvar Cancer

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Abstract

In recent years, vulvar cancer management has been revolutionised with a more conservative approach being recommended for the primary lesion, and a more rational approach to the management of the lymph nodes. Treatment has become individualised with consideration being given independently to the optimal approach for the primary lesion and regional lymph nodes. The primary vulvar lesion can be effectively treated by radical local excision, thereby sparing the psychosexual consequences of radical vulvectomy in most patients. Local recurrence occurs in up to 10% cases whether or not radical vulvectomy has been performed, and can usually be effectively treated by further surgery and/or radiation. By contrast, recurrence in the groin is usually fatal, so any patient with a T₁ lesion and more than 1 mm stromal invasion should have at least an ipsilateral inguinal-femoral lymphadenectomy performed. Postoperative groin and pelvic radiation should be given for patients with 3 or more micrometastases in lymph nodes, one macrometastasis (≥10 mm diameter), or any evidence of extracapsular nodal spread. The future role of lymphatic mapping to decrease the morbidity associated with complete inguinal-femoral lymphadenectomy awaits further investigation.

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Introduction

Carcinoma of the vulva is an uncommon malignancy, but one that is amenable to early diagnosis if symptoms and signs are appropriately investigated. Although patient and physician delay remains common, an increasing number of patients are being diagnosed with early stage disease.

Traditionally, the disease has been treated surgically, the standard operation since the first half of this century being accepted as en bloc radical vulvectomy and bilateral inguinal-femoral lymphadenectomy.^{1,2}

The psychosexual consequences of radical vulvectomy had been suspected for some time, but were not quantified until the report of Andersen and Hacker in 1983.³ They studied 15 patients who had an average interval since vulvectomy of 5 years and a mean age of 55 years. Using standard psychometric indices and comparing patients who underwent a vulvectomy with healthy women of comparable age, they reported that current sexual activity for the vulvectomy group was at the third percentile, sexual arousal at the eighth percentile, and body image at the fourth percentile. All patients experienced a major disruption of their sexuality.

Documentation of the marked psychosexual consequences of radical vulvectomy, together with a trend

towards earlier age at initial diagnosis and earlier stage disease, have led to progressive acceptance, in most centres, of the need for a more conservative approach to the treatment of this disease. Vulvar-sparing operations have been increasingly utilised in lieu of radical vulvectomy, particularly clitoral sparing operations whenever possible. It has become apparent that local recurrences occur whether or not radical vulvectomy is performed, but that most local recurrences can be successfully treated, as long as the patient is kept under regular, long-term surveillance.⁴ On the other hand, attempts to spare patients the morbidity of groin node dissection have proven to be ill-advised, because recurrence in an undissected groin carries about 90% mortality.⁵

This paper will detail the current management of patients with T₁ and T₂ squamous cell carcinoma of the vulva, with no clinically suspicious lymph nodes.

Surgical Anatomy of the Regional Lymphatic System

Vulvar cancer spreads mainly by direct extension to adjacent organs, including the vagina, urethra, and anus, and by lymphatic embolization to regional lymph nodes. Haematogenous spread to distant organs is usually a late phenomenon. An understanding of the lymphatic pathways and regional lymph nodes is critical to the

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proper management of vulvar cancer.

Iversen and Aas⁶ studied the lymphatic drainage of the vulva by injecting different areas of the organ with technetium-99m colloid in 54 patients before Wertheim hysterectomy and pelvic lymphadenectomy for Stage IB carcinoma of the cervix. These authors measured the radioactivity in the groin and pelvis with a scintillation counter. They confirmed that lymph drainage from the perineum and clitoris is bilateral, but significant bilateral flow also occurred from the anterior labium minus in all patients. Most of the radioactivity from the rest of the vulva was to the ipsilateral groin nodes, although 67% of patients had low but definite contralateral lymph flow. This suggests that ipsilateral groin dissection is appropriate for small (T₁) vulvar cancers unless the tumours involve the clitoris, perineum, or labia minora. This has been confirmed clinically; the incidence of involved contralateral nodes in patients with uninvolved ipsilateral nodes is less than 1% in patients with T₁ lesions.⁴ Both patients who had positive contralateral nodes with negative ipsilateral nodes in one report had tumours involving the labia minora.⁷

The groin lymph nodes consist of an inguinal and a femoral group. The inguinal nodes lie along the line of the inguinal ligament and along the long saphenous vein. They are situated above the fascia lata and cribriform fascia and below Camper's (superficial) fascia.

The exact location of the inguinal and femoral lymph nodes has recently been studied in two reports, one from Sydney, Australia⁸ and the other from Turin, Italy.⁹ In a study of the topography of the inguinal nodes, Nicklin and colleagues⁸ studied bipedal lymphangiograms which had been performed for patients with carcinoma of the cervix. They confirmed that the inguinal nodes were situated in the femoral triangle, and demonstrated that there were no nodes medial to the pubic tubercle and no nodes in the outer 15% to 20% of a line drawn from the anterior superior iliac spine to the pubic tubercle. However, occasional lymphatic vessels travel from the leg in this lateral groin fat to anastomose with nodes in the axilla. Limiting the lateral extent of the groin incision may potentially decrease the incidence of lymphoedema, without compromising the adequacy of the groin dissection.

The topography of the femoral nodes was investigated in a study of 50 female cadavers reported by Borgno and colleagues⁹ They reported that the femoral nodes are one to four in number, and lie on the medial side of the femoral vein, within the fossa ovalis. No nodes were located distal to the lower margin of the fossa ovalis, and none was located lateral to the femoral vein. The most cephalad femoral node is called the node of Cloquet or Rosenmuller, but this group reported that it was absent in 54% of cadavers (27 of 59). These findings suggest that, in dissecting the groin, there is no need to remove

the fascia lata lateral to the femoral vessels to resect all nodes. Preservation of this fascia decreases the risk of injury to the femoral nerve.

Lymphatic vessels from the vulva course anteriorly before turning laterally at the mons veneris and terminating mainly in the inguinal lymph nodes.¹⁰ The femoral nodes receive afferents from the inguinal nodes but also receive some direct channels through the cribriform fascia, particularly from the clitoris and anterior vulva. The presence of direct channels to femoral nodes has been confirmed clinically by several reports of involved femoral nodes in patients with uninvolved inguinal nodes.¹¹⁻¹³ The author has seen 3 such cases. One patient had an inguinal-femoral lymphadenectomy done by the author, and had one involved femoral node. The patient remains alive and well at 36 months. The other 2 patients were treated by other surgeons using inguinal lymphadenectomy only. Despite uninvolved inguinal nodes, both had recurrences within 12 months in a femoral node and died of disseminated disease over the groin, thigh, and lower abdomen. These findings suggest that groin dissection always should consist of dissection of both the inguinal and femoral nodes.

Management of T₁, N₀ - N₁ Tumours

Current management of vulvar cancer requires individualization of treatment.^{14,15} This means that in each patient, careful consideration must be given to the most appropriate operation for: 1) the primary tumour and 2) the regional lymph nodes. The optimal operation for the primary lesion (vulvectomy versus vulvar-sparing surgery) should not influence the decision regarding the need for ipsilateral or bilateral inguinal-femoral lymphadenectomy.

Prior to any treatment being offered, it is important to perform a colposcopic examination of the cervix and vagina to exclude any co-existing sites of invasive or intraepithelial neoplasia.

Management of the Primary Lesion

The most important consideration in determining the appropriate operation for a lesion 2 cm or less in diameter is the condition of the remainder of the vulva. If the lesion is unifocal and the rest of the vulva is healthy, radical local excision is the treatment of choice. Whether or not a radical vulvectomy or a radical local excision is done, deep and lateral surgical margins adjacent to the tumour will be the same. Hence, it is not surprising that the incidence of local invasive recurrence is similar, regardless of the type of vulvar procedure done (Table I).

The depth of resection should be to the fascia lata, which is coplanar with the inferior fascia of the urogenital diaphragm and the fascia overlying the symphysis pubis. There has been some uncertainty regarding the

lateral clearance required, but a clinicopathologic review of the data from UCLA indicated that local recurrence was unlikely if surgical margins of at least 10 mm were attained.¹⁶ Surgical margins of this dimension allow a significant amount of vulvar tissue to be conserved, and a particularly impressive cosmetic result is obtained if the lesion is situated in the posterior labium majus or perineum (Fig. 1).

There are 3 potential problems with respect to adequate surgical margins. Firstly, if a 10 mm margin cannot be obtained because of close proximity to the urethra, the distal 1 cm of urethra may be safely resected without compromising urinary continence. Secondly, if proximity to the anus limits adequate margins, consideration should be given to a small (e.g. 5 x 5 cm) field of postoperative external beam perineal radiation. Our own practice is to give postoperative radiation for perianal lesions if the surgical margin is less than 5 mm. Finally, if the primary lesion involves, or is immediately adjacent to the clitoris, major psychosexual sequelae are likely if the clitoris is resected. In this situation, primary radiation therapy to a small anterior vulvar field is capable of sterilising the tumour, without interfering with clitoral sensitivity (Personal communication—Jones RA).

TABLE I: INCIDENCE OF LOCAL INVASIVE RECURRENCE AFTER RADICAL LOCAL EXCISION AND RADICAL VULVECTOMY FOR T₁ SQUAMOUS CELL CARCINOMA OF THE VULVA

	No.	Recurrence	DOD
Radical local excision	165	12 (7.2%)	1 (0.6%)
Radical vulvectomy	365	3 (6.3%)	2 (0.6%)

DOD: dead of disease

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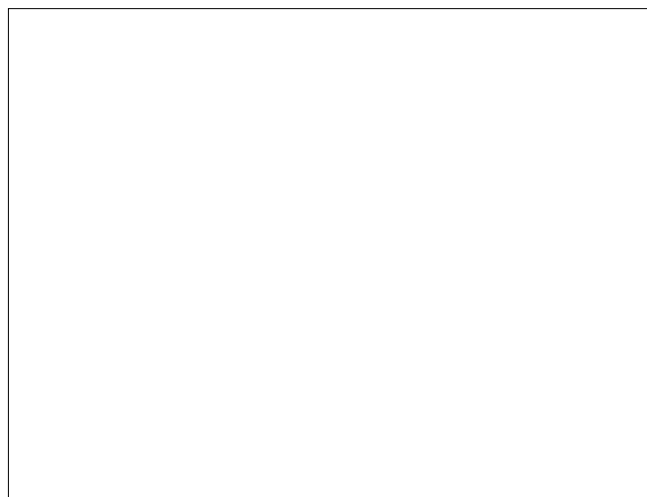


Fig. 1. Good cosmetic result following radical local excision of a perineal lesion, and bilateral groin dissection through separate incisions.

If the vulvar cancer arises in the presence of widespread intraepithelial neoplasia or dystrophy, the patient's age and wishes should be considered when determining treatment. Most elderly women will have had many years of chronic vulvar itching and will gladly accept radical vulvectomy. However, most young women will be reluctant to undergo radical vulvectomy, and it is usually possible to treat the primary tumour with radical local excision and then treat the rest of the vulva in the most appropriate manner. For example, vulvar dystrophy will require topical steroid therapy; vulvar intraepithelial neoplasia may require superficial local excision with primary closure and/or laser therapy.

If the perineum needs to be widely excised, it is important to reconstruct the perineal defect to prevent introital stenosis, and to avoid close approximation of the anus and vagina. This reconstruction is most readily facilitated with the use of rhomboid transposition flaps.¹⁷

Management of Patients with T₂ N₀ - N₁ Tumours

Patients with primary lesions more than 2 cm in diameter are usually treated with radical vulvectomy and bilateral groin dissection. However, there is increasing evidence that radical vulvectomy may be unnecessary for these larger lesions as well, and the author has not performed radical vulvectomy for an isolated T₂ tumour for the past 10 years.

Burrell and colleagues¹⁸ reported a modified radical vulvectomy in 14 patients with T₂ tumour without local recurrence. Burke and colleagues¹⁹ at the MD Anderson Hospital reported on 32 patients with invasive squamous cell carcinoma of the vulva (depth of invasion, >1 mm) and clinically uninvolved inguinal nodes who underwent radical local excision. Seventeen patients had T₁ tumours, and 15 had T₂ lesions. The diameter of the tumours ranged from 5 to 65 mm (mean 23 mm), and depth of invasion ranged from 1.5 to 13 mm (mean 4.1 mm). With a mean follow-up of 36 months, only 2 patients (6%) had a local invasive recurrence, and both were salvaged with additional surgery.

Management of the Groin Lymph Nodes

Appropriate groin dissection is the single most important factor in decreasing the mortality rate from early vulvar cancer. Unlike patients who have a vulvar recurrence, which usually can be cured with additional surgical resection, patients who have recurrent disease in an undissected groin usually die of their disease.⁵

A review of the literature during the past decade indicated that the only patients with an insignificant risk of lymph node metastases are those whose tumours invade the stroma to 1 mm or less (Table II). The Nomenclature Committee of the International Society of Gynecologic Pathologists has recommended that the depth of invasion should be measured from the most

TABLE II: NODAL STATUS IN T₁ SQUAMOUS CELL CARCINOMA OF THE VULVA VERSUS DEPTH OF STROMAL INVASION

Depth of invasion (mm)	No.	Positive nodes	Nodes (%)
<1	163	0	0
1.1 to 2	145	11	7.7
2.1 to 3	131	11	8.3
3.1 to 5	101	27	26.7
>5	38	13	34.2
Total	578	62	10.7

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superficial dermal papilla adjacent to the tumour to the deepest focus of invasion.²⁰

To determine the need for lymph node dissection, a wedge biopsy should be taken from the tumour under local anaesthesia and the depth of invasion measured. If it is less than 1 mm, the entire lesion should be excised and submitted to the pathologist for careful sectioning to exclude a more deeply invasive focus. If no focus with greater than 1 mm of stromal invasion is present, lymph node dissection may be omitted.

Midline lesions and those involving the labia minora require bilateral groin dissection. Lateral T₁ lesions may undergo a unilateral inguinal-femoral lymphadenectomy because the risk of positive contralateral nodes in the absence of involved ipsilateral nodes is less than 1%.⁵

For lateral and posterior lesions, the groin dissection may be done safely through a separate groin incision. More anteriorly placed lesions can be treated readily with an en bloc or separate incision technique.

Management of Patients with Positive Lymph Nodes

Involved groin lymph nodes place the patient at risk for positive pelvic nodes and also for recurrence in the skin of the groin and lower abdomen. In 1986, the Gynecologic Oncology Group reported the results of a study in which patients with one or more involved groin nodes were randomized to undergo either pelvic lymphadenectomy or receive bilateral groin and pelvic irradiation.²¹ Patients receiving the postoperative radiation had a significantly better survival rate at 2 years (68% versus 54%, $P=0.03$) as a result of a decreased incidence of groin recurrence (5% versus 23.6%, $P=0.02$). Significance was found only for patients with more than one involved groin node and clinically suspicious (N₂) groin nodes preoperatively. In an earlier study of 113 patients with invasive vulvar cancer, Hacker and colleagues²² reported that involved pelvic nodes were likely only in patients with three or more positive groin nodes or clinically suspicious (N₂) groin nodes. In the latter study,

patients with one microscopically involved node had a 5-year survival rate of 94%.

More recent studies have demonstrated the significance of the morphology of involved lymph nodes, allowing further discrimination among patients with positive nodes.

In 1992, Origoni and colleagues²³ reported that for patients with positive lymph nodes, there was a significant difference in survival depending on the size of the involved nodes, and the presence or absence of extracapsular spread. Patients whose involved nodes were <5mm in diameter had a 5-year survival rate of 90.9%, compared to 41.6% survival if the involved nodes were 5 to 15 mm diameter, and 20.6% for involved nodes >15 mm diameter ($P<0.001$). Similarly if nodal involvement remained intracapsular, the 5-year survival was 85.7% compared to 25% if there was extracapsular spread ($P<0.001$). Similar results were reported by Paladini et al²⁴ who reported that in a multivariate analysis, the only significant variables were FIGO Stage (III, IVA, or IVB) and the presence of extracapsular spread. Factors that were significant in a univariate analysis but not in the multivariate analysis included number of positive groin nodes, diameter of the metastasis, percentage of the node replaced with tumour, and the nodal immune response. van der Velden and colleagues²⁵ demonstrated that even for patients with one positive node, the presence of extracapsular spread decreased survival from 88% (14 of 16 patients) to 44% (7 of 16 patients).

In view of the above, the author's present recommendations for the management of patients with positive groin nodes are as follows:

1. patients with one or two micrometastases should be observed; and
2. patients with three or more micrometastases, one macrometastasis (≥ 10 mm diameter), or any evidence of extracapsular spread, should receive bilateral groin and pelvic radiation. The radiation depth-dose should be planned after obtaining a computed tomographic scan to determine the depth of the femoral vessels.

Lymphatic Mapping

In an attempt to decrease the morbidity associated with inguinal-femoral lymphadenectomy, efforts have been made to identify one or more sentinel nodes in the groin. The hypothesis is that if the sentinel node(s) is negative, all other nodes will be negative, so the patient could be spared the morbidity of groin dissection. A combination of intradermal isosulphan blue dye and intradermal radioactive technetium-99-labelled sulphur colloid, injected around the primary vulvar lesion and subsequently identified in the groin by dissection or lymphoscintigraphy, is used to identify the sentinel node(s).

This concept was initially introduced for the management of melanomas²⁶ and has subsequently been trialed as an approach to breast²⁷ and vulvar cancer.²⁸ Data at this stage are scant and preliminary, and the concept should be considered experimental. No treatment should be modified as a result of sentinel node identification until sufficient data are available to determine the false negative rate.

Conclusions

Modern management of early vulvar cancer should be individualized. Vulvar sparing surgery will usually be appropriate for the primary lesion. At least an inguinal-femoral lymphadenectomy should be performed for all patients with T₂ lesions, or for T₁ lesions with a depth of invasion >1 mm.

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