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FIGO CANCER REPORT 2015

Cancer of the vulva

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1. Staging

1.1. Anatomy

1.1.1. Primary site

Cases should be classified as carcinoma of the vulva when the primary site of growth is in the vulva. Any lesion that involves both the vagina and vulva (i.e. crosses the hymenal ring) should be classified as a carcinoma of the vulva. Tumors that present in the vulva as secondary growths, from either a genital or extragenital site, should be excluded. Malignant melanoma should be reported separately. There must be histologic confirmation of the cancer.

1.1.2. Nodal stations

The inguinal and femoral nodes are the first sites of regional spread.

1.1.3. Metastatic sites

Patients who have extrapelvic metastases or who have involvement of pelvic lymph nodes (external, hypogastric, obturator, and common iliac) are classified as having stage IVB disease.

1.2. Surgical staging classification

The staging system for vulvar cancer has been based on surgical findings since 1988. The final diagnosis is dependent upon thorough histopathologic evaluation of the operative specimen (vulva and lymph nodes). Various modifications have been made over time, with a subdivision of Stage I added in 1994. The FIGO staging of vulvar carcinoma was last changed in 2009 by the FIGO Committee on Gynecologic Oncology [1], to give better prognostic discrimination between stages (Table 1). Table 2 compares the FIGO staging with the Union of International Cancer Control "TNM" classification.

1.2.1. Histopathologic types

Approximately 80% of cases are squamous cell carcinomas, and many cases, particularly in younger women, are HPV related. Melanomas are the second most common cancer seen in cancer centers, although community-based studies have reported basal cell carcinomas to be the second most common vulvar cancer [2]. The histopathologic types are:

- squamous cell carcinoma
- melanoma
- verrucous carcinoma
- Paget's disease of vulva
- adenocarcinoma, not otherwise specified (NOS)
- basal cell carcinoma, NOS
- Bartholin's gland carcinoma.

1.2.2. Histopathologic grades (G)

- GX: Grade cannot be assessed
- G1: Well differentiated
- G2: Moderately differentiated
- G3: Poorly or undifferentiated.

2. Introduction

Carcinoma of the vulva is an uncommon tumor, representing about 4% of gynecologic malignancies. Because of the relatively small experience of individual institutions, randomized trials of therapeutic approaches are uncommon, and most studies are based on retrospective clinicopathologic reviews [3].

It is predominantly a disease of postmenopausal women, with the age-specific incidence increasing with increasing age. Although the external location of the vulva should encourage early presentation, vulvar cancers are often advanced at the time of diagnosis.

Most squamous carcinomas occur on the labia majora, but the labia minora, clitoris, and perineum may also be primary sites.

Vulvar intraepithelial neoplasia (VIN), a precursor lesion in some cases, tends to occur in younger women and may be associated with similar lesions of the cervix and vagina. A new classification of squamous VIN was introduced by the International Society for the Study of Vulvovaginal Disease (ISSVD) in 2004 [4]. The term VIN 1 is no longer used, and VIN 2 and 3 are simply called VIN. There are two types of VIN: (1) VIN, usual type (warty, basaloid, and mixed), which is HPV-related in most cases; and (2) VIN, differentiated type, which is seen particularly in older women, and is often associated with lichen sclerosus and/or squamous hyperplasia. The incidence of VIN, usual type, and the incidence of invasive vulvar cancer in premenopausal women should both decrease significantly with increasing use of HPV vaccination.

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Table 1
FIGO staging of carcinoma of the vulva.

FIGO Stage	Description
I	Tumor confined to the vulva
IA	Lesions ≤ 2 cm in size, confined to the vulva or perineum and with stromal invasion ≤ 1.0 mm[a], no nodal metastasis
IB	Lesions > 2 cm in size or with stromal invasion > 1.0 mm[a], confined to the vulva or perineum, with negative nodes
II	Tumor of any size with extension to adjacent perineal structures (lower third of urethra, lower third of vagina, anus) with negative nodes
III	Tumor of any size with or without extension to adjacent perineal structures (lower third of urethra, lower third of vagina, anus) with positive inguinofemoral nodes
IIIA	(i) With 1 lymph node metastasis (≥5 mm), or (ii) With 1–2 lymph node metastasis(es) (<5 mm)
IIIB	(i) With 2 or more lymph node metastases (≥5 m), or (ii) With 3 or more lymph node metastases (<5 mm)
IIIC	With positive nodes with extracapsular spread.
IV	Tumor invades other regional (upper 2/3 urethra, upper 2/3 vagina), or distant structures
IVA	Tumor invades any of the following: (i) upper urethral and/or vaginal mucosa, bladder mucosa, rectal mucosa, or fixed to pelvic bone, or (ii) fixed or ulcerated inguinofemoral lymph nodes
IVB	Any distant metastasis including pelvic lymph nodes

[a] The depth of invasion is defined as the measurement of the tumor from the epithelial–stromal junction of the adjacent most superficial dermal papilla to the deepest point of invasion.

Treatment of vulvar cancer used to be primarily surgical, but radiation therapy and, to a lesser extent, chemotherapy have been progressively integrated into the treatment protocol over the past 30 years. Therefore, management has evolved into an individualized multidisciplinary approach, and patients should be referred centrally to a gynecological cancer center where all relevant expertise is available [5,6]. **Level of Evidence B**

3. Screening

There is no screening procedure for vulvar cancer. However, patients with a past history of cervical or vaginal cancer should have inspection of the vulva, with or without colposcopic examination, as part of their regular follow-up. Patients with lichen sclerosus or a past history of VIN should also be kept under regular surveillance, and taught to undertake regular self-examination with a mirror.

4. Squamous cell carcinoma

4.1. Presenting symptoms

Vulvar cancer may be asymptomatic, but most patients present with a vulvar lump or ulcer, which may or may not be painful. There is often a long-standing history of pruritus, which may be due to associated vulvar dystrophy. Bleeding or discharge is an occasional presenting symptom, and patients with advanced disease may present with a lump in the groin caused by metastases to groin lymph nodes.

Table 2
Cancer of the vulva: FIGO staging compared with TNM classification.

FIGO Stage	Union for International Cancer Control (UICC)		
	T (tumor)	N (lymph nodes)	M (metastasis)
I	T1	N0	M0
IA	T1a	N0	M0
IB	T1b	N0	M0
II	T2/T3	N0	M0
IIIA	T1, T2, T3	N1a, N1b	M0
IIIB	T1, T2, T3	N2a, N2b	M0
IIIC	T1, T2, T3	N2c	M0
IVA	T4	N0–N2	M0
IVB	Any T	N3	M0

4.2. Diagnosis

If the disease appears to be entirely intraepithelial, initial assessment should consist of multiple biopsies to exclude an invasive focus. A 3 or 4 mm Keyes biopsy instrument is ideal for this purpose. Patients with multifocal lesions should have biopsies taken from several lesions.

If there appears to be invasive cancer present, a wedge or Keyes biopsy under local anesthesia in the office is usually sufficient to confirm the diagnosis. The biopsy should include some underlying stroma.

For small tumors, it is preferable not to excise the entire lesion at the time of biopsy because this makes it more difficult to plan the subsequent definitive resection.

If the lesion is 2 cm or less in diameter and depth of stromal invasion is less than or equal to 1 mm on the initial biopsy, radical local excision of the lesion must be undertaken to allow serial sectioning to properly assess the depth of invasion. If there is still no focus found with a depth of invasion greater than 1 mm, this excision will also be the definitive treatment [3].

4.3. Investigations

(1) Cervical cytology, if applicable.
(2) Colposcopy of the cervix and vagina because of the common association with other squamous intraepithelial lesions.
(3) For large lesions, a CT or MRI scan of the pelvis and groins is helpful to detect any enlarged lymph nodes in the groins or pelvis, erosion into underlying bony structures, or other evidence of metastatic disease.
(4) Routine full blood count, biochemical profile, and chest X-ray preoperatively.

4.4. Clinical practice guidelines

The clinical findings should be recorded on a staging diagram (e.g. Fig. 1). The findings according to the staging delineated in Tables 1 and 2 are usually listed on the reverse side of the diagram.

4.5. Treatment

4.5.1. Treatment of vulvar intraepithelial neoplasia

Various treatment modalities are available for treating intraepithelial lesions of the vulva [7,8]. Once the diagnosis has been established, superficial local excision of the vulvar epithelium with a 0.5–1.0-cm margin is considered adequate for lesions of the lateral aspect of the vulva. Lesions involving the labia minora may also be treated by local excision but may respond favorably to laser vaporization. Laser is also appropriate for clitoral and perianal lesions. Laser treatment of the hair-bearing skin of the vulva will usually produce depigmentation and destruction of hair follicles, with subsequent loss of hair growth. Large lesions may be treated with a skinning vulvectomy and split-thickness skin graft. **Level of Evidence C**

Two randomized controlled trials have shown promising results with the topical immune response modifier, imiquimod, with complete response rates of 35–81% reported [9,10]. Long-term follow-up of patients in one of the studies showed good sustained benefit, although the number of patients in the study was small [9]. **Level of Evidence A**

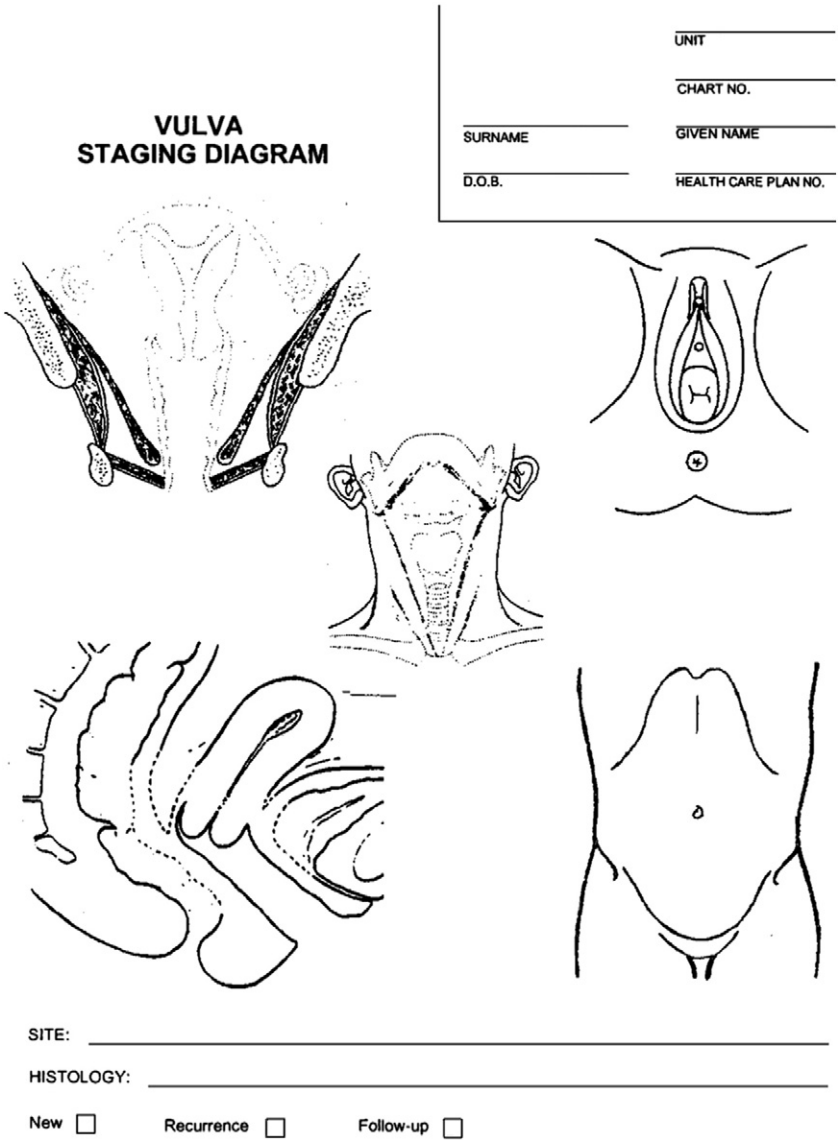

Fig. 1. Vulvar staging diagram.

4.5.2. Invasive vulvar cancer

Management of vulvar cancer must be individualized. There is no standard operation and the emphasis should be on performing the most conservative operation consistent with cure of the disease [3].

In considering surgical treatment options, it is necessary to consider independently the most appropriate management of:

(1) The primary lesion.
(2) The groin lymph nodes.

In cases of locally advanced disease, treatment options for each site should be considered independently and then in the context of the overall management of the patient, in order to select a treatment that will optimize the likelihood of cure and minimize treatment-related morbidity.

4.5.3. Microinvasive vulvar cancer (Stage IA)

Stage IA carcinoma of the vulva is defined as a single lesion measuring 2 cm or less in diameter with a depth of invasion of 1.0 mm or less, the depth being measured from the epithelial–stromal junction of the most adjacent superficial dermal papilla to the deepest point of invasion. Lesions of this extent should be managed with radical local excision. Groin dissection is not necessary for lesions of this type [11,12]. **Level of Evidence C**

4.5.4. Early vulvar cancer

Tumors confined to the vulva without suspicious lymph nodes, as determined by clinical examination, with or without ultrasonic or radiological assessment, may be considered early.

4.5.4.1. Management of the primary lesion (Fig. 2). To decrease psychosexual morbidity, a more conservative operation than radical vulvectomy usually is indicated. The procedure may be called a radical local excision, and for localized lesions, this operation is as effective as radical vulvectomy in preventing local recurrence [3,13–17].

Surgical removal should achieve lateral margins of at least 1 cm, and the deep margin should be the inferior fascia of the urogenital diaphragm, which is co-planar with the fascia lata and the fascia over the pubic symphysis [13,16–18].

If the lesion is close to the urethra, the distal 1 cm of the urethra may be resected without jeopardizing urinary continence.

If there is associated VIN, this should be superficially excised to control symptoms, to exclude other areas of superficial invasion, and to

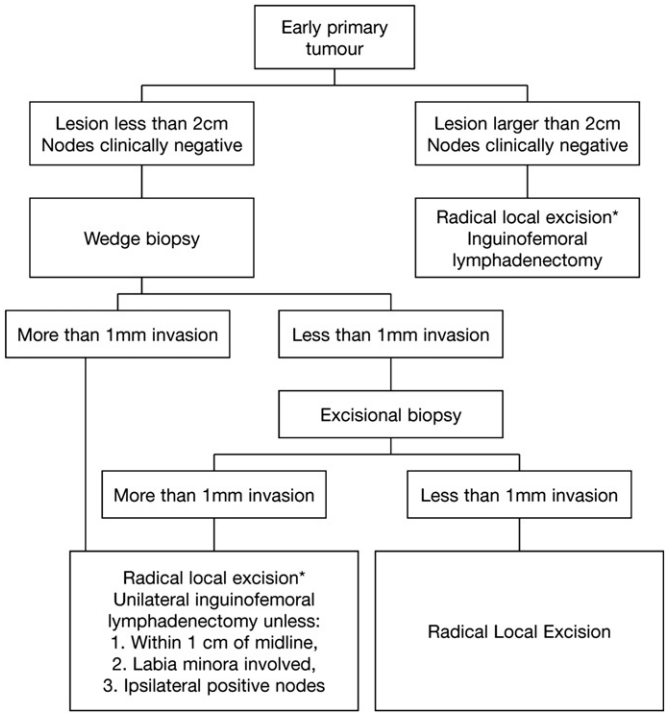

Fig. 2. Management of early vulvar cancer. * If there is associated VIN or lichen sclerosis, these areas may be superficially excised.

prevent subsequent progression to invasive cancer. This is especially true for differentiated VIN. **Level of Evidence C**

4.5.4.2. Management of groin lymph nodes. Recurrence in the groin carries a very high mortality; therefore, appropriate groin treatment is the single most important factor in reducing mortality from early vulvar cancer [3].

All patients with FIGO stage 1B or stage II lesions should have at least an ipsilateral inguinofemoral lymphadenectomy. **Level of Evidence C**

The incidence of positive contralateral nodes in patients with small lateral lesions and negative ipsilateral nodes is less than 1%, so unilateral groin dissection is appropriate for such lesions [3].

Bilateral groin dissection should be performed for midline tumors, and for those involving the anterior labia minora [19]. Large lateral tumors should probably also have bilateral dissection, and definitely if the ipsilateral nodes are positive [19].

Sentinel node excision is being increasingly practiced in many centers following the European multicenter observational study on sentinel node detection [20]. This procedure detects nodal metastasis in most patients with regional spread of disease, and is associated with a lower rate of lymphedema than complete lymphadenectomy. The study, (GROINSS-V), involved 403 women with a unifocal tumor confined to the vulva less than 4 cm in diameter, stromal invasion more than 1 mm, and clinically negative lymph nodes [20]. Sentinel nodes were identified using blue dye and radiolabelled technetium. Lymphadenectomy was omitted in sentinel node negative women. Groin recurrences occurred in 2.3% of patients, with a median follow-up of 35 months. Overall disease-specific survival was 97% after 3 years and morbidity was substantially reduced. Higher false-negative rates have been reported in other studies [21–23].

Owing to the small but definite false-negative rate with sentinel node biopsy, and the high risk of death if groin recurrence occurs, some patients, properly informed of the risks and benefits, will elect to have a full groin dissection, despite the greater complication rate [24–26]. **Level of Evidence B**

4.5.4.3. Groin dissection. It is recommended that both inguinal and femoral nodes be removed, as inguinal node dissection alone is associated with a higher incidence of groin recurrence [27]. **Level of Evidence A**

The femoral nodes are situated medial to the femoral vein within the fossa ovalis. There is no need to remove the fascia lata to dissect the femoral nodes [28]. Groin dissection may be safely performed through a triple incision approach, and this should improve primary healing compared with an en bloc resection of the vulva and groins [29]. **Level of Evidence C**

An en bloc approach may still be useful for clitoral or periclitoral lesions. To avoid skin necrosis, all subcutaneous tissue above the superficial fascia must be preserved.

Groin dissection (with postoperative radiation for patients with positive groin nodes) was found to be superior to groin irradiation in one small randomized trial [30]. Pretreatment imaging that might have detected grossly enlarged nodes was not performed in that early trial and the radiation technique used was considered inadequate to cover the at-risk inguinofemoral nodes [31]. Retrospective clinical reviews have suggested that radiation alone can control microscopic disease in the groins if adequate coverage of the inguinofemoral nodes is confirmed [32,33].

4.5.4.4. Management of patients with positive groin nodes. The Gynecologic Oncology Group demonstrated superior results for pelvic and inguinal radiation compared with pelvic node dissection for patients who had an inguinal lymph node dissection with findings of grossly positive or more than one positive node [34]. **Level of Evidence A**. A recent retrospective, multicenter German study also reported improved survival for patients with positive groin nodes who received adjuvant radiotherapy directed at the groins (positive/negative other fields) [35].

Several studies have emphasized the prognostic significance of the morphology of positive groin nodes, particularly the size of the metastasis and the presence or absence of extracapsular spread [36–38].

Patients with one small lymph node metastasis do not appear to benefit from adjuvant radiation therapy; several series suggest that their prognosis is good after inguinofemoral lymphadenectomy alone [37–39], but the number of patients in most series is too small to draw definitive conclusions. A multicenter Dutch study of 75 patients with vulvar cancer and one positive lymph node of all sizes reported that adjuvant radiation was only beneficial if extracapsular spread was present [40].

Reasonable indications for bilateral pelvic and groin irradiation in patients with positive groin nodes would be:

- The presence of extracapsular spread.
- Two or more positive groin nodes. **Level of Evidence B**

An ongoing international prospective observational trial (GROINSS-V II) is investigating the efficacy of groin radiation, without inguinofemoral lymphadenectomy, for patients with a single positive sentinel lymph node 2 mm or less in diameter. Pending the results of this study, all patients who have had a sentinel lymph node biopsy and are found to have one or more positive nodes should be treated with a full inguinofemoral lymph node dissection, followed by radiotherapy to the groins and pelvis if indicated.

4.5.4.5. Radiation fields and doses. In most cases, fields should include the inguinofemoral, external iliac, and internal iliac lymph nodes. The upper border may be extended if there is extensive inguinal involvement or suspicion of pelvic node metastasis.

One of a variety of radiation techniques can be selected, depending on the patient's body habitus and extent of disease. Treatments should always be based on three-dimensional planning using high-quality CT or MRI images.

Combined photon and electron techniques are often used to treat the regional nodes, without overdosing the femoral heads. Care must be taken to completely include both the superficial and deep inguinal

lymph nodes. In thin patients, care must be taken to avoid underdosage of superficial inguinal nodes by high-energy photon beams. If electron beams are used, the energy must be sufficient to cover the femoral nodes. In recent years, some clinicians have begun to use intensity-modulated radiation therapy (IMRT) or other inverse-planned, computer-controlled delivery techniques to treat vulvar cancer. Although these techniques can reduce acute radiation effects in skin and soft tissue, the treatment planning and delivery are complex, and the opportunity for unanticipated underdosage of the target is substantial, suggesting that these cases may be best treated by clinicians who have considerable specialized expertise.

The dose of radiation is determined by the initial extent of regional disease and any known residual. After a groin dissection with microscopic inguinal metastases, 50 Gy in 1.8–2.0 Gy fractions is usually sufficient.

If there are multiple positive nodes or if there is evidence of extracapsular extension, doses up to 60 Gy may be given to a reduced volume. Gross residual disease usually requires 60–70 Gy to achieve a high probability of regional disease control.

The effectiveness of concurrent chemotherapy in the treatment of groin and pelvic lymph nodes is unknown.

4.5.5. Advanced vulvar cancer

Patients with primary tumors extending beyond the vulva, or bulky positive groin nodes are considered to have advanced vulvar cancer. For such patients, multimodality treatment planning is particularly important.

4.5.5.1. Management of groin lymph nodes. It is desirable to determine the status of the groin nodes prior to planning the overall treatment [3]. Pelvic CT or MRI should be part of the patient's initial workup. These studies are particularly helpful in suggesting the extent of inguinal or pelvic lymphadenopathy (Fig. 3). Pelvic MRI can also provide useful information about the anatomical extent of the primary lesion, but is not mandatory.

If there are no suspicious nodes in the groin on CT scan, bilateral inguinofemoral lymphadenectomy may be performed. If final histologic assessment reveals positive nodes, adjuvant radiation to the groin and pelvis should follow the guidelines given for early stage disease. If the nodes are negative, groin and pelvic radiation may be eliminated.

Alternatively, primary chemoradiation therapy may be used to treat the primary tumor as well as the groin and pelvic nodes if surgery is deemed inappropriate for the individual patient [32,33].

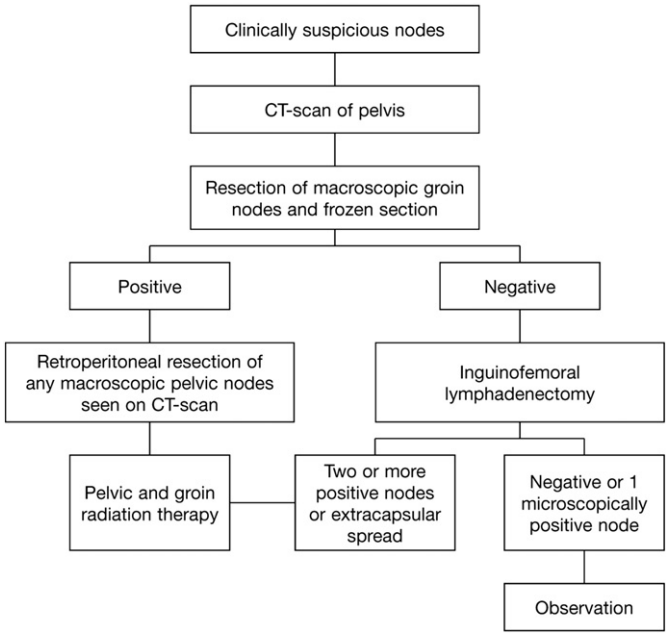

Fig. 3. Management of clinically suspicious groin nodes.

If nodes are clinically positive, a complete lymphadenectomy should be avoided because full groin dissection together with postoperative groin irradiation may result in severe lymphedema. Only enlarged nodes from the groin and pelvis should be removed if feasible, and the patient given postoperative groin and pelvic radiation [41]. **Level of Evidence C**

If there are ulcerated or fixed groin nodes, they should be resected if not infiltrating muscle or femoral vessels, as determined by imaging studies. If nodes are not felt to be resectable, they should be biopsied to confirm the diagnosis then treated with primary radiation, with or without chemotherapy. If appropriate, the nodes may be resected following radiation if there has been an incomplete response (Fig. 4) [42]. **Level of Evidence C**

4.5.5.2. Management of the primary tumor (Fig. 5). If it is possible to resect the primary lesion with clear surgical margins and without sphincter damage leading to urinary or fecal incontinence, primary surgical excision is usually the preferred treatment. It usually follows dissection of the groins, although this is not mandatory.

If primary surgery would result in the need for a bowel or urinary stoma, it is preferable to employ primary radiation therapy, sometimes followed by a more limited resection of the residual tumor or tumor bed [43,44].

Chemoradiation has been used extensively for large lesions if surgical resection would damage central structures (anus, urethra); durable complete responses without the need for post-treatment surgery have been well described [45–49].

The groin nodes and pelvis may need to be included in the treatment field depending on the status of the groin nodes, as determined initially.

Treatment with neoadjuvant cisplatin and 5-fluorouracil, or other drug combinations, has been reported in small retrospective studies to be effective for preservation of the anal sphincter and/or urethra in patients with advanced vulvar cancer [50,51]. This approach deserves further clinical research.

4.5.5.3. Radiation protocol. If the groin nodes are positive and meet the requirements described earlier for adjuvant radiation, the initial radiation treatment fields should include the pelvis, inguinal nodes, and primary site, which are treated to a total dose of at least 50 Gy. Care must be taken to adequately cover the inguinal nodes.

Some clinicians prefer to treat in an open-leg position but care must be taken to apply bolus to the vulva to avoid underdosage of potentially involved skin regions.

Areas of gross disease or particularly high risk are usually boosted either with appositional fields of electrons selected to provide an adequate dose to the surface and at depth, or with conformal external beam therapy. Gross vulvar disease probably requires 60–70 Gy to achieve local control, although investigators are currently exploring

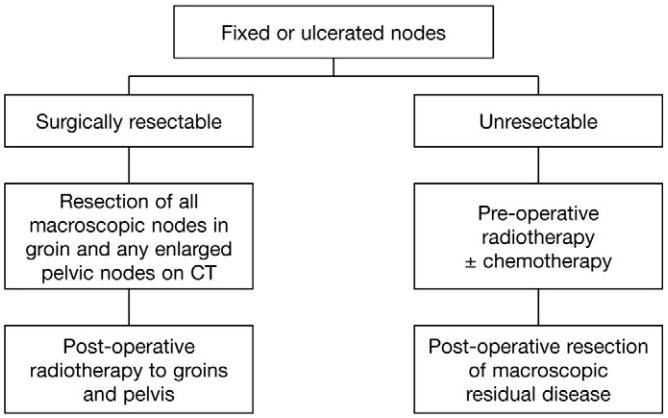

Fig. 4. Management of clinically obvious groin nodes.

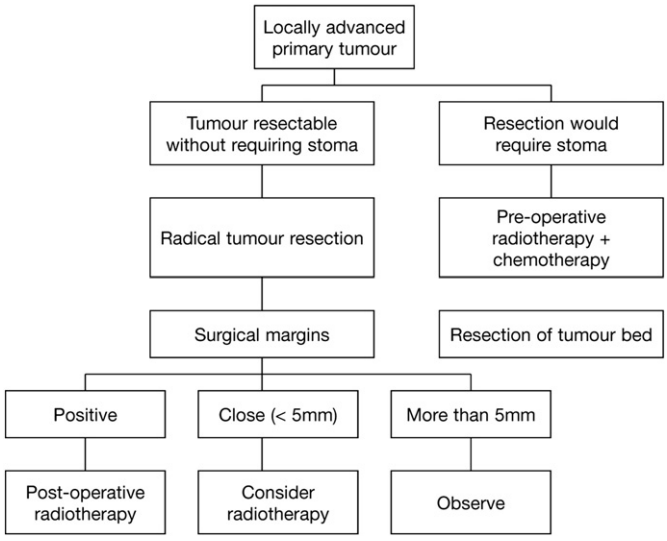

Fig. 5. Management of advanced primary tumor. Treatment should usually follow dissection of the groins. Groin and pelvic radiation should follow standard indications.

a wide variety of chemoradiation schedules, and the relationship between dose and local control remains somewhat uncertain. **Level of Evidence C**

4.5.5.4. Close surgical margins. Most recurrences from vulvar cancer occur on the vulva. Rouzier et al. [52] described two types of local recurrences, those at the primary site and those at a remote site. In an analysis of patients with vulvar cancer from the Royal Hospital for Women in Sydney [13], primary site recurrences occurred with a median disease-free interval of 21 months, and were associated with a histological margin of 8 mm or less, as previously reported [16 — 18]. Remote site recurrences occurred with a median disease-free interval of 69 months, and were more commonly associated with lichen sclerosus. Although some recent papers have not found an association between margin distance and local recurrence, these papers have not distinguished primary from remote site recurrences [53,54].

Postoperative radiation is of benefit for patients with close surgical margins (less than 5 mm), if the margins cannot be re-excised [55]. A recent study of 205 patients with vulvar cancer from Boston reported that the highest risk of vulvar recurrence was associated with margins of 5 mm or less ($P = 0.002$), and that patients who received a dose of more than or equal to 56 Gy had a lower risk of relapse than those who received less than or equal to 50.4 Gy ($P < 0.05$) [56].

In some cases, the positive margin may be boosted with brachytherapy, although this technique requires experience to avoid an excessive risk of necrosis. Alternatively, the operative bed may be treated with an appositional electron field or in some cases, carefully planned conformal external beam irradiation. **Level of Evidence C**

5. Special situations

5.1. Vulvar melanoma

Vulvar melanoma is the second most common neoplasm of the vulva. The majority of lesions involve the clitoris or labia minora. The Clark or Breslow modifications to the micro staging system should be used for the staging of vulvar melanoma rather than the more common TNM/FIGO system. These systems measure the depth of invasion in terms of the descriptive histology of the skin.

Any pigmented lesion on the vulva should be excised for diagnosis unless it has been known to be present and unchanged for some years.

In line with trends toward more conservative surgery for cutaneous melanomas, there is a trend toward more conservative resection of vulvar melanomas [57–59]. Primary lesions should be treated by radical local excision, with margins around the lesion of at least 1 cm. **Level of Evidence C**

The role of node dissection is also controversial, but the Intergroup Surgical Melanoma Program has conducted a prospective, multi-institutional randomized trial of elective node dissection versus observation for intermediate thickness cutaneous melanomas (1–4 mm) [60]. There were 740 patients entered into the trial, and elective node dissection resulted in a significantly better survival for patients 60 years of age or younger, patients with tumors 1–2 mm thick, and patients without tumor ulceration.

5.2. Bartholin's gland cancer

Cancers arising in the Bartholin's gland may be either transitional or squamous types, arising from the duct, or an adenocarcinoma from the gland itself. Adenoid cystic and adenosquamous variants have also been reported. Adenocarcinomas of the vulva occur, on average, approximately a decade earlier than invasive squamous cancers. Frequently, diagnosis is made after resection of what was thought to be a persisting Bartholin's cyst.

The standard approach for Bartholin's gland carcinomas has been radical vulvectomy and bilateral groin dissection. However, ipsilateral groin dissection and radical hemi-vulvectomy may be equally effective for early lesions [61]. Because these lesions are deep in the ischiorectal fossa, surgical margins are more likely to be close, particularly for bulky lesions, and postoperative radiation to the vulva may decrease the likelihood of local recurrence [61]. **Level of Evidence C**

If the ipsilateral groin nodes are positive, bilateral groin and pelvic radiation may decrease regional recurrence.

For adenoid cystic lesions, radical local excision alone is the treatment of choice, with adjuvant local radiation recommended for positive margins or perineural invasion [62]. **Level of Evidence C**

5.3. Paget's Disease

This is predominantly an intraepithelial lesion, but on occasion it may be associated with an underlying invasive adenocarcinoma. It is usually of primary cutaneous origin from the vulva, but may be secondary to an anorectal, urothelial, or noncutaneous genital tract carcinoma (e.g. endocervical or endometrial) [63].

The disease occurs predominantly in the menopausal or postmenopausal population. Most patients will present with vulvar discomfort and itching and on examination, an eczematoid, weeping lesion is often seen. Diagnosis is usually confirmed by biopsy, which will generally differentiate an intraepithelial from an invasive lesion [3,64].

Intraepithelial Paget's disease requires superficial local excision. It is difficult to obtain clear margins with this disease, as often the underlying histologic change will extend far beyond the macroscopic lesion. More recently, there has been a move to perform less radical resection for intraepithelial lesions, with re-excision at a later date should lesions become symptomatic or clinically visible [65]. Lesions that involve or extend into the urethra or anus can be particularly difficult to manage, and may require laser therapy.

If there is an underlying adenocarcinoma, the invasive component should be treated by radical local excision with margins of at least 1 cm. At least an ipsilateral inguinofemoral lymphadenectomy should be performed for unilateral lesions, with adjuvant radiation following the same indications as for squamous carcinomas [66]. **Level of Evidence C**

6. Pathology

The surgical specimen should be correctly orientated and photographed. Photographs should be used to indicate the origin of tissue blocks. The size of the specimen should be measured and the

dimensions of any visible tumor measured. The macroscopic tumor-free surgical margins should be measured. Sections are taken through the tumor to measure tumor depth. Sections should be taken from urethral, anal, and vaginal resection margins.

Lymph nodes should be carefully dissected out and the site from which they are removed recorded. A full cross-section of each lymph node should be embedded.

The following histological points should be noted:

(a) Tumor type: keratinizing, basaloid, bowenoid.
(b) Depth of invasion: measured from the epithelial–stromal junction of the adjacent dermal papilla to the deepest point of invasion by the tumor.
(c) Tumor grade.
(d) Histological measurement of tumor-free margins and statement as to whether the tumor is completely excised.
(e) Presence or absence of perineural or vascular space invasion.
(f) Nature of the adjacent nonmalignant squamous epithelium: VIN, lichen sclerosus, squamous hyperplasia, HPV-associated changes.
(g) Sites and number of nodes examined and number of positive nodes. Presence or absence of extracapsular extension.

Conflict of interest

The authors declare that they have no conflicts of interest.

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