# IV) Vulval Cancer – Clinical Guideline

UHDB/GYNONC/09:22/O3

1.1

## Suspected vulva malignancy

(vulva swelling/polyp/lump/ulcer/suspicious groin nodes etc)

General Examination
Pelvic Examination
*2 week wait Cancer referral*

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**Refer to cancer unit or cancer centre**

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**Suspicious of malignancy in cancer unit**

No

In or Outpatient biopsy

+/- Colposcopy

Benign

↓

Management continues in cancer unit

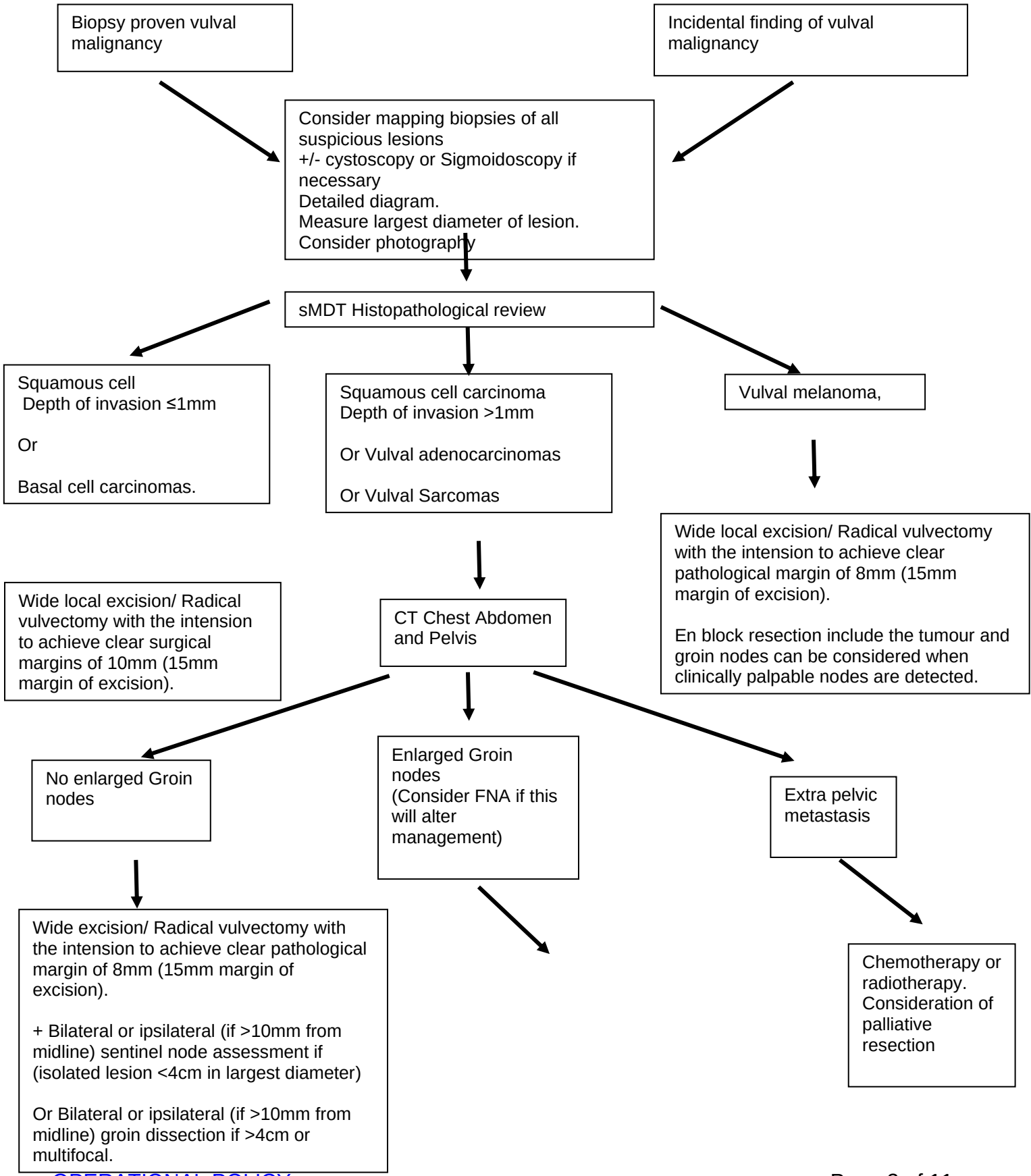
Yes

Outpatient biopsy & Prompt referral to cancer centre
Do not delay referral to obtain biopsy.
(See section 1.2)

Malignant

***If at any stage concerns regarding malignancy refer to cancer centre***

Section 1.2


Biopsy proven vulval malignancy
Incidental finding of vulval malignancy
Consider mapping biopsies of all suspicious lesions
+/- cystoscopy or Sigmoidoscopy if necessary
Detailed diagram.
Measure largest diameter of lesion.
Consider photography
sMDT Histopathological review
Squamous cell
Depth of invasion ≤1mm
Or
Basal cell carcinomas.
Squamous cell carcinoma
Depth of invasion >1mm
Or Vulval adenocarcinomas
Or Vulval Sarcomas
Vulval melanoma,
Wide local excision/ Radical vulvectomy with the intension to achieve clear pathological margin of 8mm (15mm margin of excision).
En block resection include the tumour and groin nodes can be considered when clinically palpable nodes are detected.
Wide local excision/ Radical vulvectomy with the intension to achieve clear surgical margins of 10mm (15mm margin of excision).
CT Chest Abdomen and Pelvis
No enlarged Groin nodes
Enlarged Groin nodes
(Consider FNA if this will alter management)
Extra pelvic metastasis
Wide excision/ Radical vulvectomy with the intension to achieve clear pathological margin of 8mm (15mm margin of excision).
+ Bilateral or ipsilateral (if >10mm from midline) sentinel node assessment if (isolated lesion <4cm in largest diameter)
Or Bilateral or ipsilateral (if >10mm from midline) groin dissection if >4cm or multifocal.
Chemotherapy or radiotherapy.
Consideration of palliative resection

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|---|
| Wide excision/ Radical vulvectomy with the intension to achieve clear pathological margin of 8mm (15mm margin of excision).<br><br>+ Bilateral/ipsilateral Resection of bulky nodes |

*In lateral tumours. If Ipsilateral groin dissection is +ve then completion contralateral groin dissection should be performed. If Ipsilateral Sentinel node is positive, Bilateral groin dissection should be performed.

# Vulva Cancer

## General

The flow diagrams enclosed act as a guide for referral and management of patients with suspected vulval cancer. Specific referral pathways are available regarding the primary care team to unit level gynaecological oncology and from unit level to cancer centre.

1. Primary Care Team Management.

1.1 All patients with suspected vulval cancer should be referred on the 2-week wait form.

2.1 Suspicious features of vulval cancer include:-

swelling, polyp or lump, an ulcer, colour change (whitening or pigment deposition), elevation or irregularity of the surface contour. Any ‘warts’ in a postmenopausal woman or persistent ‘warts’ in the premenopausal woman.

2. Hospital Assessment.

1.1 All patients with perceived vulval cancer should outpatient biopsy or an examination under anaesthesia with appropriate biopsies. The biopsy should be incisional with a depth greater than 1mm, not removing the entire lesion and include an area of epithelium where there is a transition of normal to abnormal tissue. If possible, the lesion should be photographed and following this the case discussed at the Multi-Disciplinary Team Meeting. In exceptional circumstances if excision is being performed to obtain diagnosis or palliate symptoms, this should be non-radical in nature to allow subsequent sentinel node assessment from the scar if applicable. If more than one lesion is present, each individual biopsy should be sampled separately, sent in separate pots and carefully labelled, so that lesion site can be identified at a later date.

2.1 All women diagnosed with vulval cancer >1mm in depth require:-

CT of chest abdo, pelvis and groins

3.1 The following investigations may be useful:

MRI pelvis to assess Loco-regional disease
FNA of suspicious nodes if node posititive may alter management.

4.1 For Vulval melanomas the additional investigations required are:

CT or MRI head

3. Staging.

1.1 The staging of vulva cancer is according to FIGO classification. (See appendix A) It is predominantly surgical.

2.1 Full histological assessment should include:-

- Histological sub-type of cancer.
- Grade of tumour.
- Exact dimensions of tumour, including accurate measurements of disease free margins.
- Depth of invasion
- Lymphovascular and/or perineural invasion (PNI)
- Preoneoplastic and non-neoplastic disease
- p16/p53 status

3.1 Nodal assessment should include the following:

Macrometastasis: >2 mm;
Micrometastasis: >0.2 mm to ≤2 mm;
ITC – individual tumour cells – microscopic clusters and single cells </= 0.2 mm

4. Surgical Management.

4.1.1 Surgery should be considered the mainstay of treatment for this disease, irrespective of the age and medical condition of the patient involved.

4.1.2 Vulva cancers require a radical wide local excision with a 15mm surgical margin (to ensure a 8mm margin at histological analysis) around the tumour. Biopsies and removal of suspicious areas should be considered at that time. However the most important prognostic marker is the clear resection margins. Vulval recurrence is more often a new primary tumour within an area of field change as indicated by the presence of lichen sclerosus or VIN at the margins.

4.1.3 If invasion is greater than 1mm in depth, then appropriate inguinal femoral assessment should be performed. The laterality of the lymph node assessment will be decided upon at the Multi-Disciplinary Team Meeting. Tumours with a medial border more then 10mm from the midline should be treated with ipsilateral lymph node assessment alone, tumours with a medial border within 10mm of midline need bilateral lymph node assessment by either the sentinel node technique or inguinal femoral groin dissection

4.1.4 If margins are involved after primary excision repeat excision should be considered.

4.1.5 Sentinel node assessment should be used for patients with:

- Primary squamous cancers measuring less than 4 cm in maximum dimension
- Macroscopic unifocal cancers
- No clinical or radiological evidence to suspect lymph node metastasis
- No known safety issues for the use of Patent Blue dye and/or technetium-99

This should be performed using both a radioactive tracer and blue dye. If a sentinel node is not found an inguinal femoral groin dissection should be performed on that side. If a histologically positive sentinel node is identified an inguinal femoral groin dissection should be performed on both sides.

In patients with micro-metastasis (≤2 mm) in the Sentinel node Radiotherapy is an acceptable alternative to groin lymphadenectomy. In those with macro-metastasis (>2 mm) bilateral groin lymphadenectomy is recommended

4.1.6 All tumours ≥4cm in size or multifocal in nature require an inguinal femoral groin dissection

4.1.7 In cases with large primary lesions and clinically suspicious nodes, a radical vulvectomy with ‘en bloc’ groin node dissection can be considered.

4.1.8 Enlarged nodes should be debulked. Ideally all nodes >2cm should be removed prior to radiotherapy.

4.1.9 In cases with fixed or ulcerated groin nodes, surgery and/or radiotherapy should be considered. Pathological assessment of these nodes should be undertaken prior to radiotherapy, preferably by fine-needle aspiration cytology, in order to maximise the chances of maintaining skin integrity and minimising the risk of wound problems.

4.1.10 In tumours which arise in a background of dVIN or Paget’s disease, consideration should be given to excising the whole of the abnormal area, although with lesser radicality, if feasible.

4.1.11 Surgery rarely has a role in Stage 4 disease. Palliative procedures may be considered to ease discomfort, which is otherwise difficult to control. In cases of fistulation of the tumour to bowel or bladder, de-functioning stomas and/ or urinary diversions or nephrostomies can be considered.

5. Radiotherapy.

1.1 Neo-adjuvant chemoradiation or primary radiation may be preferable in a few selected cases of vulval cancer involving the urethra or anus to down-stage the

tumour and limit the required surgical resection. These cases need to be discussed in length and detail at the Multi-Disciplinary Team Meeting.

2.1 Radiotherapy should start as soon as possible ideal within 6 weeks of surgical treatment.

3.1 Adjuvant radiotherapy should be considered when:-

- Surgical margins are involved and no further surgical excision is performed.
- When 2 or more lymph nodes are involved with metastatic disease or extra capsular spread is seen.
- When pathological margins are close (<2mm) but clear margins radiotherapy can be considered to reduce local recurrence

Adjuvant radiotherapy for metastatic groin nodes should include the ipsilateral groin area and where pelvic nodes are non-suspicious on imaging, the distal part of the iliac nodes with an upper limit at the level of the bifurcation of the common iliac artery

At least 50 gys using a conformal and planned approach. Radical treatment will usually require (50 Gys) to be delivered to the primary and nodal sites and consideration can be given to integral boost. The total prescribed dose is determined by the clinical context.

In advanced or irresectable disease, concurrent radiotherapy or chemo-radiation (if patients are fit enough) to vulva and lymphatic drainage areas can be given depending on the clinical context.

In all situations chemoradiation is a viable alternative to radiation treatment.

6. <u>Recurrent Disease.</u>

1.1 Restaging with CT Chest Abdo Pelvis or PET CT should be performed.

2.1 Possible options include:
• Further surgery
• Radical radiation therapy with or without chemotherapy
• Neoadjuvant chemotherapy followed by tailored therapy
• Palliative radiotherapy
• Palliative chemotherapy
• Novel approaches including immunotherapy
• Best supportive care

3.1 Local recurrence is usually managed by further local excision. Radiotherapy or chemoradiotherapy may be considered with a wide recurrent lesion if no radiotherapy previously given.

4.1 If depth of invasion is >1mm and previous sentinel node assessment has been performed a formal inguinal femoral groin dissection should be performed.

5.1 Groin recurrence may be managed by both surgery and radiotherapy (if not previously used). In irresectable disease chemo-radiation can be considered.

7. Rare cancers

1.1 **Carcinoma of the Bartholin gland**

2.1 These tumours arise from the Bartholin glands or their ducts, and classification is based on Honan's criteria. The tumour must be: in the correct position; deep in the labium majora; have normal overlying skin; and there should be some normal gland present. There can therefore be a variety of histological types of Bartholin gland carcinomas including: adenocarcinoma; squamous carcinoma; and transitional cell carcinoma.

3.1 MRI Pelvis many be useful to identify loco-regional involvement and plan surgery.

4.1 Carcinoma of the Bartholin's gland is more commonly associated with metastatic disease at presentation with 60% presenting with stage III/IV disease

5.1 There is no current data regarding the use of sentinel node biopsy, hence inguinofemoral lymphadenectomy is recommended for the management of the groins

6.1 Recommended treatment is wide local excision, with lymphadenectomy and where indicated, radiotherapy to the vulval and regional lymph nodes. Post-operative radiotherapy reduced the local recurrence rate from 27% to 7%.

7.1 **Basal cell carcinoma and verrucous carcinoma**.

8.1 These rarely metastasis to the lymphnodes and can be managed by radical excision alone. Basal cell carcinomas are radio sensitive and primary radiotherapy can be utilised if surgical resection is likely to impact on sphincter function. No preoperative imaging is required. Groin resection should only be considered if pathological nodes are present.

9.1 **Malignant melanoma**

10.1 Malignant melanoma is the second most common vulval malignancy after squamous cell carcinoma, representing 7-10% of all vulval cancers. Relapse rates are high and correlate with the depth of invasion (Breslow thickness).

11.1 Tumor size is the only significant prognostic factor for local recurrence (P = 0.003). Width of margins, lymphadenectomy rate, adjuvant treatment are not associated with recurrence or overall survival

12.1 All vulval melanoma should be discussed in both the gynaecology specialist MDT and the melanoma MDT.

13.1 Inguino-femoral lymphadenectomy has not been shown to improve survival. Sentinel lymph node detection has been used in vulval melanoma and may influence treatment choices. If clinical involved nodes traditionally an enbloc resection with tumour is performed.

14.1 Immunotherapy (Nivolumab) improves recurrence-free survival for patients with node-positive surgically resected melanoma.

15.1 Surgical resection of involved regional nodes may be considered for palliation and improve quality of life.

16.1 Surgical management should consist of a wide local excision to achieve margins free of microscopic disease by >1 mm (R0) in the least radical fashion. There is no evidence that more radical surgery is beneficial. If margins are microscopically involved (R1), further salvage surgery is normally recommended. If this is not possible, or is declined, options involve:

- Watch and wait, treating recurrences as identified and appropriate at the time
- Adjuvant radiotherapy with the aim of reducing local recurrence;
- Systemic therapy.

17.1 **Pagets disease of the vulva**

18.1 Vulval Paget's Disease (VPD) is a rare disease with only few case series presented in the literature.

19.1 VPD may be asymptomatic or present with itching, burning and irritation. VPD classically presents as an erythematous plaque with white scaling, called "cakeicing scaling". However, it can present with a variety of colours with nodules or plaque-like disease at presentation.

20.1 Whilst traditionally the VPD had been considered and associated malignancy a whole search for cancer has been now shown not to be necessary.

21.1 Treatment for VPD consists mainly of surgery +/- lymphadenectomy, if there is evidence of >1 mm depth of invasion.

22.1 Recurrent disease is common (60-70%) and is as frequent in those with microscopically clear margins compared to those with involved margins. (88). Further excision may not reduce the risk of recurrence and alternatives, including imiquimod or watchful waiting, should be strongly considered, if invasion is excluded. There are no data regarding the safety or effectiveness of sentinel lymph node biopsy in VPD with evidence of invasion >1 mm and at present lymphadenectomy, whether ipsilateral or bilateral, depending on position, would be recommended.

8. Follow Up

Refer to Appendix X (Follow up)

## Appendix A. FIGO Staging ( 2021)

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|---|---|
| Stage I: | Tumour confined to the vulva |
| Stage IA: | Tumour confined to vulva ≤2cm in diameter and invasion ≤1mm depth. |
| Stage IB: | Tumour confined to vulva > 2cm in diameter or with invasion >1mm depth. |
| Stage II: | Tumour of any size with invasion into perineal structures (lower 1/3 urethra/ lower 1/3 vagina/ 1/3 lower anus), with negative nodes. |
| Stage III: | Carcinoma extends to adjacent perineal structures and/or any number of nonfixed, nonulcerated lymph node/s. |
| Stage IIIA | Tumour of any size with extension to upper part of adjacent perineal structures, or with any number of nonfixed, nonulcerated lymph node.<br>Tumour of any size with disease extension to upper two-thirds of the urethra, upper two-thirds of the vagina, bladder mucosa, rectal mucosa, or regional lymph node metastases ≤5 mm |
| Stage IIIB | Regional lymph node* metastases >5 mm |
| Stage IIIC | Regional lymph node metastases with extracapsular spread |
| Stage IV | Carcinoma has extended beyond the true pelvis |
| Stage IVA: | Disease fixed to pelvic bone, or fixed or ulcerated regional lymph node metastases |
| Stage IVB: | Any distant metastasis |

FIGO 2021 – The depth of invasion is measured from the basement membrane of the deepest, adjacent, dysplastic, tumour-free rete ridge (or nearest dysplastic rete peg) to the deepest point of invasion.

Sources

ESGO Vulvar cancer guidelines. 2016

RCOG/BGCS Guidelines for the Diagnosis and Management of Vulval Carcinoma May 2014

BAGP 2021 FIGO Staging System for Vulvar Cancer: Summary and comparison with 2009 FIGO Staging System

British Gynaecological Cancer Society (BGCS) Vulval Cancer Guidelines: Recommendations for Practice (2020)

Radiotherapy Versus Inguinofemoral Lymphadenectomy as Treatment for Vulvar Cancer Patients With Micrometastases in the Sentinel Node: Results of GROINSS-V II (2021)

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