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CURRENT CHALLENGES AND TREATMENT STRATEGIES FOR VULVAR CANCER: DIAGNOSIS, THERAPY, AND PREVENTION

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ABSTRACT

Introduction and purpose: Vulvar cancer is a rare malignancy of the female genital tract. However, due to the increasing incidence of Human Papillomavirus (HPV) infections, there's a growing trend of this cancer affecting younger women. Often, misdiagnosis leads to delayed detection, resulting in a poor prognosis.

The aim of this study is to review the current literature concerning the epidemiology, incidence, trends, risk factors, diagnosis, and treatment of vulvar cancer, in accordance with the latest ESGO 2021 guidelines.

Description: This review provides a comprehensive overview of available treatment modalities, including surgical cytoreduction, chemotherapy, and emerging therapies such as immunotherapy and cancer vaccines. The importance of interdisciplinary care is highlighted, alongside the critical role of prevention and patient education in mitigating cancer risk.

Summary: Despite diagnostic and therapeutic challenges, the overall prognosis for patients with vulvar cancer remains generally favorable. Nevertheless, disease recurrence—though associated with relatively low mortality—requires increased clinical vigilance. Therefore, patient education on the importance of regular monitoring during remission is essential.

KEYWORDS

Vulvar Neoplasms, Vulvar Cancer, FIGO Cancer Report, Cancer Staging, Chemotherapy, Radiotherapy, Cancer Risk Factors, Guidelines, Review Literature

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Introduction and purpose

Vulvar cancer is diagnosed in approximately 6,000 individuals annually in the United States and around 45,000 cases worldwide each year. These figures indicate that vulvar cancer accounts for approximately 0.3% of all cancers and 4% of malignant tumors of the female genital tract. The number of deaths due to vulvar cancer is estimated at about 1,500 per year in the United States and approximately 17,000 globally [1-5].

A global trend has been observed toward an increasing incidence of this malignancy and its diagnosis at a younger age, which is attributed to the rising prevalence of HPV infections [1-2].

The most common histological type of vulvar cancer is squamous cell carcinoma, which accounts for approximately 80% of all cases. The second most frequent type is melanoma. Other, less common types include:

- Basal cell carcinoma
- Verrucous carcinoma
- Adenocarcinoma associated with extramammary Paget's disease (primary or secondary to rectal/genital adenocarcinoma)
 - Bartholin gland carcinoma (squamous cell, adenocarcinoma, or transitional cell carcinoma) – accounting for about 5% of vulvar cancer cases
- Sarcomas [1,6-8].

Squamous Cell Carcinoma

This malignancy is typically preceded by precancerous lesions:

- Usual-type VIN (uVIN), formerly VIN II and VIN III
- Differentiated-type VIN (dVIN), formerly referred to as VIN simplex

These forms differ in prevalence, etiology, and the risk of malignant transformation. uVIN is usually HPV-related, commonly associated with HPV types 16, 18, and 33, and occurs in younger women, around the age of 40. The risk of progression to invasive squamous cell carcinoma is approximately 20%.

dVIN accounts for about 5% of all VIN cases and is more often associated with vulvar dermatoses such as lichen sclerosus. It typically occurs in postmenopausal women over the age of 60 and carries a significantly higher risk—around 80%—of progression to vulvar carcinoma compared to uVIN [8-13].

Melanoma

The precancerous lesion for melanoma is melanoma in situ. It is characterized by a poor prognosis (15% of cases). The American Joint Committee on Cancer (AJCC) classification system is recommended over the FIGO system. Testing for c-kit and BRAF mutations is also advised [1].

Risk Factors

Age is a significant risk factor, especially for women over 60. Other important risk factors include:

- Infection with HPV, particularly types 16 and 33
- HIV infection
- Tobacco use
- Lichen sclerosus
- Chronic vulvar inflammation
- Immunodeficiency [2,14-16]

Epidemiological variations by region have been noted:

- In low-income countries, HPV-related cases are more common and occur at a younger age.
- In high-income countries, HPV-independent cases predominate and are more frequent in older women [14].

The majority of vulvar cancers occur on the labia majora and minora.

Tumors located on other vulvar structures, such as the clitoris, are rare and more frequently associated with melanoma than with squamous cell carcinoma [1]. HPV-negative lesions often present as solitary ulcers on the labia, whereas HPV-related lesions are usually multiple and multifocal [6].

Material and methods

This review was conducted based on an analysis of literature retrieved from PubMed. The following keywords were utilized during the search for relevant scholarly articles: "Vulvar Neoplasms," "Vulvar Cancer," "FIGO Cancer Report," "Cancer Staging," "Chemotherapy," "Radiotherapy," "Risk Factors," and "Guidelines." A total of 44 articles published between 1984 and 2025 were selected for inclusion and assessed for their direct relevance to the topic "Vulvar cancer – diagnosis and treatment in light of current ESGO guidelines."

Diagnosis of Vulvar Cancer According to ESGO Guidelines

The diagnostic process for vulvar cancer is multifaceted, involving a combination of thorough medical history, physical examination, advanced imaging techniques, and histopathological assessment. The absence of screening tests highlights the critical importance of clinical vigilance and prompt investigation of suspicious symptoms [1, 6].

Key components of patient evaluation include a detailed medical history and a careful physical examination of the vulva and inguinal-femoral lymph nodes. Additionally, photographs and precise documentation of any suspicious lesions are essential. Description should include lesion size, location, and whether it is solitary or multifocal.

Patients may be asymptomatic or present with symptoms such as vulvar pruritus, pain, a mass, or ulceration. Delayed diagnosis is common, often due to misinterpretation of symptoms as vulvovaginitis.

According to ESGO recommendations, the next steps include:

- Colposcopic examination
- Cervical cytology with HPV testing from the vagina or cervix [1,6,17]

Role of Biopsy in Histopathological Diagnosis

Every suspicious vulvar lesion should be biopsied for histopathological examination. Diagnosis is based on histological analysis of a biopsy or excised lesion. Biopsy is preferred over total excision, regardless of lesion size, as full excision may complicate further treatment planning.

Biopsy provides not only histological diagnosis but also assessment of prognostic markers such as p16, which is important in HPV-related squamous cell carcinoma. If p16 is negative, p53 immunohistochemistry should be performed.

Histopathological findings are classified using the FIGO (2021) and TNM staging systems. The AJCC classification should be used for melanoma [1, 6, 17].

Imaging Studies in the Diagnosis of Vulvar Cancer

Imaging plays an essential role in assessing disease extent and potential metastases. For pT1 tumors, imaging may be omitted. In all other cases, CT of the chest, abdomen, and pelvis or PET-CT is indicated. MRI is used to assess pelvic structures beyond the vulva, particularly in tumors \geq T2 or when findings are inconclusive [6, 17].

Treatment of Vulvar Cancer

The treatment of vulvar cancer is primarily based on surgical management. However, over the past two decades, the extent of surgical radicality has significantly evolved. In the past, the standard approach was radical vulvectomy combined with bilateral radical inguino-femoral lymphadenectomy, which was associated with a high risk of severe postoperative complications [18]. Currently, treatment selection is primarily guided

by the clinical stage of the disease, taking into account the FIGO classification, the patient's general health, age, as well as tumor location and size [19]. Treatment should be individualized and carried out by

a multidisciplinary team of specialists in an experienced, specialized oncological center with expertise in treating vulvar cancers. Early-stage vulvar cancer classified as stage IA is defined as a lesion ≤ 2 cm in diameter with stromal invasion ≤ 1.0 mm. The depth of invasion is assessed from the basement membrane of the deepest, adjacent, non-invasive dysplastic epithelium to the deepest point of tumor invasion. The key criterion for selecting a therapeutic strategy in cases of primary vulvar cancer lesions is the depth of stromal invasion determined by histopathological examination of the biopsy specimen. In cases where the invasion does not exceed 1 mm (T1a), the treatment of choice is wide local excision of the lesion with an adequate margin of healthy tissue. Additional inguinal lymph node removal is not necessary due to the very low risk of metastasis in this patient group. When stromal invasion exceeds 1 mm (T1b) or if the disease is classified as T2 (lesion ≤ 4 cm), further management depends on the tumor's proximity to the midline. For lesions located ≥ 2 cm from the midline, wide local excision or modified radical vulvectomy with sentinel lymph node biopsy (SLNB) on the side of the lesion is recommended. For midline lesions, wide local excision and bilateral sentinel lymph node biopsy are indicated [1]. The gold standard for treating early vulvar cancer remains surgical excision of the tumor with adequate margins of healthy tissue. Early vulvar cancers are defined as lesions confined to the vulva, without clinical, ultrasound, or radiologic evidence of regional lymph node metastasis. Radical vulvectomy is an oncologically equivalent alternative but is associated with a significantly higher risk of psychosexual complications, favoring less extensive surgical procedures in appropriately selected cases. The goal of surgery is to achieve a 2 cm surgical margin, which translates to a histopathological margin of at least 8 mm. However, newer data suggest that even with these margins, the risk of local recurrence is not completely eliminated, highlighting the importance of individualized treatment and close postoperative surveillance [20]. An integral part of vulvar cancer treatment is the assessment and treatment of regional lymph nodes, particularly the inguinal nodes, which are the primary route of metastasis and a significant prognostic factor. The preferred surgical approach involves separate incisions for tumor resection and lymphadenectomy, which improves wound healing and reduces complications. Standard management includes inguino-femoral lymphadenectomy, involving removal of both superficial and deep (femoral) inguinal lymph nodes. Depending on the clinical stage, adjuvant radiotherapy to the inguinal lymph nodes may be considered, especially from stage IB onward or in stage II with lymph node involvement [1]. In recent years, sentinel lymph node biopsy has become increasingly important in surgical treatment. It identifies the first draining lymph node from the tumor. Based on the GROINSS-V study and current guidelines, indications for SLNB include:

- Unifocal tumors confined to the vulva
- Lesions < 4 cm in diameter
- Stromal invasion > 1 mm
- No clinical or radiological signs of inguinal lymph node metastasis [1,21].

If the sentinel node contains metastases, there is a high risk that other nodes, including contralateral ones, are involved. In such cases, bilateral inguino-femoral lymphadenectomy is recommended to clear potential metastatic sites. The absence of metastases in the sentinel node, confirmed by histopathology, allows for the omission of radical inguinal lymphadenectomy, thereby reducing the risk of lymphatic complications such as lower limb edema or lymphocele [22,23]. A special subgroup consists of early-stage patients with positive inguinal lymph nodes, for whom adjuvant radiotherapy is recommended [24,25,26]. Indications for pelvic and inguinal radiation include:

- Extracapsular spread of cancer
- Two or more positive inguinal lymph nodes [27].

In patients with small vulvar tumors (up to 4 cm) and micrometastases (≤ 2 mm) in the sentinel node, inguinal radiotherapy can replace extensive lymph node dissection without increasing the recurrence risk [28]. When using external beam radiotherapy (EBRT), the radiation field should include inguino-femoral and external/internal iliac lymph nodes in most patients. In the presence of multiple or enlarged metastatic inguinal nodes, or suspected pelvic node involvement, the radiation field may need to be extended to include the pelvic region [29]. The radiation dose is determined based on the initial stage and any known residual disease [1]. For advanced vulvar cancer, assessment of inguinal lymph nodes is essential before therapeutic decisions. In patients with clinically suspicious lymph nodes, fine-needle aspiration (FNA) or surgical biopsy is recommended. Additionally, imaging techniques such as pelvic CT, MRI, and PET-CT are useful for assessing lymphadenopathy extent and detecting distant metastases [30]. If no suspicious nodes are found on clinical

exam or imaging, bilateral inguino-femoral lymphadenectomy may be considered. If nodes are confirmed to be metastasis-free, groin and pelvic radiotherapy is not necessary. In cases where metastases are confirmed histopathologically, adjuvant radiotherapy or chemoradiotherapy covering the groin and pelvic areas is recommended according to early-stage treatment protocols. For patients with clinically positive nodes, surgical removal of enlarged inguinal and pelvic lymph nodes is indicated when technically feasible, followed by postoperative radiotherapy to both areas. Complete inguinal lymphadenectomy is not advised due to the high risk of severe lymphedema when combined with radiotherapy. In cases of ulcerated or fixed inguinal lymph nodes, biopsy is recommended to confirm metastases, followed by primary radiotherapy with or without radiosensitizing chemotherapy. If the response to radiotherapy is incomplete, surgical removal of residual disease may be considered. An alternative strategy is neoadjuvant chemotherapy with cisplatin or carboplatin combined with paclitaxel to reduce nodal mass prior to planned radiotherapy [31,32,33]. For the primary tumor in advanced vulvar cancer, optimal management remains surgical removal with clear margins while sparing the anal sphincter if technically feasible. This approach provides local disease control and symptom relief (e.g., pain or discharge). When radical surgery would require pelvic exenteration and stoma formation, radiotherapy—alone or combined with chemotherapy—may be a more favorable option. Importantly, prognosis improves if the residual tumor is surgically removed after radiotherapy [33,34]. Concurrent chemoradiotherapy is a well-documented alternative for advanced vulvar cancer, especially in large tumors where primary resection would risk damaging central structures such as the anus or urethra. Cases of complete and durable responses to combined treatment have been reported. Depending on initial groin lymph node status, the radiation field may also need to cover inguinal and pelvic nodes. For advanced vulvar cancer requiring adjuvant radiotherapy due to inguinal node involvement, the field should include the vulva, inguinal nodes, and pelvic region [1,32,33,34]. The 2023 ESGO guidelines do not recommend the routine use of immunotherapy or targeted therapies in vulvar cancer. Their use should be considered individually, particularly in clinical trials or when standard treatments are insufficient. Decisions regarding these therapies should be made by a multidisciplinary team, considering patient-specific and tumor-specific factors [6].

Table 1. Treatment of Vulvar Cancer According to FIGO Stage [1].

FIGO Stage	Clinical Characteristics	Recommended Treatment
IA	Tumor ≤ 2 cm, stromal invasion ≤ 1 mm, no lymph node involvement	- Wide local excision with histologic margin ≥ 8 mm- No lymph node evaluation required
IB	Tumor > 2 cm or stromal invasion > 1 mm, no adjacent structure involvement	- Radical local excision or hemivulvectomy- Sentinel lymph node biopsy (SLNB) if tumor < 4 cm and lateralized- If SLNB is positive: <ul style="list-style-type: none"> • Metastasis ≤ 2 mm \rightarrow groin radiotherapy • Metastasis > 2 mm or extranodal extension \rightarrow inguinofemoral lymphadenectomy or radiotherapy to groin and pelvis
II	Tumor invades adjacent structures (lower urethra, vagina, anus), no lymph node involvement	- Radical vulvectomy- Resection of involved adjacent organs (e.g., partial vaginectomy, urethrectomy, proctectomy)- SLNB or inguinofemoral lymphadenectomy- Adjuvant radiotherapy if high-risk features present
III	Inguinal and/or femoral lymph node metastases	- Radical vulvectomy + inguinofemoral lymphadenectomy- Adjuvant radiotherapy to groin and pelvis (especially with > 1 positive node, metastasis > 2 mm, or extranodal extension)- Consider concurrent chemotherapy (e.g., cisplatin) as radiosensitizer
IVA	Invasion of upper urethra, bladder, rectum, pelvic bone or fixed/ulcerated inguinal nodes	- Definitive chemoradiation (cisplatin + EBRT)- Salvage surgery (e.g., pelvic exenteration) in select cases- Treatment individualized based on response
IVB	Distant metastases (e.g., lungs, liver)	- Palliative care- Systemic chemotherapy (e.g., paclitaxel + carboplatin)- Palliative radiotherapy- Symptom management and supportive care

Post-treatment Management and Long-term Care for Vulvar Cancer

Most recurrences of vulvar cancer occur within the first 1–2 years following completion of treatment; however, cases of disease recurrence beyond 5 years of follow-up have been reported in a significant number of patients [35]. Therefore, the implementation of long-term clinical surveillance is justified. Nonetheless, data regarding the optimal post-treatment surveillance strategy remain inconclusive [36]. Follow-up strategies should be individualized based on the patient's risk of recurrence and personal preferences. Clinical history and physical examination are recommended every 3–6 months for the first 2 years, then every 6–12 months for an additional 3 to 5 years, and annually thereafter. Patients at high risk of recurrence may benefit from more frequent monitoring (e.g., every 3 months during the first 2 years), while those at lower risk may be followed up at longer intervals (e.g., every 6 months). Annual cytological screening of the cervix and vagina, with optional human papillomavirus (HPV) testing, may be employed for early detection of lower genital tract dysplasia. However, their utility in identifying asymptomatic cancer recurrence is limited. Moreover, in patients who have previously undergone pelvic radiotherapy, cytologic interpretation may be confounded by radiation-induced morphological cell changes, potentially leading to false-positive results [37]. If abnormalities are detected on physical examination or if symptoms suggestive of recurrence arise, imaging studies such as computed tomography (CT) of the chest, abdomen, and pelvis; fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) of the neck, chest, abdomen, pelvis, and groins; or magnetic resonance imaging (MRI) of the pelvis should be performed. Additionally, laboratory testing including complete blood count, blood urea nitrogen (BUN), and creatinine levels is recommended [28,38]. An essential aspect of patient care involves education about signs and symptoms suggestive of recurrence or vulvar dystrophy, and encouragement of regular self-examinations. Counseling on a healthy lifestyle is also recommended, with emphasis on weight control, proper nutrition, physical activity, and sexual health—including the use of vaginal dilators and lubricants. Patients should also be encouraged to cease tobacco use and avoid psychoactive substances [39]. In cases of suspected local recurrence or distant metastases, further imaging studies such as CT or FDG-PET/CT and biopsy are necessary to confirm the diagnosis. Management of Recurrence Depends on Recurrence Site and Prior Treatments[1].

Local Recurrence Confined to the Vulva:

In patients with clinically localized vulvar recurrence and no evidence of lymph node involvement who have not previously received radiotherapy, the panel recommends surgical resection or radiotherapy as first-line treatment options. Surgery may include partial or total radical vulvectomy with unilateral or bilateral inguinofemoral lymphadenectomy (IFLN). The choice of subsequent therapy depends on surgical margin status and lymph node involvement [40]. In cases with negative margins and no nodal metastases, surveillance or external beam radiotherapy (EBRT) may be appropriate. For patients with positive margins but no nodal involvement, re-excision or EBRT—with possible addition of brachytherapy and/or concurrent chemotherapy (chemotherapy as a category 2B option)—may be considered. EBRT with concurrent chemotherapy is recommended in cases with positive lymph nodes and negative surgical margins. When both positive margins and nodal metastases are present, multimodal treatment—including EBRT, brachytherapy, concurrent chemotherapy, and/or re-resection—should be considered depending on clinical feasibility [40,41,42]. For patients who are not surgical candidates, management includes EBRT ± brachytherapy and/or concurrent chemotherapy. Surgical resection may be reconsidered if residual tumor is present. In cases of vulvar recurrence in previously irradiated patients, partial or total radical vulvectomy may be considered if clinically appropriate. Post-recurrence treatment should be followed by ongoing surveillance [40,43].

Confirmed Nodal or Distant Recurrence:

In patients with pelvic nodal involvement, distant metastases, or prior pelvic irradiation, systemic therapy and/or selective EBRT (if feasible) is recommended. In advanced cases, palliative care or best supportive care should be offered [43]. For recurrence limited to inguinofemoral (IF) or pelvic lymph nodes, surgical excision should be considered if clinically feasible. In selected cases of isolated IF or pelvic recurrence after prior radiotherapy, resection followed by systemic therapy may be appropriate. In patients who have not received prior radiotherapy, EBRT with or without concurrent chemotherapy may be employed. Regardless of treatment modality, patients should undergo continued follow-up after recurrence management [43,44]. Currently, there is no standard systemic treatment regimen for advanced or recurrent/metastatic squamous cell carcinoma (SCC) of the vulva. Treatment recommendations are primarily extrapolated from data on cervical,

anal, and other squamous cell carcinomas. Systematic reviews indicate several preferred first-line regimens, including cisplatin with paclitaxel, carboplatin with paclitaxel, and combinations including bevacizumab. Cisplatin, often used as a radiosensitizer in locally advanced vulvar cancer, is also recommended in both monotherapy and combination regimens for metastatic disease. Carboplatin serves as an alternative, supported by data suggesting non-inferiority in cervical cancer [43].

Melanoma Treatment

The treatment of choice for vulvar melanoma is wide local excision with a margin of ≥ 1 cm. Radical vulvectomy does not improve survival compared to organ-sparing surgery. The role of inguinal lymphadenectomy remains unclear, as no survival benefit has been demonstrated, although clinically suspicious lymph nodes must be removed. Sentinel lymph node biopsy is not currently considered standard care due to a high false-negative rate and the potential risk of local-regional recurrence. [1]

Vulvar Cancer Prevention

Primary Prevention

In the context of cervical precancerous lesions that increase the risk of developing cervical cancer, persistent infection with high-risk human papillomavirus (HPV), particularly type 16, plays a key etiological role. This infection is also associated with a long-term risk of developing high-grade squamous intraepithelial lesions (HSIL) and squamous cell carcinoma (SCC) of the vulva. Prophylactic HPV vaccination, a cornerstone of cervical cancer prevention strategies, has also been shown to reduce the incidence of precancerous lesions in other anogenital sites. This benefit is especially evident in women who have not been previously infected with oncogenic HPV types or types covered by the vaccine. In this population, vaccine efficacy exceeds 90% [45].

Secondary Prevention

Currently, there is no definitive evidence supporting the effectiveness of specific screening tests for vulvar cancer. However, women diagnosed with lichen sclerosus—a chronic dermatosis associated with an increased risk of vulvar cancer—should be educated and encouraged to perform regular vulvar self-examinations [46]. Early diagnosis is particularly important in patients presenting with symptoms such as chronic vulvar pruritus, or in those with clinically suspicious lesions, including pigmented changes or irregular ulcerations. In such cases, skin biopsy should be considered to exclude neoplasia.

Additionally, in women diagnosed with squamous intraepithelial lesions (SIL) of the cervix, vagina, or anus, a comprehensive vulvar examination should be an integral part of follow-up colposcopy [46,47].

Tertiary Prevention

Reducing the incidence of vulvar cancer relies heavily on the early identification and appropriate management of predisposing and precancerous lesions [45]. Currently, two main pathogenic pathways leading to vulvar squamous cell carcinoma (SCC) are recognized:

- Keratinizing SCC, which typically affects older women, often arises in the context of chronic dermatoses such as lichen sclerosus and/or differentiated vulvar intraepithelial neoplasia (dVIN).
- Warty and basaloid SCC, usually seen in younger women, is associated with persistent infection with oncogenic HPV types (particularly HPV 16, 18, 31, and 33). In this pathway, HSIL is considered the precursor lesion. These changes are often multifocal and may coexist with SIL in other areas of the lower genital tract (e.g., cervix, vagina, anus) [48].

Currently, no causal treatment exists for lichen sclerosus. Management includes avoidance of irritants (e.g., mechanical trauma, occlusive moist environments) and the use of potent or ultra-potent topical corticosteroids. In steroid-resistant cases, topical calcineurin inhibitors (e.g., tacrolimus), retinoids, or photodynamic therapy may be considered. Surgical intervention is generally reserved for cases involving functionally impairing scarring [46]. dVIN accounts for less than 5% of vulvar precancerous lesions but is associated with a significantly higher risk of progression to invasive carcinoma, a shorter time to progression, and a higher recurrence rate compared to HSIL. Unlike HSIL, dVIN is rarely associated with persistent HPV infection (less than 2%). The treatment of choice is surgical excision with 0.5–1 cm margins, allowing for thorough histopathological assessment and exclusion of occult invasion [46,49]. Multiple treatment options exist for HSIL. The most common is simple surgical excision with a 5 mm lateral and 4 mm depth margin, which allows for histological assessment of invasion. However, tissue loss may result in anatomical distortion

and psychosexual dysfunction, particularly in younger women. Alternative approaches that preserve anatomy, such as CO₂ laser therapy, do not permit histological margin assessment. Less invasive treatments, such as 5% imiquimod, are preferred for multifocal lesions, aiming to avoid scarring and sexual dysfunction [50].

Conclusions

Although vulvar cancer presents both diagnostic and therapeutic challenges, the overall outlook for patients is generally positive. Early diagnosis, combined with carefully chosen surgical and adjuvant treatments, often leads to favorable outcomes and extended survival. However, even though the mortality rate from recurrent disease is relatively low, the possibility of relapse should not be overlooked. Recurrence demands close attention from healthcare providers and consistent patient follow-up to ensure early detection and prompt management.

For this reason, educating patients about the necessity of regular follow-up appointments and ongoing self-monitoring during remission is vital. Patients need to understand that, even after successful treatment and the disappearance of symptoms, continued vigilance and adherence to scheduled check-ups remain crucial. This proactive approach enables early identification of any recurrence, greatly enhancing the effectiveness of subsequent treatment and minimizing complications. Ultimately, the best outcomes for vulvar cancer patients are achieved through a comprehensive strategy that integrates effective treatment, patient education, and systematic monitoring [1].

Disclosures

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REFERENCES

1. Olawaiye AB, Cuello MA, Rogers LJ. Cancer of the vulva: 2021 update. *Int J Gynaecol Obstet.* 2021 Oct;155 Suppl 1(Suppl 1):7-18. doi: 10.1002/ijgo.13881. PMID: 34669204; PMCID: PMC9298362.
2. Wei S, Li L, Yi T, Su L, Gao Q, Wu L, OuYang Z. Epidemiologic characteristics and a prognostic nomogram for patients with vulvar cancer: results from the Surveillance, Epidemiology, and End Results (SEER) program in the United States, 1975 to 2016. *J Gynecol Oncol.* 2023 Nov;34(6):e81. doi: 10.3802/jgo.2023.34.e81. Epub 2023 Jul 5. PMID: 37477104; PMCID: PMC10627757.
3. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin.* 2021 May;71(3):209-249. doi: 10.3322/caac.21660. Epub 2021 Feb 4. PMID: 33538338.
4. Alimena S, Sullivan MW, Philp L, Dorney K, Hubbell H, Del Carmen MG, Goodman A, Bregar A, Growdon WB, Eisenhower EL, Sisodia RC. Patient reported outcome measures among patients with vulvar cancer at various stages of treatment, recurrence, and survivorship. *Gynecol Oncol.* 2021 Jan;160(1):252-259. doi: 10.1016/j.ygyno.2020.10.022. Epub 2020 Nov 1. PMID: 33139040.
5. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. *CA Cancer J Clin.* 2021 Jan;71(1):7-33. doi: 10.3322/caac.21654. Epub 2021 Jan 12. Erratum in: *CA Cancer J Clin.* 2021 Jul;71(4):359. doi: 10.3322/caac.21669. PMID: 33433946.

6. Oonk MHM, Planchamp F, Baldwin P, Mahner S, Mirza MR, Fischerová D, Creutzberg CL, Guillot E, Garganese G, Lax S, Redondo A, Sturdza A, Taylor A, Ulrikh E, Vandecaveye V, van der Zee A, Wölber L, Zach D, Zannoni GF, Zapardiel I. European Society of Gynaecological Oncology Guidelines for the Management of Patients with Vulvar Cancer - Update 2023. *Int J Gynecol Cancer*. 2023 Jul 3;33(7):1023-1043. doi: 10.1136/ijgc-2023-004486. PMID: 37369376; PMCID: PMC10359596.
7. Michalski BM, Pfeifer JD, Mutch D, Council ML. Cancer of the Vulva: A Review. *Dermatol Surg*. 2021 Feb 1;47(2):174-183. doi: 10.1097/DSS.0000000000002584. PMID: 32947298.
8. Terlou A, Blok LJ, Helmerhorst TJ, van Beurden M. Premalignant epithelial disorders of the vulva: squamous vulvar intraepithelial neoplasia, vulvar Paget's disease and melanoma in situ. *Acta Obstet Gynecol Scand*. 2010 Jun;89(6):741-8. doi: 10.3109/00016341003739575. PMID: 20504079.
9. Voss FO, Thuijs NB, Vermeulen RFM, Wilthagen EA, van Beurden M, Bleeker MCG. The Vulvar Cancer Risk in Differentiated Vulvar Intraepithelial Neoplasia: A Systematic Review. *Cancers (Basel)*. 2021 Dec 7;13(24):6170. doi: 10.3390/cancers13246170. PMID: 34944788; PMCID: PMC8699429.
10. van de Nieuwenhof HP, van der Avoort IA, de Hullu JA. Review of squamous premalignant vulvar lesions. *Crit Rev Oncol Hematol*. 2008 Nov;68(2):131-56. doi: 10.1016/j.critrevonc.2008.02.012. Epub 2008 Apr 11. PMID: 18406622.
11. Skapa P, Robová H, Rob L, Zámečník J. Prekancerózní léze vulvy [Review of precancerous vulvar lesions]. *Cesk Patol*. 2012 Jan;48(1):15-21. Czech. PMID: 22716003.
12. Ayala M, Fatehi M. Vulvar Intraepithelial Neoplasia. 2023 Oct 18. In: *StatPearls [Internet]*. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. PMID: 31082026.
13. Bornstein J, Bogliatto F, Haefner HK, Stockdale CK, Preti M, Bohl TG, Reutter J; ISSVD Terminology Committee. The 2015 International Society for the Study of Vulvovaginal Disease (ISSVD) Terminology of Vulvar Squamous Intraepithelial Lesions. *Obstet Gynecol*. 2016 Feb;127(2):264-8. doi: 10.1097/AOG.0000000000001285. PMID: 26942352.
14. Bucchi L, Pizzato M, Rosso S, Ferretti S. New Insights into the Epidemiology of Vulvar Cancer: Systematic Literature Review for an Update of Incidence and Risk Factors. *Cancers (Basel)*. 2022 Jan 13;14(2):389. doi: 10.3390/cancers14020389. PMID: 35053552; PMCID: PMC8773873.
15. Li Z, Liu P, Wang Z, Zhang Z, Chen Z, Chu R, Li G, Han Q, Zhao Y, Li L, Miao J, Kong B, Song K. Prevalence of human papillomavirus DNA and p16INK4a positivity in vulvar cancer and vulvar intraepithelial neoplasia: a systematic review and meta-analysis. *Lancet Oncol*. 2023 Apr;24(4):403-414. doi: 10.1016/S1470-2045(23)00066-9. Epub 2023 Mar 15. Erratum in: *Lancet Oncol*. 2023 May;24(5):e192. doi: 10.1016/S1470-2045(23)00178-X. PMID: 36933562.
16. Faber MT, Sand FL, Albieri V, Norrild B, Kjaer SK, Verdoodt F. Prevalence and type distribution of human papillomavirus in squamous cell carcinoma and intraepithelial neoplasia of the vulva. *Int J Cancer*. 2017 Sep 15;141(6):1161-1169. doi: 10.1002/ijc.30821. Epub 2017 Jun 21. PMID: 28577297.
17. Restaino S, Pellecchia G, Arcieri M, Bogani G, Taliento C, Greco P, Driul L, Chiantera V, De Vincenzo RP, Garganese G, Sopracordevole F, Di Donato V, Ciavattini A, Scollo P, Scambia G, Vizzielli G, Gynecologic Oncology Group. Management of Patients with Vulvar Cancers: A Systematic Comparison of International Guidelines (NCCN-ASCO-ESGO-BGCS-IGCS-FIGO-French Guidelines-RCOG). *Cancers (Basel)*. 2025 Jan 8;17(2):186. doi: 10.3390/cancers17020186. PMID: 39857968; PMCID: PMC11764181.
18. Merlo S. Modern treatment of vulvar cancer. *Radiol Oncol*. 2020 Sep 22;54(4):371-376. doi: 10.2478/raon-2020-0053. PMID: 32960779; PMCID: PMC7585347.
19. Abu-Rustum NR, Yashar CM, Arend R, Barber E, Bradley K, Brooks R, Campos SM, Chino J, Chon HS, Crispens MA, Damast S, Fisher CM, Frederick P, Gaffney DK, Gaillard S, Giuntoli R II, Glaser S, Holmes J, Howitt BE, Kendra K, Lea J, Lee N, Mantia-Smaldone G, Mariani A, Mutch D, Nagel C, Nekhlyudov L, Podoll M, Rodabaugh K, Salani R, Schorge J, Siedel J, Sisodia R, Soliman P, Ueda S, Urban R, Wethington SL, Wyse E, Zanolli K, McMillian N, Espinosa S. Vulvar Cancer, Version 3.2024, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2024 Mar;22(2):117-135. doi: 10.6004/jnccn.2024.0013. PMID: 38503056.
20. Weinberg D, Gomez-Martinez RA. Vulvar Cancer. *Obstet Gynecol Clin North Am*. 2019 Mar;46(1):125-135. doi: 10.1016/j.ogc.2018.09.008. PMID: 30683259.
21. Barlow EL, Kang YJ, Hacker NF, Canfell K. Changing Trends in Vulvar Cancer Incidence and Mortality Rates in Australia Since 1982. *Int J Gynecol Cancer*. 2015 Nov;25(9):1683-9. doi: 10.1097/IGC.0000000000000547. PMID: 26495761.
22. Koh WJ, Greer BE, Abu-Rustum NR, Campos SM, Cho KR, Chon HS, Chu C, Cohn D, Crispens MA, Dizon DS, Dorigo O, Eifel PJ, Fisher CM, Frederick P, Gaffney DK, Han E, Higgins S, Huh WK, Lurain JR 3rd, Mariani A, Mutch D, Nagel C, Nekhlyudov L, Fader AN, Remmenga SW, Reynolds RK, Tillmanns T, Ueda S, Valea FA, Wyse E, Yashar CM, McMillian N, Scavone J. Vulvar Cancer, Version 1.2017, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2017 Jan;15(1):92-120. doi: 10.6004/jnccn.2017.0008. PMID: 28040721.

23. Covens A, Vella ET, Kennedy EB, Reade CJ, Jimenez W, Le T. Sentinel lymph node biopsy in vulvar cancer: Systematic review, meta-analysis and guideline recommendations. *Gynecol Oncol.* 2015 May;137(2):351-61. doi: 10.1016/j.ygyno.2015.02.014. Epub 2015 Feb 20. PMID: 25703673.
24. Paladini D, Cross P, Lopes A, Monaghan JM. Prognostic significance of lymph node variables in squamous cell carcinoma of the vulva. *Cancer.* 1994 Nov 1;74(9):2491-6. doi: 10.1002/1097-0142(19941101)74:9<2491::aid-cncr2820740916>3.0.co;2-5. PMID: 7923005.
25. van der Velden J, van Lindert AC, Lammes FB, ten Kate FJ, Sie-Go DM, Oosting H, Heintz AP. Extracapsular growth of lymph node metastases in squamous cell carcinoma of the vulva. The impact on recurrence and survival. *Cancer.* 1995 Jun 15;75(12):2885-90. doi: 10.1002/1097-0142(19950615)75:12<2885::aid-cncr2820751215>3.0.co;2-3. PMID: 7773938.
26. Fons G, Groenen SM, Oonk MH, Ansink AC, van der Zee AG, Burger MP, Stalpers LJ, van der Velden J. Adjuvant radiotherapy in patients with vulvar cancer and one intra capsular lymph node metastasis is not beneficial. *Gynecol Oncol.* 2009 Aug;114(2):343-5. doi: 10.1016/j.ygyno.2009.05.017. Epub 2009 May 29. PMID: 19481242.
27. Hacker NF, Eifel PJ, van der Velden J. Cancer of the vulva. *Int J Gynaecol Obstet.* 2015 Oct;131 Suppl 2:S76-83. doi: 10.1016/j.ijgo.2015.06.002. Erratum in: *Int J Gynaecol Obstet.* 2016 Mar;132(3):365. PMID: 26433678.
28. Oonk MH, Slomovitz B, Baldwin P, Van Doorn H, Van Der Velden J, De Hullu J, Slangen B, Gaarenstroom K, Vergote I, Brannstrom M, van Dorst E. Radiotherapy instead of inguinofemoral lymphadenectomy in vulvar cancer patients with a metastatic sentinel node: results of GROINSS-V II. *International journal of gynecological cancer.* 2019 Nov 1;29:A14.
29. Gaffney DK, King B, Viswanathan AN, Barkati M, Beriwal S, Eifel P, Erickson B, Fyles A, Goulart J, Harkenrider M, Jhingran A, Klopp A, Koh WJ, Lim K, Petersen I, Portelance L, Small W Jr, Stewart A, Wiebe E, Wolfson A, Yashar C, Bosch W. Consensus Recommendations for Radiation Therapy Contouring and Treatment of Vulvar Carcinoma. *Int J Radiat Oncol Biol Phys.* 2016 Jul 15;95(4):1191-200. doi: 10.1016/j.ijrobp.2016.02.043. Epub 2016 Feb 21. PMID: 27130794; PMCID: PMC5189987.
30. Gill BS, Bernard ME, Lin JF, Balasubramani GK, Rajagopalan MS, Sukumvanich P, Krivak TC, Olawaiye AB, Kelley JL, Beriwal S. Impact of adjuvant chemotherapy with radiation for node-positive vulvar cancer: A National Cancer Data Base (NCDB) analysis. *Gynecol Oncol.* 2015 Jun;137(3):365-72. doi: 10.1016/j.ygyno.2015.03.056. Epub 2015 Apr 11. PMID: 25868965.
31. Hyde SE, Valmadre S, Hacker NF, Schilthuis MS, Grant PT, van der Velden J. Squamous cell carcinoma of the vulva with bulky positive groin nodes-nodal debulking versus full groin dissection prior to radiation therapy. *Int J Gynecol Cancer.* 2007 Jan-Feb;17(1):154-8. doi: 10.1111/j.1525-1438.2006.00769.x. PMID: 17291247.
32. Montana GS, Thomas GM, Moore DH, Saxer A, Mangan CE, Lentz SS, Averette HE. Preoperative chemo-radiation for carcinoma of the vulva with N2/N3 nodes: a gynecologic oncology group study. *Int J Radiat Oncol Biol Phys.* 2000 Nov 1;48(4):1007-13. doi: 10.1016/s0360-3016(00)00762-8. PMID: 11072157.
33. Amant F, Nooij L, Annibaldi D, van Rompuy AS, Han S, van den Bulck H, Goffin F. Brief Report on 3-Weekly Paclitaxel Carboplatin Efficacy in Locally Advanced or Metastatic Squamous Vulvar Cancer. *Gynecol Obstet Invest.* 2018;83(6):620-626. doi: 10.1159/000487435. Epub 2018 Sep 18. PMID: 30227411.
34. Boronow RC, Hickman BT, Reagan MT, Smith RA, Steadham RE. Combined therapy as an alternative to exenteration for locally advanced vulvovaginal cancer. II. Results, complications, and dosimetric and surgical considerations. *Am J Clin Oncol.* 1987 Apr;10(2):171-81. doi: 10.1097/00000421-198704000-00055. PMID: 3565317.
35. Farias-Eisner R, Cirisano FD, Grouse D, Leuchter RS, Karlan BY, Lagasse LD, Berek JS. Conservative and individualized surgery for early squamous carcinoma of the vulva: the treatment of choice for stage I and II (T1-2N0-1M0) disease. *Gynecol Oncol.* 1994 Apr;53(1):55-8. doi: 10.1006/gyno.1994.1087. PMID: 8175023.
36. Hacker NF, Berek JS, Lagasse LD, Nieberg RK, Leuchter RS. Individualization of treatment for stage I squamous cell vulvar carcinoma. *Obstet Gynecol.* 1984 Feb;63(2):155-62. PMID: 6694808.
37. Chan JK, Sugiyama V, Pham H, Gu M, Rutgers J, Osann K, Cheung MK, Berman ML, Disaia PJ. Margin distance and other clinico-pathologic prognostic factors in vulvar carcinoma: a multivariate analysis. *Gynecol Oncol.* 2007 Mar;104(3):636-41. doi: 10.1016/j.ygyno.2006.10.004. Epub 2006 Nov 7. PMID: 17095080.
38. Stehman FB, Bundy BN, Thomas G, Varia M, Okagaki T, Roberts J, Bell J, Heller PB. Groin dissection versus groin radiation in carcinoma of the vulva: a Gynecologic Oncology Group study. *Int J Radiat Oncol Biol Phys.* 1992;24(2):389-96. doi: 10.1016/0360-3016(92)90699-i. PMID: 1526880.
39. Magrina JF, Gonzalez-Bosquet J, Weaver AL, Gaffey TA, Leslie KO, Webb MJ, Podratz KC. Squamous cell carcinoma of the vulva stage IA: long-term results. *Gynecol Oncol.* 2000 Jan;76(1):24-7. doi: 10.1006/gyno.1999.5638. PMID: 10620436.
40. Salani R, Khanna N, Frimer M, Bristow RE, Chen LM. An update on post-treatment surveillance and diagnosis of recurrence in women with gynecologic malignancies: Society of Gynecologic Oncology (SGO) recommendations. *Gynecol Oncol.* 2017 Jul;146(1):3-10. doi: 10.1016/j.ygyno.2017.03.022. Epub 2017 Mar 31. PMID: 28372871.

41. Mahner S, Prieske K, Grimm D, Trillsch F, Prieske S, von Amsberg G, Petersen C, Mueller V, Jaenicke F, Woelber L. Systemic treatment of vulvar cancer. *Expert Rev Anticancer Ther.* 2015 Jun;15(6):629-37. doi: 10.1586/14737140.2015.1037837. Epub 2015 May 21. PMID: 25997120.
42. Piura B, Masotina A, Murdoch J, Lopes A, Morgan P, Monaghan J. Recurrent squamous cell carcinoma of the vulva: a study of 73 cases. *Gynecol Oncol.* 1993 Feb;48(2):189-95. doi: 10.1006/gyno.1993.1032. PMID: 8428690.
43. Abu-Rustum NR, Yashar CM, Arend R, Barber E, Bradley K, Brooks R, Campos SM, Chino J, Chon HS, Crispens MA, Damast S, Fisher CM, Frederick P, Gaffney DK, Gaillard S, Giuntoli R II, Glaser S, Holmes J, Howitt BE, Kendra K, Lea J, Lee N, Mantia-Smaldone G, Mariani A, Mutch D, Nagel C, Nekhlyudov L, Podoll M, Rodabaugh K, Salani R, Schorge J, Siedel J, Sisodia R, Soliman P, Ueda S, Urban R, Wethington SL, Wyse E, Zanotti K, McMillian N, Espinosa S. Vulvar Cancer, Version 3.2024, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw.* 2024 Mar;22(2):117-135. doi: 10.6004/jnccn.2024.0013. PMID: 38503056.
44. Hopkins MP, Reid GC, Morley GW. The surgical management of recurrent squamous cell carcinoma of the vulva. *Obstet Gynecol.* 1990 Jun;75(6):1001-5. PMID: 2342725.
45. Rantshabeng PS, Moyo S, Moraka NO, Ndlovu A, MacLeod IJ, Gaseitsiwe S, Kasvosve I. Prevalence of oncogenic human papillomavirus genotypes in patients diagnosed with anogenital malignancies in Botswana. *BMC Infect Dis.* 2017 Nov 25;17(1):731. doi: 10.1186/s12879-017-2832-8. PMID: 29178840; PMCID: PMC5702116.
46. Halonen P, Jakobsson M, Heikinheimo O, Riska A, Gissler M, Pukkala E. Lichen sclerosus and risk of cancer. *Int J Cancer.* 2017 May 1;140(9):1998-2002. doi: 10.1002/ijc.30621. Epub 2017 Feb 10. PMID: 28124469.
47. Palumbo AR, Fasolino C, Santoro G, Gargano V, Rinaldi M, Arduino B, Belli M, Guida M. Evaluation of Symptoms and Prevention of Cancer in Menopause: The Value of Vulvar Exam. *Transl Med UniSa.* 2016 Nov 1;15:74-79. PMID: 27896230; PMCID: PMC5120753.
48. Rakislova N, Clavero O, Alemany L, Saco A, Quirós B, Lloveras B, Alejo M, Pawlita M, Quint W, Del Pino M, de Sanjose S, Ordi J; VVAP study group. "Histological characteristics of HPV-associated and -independent squamous cell carcinomas of the vulva: A study of 1,594 cases". *Int J Cancer.* 2017 Dec 15;141(12):2517-2527. doi: 10.1002/ijc.31006. Epub 2017 Aug 31. PMID: 28815579.
49. Casabona F, Priano V, Vallerino V, Cogliandro A, Lavagnino G. New surgical approach to lichen sclerosus of the vulva: the role of adipose-derived mesenchymal cells and platelet-rich plasma in tissue regeneration. *Plast Reconstr Surg.* 2010 Oct;126(4):210e-211e. doi: 10.1097/PRS.0b013e3181ea9386. PMID: 20885230.
50. Lawrie TA, Nordin A, Chakrabarti M. Medical and Surgical Treatments for Usual-Type Vulvar Intraepithelial Neoplasia. *JAMA Oncol.* 2016 Dec 1;2(12):1647-1648. doi: 10.1001/jamaoncol.2016.2430. PMID: 27490514.