

**American College of Radiology
ACR Appropriateness Criteria®
Staging and Follow-up of Vulvar Cancer**

Variant: 1 Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 2 cm, confined to the vulva or perineum, and with less than or equal to 1 mm stromal invasion.

Procedure	Appropriateness Category	Relative Radiation Level
US duplex Doppler and US-guided fine-needle aspiration biopsy groin	Usually Not Appropriate	○
US duplex Doppler groin	Usually Not Appropriate	○
US-guided fine needle aspiration biopsy groin	Usually Not Appropriate	○
Radiography chest	Usually Not Appropriate	☢
MRI pelvis without and with IV contrast	Usually Not Appropriate	○
MRI pelvis without IV contrast	Usually Not Appropriate	○
Lymphoscintigraphy groin	Usually Not Appropriate	☢☢
CT abdomen and pelvis with IV contrast	Usually Not Appropriate	☢☢☢
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	☢☢☢
CT pelvis with IV contrast	Usually Not Appropriate	☢☢☢
CT pelvis without IV contrast	Usually Not Appropriate	☢☢☢
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	☢☢☢☢
CT chest abdomen pelvis with IV contrast	Usually Not Appropriate	☢☢☢☢
CT chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	☢☢☢☢
CT chest abdomen pelvis without IV contrast	Usually Not Appropriate	☢☢☢☢
CT pelvis without and with IV contrast	Usually Not Appropriate	☢☢☢☢
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	☢☢☢☢

Variant: 2 Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 4 cm with greater than 1 mm stromal invasion, confined to vulva or perineum, or with minimal involvement of the urethra, vagina, or anus.

Procedure	Appropriateness Category	Relative Radiation Level
MRI pelvis without and with IV contrast	Usually Appropriate	○
US duplex Doppler and US-guided fine-needle aspiration biopsy groin	May Be Appropriate	○
MRI pelvis without IV contrast	May Be Appropriate (Disagreement)	○
Lymphoscintigraphy groin	May Be Appropriate	☢☢
US duplex Doppler groin	Usually Not Appropriate	○
US-guided fine needle aspiration biopsy groin	Usually Not Appropriate	○
Radiography chest	Usually Not Appropriate	☢
CT abdomen and pelvis with IV contrast	Usually Not Appropriate	☢☢☢
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	☢☢☢
CT pelvis with IV contrast	Usually Not Appropriate	☢☢☢
CT pelvis without IV contrast	Usually Not Appropriate	☢☢☢

CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	☠☠☠☠
CT chest abdomen pelvis with IV contrast	Usually Not Appropriate	☠☠☠☠
CT chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	☠☠☠☠
CT chest abdomen pelvis without IV contrast	Usually Not Appropriate	☠☠☠☠
CT pelvis without and with IV contrast	Usually Not Appropriate	☠☠☠☠
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	☠☠☠☠

Variant: 3 Initial staging of pretreatment vulvar cancer: Primary tumor is greater than 4 cm or tumor of any size with more than minimal involvement of the urethra, vagina, or anus.

Procedure	Appropriateness Category	Relative Radiation Level
MRI pelvis without and with IV contrast	Usually Appropriate	○
CT chest abdomen pelvis with IV contrast	Usually Appropriate	☠☠☠☠
FDG-PET/CT skull base to mid-thigh	Usually Appropriate	☠☠☠☠
US duplex Doppler and US-guided fine-needle aspiration biopsy groin	May Be Appropriate (Disagreement)	○
US-guided fine needle aspiration biopsy groin	May Be Appropriate (Disagreement)	○
MRI pelvis without IV contrast	May Be Appropriate	○
CT abdomen and pelvis with IV contrast	May Be Appropriate	☠☠☠
CT abdomen and pelvis without IV contrast	May Be Appropriate (Disagreement)	☠☠☠
CT pelvis with IV contrast	May Be Appropriate	☠☠☠
CT chest abdomen pelvis without IV contrast	May Be Appropriate (Disagreement)	☠☠☠☠
US duplex Doppler groin	Usually Not Appropriate	○
Radiography chest	Usually Not Appropriate	☠
Lymphoscintigraphy groin	Usually Not Appropriate	☠☠
CT pelvis without IV contrast	Usually Not Appropriate	☠☠☠
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	☠☠☠☠
CT chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	☠☠☠☠
CT pelvis without and with IV contrast	Usually Not Appropriate	☠☠☠☠

Variant: 4 Post-treatment assessment of clinically suspected recurrence of known vulvar cancer.

Procedure	Appropriateness Category	Relative Radiation Level
MRI pelvis without and with IV contrast	Usually Appropriate	○
CT chest abdomen pelvis with IV contrast	Usually Appropriate	☠☠☠☠
FDG-PET/CT skull base to mid-thigh	Usually Appropriate	☠☠☠☠
US duplex Doppler and US-guided fine-needle aspiration biopsy groin	May Be Appropriate (Disagreement)	○
US-guided fine needle aspiration biopsy groin	May Be Appropriate (Disagreement)	○
MRI pelvis without IV contrast	May Be Appropriate	○
CT abdomen and pelvis with IV contrast	May Be Appropriate	☠☠☠
CT abdomen and pelvis without IV contrast	May Be Appropriate	☠☠☠

	(Disagreement)	
CT pelvis with IV contrast	May Be Appropriate (Disagreement)	☹☹☹
CT pelvis without IV contrast	May Be Appropriate (Disagreement)	☹☹☹
CT chest abdomen pelvis without IV contrast	May Be Appropriate (Disagreement)	☹☹☹☹
US duplex Doppler groin	Usually Not Appropriate	○
Radiography chest	Usually Not Appropriate	☹
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	☹☹☹☹
CT chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	☹☹☹☹
CT pelvis without and with IV contrast	Usually Not Appropriate	☹☹☹☹

Panel Members

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Summary of Literature Review

Introduction/Background

Vulvar cancer is a rare gynecologic malignancy. In the United States, it is estimated that approximately 6,120 women will present with vulvar cancer, and 1,350 will succumb to their disease in 2020 [1]. Most patients are diagnosed with early-stage disease, and the majority of tumors originate in the labia majora [2,3]. The 5-year survival rate is 86% for patients with vulvar-confined disease but is reduced to 57% for patients with regional lymph node metastases, and 17% for patients with distant metastases [4].

Squamous cell carcinoma (SCC) is the predominant histotype of vulvar cancer, accounting for 90% of cases; thus, it is the focus of this discussion. Up to 69% of vulvar cancer is attributed to chronic human papillomavirus (HPV) infection, in particular high-risk strains such as HPV-16 and HPV-18 [5]. Other risk factors include older age, tobacco use, chronic inflammation of the vulva, and immune-compromised state [6].

The International Federation of Obstetrics and Gynecology (FIGO) and The American Joint Committee on Cancer (AJCC) TNM systems are both used to stage vulvar cancer and are closely aligned [7-9].

Initial evaluation of patients with vulvar lesions consists of careful clinical examination and punch biopsies of all suspicious vulvar lesions. Care must be taken to include the underlying stroma and to avoid necrotic areas. Lesion size, location relative to the midline, relationship to the adjacent organs (urethra, vagina, anus), and presence of multifocal disease are noted on physical examination. Clinical palpation of groin lymph nodes is performed, although this approach is

limited by the high false-negative rate [10].

The status of inguinofemoral lymph nodes (IFLNs) is the most important prognostic factor in vulvar cancer. The likelihood of lymph node metastases is estimated by primary tumor size, depth of stromal invasion, and presence of lymphovascular space invasion [11-15]. Traditionally, IFLN assessment entailed complete lymphadenectomy. High morbidity of this procedure and the fact that only a third of patients with early-stage disease have lymph node metastases at diagnosis led to a major shift toward less invasive assessment strategies including a combination of imaging, sentinel lymph node (SLN) mapping, and/or biopsy [16-21]. The SLN is the lymph node at the highest risk of metastasis because it is the first lymph node to receive lymphatic drainage from the primary tumor. Several prospective multi-institutional trials established the feasibility, safety, and effectiveness of SLN evaluation in early-stage vulvar cancer [16,19-23].

The peer-reviewed literature about the role of imaging in vulvar cancer is limited, likely because vulvar cancer is uncommon. Many studies report on patients with combined histotypes of vulvar cancer, wide range of disease stages, primary and recurrent disease, and vulvar and vaginal cancers combined. The imaging techniques are not uniform, and the descriptions of imaging studies are often limited with regard to the area imaged and the use of intravenous (IV) contrast. The above limits our ability to draw conclusions and provide evidence-based imaging recommendations.

Special Imaging Considerations

Vaginal gel is optional with MRI pelvis without and with IV contrast or MRI pelvis without IV contrast. Vaginal gel may be useful to delineate the extent of vaginal involvement by primary tumor.

Discussion of Procedures by Variant

Variant 1: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 2 cm, confined to the vulva or perineum, and with less than or equal to 1 mm stromal invasion.

For early-stage disease, the present-day surgical approach consists of conservative vulvar resection (with at least 1 cm of tumor-free margin) and IFLN assessment carried out via two separate incisions [6]. Primary tumors ≤ 2 cm, confined to the vulva and/or perineum and with ≤ 1 mm stromal invasion (TNM T1a or FIGO IA) represent a special case because lymph node assessment with either imaging or SLN mapping or biopsy is not required because of the $< 1\%$ risk of metastasis [24].

Variant 1: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 2 cm, confined to the vulva or perineum, and with less than or equal to 1 mm stromal invasion.

A. CT Abdomen and Pelvis

There is no relevant literature regarding the use of CT abdomen and pelvis in the evaluation of primary tumors ≤ 2 cm, confined to the vulva and/or perineum, and with ≤ 1 mm of stromal invasion.

Variant 1: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 2 cm, confined to the vulva or perineum, and with less than or equal to 1 mm stromal invasion.

B. CT Chest, Abdomen, and Pelvis

There is no relevant literature regarding the use of CT chest, abdomen, and pelvis in the evaluation of primary tumors ≤ 2 cm, confined to the vulva and/or perineum, and with ≤ 1 mm of stromal invasion.

Variant 1: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 2 cm, confined to the vulva or perineum, and with less than or equal to 1 mm stromal invasion.

C. CT Pelvis

There is no relevant literature regarding the use of CT pelvis in the evaluation of primary tumors ≤ 2 cm, confined to the vulva and/or perineum, and with ≤ 1 mm of stromal invasion.

Variant 1: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 2 cm, confined to the vulva or perineum, and with less than or equal to 1 mm stromal invasion.

D. FDG-PET/CT Skull Base to Mid-Thigh

There is no relevant literature regarding the use of fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-PET/CT in the evaluation of primary tumors ≤ 2 cm, confined to the vulva and/or perineum, and with ≤ 1 mm of stromal invasion.

Variant 1: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 2 cm, confined to the vulva or perineum, and with less than or equal to 1 mm stromal invasion.

E. Lymphoscintigraphy Pelvis

There is no relevant literature regarding the use of lymphoscintigraphy in the evaluation of primary tumors ≤ 2 cm, confined to the vulva and/or perineum, and with ≤ 1 mm of stromal invasion.

Variant 1: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 2 cm, confined to the vulva or perineum, and with less than or equal to 1 mm stromal invasion.

F. MRI Pelvis

There is no relevant literature regarding the use of pelvic MRI in the evaluation of primary tumors ≤ 2 cm, confined to the vulva and/or perineum, and with ≤ 1 mm of stromal invasion. Nevertheless, this procedure can be useful to confirm the size and extent of tumor.

Variant 1: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 2 cm, confined to the vulva or perineum, and with less than or equal to 1 mm stromal invasion.

G. Radiography Chest

There is no relevant literature regarding the use of radiography in the evaluation of primary tumors ≤ 2 cm, confined to the vulva and/or perineum, and with ≤ 1 mm of stromal invasion.

Variant 1: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 2 cm, confined to the vulva or perineum, and with less than or equal to 1 mm stromal invasion.

H. US Duplex Doppler and US-Guided Fine-Needle Aspiration Biopsy Groin

There is no relevant literature regarding the use of ultrasound (US) duplex Doppler and US-guided fine-needle aspiration biopsy (FNAB) in the evaluation of primary tumors ≤ 2 cm, confined to the vulva and/or perineum, and with ≤ 1 mm of stromal invasion.

Variant 1: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 2 cm, confined to the vulva or perineum, and with less than or equal to 1 mm stromal invasion.

I. US Duplex Doppler Groin

There is no relevant literature regarding the use of US duplex Doppler in the evaluation of primary tumors ≤ 2 cm, confined to the vulva and/or perineum, and with ≤ 1 mm of stromal invasion.

Variant 1: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 2 cm, confined to the vulva or perineum, and with less than or equal to 1 mm stromal invasion.

J. US-Guided Fine-Needle Aspiration Biopsy Groin

There is no relevant literature regarding the use of US-guided FNAB in the evaluation of primary tumors ≤ 2 cm, confined to the vulva and/or perineum, and with ≤ 1 mm of stromal invasion.

Variant 2: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 4 cm with greater than 1 mm stromal invasion, confined to vulva or perineum, or with minimal involvement of the urethra, vagina, or anus.

For early-stage disease, present-day surgical approach consists of conservative vulvar resection (with at least 1 cm of tumor-free margin) and IFLN assessment carried out via two separate incisions [6]. If no lymph node metastases are apparent at clinical assessment, the extent of lymph node evaluation is determined by the size of the primary tumor, the depth of stromal invasion, and location of the primary tumor relative to the midline [6].

Primary tumors ≤ 4 cm with > 1 mm stromal invasion confined to the vulva or perineum or with minimal involvement of the urethra, vagina, or anus (TNM T1b/smaller T2 or FIGO IB/smaller II) situated ≥ 2 cm away from the midline are approached with unilateral IFLN assessment. In contrast, same stage tumors located within 2 cm of midline have higher risk of bilateral lymph node spread and require bilateral IFLN evaluation [6].

If clinical and/or imaging evaluation shows no apparent IFLN metastases, SLN mapping is performed as detailed below. If IFLN metastases are suspected based on clinical and/or imaging evaluation, either minimally invasive lymph node sampling with US-guided FNAB and/or IFLN dissection may be performed.

Variant 2: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 4 cm with greater than 1 mm stromal invasion, confined to vulva or perineum, or with minimal involvement of the urethra, vagina, or anus.

A. CT Abdomen and Pelvis

CT of the abdomen and pelvis is not indicated in patients with clinical early-stage disease. There is no relevant literature detailing the role of CT in the evaluation of primary tumor size and extent, which is likely explained by the limited soft-tissue contrast of CT. Lymph node morphologic characteristics including size enlargement and abnormal pattern of enhancement are the main criteria used to detect lymph node metastases on CT. If IFLN metastases are suspected on imaging, SLN mapping is not recommended. Instead, complete lymphadenectomy or, alternatively, US-guided FNAB is performed [6]. Normal imaging findings do not exclude IFLN metastases (because of inadequate sensitivity) and do not alleviate the need for SLN mapping and sampling.

Land et al [25] reported on 44 patients with primary vulvar SCC of various tumor stages. Of these,

23 patients were imaged with both CT and US or US-guided FNAB, 6 with CT alone, and 15 with US or US-guided FNAB alone prior to undergoing lymphadenectomy. The authors did not specify whether CT imaging extended beyond the pelvis or if IV contrast was administered. Long-axis diameter ≥ 10 mm, presence of necrosis, or evidence of extranodal disease were considered suspicious for IFLN metastases. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of CT was 58%, 75%, 58%, and 75%, US alone was 87%, 69%, 48%, and 94%, and US-guided FNAB was 80%, 100%, 100%, and 93%, respectively.

Variant 2: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 4 cm with greater than 1 mm stromal invasion, confined to vulva or perineum, or with minimal involvement of the urethra, vagina, or anus.

B. CT Chest, Abdomen, and Pelvis

CT of the chest, abdomen, and pelvis is not indicated in patients with clinical early-stage disease. There is no relevant literature detailing the role of CT in the evaluation of primary tumor size and extent, which is likely explained by the limited soft-tissue contrast of CT. Lymph node enlargement and abnormal pattern of enhancement are the main criteria used to detect lymph node metastases on CT. If IFLN metastases are suspected on imaging, SLN mapping is not recommended. Instead, complete lymphadenectomy or, alternatively, US-guided FNAB is performed [6]. Normal imaging findings do not exclude IFLN metastases (because of inadequate sensitivity) and do not alleviate the need for SLN mapping and sampling.

Andersen et al [26] prospectively evaluated 27 patients with vulvar cancer (23 primary and 4 recurrent) who underwent contrast-enhanced CT scan of the chest, abdomen, and pelvis prior to treatment. Most patients had tumors ≤ 4 cm; only 4 patients had tumors >4 cm. IFLN metastases were diagnosed if short-axis diameter was >10 mm and/or abnormal pattern of contrast enhancement was observed. CT had sensitivity of 60%, specificity of 90%, PPV of 37.5%, and NPV of 95.7% for detection of IFLN metastases. CT did not reveal distant metastases from vulvar cancer or alter original treatment plan in any patients. Incidental synchronous cancers were detected in two patients.

Land et al [25] reported on 44 patients with primary vulvar SCC of various tumor stages. Of these, 23 patients were imaged with both CT and US or US-guided FNAB, 6 with CT alone, and 15 with US or US-guided FNAB alone prior to undergoing lymphadenectomy. The authors did not specify whether CT imaging extended beyond the pelvis or whether IV contrast was administered. Long-axis diameter ≥ 10 mm, presence of necrosis, or evidence of extranodal disease, were considered suspicious for IFLN metastases. The sensitivity, specificity, PPV, and NPV of CT was 58%, 75%, 58%, and 75%; US alone was 87%, 69%, 48%, and 94%; and US-guided FNAB was 80%, 100%, 100%, and 93%, respectively.

Variant 2: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 4 cm with greater than 1 mm stromal invasion, confined to vulva or perineum, or with minimal involvement of the urethra, vagina, or anus.

C. CT Pelvis

CT of the pelvis is not indicated in patients with clinical early-stage disease. There is no relevant literature about the role of CT in the evaluation of primary tumor size and extent, likely explained by the limited soft-tissue contrast of CT. Lymph node enlargement and abnormal pattern of enhancement are the main criteria used to detect lymph node metastases on CT. If IFLN metastases are suspected on imaging, SLN mapping is not recommended. Instead, complete

lymphadenectomy or, alternatively, US-guided FNAB is performed [6]. Normal imaging findings do not exclude IFLN metastases (because of inadequate sensitivity) and do not alleviate the need for SLN mapping and sampling.

Land et al [25] reported on 44 patients with primary vulvar SCC of various tumor stages. Of these, 23 patients were imaged with both CT and US or US-guided FNAB, 6 with CT alone, and 15 with US or US-guided FNAB alone prior to undergoing lymphadenectomy. The authors did not specify whether CT imaging extended beyond the pelvis or whether IV contrast was administered. Long-axis diameter ≥ 10 mm, presence of necrosis, or evidence of extranodal disease were considered suspicious for IFLN metastases. The sensitivity, specificity, PPV, and NPV of CT was 58%, 75%, 58%, and 75%; US alone was 87%, 69%, 48%, and 94%; and US-guided FNAB was 80%, 100%, 100%, and 93%, respectively.

Variant 2: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 4 cm with greater than 1 mm stromal invasion, confined to vulva or perineum, or with minimal involvement of the urethra, vagina, or anus.

D. FDG-PET/CT Skull Base to Mid-Thigh

FDG-PET/CT is not indicated in patients with clinical early-stage disease. There is no relevant literature about the role of FDG-PET/CT in the evaluation of primary tumor size and extent. If findings on FDG-PET/CT are suspicious for lymph node metastases, SLN mapping is not recommended. Instead, complete lymphadenectomy or, alternatively, US-guided FNAB is performed [6]. Normal imaging findings do not exclude IFLN metastases (because of inadequate sensitivity) and do not alleviate the need for SLN mapping and sampling.

Several recent studies examined the value of FDG-PET/CT in the detection of lymph node metastases. Kamran et al [27] retrospectively evaluated the performance of FDG-PET/CT prior to lymphadenectomy in 20 patients with primary vulvar SCC (size unspecified) and > 1 mm of stromal invasion. They found that on a patient-by-patient basis, FDG-PET/CT demonstrated a sensitivity of 50%, specificity of 100%, PPV of 100%, and NPV of 57.1%.

Crivellaro et al [28] retrospectively evaluated 29 patients with clinical early-stage primary vulvar cancer (primary tumors < 4 cm and stromal invasion > 1 mm) who were imaged with FDG-PET/CT prior to lymphadenectomy. The sensitivity, specificity, PPV, and NPV of FDG-PET/CT was 53%, 85%, 73%, 76%, and 67% on a groin-based analysis, and 50%, 67%, 59%, 59% on a patient-based analysis, respectively. The authors concluded that FDG-PET/CT had low sensitivity and moderate specificity for detecting IFLN metastases in early-stage disease.

Several recent studies focused on the impact of FDG-PET or FDG-PET/CT on prognosis and management of patients with primary and recurrent vulvar cancer [29,30]. Lin et al [29] studied 23 women with various vulvar malignancies (17 patients with primary tumors of various histotypes ≥ 2 cm with ≥ 1 cm stromal invasion and 6 recurrent tumors) all of who underwent CT/MRI and 38 FDG-PET or FDG-PET/CT scans. The findings from FDG-PET or FDG-PET/CT had a positive impact in the management of four patients. One patient was upstaged by identifying a metastasis to the pancreas. In one patient, PET confirmed the absence of distant metastasis, allowing pelvic lymph node resection with curative intent, and in two patients there was no FDG uptake in the left para-aortic and left pelvic nodes that were falsely positive on CT. The findings from FGD-PET had a negative impact in the management of one patient who had a false-positive pelvic lymph node, resulting in unnecessary left pelvic lymph node dissection.

Robertson et al [30] reported on 50 patients who were enrolled in the National Oncologic PET Registry and underwent 83 FDG-PET/CT studies for suspected or known primary or recurrent vulvar or vaginal cancer. Fifty-four of 83 (65%) studies were performed in patients with vulvar cancer, and the remaining 29 of 83 (35%) studies were performed in patients with vaginal cancer. The authors did not specify numbers of patients with vulvar cancer (including primary versus recurrent disease) or disease stages of primary tumors. The physician's prognostic impression changed following 29 of 54 (54%) FDG-PET/CT studies obtained in patients with primary or recurrent vulvar cancer. Furthermore, the management approach was altered following 30 of 83 (36%) FDG-PET/CT studies.

Variant 2: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 4 cm with greater than 1 mm stromal invasion, confined to vulva or perineum, or with minimal involvement of the urethra, vagina, or anus.

E. Lymphoscintigraphy Pelvis

SLN evaluation is performed in patients with unifocal primary tumors ≤ 4 cm (except primary tumors ≤ 2 cm, confined to the perineum and with ≤ 1 mm of stromal invasion, which do not require SLN mapping), absence of prior vulvar surgery (which can disrupt lymphatic flow), and absence of lymph node metastases at clinical and/or imaging assessment [19,21].

Combination of radiocolloid (usually Tc-99m sulfur colloid) and blue dye (most commonly isosulfan blue 1%) has a superior SLN detection rate (97.7%) compared with either Tc-99m sulfur colloid (94%) or blue dye (68.7%) alone [21,23]. Radiocolloid is injected intradermally around the tumor 2 to 4 hours prior to surgery. Preoperative lymphoscintigraphy may help with approximate SLN localization, whereas the intraoperative handheld gamma probe allows more precise SLN detection and localization. Blue dye is injected in the operating room 15 to 30 minutes prior the procedure and localizes transiently to SLN aiding intraoperative visualization and removal of blue-stained lymph nodes [6].

If the SLN is negative for metastatic spread on pathologic evaluation, lymphadenectomy is omitted [6]. If an ipsilateral SLN is not identified, complete lymphadenectomy is recommended [6]. If SLN is involved by tumor, management options include bilateral lymphadenectomy or external beam radiation therapy (EBRT) with or without chemotherapy [6].

In situations when lymph node metastases are suspected because of imaging, SLN is not recommended. Instead, complete lymphadenectomy or, alternatively, US-guided FNAB is performed [6].

Variant 2: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 4 cm with greater than 1 mm stromal invasion, confined to vulva or perineum, or with minimal involvement of the urethra, vagina, or anus.

F. MRI Pelvis

MRI with IV contrast is the best available imaging modality to define local extent of primary tumor because MRI has superior soft-tissue contrast and multiplanar capability. MRI is considered for patients with primary tumors > 2 cm and > 1 mm of stromal invasion, or primary tumors with close proximity to or involvement of the urethra, vagina, and anus because MRI can aid primary treatment planning [6].

Two prior retrospective studies examined the accuracy of MRI for assessment of primary tumor

extent [31,32]. Sohaib et al [31] evaluated 22 patients with primary vulvar SCC who underwent MRI (18 unenhanced and 4 contrast-enhanced MRI scans) prior to surgery. MRI correctly staged primary tumor extent (T stage) in 70% of patients. Kataoka et al [32] reported on 49 patients with vulvar cancer (36 primary and 13 recurrent). In 36 patients with primary vulvar cancer, the accuracy of both unenhanced and contrast-enhanced MRI for assessment of tumor size (≤ 2 cm versus > 2 cm) was 86%. The overall staging accuracy of contrast-enhanced MRI was 85% compared to 69.4% for unenhanced MRI.

In addition to primary tumor size/extent, MRI can assess IFLN basins [32-34]. Similar to CT and FDG-PET/CT, if findings on MRI are suspicious for lymph node metastases, SLN is not recommended. Instead, complete lymphadenectomy or, alternatively, US-guided FNAB is indicated [6]. Normal findings do not reliably exclude IFLN metastases (because of inadequate sensitivity) and do not alleviate the need for SLN sampling.

The aforementioned study by Sohaib et al [31] evaluated MRI (18 unenhanced and 4 contrast-enhanced MRI) to assess primary tumor stage (T stage) and evaluate IFLN status in 22 patients with primary vulvar cancer. Short-axis diameter was the only criterion used to characterize lymph nodes. On a groin-based analysis, the sensitivity and specificity of MRI was 40% and 97% using ≥ 10 mm short-axis diameter cutoff to diagnose superficial inguinal lymph node metastases, and 50% and 100% using ≥ 8 mm short-axis diameter cutoff to diagnose deep inguinal lymph node metastases.

Hawnaur et al [35] used unenhanced MRI to evaluate IFLN in 10 patients with primary vulvar cancer. Lymph node metastases were diagnosed if any of the following criteria were present: long-axis diameter > 21 mm, short-axis diameter > 10 mm, long- to short-axis diameter ratio $< 1.3:1$, irregular contour, and cystic changes within a lymph node. On a groin-based analysis, MRI had the sensitivity of 89%, specificity of 91%, PPV of 89%, NPV of 91%, and accuracy of 90%.

Bipat et al [33] evaluated 60 patients with vulvar cancer (57 vulvar SCC) who were imaged with contrast-enhanced MRI prior to SLN mapping or lymphadenectomy. On a groin-based analysis, using short-axis diameter ≥ 8 mm to diagnose lymph node metastasis, contrast-enhanced MRI had a sensitivity of 52%, specificity of 85% to 88%, PPV of 46% to 52%, and NPV of 87% to 89% for two observers. Singh et al [34] studied 39 women who were imaged with unenhanced MRI prior to lymphadenectomy. Two of the three criteria had to be met to diagnose lymph node metastases: 1) short-axis diameter > 10 mm; 2) irregular or rounded shape; or 3) increased signal intensity on short tau inversion recovery imaging or heterogeneous signal intensity on T2-weighted imaging. Using this approach, on a groin-by-groin basis, unenhanced MRI had sensitivity of 85.7%, specificity of 82.1%, PPV of 64.3%, and NPV of 93.9%.

Finally, Kataoka et al [32] evaluated 49 patients with vulvar cancer (36 primary and 13 recurrent) and groin exploration with SLN mapping or lymphadenectomy. On a groin-by groin basis, the ratio of short-axis to long-axis diameter > 0.75 and reader's gestalt of lymph node metastases had a sensitivity of 86.7% and 93.3%, specificity of 81.3% and 75%, and accuracy of 84.8% and 87%, respectively.

Variant 2: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 4 cm with greater than 1 mm stromal invasion, confined to vulva or perineum, or with minimal involvement of the urethra, vagina, or anus.

G. Radiography Chest

There is no relevant literature to support the use of routine pretreatment radiographs in patients with clinical early-stage vulvar cancer.

There is only one report regarding the role of chest radiography for the initial staging of patients with vulvar cancer. Andersen et al [26] prospectively evaluated 27 patients with vulvar cancer (23 primary and 4 recurrent). Chest radiographs were performed in 24 of 27 patients, and contrast-enhanced CT scan of the chest, abdomen, and pelvis was obtained in all 27 patients. Only 1 of 24 chest radiographs revealed a clinically important finding (pulmonary metastases) from an asymptomatic and at that time unknown adenocarcinoma of the cecum. Chest radiographs did not alter initial gynecologic management in any of the patients.

Variant 2: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 4 cm with greater than 1 mm stromal invasion, confined to vulva or perineum, or with minimal involvement of the urethra, vagina, or anus.

H. US Duplex Doppler and US-guided Fine-Needle Aspiration Biopsy Groin

There is no relevant literature to support the use of US with Doppler and US-guided FNAB for the assessment of primary tumor extent. A number of studies evaluated groin US with Doppler and US-guided FNAB for IFLN assessment [25,36-38]. Combined US and US-guided FNAB is the most accurate approach to confirm IFLN metastases that are suspected based on clinical and/or imaging assessment. The advantage of this sampling approach is that it is minimally invasive; the limitation is the potential risk of undersampling in the setting of micrometastases.

De Gregorio et al [36] evaluated 60 patients with primary vulvar cancer (55 with vulvar SCC) for sonographic evidence of lymph node involvement (absence of fatty hilum, irregular shape, cortical thickness ≥ 4 mm, and peripheral vascularization) prior to SLN mapping or lymphadenectomy. For the detection of lymph node metastases, US with Doppler had a sensitivity of 76.3%, specificity of 91.3%, PPV of 82.9%, and NPV of 87.5%.

Hall et al [38] reported on 44 patients with primary SCC of the vulva who underwent groin US with Doppler and, if suspicious findings were found on US, US-guided FNAB prior to surgical management. On US with Doppler, lymph nodes were characterized as suspicious based on the circular shape (long- to short-axis diameter ≤ 2) or irregular configuration and/or absent echogenic fatty hilum. FNAB was performed on the largest or most abnormal lymph node in each groin. The sensitivity and specificity for detecting metastatic involvement were 86% and 96% for US with Doppler alone but increased to 93% and 100% for US-guided FNAB, respectively.

The aforementioned study by Land et al [25] reported on 44 patients with primary vulvar SCC who underwent imaging with one or more of the following modalities: CT, US, and/or US-guided FNAB prior to lymphadenectomy. The sensitivity, specificity, PPV, and NPV for US alone was 87%, 69%, 48%, and 94%, respectively, and for US-guided FNAB it was 80%, 100%, 93%, and 100%, respectively.

Variant 2: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 4 cm with greater than 1 mm stromal invasion, confined to vulva or perineum, or with minimal involvement of the urethra, vagina, or anus.

I. US Duplex Doppler Groin

There is no relevant literature to support the use of US with duplex Doppler for the assessment of primary tumor extent. A number of studies evaluated groin US with Doppler and US-guided FNAB

for IFLN assessment [25,36-38]. Combined US and US-guided FNAB is the most accurate approach to confirm IFLN metastases that are suspected based on clinical and/or imaging assessment. The advantage of this sampling approach is that it is minimally invasive; the limitation is the potential risk of undersampling in the setting of micrometastases.

De Gregorio et al [36] evaluated 60 patients with primary vulvar cancer (55 with vulvar SCC) for sonographic evidence of lymph node involvement (absence of fatty hilum, irregular shape, cortical thickness ≥ 4 mm, and peripheral vascularization) prior to SLN mapping or lymphadenectomy. For the detection of lymph node metastases, US with Doppler had a sensitivity of 76.3%, specificity of 91.3%, PPV of 82.9%, and NPV of 87.5%.

Hall et al [38] reported on 44 patients with primary SCC of the vulva who underwent groin US with Doppler and, if suspicious findings were found on US, US-guided FNAB prior to surgical management. On US with Doppler, lymph nodes were characterized as suspicious based on the circular shape (long- to short-axis diameter ≤ 2) or irregular configuration and/or absent echogenic fatty hilum. FNAB was performed on the largest or most abnormal lymph node in each groin. The sensitivity and specificity for detecting metastatic involvement were 86% and 96% for US with Doppler alone but increased to 93% and 100% for US-guided FNAB, respectively.

The aforementioned study by Land et al [25] reported on 44 patients with primary vulvar SCC who were imaged with one or more of the following modalities: CT, US and/or US-guided FNAB prior to lymphadenectomy. The sensitivity, specificity, PPV, and NPV for US alone was 87%, 69%, 48%, and 94%, respectively, and for US-guided FNAB it was 80%, 100%, 93%, and 100%, respectively.

Variant 2: Initial staging of pretreatment vulvar cancer: Primary tumor is less than or equal to 4 cm with greater than 1 mm stromal invasion, confined to vulva or perineum, or with minimal involvement of the urethra, vagina, or anus.

J. US-Guided Fine-Needle Aspiration Biopsy Groin

There is no relevant literature to support the use of US-guided FNAB for the assessment of primary tumor extent. A number of studies evaluated groin US with Doppler and US-guided FNAB for IFLN assessment [25,36-38]. Combined US and US-guided FNAB is the most accurate approach to confirm IFLN metastases that are suspected based on clinical and/or imaging assessment. Sampling is minimally invasive. Limitations of US include its risk of undersampling of micrometastases.

Hall et al [38] reported on 44 patients with primary SCC of the vulva who underwent groin US with Doppler and, if suspicious findings were found on US, US-guided FNAB prior to surgical management. On US with Doppler, lymph nodes were characterized as suspicious based on the circular shape (long- to short-axis diameter ≤ 2) or irregular configuration and/or absent echogenic fatty hilum. FNAB was performed on the largest or most abnormal lymph node in each groin. The sensitivity and specificity for detecting metastatic involvement were 86% and 96% for US with Doppler alone but increased to 93% and 100% for US-guided FNAB, respectively.

The aforementioned study by Land et al [25] reported on 44 patients with primary vulvar SCC who were imaged with one or more of the following modalities: CT, US, and/or US-guided FNAB prior to lymphadenectomy. The sensitivity, specificity, PPV, and NPV for US alone was 87%, 69%, 48%, and 94%, respectively, and for US-guided FNAB 80%, 100%, 93%, and 100%, respectively.

Variant 3: Initial staging of pretreatment vulvar cancer: Primary tumor is greater than 4 cm or tumor of any size with more than minimal involvement of the urethra, vagina, or anus.

Patients with primary tumors >4 cm or tumors of any size with more than minimal involvement of urethra, vagina, or anus (TNM larger T2/T3 or larger FIGO II, FIGO III/IVA) are treated primarily with concurrent EBRT and chemotherapy [39,40]. This group of patients has >8% risk of IFLN basin metastases and are not candidates for SLN mapping and biopsy. For radiation planning, IFLN assessment with imaging and subsequent IFLN lymphadenectomy or US-guided FNAB is recommended. If lymph node metastases are identified at imaging and confirmed at lymphadenectomy or US-guided FNAB, the radiation field should encompass primary tumor, pelvis, and groin nodal basin. If no lymph node metastases are detected at imaging and subsequent lymphadenectomy, reduced EBRT coverage may be considered.

Patients presenting with distant metastases beyond the pelvis (TNM any T or N designation and M1 beyond pelvis or FIGO IVB) are treated primarily with chemotherapy and, when appropriate, EBRT for locoregional disease control and symptom palliation.

Variant 3: Initial staging of pretreatment vulvar cancer: Primary tumor is greater than 4 cm or tumor of any size with more than minimal involvement of the urethra, vagina, or anus.

A. CT Abdomen and Pelvis

Contrast-enhanced CT of abdomen and pelvis may be considered in patients with primary tumors >4 cm; urethral, vaginal, or anal involvement; or clinical suspicion for lymph node metastases. However, CT of chest, abdomen, and pelvis or FDG-PET/CT is preferred in this group. Size enlargement and abnormal pattern of enhancement are the main criteria used to detect lymph node metastases on CT. Complete lymphadenectomy or, alternatively, US-guided FNAB is performed if imaging findings are suspicious for lymph node metastases [6].

Land et al [25] reported on 44 patients with primary vulvar SCC of various tumor stages. Of these, 23 patients were imaged with both CT and US or US-guided FNAB, 6 with CT alone, and 15 with US or US-guided FNAB alone prior to undergoing lymphadenectomy. The authors did not specify whether CT imaging extended beyond the pelvis or whether IV contrast was administered. Long-axis diameter ≥ 10 mm, presence of necrosis, and evidence of extranodal disease were considered suspicious for IFLN metastases. The sensitivity, specificity, PPV, and NPV of CT was 58%, 75%, 58%, and 75%; US alone was 87%, 69%, 48%, and 94%; and US-guided FNAB was 80%, 100%, 100%, and 93%, respectively.

Variant 3: Initial staging of pretreatment vulvar cancer: Primary tumor is greater than 4 cm or tumor of any size with more than minimal involvement of the urethra, vagina, or anus.

B. CT Chest, Abdomen, and Pelvis

Contrast-enhanced CT of chest, abdomen, and pelvis may be considered for patients with primary tumors >4 cm; urethral, vaginal, or anal involvement; or clinical suspicion for lymph node metastases. Size enlargement and abnormal pattern of enhancement are the main criteria used to detect lymph node metastases on CT. Complete lymphadenectomy or, alternatively, US-guided FNAB is performed if imaging findings are suspicious for lymph node metastases [6].

Andersen et al [26] prospectively evaluated 27 patients with vulvar cancer (23 primary and 4 recurrent) who underwent contrast-enhanced CT scan of the chest, abdomen, and pelvis prior to treatment. Most patients had tumors ≤ 4 cm; only four patients had tumors >4 cm. IFLN metastases were diagnosed if short-axis diameter was > 10 mm and/or abnormal pattern of contrast

enhancement were observed. CT had sensitivity of 60%, specificity of 90%, PPV of 37.5%, and NPV of 95.7% for detection of IFLN metastases. CT did not reveal distant metastases from vulvar cancer or alter original treatment plan in any patients. Incidental synchronous cancers were detected in 2 patients.

Land et al [25] reported on 44 patients with primary vulvar SCC of various tumor stages. Of these, 23 patients were imaged with both CT and US or US-guided FNAB, 6 with CT alone, and 15 with US or US-guided FNAB alone prior to undergoing lymphadenectomy. The authors did not specify whether CT imaging extended beyond the pelvis or if IV contrast was administered. Long-axis diameter ≥ 10 mm, presence of necrosis, or evidence of extranodal disease, were considered suspicious for IFLN metastases. The sensitivity, specificity, PPV, and NPV of CT was 58%, 75%, 58%, and 75%; US alone was 87%, 69%, 48%, and 94%; and US-guided FNAB was 80%, 100%, 100%, and 93%, respectively.

Variant 3: Initial staging of pretreatment vulvar cancer: Primary tumor is greater than 4 cm or tumor of any size with more than minimal involvement of the urethra, vagina, or anus.

C. CT Pelvis

Contrast-enhanced CT of pelvis may be considered in patients with primary tumors >4 cm; urethral, vaginal, or anal involvement; or clinical suspicion for lymph node metastases. However, CT of chest, abdomen, and pelvis or FDG-PET/CT is preferred in this group. Size enlargement and abnormal pattern of enhancement are the main criteria used to detect lymph node metastases on CT. Complete lymphadenectomy or, alternatively, US-guided FNAB is performed if imaging findings are suspicious for lymph node metastases [6].

Land et al [25] reported on 44 patients with primary vulvar SCC of various tumor stages. Of these, 23 patients were imaged with both CT and US or US-guided FNAB, 6 with CT alone, and 15 with US or US-guided FNAB alone prior to undergoing lymphadenectomy. The authors did not specify whether CT imaging extended beyond the pelvis or whether IV contrast was administered. Long-axis diameter ≥ 10 mm, presence of necrosis, or evidence of extranodal disease were considered suspicious for IFLN metastases. The sensitivity, specificity, PPV, and NPV of CT was 58%, 75%, 58%, and 75%; US alone was 87%, 69%, 48%, and 94%; and US-guided FNAB was 80%, 100%, 100%, and 93%, respectively.

Variant 3: Initial staging of pretreatment vulvar cancer: Primary tumor is greater than 4 cm or tumor of any size with more than minimal involvement of the urethra, vagina, or anus.

D. FDG-PET/CT Skull Base to Mid-Thigh

FDG-PET/CT is considered in patients with primary tumors >4 cm; urethral, vaginal, or anal involvement; or clinical suspicion for lymph node metastases. Complete lymphadenectomy or, alternatively, US-guided FNAB is performed if imaging findings are suspicious for lymph node metastases [6].

Several recent studies examined the value of FDG-PET/CT in the detection of lymph node metastases. Kamran et al [27] retrospectively evaluated the performance of FDG-PET/CT prior to lymphadenectomy in 20 patients with primary vulvar SCC (size unspecified) and >1 mm of stromal invasion. He found that on a patient-by-patient basis, FDG-PET/CT demonstrated a sensitivity of 50%, specificity of 100%, PPV of 100%, and NPV of 57.1%.

Garganese et al [41] reported on FDG-PET/CT in 47 patients with vulvar cancer (44 primary and 3

recurrent) who underwent inguinofemoral lymphadenectomy because they were not candidates for SLN evaluation because of primary tumor >4 cm (n = 12), multifocal tumor (n = 9), prior surgery (n = 16), IFLN involvement (n = 7) or recurrent disease (n = 3). On a groin-based analysis, FDG-PET/CT demonstrated a sensitivity of 56%, specificity of 88%, PPV of 38%, NPV of 93%, and accuracy of 84% in detecting nodal metastases.

Several recent studies focused on the impact of FDG-PET or FDG-PET/CT on prognosis and management of patients with primary and recurrent vulvar cancer [29,30]. Lin et al [29] studied 23 women with various vulvar malignancies (17 patients with primary tumors of various histotypes ≥ 2 cm with ≥ 1 cm stromal invasion and 6 recurrent tumors) all of who underwent CT or MRI and 38 had FDG-PET or FDG-PET/CT scans. The findings from FDG-PET or FDG-PET/CT had a positive impact in the management of four patients. One patient was upstaged by identification of a metastasis to the pancreas. In one patient, PET confirmed the absence of distant metastasis, allowing pelvic lymph node resection with curative intent, and in two patients there was no FDG uptake in left para-aortic and left pelvic nodes that were falsely positive on CT. The findings from FDG-PET had a negative impact in the management of one patient who had a false-positive pelvic lymph node, resulting in an unnecessary left pelvic lymph node dissection.

Robertson et al [30] reported on 50 patients who were enrolled in the National Oncologic PET Registry and underwent 83 FDG-PET/CT studies for suspected or known primary or recurrent vulvar or vaginal cancer. Fifty-four of 83 (65%) studies were performed in patients with vulvar cancer, the remaining 29 of 83 (35%) studies in patients with vaginal cancer. The authors did not specify numbers of patients with vulvar cancer (including primary versus recurrent disease) or disease stages of primary tumors. The physician's prognostic impression changed following 29 of 54 (54%) FDG-PET/CT studies obtained in patients with primary or recurrent vulvar cancer. Furthermore, the management approach was altered following 30 of 83 (36%) FDG-PET/CT studies.

Variant 3: Initial staging of pretreatment vulvar cancer: Primary tumor is greater than 4 cm or tumor of any size with more than minimal involvement of the urethra, vagina, or anus.

E. Lymphoscintigraphy Groin

Lymphoscintigraphy and SLN mapping are not indicated in patients with primary tumor >4 cm or tumor of any size with more than minimal involvement of the urethra, vagina, or anus.

De Gregorio et al [36] evaluated 60 patients with primary vulvar cancer (55 with vulvar SCC) for sonographic evidence of lymph node involvement (absence of fatty hilum, irregular shape, cortical thickness ≥ 4 mm, and peripheral vascularization) prior to SLN mapping or lymphadenectomy. For the detection of lymph node metastases, US with Doppler had a sensitivity of 76.3%, specificity of 91.3%, PPV of 82.9%, and NPV of 87.5%.

Hall et al [38] reported on 44 patients with primary SCC of the vulva who underwent groin US with Doppler and, if suspicious findings were found on US, US-guided FNAB prior to surgical management. On US with Doppler, lymph nodes were characterized as suspicious based on the circular shape (long- to short-axis diameter ≤ 2) or irregular configuration and/or absent echogenic fatty hilum. FNAB was performed on the largest or most abnormal lymph node in each groin. The sensitivity and specificity for detecting metastatic involvement were 86% and 96% for US with Doppler alone but increased to 93% and 100% for US-guided FNAB, respectively.

The aforementioned study by Land et al [25] reported on 44 patients with primary vulvar SCC who

were imaged with one or more of the following modalities: CT, US, and/or US-guided FNAB prior to lymphadenectomy. The sensitivity, specificity, PPV, and NPV for US alone was 87%, 69%, 48%, and 94%, respectively, and for US-guided FNAB 80%, 100%, 93%, and 100%, respectively.

Variant 3: Initial staging of pretreatment vulvar cancer: Primary tumor is greater than 4 cm or tumor of any size with more than minimal involvement of the urethra, vagina, or anus.

F. MRI Pelvis

MRI with IV contrast is the best available imaging modality to define local extent of primary tumor because MRI has superior soft-tissue contrast and multiplanar capability. MRI is considered for patients with primary tumors >2 cm and >1 mm of stromal invasion, or primary tumors with close proximity to or involvement of the urethra, vagina, and anus because MRI can aid primary treatment planning [6].

Two prior retrospective studies examined the accuracy of MRI for assessment of primary tumor extent [31,32]. Sohaib et al [31] evaluated 22 patients with primary vulvar SCC who underwent MRI (18 unenhanced and 4 contrast-enhanced MRI scans) prior to surgery. MRI correctly staged primary tumor extent (T stage) in 70% of patients. Kataoka et al [32] reported on 49 patients with vulvar cancer (36 primary and 13 recurrent). In 36 patients with primary vulvar cancer, the accuracy of both unenhanced and contrast-enhanced MRI for assessment of tumor size (≤ 2 cm versus > 2 cm) was 86%. The overall staging accuracy of contrast-enhanced MRI was 85% compared with 69.4% of unenhanced MRI.

In addition to primary tumor, MRI can assess IFLN basins [32-34]. Similar to CT and FDG-PET/CT, if findings on MRI are suspicious for lymph node metastases, complete lymphadenectomy or, alternatively, US-guided FNAB is indicated [6].

The aforementioned study by Sohaib et al [31] evaluated MRI (18 unenhanced and 4 contrast-enhanced MRI) to assess primary tumor stage (T stage) and evaluate IFLN status in 22 patients with primary vulvar cancer. Short-axis diameter was the only criterion used to characterize lymph nodes. On a groin-based analysis, the sensitivity and specificity of MRI was 40% and 97% using ≥ 10 mm short-axis diameter cutoff to diagnose superficial inguinal lymph node metastases, and 50% and 100% using ≥ 8 mm short-axis diameter cutoff to diagnose deep inguinal lymph node metastases.

Hawnaur et al [35] used unenhanced MRI to evaluate IFLN in 10 patients with primary vulvar cancer. Lymph node metastases were diagnosed if any of the following criteria were present: long-axis diameter > 21 mm, short-axis diameter > 10 mm, long- to short-axis diameter ratio $< 1.3:1$, irregular contour, and cystic changes within a lymph node. On a groin-based analysis, MRI had the sensitivity of 89%, specificity of 91%, PPV of 89%, NPV of 91%, and accuracy of 90%.

Bipat et al [33] evaluated 60 patients with vulvar cancer (57 vulvar SCC) who were imaged with contrast-enhanced MRI prior to SLN mapping or lymphadenectomy. On a groin-based analysis, using short-axis diameter ≥ 8 mm to diagnose lymph node metastasis, contrast-enhanced MRI had sensitivity of 52%, specificity of 85% to 88%, PPV of 46% to 52%, and NPV of 87% to 89% for two observers. Singh et al [34] studied 39 women who were imaged with unenhanced MRI prior to lymphadenectomy. Two of the three criteria had to be met to diagnose lymph node metastases: 1) short-axis diameter > 10 mm; 2) irregular or rounded shape; or 3) increased signal intensity on short tau inversion recovery imaging or heterogeneous signal intensity on T2-weighted imaging. Using this approach, on a groin-by-groin basis, unenhanced MRI had sensitivity of 85.7%,

specificity of 82.1%, PPV of 64.3%, and NPV of 93.9%.

Finally, Kataoka et al [32] evaluated 49 patients with vulvar cancer (36 primary and 13 recurrent) and groin exploration with SLN mapping or lymphadenectomy. On a groin-by groin basis, the ratio of short-axis to the long-axis diameter >0.75 and reader's gestalt of lymph node metastases had a sensitivity of 86.7% and 93.3%, specificity of 81.3% and 75%, and accuracy of 84.8% and 87%, respectively.

Variant 3: Initial staging of pretreatment vulvar cancer: Primary tumor is greater than 4 cm or tumor of any size with more than minimal involvement of the urethra, vagina, or anus.

G. Radiography Chest

There is only one report regarding the role of chest radiography for the initial staging of patients with vulvar cancer. Andersen et al [26] prospectively evaluated 27 patients with vulvar cancer (23 primary and 4 recurrent). Chest radiographs was performed in 24 of 27 patients and contrast-enhanced CT scan of the chest, abdomen, and pelvis was performed in all 27 patients. Only 1 of 24 chest radiographs revealed a clinically important finding (ie, pulmonary metastases) from an asymptomatic and at that time unknown adenocarcinoma of the cecum. Chest radiographs did not alter initial gynecologic management in any of the patients.

Variant 3: Initial staging of pretreatment vulvar cancer: Primary tumor is greater than 4 cm or tumor of any size with more than minimal involvement of the urethra, vagina, or anus.

H. US Duplex Doppler and US-guided Fine-Needle Aspiration Biopsy Groin

There is no relevant literature to support the use of US with Doppler and US-guided FNAB for the assessment of primary tumor extent. A number of studies evaluated groin US with Doppler and US-guided FNAB for IFLN assessment [25,36-38]. Combined US and US-guided FNAB is the most accurate approach to confirm IFLN metastases that are suspected based on clinical and/or imaging assessment. The advantage of this sampling approach is that it is minimally invasive; the limitation is the potential risk of undersampling in the setting of micrometastases.

Variant 3: Initial staging of pretreatment vulvar cancer: Primary tumor is greater than 4 cm or tumor of any size with more than minimal involvement of the urethra, vagina, or anus.

I. US Duplex Doppler Groin

There is no relevant literature to support the use of US with Doppler for the assessment of primary tumor extent. A number of studies evaluated groin US with Doppler and US-guided FNAB for IFLN assessment [25,36-38]. Combined US and US-guided FNAB is the most accurate approach to confirm IFLN metastases that are suspected based on clinical and/or imaging assessment. The advantage of this sampling approach is that it is minimally invasive; the limitation is the potential risk of undersampling in the setting of micrometastases.

De Gregorio et al [36] evaluated 60 patients with primary vulvar cancer (55 with vulvar SCC) for sonographic evidence of lymph node involvement (absence of fatty hilum, irregular shape, cortical thickness ≥ 4 mm, and peripheral vascularization) prior to SLN mapping or lymphadenectomy. For the detection of lymph node metastases, US with Doppler had a sensitivity of 76.3%, specificity of 91.3%, PPV of 82.9%, and NPV of 87.5%.

Hall et al [38] reported on 44 patients with primary SCC of the vulva who underwent groin US with Doppler and, if suspicious findings were found on US, US-guided FNAB prior to surgical management. On US with Doppler, lymph nodes were characterized as suspicious based on the

circular shape (long- to short-axis diameter ≤ 2) or irregular configuration and/or absent echogenic fatty hilum. FNAB was performed on the largest or most abnormal lymph node in each groin. The sensitivity and specificity for detecting metastatic involvement were 86% and 96% for US with Doppler alone but increased to 93% and 100% for US-guided FNAB, respectively.

The aforementioned study by Land et al [25] reported on 44 patients with primary vulvar SCC who were imaged with one or more of the following modalities: CT, US, and/or US-guided FNAB prior to lymphadenectomy. The sensitivity, specificity, PPV, and NPV for US alone was 87%, 69%, 48%, and 94%, respectively, and for US-guided FNAB 80%, 100%, 93%, and 100%, respectively.

Variant 3: Initial staging of pretreatment vulvar cancer: Primary tumor is greater than 4 cm or tumor of any size with more than minimal involvement of the urethra, vagina, or anus.

J. US-Guided Fine-Needle Aspiration Biopsy Groin

There is no relevant literature to support the use of US-guided FNAB for the assessment of primary tumor extent. A number of studies evaluated groin US with Doppler and US-guided FNAB for IFLN assessment [25,36-38]. Combined US and US-guided FNAB is the most accurate approach to confirm IFLN metastases that are suspected based on clinical and/or imaging assessment. The advantage of this sampling approach is that it is minimally invasive; the limitation is the potential risk of undersampling in the setting of micrometastases.

Hall et al [38] reported on 44 patients with primary SCC of the vulva who underwent groin US with Doppler and, if suspicion on US with Doppler, lymph nodes were characterized as suspicious based on the circular shape (long- to short-axis diameter ≤ 2) or irregular configuration and/or absent echogenic fatty hilum. FNAB was performed on the largest or most abnormal lymph node in each groin findings were found on US, US-guided FNAB prior to surgical management. The sensitivity and specificity for detecting metastatic involvement were 86% and 96% for US with Doppler alone but increased to 93% and 100% for US-guided FNAB, respectively.

The aforementioned study by Land et al [25] reported on 44 patients with primary vulvar SCC who were imaged with one or more of the following modalities: CT, US, and/or US-guided FNAB prior to lymphadenectomy. The sensitivity, specificity, PPV, and NPV for US alone was 87%, 69%, 48%, and 94%, respectively, and for US-guided FNAB 80%, 100%, 93%, and 100%, respectively.

Variant 4: Post-treatment assessment of clinically suspected recurrence of known vulvar cancer.

Most vulvar cancers relapse within the first 2 years after initial treatment, but up to one-third recur ≥ 5 years after initial management, which points to the importance of long-term follow-up [42]. No direct evidence is available to inform the post-treatment surveillance; thus, the surveillance approach is extrapolated from the experience with the more common cervical cancer and consists of regular clinical history, physical examination, and cytology [43]. Imaging workup is recommended only in the presence of symptoms or clinical findings suspicious for recurrence [43].

Vulvar region, IFLN basins, multisite, and distant metastases are the most common locations of recurrence in decreasing order of frequency [13]. If the relapse is confirmed pathologically, FDG-PET/CT is recommended to detect lymph node and distant metastases, whereas MRI of pelvis aids the assessment of local tumor extent [44-46].

Treatment of recurrent vulvar cancer is determined by the tumor extent (vulva-confined, nodal

recurrence, distant recurrence) and history of prior EBRT. Detailed discussion is beyond the scope of this guideline and is addressed comprehensively elsewhere [6]. In general, nonirradiated vulva-confined recurrent tumors are approached with multimodal strategy including surgical resection or IFLN dissection, and/or chemoradiotherapy. Surgery is the only potentially curative option in previously irradiated vulva-confined tumors. Similarly, if there is no prior EBRT, isolated lymph node or distant metastases are managed with multimodal approach; surgical resection and systemic therapy may be considered if there was prior EBRT. If there are multiple lymph node or distant metastases and prior EBRT, systemic therapy and best supporting care are advised [6].

Variant 4: Post-treatment assessment of clinically suspected recurrence of known vulvar cancer.

A. CT Abdomen and Pelvis

Contrast-enhanced CT of the abdomen and pelvis may be considered in patients with suspected vulvar cancer recurrence. However, contrast-enhanced CT of the chest, abdomen, and pelvis or FDG-PET/CT is preferred in this group. Size enlargement and abnormal pattern of enhancement are the main criteria used to detect lymph node metastases on CT.

Andersen et al [26] prospectively evaluated 27 patients with vulvar cancer (23 primary and 4 recurrent) who underwent contrast-enhanced CT scan of the chest, abdomen, and pelvis prior to treatment. IFLN metastases were diagnosed if short-axis diameter was >10 mm and/or abnormal pattern of contrast enhancement were observed. CT had sensitivity of 60%, specificity of 90%, PPV of 37.5%, and NPV of 95.7% for detection of IFLN metastases. CT did not reveal distant metastases from vulvar cancer or alter original treatment plan in any patients. Incidental synchronous cancers were detected in two patients.

Variant 4: Post-treatment assessment of clinically suspected recurrence of known vulvar cancer.

B. CT Chest, Abdomen, and Pelvis

Contrast-enhanced CT of the chest, abdomen, and pelvis is usually appropriate in patients with suspected vulvar cancer recurrence. Andersen et al [26] prospectively evaluated 27 patients with vulvar cancer (23 primary and 4 recurrent) who underwent contrast-enhanced CT scan of the chest, abdomen, and pelvis prior to treatment. IFLN metastases were diagnosed if short-axis diameter was >10 mm and/or abnormal pattern of contrast enhancement were observed. CT had sensitivity of 60%, specificity of 90%, PPV of 37.5%, and NPV of 95.7% for detection of IFLN metastases.

Variant 4: Post-treatment assessment of clinically suspected recurrence of known vulvar cancer.

C. CT Pelvis

Contrast-enhanced CT of the pelvis may be considered in patients with suspected vulvar cancer recurrence. However, contrast-enhanced CT of chest, abdomen, and pelvis or FDG-PET/CT is preferred in this group.

Variant 4: Post-treatment assessment of clinically suspected recurrence of known vulvar cancer.

D. FDG-PET/CT Skull Base to Mid-Thigh

FDG-PET/CT is usually appropriate in patients with suspected vulvar cancer recurrence. FDG-PET/CT, alone or in combination with MRI, can facilitate treatment planning prior to pelvic exenteration for recurrent gynecologic cancers.

Burger et al [46] reported on 33 patients with recurrent gynecologic malignancies and found that the area under the curves for FDG-PET/CT detection of bladder or rectal invasion ranged from 0.74 to 0.96. In addition, FDG-PET provided relevant prognostic information, with significant associations between FDG uptake metrics incorporating tumor volume (total lesion glycolysis and metabolic tumor volume) and overall survival ($P \leq .001$); as well as between metabolic tumor volume and progression-free survival ($P = .001$) [46]. MRI was performed in addition to FDG-PET/CT in 31 of these 33 patients [45]. Compared with MRI or FDG-PET/CT, fused FDG-PET/MRI correctly improved readers' diagnostic confidence in detecting bladder, rectal, or pelvic sidewall invasion in up to 52% of patients [45]. Fused FDG-PET/MRI also had a positive impact on inter-reader variability; inter-reader agreement was consistently in the highest ("almost perfect") range only for FDG-PET/MRI ($\kappa = 0.84-1.0$) [45]. The main limitation of the two above described studies is that although all patients had recurrent gynecologic cancer, very few of them (<7) were vulvar in origin.

Garganese et al [41] reported on FDG-PET/CT in 47 patients with vulvar cancer (44 primary and 3 recurrent) who underwent inguofemoral lymphadenectomy because they were not candidates for SLN evaluation because of primary tumor >4 cm ($n = 12$), multifocal tumor ($n = 9$), prior surgery ($n = 16$), IFLN involvement ($n = 7$) or recurrent disease ($n = 3$). On a groin-based analysis, FDG-PET/CT demonstrated a sensitivity of 56%, specificity of 88%, PPV of 38%, NPV of 93%, and accuracy of 84% in detecting nodal metastases.

Several recent studies focused on the impact of FDG-PET or FDG-PET/CT on prognosis and management of patients with primary and recurrent vulvar cancer [29,30]. Lin et al [29] studied 23 women with various vulvar malignancies (17 patients with primary tumors of various histotypes ≥ 2 cm with ≥ 1 cm stromal invasion and 6 recurrent tumors) all of who underwent CT or MRI and 38 who had FDG-PET or FDG-PET/CT scans. The findings from FDG-PET or FDG-PET/CT had a positive impact in the management of four patients. One patient was upstaged because a metastasis to the pancreas was identified. In one patient, PET confirmed the absence of distant metastasis, thus allowing pelvic lymph node resection with curative intent, and in two patients, there was no FDG uptake in left para-aortic and left pelvic nodes that were falsely positive on CT. The findings from FGD-PET had a negative impact in the management of one patient who had a false-positive pelvic lymph node, which resulted in an unnecessary left pelvic lymph node dissection.

Robertson et al [30] reported on 50 patients who were enrolled in the National Oncologic PET Registry and underwent 83 FDG-PET/CT studies for suspected or known primary or recurrent vulvar or vaginal cancer. Fifty-four of 83 (65%) studies were performed in patients with vulvar cancer, and the remaining 29 of 83 (35%) studies were performed in patients with vaginal cancer. The authors did not specify the number of patients with vulvar cancer (including primary versus recurrent disease) or disease stages of primary tumors. The physician's prognostic impression changed following 29 of 54 (54%) FDG-PET/CT studies obtained in patients with primary or recurrent vulvar cancer. Furthermore, the management approach was altered following 30 of 83 (36%) FDG-PET/CT studies.

Variant 4: Post-treatment assessment of clinically suspected recurrence of known vulvar cancer.

E. MRI Pelvis

MRI of the pelvis has superior soft-tissue contrast and multiplanar capability. Thus, MRI is the

preferred imaging modality to define local extent of suspected or confirmed recurrent vulvar cancers, especially those in close proximity to or involving the urethra, vagina, and anus as it can aid treatment planning [6]. Contrast-enhanced imaging is advised [6].

MRI may also aid the evaluation of recurrent disease in pelvic nodes. Kataoka et al [32] evaluated 49 patients with vulvar cancer (36 primary and 13 recurrent) and groin exploration with SLN mapping or lymphadenectomy. On a groin-by-groin basis, the ratio of short-axis to the long-axis diameter >0.75 and reader's gestalt of lymph node metastases had a sensitivity of 86.7% and 93.3%, specificity of 81.3% and 75%, and accuracy of 84.8% and 87%, respectively.

Variant 4: Post-treatment assessment of clinically suspected recurrence of known vulvar cancer.

F. Radiography Chest

Routine radiography is usually not indicated in the evaluation of clinically suspected recurrence of vulvar cancer. There is only one report regarding the role of chest radiography for the initial staging of patients with vulvar cancer. Andersen et al [26] prospectively evaluated 27 patients with vulvar cancer (23 primary and 4 recurrent). Chest radiographs was performed in 24 of 27 patients and contrast-enhanced CT scan of the chest, abdomen, and pelvis was performed in all 27 patients. Only 1 of 24 chest radiographs revealed a clinically important finding (pulmonary metastases) from an asymptomatic and at that time unknown adenocarcinoma of the cecum. Chest radiographs did not alter initial gynecologic management in any of the patients.

Variant 4: Post-treatment assessment of clinically suspected recurrence of known vulvar cancer.

G. US Duplex Doppler and US-guided Fine-Needle Aspiration Biopsy Groin

There is no relevant literature to support or refute the use of US with Doppler and US-guided FNAB for the assessment of suspected vulvar cancer recurrence. Nevertheless, this procedure may be useful to confirm suspected IFLN metastases.

Variant 4: Post-treatment assessment of clinically suspected recurrence of known vulvar cancer.

H. US Duplex Doppler Groin

There is no relevant literature to support or refute the use of US with Doppler for the assessment of suspected vulvar cancer recurrence.

Variant 4: Post-treatment assessment of clinically suspected recurrence of known vulvar cancer.

I. US-guided Fine-Needle Aspiration Biopsy Groin

There is no relevant literature to support or refute the use of US-guided FNAB for the assessment of suspected vulvar cancer recurrence.

Summary of Recommendations

- **Variant 1:** For the initial staging of pretreatment vulvar cancer where the primary tumor is ≤ 2 cm, confined to the vulva or perineum, and with ≤ 1 mm stromal invasion, imaging is usually not appropriate.
- **Variant 2:** For the initial staging of pretreatment vulvar cancer where the primary tumor is ≤ 4 cm with >1 mm stromal invasion, when confined to the vulva or perineum, or with minimal

involvement of the urethra, vagina, or anus, MRI pelvis without and with IV contrast is usually appropriate to define the extent of primary tumor and to assess IFLN basins. No agreement was reached about the role of MRI pelvis without IV contrast. Lymphoscintigraphy of the pelvis may be appropriate for SLN detection and localization. US duplex Doppler and US-guided FNAB groin may be appropriate to confirm IFLN metastases that are suspected based on clinical and/or imaging assessment.

- **Variante 3:** For the initial staging of pretreatment vulvar cancer with a primary tumor >4 cm or tumor of any size with more than minimal involvement of the urethra, vagina, or anus, MRI pelvis without and with IV contrast and FDG-PET/CT skull base to mid-thigh are both usually appropriate and complementary to each other for comprehensive staging. CT chest, abdomen, and pelvis with IV contrast is a usually appropriate alternative to MRI pelvis without and with IV contrast. No agreement was reached about the role of CT abdomen and pelvis without IV contrast or CT chest, abdomen, and pelvis without IV contrast. No agreement was reached about the role of US duplex Doppler and US-guided FNAB groin. Nevertheless, US duplex Doppler and US-guided FNAB groin may be appropriate to confirm IFLN metastases that are suspected based on clinical and/or imaging assessment.
- **Variante 4:** For the post-treatment assessment of clinically suspected recurrence of known vulvar cancer, MRI pelvis without and with IV contrast and FDG-PET/CT skull base to mid-thigh are both usually appropriate and complementary to each other to accurately define the extent of suspected or confirmed recurrent vulvar cancer. CT chest, abdomen, and pelvis with IV contrast is a usually appropriate alternative to MRI pelvis without and with IV. No agreement was reached about the role of CT abdomen and pelvis without IV contrast, CT chest, abdomen, and pelvis without IV contrast, CT pelvis with IV contrast, and CT pelvis without IV contrast. No agreement was reached about the role of US duplex Doppler and US-guided FNAB groin, and US-guided FNAB groin. Nevertheless, US duplex Doppler and US-guided FNAB groin may be appropriate to confirm IFLN metastases that are suspected based on clinical and/or imaging assessment.

Supporting Documents

The evidence table, literature search, and appendix for this topic are available at <https://acsearch.acr.org/list>. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents, please go to the ACR website at <https://www.acr.org/Clinical-Resources/Clinical-Tools-and-Reference/Appropriateness-Criteria>.

Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an

		alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® [Radiation Dose Assessment Introduction](#) document.

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
0	0 mSv	0 mSv
	<0.1 mSv	<0.03 mSv
	0.1-1 mSv	0.03-0.3 mSv
	1-10 mSv	0.3-3 mSv
	10-30 mSv	3-10 mSv
	30-100 mSv	10-30 mSv

*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."

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Disclaimer

The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

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