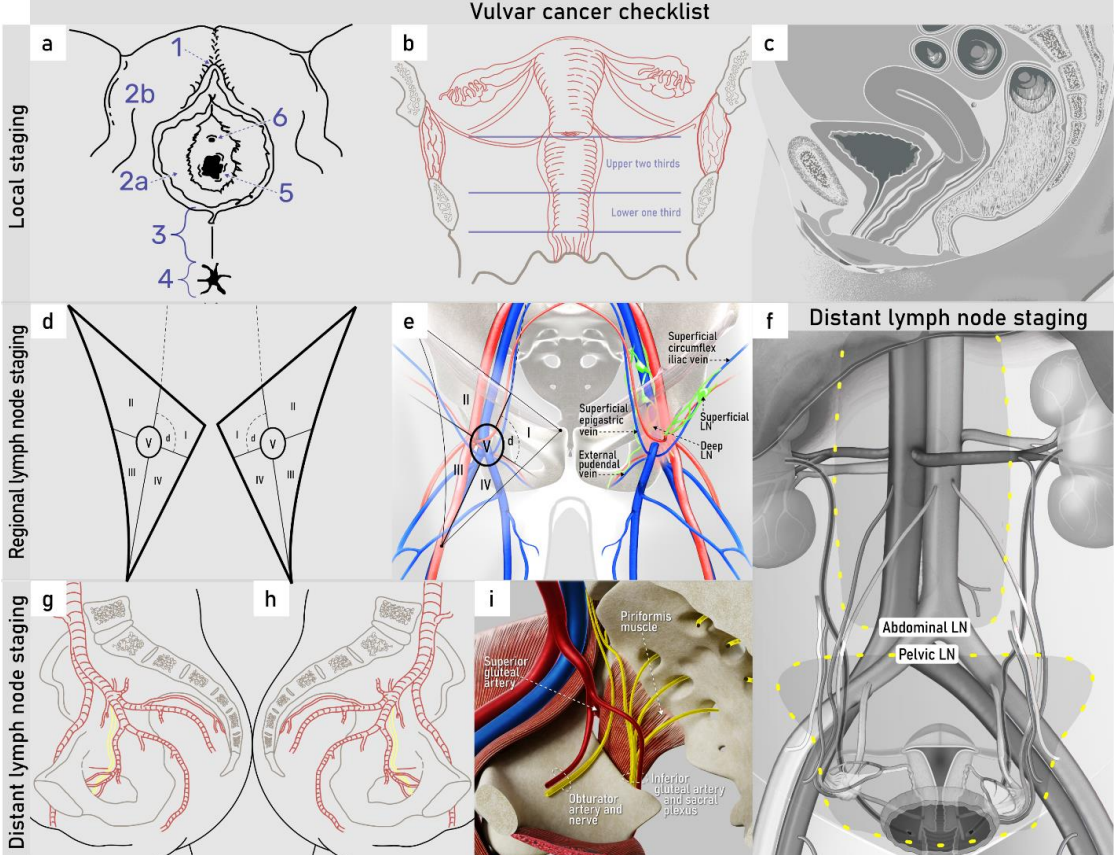


APPENDIX S1 VULVAR CANCER

- 1.1 Standardized ultrasound report for vulvar cancer assessment
- 1.2 FIGO / TNM staging
- 1.3 Methodology

1.1. Standardized ultrasound report for vulvar cancer assessment

Ultrasound parameter	Description of vulvar cancer
Tumor identification	<ul style="list-style-type: none"> Yes/No. If yes, assess tumor echogenicity and perfusion using Color Score.^{\$}
Tumor site of origin	<ul style="list-style-type: none"> Labia majora/minora Clitoris Perineum*
Tumor location	<ul style="list-style-type: none"> Non-lateralized (medial border <1 cm from midline) versus lateralized tumors Uni-/multifocal
Tumor size (millimeters)	<ul style="list-style-type: none"> Greatest dimension
Local extent	<ul style="list-style-type: none"> Subcutaneous perineal space (tela subcutanea) Superficial (Colles) perineal fascia, perineal muscles (superficial perineal space) Inferior fascia of urogenital diaphragm (perineal membrane), pelvic floor muscles (e.g., lower level – sphincters and erectile muscles of the urogenital and intestinal tract) Urethro-/vesicovaginal, rectovaginal) septum, paracolpium right/left Vagina/urethra (lower third versus upper two thirds) Anus Pelvic bone and others
Bladder and rectal invasion	<p>Sliding sign⁽¹⁾:</p> <ul style="list-style-type: none"> positive sliding sign (the tumor slides over the bladder and/or rectum) negative sliding sign (tumor is fixed against bladder and/or rectum) <p>Bladder and/or rectal involvement grading⁽²⁾:</p> <ul style="list-style-type: none"> Grade 0: Intact echogenic layer of fibrous and fat tissue between the bladder and/or the rectum and vagina and/or the cervix. Grade 1: Disruption of the echogenic outer layer of the bladder and/or rectum but no other signs of invasion Grade 2: Disruption of the hyperechogenic muscle layer but no abnormalities of the inner wall architecture. Grade 3: Disruption of all layers with intraluminal tumor spread. <p>In case of bladder trigone involvement: ureteric infiltration right/left (yes/no)</p>
Regional (inguinofemoral) lymph nodes	<p>Description of site, number, laterality (Figure S1)</p> <p>Assessment by standardized VITA terms using the classification LN1 – LN5⁽³⁾:</p> <ul style="list-style-type: none"> LN1: Normal finding LN2: Benign finding LN3: Indeterminate, probably benign finding LN4: Probably malignant finding LN5: Malignant finding
Distant spread	<ul style="list-style-type: none"> Distant lymph nodes (site, number, laterality if appropriate, lymph node status LN1-LN5, see above) Other distant spread
Other findings	<ul style="list-style-type: none"> Related / unrelated gynecologic/non-gynecologic pathologies (vagina, cervix, uterus, ovaries and others)

Staging system	<ul style="list-style-type: none">TNM and FIGO staging system^(4, 5)Comments and recommendations to additional diagnostic tests to the referring specialist and to multidisciplinary team meeting
<p><i>*Lesions that clearly arise from the vulva and extend onto the perineum and potentially involve the anus should be classified as vulvar and vice versa. For lesions localized to the perineum that do not clearly arise from either the vulva or the anus, should be classified as ‘perineum favor vulva’ or ‘perineum favor anus’ (based on clinical examination).</i></p> <p><i>§Color Score following IOTA (International Ovarian Tumor Analysis) terms and definitions (Color Score 1, no perfusion; Color Score 2, minimal perfusion; Color score 3, moderate flow; Color score 4, highly vascularized).⁽⁶⁾</i></p>	
<p>Vulvar cancer checklist</p> 	
<p>Figure S1 Schematic documentation of vulvar cancer staging by ultrasound. Ultrasound documents the location and extension of primary tumor (local staging, a-c), and any suspicious lymph nodes (size of lymph node and intranodal metastasis, the number of lymph nodes involved, the presence or absence of extracapsular spread and others)(d-f). For local staging, schematics showing vulvar anatomy (a), 1-clitoris (glans clitoris and clitoral hood), 2a- labia minora, 2b- labia majora, 3- perineum, 4- perianal region, 5- vaginal opening, 6- urethra; coronal view of pelvic anatomy (b); sagittal view of pelvic anatomy (c). The regional lymph nodal status is documented by ultrasound according to a standardized report published in 2021 by the Vulvar International Tumor Analysis (VITA) collaborative group (d, e).⁽³⁾ For describing location of superficial lymph nodes in the groins using Daseler regions (I-V), the femoral triangle is divided into 4 quadrants by the femoral vein and a virtual line drawn perpendicular to it passing through the saphenofemoral junction: superomedial region (I); superolateral region (II); inferolateral region (III); and inferomedial region (IV). The central zone (V) is circled. Deep lymph nodes in the groins are located medially to the femoral vein and cranially to the lower margin of oval fossa (d, e). In the scheme (d), the location of deep lymph nodes is marked as ‘d’. Distant lymph nodes for the vulvar cancer (g-f).</p>	
<p>Table S1 Ultrasound checklist on vulvar cancer based the consensus of the authors</p>	

1.2. 2021 FIGO staging system / 8th TNM classification for vulvar cancer

FIGO	T	N	M	DEFINITION
IA	T1a	N0	M0	Lesion(s) 2 cm or less, confined to the vulva and/or perineum, and with stromal invasion of 1.0 mm or less. No regional lymph nodes.
IB	T1b	N0	M0	Lesion(s) more than 2 cm, or any size with stromal invasion of more than 1.0 mm, confined to the vulva and/or perineum. No metastases in regional lymph nodes.
II	T2	N0	M0	Lesion(s) of any size with extension to adjacent perineal structures (lower/distal third of the urethra, lower/distal third of the vagina, anal involvement). No metastases in regional lymph nodes.
IIIA	T1, T2	N1a, N1b	M0	T1 or T2 lesion(s). One or two lymph-node metastases each less than 5 mm (N1a), or one lymph-node metastasis 5 mm or larger (N1b).
IIIB	T1, T2	N2a, N2b	M0	T1 or T2 lesion(s). Three or more lymph-node metastases each less than 5 mm (N2a), or two or more lymph-node metastases 5 mm or larger (N2b).
IIIC	T1, T2	N2c	M0	T1 or T2 lesion(s). Extranodal lymph-node extension (N2c).
IVA	T1, T2 T3	N3 Any N	M0	T1 or T2 lesion(s) with fixed or ulcerated regional lymph-node metastases (N3). Lesion (s) of any size with extension to any one or more of the following: upper/proximal two thirds of the urethra, upper/proximal two thirds of the vagina, bladder mucosa, rectal mucosa, fixed to pelvic bone (T3), with or without regional lymph-node metastasis.
IVB	Any T	Any N	M1	Any distant metastasis (including pelvic nodes).

Table S2 TNM and FIGO staging for vulvar cancer ^(4, 5, 7)

1.3. Methodology of loco-regional ultrasound staging in vulvar cancer

The routine ultrasound staging for vulvar cancer starts with the transperineal approach in combination with transvaginal or transrectal approach to assess the primary tumor and its spread but also to exclude other unrelated pelvic pathologies. It is always followed by systematic transabdominal approach and finally the transcutaneous approach for inguinofemoral nodal evaluation (Figure S2).

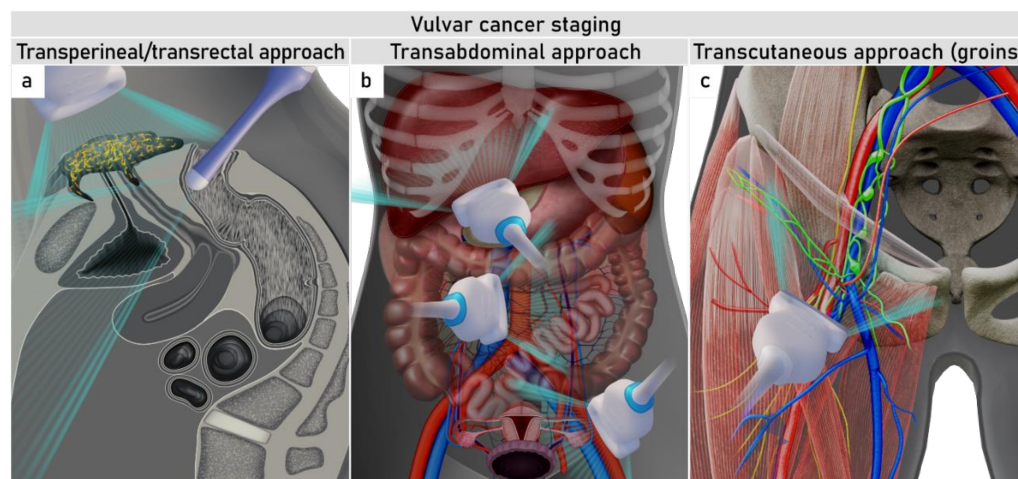


Figure S2 Ultrasound approaches for vulvar cancer staging. Transperineally applied convex or linear array probe for primary tumor assessment in combination with transrectally inserted endoluminal probe to bypass obstruction of the vaginal introitus by a large vulvar cancer (a). Transabdominal approach using a convex array probe for evaluation of distant metastases (b). Transcutaneous approach with linear array probe for inguinofemoral lymph nodes evaluation (c).

There are only limited data on the sonographic features of vulvar cancer. **The transperineal approach** is useful to assess the size of hypoechoic, highly vascularized tumor/-s (if multifocal vulvar cancer) and its extent and relationship with the surrounding structures (Figure S2). Due to tumor growth, hypoechoic tumor spikes or nodular projections may disrupt hyperechoic septa with or without infiltration of the surrounding organs. The convex or linear probe is gently applied on the surface of the primary organ/tumor, and it is examined in sagittal and transverse planes. The sagittal plane is used to assess the caudo-cranial and ventro-dorsal extension of the disease and its relationship with the urethra, the urethrovaginal septum, anus/rectum, and the rectovaginal septum as well as its infiltration into the vagina. The transverse plane, with the probe slightly angled to oblique section and perpendicular to the long axis of the urethra, offers a symmetrical section of the vulva (latero-lateral section). This may be useful in the evaluation of the clitoris, labia minora and majora, bulb of the vestibule, bulbospongiosus and transverse muscles, and others. **The transrectal approach** may be an alternative to the transvaginal route to overcome the obstruction caused by the disease and to assess the integrity of the surrounding structures (Figure S2). In addition, distant (pelvic) lymph nodes are visualized with high resolution by this transrectal or transvaginal approach. Other pelvic pathologies can also be excluded at the same time. **The transabdominal approach** with a convex probe is used to evaluate distant (pelvic and abdominal) lymph nodes and other abdominal spread (Figure S2). **The transcutaneous approach** using linear array probe assessment is the standard approach for visualizing regional (inguinofemoral) lymph nodes (Figure S2). The methodologic assessment of vulvar lymph nodes by ultrasound was previously reported in the VITA consensus.⁽³⁾ High-quality ultrasound examination must be complemented by a structured ultrasound report to communicate clinically relevant information to the referring physician. Localization of the tumor and infiltrated regional and distant lymph nodes ought to be documented in a schematic drawing (Figure S1) within a systematic checklist (Table S1).

Supplemental references

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