Urology CHEAT SHEETS

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EAU-ASCO Collaborative Guidelines on Penile Cancer

Epidemiology, aetiology, classification, staging and diagnosis

EPIDEMIOLOGY AND AETIOLOGY:

Penile carcinoma is usually a squamous cell carcinoma (SCC) (95%) and there are several recognised subtypes of penile SCC with different clinical features and natural history. Penile SCC usually arises from the epithelium of the inner prepuce or the glans.
In industrialised countries is uncommon, with an overall incidence of around 1/100,000 males.

The incidence of penile cancer increases with age, with a peak in the sixth decade and it is common in regions with a high prevalence of human papillomavirus (HPV). Approximately one-third to half of cancer cases are attributed to HPV-associated carcinogenesis. There are no reports linking this cancer to human immunodeficiency virus (HIV) or acquired immune deficiency syndrome (AIDS).

Other predisposing factors have been reported, including phimosis, chronic penile inflammation, lichen sclerosus, sporalene and ultraviolet A phototherapy, smoking, multiple sexual partners and early age of first intercourse.

PATHOLOGY:

Different histological types of penile SCC with different growth patterns, clinical aggressiveness and HPV associations have been identified. Numerous mixed forms exist such as the warty-basaloid form, with 50-60% the most common mixed form, the usual-verrucous (hybrid), usual-warty, usual-basaloid and the usual-papillary, as well as other rarer combinations.

Pathological subtype, perineural invasion, lymphovascular invasion, depth of invasion and grade in the primary tumour are strong predictors of poor prognosis and high cancer-specific mortality. Tumour grade is a predictor of metastatic spread, and lymphatic invasion is a predictor of metastasis.

Recommendations	Strength rating
The pathological evaluation of penile carcinoma specimens must include the pTNM (see Chapter 4) stage and an assessment of tumour grade.	Strong
The pathological evaluation of penile carcinoma specimens must include an assessment of p16 by immunohistochemistry.	Strong
The pathological evaluation of penile carcinoma specimens should follow the ICCR dataset synoptic report.	Strong

ICCR = International Collaboration on Cancer Reporting.

STAGING AND CLASSIFICATION SYSTEMS:

UICC/AJCC 8th edition TNM clinical and pathological classification of penile cancer.

Clinical classification	
T - Primary Tumour	
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma *in situ* (Penile Intraepithelial Neoplasia – PeIN)
Ta	Non-invasive verrucous carcinoma*
T1	Tumour invades subepithelial connective tissue
T1a	Tumour invades subepithelial connective tissue without lymphovascular invasion or perineural invasion and is not poorly differentiated
T1b	Tumour invades subepithelial connective tissue with lymphovascular invasion or perineural invasion or is poorly differentiated
T2	Tumour invades corpus spongiosum with or without invasion of the urethra
T3	Tumour invades corpus cavernosum with or without invasion of the urethra
T4	Tumour invades other adjacent structures
N - Regional Lymph Nodes	
cNX	Regional lymph nodes cannot be assessed
cN0	No palpable or visibly enlarged inguinal lymph nodes
cN1	Palpable mobile unilateral inguinal lymph node
cN2	Palpable mobile multiple or bilateral inguinal lymph nodes
cN3	Fixed inguinal nodal mass *or* pelvic lymphadenopathy, unilateral or bilateral
M - Distant Metastasis	
cM0	No distant metastasis
cM1	Distant metastasis
Pathological classification	
The pT categories correspond to the clinical T categories. The pN categories are based upon biopsy or surgical excision	
pN - Regional Lymph Nodes	
pNX	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastasis
pN1	Metastasis in one or two inguinal lymph nodes
pN2	Metastasis in more than two unilateral inguinal nodes or bilateral inguinal lymph nodes
pN3	Metastasis in pelvic lymph node(s), unilateral *or* bilateral or extranodal extension of regional lymph node metastasis
pM - Distant Metastasis	
pM1	Distant metastasis microscopically confirmed
G - Histopathological Grading	
GX	Grade of differentiation cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated
G4	Undifferentiated

DIAGNOSTIC EVALUATION AND STAGING:

PRIMARY LESION AND REGIONAL LYMPH NODES:

Primary penile carcinoma are usually clinically evident lesions often presenting as raised or ulcerous lesions which can be locally destructive.

Non-palpable inguinal nodes: likelihood of micro-metastatic disease is about 25%. Imaging studies are not helpful in staging clinically normal inguinal region. Further management should be guided by pathological risk factors of the primary tumour.

Palpable inguinal nodes: are highly indicative of lymph node metastases. Pelvic CT can be used to assess the pelvic lymph nodes. Imaging with 18FDG-PET/CT has shown high sensitivity and specificity for confirming metastatic nodes.

DISTANT METASTASES:

Staging for systemic metastases should be performed in patients with positive inguinal nodes. Abdominal and pelvic CT should be done plus a chest X-ray, although a thoracic CT is more sensitive. PET/CT is also an option.

Recommendations	Strength rating
Primary tumour	
Perform a detailed physical examination of the penis and external genitalia, recording morphology, size and location of the penile lesion, including extent and invasion of penile (adjacent) structures.	Strong
Perform magnetic resonance imaging (MRI) of the penis/primary tumour (artificial erection not mandatory) when there is uncertainty regarding corporal invasion and/or the feasibility of (organ-sparing) surgery. If MRI is not available, offer ultrasound (US) as alternative option.	Weak
Obtain a pre-treatment biopsy of the primary lesion when malignancy is not clinically obvious, or when non-surgical treatment of the primary lesion is planned (e.g., topical agents, laser, radiotherapy).	Strong
Inguinal lymph nodes (LN)	
Perform a physical examination of both groins. Record the number, laterality and characteristics of any palpable/suspicious inguinal nodes.	Strong
Clinically node-negative (cN0)	
If there are no palpable/suspicious nodes (cN0) at physical examination, offer surgical LN staging to all patients at high risk of having micro-metastatic disease (T1b or higher).	Strong
In case of T1a G2 disease, also discuss surveillance as an alternative to surgical staging with patients willing to comply with strict follow-up.	Weak
When surgical staging is indicated, offer dynamic sentinel node biopsy (DSNB). If DSNB is not available and referral is not feasible, or if preferred by the patient after being well informed, offer inguinal lymph node dissection (ILND) (open or video-endoscopic).	Strong
If DSNB is planned, perform inguinal US first, with fine needle aspiration cytology (FNAC) of sonographically abnormal LNs.	Strong
Clinically node-positive (cN+)	
If there is a palpable/suspicious node at physical examination (cN+), obtain (image-guided) biopsy to confirm nodal metastasis before initiating treatment.	Strong
In cN+ patients, stage the pelvis and exclude distant metastases with ^{18}F-fluoro-2-deoxy-D-glucose positron emission tomography (^{18}FDG-PET) computed tomography (CT) or CT of the chest and abdomen before initiating treatment.	Strong