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EAU-ASCO Collaborative Guidelines on Penile Cancer		
Topic	**Recommendation**	**Strength**
Pathological assessment of tumour specimens	The pathological evaluation of penile carcinoma specimens must include the pTNM stage and an assessment of tumour grade.	S
	The pathological evaluation of penile carcinoma specimens must include an assessment of p16 by immunohistochemistry.	S
	The pathological evaluation of penile carcinoma specimens should follow the ICCR dataset synoptic report.	S
Diagnosis and staging of penile cancer	*Primary tumor*	
	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.	S
	Perform 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 US as alternative option.	W
	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).	S
	Inguinal lymph nodes	
	Perform a physical examination of both groins. Record the number, laterality and characteristics of any palpable/suspicious inguinal nodes.	S
	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).	S
	In case of T1a G2 disease, also discuss surveillance as an alternative to surgical staging with patients willing to comply with strict follow-up.	W
	When surgical staging is indicated, offer DSNB. If DSNB is not available and referral is not feasible, or if preferred by the patient after being well informed, offer ILND (open or video-endoscopic).	S
	If DSNB is planned, perform inguinal US first, with FNAC of sonographically abnormal LNs.	S

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	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.	S
	In cN+ patients, stage the pelvis and exclude distant metastases with ^{18}FDG-PET CT or CT of the chest and abdomen before initiating treatment.	S
Local treatment of penile carcinoma	Offer a balanced and individualised discussion on benefits and harms of possible treatments options with the goal of shared decision making.	S
	Inform patients of the higher risk of local recurrence when using organ-sparing treatments compared to amputative surgery.	S
	Topical therapy	
	Offer topical therapy with 5-fluorouracil or imiquimod to patients with biopsy-confirmed PeIN.	W
	Clinically assess treatment effects after a treatment-free interval and in cases of doubt perform a biopsy. If topical treatment fails, it should not be repeated.	W
	Laser ablation	
	Offer laser ablation using CO2 or Nd:YAG laser to patients with biopsy-confirmed PeIN, Ta or T1 lesions.	W
	Organ-sparing treatment: surgery (circumcision, wide local excision, glansectomy and glans resurfacing)	
	Offer organ-sparing surgery and reconstructive techniques to patients with lesions confined to the glans and prepuce (PeIN, Ta, T1–T2) and who are willing to comply with strict follow-up.	S
	Perform intra-operative frozen section analysis of resection margins in cases of doubt on the completeness of resection.	W
	Offer salvage organ-sparing surgery to patients with small recurrences not involving the corpora cavernosa.	W
	Organ-sparing treatment: radiotherapy (EBRT and brachytherapy)	
	Offer radiotherapy to selected patients with biopsy-confirmed T1 or T2 lesions.	S
	Amputative surgery (partial- and total penectomy)	
	Offer partial penectomy, with or without reconstruction, to patients with invasion of the corpora cavernosa (T3) and those not willing to undergo organ-sparing surgery or not willing to comply with strict follow-up.	S
	Offer total penectomy with perineal urethrostomy to patients with large invasive tumours not amenable to partial amputation.	S

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	Offer amputative surgery to patients with large local recurrences or corpora cavernosa involvement	W
	Multimodal therapy	
	Offer induction chemotherapy followed by surgery to responders, or chemo-radiotherapy to patients with non-resectable advanced primary lesions, or to patients with locally advanced-disease who refuse surgical management.	W
Radical inguinal lymph node dissection in cN1-2 disease	In patients with cN1 disease offer either ipsilateral: • fascial-sparing inguinal lymph node dissection • open radical ILND; sparing the saphenous vein, if possible	S
	In patients with cN2 disease offer ipsilateral open radical ILND; sparing the saphenous vein, if possible.	S
	Offer minimally-invasive inguinal LN dissection to patients with cN1–2 disease only as part of a clinical trial.	S
	Offer chemotherapy as an alternative approach to upfront surgery in selected patients with bulky mobile inguinal nodes or bilateral disease (cN2) who are candidates for cisplatin and taxane-based chemotherapy.	W
	Complete surgical inguinal and pelvic nodal management within 3 months of diagnosis (unless the patient has undergone prior neoadjuvant chemotherapy).	W
Prophylactic pelvic lymph node dissection	Offer open or minimally-invasive prophylactic ipsilateral pelvic lymphadenectomy to patients if: • three or more inguinal nodes are involved on one side on pathological examination • extranodal extension is reported on pathological examination	W
	Complete surgical inguinal and pelvic nodal management within 3 months of diagnosis (unless the patient has undergone neoadjuvant chemotherapy).	W
Surgical management of cN3 disease	Offer NAC using a cisplatin- and taxane-based combination to chemotherapy-fit patients with pelvic lymph node involvement or those with extensive inguinal involvement (cN3), in preference to up front surgery.	W
	Offer surgery to patients responding to NAC in whom resection is feasible.	S
	Offer surgery to patients who have not progressed during NAC, but resection is feasible. See also (chemo)radiation.	W
	Do not offer Video Endoscopic Inguinal lymphadenectomy.	S
Neoadjuvant and adjuvant chemotherapy	Offer neoadjuvant chemotherapy using a cisplatin- and taxane-based combination to chemotherapy-fit patients with pelvic lymph node involvement or those with extensive inguinal involvement (cN3), in preference to up front surgery.	W
	Offer chemotherapy as an alternative approach to upfront surgery to selected patients with bulky mobile inguinal nodes or bilateral disease (cN2) who are candidates for cisplatin and taxane-based chemotherapy.	W

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	Have a balanced discussion of risks and benefits of adjuvant chemotherapy with high-risk patients with surgically resected disease, in particular with those with pathological pelvic LN involvement (pN3). See also section on post-operative radiotherapy.	W
Pre- and post-operative radiotherapy	Offer adjuvant radiotherapy (with or without chemo sensitisation) to patients with pN2/N3 disease, including those who received prior neoadjuvant chemotherapy.	W
	Offer definitive radiotherapy (with or without chemo sensitisation) to patients unwilling or unable to undergo surgery for lymph node dissection.	W
	Offer radiotherapy (with or without chemo sensitisation) to cN3 patients who are not candidates for multi-agent chemotherapy.	W
Systemic and palliative therapies for advanced penile cancer	*Systemic therapies*	
	Offer patients with distant metastatic disease, platinum-based chemotherapy as the preferred approach to first-line palliative systemic therapy.	W
	Do not offer bleomycin because of the pulmonary toxicity risk.	S
	Offer patients with progressive disease under platinum chemotherapy the opportunity to enroll in clinical trials, including experimental therapies within phase I or basket trials.	S
	Radiotherapy	
	Offer radiotherapy for symptom control (palliation) in advanced disease.	S
Follow-up and quality of life	Deliver penile cancer care as part of an extended multi-disciplinary team comprising of urologists specialising in penile cancer, specialist nurses, pathologists, uro-radiologists, nuclear medicine specialists, medical and radiation oncologists, lymphoedema therapists, psychologists, counsellors, palliative care teams for early symptom control, reconstructive surgeons, vascular surgeons, sex therapists.	S
	Follow-up men after penile cancer treatment, initially three-monthly for 2 years then less frequently to assess for recurrent disease and to offer patient support services through the extended multi-disciplinary team. At discharge, recommend self-examination with easy access back to the clinic as local recurrence can occur late.	S
	Discuss the psychological impact of penile cancer and its treatments with the patient and offer psychological support and counselling services.	S
	Discuss the negative impact of treatments for the primary tumour on penile appearance, sensation, urinary and sexual function so that the patient is better prepared for the challenges he may face.	S
	Discuss the potential impact of lymphoedema as a consequence of inguinal and pelvic lymph node treatment with the patient and assess patients for it at follow-up and refer to lymphoedema therapists early.	S

Abbreviations. ^{18}FDG-PET, ^{18}F-fluoro-2-deoxy-D-glucose positron emission tomography; cN+, clinically-node positive; cN0, clinically-node negative; cN1, clinical N1 disease; cN2, clinical N2 disease; cN3, clinical N3 disease; CT, computed tomography; DSNB, dynamic sentinel node biopsy; FNAC, fine needle aspiration cytology; ICCR, International Collaboration on Cancer Reporting; ILND, inguinal lymph node dissection; LN, lymph node; MRI, magnetic resonance imaging; NAC, neoadjuvant chemotherapy; PeIN, penile intra-epithelial neoplasia; S, strong; US, ultrasound; W, weak