

Penile cancer practice guidelines

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We present a condensed version of the ESMO clinical practice guidelines on penile cancer.¹

Penile cancer is an uncommon but ominous disease. In the last few years there has been a shift towards penile-preserving techniques, because besides local control, an important aim of surgery is to preserve the functionality and sexual function of the penis. This has an important impact on the patient's self-esteem, quality of life and general mental health. Despite the rarity of the disease we gradually achieve more insight in the proper staging and treatment of this malignancy.

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Introduction

Penile cancer is an uncommon but ominous disease. Important risk factors include lack of hygiene, religious, social and cultural habits. The disease is facilitated by phimosis and may be preceded by chronic inflammations and condylomata.^{2,3} Penile cancer is generally an aggressive disease characterised by early locoregional lymph node spread and later metastases in distant sites.

Diagnosis and treatment

Primary tumour (Figure 1)

Accurate diagnosis and staging of the primary tumour are of the greatest importance for appropriate treatment. Penile cancer should preferably be staged according to the TNM classification (Table 1). A thorough physical examination is necessary to record the characteristics of the lesion, as well as a cytological and/or histological diagnosis, whereby an incisional or excisional biopsy is advised. MRI (combined with intracavernous injection of PG E1) can be helpful if there is any doubt as to the presence of corpora cavernosa invasion and to determine whether limited surgery is possible.⁴

Local recurrence after conservative surgery does not seem to have a negative impact on long-term survival. Furthermore a margin of <5 mm is adequate for most tumours.⁵ The recurrence rate with these resection margins is less than 5%. This led to a shift towards penile-

preserving techniques. Besides local control, an important aim of surgery is to preserve functionality and sexual function of the penis. This has a major impact on the patient's self-esteem, quality of life and general mental health. There's only very few data about functional and psychosexual outcome of organ preservation by radiotherapy.⁶ There are no direct comparisons between radiotherapy and the newer penile-preserving techniques, and studies with chemotherapy are very limited.

The role of salvage surgery after radio- and/or chemotherapy remains controversial. A limited number of patients, where positive resection margins are anticipated, could benefit from pre surgical down-staging.

Regional lymph nodes (Figure 2)

Penile cancer drains primarily to the inguinal nodes. Usually the primary tumour and regional lymph nodes are treated separately. Patients with low risk disease (T1G1) do not need further nodal assessment after local treatment.² If there are no lymph nodes palpable, a dynamic sentinel node biopsy (DSNB) is advised for intermediate (T1G2) or high-risk (T1G3 or greater) malignancy. Early detection and resection of lymph node metastases by DSNB improves survival in comparison with a surveillance policy.⁷ As an alternative, ultrasound-guided fine-needle aspiration cytology (FNAC) of visualised nodes can be used.² If the lymph nodes are palpable, FNAC biopsy and/or

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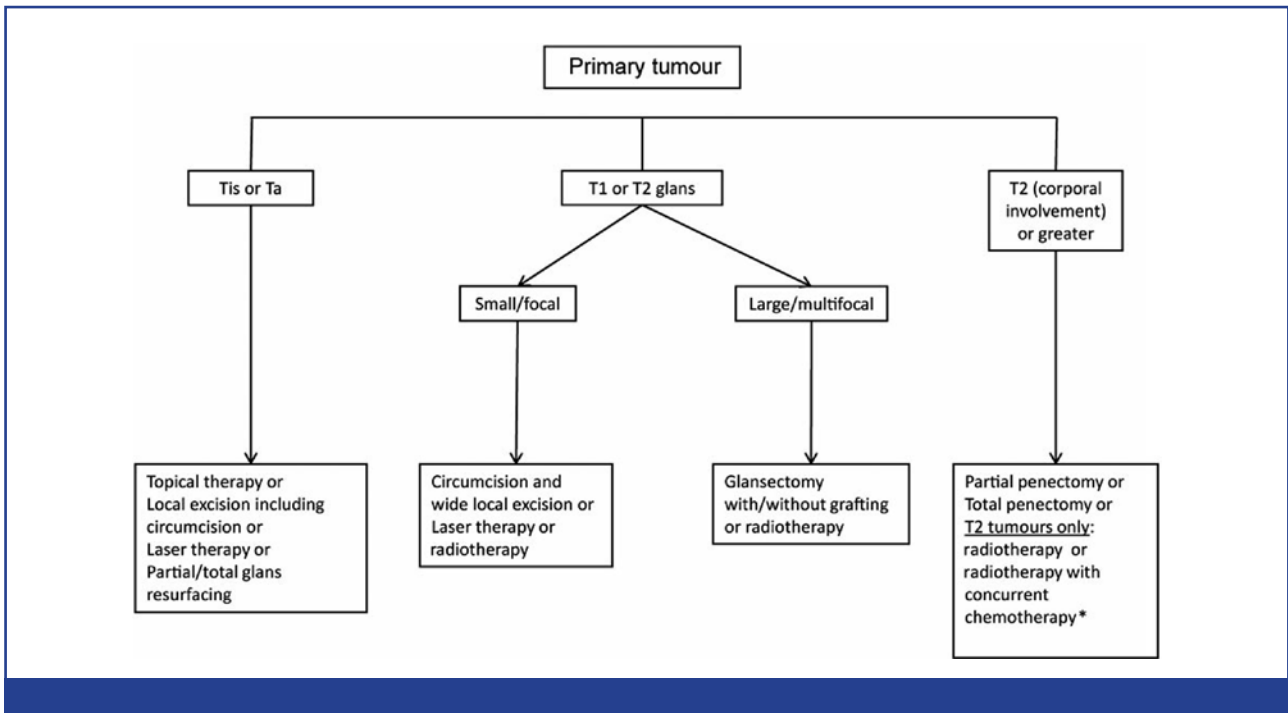


Figure 1. Guidelines on treatment strategies for the primary tumour.

histology must be performed. In clinically suspicious nodes with a negative biopsy a repeat biopsy or node excision is advised.⁸ Half of palpable inguinal nodes are enlarged because of inflammatory changes, but those

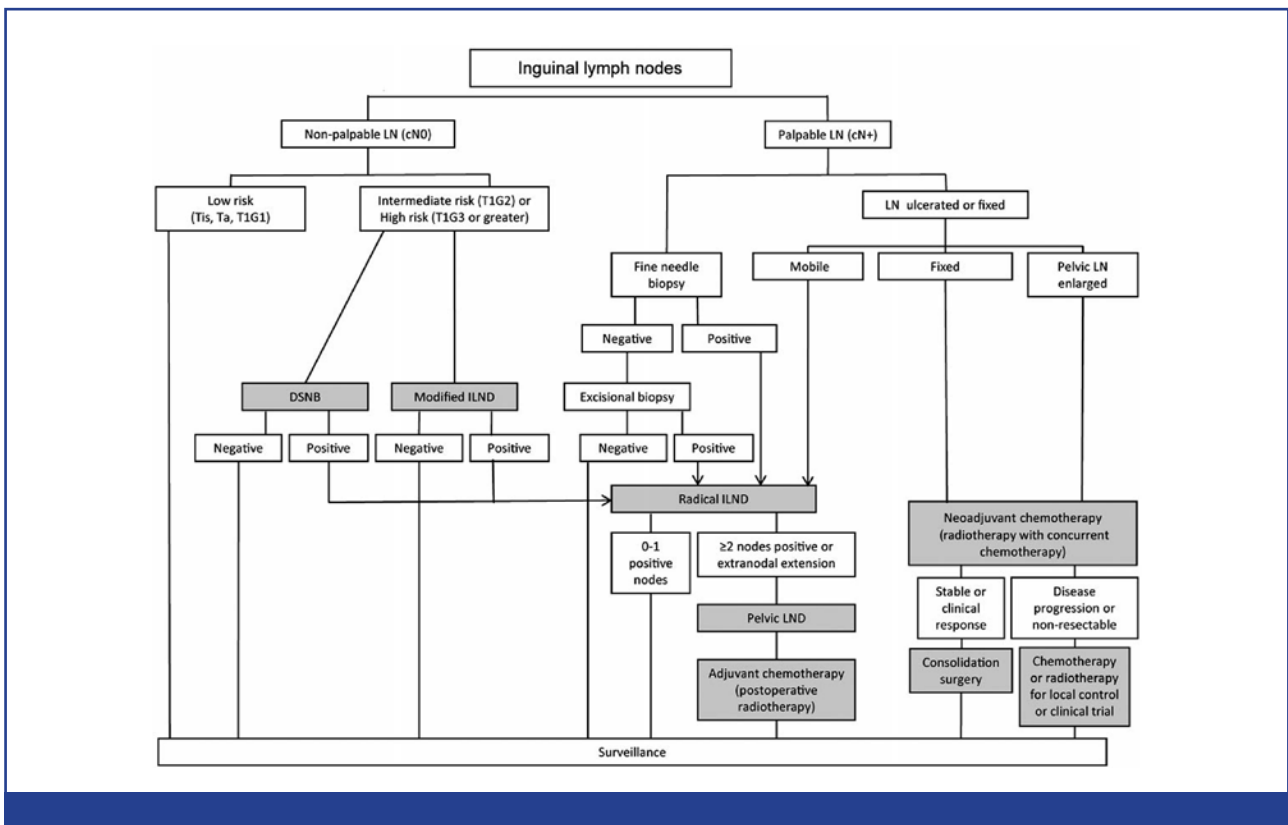


Figure 2. Guidelines on treatment strategies for the regional LNs.

LN: lymph nodes, ILND: inguinal lymphadenectomy, DSNB: dynamic sentinel node biopsy.

Table 1. American Joint Committee on Cancer/Union for International Cancer Control (AJCC/UICC) seventh 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
Ta	Non-invasive verrucous carcinoma, not associated with destructive invasion
T1	Tumour invades sub-epithelial connective tissue
T1a	Without lymphovascular invasion and well or moderately differentiated (T1G1-2)
T1b	With lymphovascular invasion or poorly differentiated/undifferentiated (T1G3-4)
T2	Tumour invades corpus spongiosum/corpora cavernosa
T3	Tumour invades urethra
T4	Tumour invades other adjacent structures
N: Regional lymph nodes	
NX	Regional lymph nodes cannot be assessed
N0	No palpable or visibly enlarged inguinal lymph node
N1	Palpable mobile unilateral inguinal lymph node
N2	Palpable mobile multiple or bilateral inguinal lymph nodes
N3	Fixed inguinal nodal mass or pelvic lymphadenopathy, unilateral or bilateral
M: Distant metastasis	
M0	No distant metastasis
M1	Distant metastasis
Pathological classification	
The pT categories correspond to the 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	Intra-nodal metastasis in a single inguinal lymph node
pN2	Metastasis in multiple 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	
pM0	No distant metastasis
pM1	Distant metastasis
G: Histological grading	
GX	Grade of differentiation cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3-4	Poorly differentiated/undifferentiated

who become palpable during follow-up are malignant in nearly 100% of cases.⁹

Lymphadenectomy is the standard treatment of patients with inguinal lymph node metastases.¹⁰

The role of adjuvant postoperative radiation remains controversial. The incidence of inguinal failure after lymphadenectomy varies between 25% and 77%.¹¹⁻¹³

Chen et al. reported in a small series of patients that postoperative radiotherapy reduced the recurrence rate from

60% to 11%.¹⁴ Nevertheless larger series confirming these results are lacking.

A few retrospective studies suggest some benefit of radiotherapy with concurrent cisplatin-based chemotherapy in locally advanced unresectable disease, but prospective studies of these treatment strategies are unavailable in penile cancer.¹⁵⁻¹⁶

Neoadjuvant chemotherapy followed by radical surgery is advisable in unresectable or recurrent lymph node

metastases.¹⁷⁻¹⁹ Adjuvant chemotherapy is recommended in pN2-3 patients.²⁰

Distant metastases

For detection of pelvic lymph node metastases, scanning with 18F-FDG PET-CT appears encouraging with great accuracy and also identifies more distant metastases in patients with inguinal node-positive penile cancer.²¹ A bone scan is advised in symptomatic patients. A sustained palliative response has been observed with combination chemotherapy using cisplatin and gemcitabine for the management of metastatic penile cancer.²² The overall survival of patients with metastatic disease (beyond the pelvic nodes) is 0% at five years and <10% at two years. Patients who present with metastatic disease have a very poor prognosis and early consideration of palliative care is recommended.

Follow-up

After penile-preserving treatment, a follow-up visit every three months is advised in the first two years and every six months in the following three years. After penectomy, the intervals of follow-up visits are biannually in the first two years and annually in the following three years.²³ Follow-up can stop after five years in well educated and motivated patients who are able to perform self-examination.

Conclusion

As more people achieve long-term survival after cancer, infertility and sexual dysfunction are increasingly recognised as negative consequences that affect quality of life. Early referral to specialised centres for correct diagnosis and staging is recommended. Selection of appropriate treatments and follow-up are fundamental for the best oncologic results and quality of life for penile cancer patients. Penile-sparing surgery allows for a better quality of life than penectomy and must be considered whenever feasible. In patients with recurrent or advanced disease, adjuvant and neoadjuvant chemotherapy showed promising results. Psychological support should be offered at a low threshold.

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