

PROGNOSIS:

Prognostic factors for survival in primary urethral carcinoma (UC) are: age, gender, race, tumour stage and grade, nodal stage, presence of distant metastasis, histological type, tumour size, tumour location, concomitant bladder cancer and type and modality of treatment.

In locally-advanced urothelial- and squamous cell carcinoma (SCC) of the urethra, **treatment in reference centres improves overall survival (OS)**.

DISEASE MANAGEMENT:

Treatment of primary localised urethral carcinoma in males:

In distal urethral tumours performing a partial urethrectomy with a minimal safety margin does not increase the risk of local recurrence.

Recommendations	Strength rating
Offer distal urethrectomy as an alternative to penile amputation in localised distal urethral tumours, if negative surgical margins can be achieved intra-operatively.	Weak
Ensure complete circumferential assessment of the proximal urethral margin if penile preserving surgery is intended.	Strong

Treatment of primary localised urethral carcinoma in females:

In females with distal urethral tumours, urethra-sparing surgery and local radiotherapy (RT) represent alternatives to primary urethrectomy but are associated with increased risk of tumour recurrence and local toxicity.

Recommendations	Strength rating
Offer urethra-sparing surgery, as an alternative to primary urethrectomy, to females with distal urethral tumours, if negative surgical margins can be achieved intra-operatively.	Weak
Offer local radiotherapy, as an alternative to urethral surgery, to females with localised urethral tumours but discuss local toxicity.	Weak

Multimodal treatment in locally-advanced urethral carcinoma in both males and females:

Multimodal therapy in primary urethral carcinoma consists of definitive surgery plus chemotherapy with additional RT. Its use has decreased over time. Treatment in reference centres was reported to result in higher utilisation of neoadjuvant- and multimodal treatment and improved OS in patients with locally advanced urothelial- and SCC primary urethral carcinoma.

Recommendations	Strength rating
Refer patients with advanced urethral carcinoma to academic centres.	Strong
Discuss treatment of patients with locally-advanced urethral carcinoma within a multidisciplinary team of urologists, radiation-oncologists, and oncologists.	Strong
In locally-advanced urethral carcinoma, use cisplatin-based chemotherapeutic regimens with curative intent prior to surgery.	Weak
In locally-advanced squamous cell carcinoma (SCC) of the urethra, offer the combination of curative radiotherapy (RT) with radiosensitising chemotherapy for definitive treatment and genital preservation.	Weak
Offer salvage surgery or RT to patients with urethral recurrence after primary treatment.	Weak
Offer inguinal lymph node (LN) dissection to patients with limited LN-positive urethral SCC.	Weak

Treatment of urothelial carcinoma of the prostate:

Recommendations	Strength rating
Offer a urethra-sparing approach with transurethral resection (TUR) and bacillus-Calmette Guérin (BCG) to patients with non-invasive urethral carcinoma or carcinoma <i>in situ</i> of the prostatic urethra and prostatic ducts.	Strong
In patients not responding to BCG, or in patients with extensive ductal or stromal involvement, perform a cystoprostatectomy with extended pelvic lymphadenectomy.	Weak

Metastatic disease: Systemic therapy in metastatic disease should be selected based on the histology of the tumour. The EAU Guidelines on Muscle-invasive and Metastatic Bladder Cancer can be followed if UC is the predominant histology.

Figure 1: Flowchart of the management of primary urethral carcinoma

* Ensure complete circumferential assessment if penile-preserving/urethra-sparing surgery or partial urethrectomy is intended.
 ** Squamous cell carcinoma.
 *** Regional lymphadenectomy should be considered in clinically enlarged lymph nodes.
 **** Consider neoadjuvant chemotherapy
 ***** In extensive or BCG-unresponsive disease: consider (primary) cystoprostatectomy +/- urethrectomy + lymphadenectomy.
 BCG = bacillus Calmette-Guérin; CT = computed tomography; MRI = magnetic resonance imaging; PUC = primary urethral carcinoma; TUR = transurethral resection

