

## Epidemiology, classification, diagnosis and prognosis

### EPIDEMIOLOGY:

Upper urinary tract urothelial carcinomas (UTUCs) are uncommon and account for only 5–10% of UCs. Peak incidence in individuals aged 70–90 years. Pyelocaliceal tumours are twice as common as ureteral tumours. Multifocal tumours are found in 10–20%.

Concomitant CIS: 11- 36%. Concurrent bladder cancer: 17%.

2/3 have invasive disease at diagnosis compared to 15–25% with muscle-invasive bladder tumours. 9% of patients present with metastasis.

Genomic characterisation of UTUC provides information regarding the risk of bladder recurrence and can identify tumours associated with Lynch syndrome. Patients identified at high risk for Lynch syndrome should undergo DNA sequencing for patient and family counselling.

| Recommendations   | Strength rating |
|---|-----------------|
| Evaluate patient and family history based on the Amsterdam criteria to identify patients with upper tract urothelial carcinoma. | Weak            |
| Evaluate patient exposure to smoking and aristolochic acid.   | Weak            |

### HISTOLOGY AND CLASSIFICATION:

Almost always urothelial carcinomas and pure non-urothelial histology is rare.

Pure squamous cell carcinoma is often assumed to be associated with chronic inflammatory diseases and infections arising from urolithiasis.

Urothelial carcinoma with divergent squamous differentiation is present in approximately 15% of cases.

UTUCs with variant histology are high-grade and have a worse prognosis compared with pure UC.

### STAGING: TNM, 2017:

| T - Primary tumour       |   |
|--------------------------|---|
| TX                       | Primary tumour cannot be assessed   |
| T0                       | No evidence of primary tumour   |
| Ta                       | Non-invasive papillary carcinoma  |
| Tis                      | Carcinoma <i>in situ</i>  |
| T1                       | Tumour invades subepithelial connective tissue  |
| T2                       | Tumour invades muscularis   |
| T3                       | (Renal pelvis) Tumour invades beyond muscularis into peripelvic fat or renal parenchyma (Ureter) Tumour invades beyond muscularis into periureteric fat |
| T4                       | Tumour invades adjacent organs or through the kidney into perinephric fat   |
| N - Regional lymph nodes |   |
| NX                       | Regional lymph nodes cannot be assessed   |
| N0                       | No regional lymph node metastasis   |
| N1                       | Metastasis in a single lymph node 2 cm or less in the greatest dimension  |
| N2                       | Metastasis in a single lymph node more than 2 cm, or multiple lymph nodes   |
| M - Distant metastasis   |   |
| M0                       | No distant metastasis   |
| M1                       | Distant metastasis  |

TNM = Tumour, Node, Metastasis (classification).

### DIAGNOSIS:

- Symptoms:

**Most common symptom: visible or nonvisible haematuria (70–80%)**

Flank pain (clot or tumour obstruction or less often due to local growth).

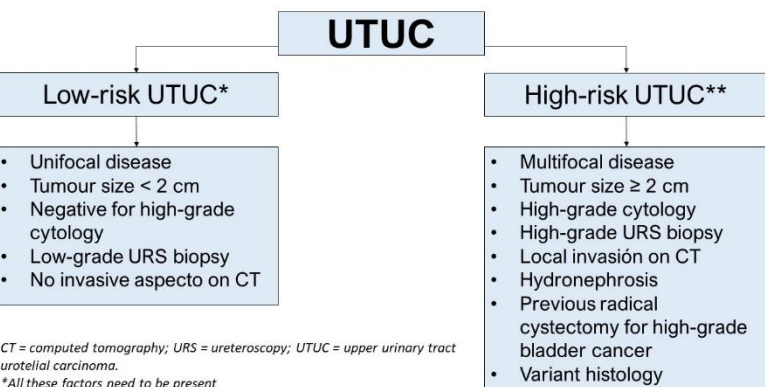
- Imaging, cystoscopy, cytology and diagnostic ureteroscopy:

| Summary of evidence   | LE |
|---|----|
| The diagnosis and staging of UTUC is best done with computed tomography urography and URS.                  | 2a |
| Selective urinary cytology has high sensitivity in high-grade tumours, including carcinoma <i>in situ</i> . | 3  |
| Urethroscopy can detect concomitant bladder cancer.   | 2a |

| Recommendations  | Strength rating |
|--|-----------------|
| Perform a urethroscopy to rule out bladder tumour.   | Strong          |
| Perform a computed tomography (CT) urography for diagnosis and staging.  | Strong          |
| Use diagnostic ureteroscopy and biopsy if imaging and cytology are not sufficient for the diagnosis and/or risk-stratification of the tumour.                | Strong          |
| Magnetic resonance urography or <sup>18</sup> F-Fluorodeoxyglucose positron emission tomography/computed tomography may be used when CT is contra-indicated. | Weak            |

### PROGNOSIS:

#### Risk stratification of non-metastatic UTUC

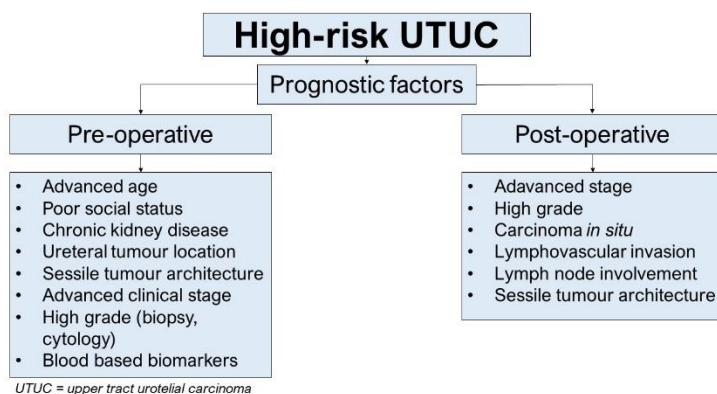


CT = computed tomography; URS = ureteroscopy; UTUC = upper urinary tract urothelial carcinoma.

\*All these factors need to be present

\*\*Any of these factors need to be present

#### UTUC - prognostic factors included in prognostic models



UTUC = upper tract urothelial carcinoma

| Summary of evidence  | LE |
|--|----|
| Important prognostic factors for risk stratification include tumour multifocality, size, stage, grade, hydronephrosis and variant histology. | 3  |
| Models are available to predict non-organ confined disease and altered prognosis after RNU.  | 3  |
| Patient, tumour and treatment-related factors impact risk of bladder recurrence.   | 3  |
| Currently, no prognostic biomarkers are validated for clinical use.  | 3  |

| Recommendation   | Strength rating |
|--|-----------------|
| Use prognostic factors to risk-stratify patients for therapeutic guidance. | Weak            |