

EAU GUIDELINES ON UROTHELIAL CARCINOMA OF THE UPPER URINARY TRACT (UTUCs)

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Epidemiology

UTUC are uncommon and account for only 5-10% of urothelial cell carcinomas (UCs). They have a similar morphology to bladder carcinomas and nearly all UTUCs are urothelial in origin.

Staging and grading systems

The UICC 2017 TNM (Tumour, Node, Metastasis Classification) for renal pelvis and ureter is used for staging (Table 1).

Tumour grade

The 2004/2016 WHO classification distinguishes between non-invasive tumours:

- papillary urothelial neoplasia of low malignant potential;
- low-grade urothelial carcinomas;
- high-grade urothelial carcinomas.

As well as flat lesions (carcinoma *in situ*) and invasive carcinoma.

Upper urinary tract tumours with low malignant potential are very rare.

Table 1: TNM Classification 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 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

Diagnosis

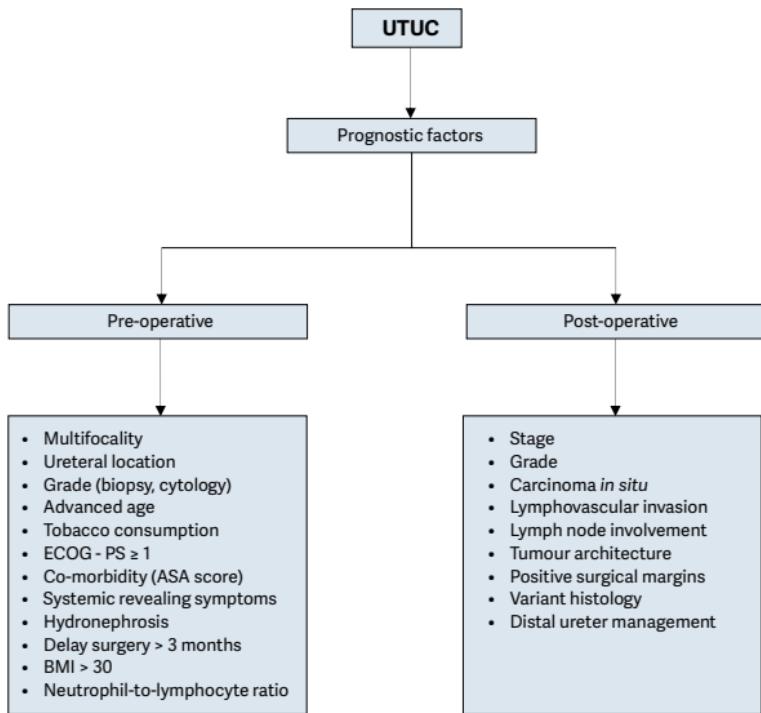
UTUCs are diagnosed using imaging, cystoscopy, urinary cytology and diagnostic ureteroscopy. In case conservative management is considered, a pre-operative ureteroscopic assessment is needed.

Recommendations	Strength rating
Perform cystoscopy to rule out bladder tumour.	Strong
Perform computed tomography (CT) of chest, abdomen and pelvis for staging.	Strong
Use diagnostic ureteroscopy and biopsy only if the result will influence the type of treatment.	Strong
Use CT for staging the chest.	Strong
If CT is contra-indicated, magnetic resonance imaging may be used for imaging the abdomen and pelvis.	Strong

Prognosis

Invasive UTUC usually have a very poor prognosis. The main prognostic factors are listed in Figure 1.

Figure 1: UTUCs: Prognostic factors

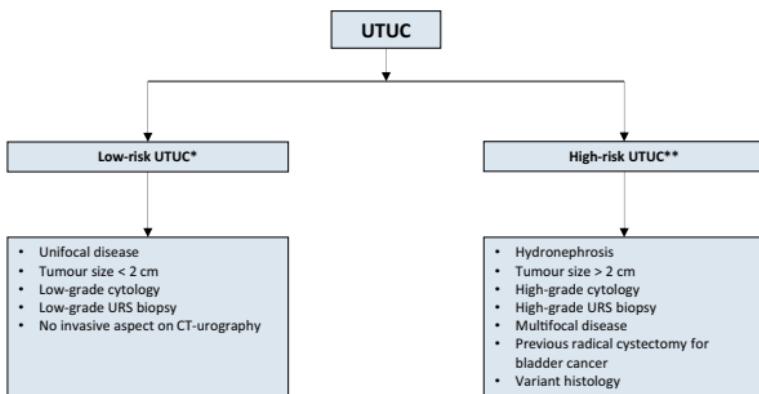


ASA = American Society of Anesthesiologists; BMI = body mass index; ECOG PS = Eastern Cooperative Oncology Group performance status performance score; UTUC = upper urinary tract urothelial carcinoma.

Risk stratification

It is necessary to 'risk-stratify' UTUC cases before treatment to identify those patients who are more suitable for kidney-sparing management rather than radical extirpative surgery (Figure 2).

Figure 2: Pre-intervention risk stratification of UTUCs



*All of these factors need to be present.

** Any of these factors need to be present.

CTU = computed tomography urography; URS = ureteroscopy;

UTUC = upper urinary tract urothelial carcinoma.

Disease management (see also Figures 3 & 4)

Localised disease

Kidney-sparing surgery

Kidney-sparing surgery for low-risk UTUC consists of surgery preserving the upper urinary renal unit and should be discussed in all low-risk cases, irrespective of the status of the contralateral kidney. Kidney-sparing surgery potentially allows avoiding the morbidity associated with open radical surgery without compromising oncological outcomes and kidney function. Kidney-sparing surgery can also be considered in select patients with serious renal insufficiency or solitary kidney (i.e. imperative indications).

Recommendations	Strength rating
Offer kidney-sparing management as primary treatment option to patients with low-risk tumours.	Strong
Offer kidney-sparing management to patients with high-risk distal ureteral tumours.	Weak
Offer kidney-sparing management to patients with solitary kidney and/or impaired renal function, providing that it will not compromise survival. This decision will have to be made on a case-by-case basis with the patient.	Strong
Use a laser for endoscopic treatment of upper tract urothelial carcinoma.	Weak

The instillation of Bacillus Calmette-Guérin or mitomycin C in the urinary tract by percutaneous nephrostomy or via a ureteric stent is technically feasible after kidney-sparing management or for treatment of carcinoma *in situ*. However, the benefits have not been confirmed.

Radical nephroureterectomy (RNU)

Open RNU with bladder cuff excision is the standard treatment for high-risk UTUC, regardless of tumour location.

Adjuvant chemotherapy after RNU reduces the risk of recurrence by more than 50% as compared to surgery alone.

In high-risk patients, neoadjuvant chemotherapy has been associated with significant downstaging at surgery and ultimately survival benefit as compared to RNU alone.

Recommendations	Strength rating
Perform radical nephroureterectomy in patients with high-risk tumours.	Strong
Technical steps of radical nephroureterectomy	
Remove the bladder cuff.	Strong
Perform a lymphadenectomy in patients with high-risk tumours.	Weak
Offer a post-operative bladder instillation of chemotherapy to lower the intravesical recurrence rate.	Strong

Metastatic disease

Radical nephroureterectomy has no benefit in metastatic (M+) disease, but may be used in palliative care. As UTUCs are urothelial tumours, platinum-based chemotherapy should provide similar results to those in bladder cancer. Currently, insufficient data are available to provide any recommendations.

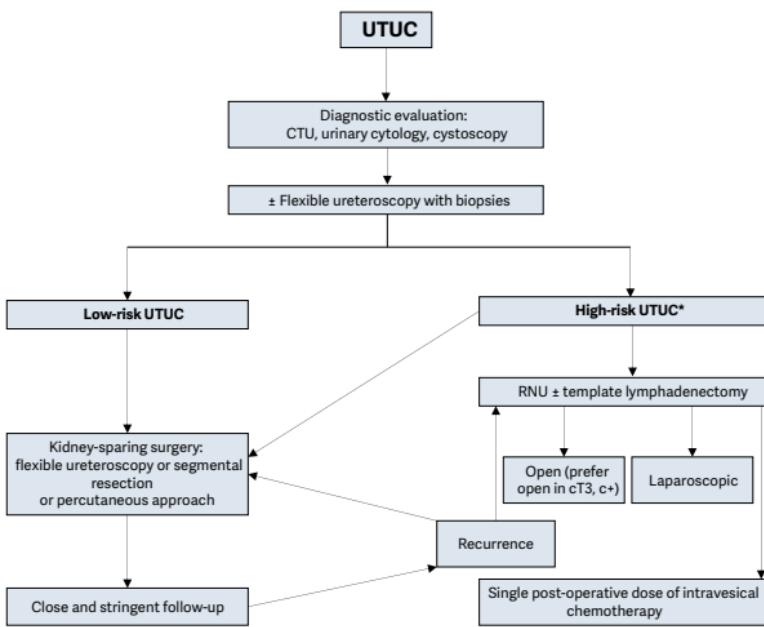
Radiotherapy is no longer relevant nowadays, neither as a sole treatment option, nor as an adjunct to chemotherapy.

Follow-up after initial treatment

In all cases, there should be strict follow-up after radical management to detect metachronous bladder tumours, as well as invasive tumours, local recurrence and distant metastases. When kidney-sparing surgery is performed, the ipsilateral upper urinary tract requires careful follow-up due to the high risk of recurrence.

Recommendations	Strength rating
After radical nephroureterectomy:	
<i>Low-risk tumours</i>	
Perform cystoscopy at three months. If negative, perform subsequent cystoscopy nine months later and then yearly, for five years.	Weak
<i>High-risk tumours</i>	
Perform cystoscopy and urinary cytology at three months. If negative, repeat subsequent cystoscopy and cytology every three months for a period of two years, and every six months thereafter until five years, and then yearly.	Weak
Perform computed tomography (CT) urography and chest CT every six months for two years, and then yearly.	Weak
After kidney-sparing management:	
<i>Low-risk tumours</i>	
Perform cystoscopy and CT urography at three and six months, and then yearly for five years.	Weak
Perform ureteroscopy at three months.	Weak
<i>High-risk tumours</i>	
Perform cystoscopy, urinary cytology, CT urography and chest CT at three and six months, and then yearly.	Weak
Perform ureteroscopy and urinary cytology <i>in situ</i> at three and six months.	Weak

Figure 3: Proposed flowchart for the management of UTUC

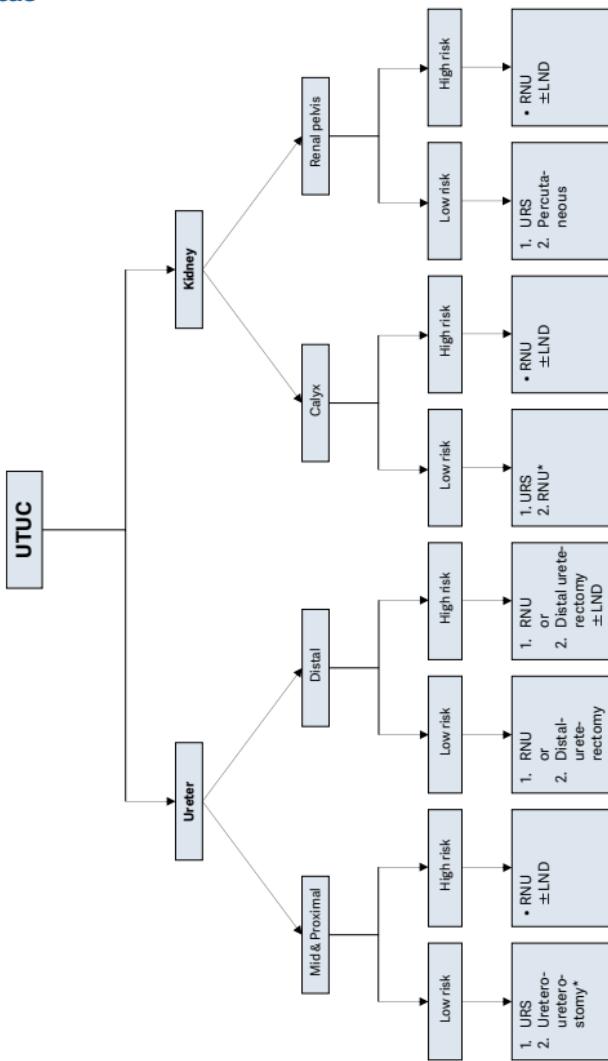


* In patients with a solitary kidney, consider a more conservative approach.

CTU = computed tomography urography;

RNU = nephroureterectomy; UTUC = upper urinary tract urothelial carcinoma.

Figure 4: Surgical treatment according to location and risk status



1. First treatment option

2. Secondary treatment option

*In case not amendable to endoscopic management.

*This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-04-2), available to all members of the European Association of Urology at their website:
<http://www.uroweb.org/guidelines/>.*