

# GUIDELINES ON UROTHELIAL CARCINOMAS OF THE UPPER URINARY TRACT (UTUCs)

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M. Rouprêt, M. Babjuk, E. Compérat, R. Zigeuner, R. Sylvester, M. Burger, A. Böhle, B.W.G. Van Rhijn, E. Kaasinen, J. Palou, S.F. Shariat

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## Epidemiology

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

## Staging and grading systems

The UICC 2009 TNM (Tumour, Node, Metastasis Classification) for renal pelvis and ureter is used for staging (Table 1).

## Tumour grade

There are currently two main classifications used for UTUCs; the 1973 WHO classification, which classifies tumours into three grades, G1, G2 and G3, and the 2004 WHO classification, which classifies tumours into three groups:

- Papillary urothelial neoplasia of low malignant potential;
- Low-grade carcinomas;
- High-grade carcinomas.

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

**Table 1: TNM Classification 2009****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 but not more than 5 cm in the greatest dimension, or multiple lymph nodes, none more than 5 cm in greatest dimension
N3	Metastasis in a lymph node more than 5 cm in greatest dimension

**M - Distant Metastasis**

M0	No distant metastasis
M1	Distant metastasis

## Diagnosis

UTUCs are diagnosed using imaging, cystoscopy, urinary cytology and diagnostic ureteroscopy. The benefits of

ureteroscopy for pre-operative assessment should also be discussed with the patient.

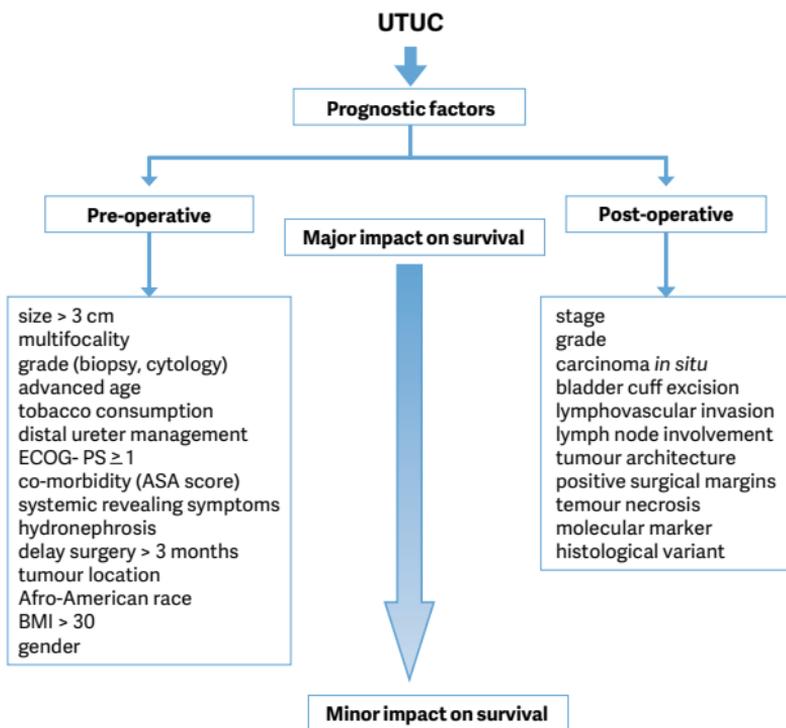
<b>Recommendations for the diagnosis of UTUCs</b>	<b>GR</b>
Urinary cytology should be performed as part of a standard diagnostic work-up.	A
A cystoscopy should be done to rule out concomitant bladder tumour.	A
CTU must be part of the diagnostic work-up.	A
Diagnostic ureteroscopy and biopsy should be performed, certainly in cases where additional information will impact treatment decisions.	C
Retrograde ureteropyelography is an optional tool for the detection of UTUC.	C

*CTU = Computed tomography urography; GR = grade of recommendation.*

## **Prognosis**

UTUCs invading the muscle wall usually have a very poor prognosis. Recognised prognostic facts, as listed in Figure 1.

**Figure 1: UTUCs - Prognostic factors**

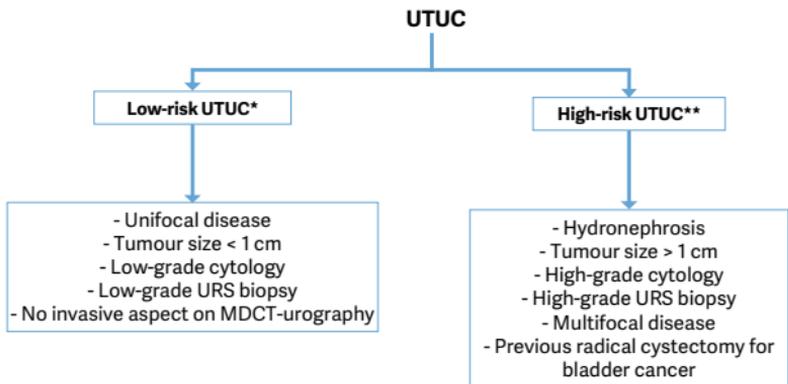


ASA = American Society of Anesthesiologists; BMI = body mass index; ECOG = Eastern Cooperative Oncology Group.

### **Risk stratification**

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

**Figure 2: UTUCs - Risk stratification**



\* All of these factors need to be present

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

MDCT = multidetector-row computed tomography;

URS = ureterorenoscopy.

## Disease management

### Localised disease

#### *Kidney-sparing surgery (low-risk UTUCs)*

Conservative management of low-risk UTUCs consists of surgery preserving the upper urinary renal unit. It is used in imperative cases (renal insufficiency, solitary functional kidney). It can also be discussed in low-risk patients in case of a functional contralateral kidney. Kidney-sparing surgery in low-risk UTUCs potentially allows avoiding the morbidity associated with open radical surgery without compromising oncological outcomes and kidney function.

<b>Recommendations for the kidney-sparing management of low-risk UTUCs</b>	
<b>Indications</b>	<b>GR</b>
Unifocal tumour.	B
Small tumour (size < 1 cm).	B
Low-grade tumour (cytology or biopsies).	B
No evidence of an infiltrative lesion on CTU.	B
Understanding of close follow-up.	B
<b>Techniques used according to location</b>	
Laser should be used for endoscopic treatment.	C
Flexible is preferable to rigid ureteroscopy; renal pelvic, distal-, mid- and proximal ureter.	C
Percutaneous approach is an option for low-grade tumours not accessible by ureteroscopic approach.	C
<b>Surgical open approach</b>	
<i>Renal pelvis or calyces:</i> Partial pyelectomy or partial nephrectomy is seldom indicated.	C
<i>Ureter-Mid &amp; proximal:</i> Ureteroureterostomy is indicated for tumours that cannot be removed completely endoscopically.	C
<i>Distal:</i> Complete distal ureterectomy and neocystostomy are indicated for tumours in the distal ureter that cannot be removed completely endoscopically.	C

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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 conservative treatment of UTUCs. However, the benefits have not been confirmed.

### Advanced disease

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

Radiotherapy is scarcely relevant nowadays, both as a unique therapy and associated with chemotherapy as a tumour adjuvant.

### Follow-up after initial treatment

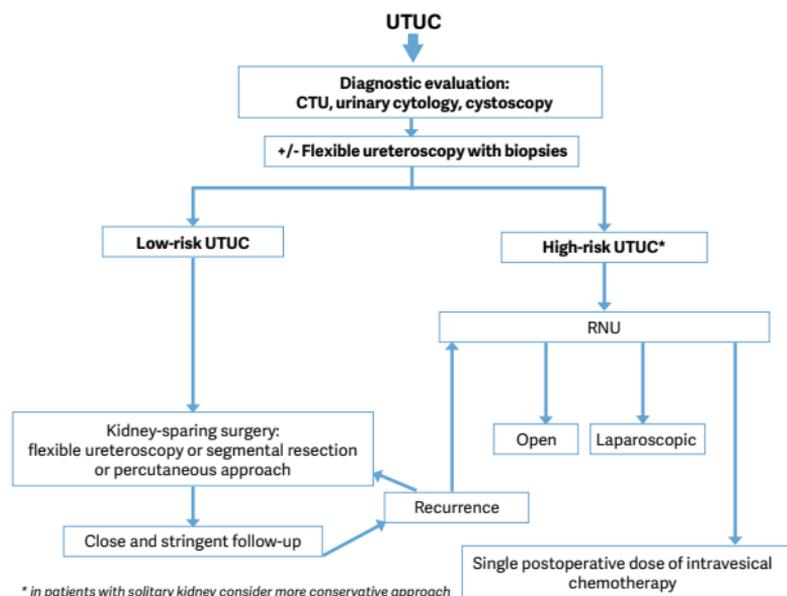
In all cases, there should be strict follow-up after radical management to detect metachronous bladder tumours, as well as invasive tumours, local recurrence and distant metastases. In conservative management, the ipsilateral upper urinary tract requires careful follow-up due to the high risk of recurrence.

<b>Recommendation for follow-up of UTUC after initial treatment</b>	<b>GR</b>
<b>After radical management, over at least 5 years</b>	
<b>Non-invasive tumour</b>	
Cystoscopy/urinary cytology at 3 months and then yearly.	C
CT every year.	C
<b>Invasive tumour</b>	
Cystoscopy/urinary cytology at 3 months and then yearly.	C
CTU every 6 months for 2 years and then yearly.	C
<b>After conservative management, over at least 5 years</b>	
Urinary cytology and CTU at 3 months, 6 months and then yearly.	C

Cystoscopy, ureteroscopy and cytology <i>in situ</i> at 3 months, 6 months, every 6 months for 2 years and then yearly.	C
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**Figure 3: Proposed flowchart for the management of UTUC**



CTU = computed tomography urography;  
RNU = nephroureterectomy.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN: 978-90-79754-80-9), available to all members of the European Association of Urology at their website: <http://www.uroweb.org/guidelines/>.