

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

(Text update April 2014)

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Eur Urol 2011 Apr;59(4):584-94

Eur Urol 2013 Jun;63(6):1059-71

Introduction

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.

Classification

Table 1: TNM classification 2009 for renal pelvis and ureter

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

Tumour grade

There are currently two main classifications used for UTUCs.

They are 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, and high-grade carcinomas. Upper urinary tract tumours with low malignant potential are very rare.

Diagnosis

UTUCs are diagnosed using imaging, cystoscopy, urinary cytology and diagnostic ureteroscopy. The benefits of ureteroscopy in pre-operative assessment should also be discussed with the patient.

Recommendations for the diagnosis of UTUCs	GR
Urinary cytology	A
Cystoscopy to rule out a concomitant bladder tumour	A
CT urography	A
Diagnostic ureteroscopy and biopsy	C
Retrograde ureteropyelography	C

Prognostic factors

UTUCs that invade the muscle wall usually have a very poor prognosis. Recognised prognostic factors in decreasing order of importance include: tumour stage and grade; concomitant carcinoma *in situ* (CIS); age; lymphovascular invasion; tumour architecture; extensive tumour necrosis; molecular markers; tumour location; and gender.

Risk stratification

It is necessary to 'risk stratify' UTUC cases (i.e., with a functional contralateral kidney) before treatment to identify those patients (and tumours) who are more suitable for conservative treatment rather than radical extirpative surgery. Patients with a normal contralateral kidney can be classified at the time of

diagnosis as having 'low-risk UTUC' or 'high-risk UTUC,' based on patient and/or clinical factors.

Management

Localised disease in UTUCs

Radical management (radical nephroureterectomy, [RNU])

The radical management of UTUCs consists of open surgery RNU with excision of the bladder cuff. This is the gold standard treatment for UTUCs, regardless of tumour location. It includes resection of the distal ureter and its orifice because of the high risk of recurrence in this area. Lymph node dissection is also carried out as part of treatment and to provide optimal staging.

Recommendations for RNU for UTUC	
Indications	GR
Suspicion of infiltrating UTUC on imaging	B
High-grade tumour (urinary cytology)	B
Multifocality (with two functional kidneys)	B
Non-invasive but large (i.e. > 1 cm) UTUC	B
Choice of technique	
Open- and laparoscopic access are equivalent in terms of efficacy in T1-T2/N0 tumours	B
Bladder cuff removal is imperative	A
Several techniques for bladder cuff excision are acceptable, except stripping	C
Lymphadenectomy is recommended in cases of invasive UTUC	C
Postoperative instillation (chemotherapy) is recommended after RNU to avoid bladder recurrence	B

Conservative management (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) or in selected elective cases (functional contralateral kidney) for low-grade, low-stage tumours. The choice of technique (ureteroscopy, segmental resection, percutaneous access) depends on technical constraints, the anatomical location of the tumour, and the experience of the surgeon.

Recommendations for the conservative management of low-risk UTUCs	
Indications	GR
Unifocal tumour	B
Small tumour (size < 1 cm)	B
Low-grade tumour (cytology or biopsies)	B
No evidence of an infiltrative lesion on CT urography	B
Understanding of close follow-up	B
Techniques	
Laser should be used in the case of endoscopic treatment	C
Flexible ureteroscopy is preferable over rigid ureteroscopy	C
A percutaneous approach is an option for small, low-grade, caliceal tumours unsuitable for ureteroscopic treatment	C
Ureteroureterostomy is indicated for non-invasive, low-grade tumours of the proximal ureter or mid-ureter that cannot be removed completely by endoscopic means	C
Complete distal ureterectomy and neocystostomy is indicated for non-invasive, low-grade tumours in the distal ureter that cannot be removed completely by endoscopic means and for high-grade, locally-invasive tumours	C

The instillation of Bacillus Calmette-Guérin (BCG) 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 in UTUCs

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.

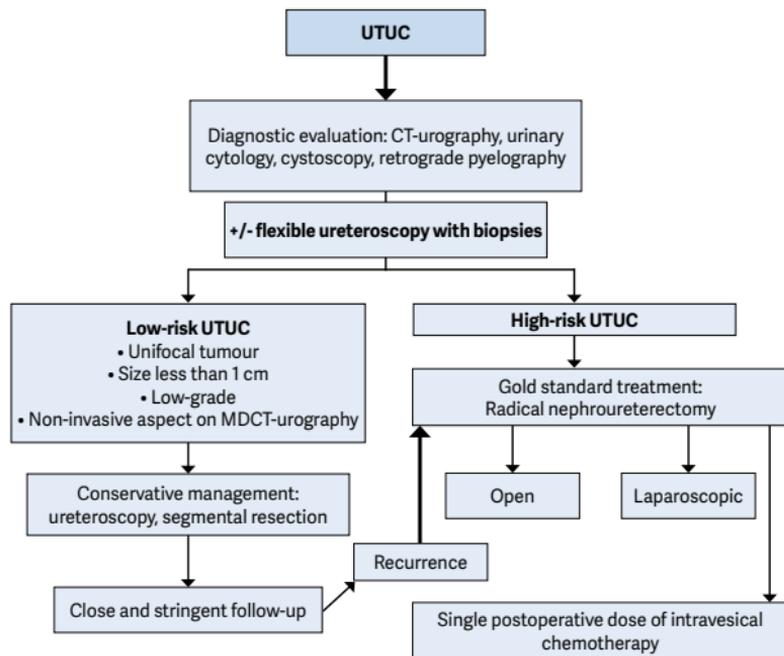
Follow-up after initial treatment

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.

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

CT urography every 6 months for 2 years and then yearly	C
After conservative management, over at least 5 years	
Urinary cytology and CT urography 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

Figure 1: Proposed flowchart for the management of UTUC



This short booklet text is based on the more comprehensive EAU guidelines (ISBN: 978-90-79754-65-6), available to all members of the European Association of Urology at their website, <http://www.uroweb.org>.