Upper Urinary Tract Cancer: Importance of Risk stratification to choose wisely between radical surgery & kidney-sparing management

Conflict of Interest Disclosure

I have the following potential conflicts of interest to report:

- Consultant and advisory role: Ipsen, Sanofi Pasteur, Roche, Astellas, Arquer, Janssen, Ceipheid, Astra-Zeneca, Coloplast, Bouchara-Recordati, Lilly

- ESOU chairman
- Member of the EAU- guidelines panel NMIBC
- Head of the French association- guidelines panel Bladder Cancer
- I am a urologist, not an oncologist…
Guidelines on Urothelial Carcinomas of the Upper Urinary Tract

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Survival

5-year specific survival (%)

<table>
<thead>
<tr>
<th>Stage</th>
<th>pTa, pT1</th>
<th>pT2</th>
<th>pT3</th>
<th>pT4/N+</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt; 10</td>
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<td></td>
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<td>&lt; 50</td>
</tr>
<tr>
<td></td>
<td>80-100</td>
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<table>
<thead>
<tr>
<th>Grade</th>
<th>low</th>
<th>high</th>
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<tbody>
<tr>
<td></td>
<td>65-85</td>
<td>20-40</td>
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<thead>
<tr>
<th>Location</th>
<th>Renal Pelvis</th>
<th>Ureter</th>
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<tr>
<td></td>
<td>70-90</td>
<td>30-50</td>
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UTUC

EAU guidelines, Eur Urol,

UTUC – Risk stratification

Imaging (CTU/MRU) is the best diagnostic instrument we currently have for tumour staging
Endoscopic evaluation combined with histology are the best diagnostic instruments we currently have for tumour grading.

**UTUC – Risk stratification**

**High Risk UTUC**

**KEY PARAMETER**

- multifocal disease
- CIS

*an increase in the proportion of UTCIS from 7.2% to 31% from 1973 to 2005*
Patient selection = Risk stratification

Diagnosis

Computed Tomography
Urography
Gold standard: Radical Surgery high risk tumor

- NEPHROURETERECTOMY

Roupret et al., Eur Urol, 2018

Risk stratification of UTUC

Low-risk UTUC*

- unifocal disease
- tumour size < 2 cm
- low-grade cytology
- low-grade URS biopsy
- no invasive aspect on MDCT-urography

* All of these factors need to be present

High-risk UTUC **

- hydroureter
- tumour size > 2 cm
- high-grade cytology
- high-grade URS biopsy
- multifocal disease
- previous radical cystectomy for bladder cancer

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

Pre-operative
- size > 3 cm
- multifocality
- grade (biopsy, cytology)
- advanced age
- tobacco consumption
- distal ureter management
- ECOG-PS ≥1
- co-morbidity (ASA score)
- systemic revealing symptoms
- hydronephrosis
- delay surgery > 3 months
- tumor location
- Afro-American race
- BMI > 30
- gender

Major impact on survival
- stage
- grade
- carcinoma in situ
- bladder cuff excision
- lymphovascular invasion
- lymph node involvement
- tumor architecture
- positive surgical margins
- tumor necrosis
- molecular marker
- histological variant

Post-operative

Minor impact on survival

Overtreatment?
Conclusions: Our systematic review suggests similar survival after KSS versus RNU only for low-grade and noninvasive UTUC when using URS or PC. However, patients with high-

sub-optimal vs. over treatment
Diagnostics and guidelines

Pitfalls
Small samples
20% non diagnostic
Lamina propria
Effect instrumentation
Misinterpretation

MUSCLE INVASIVE UTUC?
UTUC similar to Bladder tumour in a diverticula

$\pm$ muscularis mucosae hyperthrophique

Image Enhancement Techniques

Hansel, Hum Pathol. 2011
Impaired vision

Irrigation, no aspiration!

Technique

Inspection
No touch technique
**CONFOCAL LASER ENDOMICROSCOPY**

Cell Vizio system Mauna Kea Technologies

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**UTUC - CLE**

488nm laser as light source and fluoresceine as contrast agent

Cell Vizio system Mauna Kea Technologies
Correlation Between Confocal Laser Endomicroscopy (Cellvizio®) and Histological Grading of Upper Tract Urothelial Carcinoma: A Step Forward for a Better Selection of Patients Suitable for Conservative Management

Alberto Breda, Angelo Territo, Andrea Guttila, Francesco Sanguedolce, Martina Manfredi, Luigi Quaresima, Jose M. Gayà, Ferran Algaba, Joan Palou, Humberto Villavicencio

N=14 patients

+ correlation in HG
**About the OLYMPUS Trial**

OLYMPUS (Optimized Delivery of Mitomycin for Primary UTUC Study) is an open-label, single-arm Phase 3 clinical trial of MitoGel to evaluate the safety, tolerability and tumor ablative effect of MitoGel in low grade UTUC patients. The trial, designed to be a single pivotal study for the approval of MitoGel in low-grade UTUC, is anticipated to enroll approximately 70 patients in clinical sites in the U.S. and Europe. The trial will also evaluate the durability of the tumor ablative effect of MitoGel.

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**UTUC**

- **Diagnostic evaluation:** CTU, urinary cytology, cystoscopy
- +/- Flexible ureteroscopy with biopsies

**Low-risk UTUC**

- Kidney-sparing surgery: flexible ureteroscopy or segmental resection or percutaneous approach
- Close and stringent follow-up

**High-risk UTUC**

- RNU
  - Open (prefer open in cT3, cN+)
  - Laparoscopic
- Single postoperative dose of intravesical chemotherapy

*In patients with solitary kidney, consider a more conservative approach*
TAKE HOME MESSAGES

1. Risk stratification assessment is feasible in UTUC
2. KSS ? In any low-risk UTUC!
3. Peri Operative systemic treatment in high-risk UTUC
4. Radical NUT remain the gold standard in more than 75% of cases

Upper Urinary Tract Cancer:
Importance of Risk stratification to choose wisely between radical surgery & kidney-sparing management

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