Minimally Invasive Treatment of Upper Tract TCC

Pr Alexandre de la Taille
CHU Mondor, Créteil – INSERMU955Eq07
adelataille@hotmail.com
The 9th Congress of the Lebanese Urology Society

Sept. 29 - Oct. 1, 2016
Hilton Habtoor Hotel, Beirut - Lebanon

CME Credits
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Management of UT TCC with kidney-sparing approach

• Why? The Rational

• Is it safe? Is it equal?

• Who? Selection is the key!
Radical Nephro-Ureterectomy = Standard
N=2244

<table>
<thead>
<tr>
<th>Pathologic T classification, no. (%)</th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>pT0</td>
<td>15 (0.7)</td>
<td></td>
</tr>
<tr>
<td>pTa</td>
<td>516 (23.0)</td>
<td></td>
</tr>
<tr>
<td>pTis</td>
<td>46 (2.0)</td>
<td></td>
</tr>
<tr>
<td>pT1</td>
<td>537 (23.9)</td>
<td></td>
</tr>
<tr>
<td>pT2</td>
<td>444 (19.8)</td>
<td></td>
</tr>
<tr>
<td>pT3</td>
<td>606 (27.0)</td>
<td></td>
</tr>
<tr>
<td>pT4</td>
<td>80 (3.6)</td>
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</table>

Pathologic tumor grade, no. (%)

| Low                      | 406 (18.1) |   |
| High                     | 1838 (81.9) |   |

Cha et al., Eur Urol 2012

~25%

~18%
Chronic Kidney Disease

• Chronic kidney disease is common in patients with UTUC
  – **Prior to RNU:** > 50% have eGFR below 60 mL/min/1.73 m$^2$
  – **After RNU:** > 75% have eGFR below 60

Median decline: ~20 mL/min

[Graph showing eGFR decline with postoperative eGFR showing no recovery]

Xylinas, Shariat et al., BJUI 2012
Kaag et al., Eur Urol, 2010
Lane et al., Cancer 2010
Kidney-sparing surgery

Is it Safe?

- Endoscopic approach
- Percutaneous approach
- Segmental Ureterectomy
→ Useful for

1. Diagnosis
2. Risk-stratification: aspect of tumor, biopsy

Rouprêt et al., Eur Urol 2015
Chromecki et al., Nat Rev Urol 2011
Risk of intravesical recurrence

- N=630 NephroUreterectomy (RNU) - 282 had URS before RNU

Diagnostic URS increased risk of intravesical recurrence

5-yr IVR-free survival was 43% vs 64% (p<0.001)

- N=104 URS than RNU patients
  
  Group 1: No URS
  
  Group 2: URS immediately before RNU
  
  Group 3: >5 days btw URS & RNU

  IVR rate significantly greater in group 3 than in the other 2 groups (p=0.004)

  Group 3 was a independent predictor of IVR (HR 3.82)

Sung et al., Plos One 2015

Lee et al., Clin Genitourin Cancer 2016
Single postop intravesical instillation of chemo after RNU!

- RCT of 284 pts
- MMC vs standard
- Endpoint: bladder recurrence
  - 1-yr 16% vs 27% (p=0.03)
  - Biopsy not mandated
  - MMC given 7-10d postop

O’Brien et al., Eur Urol 2011

- RCT of 77 pts
- Pirarubicin (THP) vs standard
- Endpoint: bladder recurrence
  - 2-yr 17% vs 42% (p=0.025)
  - Biopsy mandated
  - THP given 48hr postop

Ito et al., JCO 2013
Cancer-specific outcomes with ureteroscopic management

- **N=20 patients, 85% LG**
  - Upper tract Recurrence: 25%
  - CSS: 95%

- **N=80 patients, 66 LG & 14 HG**
  - Upper tract Recurrence: 81%
  - CSS: 87%

Fajkovic et al., World Journal, 2013
Grasso et al., BJU Int, 2012
Radical nephroureterectomy versus endoscopic procedures for the treatment of localised upper tract urothelial carcinoma: A meta-analysis and a systematic review of current evidence from comparative studies

1. KSS associated with higher intraluminal recurrence
2. But NO difference in CSS and OS
3. Heterogeneous data; Low level of evidence: 3b

Yakoubi et al., EJSO 2014
Percutaneous approach

Common technical principles with urinary stone
- lower pole calyx tumor
- theoretical seeding risk
Percutaneous management

- **N=24 patients, 17 LG, 7HG**  
  - Upper tract recurrence: 13%  
  - CSS: 83%

  *Rouprêt et al., Eur Urol 2007*

- **N=89 patients, 50 LG, 39 HG**  
  - Upper tract recurrence: 33%  
  - CSS: 68%

  *Rastinehad et al., Urology 2009*

<table>
<thead>
<tr>
<th>Table 4 – Prognostic factors for survival in patients undergoing percutaneous endoscopic surgery</th>
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</thead>
<tbody>
<tr>
<td><strong>p value (univariate log-rank test)</strong></td>
</tr>
<tr>
<td>Tumour stage</td>
</tr>
<tr>
<td>Grade</td>
</tr>
<tr>
<td>Age &lt;70 yr</td>
</tr>
<tr>
<td>Tumour diameter &gt;2 cm</td>
</tr>
<tr>
<td>Multifocality</td>
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</table>
Segmental Distal Ureterectomy

- Criteria for segmental resection:
  1. Solitary tumor
  2. Lower 1/3 of ureter
  3. Stage ≤ pT2

- Smaller studies
  - 35 patients: RFS: 84%, CSS: 92%
  - 43 patients: RFS: 84%, CSS: 86%
  - 49 patients: CSS: 77%, OS: 72%

- Technique does not matter: Robotic vs. Open vs. Laparoscopic

Hung et al., Int Urol Nephrol 2014
Dalpiaz et al., Urol Oncol 2014
Fukushima et al., Int Journal Urol 2014

FEASIBLE AND SAFE IN WELL SELECTED PATIENTS
Instillation techniques

- Under low pressure & absence of infection
  - **Antegrade** through nephrostomy tube
  - **Retrograde** into a ureteral catheter
  - **Via reflux** with ureteral stent or iatrogenically induced reflux
    - Only 56% have reflux on cystogram
    - Mean volume needed 170cc
Kidney-sparing surgery

• Why? The Rational.

• Is it safe? Is it equal?

• Who? Selection is the key.
Diagnosis of UTUC: Endoscopy and Biopsy
Is URS grading good enough?

- 238 patients URS biopsies followed by RNU
  - **High grade**, but not stage, associated with **high pathology grade**
    (HR: 16.6, p<0.0001)
    *Clements et al., J of Endourol 2012*

- 54 patients URS biopsies first followed by RNU
  - **Grade concordance: 93%;** Stage concordance: 43%
  - **Biopsy volume** did **not affect** assessment of grade or stage
    *Rojas et al., Urol Oncol 2013*

- 184 patients URS biopsies first followed by RNU
  - Greater rate of tumor **upgrading, particularly in low-grade**
    96% of patients with grade 1 had the tumor upgraded
    *Wang et al., J Urol 2011*
Re-URS within 6-8 weeks to increase grade diagnosis

- N=40 first URS than RNU
  - 22% up-graded & 45% upstaged

<table>
<thead>
<tr>
<th>Surgical Stage</th>
<th>No. Biopsy Stage Ta</th>
<th>No. Biopsy Stage T1+</th>
</tr>
</thead>
<tbody>
<tr>
<td>pTa</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>pT1–pT3</td>
<td>10*</td>
<td>5</td>
</tr>
<tr>
<td>Totals</td>
<td>22</td>
<td>5</td>
</tr>
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</table>

Guarnizo et al., J Urol 2000

- N=65 initial biopsy followed by re-biopsy in 6 weeks
  - 28% upgraded & 32% upstaged → 43% reclassified

Smith et al., Urology 2011

- N=41 initial biopsy followed by re-biopsy in 6-8 weeks
  - 51.2% cancers found
  → re-URS lowered recurrence and progression

Villa et al., WJUrology 2016
New Technologies

- Digital ureteroscopy
- Narrow band imaging (NBI) and SPIES
- Fluorescence (Hexvix)
- Endoluminal Ultrasound
- Optical Coherence Tomography
- Confocal laser endomicroscopy
Clinical Risk Stratification of UTUC

Low-risk UTUC*
- Unifocal disease
- Tumour size (< 1 cm)
- Low-grade cytology
- Low-grade URS biopsy
- No invasive on MDCT-urography

High-risk UTUC**
- Multifocal disease
- Tumour size > 1 cm
- High-grade cytology
- High-grade URS biopsy
- Invasive on MDCT-urography
- (Hydronephrosis)
- MIBC on previous radical cystectomy

* All need to be present

** Any need to be present

Roupret et al., EAU GUIDELINES 2016
CONCLUSION
Surgical treatment according to location & risk status

URETER

MID & PROXIMAL
Low risk  High risk

1. URS (2. Uretero-ureterostomy)

DISTAL
Low risk  High risk

✓ RNU ✓ URS ✓ RNU ✓ RNU
✓ distal ureterectomy ✓ distal ureterectomy ✓ distal ureterectomy
✓ +/- LND ✓ +/- LND ✓ +/- LND

KIDNEY

CALYX
Low risk  High risk

1. URS 2. RNU*

 ✓ RNU ✓ RNU ✓ RNU
 ✓ +/- LND ✓ +/- LND ✓ +/- LND

RENAL PELVIS
Low risk  High risk

1. URS 2. PERC

✓ RNU ✓ RNU ✓ RNU
✓ +/- LND ✓ +/- LND ✓ +/- LND

* in case not amendable to endoscopic management

Roupret, Shariat.,
EAU GUIDELINES 2016
TAKE HOME MESSAGES

• Flexible URS for diagnostic / evaluation +++

• Cons. ttt/ UTUC for LOW grade disease
  Patient Selection +++

• 2016 Guidelines and …
  — DIGITAL Flexible URS +++
  — New tools for better detection: NBI
  — Place of Early Second LOOK after initial ttt

• Need +++ for more evaluation/publications