Endoscopic Management of Upper Tract Urothelial Cell Carcinoma

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UTUC

- Epidemiology
- Treatment options
- Indications for Endoscopic management
- Technique
- Outcomes
- Follow up and adjuvant treatments
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Epidemiology

- Estimated annual incidence 2:100,000 in Western countries
- Peak age 70s to 80s
- 3 x more prevalent in men
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Epidemiology

• Renal UTUC ~ 2 x more common than ureteral UTUC
• 17% cases with concurrent bladder CA
• 60% are invasive at diagnosis
  – Compared to 15-25% of bladder CA

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Epidemiology

- Recurrence in bladder 22-47%
- Recurrence in the contralateral upper tract 2-6%
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Treatment Options

• Radical Nephro-ureterectomy (RNU)
  – Open
  – Laparoscopic
  – Robotic

• Endoscopic treatment
  – Ureteroscopic (URS) ablation
  – Percutaneous resection (PR)
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Indications for Endoscopic Management

• Imperative indications:
  – Solitary kidney
  – Renal insufficiency
  – Bilateral disease

• Elective indications:
  – Low grade, low stage disease amenable to endoscopic treatment
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Endoscopic Biopsy

• Controversy exists on the reliability of ureteroscopic biopsy ability to appropriately grade disease
• Endoscopic biopsy generally not effective on determining stage
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**Ureteroscopic Biopsy Accuracy**

Studies comparing percent change from URS biopsy grade to grade from RNU specimen

<table>
<thead>
<tr>
<th>Study</th>
<th>Low/Moderate Grade</th>
<th>High Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keeley FX et al, J Urol 1997</td>
<td>90%</td>
<td>91.6%</td>
</tr>
<tr>
<td>Rojas CP et al Urol Oncol 2013</td>
<td>62.5%</td>
<td>97.8%</td>
</tr>
<tr>
<td>Wang JK et al Urology 2012</td>
<td>63.0%ǂ</td>
<td>91%</td>
</tr>
</tbody>
</table>

ǂ Includes Grade 1 or 2 tumors which were upgraded to grade 3 on RNU
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Endoscopic Biopsy Technique

• Can be performed with either semi-rigid or flexible ureteroscopy
  – Cold cup biopsy forceps
  – Baskets
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Endoscopic Biopsy
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Ureteroscopic Ablation Technique

• Can be performed with either semi-rigid or flexible ureteroscopy
  – Holmium laser
  – Flexible bugbee electrode
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Ureteroscopic Ablation Technique

• Laser settings:
  – Typically use 0.6 – 1 J and 5 – 10 Hz
• Stay just on surface of tumor
  – Need contact to ablate
• “Defocus” laser to get hemostasis
  – Similar to holmium laser BPH surgery
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Ureteroscopic Ablation Technique

• Visibility typically limiting factor
  – Decreased from bleeding and debris

• Ureteral access sheath helpful to maintain visualization
  – Allows multiple passes of the scope for biopsies as well

• In cases of decreased visibility, leave a stent and stage procedure
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Ureteroscopic Ablation
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Percutaneous Ablation Technique

• Obtain access similar to percutaneous nephrolithotomy
• Preferably access calyx uninvolved with tumor
• Choose calyx that will allow access to the tumor with a rigid scope
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Percutaneous Ablation Technique

• Place a standard 25 or 27 Fr resectoscope via the tract
• Can use loop, roller ball, bipolar Button
  – Care must be taken to avoid resecting too deep especially in renal pelvis and infundibulum
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Percutaneous Ablation Technique

• Always leave drainage
  – Either JJ stent or nephrostomy tube
  – Nephrostomy preferable if adjuvant topical therapy planned
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Percutaneous Resection
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Endoscopic Management

- Endoscopic management seems to be increasingly utilized

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Endoscopic Management Outcomes

- Pooled recurrence and DSS for UTUCC managed endoscopically

**For low grade disease, recurrence rate 23%-35% for PR, ~50% for URS. DSS 96-100%**

**For high grade disease, recurrence rate ~40% for PR, 60-76% for URS. DSS ~60-80%**

<table>
<thead>
<tr>
<th>UT recurrence</th>
<th>11/47 (23)</th>
<th>17/56 (30)</th>
<th>20/50 (40)</th>
<th>26/75 (35)</th>
<th>22/52 (42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSS</td>
<td>46/47 (98)</td>
<td>41/42 (98)</td>
<td>21/35 (60)</td>
<td>25/25 (100)</td>
<td>7/13</td>
</tr>
</tbody>
</table>

Cutress ML, et al. BJU Int 110 (2012), 614–628
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Endoscopic Management Outcomes

<table>
<thead>
<tr>
<th></th>
<th>DSS</th>
<th>OS</th>
<th>Metastatic Progression</th>
<th>Renal preservation</th>
</tr>
</thead>
<tbody>
<tr>
<td>URS</td>
<td>91%</td>
<td>72%</td>
<td>9%</td>
<td>81%</td>
</tr>
<tr>
<td>PR</td>
<td>89%</td>
<td>79%</td>
<td>6%</td>
<td>78%</td>
</tr>
</tbody>
</table>

- Pooled data from large review
  - 37 month follow up
  - Only limited studies had data on metastasis
  - Longer follow up may demonstrate worse renal preservation (68%)

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Endoscopic Management Vs Lap Nephro-U

- 59 URS/PR vs 70 LNU
- Median follow up 50 months
- For low grade disease, similar survival

UTUC Surveillance

• No clearly defined follow up
• Surveillance regimens extrapolated from bladder
• Important to remember recurrence can occur in the bladder
UTUC Surveillance
EAU Guidelines

• Recommended for at least 5 years:
  – Urine cytology and CT Urogram at 3 and 6 month, then annually
  – Cysto/URS with selective cytology at 3, 6 months, then q6 month over 2 years
  – Cysto/URS with selective cytology annually after the first 2 years
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Adjuvant Therapy

- Number of methods described for topical therapy for upper tract:
  - JJ stent with reflux
  - Open ended ureteral catheter
  - Nephrostomy tubes
• Gupta et al described technique for application of BCG/IFN to the upper tracts in the office for CIS
  – Place a 5 Fr open ended catheter
  – Confirm with a retrograde or free flow of urine
  – Infuse BCG/IFN under low pressure for 1 hour
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Adjuvant Therapy

- Repeat URS with selective cytology 4 to 6 weeks after last dose
- Complete response 82% (9/11)
- Offered maintenance BCG/IFN with similar regimen as used in bladder

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Adjuvant Therapy

- Retrospective study of 89 renal units (RU) treated with PR for UTUCC
  - 56% low grade, 44% high grade
- 50 RU underwent adjuvant BCG via nephrostomy
  - No difference in grade or stage for BCG vs no BCG

# UTUC

## Adjuvant Therapy

<table>
<thead>
<tr>
<th></th>
<th>No BCG</th>
<th>BCG</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recurrence (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low grade</td>
<td>26%</td>
<td>33%</td>
</tr>
<tr>
<td>High grade</td>
<td>38%</td>
<td>39%</td>
</tr>
<tr>
<td><strong>Progression (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low grade</td>
<td>17%</td>
<td>15%</td>
</tr>
<tr>
<td>High grade</td>
<td>25%</td>
<td>26%</td>
</tr>
<tr>
<td><strong>Recurrence Free survival (mo)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low grade</td>
<td>102</td>
<td>104</td>
</tr>
<tr>
<td>High grade</td>
<td>41</td>
<td>69</td>
</tr>
</tbody>
</table>

Conclusions

- Endoscopic management for UTUCC can be effectively performed
- Indications include solitary kidney, bilateral disease, renal insufficiency
- Biopsy should be performed to confirm grade
Conclusions

- In general, outcomes for low grade disease better than for high grade disease
- Patient’s require close endoscopic follow up
- Unclear the benefit of adjuvant topical therapy