Transitional Cell Cancer of the Renal Pelvis and Ureter Treatment (PDQ®): Treatment - Health Professional Information [NCI]

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General Information About Transitional Cell Cancer of the Renal Pelvis and Ureter

Incidence and Mortality

Transitional cell carcinoma of the renal pelvis, accounting for only 7% of all kidney tumors, and transitional cell cancer of the ureter, accounting for only 1 of every 25 upper tract tumors, are curable in more than 90% of patients if they are superficial and confined to the renal pelvis or ureter. Patients with deeply invasive tumors that are still confined to the renal pelvis or ureter have a 10% to 15% likelihood of cure. Patients with tumors with penetration through the urothelial wall or with distant metastases usually cannot be cured with currently available forms of treatment.

Prognosis

The major prognostic factor at the time of diagnosis of upper tract transitional cell cancer is the depth of infiltration into or through the uroepithelial wall.

Most superficial tumors are likely to be well differentiated, while infiltrative tumors are likely to be poorly differentiated. The incidence of synchronous or metachronous contralateral upper tract cancers ranges from 2% to 4%; the incidence of subsequent bladder cancer after prior upper tract transitional cell cancer ranges from 30% to 50%.[1] When involvement of the upper tract is diffuse (involving both the renal pelvis and ureter), the likelihood of subsequent development of bladder cancer increases to 75%. DNA ploidy has not added significant prognostic information beyond that provided by stage and grade.[2]

Diagnostics

Even if ureteroscopy and pyeloscopy are successfully implemented, accurate assessment of depth of invasion is difficult.

Treatment Management and Survivorship
Total excision of the ureter with a bladder cuff, renal pelvis, and kidney is recommended in an attempt to provide the greatest likelihood of cure.

References:


Cellular Classification of Transitional Cell Cancer of the Renal Pelvis and Ureter

The majority of upper tract uroepithelial tumors are of transitional cell histology. Squamous cell cancer of the urinary tract constitutes less than 15% of the tumors of the renal pelvis and a smaller percentage of ureteral tumors and is often associated with chronic calculus disease and infection.

Grade of transitional cell cancer of the upper tract has generally been found to correlate with stage. Superficial tumors are generally grade I or II, whereas the majority of infiltrative tumors are grades III and IV. Prognosis is worse for patients with high-grade (grades III and IV) tumors than for those with low-grade (grades I and II) tumors.

Stage Information for Transitional Cell Cancer of the Renal Pelvis and Ureter

Though comparable in many respects to staging systems described for bladder cancer, unique structural aspects of the renal pelvis and ureter have led to several differences in the classification schema of tumors that involve the upper tracts. Clinical staging is based on a combination of radiographic procedures (e.g., intravenous pyelogram and computed tomographic scans) and, more recently, ureteroscopy and biopsy.

The advent of rigid and flexible ureteroscopic techniques has permitted endoscopic access to the ureter and renal pelvis. This may permit greater accuracy in preoperative definition of the stage and grade of an upper tract neoplasm. In addition, fulguration and endourological access permit resection or laser coagulation of highly selected low-stage, low-grade lesions of the ureters.[1] However, this approach is still under clinical evaluation since there is the possibility of inaccurate assessment of the stage and extent of disease, and the adequacy and risks of such treatment have not yet been defined.[2,3,4,5]
Because of the inaccessibility of ureteral and pelvic anatomy, accurate staging requires pathologic analysis of the surgically excised specimen.

**Definitions of TNM**

The American Joint Committee on Cancer (AJCC) has designated staging by TNM classification to define carcinoma of the renal pelvis and ureter.[6]

### Table 1. Primary Tumor (T)\(^a\)

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumor cannot be assessed.</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor.</td>
</tr>
<tr>
<td>Ta</td>
<td>Papillary noninvasive carcinoma.</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma <em>in situ</em>.</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor invades subepithelial connective tissue.</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor invades the muscularis.</td>
</tr>
<tr>
<td>T3</td>
<td>(For renal pelvis only) Tumor invades beyond muscularis into peripelvic fat or the renal parenchyma. (For ureter only) Tumor invades beyond muscularis into periureteric fat.</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor invades adjacent organs, or through the kidney into the perinephric fat.</td>
</tr>
</tbody>
</table>


### Table 2. Regional Lymph Nodes (N)\(^a, b\)

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed.</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis.</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in a single lymph node, ≤2 cm in greatest dimension.</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis in a single lymph node, &gt;2 cm but not &gt;5 cm in greatest dimension; or multiple lymph nodes, none &gt;5 cm in greatest dimension.</td>
</tr>
<tr>
<td>N3</td>
<td>Metastasis in a lymph node, &gt;5 cm in greatest dimension.</td>
</tr>
</tbody>
</table>


\(^b\) Laterality does not affect the N classification.
Table 3. Distant Metastasis (M)^a

<table>
<thead>
<tr>
<th>M0</th>
<th>No distant metastasis.</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1</td>
<td>Distant metastasis.</td>
</tr>
</tbody>
</table>


Table 4. Anatomic Stage/ Prognostic Groups^a

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>0a</td>
<td>Ta</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>0is</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>II</td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>III</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IV</td>
<td>T4</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>N3</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>


Patients may also be designated as having localized, regional, or metastatic disease, as follows:

**Localized**

Patients with localized disease may be classified into three groups:

- Group 1: Low-grade tumor confined to the urothelium without lamina propria invasion ("Papilloma" Grade I transitional cell cancer).
- Group 2: Grade I-III carcinomas without demonstrable subepithelial invasion or focal microscopic invasion or papillary carcinomas with carcinoma in situ and/or carcinoma in situ elsewhere in the urothelium.
- Group 3: High-grade tumors that have infiltrated the renal pelvic wall or renal parenchyma or both but are still confined to the kidney. Infiltration of muscle in the upper tract may not be associated with as much potential for distant dissemination as appears to be the case for bladder cancer.

**Regional**
• Group 4: Extension of tumors beyond the renal pelvis or parenchyma and invasion of peripelvic and perirenal fat, lymph nodes, hilar vessels, and adjacent tissues.

Metastatic

• Spread of the tumor to distant tissues.

Each of these classifications has been subclassified into categories of unicentricity or multicentricity. The latter category indicates a more pervasive tumor diathesis and generally a less favorable prognosis.

Although the classifications listed above have prognostic significance, they can only be determined at the time of nephroureterectomy, which is the treatment of choice for patients with this disease. Because of the high incidence of tumor recurrence within the intramural ureter among patients who have had incomplete excision of this area, nephroureterectomy should include the entire ureter and a margin of periureteral orifice mucosa (i.e., bladder cuff).

A TNM system for staging has been established and has demonstrated accurate predictions of survival. The TNM staging system may be a better predictor of prognosis than tumor grade, though both are strongly predictive of survival. Median survival for patients with tumors confined to the subepithelial connective tissue was 91.1 months compared to 12.9 months for patients with tumors invading the muscularis and beyond in one report. Flow cytometry analysis identifies low-stage, low-grade tumors at high risk of recurrence by virtue of their aneuploid histograms.[7,8]

References:

Treatment Option Overview

The rarity of synchronous bilateral renal pelvic neoplasia, the low incidence of asynchronous development of contralateral upper tract tumors, and the increased risk of tumor recurrence in the ipsilateral ureter distal to the original pelvic tumor are the rationale for total nephroureterectomy with bladder cuff for most patients with renal pelvic transitional cell cancers and ureteral cancers.

Contemplation of anything less than total excision must take into account the potential risk for tumor recurrence anywhere in the upper tract unit. In other than unifocal, low-grade, low-stage renal pelvic tumors, the probable extensive involvement of both contiguous and noncontiguous sites would appear to make segmental excision an unnecessary option with a potentially serious risk. However, an operative possibility includes segmental excision of a particular lesion. If the extent of a tumor can be determined by intraoperative assessment, and frozen section histologic diagnosis confirms low-grade, unifocal tumor of limited size, then segmental excision is possible. However, this approach should be reserved for highly selected patients. This includes those patients who have a solitary kidney or those with decreased renal function and who require maximal preservation of renal tissue. The likelihood of tumor recurrence in this setting, and of extension of disease outside the renal pelvis once the pelvis has been violated, is a serious risk that must be heavily weighed in offering a patient this therapeutic option.

Ureteral transitional cell cancer may more readily offer the possibility of segmental excision if the absence of proximal disease can be documented. In this setting, attention is focused on the ease of reconstruction of the ureter and restoration of ureterovesical continuity. This is most feasible if the cancer is in the distal ureter. If partial ureterectomy is possible and proximal disease has been excluded, then segmental excision and ureteral reimplantation can be performed.

Systematic regional lymph node dissection in conjunction with nephroureterectomy or segmental excision has not been found to enhance the effectiveness of surgery if tumors are of high grade or high stage, since in these instances the overall results are so poor. Correspondingly, lymph node involvement is uncommon in low-stage disease, and lymphadenectomy is therefore unlikely to remove additional tumor. Thus, lymph node dissection at the time of nephrectomy may offer prognostic information, but little, if any, therapeutic benefit.
Localized Transitional Cell Cancer of the Renal Pelvis and Ureter

Standard treatment options:

1. Nephroureterectomy with cuff of bladder.
2. Segmental resection of ureter, only if the tumor is superficial and located in the distal third of the ureter.

Treatment options under clinical evaluation:

The development of new instrumentation for endourological treatment of upper tract transitional cell cancer has provided new options for regional management of these cancers. Introduction of electrofulguration and resection instruments or laser probes either transureterally or percutaneously may permit destruction of a primary cancer. Introduction of cytotoxic agents has also been employed. Although a biopsy can be taken for staging purposes, the accuracy of this remains to be determined. The efficacy of treatment by these maneuvers has not been established.

1. Electroresection and fulguration or laser fulguration, if the tumor is superficial.
2. Any parenchymal sparing procedure (segmental resection; ureteroscopic or percutaneous resection/fulguration/laser destruction) if the renal unit is solitary or renal function is depressed.
3. Intrapelvic or intraureteral cytotoxic/immunotherapy. The dramatic successes that have been reported with intravesical cytotoxic (thiotepa, mitomycin, doxorubicin) or immunologic/inflammatory (BCG, interferon) therapy for superficial transitional cell cancers in the bladder have led to the occasional use of these agents in the treatment of upper tract cancers. Long-term follow-up of the results of such treatments has generally not been reported, and the efficacy of this approach cannot be assessed, largely because experience has been limited to those patients whose compromised clinical status (solitary kidney, renal failure, medical risks for surgery) may have influenced clinical outcome. The use of this approach will be limited by the extent of disease in the renal pelvis, the access that these agents may have to the area of disease, the sensitivity of the cancer being treated, and the adequacy and accuracy of initial tumor staging and continued monitoring.
4. Laser vaporization/coagulation. Transurethral and percutaneous access to the upper tract have permitted the use of laser therapy in the control of superficial upper tract transitional cell cancers. This approach is dependent on accurate staging and adequate visualization of the lesions that need to be coagulated. Results of this approach are at present too preliminary to assess. Therapeutic efficacy, however, will depend on staging accuracy on initial treatment and ease of monitoring such patients for disease recurrence and possible progression.

Current Clinical Trials

Check the list of NCI-supported cancer clinical trials that are now accepting patients with localized transitional cell cancer of the renal pelvis and ureter. The list of clinical trials can be further narrowed by location, drug, intervention, and other criteria.
Regional Transitional Cell Cancer of the Renal Pelvis and Ureter

Treatment of extensive regional disease has thus far not had well-documented success by either radiation or systemic chemotherapy. Patients with extensive regional disease should be considered for clinical trials.

Current Clinical Trials

Check the list of NCI-supported cancer clinical trials that are now accepting patients with regional transitional cell cancer of the renal pelvis and ureter. The list of clinical trials can be further narrowed by location, drug, intervention, and other criteria.

General information about clinical trials is also available from the NCI website.

Metastatic Transitional Cell Cancer of the Renal Pelvis and Ureter

The prognosis for any patient with metastatic or recurrent transitional cell cancer is poor. The proper management of recurrence depends on the sites of recurrence, extent of prior therapy, and individual patient considerations. Chemotherapy regimens that have been shown effective for metastatic bladder cancer have generally been applied to transitional cell cancers arising from other sites. Patients with distant metastases have a poor prognosis and can be appropriately offered treatment on a clinical trial.

In patients with metastatic or recurrent transitional cell carcinoma of the bladder, combination chemotherapy has produced high response rates and occasional complete responses.[1,2] Results from a randomized trial that compared methotrexate, vinblastine, doxorubicin, and cisplatin (M-VAC) to single-agent cisplatin in advanced bladder cancer show a significant advantage with M-VAC in both response rate and median survival. The overall response rate with M-VAC in this cooperative group trial was 39%.[3]

Other chemotherapy agents that have shown activity in metastatic transitional cell cancer include the following:[4,5,6,7,8][Level of evidence: 3iiiDiv]

- Paclitaxel.
- Ifosfamide.
- Gallium nitrate.
- Gemcitabine.
- Pemetrexed.
Ifosfamide, gallium, and pemetrexed have shown limited activity in patients previously treated with cisplatin.

**Current Clinical Trials**

Check the list of NCI-supported cancer clinical trials that are now accepting patients with metastatic transitional cell cancer of the renal pelvis and ureter. The list of clinical trials can be further narrowed by location, drug, intervention, and other criteria.

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**References:**


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References:


Changes to This Summary (10 / 01 / 2015)

The PDQ cancer information summaries are reviewed regularly and updated as new information becomes available. This section describes the latest changes made to this summary as of the date above.

Editorial changes were made to this summary.

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This PDQ cancer information summary for health professionals provides comprehensive, peer-reviewed, evidence-based information about the treatment of transitional cell cancer of the renal pelvis and ureter. It is intended as a resource to inform and assist clinicians who care for cancer patients. It does not provide formal guidelines or recommendations for making health care decisions.

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- Timothy Gilligan, MD (Cleveland Clinic Taussig Cancer Institute)

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