Protocol for the Examination of Specimens from Patients with Carcinoma of the Ureter and Renal Pelvis

Protocol applies to invasive, noninvasive and in situ carcinomas of the ureter and renal pelvis.

Version: UreterRenalPelvis 1.0.0.0  Protocol Posting Date: February 2017
Includes pTNM requirements from the 7th Edition, AJCC Staging Manual

Procedures
• Biopsy
• Nephroureterectomy or Ureterectomy

Accreditation Requirements
This protocol can be utilized for a variety of procedures and tumor types for clinical care purposes. For accreditation purposes, only the definitive primary cancer resection specimen is required to have the core and conditional data elements reported in a synoptic format.

• Core data elements are required in reports to adequately describe appropriate malignancies. For accreditation purposes, essential data elements must be reported in all instances, even if the response is "not applicable" or "cannot be determined."

• Conditional data elements are only required to be reported if applicable as delineated in the protocol. For instance, the total number of lymph nodes examined must be reported, but only if nodes are present in the specimen.

• Optional data elements are identified with "+" and although not required for CAP accreditation purposes, may be considered for reporting as determined by local practice standards.

The use of this protocol is not required for recurrent tumors or for metastatic tumors that are resected at a different time than the primary tumor. Use of this protocol is also not required for pathology reviews performed at a second institution (ie, secondary consultation, second opinion, or review of outside case at second institution).

CAP Laboratory Accreditation Program Protocol Required Use Date: November 2017*
* Beginning January 1, 2018, the 8th edition AJCC Staging Manual should be used for reporting pTNM. The CAP will offer a revised 8th edition version of this protocol by mid-year 2017.

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CAP Ureter, Renal Pelvis Protocol Revision History

Summary of Changes
The following changes have been made since the October 2013 release.

URETER, RENAL PELVIS: Biopsy

The following data elements have been modified:
  - Histologic Type
  - Associated Epithelial Lesions
  - Additional Pathologic Findings

The following data elements have been deleted:
  - Tumor Type
  - Pathologic Staging (pTNM)

RENAL PELVIS AND URETER: Resection/Nephroureterectomy, Partial or Complete/Ureterectomy

The following data elements have been modified:
  - Procedure
  - Histologic Type
  - Associated Epithelial Lesions
  - Microscopic Tumor Extension
  - Margins
  - Lymph Node Dissection
  - Additional Pathologic Findings
  - Pathologic Findings in Ipsilateral Nonneoplastic Renal Tissue

The following data elements have been added:
  - Tumor Location
  - Tumor Focality
  - Lymph Node Dissection

The following data element has been deleted:
  - Tumor Type

URETER: Resection

This case summary was combined with the Renal Pelvis: Resection/Nephroureterectomy case summary.
Surgical Pathology Cancer Case Summary

Protocol posting date: February 2017

URETER, RENAL PELVIS: Biopsy

Note: Use of case summary for biopsy specimens is optional.

Select a single response unless otherwise indicated.

+ Specimen (Note A)
  + ___ Renal pelvis
  + ___ Ureter
  + ___ Other (specify): ____________________________
  + ___ Not specified

+ Specimen Laterality
  + ___ Left
  + ___ Right
  + ___ Not specified

+ Histologic Type (select all that apply) (Note B)

Urothelial
  ___ Papillary urothelial carcinoma, noninvasive
  ___ Papillary urothelial carcinoma, invasive
  ___ Urothelial carcinoma in situ
  ___ Urothelial carcinoma, invasive
  ___ Urothelial carcinoma, nested (including large nested) variant
  ___ Urothelial carcinoma, microcystic variant
  ___ Urothelial carcinoma, micropapillary variant
  ___ Urothelial carcinoma, lymphoepithelioma-like variant
  ___ Urothelial carcinoma, plasmacytoid / signet ring / diffuse variant
  ___ Urothelial carcinoma, sarcomatoid variant
  ___ Urothelial carcinoma, giant cell variant
  ___ Urothelial carcinoma, poorly differentiated variant
  ___ Urothelial carcinoma, lipid-rich variant
  ___ Urothelial carcinoma, clear cell variant
  ___ Urothelial carcinoma with squamous differentiation
    + Specify percentage of squamous differentiation: _____%
  ___ Urothelial carcinoma with glandular differentiation
    + Specify percentage of glandular differentiation: _____%
  ___ Urothelial carcinoma with trophoblastic differentiation
    + Specify percentage of trophoblastic differentiation: _____%
  ___ Urothelial carcinoma with Müllerian differentiation
    + Specify percentage of Müllerian differentiation: _____%

Squamous
  ___ Pure squamous cell carcinoma
  ___ Verrucous carcinoma
  ___ Squamous cell carcinoma in situ (no invasive carcinoma identified)

Glandular
  ___ Adenocarcinoma
  ___ Adenocarcinoma, enteric

+ Data elements preceded by this symbol are not required for accreditation purposes These optional elements may be clinically important but are not yet validated or regularly used in patient management.
___ Adenocarcinoma, mucinous
___ Adenocarcinoma, mixed
___ Adenocarcinoma in situ (no invasive carcinoma identified)

Tumors of Müllerian Type
___ Clear cell carcinoma
___ Endometrioid carcinoma

Neuroendocrine Tumors
___ Small cell neuroendocrine carcinoma
   + Specify percentage of small cell neuroendocrine component: _____%
___ Large cell neuroendocrine carcinoma
   + Specify percentage of large cell neuroendocrine component: _____%
___ Well-differentiated neuroendocrine carcinoma
   + Specify percentage of well-differentiated neuroendocrine component: _____%
+ ___ Other histologic type not listed (specify): ____________________________

+ Associated Epithelial Lesions (select all that apply) (Note C)
  + ___ None identified
  + ___ Urothelial papilloma
  + ___ Urothelial papilloma, inverted type
  + ___ Papillary urothelial neoplasm, low malignant potential (PUNLMP)
  + ___ Urothelial proliferation of uncertain malignant potential
  + ___ Urothelial dysplasia
  + ___ Cannot be determined

+ Histologic Grade (Note C)
  + ___ Not applicable
  + ___ Cannot be determined

  + For urothelial carcinoma, other variants, or divergent differentiation
  + ___ Low-grade
  + ___ High-grade

  + For squamous cell carcinoma or adenocarcinoma
  + ___ GX: Cannot be assessed
  + ___ G1: Well-differentiated
  + ___ G2: Moderately differentiated
  + ___ G3: Poorly differentiated
  + ___ Other (specify): ____________________________

+ Tumor Configuration (select all that apply)
  + ___ Papillary
  + ___ Solid/nodule
  + ___ Flat
  + ___ Ulcerated
  + ___ Cannot be determined
  + ___ Other (specify): ____________________________

+ Presence of Muscularis Propria for Determining T Category (Note D)
  + ___ Muscularis propria not identified
  + ___ Muscularis propria present
  + ___ Cannot be determined

+ Data elements preceded by this symbol are not required for accreditation purposes These optional elements may be clinically important but are not yet validated or regularly used in patient management.
+ Microscopic Tumor Extension (Note E)
+ ___ Cannot be assessed
+ ___ No evidence of primary tumor
+ ___ Noninvasive papillary carcinoma
+ ___ Carcinoma in situ
+ ___ Tumor invades subepithelial connective tissue
+ ___ Tumor invades the muscularis
+ ___ Tumor invades beyond muscularis into peripelvic fat or the renal parenchyma (for renal pelvis only)
+ ___ Tumor invades beyond muscularis into periureteric fat (for ureter only)
+ ___ Tumor invades adjacent organs, or through the kidney into the perinephric fat

+ Additional Pathologic Findings (select all that apply)
+ ___ Inflammation/regenerative changes
+ ___ Therapy-related changes
+ ___ Cautery artifact
+ ___ Cystitis cystica et glandularis
+ ___ Keratinizing squamous metaplasia
+ ___ Intestinal metaplasia
+ ___ Other (specify): ________________________________

+ Comment(s)
Surgical Pathology Cancer Case Summary

Protocol web posting date: February 2017

RENALE PELVIS AND URETER: Resection/Nephroureterectomy, Partial or Complete/Ureterectomy

Select a single response unless otherwise indicated.

Procedure (Note F)
___ Nephroureterectomy, partial
___ Nephroureterectomy, complete
___ Ureterectomy
___ Other (specify): ____________________________
___ Not specified

Specimen Laterality
___ Right
___ Left
___ Not specified

Tumor Site
___ Ureter
___ Renal pelvis
___ Ureter and renal pelvis
___ Kidney
___ Cannot be determined

Tumor Focality
___ Unifocal
___ Multifocal (≥2)
___ Cannot be determined

+ Tumor Size
+ Greatest dimension: ___ cm
+ Additional dimensions: ___ x ___ cm
+ ___ Cannot be determined

Histologic Type (select all that apply) (Note B)

Urothelial
___ Papillary urothelial carcinoma, noninvasive
___ Papillary urothelial carcinoma, invasive
___ Urothelial carcinoma in situ
___ Urothelial carcinoma, invasive
___ Urothelial carcinoma, nested (including large nested) variant
___ Urothelial carcinoma, microcystic variant
___ Urothelial carcinoma, micropapillary variant
___ Urothelial carcinoma, lymphoepithelioma-like variant
___ Urothelial carcinoma, plasmacytoid / signet ring / diffuse variant
___ Urothelial carcinoma, sarcomatoid variant
___ Urothelial carcinoma, giant cell variant
___ Urothelial carcinoma, poorly differentiated variant
___ Urothelial carcinoma, lipid-rich variant
___ Urothelial carcinoma, clear cell variant
___ Urothelial carcinoma with squamous differentiation

+ Data elements preceded by this symbol are not required for accreditation purposes. These optional elements may be clinically important but are not yet validated or regularly used in patient management.
+ Specify percentage of squamous differentiation: _____%
  ___ Urothelial carcinoma with glandular differentiation
   + Specify percentage of glandular differentiation: _____%
  ___ Urothelial carcinoma with trophoblastic differentiation
   + Specify percentage of trophoblastic differentiation: _____%
  ___ Urothelial carcinoma with Müllerian differentiation
   + Specify percentage of Müllerian differentiation: _____%

Squamous
  ___ Pure squamous cell carcinoma
  ___ Verrucous carcinoma
  ___ Squamous cell carcinoma in situ (no invasive carcinoma identified)

Glandular
  ___ Adenocarcinoma
  ___ Adenocarcinoma, enteric
  ___ Adenocarcinoma, mucinous
  ___ Adenocarcinoma, mixed
  ___ Adenocarcinoma in situ (no invasive carcinoma identified)

Tumors of Müllerian Type
  ___ Clear cell carcinoma
  ___ Endometrioid carcinoma

Neuroendocrine Tumors
  ___ Small cell neuroendocrine carcinoma
     + Specify percentage of small cell neuroendocrine component: _____%
  ___ Large cell neuroendocrine carcinoma
     + Specify percentage of large cell neuroendocrine component: _____%
  ___ Well-differentiated neuroendocrine carcinoma
     + Specify percentage of well-differentiated neuroendocrine component: _____%
  ___ Other histologic type not listed (specify): ____________________________

+ Associated Epithelial Lesions (select all that apply) (Note C)
  + ___ None identified
  + ___ Urothelial papilloma
  + ___ Urothelial papilloma, inverted type
  + ___ Papillary urothelial neoplasm, low malignant potential (PUNLMP)
  + ___ Urothelial proliferation of uncertain malignant potential
  + ___ Urothelial dysplasia
  + ___ Cannot be determined

Histologic Grade (Note C)
  ___ Not applicable
  ___ Cannot be determined

For urothelial carcinoma, other variants, or divergent differentiation:
  ___ Low-grade
  ___ High-grade
  ___ Other (specify): ____________________________

For squamous cell carcinoma or adenocarcinoma:
  ___ GX: Cannot be assessed
  ___ G1: Well-differentiated
  ___ G2: Moderately differentiated

+ Data elements preceded by this symbol are not required for accreditation purposes. These optional elements may be clinically important but are not yet validated or regularly used in patient management.
G3: Poorly differentiated

Other (specify): ____________________________

Microscopic Tumor Extension (Note E)

Cannot be assessed
No evidence of primary tumor
Noninvasive papillary carcinoma
Carcinoma in situ
Tumor invades subepithelial connective tissue
Tumor invades the muscularis
Tumor invades beyond muscularis into periureteral fat or peripelvic fat or the renal parenchyma
Tumor invades adjacent organs, or through the kidney into the perinephric fat

Tumor Configuration (select all that apply)

Papillary
Solid/nodule
Flat
Ulcerated
Cannot be determined
Other (specify): ____________________________

Margins (select all that apply) (Note G)

Cannot be assessed
Involved by invasive carcinoma
Proximal ureteral margin
Distal ureteral margin
Deep soft tissue margin
Other margin(s) (specify)#: ____________________________
Involved by carcinoma in situ/noninvasive high-grade urothelial carcinoma
Proximal ureteral margin
Distal ureteral margin
Other margin(s) (specify)#: ____________________________
Uninvolved by invasive carcinoma/carcinoma in situ/noninvasive high-grade urothelial carcinoma
Distance of carcinoma from closest margin: ___ mm
Specify closest margin: ____________________________
Other significant changes at margin (specify margin): ____________________________
Low-grade dysplasia
Noninvasive low-grade urothelial carcinoma

Lymphovascular Invasion (Note H)

Not identified
Present
Cannot be determined

Regional Lymph Nodes

No lymph nodes submitted or found

Lymph Node Examination (required only if lymph nodes are present in the specimen)

Number of Lymph Nodes Involved: ______
Number cannot be determined (explain): ____________________________

Number of Lymph Nodes Examined: ______

Notes:
- If the specimen is received unoriented, precluding identification of margins as distal or proximal, it should be denoted here.
- Data elements preceded by this symbol are not required for accreditation purposes. These optional elements may be clinically important but are not yet validated or regularly used in patient management.
Number cannot be determined (explain): ____________________

+ Size of Largest Metastatic Deposit (millimeter): ___ mm
  + Specify Location: ___________

+ Size of Largest Lymph Node Involved (centimeter): ___ cm
  + Specify Location: ___________

+ Extranodal Extension
  + ___ Not identified
  + ___ Present
  + ___ Cannot be determined

Pathologic Stage Classification (pTNM, AJCC 7th Edition) (Note E)

TNM Descriptors (required only if applicable) (select all that apply)
  ___ m (multiple)
  ___ r (recurrent)
  ___ y (posttreatment)

Primary Tumor (pT)
  ___ pTX: Cannot be assessed
  ___ pT0: No evidence of primary tumor
  ___ pTa: Papillary noninvasive carcinoma
  ___ pTis: Flat carcinoma in situ
  ___ pT1: Tumor invades subepithelial connective tissue (lamina propria)
  ___ pT2: Tumor invades muscularis propria
  ___ pT3: Tumor invades beyond muscularis into periuretreal fat or peripelvic fat or the renal parenchyma
  ___ pT4: Tumor invades adjacent organs, or through the kidney into the perinephric fat

Regional Lymph Nodes (pN)
  ___ pNX: Cannot be assessed
  ___ pN0: No regional lymph node metastasis
  ___ pN1: Metastasis in a single regional lymph node, 2 cm or less in greatest dimension
  ___ pN2: Metastasis in a single regional lymph node, more than 2 cm but not more than 5 cm in greatest dimension, or multiple lymph nodes, none more than 5 cm in greatest dimension
  ___ pN3: Metastasis in a regional lymph node more than 5 cm in greatest dimension

Distant Metastasis (pM) (required only if applicable)
  ___ pM1: Distant metastasis
    Specify site(s), if known: ____________________________

+ Additional Pathologic Findings (select all that apply)
  + ___ Inflammation/regenerative changes
  + ___ Therapy-related changes (specify): ____________________________
  + ___ Cautery artifact
  + ___ Cystitis cystica et glandularis
  + ___ Keratinizing squamous metaplasia
  + ___ Intestinal metaplasia
  + ___ Other (specify): ____________________________

Data elements preceded by this symbol are not required for accreditation purposes. These optional elements may be clinically important but are not yet validated or regularly used in patient management.
Pathologic Findings in Ipsilateral Nonneoplastic Renal Tissue (select all that apply) (Note I)

___ No or insufficient renal parenchyma

Significant pathologic alterations:

___ None identified

___ Glomerular disease (specify type): __________________

___ Tubulointerstitial disease (specify type): __________________

___ Vascular disease (specify type): __________________

___ Inflammation (specify type): __________________

___ Other (specify): __________________

+ Comment(s)

+ Data elements preceded by this symbol are not required for accreditation purposes. These optional elements may be clinically important but are not yet validated or regularly used in patient management.
Explanatory Notes

A. History
A relevant history is important for interpretation of all upper urinary tract (renal pelvis and ureter) specimens. A history of renal stones, recent urinary tract procedures, infections, or obstruction can influence the interpretation of random biopsies obtained from patients with hematuria. Any neoplasms previously diagnosed should be specified, including the histologic type, primary site, and histologic grade. Primary tumors may be associated with hereditary nonpolyposis colon cancer (HNPCC) syndrome (Lynch syndrome II). Renal pelvic tumors are more often seen in analgesic abusers, who often have analgesic nephropathy, including papillary necrosis. If prior therapy has been given, it should be described (systemic or intravesical chemotherapy, immunotherapy, radiation, etc). The method of collection and date also should be specified in urine cytology specimens. Cytologic specimens from the ureter or renal pelvis may be over-interpreted if their site of sampling is not stated.

B. Histologic Type
Like the urinary bladder, the vast majority (more than 95%) of carcinomas of the renal pelvis and ureter are urothelial in origin. The most recent 2016 World Health Organization (WHO) classification of tumors of the urothelial tract, including urethra, urinary bladder, ureter, and renal pelvis, is provided in this note. Benign tumors are included in this classification because, within the same patient, a spectrum of differentiation from benign to malignant tumors may be seen, either at the same time or over the clinical course of the disease. The full spectrum of invasive urothelial carcinoma and its variants as found in the urinary bladder may also be found in the upper tract. The distinction between a urothelial carcinoma with divergent squamous, glandular, or Müllerian differentiation, and a pure squamous cell carcinoma, adenocarcinoma or Müllerian is rather arbitrary. Most authorities, including the 2016 WHO classification, require a pure histology of squamous cell carcinoma, adenocarcinoma or Müllerian to designate a tumor as such, all others with recognizable papillary, invasive, or flat carcinoma in situ (CIS) urothelial component being considered as urothelial carcinoma with divergent differentiation. A malignant neoplasm with small cell neuroendocrine carcinoma component arising in the urinary tract is designated as small cell carcinoma.

Lynch syndrome, also known as hereditary nonpolyposis colorectal cancer, predisposes patients to urological cancer, particularly upper tract urothelial carcinoma. Upper tract urothelial carcinoma develops in up to 28% of patients with known Lynch syndrome. Therefore, pathologists should be aware of Lynch syndrome and their important role of identifying Lynch syndrome patients by considering appropriate tissue tests. Recently several guidelines have been published regarding when and what tissue testing is appropriate for screening patients with upper tract urothelial carcinoma.

2016 WHO Classification of Tumors of the Urothelial Tract

Urothelial tumors
Infiltrating urothelial carcinoma
- Nested, including large nested
- Microcystic
- Micropapillary
- Lymphoepithelioma-like
- Plasmacytoid/signet ring cell/diffuse
- Sarcomatoid
- Giant cell
- Poorly differentiated

Noninvasive urothelial lesions
- Urothelial carcinoma in situ
- Noninvasive papillary urothelial carcinoma, low grade
- Noninvasive papillary urothelial carcinoma, high grade
- Papillary urothelial neoplasm of low malignant potential
- Urothelial papilloma
- Inverted urothelial papilloma
- Urothelial proliferation of uncertain malignant potential
Urothelial dysplasia

**Squamous cell neoplasms**
- Pure squamous cell carcinoma
- Verrucous carcinoma
- Squamous cell papilloma

**Glandular neoplasms**
- Adenocarcinoma, NOS
  - Enteric
  - Mucinous
  - Mixed
- Villous adenoma

**Tumors of Mullerian type**
- Clear cell carcinoma
- Endometrioid carcinoma

**Neuroendocrine tumors**
- Small cell neuroendocrine carcinoma
- Large cell neuroendocrine carcinoma
- Well-differentiated neuroendocrine tumor
- Paraganglioma

**C. Histologic Grade**
The grading system is identical to that for urinary bladder neoplasms. Flat intraepithelial lesions and papillary and invasive lesions are graded separately. There has been significant controversy in the classification of these lesions. Due to variable classification systems and the need for a universally acceptable system, the World Health Organization/International Society of Urological Pathology (WHO/ISUP) consensus classification was proposed. This system is utilized in the WHO 2004 classification, the 2004 Armed Forces Institute of Pathology (AFIP) fascicle, and 2016 WHO classification, and has been validated by many studies to be prognostically significant. Other systems (that were being used previously) may still be used according to institutional preference. Urothelial carcinomas of the renal pelvis tend to more often be high grade compared to urinary bladder carcinomas.

Flat and papillary urothelial hyperplasia has been renamed as “urothelial proliferation of uncertain malignant potential” in 2016 WHO classification.

Squamous carcinomas and adenocarcinomas may be graded as well-differentiated, moderately differentiated, and poorly differentiated.

**D. Extent of Invasion**
Depth of invasion and pathologic stage are the most important prognostic indicators for patients with neoplasms of the upper urinary tract. A critical role of the surgical pathologist is to diagnose the depth and extent of invasion into the subepithelial connective tissue/lamina propria (pT1), muscularis propria (pT2), or beyond (pT3 or pT4). The patterns of invasion are similar to the urinary bladder, except that for renal pelvis carcinoma, the type of tumor involvement of the kidney, when present, impacts stage. Also, it is important to note that the lamina propria is absent beneath the urothelium lining the renal papillae in the pelvis and is thin along the minor calyces. As in the urinary bladder, in papillary tumors, invasion occurs most often at the base of the tumor and very infrequently in the stalk. Tumor infiltrating the lamina propria is pT1 and, like the urinary bladder, there is no accepted approach for assessing depth of lamina propria invasion. However, pathologists are encouraged to provide some assessment as to the extent of lamina propria invasion (ie, focal versus extensive, or depth in millimeters, or by level – above, at, or below muscularis mucosae). Designation of a tumor as merely muscle-invasive is inappropriate, but the type of muscle invasion, ie, muscularis mucosae (pT1 tumors) versus muscularis propria (pT2 tumors) invasion, needs to be clearly stated. Descriptive terminology, such as “urothelial carcinoma with muscle invasion, indeterminate for type of muscle invasion,” may be used when it is not possible to be certain
whether the type of muscle invaded by the tumor is hypertrophic muscularis mucosae or muscularis propria. For renal pelvic tumors, in-situ extension of carcinoma into renal collecting ducts and renal tubules does not affect stage, while carcinoma invading into the renal parenchyma is pT3. Renal pelvic carcinoma that invades through the kidney into perinephric fat is pT4. Patients with upper tract urothelial carcinoma often present at higher stage compared to patients with urinary bladder carcinoma.

E. TNM and Stage Groupings

The TNM Staging System for carcinomas of the ureter and renal pelvis of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) is recommended and shown below. By AJCC/UICC convention, the designation “T” refers to a primary tumor that has not been previously treated. The symbol “p” refers to the pathologic classification of the TNM, as opposed to the clinical classification, and is based on gross and microscopic examination. pT entails a resection of the primary tumor or biopsy adequate to evaluate the highest pT category, pN entails removal of nodes adequate to validate lymph node metastasis, and pM implies microscopic examination of distant lesions. Clinical classification (cTNM) is usually carried out by the referring physician before treatment during initial evaluation of the patient or when pathologic classification is not possible.

Pathologic staging is usually performed after surgical resection of the primary tumor. Pathologic staging depends on pathologic documentation of the anatomic extent of disease, whether or not the primary tumor has been completely removed. If a biopsied tumor is not resected for any reason (eg, when technically unfeasible) and if the highest T and N categories or the M1 category of the tumor can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer.

Primary Tumor (T) (Figure 1)
The suffix “m” should be added to the appropriate T category to indicate multiple tumors. The suffix “is” may be added to any T to indicate the presence of associated carcinoma in situ.

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Figure 1. Depiction of pTa, pT1, pT2, and pT3.
Anatomic Stage/Prognostic Groups

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tumor Size (T)</th>
<th>Nodes (N)</th>
<th>Metastasis (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>
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<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>N1,2,3</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

*M0 is defined as no distant metastasis.

TNM Descriptors

For identification of special cases of TNM or pTNM classifications, the “m” suffix and “y” and “r” prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

The “m” suffix indicates the presence of multiple primary tumors in a single site and is recorded in parentheses: pT(m)NM.

The “y” prefix indicates those cases in which classification is performed during or following initial multimodality therapy (ie, neoadjuvant chemotherapy, radiation therapy, or both chemotherapy and radiation therapy). The cTNM or pTNM category is identified by a “y” prefix. The ycTNM or ypTNM categorizes the extent of tumor actually present at the time of that examination. The “y” categorization is not an estimate of tumor prior to multimodality therapy (ie, before initiation of neoadjuvant therapy).

The “r” prefix indicates a recurrent tumor when staged after a documented disease-free interval, and is identified by the “r” prefix: rTNM.

Additional Descriptors

Residual Tumor (R)

Tumor remaining in a patient after therapy with curative intent (eg, surgical resection for cure) is categorized by a system known as R classification, shown below.

RX Presence of residual tumor cannot be assessed
R0 No residual tumor
R1 Microscopic residual tumor
R2 Macroscopic residual tumor

For the surgeon, the R classification may be useful to indicate the known or assumed status of the completeness of a surgical excision. For the pathologist, the R classification is relevant to the status of the margins of a surgical resection specimen. That is, tumor involving the resection margin on pathologic examination may be assumed to correspond to residual tumor in the patient and may be classified as macroscopic or microscopic according to the findings at the specimen margin(s).

F. Sections for Microscopic Evaluation

Tissue samples include ureteroscopic biopsies, needle biopsies, segmental ureterectomy specimens, and radical nephroureterectomy with urinary bladder cuff resection specimens.

Ureteroscopic biopsies are entirely submitted. Since these are often minute in size, one approach to processing is to submit the biopsy sample for cytology cell block preparation.

Needle core biopsies of renal masses, including urothelial carcinoma involving the kidney, should be completely submitted.
Segmental ureterectomy is performed for tumors of the proximal or mid ureter. The length and diameter of the intact ureter is recorded, with a search for a mass by palpation and visual inspection. Proximal and distal cross-section margins are taken, and the outer aspect of the ureter is inked. The ureter is then opened longitudinally and assessed for mucosal abnormalities. After fixation in 10% formalin, sections are taken to demonstrate the deepest invasion of any lesion(s). At least one section of uninvolved ureter should be submitted.

Radical nephroureterectomy with bladder cuff. Gross examination and sampling should document the relationship of tumor to adjacent renal parenchyma, peripelvic fat, nearest soft tissue margin, and ureter. Sections of grossly unremarkable kidney, pelvis, and ureter should be obtained. The important urothelial margin is the urinary bladder cuff, which can be sampled as shave sections.

**Lymph Nodes**

Regional lymph nodes are not always submitted or identified in cases of resection, but evaluation of these nodes is important. Submit one section from each grossly positive lymph node. All other lymph nodes should be entirely submitted, as presence of nodal disease may be used as an indication for adjuvant therapy. Limited data indicate that the presence of extranodal extension may be clinically significant.

The regional lymph nodes for the renal pelvis are renal hilar, paracaval, aortic, and retroperitoneal. The regional lymph nodes for the ureter are renal hilar, iliac (common, internal [hypogastric], external), paracaval, periureteral, and pelvic.

Involvement of lymph nodes beyond the regional lymph nodes is considered distant metastasis (M1).

**G. Margins**

Resection margins, including those mentioned in Note F, should be carefully specified. Statements about deep soft tissue margins should specify whether peritoneal surfaces are involved by tumor. In renal pelvis, ureter, and nephroureterectomy specimens, the margins may include radial hilar soft tissue margin; bladder cuff; and ureteral, renal parenchymal, and Gerota’s fascia margins, depending on the type of surgical specimen.

**H. Lymph-Vascular Invasion**

Urothelial carcinoma may invade blood vessels or lymphatic channels. This is an important prognostic factor in upper urinary tract urothelial carcinoma. In suspicious cases, blood vessels can be highlighted by immunohistochemical staining for factor VIII-related antigen, CD31 or CD34. Staining can help resolve the problem of differentiating lyphatic versus artifactual space formation by tumor cells, a frequent finding seen in urothelial tumors invading the lamina propria. Retraction artifact is also prominent in the “micropapillary variant” of urothelial carcinoma.

**I. Pathologic Findings in Nonneoplastic Kidney**

It is important to recognize that medical kidney diseases may be present in nonneoplastic renal tissue in nephrectomy and nephroureterectomy specimens. Arterionephrosclerosis (or hypertensive nephropathy) and diabetic nephropathy are seen in approximately 30% and 20% of cases, respectively. Other medical renal diseases that have been identified include thrombotic microangiopathy, focal segmental glomerulosclerosis, and IgA nephropathy. The findings of greater than 20% global glomerulosclerosis or advanced diffuse diabetic glomerulosclerosis are predictive of significant decline in renal function 6 months after radical nephrectomy. Evaluation for medical renal disease should be performed in each case; PAS and/or Jones methenamine silver stains should applied if necessary. Consultation with a nephropathologist should be pursued as needed.

However, no studies have specifically measured peritumoral-related changes in the renal cortex. Some tumors have no peritumoral changes. Oncocytoma is the best example. While some large tumors often have a large zone of peritumoral changes compared with smaller tumors. The pseudocapsule may contain sclerotic glomeruli, tubular atrophy and show fibrointimal thickening of arteries, followed by a zone of several millimeters of acute tubular injury, none of which is representative of the cortex elsewhere. A judgement whether the amount of non-neoplastic renal parenchyma is sufficient for evaluation of medical kidney diseases should be made on a case by case basis. Two studies have used 1-5 mm as the cut-off for insufficient renal parenchyma. Five mm of non-neoplastic renal parenchyma is a reasonable recommendation.
References


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