Protocol for the Examination of Specimens From Patients With Carcinoma of the Ureter and Renal Pelvis

Protocol applies to invasive and in-situ carcinomas and/or associated epithelial lesions of the ureter and renal pelvis.

Based on AJCC/UICC TNM, 7th edition
Protocol web posting date: July 2012

Procedures
• Biopsy
• Nephroureterectomy or Ureterectomy

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CAP Ureter, Renal Pelvis Protocol Revision History

Version Code
The definition of the version code can be found at www.cap.org/cancerprotocols.

Version: UreterRenalPelvis 3.3.0.0

Summary of Changes
The following changes have been made since the June 2012 release.

RENAL PELVIS: Resection/Nephroureterectomy; URETER: Resection

Pathologic Findings in Ipsilateral Nonneoplastic Renal Tissue (select all that apply)
This element was added to the Renal Pelvis Resection/Nephroureterectomy case summary and deleted from the Ureter Resection case summary.

The following changes have been made since the November 2011 release.

URETER, RENAL PELVIS: Biopsy

Note: The word “checklist” was changed to “case summary.”

Histologic Grade (select all that apply)
“Select all that apply” was added. “Adenocarcinoma and squamous cell carcinoma” was changed to “Squamous cell carcinoma or adenocarcinoma,” and “Other carcinoma” was added.

+ Microscopic Tumor Extension: This reporting element was added.

Additional Pathologic Findings: “Ureteritis or pyelitis cystica and/or glandularis” was changed to “Ureteritis or pyelitis cystica et glandularis.”

RENAL PELVIS: Resection/Nephroureterectomy

Histologic Grade and Microscopic Tumor Extension: These elements were changed/added, as above.

Margins: Reporting on margins was changed to include noninvasive high-grade urothelial carcinoma and other significant changes at the margin, as follows:

Margins (select all that apply)
___ Cannot be assessed
___ Margin(s) involved by invasive carcinoma
    Specify margin(s): ___________________________
___ Margins(s) involved by carcinoma in situ/noninvasive high-grade urothelial carcinoma
    Specify margin(s): ___________________________
___ Margins 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
Additional Pathologic Findings: “Pyelitis cystica and/or glandularis” was changed to “Pyelitis cystica et glandularis.”

URETER: Resection

Histologic Grade and Microscopic Tumor Extension: These elements were changed/added, as above.

Microscopic Tumor Extension: “Peripelvic” was changed to “periureteric”; “or through the kidney into the perinephric fat” was deleted from the last entry, as follows:

- Tumor invades beyond muscularis into periureteric fat
- Tumor invades adjacent organs

Margins: Reporting on margins was changed to include noninvasive high-grade urothelial carcinoma and other significant changes at the margin and a note was added, as follows:

Margins (select all that apply)
- Cannot be assessed
- Margin(s) involved by invasive carcinoma
  - Proximal mucosal margin
  - Distal mucosal margin
  - Deep soft tissue margin
  - Other margin(s) (specify)*: _________________________
- Margin(s) involved by carcinoma in situ/noninvasive high-grade urothelial carcinoma
  - Proximal mucosal margin
  - Distal mucosal margin
  - Other margin(s) (specify)*: _________________________
- Margins uninvolved by invasive carcinoma/carcinoma in situ/noninvasive high-grade urothelial carcinoma
  + Distance of carcinoma from closest margin: ___ mm
  + Specify margin(s)*: _________________________
  + Other significant changes at margin (specify margin)*: _________________________
  + Low-grade dysplasia
  + Noninvasive low-grade urothelial carcinoma

* If the specimen is received unoriented, precluding identification of margins as distal or proximal, it should be denoted here.

Additional Pathologic Findings: “Ureteritis cystica and/or glandularis” was changed to “Ureteritis cystica et glandularis.”

Explanatory Notes

Lymph Nodes: The following paragraphs were added:
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).
Surgical Pathology Cancer Case Summary

Protocol web posting date: July 2012

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 (Note B)
+ __ Urothelial (transitional cell) carcinoma
+ __ Urothelial (transitional cell) carcinoma with squamous differentiation
+ __ Urothelial (transitional cell) carcinoma with glandular differentiation
+ __ Urothelial (transitional cell) carcinoma with variant histology
  (specify): __________________________
+ __ Squamous cell carcinoma, typical
+ __ Squamous cell carcinoma, variant histology (specify): __________________________
+ __ Adenocarcinoma, typical
+ __ Adenocarcinoma, variant histology (specify): __________________________
+ __ Small cell carcinoma
+ __ Undifferentiated carcinoma (specify): __________________________
+ __ Mixed cell type (specify): __________________________
+ __ Other (specify): __________________________
+ __ Carcinoma, type cannot be determined

+ Associated Epithelial Lesions (select all that apply) (Note C)
+ __ None identified
+ __ Urothelial (transitional cell) papilloma, inverted type
+ __ Papillary urothelial (transitional cell) neoplasm, low malignant potential
  (WHO/ISUP 1998; WHO 2004)
+ __ Cannot be determined

+ Data elements preceded by this symbol are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.
**Histologic Grade (select all that apply) (Note C)**
- Not applicable
- Cannot be determined
- Urothelial carcinoma
  - Low-grade
  - High-grade
  - Other (specify): ____________________________
- Squamous cell carcinoma or adenocarcinoma
  -GX: Cannot be assessed
  - G1: Well differentiated
  - G2: Moderately differentiated
  - G3: Poorly differentiated
  - Other (specify): ____________________________
- Other carcinoma
  - Low-grade
  - High-grade
  - Other (specify): ____________________________

**Tumor Configuration (select all that apply)**
- Papillary
- Solid/nodule
- Flat
- Ulcerated
- Indeterminate
- Other (specify): ____________________________

**Adequacy of Material for Determining T Category (Note D)**
- Muscularis propria not identified
- Muscularis propria present
- Indeterminate

**Microscopic Tumor Extension (Note E)**
- Cannot be assessed
- No evidence of primary tumor
- Papillary noninvasive 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

**Pathologic Staging (pTNM) (Note E)**
- TNM Descriptors (select all that apply)
  - None
  - m (multiple primary tumors)
  - r (recurrent)
  - y (posttreatment)
Primary Tumor (pT)
+ ___ pTX: Cannot be assessed
+ ___ pT0: No evidence of primary tumor
+ ___ pTa: Noninvasive papillary carcinoma
+ ___ pTis: Flat carcinoma in situ
+ ___ pT1: Tumor invades subepithelial connective tissue (lamina propria)
+ ___ pT2: Tumor invades muscularis propria

Additional Pathologic Findings (select all that apply)
+ ___ Urothelial carcinoma in situ
+ ___ Urothelial dysplasia (low-grade intraurothelial neoplasia)
+ ___ Inflammation/regenerative changes
+ ___ Therapy-related changes
+ ___ Cautery artifact
+ ___ Ureteritis or pyelitis cystica et glandularis
+ ___ Keratinizing squamous metaplasia
+ ___ Intestinal metaplasia
+ ___ Other (specify): ____________________________

Comment(s)
Surgical Pathology Cancer Case Summary

Protocol web posting date: July 2012

RENAL PELVIS: Resection/Nephroureterectomy, Partial or Complete

Select a single response unless otherwise indicated.

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

Specimen Laterality
___ Right
___ Left
___ Not specified

Tumor Size
Greatest dimension: ___ cm
+ Additional dimensions: ___ x ___ cm
___ Cannot be determined (see Comment)

Histologic Type (Note B)
___ Urothelial (transitional cell) carcinoma
___ Urothelial (transitional cell) carcinoma with squamous differentiation
___ Urothelial (transitional cell) carcinoma with glandular differentiation
___ Urothelial (transitional cell) carcinoma with variant histology
  (specify): ____________________________
___ Squamous cell carcinoma, typical
___ Squamous cell carcinoma, variant histology
  (specify): ____________________________
___ Adenocarcinoma, typical
___ Adenocarcinoma, variant histology (specify): ____________________________
___ Small cell carcinoma
___ Undifferentiated carcinoma (specify): ____________________________
___ Mixed cell type (specify): ____________________________
___ Other (specify): ____________________________
___ Carcinoma, type cannot be determined

Associated Epithelial Lesions (select all that apply) (Note C)
___ None identified
___ Urothelial (transitional cell) papilloma, inverted type
___ Papillary urothelial (transitional cell) neoplasm, low malignant potential
  (WHO/ISUP 1998; WHO 2004)
___ Cannot be determined

Data elements preceded by this symbol are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.
Histologic Grade (select all that apply) (Note C)
___ Not applicable
___ Cannot be determined
___ Urothelial carcinoma
    ___ Low-grade
    ___ High-grade
    ___ Other (specify): ____________________________
___ Squamous cell carcinoma or adenocarcinoma
    ___ GX: Cannot be assessed
    ___ G1: Well differentiated
    ___ G2: Moderately differentiated
    ___ G3: Poorly differentiated
    ___ Other (specify): ____________________________
___ Other carcinoma
    ___ Low-grade
    ___ High-grade
    ___ Other (specify): ____________________________

Microscopic Tumor Extension (Note E)
___ Cannot be assessed
___ No evidence of primary tumor
___ Papillary noninvasive carcinoma
___ Carcinoma in situ
___ Tumor invades subepithelial connective tissue
___ Tumor invades the muscularis
___ Tumor invades beyond muscularis into 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
  + ___ Indeterminate
  + ___ Other (specify): ____________________________

Margins (select all that apply) (Note G)
___ Cannot be assessed
___ Margin(s) involved by invasive carcinoma
    Specify margin(s): ____________________________
___ Margin(s) involved by carcinoma in situ/noninvasive high-grade urothelial carcinoma
    Specify margin(s): ____________________________
___ Margins 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

+ Data elements preceded by this symbol are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.
+ Lymph-Vascular Invasion (Note H)
+ ___ Not identified
+ ___ Present
+ ___ Indeterminate

Pathologic Staging (pTNM) (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 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
___ No nodes submitted or found

Number of Lymph Nodes Examined
Specify: ___
___ Number cannot be determined (explain): ______________________

Number of Lymph Nodes Involved (any size)
Specify: ___
___ Number cannot be determined (explain): ______________________

Distant Metastasis (pM)
___ Not applicable
___ pM1: Distant metastasis
       + Specify site(s), if known: ________________________
+ Additional Pathologic Findings (select all that apply)
+ ___ Urothelial carcinoma in situ
+ ___ Urothelial dysplasia (low-grade intraurothelial neoplasia)
+ ___ Inflammation/regenerative changes
+ ___ Therapy-related changes
+ ___ Pyelitis cystica et glandularis
+ ___ Keratinizing squamous metaplasia
+ ___ Intestinal metaplasia
+ ___ Lithiasis
+ ___ Other (specify): __________________________

Pathologic Findings in Ipsilateral Nonneoplastic Renal Tissue (select all that apply) (Note 1)
___ Insufficient tissue (partial nephrectomy specimen with <5 mm of adjacent nonneoplastic renal tissue)
___ Significant pathologic alterations
   ___ None identified
   ___ Glomerular disease (type): ________________
   ___ Tubulointerstitial disease (type): ________________
   ___ Vascular disease (type): ________________
   ___ Inflammation (type): ________________
   ___ Other (specify): ________________

+ Comment(s)
Surgical Pathology Cancer Case Summary

Protocol web posting date: July 2012

URETER: Resection

Select a single response unless otherwise indicated.

Procedure
___ Ureterectomy
___ Nephroureterectomy
___ Other (specify): ____________________________
___ Not specified

Specimen Laterality
___ Right
___ Left
___ Not specified

Tumor Size
Greatest dimension: ___
+ Additional dimensions: ___ x ___
___ Cannot be determined (see Comment)

Histologic Type (Note B)
___ Urothelial (transitional cell) carcinoma
___ Urothelial (transitional cell) carcinoma with squamous differentiation
___ Urothelial (transitional cell) carcinoma with glandular differentiation
___ Urothelial (transitional cell) carcinoma with variant histology (specify): ____________________________
___ Squamous cell carcinoma, typical
___ Squamous cell carcinoma, variant histology (specify): ____________________________
___ Adenocarcinoma, typical
___ Adenocarcinoma, variant histology (specify): ____________________________
___ Small cell carcinoma
___ Undifferentiated carcinoma (specify): ____________________________
___ Mixed cell type (specify): ____________________________
___ Other (specify): ____________________________
___ Carcinoma, type cannot be determined

Associated Epithelial Lesions (select all that apply) (Note C)
___ None identified
___ Urothelial (transitional cell) papilloma, inverted type
___ Papillary urothelial (transitional cell) neoplasm, low malignant potential (WHO/ISUP 1998; WHO 2004)
___ Cannot be determined

+ Data elements preceded by this symbol are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.
Histologic Grade (select all that apply) (Note C)
___ Not applicable
___ Cannot be determined
___ Urothelial carcinoma
     ___ Low-grade
     ___ High-grade
     ___ Other (specify): ____________________________
___ Squamous cell carcinoma or adenocarcinoma
     ___ GX: Cannot be assessed
     ___ G1: Well differentiated
     ___ G2: Moderately differentiated
     ___ G3: Poorly differentiated
     ___ Other (specify): ____________________________
___ Other carcinoma
     ___ Low-grade
     ___ High-grade
     ___ Other (specify): ____________________________

Microscopic Tumor Extension (Note E)
___ Cannot be assessed
___ No evidence of primary tumor
___ Papillary noninvasive carcinoma
___ Carcinoma in situ
___ Tumor invades subepithelial connective tissue
___ Tumor invades the muscularis
___ Tumor invades beyond muscularis into periureteric fat
___ Tumor invades adjacent organs

+ Tumor Configuration (select all that apply)
  + ___ Papillary
  + ___ Solid/nodule
  + ___ Ulcerated
  + ___ Flat
  + ___ Indeterminate
  + ___ Other (specify): ____________________________

Margins (select all that apply) (Note G)
___ Cannot be assessed
___ Margin(s) involved by invasive carcinoma
     ___ Proximal mucosal margin
     ___ Distal mucosal margin
     ___ Deep soft tissue margin
     ___ Other margin(s) (specify)*: ____________________________
___ Margins(s) involved by carcinoma in situ/noninvasive high-grade urothelial carcinoma
     ___ Proximal mucosal margin
     ___ Distal mucosal margin
     ___ Other margin(s) (specify)*: ____________________________

* Data elements preceded by this symbol are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.
__ Margins uninvolved by invasive carcinoma/carcinoma in situ/noninvasive high-grade urothelial carcinoma
  + Distance of carcinoma from closest margin: ___ mm
  + Specify margin(s)*: ______________________________
  + Other significant changes at margin (specify margin)*: ______________________________
    + ___ Low-grade dysplasia
    + ___ Noninvasive low-grade urothelial carcinoma

* if the specimen is received unoriented, precluding identification of margins as distal or proximal, it should be denoted here.

+ Lymph-Vascular Invasion (Note H)
  + ___ Not identified
  + ___ Present
  + ___ Indeterminate

Pathologic Staging (pTNM) (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: Carcinoma in situ
__ pT1: Tumor invades subepithelial connective tissue (lamina propria)
__ pT2: Tumor invades the muscularis propria
__ pT3: Tumor invades beyond muscularis propria into periureteric fat
__ pT4: Tumor invades adjacent organs

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
__ No nodes submitted or found

Number of Lymph Nodes Examined
Specify: ___
__ Number cannot be determined (explain): ______________________________

Number of Lymph Nodes Involved (any size)
Specify: ___
__ Number cannot be determined (explain): ______________________________

+ Data elements preceded by this symbol are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.
Distant Metastasis (pM)
___ Not applicable
___ pM1: Distant metastasis
   + Specify site(s), if known: __________________________

+ Additional Pathologic Findings (select all that apply)
+ ___ Urothelial carcinoma in situ
+ ___ Urothelial dysplasia (low-grade intraurothelial neoplasia)
+ ___ Inflammation/regenerative changes
+ ___ Therapy-related changes
+ ___ Ureteritis cystica et glandularis
+ ___ Keratinizing squamous metaplasia
+ ___ Intestinal metaplasia
+ ___ Other (specify): __________________________

+ Comment(s)
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 non-polyposis 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. A working histologic classification encompassing the wide histologic diversity and histologic range within the different types of carcinomas of the urothelial tract is tabulated 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. Of note, unusual histomorphological variants seem to be more common in the upper tract, including carcinomas with micropapillary, lymphoepithelioma-like, sarcomatoid, squamous, clear cell, glandular, rhabdoid, signet-ring, and plasmacytoid features or areas. The distinction between a urothelial carcinoma with aberrant squamous or glandular differentiation and a primary squamous cell carcinoma or adenocarcinoma is rather arbitrary. Most authorities require a pure histology of squamous cell carcinoma or adenocarcinoma 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 aberrant differentiation.

Classification of Neoplasms of the Ureter and Renal Pelvis, Including Urothelial (Transitional Cell) Carcinoma and Its Variants


- Benign
  - Urothelial papilloma
  - Inverted papilloma
- Papillary urothelial neoplasm of low malignant potential

- Malignant
  - Papillary**
    - Typical, noninvasive
    - Typical, with invasion
    - Variant
      - With squamous or glandular differentiation
  - Micropapillary
  - Nonpapillary
    - Carcinoma in situ
    - Invasive carcinoma
    - Variants containing or exhibiting
      - Deceptively benign features
Nested pattern (resembling von Brunn’s nests)
Small tubular pattern
Microcystic pattern
Inverted pattern
Squamous differentiation
Glandular differentiation
Micropapillary histology
Sarcomatoid foci ("sarcomatoid carcinoma")
Urothelial carcinoma with unusual cytoplasmic features
  Clear cell
  Plasmacytoid
Urothelial carcinoma with syncytiotrophoblasts
Unusual stromal reactions
  Pseudosarcomatous stroma
  Stromal osseous or cartilaginous metaplasia
  Osteoclast-type giant cells
  With prominent lymphoid infiltrate

Squamous Cell Carcinoma
  Typical
  Variant
    Verrucous carcinoma
    Basaloid squamous cell carcinoma
    Sarcomatoid carcinoma

Adenocarcinoma
  Histologic variants
    Typical intestinal type
    Mucinous (including colloid)
    Signet-ring cell
    Clear cell
    Hepatoid
    Mixture of above patterns – adenocarcinoma not otherwise specified (NOS)

Tumors of Mixed Cell Types
Undifferentiated Carcinoma###
  Small cell carcinoma
  Large cell neuroendocrine carcinoma
  Lymphoepithelioma-like carcinoma
  Giant cell carcinoma
  Not otherwise specified

Metastatic Carcinoma

* Modified from Amin et al.7

** Papillary tumors may be invasive or noninvasive.

### Refers to tumors that are undifferentiated by light microscopy.

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.8 This system is utilized in the WHO 2004 “blue book”1
and the 2004 AFIP Fascicle.\textsuperscript{2} Urothelial carcinomas of the renal pelvis tend to more often be high-grade\textsuperscript{3,9} compared to urinary bladder carcinomas.

**WHO/ISUP (1998) and WHO 2004 Consensus Classification for Urothelial (Transitional Cell) Lesions**

- **Normal**
  - Normal#
- **Hyperplasia**
  - Flat hyperplasia
  - Papillary hyperplasia
- **Flat Lesions with Atypia**
  - Reactive (inflammatory) atypia
  - Atypia of unknown significance
  - Dysplasia (low-grade intraurothelial neoplasia)
  - Carcinoma in situ (high-grade intraurothelial neoplasia)##
- **Papillary Neoplasms**
  - Papilloma
  - Inverted papilloma
  - Papillary neoplasm of low malignant potential
  - Papillary carcinoma, low-grade
  - Papillary carcinoma, high-grade###
- **Invasive Neoplasms**
  - Lamina propria invasion
  - Muscularis propria invasion

# May include cases formerly diagnosed as “mild dysplasia.”

## Includes cases with “severe dysplasia.”

### Option exists to add comment as to the presence of marked anaplasia.

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.\textsuperscript{10,11} 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.\textsuperscript{12} 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 (i.e., 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, i.e., 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.\textsuperscript{3,9}

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.\textsuperscript{13}

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.
Figure 1. Depiction of pTa, pT1, pT2, and pT3.

Anatomic Stage/Prognostic Groups

<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>
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<tr>
<td>II</td>
<td>T2</td>
<td>N0</td>
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<td>N0</td>
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<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 overnight fixation in 10% formalin, sections are taken to demonstrate the deepest invasion of any lesion(s). At least 1 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 1 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.
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 lymphatic 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.

References
Background Documentation


