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

Version: 2.3.0.0
Protocol Posting Date: September 2023
The use of this protocol is recommended for clinical care purposes but is not required for accreditation purposes.

This protocol may be used for the following procedures AND tumor types:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy</td>
<td>Includes specimens designated biopsy or endoscopic transurethral resection</td>
</tr>
<tr>
<td>Tumor Type</td>
<td>Description</td>
</tr>
<tr>
<td>Carcinomas</td>
<td>Includes invasive carcinomas of the urinary tract, including urothelial</td>
</tr>
<tr>
<td></td>
<td>carcinoma, its morphological subtypes, and other carcinoma (such as</td>
</tr>
<tr>
<td></td>
<td>squamous cell carcinoma, adenocarcinoma, Müllerian carcinoma,</td>
</tr>
<tr>
<td></td>
<td>neuroendocrine carcinoma)</td>
</tr>
</tbody>
</table>

The following should NOT be reported using this protocol:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resection</td>
<td>(consider the Ureter and Renal Pelvis Resection protocol)</td>
</tr>
<tr>
<td>Cytologic</td>
<td>specimens</td>
</tr>
</tbody>
</table>

The following tumor types should NOT be reported using this protocol:

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoma</td>
<td>(consider the Lymphoid Neoplasm protocols)</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>(consider the Soft Tissue protocol)</td>
</tr>
<tr>
<td>Renal cortical and medullary tumors</td>
<td>(consider the separate Kidney protocol)</td>
</tr>
</tbody>
</table>

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With guidance from the CAP Cancer and CAP Pathology Electronic Reporting Committees.
* Denotes primary author.

Accreditation Requirements
The use of this case summary is recommended for clinical care purposes but is not required for accreditation purposes. The core and conditional data elements are routinely reported. Non-core data elements are indicated with a plus sign (+) to allow for reporting information that may be of clinical value.
Summary of Changes
v 2.3.0.0

- WHO 5th Edition update to content and Explanatory Notes
- LVI question update from “Lymphovascular Invasion” to “Lymphatic and/or Vascular Invasion”
CASE SUMMARY: (URETER, RENAL PELVIS: Biopsy)

Standard(s): AJCC-UICC 8

This case summary is recommended for reporting biopsy specimens, but is not required for accreditation purposes.

SPECIMEN

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

Specimen Laterality
___ Right
___ Left
___ Not specified

TUMOR

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

Urothelial
___ Papillary urothelial carcinoma, noninvasive
___ Urothelial carcinoma in situ
___ Urothelial carcinoma, invasive (conventional)
___ Urothelial carcinoma, micropapillary
___ Urothelial carcinoma, nested
___ Urothelial carcinoma, tubular and microcystic
___ Urothelial carcinoma, lymphoepithelioma-like
___ Urothelial carcinoma, plasmacytoid
___ Urothelial carcinoma, sarcomatoid
___ Urothelial carcinoma, giant cell
___ Urothelial carcinoma, poorly differentiated
___ Urothelial carcinoma, lipid-rich
___ Urothelial carcinoma, clear cell (glycogen-rich)
___ Urothelial carcinoma with squamous differentiation
___ Urothelial carcinoma with glandular differentiation
___ Urothelial carcinoma with trophoblastic differentiation
___ Urothelial carcinoma with Müllerian differentiation

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

Glandular
___ Adenocarcinoma, NOS
___ Adenocarcinoma, enteric
___ Adenocarcinoma, mucinous
___ Adenocarcinoma, mixed
___ Adenocarcinoma, signet-ring cell
___ Adenocarcinoma in situ (no invasive carcinoma identified)

**Müllerian**
___ Clear cell adenocarcinoma
___ Endometrioid carcinoma

**Neuroendocrine**
___ Small cell neuroendocrine carcinoma
___ Large cell neuroendocrine carcinoma
___ Well-differentiated neuroendocrine carcinoma

**Other**
___ Other histologic type not listed (specify): _________________
___ Carcinoma, type cannot be determined: _________________

**+Specify Percentages of Histologic Subtypes and Divergent Differentiations Present (totaling 100%)# (select all that apply)**
# Applicable for mixed subtypes, divergent differentiations, and other carcinomas
___ Urothelial carcinoma, invasive (conventional): _________________ %
___ Urothelial carcinoma, micropapillary: _________________ %
___ Urothelial carcinoma, nested: _________________ %
___ Urothelial carcinoma, large nested: _________________ %
___ Urothelial carcinoma, tubular and microcystic: _________________ %
___ Urothelial carcinoma, lymphoepithelioma-like: _________________ %
___ Urothelial carcinoma, plasmacytoid: _________________ %
___ Urothelial carcinoma, sarcomatoid: _________________ %
___ Urothelial carcinoma, giant cell: _________________ %
___ Urothelial carcinoma, poorly differentiated: _________________ %
___ Urothelial carcinoma, lipid-rich: _________________ %
___ Clear cell (glycogen-rich): _________________ %
___ Squamous differentiation: _________________ %
___ Glandular (adenocarcinoma) differentiation: _________________ %
___ Trophoblastic differentiation: _________________ %
___ Müllerian differentiation: _________________ %
___ Small cell neuroendocrine carcinoma: _________________ %
___ Large cell neuroendocrine carcinoma: _________________ %
___ Other (specify): _________________

**+Histologic Type Comment: _________________**

**Histologic Grade (Note C)**
For urothelial carcinoma, other variants, or divergent differentiation
___ Low-grade
___ High-grade

For squamous cell carcinoma or adenocarcinoma
___ G1, well-differentiated
___ G2, moderately differentiated
___ G3, poorly differentiated
___ GX, cannot be assessed: _________________

**Other**
___ Other (specify): _________________
___ Cannot be assessed: _________________
___ Not applicable: _________________
Tumor Extent (Note D)
___ Noninvasive papillary carcinoma
___ Carcinoma in situ
___ Invades subepithelial connective tissue
___ Invades muscularis
___ Invades beyond muscularis into peripelvic fat or renal parenchyma (for renal pelvis only)
___ Invades beyond muscularis into periureteric fat (for ureter only)
___ Invades adjacent organs or through the kidney into perinephric fat: _________________
___ Cannot be determined: _________________

+Lymphatic and/or Vascular Invasion
___ Not identified
___ Present
___ Cannot be determined: _________________

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

Muscularis (for determining T category) (Note D)
___ Not identified
___ Present in specimen
___ Cannot be determined: _________________

+Tumor Comment: _________________

ADDITIONAL FINDINGS

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

+Additional Findings (select all that apply)
___ Inflammation / regenerative changes
___ Therapy-related changes
___ Cautery artifact
___ Ureteritis cystica et glandularis
___ Non-keratinizing squamous metaplasia
___ Keratinizing squamous metaplasia
___ Intestinal metaplasia
CAP Approved

___ Other (specify): ____________________

COMMENTS

Comment(s): ____________________
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 2022 World Health Organization (WHO) classification of tumors of the urinary tract, including for 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 subtypes (variants) as found in the urinary bladder may also be found in the upper tract. In cases of mixed urothelial subtypes and/or divergent differentiations, each component should be reported, including admixed neuroendocrine carcinoma if present. The distinction between a urothelial carcinoma with divergent squamous, glandular, or Müllerian differentiation, and a pure squamous cell carcinoma, adenocarcinoma or Müllerian is important. The 2022 WHO classification, requires 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.

Lynch syndrome, also known as hereditary nonpolyposis colorectal cancer, predisposes patients to urological cancer, particularly upper tract urothelial carcinoma. Lynch syndrome develops in up to 28% of patients with known Lynch syndrome. Therefore, pathologists should be aware of Lynch syndrome and their important role in 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.

2022 WHO Classification of Epithelial Tumors of the Urothelial Tract

Urothelial tumors

Invasive urothelial carcinoma
- Conventional urothelial carcinoma
- Urothelial carcinoma with squamous differentiation
- Urothelial carcinoma with glandular differentiation
- Urothelial carcinoma with trophoblastic differentiation
- Nested urothelial carcinoma
- Tubular and microcystic urothelial carcinomas
- Micropapillary urothelial carcinoma
- Lymphoepithelioma-like urothelial carcinoma
- Plasmacytoid urothelial carcinoma
Giant cell urothelial carcinoma
Lipid-rich urothelial carcinoma
Clear cell (glycogen-rich) urothelial carcinoma
Urothelial carcinoma, poorly differentiated

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

Squamous cell neoplasms
Squamous cell carcinoma
Verrucous carcinoma
Squamous papilloma

Glandular neoplasms
Adenocarcinoma, NOS
Enteric
Mucinous
Mixed
Signet-ring cell
Adenocarcinoma in situ

Villous adenoma

Urachal and diverticular neoplasms
Urachal carcinoma
Diverticular carcinoma

Tumors of Mullerian type
Clear cell adenocarcinoma
Endometrioid carcinoma

Neuroendocrine neoplasms
Small cell neuroendocrine carcinoma
Large cell neuroendocrine carcinoma
Mixed neuroendocrine neoplasm
Well-differentiated neuroendocrine tumor
Paraganglioma

References
C. Histologic Grade

Flat intraepithelial lesions and papillary and invasive lesions are graded separately. In the 1973 WHO classification, papillary lesions were classified as papillomas and transitional cell carcinomas, grades 1, 2, and 3. Due to the need for a universally acceptable system, the World Health Organization/International Society of Urological Pathology (WHO/ISUP) consensus classification was proposed in 1998. This system is adopted in the 2004 WHO classification and has been validated by many studies to be prognostically significant. The 2016 WHO and 2022 WHO systems used essentially the same classification with minor modifications. Other systems may still be used according to institutional preference. Tumor grade according to both the 2004 WHO system and the 1973 WHO system may be concurrently used.

The vast majority of invasive urothelial carcinoma are high-grade with uncommon cases of invasive low-grade tumors reported. Invasive urothelial carcinoma subtypes are graded as high-grade tumors, although these tumors should not be considered as a homogenous group in terms of behavior. Pure squamous carcinomas and adenocarcinomas are graded based on tumor differentiation as well-differentiated, moderately differentiated, and poorly differentiated.

References


**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.\(^1\)\(^2\)\(^3\) A critical role of the surgical pathologist is to diagnose the depth and extent of invasion into the subepithelial connective tissue/lamina propria (T1), muscularis propria (T2). 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 T1, and like the urinary bladder, there is no accepted approach for assessing depth of lamina propria invasion. Designation of a tumor if muscularis propria muscle-invasive or not is important. Upper tract papillary urothelial carcinoma may also have inverted non-invasive growth pushing into subepithelial structures (Ta) that must be distinguished from true invasion of subepithelial structures. 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 T3.

**References**

