Sponsored by ISUP

Carcinoma of the Renal Pelvis and Ureter Histopathology Reporting Guide Nephroureterectomy and Ureterectomy Specimen

ICCR

Family/Last name

Given name(s)

Date of birth DD – MM – YYYY

Patient identifiers

Date of request DD – MM – YYYY

Accession/Laboratory number

Elements in **black text** are CORE. Elements in **grey text** are NON-CORE.

☐ indicates multi-select values ◯ indicates single select values

SCOPE OF THIS DATASET

CLINICAL INFORMATION (Note 1)

- ◯ Information not provided
- ◯ Information provided (select all that apply)
  - ☐ Previous history of urinary tract disease or distant metastasis
    - ☐ Carcinoma in situ, flat
    - ☐ Non-invasive papillary
    - ☐ Invasion into lamina propria
    - ☐ Invasion of muscularis propria or beyond
    - ☐ Distant metastasis
    - ☐ Other, *specify*
  - ☐ Previous therapy
    - ☐ Bacillus Calmette-Guerin (BCG)
    - ☐ Immunotherapy
    - ☐ Radiation therapy
    - ☐ Chemotherapy, systemic
    - ☐ Chemotherapy, intravesical, *specify*
    - ☐ Other, *specify*
  - ☐ Other clinical information, *specify*

OPERATIVE PROCEDURE (Note 2)

- ◯ Not specified
- ◯ Nephroureterectomy
- ◯ Ureterectomy, partial
- ◯ Ureterectomy, complete
- ◯ Ureterectomy with cystectomy
- ◯ Ureterectomy with cystoprostatectomy
- ◯ Other, *specify*

ADDITIONAL SPECIMEN(S) SUBMITTED (Note 3)

- ◯ Not submitted
- ◯ Submitted, *specify*

TUMOUR SITE (select all that apply) (Note 4)

- ◯ Not specified
- ◯ No macroscopically visible tumour
- ☐ Ureter
  - ◯ Left ◯ Right ◯ Laterality not specified
- ☐ Renal pelvis
  - ◯ Left ◯ Right ◯ Laterality not specified
- ☐ Other, *specify*

TUMOUR FOCALITY (Note 5)

- ◯ Unifocal
- ◯ Multifocal

TUMOUR DIMENSIONS (Note 6)

- ◯ No macroscopically visible tumour

Maximum tumour dimension (largest tumour)

mm

Additional dimensions (largest tumour)

mm X mm

MACROSCOPIC EXTENT OF INVASION (select all that apply) (Note 7)

- ◯ No macroscopically visible tumour
- ◯ Non-invasive tumour visible
- ☐ Invasion into wall
- ☐ Invasion into periureteral/peripelvic tissue
- ☐ Invasion into renal parenchyma
- ☐ Invasion into perinephric fat
- ☐ Involvement of other adjacent structures, *specify*

BLOCK IDENTIFICATION KEY (Note 8)

(List overleaf or separately with an indication of the nature and origin of all tissue blocks)

Version 2.0 Published December 2025 ISBN: 978-1-922324-75-7

HISTOLOGICAL TUMOUR TYPE (Note 9)

(Value list based on the World Health Organization Classification of Urinary and Male Genital Tumours, 5th Edition (2022))

- ◯ Urothelial carcinoma
- ◯ Squamous cell carcinoma
- ◯ Adenocarcinoma
- ◯ Neuroendocrine carcinoma
  - ◯ Small cell neuroendocrine carcinoma
  - ◯ Large cell neuroendocrine carcinoma
  - ◯ Carcinoma mixed with neuroendocrine carcinoma
    - ____ %
- ◯ Other, *specify*

Histologic subtype and divergent differentiation (urothelial carcinoma)

- ◯ Not identified
- ◯ Present, *specify subtype and percentage* (select all that apply)
  - ☐ Squamous ____ %
  - ☐ Glandular ____ %
  - ☐ Nested ____ %
  - ☐ Micropapillary ____ %
  - ☐ Plasmacytoid ____ %
  - ☐ Sarcomatoid ____ %
  - ☐ Other, *specify* ____ %

Comments

NON-INVASIVE CARCINOMA[a] (select all that apply) (Note 10)

- ◯ Not identified
- ◯ Indeterminate
- ☐ Carcinoma in situ
  - ◯ Focal ◯ Multifocal
- ☐ Papillary urothelial carcinoma
- ☐ Other, *specify*

[a] *Core in cases of non-invasive carcinoma requiring cystectomy; non-core for all other.*

ASSOCIATED EPITHELIAL LESIONS (Note 11)

- ◯ Not identified
- ◯ Present, *specify*

HISTOLOGICAL TUMOUR GRADE[b] (Note 12)

- ◯ Not applicable
- ◯ Cannot be assessed

Urothelial carcinoma[c]

- ◯ 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*

[b] *If more than one foci with different grades, record the highest grade.*

[c] *In cases with heterogeneous grades, the cutoff for high grade is 5%.*

MICROSCOPIC EXTENT OF INVASION (select all that apply) (Note 13)

- ◯ Cannot be assessed
- ◯ No evidence of primary tumour
- ☐ Papillary urothelial carcinoma, non-invasive
- ☐ Carcinoma in situ, flat
- ☐ Tumour invades subepithelial connective tissue (lamina propria)
- ☐ Tumour invades muscularis
- ☐ Tumour invades beyond muscularis into periureteric or peripelvic (renal sinus) fat
- ☐ Tumour invades into the renal parenchyma
- ☐ Tumour invades through the kidney into the perinephric fat
- ☐ Tumour invades adjacent structures, *specify*

LYMPHOVASCULAR INVASION (Note 14)

- ◯ Not identified
- ◯ Indeterminate
- ◯ Present

ISBN: 978-1-922324-75-7

MARGIN STATUS (Note 15)

- ◯ Cannot be assessed
- ◯ Not involved
- ◯ Involved
  - ◯ Invasive carcinoma (select all that apply)
    - ☐ Distal[d]
    - ☐ Proximal[d]
    - ☐ Circumferential bladder cuff
    - ☐ Soft tissue (periureteral, perirenal)
    - ☐ Other, *specify*
  - ◯ Carcinoma in situ/non-invasive papillary urothelial carcinoma (select all that apply)
    - ☐ Distal mucosa
    - ☐ Proximal mucosa
    - ☐ Other, *specify*

[d] *Relative to kidney as reference point.*

LYMPH NODE STATUS (Note 16)

- ◯ No nodes submitted or found

Number of lymph nodes examined

- ◯ Not involved
- ◯ Involved

Number of involved lymph nodes

- ◯ Number cannot be determined

Location of involved lymph nodes, *specify*

Maximum dimension of largest deposit ____ mm

Extranodal extension

◯ Not identified ◯ Present

COEXISTENT PATHOLOGY (Note 17)

Non-neoplastic renal tissue

- ◯ Not applicable
- ◯ Insufficient tissue
- ◯ No significant pathologic alterations
- ◯ Significant pathologic alterations, *specify*

Other histopathological features

- ◯ None identified
- ◯ Present, *specify*

ANCILLARY STUDIES (Note 18)

- ◯ Not performed
- ◯ Performed, *record test(s), methodology and result(s)*

Representative blocks for ancillary studies, *specify those blocks best representing tumour and/or normal tissue for further study*

HISTOLOGICALLY CONFIRMED DISTANT METASTASES (Note 19)

- ◯ Not identified
- ◯ Present (M1), *specify site(s)*

PATHOLOGICAL STAGING (UICC TNM 9th edition)[e] (Note 20)

TNM Descriptors (only if applicable) (select all that apply)

- ☐ m - multiple primary tumours
- ☐ y - post-therapy
- ☐ r - recurrent

Primary tumour (pT)

- ◯ TX[f] Primary tumour cannot be assessed
- ◯ T0 No evidence of primary tumour
- ◯ Ta Non-invasive papillary carcinoma
- ◯ Tis Carcinoma in situ
- ◯ T1 Tumour invades subepithelial connective tissue
- ◯ T2 Tumour invades muscularis
- ◯ T3 Renal pelvis: Tumour invades beyond muscularis into peripelvic fat or renal parenchyma
  Ureter: Tumour invades beyond muscularis into periureteric fat
- ◯ T4 Tumour invades adjacent organs or through the kidney into perinephric fat

Regional lymph nodes (pN)

- ◯ NX[f] Regional lymph nodes cannot be assessed
- ◯ N0 No regional lymph node metastasis
- ◯ N1 Metastasis in a single lymph node 2 cm or less in greatest dimension
- ◯ N2 Metastasis in a single lymph node more than 2 cm or multiple lymph nodes

[e] *Reproduced with permission. Source: UICC TNM Classification of Malignant Tumours, 9th Edition, eds by James Brierley, Meredith Giuliani, Brian O'Sullivan, Brian Rous, Elizabeth Van Eycken. 2025, Publisher Wiley (incorporating errata published 12th October 2025).*

[f] *TX and NX should be used only if absolutely necessary.*

ISBN: 978-1-922324-75-7

Definitions

CORE elements

Core elements are those which are essential for the clinical management, staging or prognosis of the cancer. These elements will either have evidentiary support at Level III-2 or above (based on prognostic factors in the National Health and Medical Research Council (NHMRC) levels of evidence[1]). In rare circumstances, where level III-2 evidence is not available an element may be made a core element where there is unanimous agreement by the Dataset Authoring Committee (DAC). An appropriate staging system, e.g., Pathological TNM staging, would normally be included as a core element.

Non-morphological testing e.g., molecular or immunohistochemical testing is a growing feature of cancer reporting. However, in many parts of the world this type of testing is limited by the available resources. In order to encourage the global adoption of ancillary tests for patient benefit, International Collaboration on Cancer Reporting (ICCR) recommends that some ancillary testing in ICCR Datasets is included as core elements. Where the technical capability does not yet exist, laboratories may consider temporarily using these data elements as non-core items.

The summation of all core elements is considered to be the minimum reporting standard for a specific cancer.

NON-CORE elements

Non-core elements are those which are unanimously agreed should be included in the dataset but are not supported by level III-2 evidence. These elements may be clinically important and recommended as good practice but are not yet validated or regularly used in patient management.

Key information other than that which is essential for clinical management, staging or prognosis of the cancer such as macroscopic observations and interpretation, which are fundamental to the histological diagnosis and conclusion e.g., macroscopic tumour details, may be included as either core or non-core elements by consensus of the DAC.

⬆ Back

Scope

The dataset has been developed for the pathology reporting of resection specimens from patients with primary carcinoma of the renal pelvis and ureter. The protocol applies to carcinomas (non-invasive and invasive), with or without associated epithelial lesions. Biopsy specimens are dealt with in a separate ICCR dataset.[2]

For bilateral tumours, complete a separate dataset for each.

The second edition of this dataset includes changes to align the dataset with the World Health Organization (WHO) Classification of Urinary and Male Genital Tumours, 5th edition, 2022.[3] The ICCR dataset includes 5th edition Corrigenda, July 2024.[4] In development of this dataset, the DAC considered evidence up until October 2025.

A list of changes in this dataset edition can be accessed here.

The authors of this dataset can be accessed here.

⬆ Back

Note 1 – Clinical information (Core and Non-core)

Presence or absence of clinical information is a core item, whereas details of the clinical information are non-core, since information may not be provided.

In addition to demographic information about the patient and details of destination of the report, several items of clinical information can help the pathologist in the handling and reporting of specimens of the upper urinary tract. Knowledge of any relevant history is critical in the accurate diagnosis of tumours throughout the urinary tract.[5-7] This may be relevant to the specific diagnosis being entertained. This is a non-core element since it is the responsibility of the clinician requesting pathological examination to provide information that will have an impact on the diagnostic process.

Specific observations of the upper tract epithelium are usually not available, but when present may be like those described in the urinary bladder. Bacillus Calmette-Guerin (BCG) and other 'intravesical' agents are used in upper tract tumours and these can affect the appearance of the upper tract lining.[8]

Back

Note 2 – Operative procedure (Core)

Documentation of the specific procedure performed should be a standard part of any pathology report. The term 'partial' refers to cases where the entire ureter is not removed.

A complete (radical) nephroureterectomy includes a cuff of bladder wall tissue. This is the standard operation for high risk urothelial carcinoma irrespective of location.[9,10]

In the past the role for segmental ureterectomy in urothelial carcinoma has been largely limited to patients with specific indication, in particular patients with an absent or non-functioning kidney on the opposite side. More recently, this approach has also been used in patients with a normal functioning contralateral kidney, particularly those patients with low risk disease.[9,11,12] Low risk upper tract urothelial carcinomas are defined by the European Association of Urology (EAU) and American Urological Association (AUA)/Society of Urologic Oncology (SUO) as unifocal tumours with negative cytology, low grade histology on ureteroscopic biopsy and non-invasive pattern on multidetector computed tomography urography.[9,13] EAU also requires them to be <10 millimetres (mm) in size.[9] The latest EAU and AUA/SUO guidelines recommend kidney sparing surgery, segmental resection or percutaneous approach for low risk upper urinary tract cancer.[9,13] When segmental ureterectomy specimens are submitted for pathological examination, the proximal and distal ends should be oriented for proper margin assessment.

Back

Note 3 – Additional specimen(s) submitted (Core)

If any additional tissues are resected, their documentation is a necessary part of the final pathology report.

Back

Note 4 – Tumour site (Core)

Studies evaluating the significance of tumour location of upper tract urothelial carcinoma have had inconsistent results.[10,14-17] Recent research has demonstrated that tumour location is not a significant factor in determining prognosis after stage matching.[18-20]

Several reports have also demonstrated that tumour location is a significant predictor of subsequent development of intravesical disease. These reports have consistently noted an increased risk associated with ureteral rather than renal pelvic origin.[21,22] It has also been found that location in the lower ureter is associated with a higher risk than the upper ureter.[23]

Further knowledge of the gross location of the tumour is important in the evaluation of histologic sections. In cases where examination of the sections does not show the relationship of the tumour to renal parenchyma, a gross description describing location as renal pelvis should prompt re-examination of the specimen and submission of additional sections as appropriate.

The highest pT category, and size of tumour, should be recorded as the index tumour in multifocal cases, according to the general concept of Union for International Cancer Control (UICC)/American Joint Committee on Cancer (AJCC).[24,25]

Back

Note 5 – Tumour focality (Non-core)

A large meta-analysis found tumour multifocality to be a significant predictor of subsequent development of an intravesical tumour.[21] In this study other significant pathologic predictors of an increased risk for intravesical recurrence were tumour location (ureter), pT stage, and tumour necrosis; features that were not significant were tumour size, tumour grade, concomitant carcinoma in situ (CIS) and lymphovascular invasion (LVI). In a different meta-analysis predictors of intravesical recurrence were location (ureter higher), pT stage, and tumour size; features that were not significant were concomitant CIS, multifocality and tumour grade.[22,26]

In the most recent EAU guidelines,[9] multifocality is not listed as a significant prognostic indicator postoperatively. It is listed as significant preoperatively. In contrast, in a comprehensive literature review, Lughezzani et al (2012)[27] concluded that multifocality was an independent predictor of cancer specific survival. This reflected several large series in the literature.[28,29]

Back

Note 6 – Tumour dimensions (Non-core)

Tumour size is a prognostic factor in upper tract tumours which is assessed by urologists prior to surgical resection.[30] In the current EAU guidelines tumour size is not considered to be prognostic post-resection.[9] Small (<20 mm) are considered part of the definition of low risk disease.[9] A recent comprehensive review did, however, conclude that size was a significant predictor of progression-free and recurrence free survival.[30] Given the limited size of the referenced studies this parameter requires additional larger studies to confirm its independent significance. Nevertheless, tumour size remains an integral part of the gross description and documentation (at least the largest tumour dimension) should be recorded.[24,25]

Back

Note 7 – Macroscopic extent of invasion (Non-core)

In contrast to the urinary bladder, the gross evaluation of tumour extent is not an element of the pathologic staging system. Nonetheless, estimating the gross extent of disease can help in block selection and reporting cases if there is a discrepancy between the gross evaluation and the microscopic findings. When a discrepancy is found between the two, this should be resolved by re-evaluating the gross appearance and submitting additional blocks if appropriate. It is recognised that the gross estimation may both over and underestimate the microscopic extent of disease and assignment of pathologic stage is based on the latter.

Back

Note 8 – Block identification key (Non-core)

The origin/designation of all tissue blocks should be recorded. This information should ideally be documented in the final pathology report and is particularly important should the need for internal or external review arise. The reviewer needs to be clear about the origin of each block to provide an informed specialist opinion. If this information is not included in the final pathology report, it should be available on the laboratory computer system and relayed to the reviewing pathologist. It may be useful to have a digital image of the specimen and record of the origin of the tumour blocks in some cases.

Recording the origin/designation of tissue blocks also facilitates retrieval of blocks for further immunohistochemical or molecular analysis, research studies or clinical trials.

Back

Note 9 – Histological tumour type (Core and Non-core)

The WHO Classification of Urinary and Male Genital Tumours, 5th edition, 2022, is utilised for assigning histological tumour type (Table 1).[3] The ICCR dataset includes 5th edition Corrigenda, July 2024.[4] Like in the previous edition, in the 2022 WHO a tumour is classified as a urothelial carcinoma if there is any identifiable urothelial component, including urothelial CIS.[3] An exception to this rule is for neuroendocrine carcinomas (small cell neuroendocrine carcinoma, large cell neuroendocrine carcinoma and mixed neuroendocrine neoplasms). The 5th edition WHO has created a separate chapter for all tumours with neuroendocrine differentiation.[3] For mixed neuroendocrine cases, the other elements should be reported with an estimated percentage. This would be managed by placing the other component in the histological tumour type element. For example, a mixed tumour with 70% small cell neuroendocrine carcinoma and 30% urothelial carcinoma would be reported under the histological tumour type as *Neuroendocrine mixed neoplasm* and then under histological tumour type – Other, specify - *urothelial carcinoma (30%)*.

Well differentiated neuroendocrine tumours (formerly 'carcinoids') and paraganglioma are described in separate chapters in the 2022 WHO 'Blue book'.[3] In the carcinoma group, the small cell neuroendocrine carcinoma is the most common. About one-half of cases are pure and one-half are mixed with another component with urothelial carcinoma being most frequent. Therefore, cases with mixed differentiation are included in this category. There does remain some controversy regarding the percentage of the neuroendocrine component required to classify a tumour as a neuroendocrine carcinoma. From a practical standpoint, cases with a small cell neuroendocrine carcinoma component irrespective of the amount are managed as small cell neuroendocrine carcinoma.[31] The National Comprehensive Cancer Network (NCCN)

includes tumours with any small cell component in the category of non-urothelial carcinoma.[31] The larger series in the literature include cases with only focal small cell neuroendocrine carcinoma.[31-35]

The diagnosis is defined by morphologic criteria and most cases demonstrate evidence of neuroendocrine differentiation by immunohistochemistry. The most specific immunohistochemical markers are chromogranin A and synaptophysin, while CD56 although sensitive is not very specific.[36-38] TTF-1 is expressed in more than 50% of cases.[39-43] In cases with pure small cell morphology the possibility of direct spread from an adjacent organ or metastasis must be clinically excluded.[44] Recent research could demonstrate that small cell bladder cancer microscopically resembles aggressive small cell lung cancer, shares DNA changes similar to small cell lung cancer and expresses many genes that urothelial bladder cancer does not, possibly explaining aggressive activity.[44]

Like the previous edition, the 2022 WHO classification includes the category of Müllerian tumours.[3] For the purposes of the dataset this consists primarily of clear cell adenocarcinoma and rare examples of endometrioid carcinoma. These tumours are morphologically the same as their counterparts in the female genital tract, although their histogenesis of clear cell adenocarcinoma is controversial.[3] They are rare tumours and when clear cell adenocarcinoma presents as a primary bladder tumour it represents secondary involvement most often originating in a urethral diverticulum.[45] Diagnosis therefore requires clinical correlation to support diagnosis as a primary bladder tumour. Clear cell adenocarcinoma and endometrioid carcinoma may arise from endometriosis or rarely Müllerianosis.[46-50] Clear cell adenocarcinoma must also be distinguished from urothelial carcinoma with clear aspects of the cytoplasm.[51] Müllerian type clear cell adenocarcinoma has similar immunohistochemical profile to primary tumours of the female genital tract so immunohistochemistry cannot be used to distinguish a primary from a secondary origin.[52]

Histological subtypes and divergent differentiation (urothelial carcinoma)

The 2022 WHO classification includes a number of recognised morphologic subtypes as outlined in Table 1.[3] According to the 2022 WHO classification, all subtypes are considered high grade.[3] The urothelial carcinoma has a remarkable capacity for morphologic changes the number of subtypes that have been described in the literature is extensive.[53] In general the subtypes that have been specifically recognised fall into three broad categories. Those with a deceptively bland morphology, such as the nested subtype, which could be misdiagnosed as benign. In the second category are tumours that have a morphology that mimics other tumours. Lastly are those tumours that have important prognostic or therapeutic implications.[54]

The importance of subtypes in clinical management decisions has been receiving increasing clinical attention.[55,56] Some subtypes have been highlighted because of the high frequency of under staging.[5] There are an increasing number of therapeutic algorithms that incorporate subtypes as a significant factor.[57] For T1 urothelial carcinoma, the presence of a histological subtype is one feature that is used in determining whether to consider immediate cystectomy.[31]

Rather than making reporting of specific subtypes that have some supporting data core and others lacking data non-core, the consensus of the DAC was to make the entire category a core element.

Reporting the percentage of subtypes when present is non-core (this is recommended in the WHO 2022 monograph[3]). The data supporting this is very limited and only available for selected subtypes (micropapillary, sarcomatoid and lymphoepithelioma-like), with divergent differentiation (glandular, squamous). There is also insufficient data available for setting specific amounts of each specific subtype in order for it to be clinically significant. Given the lack of data, if subtypes are identified, it should be reported and the estimated percentage of the tumour it makes up reported. For cases with more than one subtype present, the percentage of each is recommended to be documented (non-core).

Table 1: 5th edition of the World Health Organization classification of tumours of the urothelial tract.[3]

Descriptor	ICD-O codes[a]
Urothelial tumours	
Non-invasive urothelial neoplasms	
Papillary urothelial neoplasm of low malignant potential	8130/1
Non-invasive papillary urothelial carcinoma, low grade	8130/2
Non-invasive papillary urothelial carcinoma, high grade	8130/2
Urothelial carcinoma in situ	8120/2
Dysplasia	
Invasive urothelial carcinoma	8120/3
Nested	
Tubular microcystic	
Micropapillary	8131/3
Lymphoepithelioma-like	8082/3
Plasmacytoid	
Sarcomatoid	8122/3
Giant cell	8031/3
Poorly differentiated	8020/3
Lipid-rich	
Clear cell	
Squamous cell neoplasms	
Pure squamous cell carcinoma	8070/3
Verrucous carcinoma	8051/3
Glandular neoplasms	
Adenocarcinoma, not otherwise specified (NOS)	8140/3
Enteric	8144/3
Mucinous	8480/3
Mixed	8140/3
Tumours of Müllerian type	
Clear cell adenocarcinoma	8310/3
Endometrioid carcinoma	8380/3
Neuroendocrine tumours	
Small cell neuroendocrine carcinoma	8041/3
Large cell neuroendocrine carcinoma	8013/3
Mixed neuroendocrine neoplasms	
Well differentiated neuroendocrine tumour	8240/3
Paraganglioma[b]	8693/3

[a] The morphology codes are from the International Classification of Diseases for Oncology (ICD-O).[58] Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumours. Subtype labels are indented. Incorporates all relevant changes from the 5th edition Corrigenda, July, 2024.[4]

[b] Paraganglioma is not an epithelial derived tumour.

Back

Note 10 – Non-invasive carcinoma (Core)

There is substantial data that the presence of concomitant urothelial CIS is associated with a worse recurrence-free and cancer-specific survival.[27,59-62] It is therefore important in these specimens to sample grossly normal portions of the resected ureter and renal pelvis for evaluation. These studies have not specifically recorded the extent of the associated CIS. For the purposes of this dataset, the dataset authors have divided CIS into focal and multifocal and arbitrarily defined these as involvement of a single versus multiple blocks. There is evidence that the extent of CIS is significant and distinguishing between a single focus and diffuse (or multifocal) disease is important.[63]

Back

Note 11 – Associated epithelial lesions (Non-core)

A variety of neoplastic lesions that fall short of carcinoma are recognised in the urinary tract. These include papillary lesions such as urothelial papilloma and inverted urothelial papilloma. Similarly, flat lesions such as urothelial dysplasia, keratinising squamous metaplasia with dysplasia and intestinal metaplasia with dysplasia can be seen. Identification of these may have diagnostic implications (e.g., the presence of keratinising squamous metaplasia with dysplasia supporting the diagnosis of primary squamous cell carcinoma) but do not have known proven prognostic or clinical significance. Therefore, the reporting of such findings, is considered non-core in the context of a carcinoma diagnosis.

Back

Note 12 – Histological tumour grade (Core)

Please note that this commentary is generic and most of the data is derived from studies of urothelial carcinoma of the bladder and to a less extent urothelial carcinoma in other anatomic sites.

Histologic grading of urothelial tumours is best considered in two categories, non-invasive papillary tumours and invasive carcinomas. For non-invasive papillary tumours the 2022 WHO[3] remains the same as in the 2004 and 2016 WHO and continues to be recommend the grading system, which was first put forward by the International Society of Urological Pathology (ISUP) in 1998.[64] The system is now recommended by almost all major pathology and urology organisations as the preferred grading system.[6,65]

In the 2022 WHO system, the lowest category is papillary urothelial neoplasm of low malignant potential (PUNLMP) which will not invade or metastasise.[3,66] This entity is rare (3.8% de novo), the risk of progression is minimal.[67] Papillary carcinomas are classified as low or high grade.[3] There are significant differences in the risk of progression to invasive carcinoma and death from bladder cancer between low and high grade categories.[68-70] The grade of non-invasive papillary carcinoma is the major variable in the choice of therapy in these patients.[71] Other features of importance in predicting outcome of patients with Ta papillary tumours are number of tumours/multifocality,[70,72-74] tumour size,[70,75-77] the presence of associated CIS,[70] and a history

of prior recurrence.[70] It has also been suggested that for low grade papillary tumours the frequency of follow up cystoscopies can be reduced.[71]

Grade heterogeneity is not uncommon in papillary urothelial carcinoma being reported in up to 32% of cases.[78,79] The 2022 WHO recommends grading based on the highest grade component and recommends the cut of 5% for high grade tumours.[3] Tumours with up to 5% high grade component would be categorised as low grade and it may be useful to state the proportion of high grade disease.[3]

The great majority of invasive urothelial carcinomas are high grade. According to the 2022 'Blue book', rare low grade invasive urothelial carcinomas lacking marked nuclear atypia are recognised but no standard criteria have been established to diagnose these as low grade.[3,6] Some authors have suggested that such low grade tumours have a more favourable outcome and therefore it is recommended that all invasive urothelial carcinomas be assigned a grade.[3,6]

For pure squamous and adenocarcinomas, a three tier system 'well differentiated', 'moderately differentiated' or 'poorly differentiated' is recommended.[3]

The ICCR dataset recommends the use of the 5th edition WHO grade as a core element.[3,80] The use of the 1973 WHO grading system for papillary tumours remains in use in some regions and one published guideline specifically recommends the reporting of both the current WHO grade with the 1973 grade,[71,81,82] while others allow for the 1973 grade to be provided by institutional choice.[3,5,65] It is beyond the scope of this commentary to provide a detailed argument for or against the 1973 WHO. Interested readers can review those discussions elsewhere.[81-83]

Back

Note 13 – Microscopic extent of invasion (Core)

Pathologic stage is a major prognostic indicator postoperatively. It is included in all three of the published nomograms based on the largest datasets available in the literature.[84-86] The diagnosis of invasion in upper tract tumours can be complicated by the distortion induced by the expansile mass growing in a confined space. This can result in thinning of the wall in the ureter or renal pelvis. Tumours with inverted architecture can compress the muscularis propria (MP) with near complete absence of this layer in tissue sections and diagnosis of invasion requires identification of a clearly infiltrative component. Given the very thin layer of subepithelial connective tissue in the ureter and renal pelvis, there is essentially no identifiable muscularis mucosae and invasion of any smooth muscle should be considered to represent pT2 disease. Tumours infiltrating the fat beyond smooth muscle are considered pT3.

For tumours arising in the renal pelvis involvement of the renal parenchyma is an important element in the staging system. Invasion of the renal parenchyma is included in the definition of pT3 disease. This must be distinguished from in situ spread of the tumour into the collecting ducts of the kidney which does not impact stage assignment.

Invasive carcinomas can also extend through the renal parenchyma and extend into the perinephric fat. Those tumours are staged as pT4. Microscopic invasion limited to renal medulla cases demonstrated better prognosis than those of extensive microscopic invasion into renal cortex and/or adjacent adipose tissue.[18,87] Direct invasion of an adjacent organ, including the adrenal gland, is also staged as pT4.

Back

Note 14 – Lymphovascular invasion (Core)

Lymphovascular invasion (LVI) has been repeatedly found to be an important prognostic indicator for urothelial carcinoma of the upper tracts. The most recent EAU guidelines conclude that it is an independent predictor of outcome in these tumours.[9] There are many other studies where it has been reported to be an independent predictor as well.[18,88]

As in other datasets the use of special stains and/or IHC to determine the presence or absence of LVI is considered optional. In the major studies referenced above, IHC was not routine part of the evaluation.

Back

Note 15 – Margin status (Core)

Positive surgical margins (generally the bladder cuff in nephroureterectomy specimens) have been correlated with an increased risk of subsequent intravesical tumours.[89,90] In a meta-analysis by Seisen et al (2015),[21] margin positivity was a statistically significant indicator for bladder recurrence.

Positive surgical margins have also been correlated with increased risk of distant metastases and cancer specific survival.[91] However, these findings are not consistent,[92] and margin positivity was not a significant predictor of cancer specific survival in the meta-analysis by Siesen et al (2015).[21] Of interest, margin status was not included in the nomograms developed by Cha et al (2012)[86] and Seisen et al (2014).[85]

In assessing microscopic margin status, invasive carcinoma should be selected if both invasive carcinoma and CIS are present. If non-invasive low grade tumour or CIS alone is present at the margin, this finding should be recorded.

Back

Note 16 – Lymph node status (Core and Non-core)

The staging system for tumours of the renal pelvis and ureter differs from the urinary bladder in that both the number of positive lymph nodes the size of the metastases are used to assign the pN category.[24,25] It is therefore necessary to document the number of positive lymph nodes (one or greater than one) and the greatest dimension of the metastasis (20 mm cut-point). For carcinomas of the renal pelvis, the renal hilar, paracaval, aortic and retroperitoneal lymph nodes, not otherwise specified (NOS), are considered regional.[93,94] For carcinomas of the ureter, regional lymph nodes include renal hilar, Iliac (common, internal/hypogastric, external), paracaval, periureteral, and pelvic, NOS. Involvement of lymph nodes other than those defined above is considered to represent pM1 disease.[24,25]

Template-based lymph node dissection is a beneficial approach for both staging and prognostic purposes.[95,96] There are limited published data indicating that the number of lymph nodes removed, the number of positive nodes and the lymph node density (percentage positive nodes) are significant prognostic indicators in patients with lymph node positive upper tract carcinoma.[97,98] In contrast, another study found that the number of nodes removed or the number of positive nodes did not correlate with outcome;[99,100] however, lymph node density was significant.[100] Similarly Fajkovic et al (2012)[101] did not show a significant correlation between the number of nodes removed or the number of positive nodes and outcome.

For patients with node-negative disease it has been reported that the number of nodes resected correlates with the likelihood that the patient is a true pN0.[102] With only one lymph node, the authors estimated that 44% of true pN+ cases would be misclassified as pN0. Another study reported that removal of eight lymph nodes had a >75% probability of finding a positive lymph node and with 13 lymph nodes a >90% probability was achieved.[103] The role of lymph node dissection, however, is controversial. A meta-analysis demonstrated that lymph node dissection predicts patients' outcome including cancer-specific survival and overall survival. In addition, it reduces recurrence and increases survival in lymph node negative patients, although it does not impact outcome in lymph node positive patients.[96,104,105] Interestingly, a recent study demonstrated that pN1 and pN2 patients show the same outcome.[106]

In the 2023 EAU guidelines for upper tract carcinoma it is stated that "extranodal extension is a powerful predictor of clinical outcome in upper tract urothelial carcinomas and positive lymph node metastases".[9] This conclusion was based on a study by Fajkovic et al (2012)[101] in which the presence of extranodal extension was an independent predictor of tumour recurrence and cancer specific mortality. In another study the presence of extranodal extension was 'marginally' associated with a worse prognosis.[107]

The presence of micrometastases, detected by IHC and/or polymerase chain reaction (PCR), is not a prognostic factor.[108,109] A study showed that pN- with IHC positive patients demonstrated intermediate prognosis between pN-, IHC negative and pN+ patients.[110] Further validation studies are needed. Artificial intelligence may also aid to assist in detecting lymph node metastasis, including micro-metastases.[111] However, their utilities in practice are needed to validate.

Back

Note 17 – Coexistent pathology (Core and Non-core)

It is important to recognise that medical kidney diseases may be present in non-neoplastic renal tissue in nephrectomy specimens.[112-114] Similar findings may be present in nephroureterectomy specimens and likely would have similar clinical significance although specific studies are not yet available. Assessment of the non-neoplastic kidney may be complicated by changes related to urinary tract obstruction with hydronephrosis and other sequelae.

Back

Note 18 – Ancillary studies (Non-core)

In addition to specifying ancillary studies performed, results should be provided (if available).

The 2023 EAU guidelines recommend evaluation for Hereditary Nonpolyposis Colorectal Cancer (HNPCC or Lynch syndrome) at the time of medical history taking.[9] They also recommend DNA sequencing to identify hereditary cancers misclassified as sporadic. In a recent comprehensive review,[115] the authors recommend tissue testing of upper tract urothelial carcinomas (IHC and/or molecular) similar to gastrointestinal tract guidelines in any one of the following situations: (i) the patient is <60 years of age; or (ii) there is a family history of an upper tract urothelial carcinoma, endometrial carcinoma, or a colon cancer diagnosis in a relative <60 years of age; or (iii) if there is a personal history of colon or endometrial cancer. However, no consensus for a screening protocol has been established.[116]

The prognosis of upper tract urothelial carcinoma and other HNPCC associated genitourinary neoplasms has not been established due to their rarity.

It has been shown that upper tract tumours associated with microsatellite instability frequently have an inverted growth pattern.[117] Various studies indicate that these tumours are more responsive to adjuvant chemotherapy.[116,118-120] After referral for genetic counselling and consent, multiple testing strategies are recommended.

Back

Note 19 – Histologically confirmed distant metastases (Core)

Documentation of known metastatic disease is an important part of the pathology report. Such information, if available, should be recorded with as much detail as is available including the site and reference to any relevant prior surgical pathology or cytopathology specimens.

Back

Note 20 – Pathological staging (Core)

The pathologic staging must be provided on the pathology report and is therefore a core element. Staging data should be assessed according to the 9th edition UICC/8th edition AJCC Cancer Staging Manuals.[24,25] Pathologic stage is the single most important prognostic parameter for patients that have undergone nephroureterectomy or ureterectomy for upper tract carcinoma.[27] Pathologic stage is also a significant predictor of subsequent intravesical recurrence.[21] Stage may also be an important parameter in the consideration of the use of adjuvant chemotherapy or immune checkpoint inhibitor therapy.[121,122] Accurate assignment of pathologic stage is therefore of considerable clinical significance. A careful gross examination with appropriate submission of sections is integral to the determination of pathologic stage. Knowledge of the anatomical origin of the sections can also be important to interpretation of the microscopic findings given the complex anatomy, particularly in the renal hilar region.

Understanding the anatomy and histology of the various parts of the upper tract are important to the subsequent interpretation of the specimen.[123] As discussed earlier, throughout the upper tract the subepithelial connective tissue tends to be very thin and is often distorted by the intraluminal tumour. The MP can be similarly attenuated. Further in the region of the renal sinus and calyces there may be no visible muscle fibres and the distinction of subepithelial connective tissue invasion (pT1) from the renal sinus connective tissue (pT3) may be quite arbitrary. In such cases identification of a convincing focus of invasion can change the stage assignment from pTa to pT2 or even pT3.[18,124] In the area of the renal papillae the urothelium sits on the renal parenchyma with an essentially invisible zone of subepithelial connective tissue such that virtually any invasion will result in designation as pT3a tumour. Cases showing tumour cell spreading into collecting ducts without invasion should not be overgraded as ‘pT3a’.

For tumours in the renal sinus and calyces the relationship of the tumour with the renal parenchyma can be complex. Non-invasive tumour extending into the renal collecting ducts does not constitute renal parenchyma invasion and over staging as pT3 must be avoided. Fortunately, when urothelial carcinoma invades renal parenchyma it almost always elicits a stroma response, and this can be helpful in difficult cases.

Invasive carcinomas can also invade through the full width of the renal parenchyma and extend into the perinephric fat. Those tumours are staged as pT4. This needs to be distinguished from involvement of sinus fat in cases with renal parenchyma invasion that would still be considered pT3.

Assessment of pathological stage can also be challenging in tumours with an inverted architecture. In the urinary bladder it is distinctly unusual to see non-invasive tumours with inverted architecture grow into the MP and so finding large pushing tumour fronts there suggests the diagnosis of invasion, perhaps related to a large, nested pattern. In the renal pelvis and calyces this becomes more problematic given the histological anatomy of that location. Non-invasive tumours with inverted architecture can push on renal sinus fat. Problematic cases should be extensively sampled to document unequivocal invasion.

Reporting of pathological staging categories (pT,pN,pM) is based on the evidence available to the pathologist at the time of reporting. As indicated in UICC TNM9 and AJCC8,[24,25] the final stage grouping of a patient's tumour is based on a combination of pathological staging and other clinical and imaging information.

Back

References

1 Merlin T, Weston A and Tooher R (2009). Extending an evidence hierarchy to include topics other than treatment: revising the Australian 'levels of evidence'. *BMC Med Res Methodol* 9:34.

2 International Collaboration on Cancer Reporting (2025). *Urinary Tract Carcinoma Histopathology Reporting Guide – Biopsy and Transurethral Resection Specimen. 2nd edition.* Available from: https://www.iccr-cancer.org/datasets/published-datasets/urinary-male-genital/ut-biopsy-and-tr/ (Accessed 18 December 2025).

3 WHO Classification of Tumours Editorial Board (2022). *Urinary and Male Genital Tumours, WHO Classification of Tumours, 5th edition, Volume 8*, IARC Publications, Lyon.

4 WHO Classification of Tumours Editorial Board (2022). *Urinary and Male Genital Tumours, WHO Classification of Tumours, 5th edition, Volume 8 - Corrigenda July 2024.* Available from: https://publications.iarc.who.int/_publications/media/download/7194/8d1c6dc5f87fee7cb7a25cbbea7818910a207c2c.pdf (Accessed 1st December 2025).

5 Hansel DE, Amin MB, Comperat E, Cote RJ, Knuchel R, Montironi R, Reuter VE, Soloway MS, Umar SA and Van der Kwast TH (2013). A contemporary update on pathology standards for bladder cancer: transurethral resection and radical cystectomy specimens. *Eur Urol* 63(2):321–332.

6 Amin MB, Smith SC, Reuter VE, Epstein JI, Grignon DJ, Hansel DE, Lin O, McKenney JK, Montironi R, Paner GP, Al-Ahmadie HA, Algaba F, Ali S, Alvarado-Cabrero I, Bubendorf L, Cheng L, Cheville JC, Kristiansen G, Cote RJ, Delahunt B, Eble JN, Genega EM, Gulmann C, Hartmann A, Langner C, Lopez-Beltran A, Magi-Galluzzi C, Merce J, Netto GJ, Oliva E, Rao P, Ro JY, Srigley JR, Tickoo SK, Tsuzuki T, Umar SA, Van der Kwast T, Young RH and Soloway MS (2015). Update for the practicing pathologist: The International Consultation On Urologic Disease-European association of urology consultation on bladder cancer. *Mod Pathol* 28(5):612–630.

7 College of American Pathologists (2025). *Protocol for the Examination of Resection Specimens from Patients with Carcinoma of the Ureter or Renal Pelvis*. Available from: https://documents.cap.org/documents/New-Cancer-Protocols-March-2025/UreterRenalPelvis.Res_2.4.0.0.REL.CAPCP.pdf (Accessed 1st December 2025).

8 Tyrrell J, Chui W, Kealey J and Sengupta S (2024). The Utility of Intraluminal Therapies in Upper Tract Urothelial Carcinoma: A Narrative Review. *Cancers (Basel)* 16(10):1931.

9 Rouprêt M, Seisen T, Birtle AJ, Capoun O, Compérat EM, Dominguez-Escrig JL, Gürses Andersson I, Liedberg F, Mariappan P, Hugh Mostafid A, Pradere B, van Rhijn BWG, Shariat SF, Rai BP, Soria F, Soukup V, Wood RG, Xylinas EN, Masson-Lecomte A and Gontero P (2023). European Association of Urology Guidelines on Upper Urinary Tract Urothelial Carcinoma: 2023 Update. *Eur Urol* 84(1):49–64.

10 Leow JJ, Orsola A, Chang SL and Bellmunt J (2015). A contemporary review of management and prognostic factors of upper tract urothelial carcinoma. *Cancer Treat Rev* 41(4):310–319.

11 Seisen T, Colin P and Roupret M (2015). Risk-adapted strategy for the kidney-sparing management of upper tract tumours. *Nat Rev Urol* 12(3):155–166.

12 Lucca I, Klatte T, Roupret M and Shariat SF (2015). Kidney-sparing surgery for upper tract urothelial cancer. *Curr Opin Urol* 25(2):100–104.

13 Coleman JA, Clark PE, Bixler BR, Buckley DI, Chang SS, Chou R, Hoffman-Censits J, Kulkarni GS, Matin SF, Pierorazio PM, Potretzke AM, Psutka SP, Raman JD, Smith AB and Smith L (2023). Diagnosis and Management of Non-Metastatic Upper Tract Urothelial Carcinoma: AUA/SUO Guideline. *J Urol* 209(6):1071–1081.

14 Milojevic B, Djokic M, Sipetic-Grujicic S, Milenkovic-Petronic D, Vuksanovic A, Bumbasirevic U, Vukovic I, Dragicevic D and Tulic C (2012). Upper urinary tract transitional cell carcinoma: location is not correlated with prognosis. *BJU Int* 109(7):1037–1042.

15 Favaretto RL, Shariat SF, Chade DC, Godoy G, Adamy A, Kaag M, Bochner BH, Coleman J and Dalbagni G (2010). The effect of tumor location on prognosis in patients treated with radical nephroureterectomy at Memorial Sloan-Kettering Cancer Center. *Eur Urol* 58(4):574–580.

16 Raman JD, Ng CK, Scherr DS, Margulis V, Lotan Y, Bensalah K, Patard JJ, Kikuchi E, Montorsi F, Zigeuner R, Weizer A, Bolenz C, Koppie TM, Isbarn H, Jeldres C, Kabbani W, Remzi M, Waldert M, Wood CG, Roscigno M, Oya M, Langner C, Wolf JS, Strobel P, Fernandez M, Karakiewcz P and Shariat SF (2010). Impact of tumor location on prognosis for patients with upper tract urothelial carcinoma managed by radical nephroureterectomy. *Eur Urol* 57(6):1072–1079.

17 Yafi FA, Novara G, Shariat SF, Gupta A, Matsumoto K, Walton TJ, Fritsche HM, El-Hakim A, Trischler S, Martinez-Salamanca JI, Seitz C, Ficarra V, Zattoni F, Karakiewicz PI and Kassouf W (2012). Impact of tumour location versus multifocality in patients with upper tract urothelial carcinoma treated with nephroureterectomy and bladder cuff excision: a homogeneous series without perioperative chemotherapy. *BJU Int* 110(2 Pt 2):E7–13.

18 Sano T, Kato M, Sassa N, Sadachi R, Hirakawa A, Kamihira O, Hirabayashi T, Nishikimi T, Katsuno S, Kimura T, Hattori R, Gotoh M and Tsuzuki T (2021). pT3 subclassification of renal pelvic cancer considering the tumor location improves the patients' prognostic accuracy. *Virchows Arch* 478(6):1089–1097.

19 Liu K, Leung DK, Wong CH, Ko IC, Horuz R, Gontero P, Laguna P, de la Rosette J and Teoh JY (2025). Influence of tumour location on the survival outcomes of upper tract urothelial carcinoma treated with radical nephroureterectomy. *World J Urol* 43(1):261.

20 Lwin AA, Hsu CH and Chipollini J (2020). Urothelial Carcinoma of the Renal Pelvis and Ureter: Does Location Make a Difference? *Clin Genitourin Cancer* 18(1):45–49.e41.

21 Seisen T, Granger B, Colin P, Leon P, Utard G, Renard-Penna R, Comperat E, Mozer P, Cussenot O, Shariat SF and Roupret M (2015). A Systematic Review and Meta-analysis of Clinicopathologic Factors Linked to Intravesical Recurrence After Radical Nephroureterectomy to Treat Upper Tract Urothelial Carcinoma. *Eur Urol* 67(6):1122–1133.

22 Yuan H, Chen X, Liu L, Yang L, Pu C, Li J, Bai Y, Han P and Wei Q (2014). Risk factors for intravesical recurrence after radical nephroureterectomy for upper tract urothelial carcinoma: a meta-analysis. *Urol Oncol* 32(7):989–1002.

23 Otsuka M, Taguchi S, Nakagawa T, Kawai T, Morikawa T, Miyazaki H, Fujimura T, Fukuhara H, Kume H and Homma Y (2016). Lower ureteral lesion is an independent predictor of intravesical recurrence after radical nephroureterectomy for upper tract urothelial carcinoma. *Urol Oncol* 34(2):59.e59–59.e13.

24 Brierley JD, Giuliani M, O'Sullivan B, Rous B and Van Eycken E (eds) (2025). *Union for International Cancer Control. TNM Classification of Malignant Tumours, 9th Edition*, Wiley, USA.

25 Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, Gershenwald JE, Compton CC, Hess KR, Sullivan DC, Jessup JM, Brierley JD, Gaspar LE, Schilsky RL, Balch CM, Winchester DP, Asare EA, Madera M, Gress DM and Meyer LR (eds) (2017). *AJCC Cancer Staging Manual. 8th ed.*, Springer, New York.

26 Sheu ZL, Huang CP, Chang CH, Chen CH, Hong JH, Weng HY, Tai TY, Chung SD, Lo CW, Hsueh TY, Tsai YC, Jiang YH, Chiang BJ, Chen YT, Lin JT, Lin WY, Jou YC, Tseng JS, Wu CC, Wu WJ and Yeh HC (2021). Tumor distribution affects bladder recurrence but not survival outcome of multifocal upper tract urothelial carcinoma treated with radical nephroureterectomy. *Sci Rep* 11(1):19059.

27 Lughezzani G, Burger M, Margulis V, Matin SF, Novara G, Roupret M, Shariat SF, Wood CG and Zigeuner R (2012). Prognostic factors in upper urinary tract urothelial carcinomas: a comprehensive review of the current literature. *Eur Urol* 62(1):100–114.

28 Kamihira O, Hattori R, Yamaguchi A, Kawa G, Ogawa O, Habuchi T, Kawauchi A, Uozumi J, Yokoi S, Tsujihata M, Hasui Y, Miyakoda K, Tada H, Ono Y and Naito S (2009). Laparoscopic radical nephroureterectomy: a multicenter analysis in Japan. *Eur Urol* 55(6):1397–1407.

29 Ouzzane A, Colin P, Xylinas E, Pignot G, Ariane MM, Saint F, Hoarau N, Adam E, Azemar MD, Bensadoun H, Cormier L, Cussenot O, Houlgatte A, Karsenty G, Bruyere F, Maurin C, Nouhaud FX, Phe V, Polguer T, Roumiguie M, Ruffion A and Roupret M (2011). Ureteral and multifocal tumours have worse prognosis than renal pelvic tumours in urothelial carcinoma of the upper urinary tract treated by nephroureterectomy. *Eur Urol* 60(6):1258–1265.

30 Collà Ruvolo C, Nocera L, Stolzenbach LF, Wenzel M, Califano G, Tian Z, Verze P, Shariat SF, Saad F, Briganti A, Mirone V and Karakiewicz PI (2022). Tumor Size Predicts Muscle-invasive and Non-organ-confined Disease in Upper Tract Urothelial Carcinoma at Radical Nephroureterectomy. *Eur Urol Focus* 8(2):498–505.

31 Flaig TW, Spiess PE, Abern M, Agarwal N, Bangs R, Buyyounouski MK, Chan K, Chang SS, Chang P, Friedlander T, Greenberg RE, Guru KA, Herr HW, Hoffman-Censits J, Kaimakliotis H, Kishan AU, Kundu S, Lele SM, Mamtani R, Mian OY, Michalski J, Montgomery JS, Parikh M, Patterson A, Peyton C, Plimack ER, Preston MA, Richards K, Sexton WJ, Siefker-Radtke AO, Stewart T, Sundi D, Tollefson M, Tward J, Wright JL, Cassara CJ and Gurski LA (2024). NCCN Guidelines® Insights: Bladder Cancer, Version 3.2024. *J Natl Compr Canc Netw* 22(4):216–225.

32 Choong NW, Quevedo JF and Kaur JS (2005). Small cell carcinoma of the urinary bladder. The Mayo Clinic experience. *Cancer* 103(6):1172–1178.

33 Siefker-Radtke AO, Dinney CP, Abrahams NA, Moran C, Shen Y, Pisters LL, Grossman HB, Swanson DA and Millikan RE (2004). Evidence supporting preoperative chemotherapy for small cell carcinoma of the bladder: a retrospective review of the M. D. Anderson cancer experience. *J Urol* 172(2):481–484.

34 Mackey JR, Au HJ, Hugh J and Venner P (1998). Genitourinary small cell carcinoma: determination of clinical and therapeutic factors associated with survival. *J Urol* 159(5):1624–1629.

35 Lynch SP, Shen Y, Kamat A, Grossman HB, Shah JB, Millikan RE, Dinney CP and Siefker-Radtke A (2013). Neoadjuvant chemotherapy in small cell urothelial cancer improves pathologic downstaging and long-term outcomes: results from a retrospective study at the MD Anderson Cancer Center. *Eur Urol* 64(2):307–313.

36 Amin MB, Trpkov K, Lopez-Beltran A and Grignon D (2014). Best practices recommendations in the application of immunohistochemistry in the bladder lesions: report from the International Society of Urologic Pathology consensus conference. *Am J Surg Pathol* 38(8):e20–34.

37 Selberherr A, Koperek O, Riss P, Scheuba C, Kaderli R, Perren A and Niederle B (2019). Neuroendocrine Liver Metastasis-a Specific Set of Markers to Detect Primary Tumor Sites. *Endocr Pathol* 30(1):31–34.

38 Agaimy A, Erlenbach-Wünsch K, Konukiewitz B, Schmitt AM, Rieker RJ, Vieth M, Kiesewetter F, Hartmann A, Zamboni G, Perren A and Klöppel G (2013). ISL1 expression is not restricted to pancreatic well-differentiated neuroendocrine neoplasms, but is also commonly found in well and poorly differentiated neuroendocrine neoplasms of extrapancreatic origin. *Mod Pathol* 26(7):995–1003.

39 Agoff SN, Lamps LW, Philip AT, Amin MB, Schmidt RA, True LD and Folpe AL (2000). Thyroid transcription factor-1 is expressed in extrapulmonary small cell carcinomas but not in other extrapulmonary neuroendocrine tumors. *Mod Pathol* 13(3):238–242.

40 Jones TD, Kernek KM, Yang XJ, Lopez-Beltran A, MacLennan GT, Eble JN, Lin H, Pan CX, Tretiakova M, Baldridge LA and Cheng L (2005). Thyroid transcription factor 1 expression in small cell carcinoma of the urinary bladder: an immunohistochemical profile of 44 cases. *Hum Pathol* 36(7):718–723.

41 Wang G, Yuan R, Zhou C, Guo C, Villamil C, Hayes M, Eigl BJ and Black P (2021). Urinary Large Cell Neuroendocrine Carcinoma: A Clinicopathologic Analysis of 22 Cases. *Am J Surg Pathol* 45(10):1399–1408.

42 Zhou HH, Liu LY, Yu GH, Qu GM, Gong PY, Yu X and Yang P (2017). Analysis of Clinicopathological Features and Prognostic Factors in 39 Cases of Bladder Neuroendocrine Carcinoma. *Anticancer Res* 37(8):4529–4537.

43 Virarkar M, Vulasala SS, Gopireddy D, Morani AC, Daoud T, Waters R and Bhosale P (2022). Neuroendocrine Neoplasms of the Female Genitourinary Tract: A Comprehensive Overview. *Cancers (Basel)* 14(13):3218.

44 Hoffman-Censits J, Choi W, Pal S, Trabulsi E, Kelly WK, Hahn NM, McConkey D, Comperat E, Matoso A, Cussenot O, Cancel-Tassin G, Fong MHY, Ross J, Madison R and Ali S (2021). Urothelial Cancers with Small Cell Variant Histology Have Confirmed High Tumor Mutational Burden, Frequent TP53 and RB Mutations, and a Unique Gene Expression Profile. *Eur Urol Oncol* 4(2):297–300.

45 Kosem M and Sengul E (2005). Clear cell adenocarcinoma of the urinary bladder. *Scand J Urol Nephrol* 39(1):89–92.

46 Loizzi V, Cormio G, Leone L, Falagario M, Longo S, Resta L and Selvaggi L (2015). A rare case of primary clear-cell adenocarcinoma of the bladder arising from bladder endometriosis. *J Obstet Gynaecol* 35(7):758–760.

47 Lah K, Desai D, Hadway P, Perry-Keene J and Coughlin G (2013). Primary vesical clear cell adenocarcinoma arising in endometriosis: a rare case of mullerian origin. *Anticancer Res* 33(2):615–617.

48 al-Izzi MS, Horton LW, Kelleher J and Fawcett D (1989). Malignant transformation in endometriosis of the urinary bladder. *Histopathology* 14(2):191–198.

49 Allen D, O'Brien T, Pingle P and Chandra A (2005). Endometrioid adenocarcinoma of the bladder. *Histopathology* 46(2):232–233.

50 Drew PA, Murphy WM, Civantos F and Speights VO (1996). The histogenesis of clear cell adenocarcinoma of the lower urinary tract. Case series and review of the literature. *Hum Pathol* 27(3):248–252.

51 Sung MT, Zhang S, MacLennan GT, Lopez-Beltran A, Montironi R, Wang M, Tan PH and Cheng L (2008). Histogenesis of clear cell adenocarcinoma in the urinary tract: evidence of urothelial origin. *Clin Cancer Res* 14(7):1947–1955.

52 Claps F, van de Kamp MW, Mayr R, Bostrom PJ, Shariat SF, Hippe K, Bertz S, Neuzillet Y, Sanders J, Otto W, van der Heijden MS, Jewett MAS, Stöhr R, Zlotta AR, Trombetta C, Eckstein M, Mertens LS, Burger M, Soorojebally Y, Wullich B, Bartoletti R, Radvanyi F, Pavan N, Sirab N, Mir MC, Pouessel D, van der Kwast TH, Hartmann A, Lotan Y, Bussani R, Allory Y and van Rhijn BWG (2023). Prognostic impact of variant histologies in urothelial bladder cancer treated with radical cystectomy. *BJU Int* 132(2):170–180.

53 Warrick JI, Al-Ahmadie H, Berman DM, Black PC, Flaig TW, Höglund M, Bubendorf L, van der Kwast TH and Cheng L (2024). International Society of Urological Pathology Consensus Conference on Current Issues in Bladder Cancer. Working Group 4: Molecular Subtypes of Bladder Cancer-Principles of Classification and Emerging Clinical Utility. *Am J Surg Pathol* 48(1):e32–e42.

54 Lopez-Beltran A (2008). Bladder cancer: clinical and pathological profile. *Scand J Urol Nephrol Suppl*(218):95–109.

55 Xylinas E, Rink M, Robinson BD, Lotan Y, Babjuk M, Brisuda A, Green DA, Kluth LA, Pycha A, Fradet Y, Faison T, Lee RK, Karakiewicz PI, Zerbib M, Scherr DS and Shariat SF (2013). Impact of histological variants on oncological outcomes of patients with urothelial carcinoma of the bladder treated with radical cystectomy. *Eur J Cancer* 49(8):1889–1897.

56 Kim SP, Frank I, Cheville JC, Thompson RH, Weight CJ, Thapa P and Boorjian SA (2012). The impact of squamous and glandular differentiation on survival after radical cystectomy for urothelial carcinoma. *J Urol* 188(2):405–409.

57 Shah JB, McConkey DJ and Dinney CP (2011). New strategies in muscle-invasive bladder cancer: on the road to personalized medicine. *Clin Cancer Res* 17(9):2608–2612.

58 Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin L, Parkin DM and Whelan S (eds) (2020). *International Classification of Diseases for Oncology, Third edition, Second revision ICD-O-3.2*. Available from: http://www.iacr.com.fr/index.php?option=com_content&view=category&layout=blog&id=100&Itemid=577 (Accessed 1st December 2025).

59 Novara G, Matsumoto K, Kassouf W, Walton TJ, Fritsche HM, Bastian PJ, Martinez-Salamanca JI, Seitz C, Lemberger RJ, Burger M, El-Hakim A, Baba S, Martignoni G, Gupta A, Karakiewicz PI, Ficarra V and Shariat SF (2010). Prognostic role of lymphovascular invasion in patients with urothelial carcinoma of the upper urinary tract: an international validation study. *Eur Urol* 57(6):1064–1071.

60 Wheat JC, Weizer AZ, Wolf JS, Jr., Lotan Y, Remzi M, Margulis V, Wood CG, Montorsi F, Roscigno M, Kikuchi E, Zigeuner R, Langner C, Bolenz C, Koppie TM, Raman JD, Fernandez M, Karakiewizc P, Capitanio U, Bensalah K, Patard JJ and Shariat SF (2012). Concomitant carcinoma in situ is a feature of aggressive disease in patients with organ confined urothelial carcinoma following radical nephroureterectomy. *Urol Oncol* 30(3):252–258.

61 Otto W, Shariat SF, Fritsche HM, Gupta A, Matsumoto K, Kassouf W, Martignoni G, Walton TJ, Tritschler S, Baba S, Bastian PJ, Martinez-Salamanca JI, Seitz C, Pycha A, Burger M, Karakiewicz PI, Ficarra V and Novara G (2011). Concomitant carcinoma in situ as an independent prognostic parameter for recurrence and survival in upper tract urothelial carcinoma: a multicenter analysis of 772 patients. *World J Urol* 29(4):487–494.

62 Mbeutcha A, Rouprêt M, Kamat AM, Karakiewicz PI, Lawrentschuk N, Novara G, Raman JD, Seitz C, Xylinas E and Shariat SF (2017). Prognostic factors and predictive tools for upper tract urothelial carcinoma: a systematic review. *World J Urol* 35(3):337–353.

63 Kwong JCC, Pace K, Al-Daqqaq Z, Chelliahpillai Y, Lee S, Kim K, Ringa M, Ali A, Wettstein M, Chan A, Lajkosz K, van der Kwast T, Perlis N, Lee JY, Hamilton RJ, Fleshner NE, Finelli A, Jamal M, Papanikolaou F, Short T, Feifer A, Kulkarni GS and Zlotta AR (2025). Impact of concomitant carcinoma in situ distribution on non-muscle-invasive bladder cancer progression risk. *BJU Int* 136(2):236–244.

64 Epstein JI, Amin MB, Reuter VR and Mostofi FK (1998). The World Health Organization/International Society of Urological Pathology consensus classification of urothelial (transitional cell) neoplasms of the urinary bladder. Bladder Consensus Conference Committee. *Am J Surg Pathol* 22(12):1435–1448.

65 College of American Pathologists (2023). *Protocol for the Examination of Cystectomy Specimens From Patients With Carcinoma of the Urinary Bladder*. Available from: https://documents.cap.org/protocols/Bladder_4.2.0.0.REL_CAPCP.pdf (Accessed 1st December 2025).

66 Cheng L, Neumann RM, Nehra A, Spotts BE, Weaver AL and Bostwick DG (2000). Cancer heterogeneity and its biologic implications in the grading of urothelial carcinoma. *Cancer* 88(7):1663–1670.

67 Hentschel AE, van Rhijn BWG, Bründl J, Compérat EM, Plass K, Rodríguez O, Henríquez JDS, Hernández V, de la Peña E, Alemany I, Turturica D, Pisano F, Soria F, Čapoun O, Bauerová L, Pešl M, Bruins HM, Runneboom W, Herdegen S, Breyer J, Brisuda A, Scavarda-Lamberti A, Calatrava A, Rubio-Briones J, Seles M, Mannweiler S, Bosschieter J, Kusuma VRM, Ashabere D, Huebner N, Cotte J, Mertens LS, Cohen D, Lunelli L, Cussenot O, Sheikh SE, Volanis D, Coté JF, Rouprêt M, Haitel A, Shariat SF, Mostafid AH, Nieuwenhuijzen JA, Zigeuner R, Dominguez-Escrig JL, Hacek J, Zlotta AR, Burger M, Evert M, Hulsbergen-van de Kaa CA, van der Heijden AG, Kiemeney L, Soukup V, Molinaro L, Gontero P, Llorente C, Algaba F, Palou J, N'Dow J, Babjuk M, van der Kwast TH and Sylvester RJ (2020). Papillary urothelial neoplasm of low malignant potential (PUN-LMP): Still a meaningful histo-pathological grade category for Ta, noninvasive bladder tumors in 2019? *Urol Oncol* 38(5):440–448.

68 Burger M, van der Aa MN, van Oers JM, Brinkmann A, van der Kwast TH, Steyerberg EC, Stoehr R, Kirkels WJ, Denzinger S, Wild PJ, Wieland WF, Hofstaedter F, Hartmann A and Zwarthoff EC (2008). Prediction of progression of non-muscle-invasive bladder cancer by WHO 1973 and 2004 grading and by FGFR3 mutation status: a prospective study. *Eur Urol* 54(4):835–843.

69 Pan CC, Chang YH, Chen KK, Yu HJ, Sun CH and Ho DM (2010). Prognostic significance of the 2004 WHO/ISUP classification for prediction of recurrence, progression, and cancer-specific mortality of non-muscle-invasive urothelial tumors of the urinary bladder: a clinicopathologic study of 1,515 cases. *Am J Clin Pathol* 133(5):788–795.

70 Sylvester RJ, van der Meijden AP, Oosterlinck W, Witjes JA, Bouffioux C, Denis L, Newling DW and Kurth K (2006). Predicting recurrence and progression in individual patients with stage Ta T1 bladder cancer using EORTC risk tables: a combined analysis of 2596 patients from seven EORTC trials. *Eur Urol* 49(3):466–465.

71 Babjuk M, Burger M, Capoun O, Cohen D, Compérat EM, Dominguez Escrig JL, Gontero P, Liedberg F, Masson-Lecomte A, Mostafid AH, Palou J, van Rhijn BWG, Rouprêt M, Shariat SF, Seisen T, Soukup V and Sylvester RJ (2022). European Association of Urology Guidelines on Non-muscle-invasive Bladder Cancer (Ta, T1, and Carcinoma in Situ). *Eur Urol* 81(1):75–94.

72 Kiemeney LA, Witjes JA, Heijbroek RP, Verbeek AL and Debruyne FM (1993). Predictability of recurrent and progressive disease in individual patients with primary superficial bladder cancer. *J Urol* 150(1):60–64.

73 Lutzeyer W, Rubben H and Dahm H (1982). Prognostic parameters in superficial bladder cancer: an analysis of 315 cases. *J Urol* 127(2):250–252.

74 Parmar MK, Freedman LS, Hargreave TB and Tolley DA (1989). Prognostic factors for recurrence and followup policies in the treatment of superficial bladder cancer: report from the British Medical Research Council Subgroup on Superficial Bladder Cancer (Urological Cancer Working Party). *J Urol* 142(2 Pt 1):284–288.

75 Kilinc MF, Sonmez NC, Dalkilic A, Arisan S and Guney S (2014). Analysis of results of recurrence and progression rates of high-grade Ta bladder cancer and comparison with results of high-grade T1. *Urologia* 81(4):237–241.

76 Dalesio O, Schulman CC, Sylvester R, De Pauw M, Robinson M, Denis L, Smith P and Viggiano G (1983). Prognostic factors in superficial bladder tumors. A study of the European Organization for Research on Treatment of Cancer: Genitourinary Tract Cancer Cooperative Group. *J Urol* 129(4):730–733.

77 Millan-Rodriguez F, Chechile-Toniolo G, Salvador-Bayarri J, Palou J, Algaba F and Vicente-Rodriguez J (2000). Primary superficial bladder cancer risk groups according to progression, mortality and recurrence. *J Urol* 164(3 Pt 1):680–684.

78 Ryu D, Kim TM, Lee YH and Ha US (2023). Longitudinal Analyses of Mutational Subclonal Architecture and Tumor Subtypes in Recurrent Bladder Cancer. *Int J Mol Sci* 24(9):8418.

79 Häggström C, Rowley M, Liedberg F, Coolen ACC and Holmberg L (2023). Latent heterogeneity of muscle-invasive bladder cancer in patient characteristics and survival: A population-based nation-wide study in the Bladder Cancer Data Base Sweden (BladderBaSe). *Cancer Med* 12(12):13856–13864.

80 Netto GJ, Amin MB, Berney DM, Compérat EM, Gill AJ, Hartmann A, Menon S, Raspollini MR, Rubin MA, Srigley JR, Hoon Tan P, Tickoo SK, Tsuzuki T, Turajlic S, Cree I and Moch H (2022). The 2022 World Health Organization Classification of Tumors of the Urinary System and Male Genital Organs-Part B: Prostate and Urinary Tract Tumors. *Eur Urol* 82(5):469–482.

81 Lopez-Beltran A, Bassi PF, Pavone-Macaluso M and Montironi R (2004). Handling and pathology reporting of specimens with carcinoma of the urinary bladder, ureter, and renal pelvis. A joint proposal of the European Society of Uropathology and the Uropathology Working Group. *Virchows Arch* 445(2):103–110.

82 The Royal College of Pathologists (2025). *Dataset for histological reporting of tumours of the urinary collecting system (renal pelvis, ureter, urinary bladder and urethra).* Available from: https://www.rcpath.org/static/e2c11ff6-780a-471e-a21a4dc48788d35b/92498480-8076-4269-9ea6fd7dbed1e102/g044-histopathological-reporting-of-tumours-of-the-urinary-collecting-system.pdf (Accessed 1st December 2025).

83 Varma M, Delahunt B and Kwast TV (2020). Reply to Eva Compérat, Mahul Amin, Victor Reuter's Editorial Reply re: Murali Varma, Brett Delahunt, Theodorus van der Kwast. Grading Noninvasive Bladder Cancer: World Health Organisation 1973 or 2004 May Be the Wrong Question. Eur Urol 2019;76:413-5: Precision Medicine Requires More Not Fewer Grade Categories. *Eur Urol* 77(1):e28–e29.

84 Roupret M, Hupertan V, Seisen T, Colin P, Xylinas E, Yates DR, Fajkovic H, Lotan Y, Raman JD, Zigeuner R, Remzi M, Bolenz C, Novara G, Kassouf W, Ouzzane A, Rozet F, Cussenot O, Martinez-Salamanca JI, Fritsche HM, Walton TJ, Wood CG, Bensalah K, Karakiewicz PI, Montorsi F, Margulis V and Shariat SF (2013). Prediction of cancer specific survival after radical nephroureterectomy for upper tract urothelial carcinoma: development of an optimized postoperative nomogram using decision curve analysis. *J Urol* 189(5):1662–1669.

85 Seisen T, Colin P, Hupertan V, Yates DR, Xylinas E, Nison L, Cussenot O, Neuzillet Y, Bensalah K, Novara G, Montorsi F, Zigeuner R, Remzi M, Shariat SF and Roupret M (2014). Postoperative nomogram to predict cancer-specific survival after radical nephroureterectomy in patients with localised and/or locally advanced upper tract urothelial carcinoma without metastasis. *BJU Int* 114(5):733–740.

86 Cha EK, Shariat SF, Kormaksson M, Novara G, Chromecki TF, Scherr DS, Lotan Y, Raman JD, Kassouf W, Zigeuner R, Remzi M, Bensalah K, Weizer A, Kikuchi E, Bolenz C, Roscigno M, Koppie TM, Ng CK, Fritsche HM, Matsumoto K, Walton TJ, Ehdaie B, Tritschler S, Fajkovic H, Martinez-Salamanca JI, Pycha A, Langner C, Ficarra V, Patard JJ, Montorsi F, Wood CG, Karakiewicz PI and Margulis V (2012). Predicting clinical outcomes after radical nephroureterectomy for upper tract urothelial carcinoma. *Eur Urol* 61(4):818–825.

87 Wong MN, Wu DJ, Lee CT and Zynger DL (2023). Renal Pelvic Urothelial Carcinoma With Invasion Into Renal Medulla Can Be Redefined as pT2 to Improve Correlation With Survival. *Mod Pathol* 36(6):100140.

88 Stangl-Kremser J, Muto G, Grosso AA, Briganti A, Comperat E, Di Maida F, Montironi R, Remzi M, Pradere B, Soria F, Albisinni S, Roupret M, Shariat SF, Minervini A, Teoh JY, Moschini M, Cimadamore A and Mari A (2022). The impact of lymphovascular invasion in patients treated with radical nephroureterectomy for upper tract urothelial carcinoma: An extensive updated systematic review and meta-analysis. *Urol Oncol* 40(6):243–261.

89 Abouassaly R, Alibhai SM, Shah N, Timilshina N, Fleshner N and Finelli A (2010). Troubling outcomes from population-level analysis of surgery for upper tract urothelial carcinoma. *Urology* 76(4):895–901.

90 Bolenz C, Fernandez MI, Trojan L, Herrmann E, Becker A, Weiss C, Alken P, Strobel P and Michel MS (2008). Lymphovascular invasion and pathologic tumor stage are significant outcome predictors for patients with upper tract urothelial carcinoma. *Urology* 72(2):364–369.

91 Hurel S, Roupret M, Ouzzane A, Rozet F, Xylinas E, Zerbib M, Berod AA, Ruffion A, Adam E, Cussenot O, Houlgatte A, Phe V, Nouhaud FX, Bensadoun H, Delage F, Guillotreau J, Guy L, Karsenty G, De La Taille A and Colin P (2013). Impact of lymphovascular invasion on oncological outcomes in patients with upper tract urothelial carcinoma after radical nephroureterectomy. *BJU Int* 111(8):1199–1207.

92 Park J, Habuchi T, Arai Y, Ohyama C, Inoue T, Hatakeyama S, Jeon SS, Kwon GY, Kwak C, Moon KC, Kim CS and Ahn H (2014). Reassessment of prognostic heterogeneity of pT3 renal pelvic urothelial carcinoma: analysis in terms of proposed pT3 subclassification systems. *J Urol* 192(4):1064–1071.

93 Seisen T, Shariat SF, Cussenot O, Peyronnet B, Renard-Penna R, Colin P and Rouprêt M (2017). Contemporary role of lymph node dissection at the time of radical nephroureterectomy for upper tract urothelial carcinoma. *World J Urol* 35(4):535–548.

94 Kondo T and Tanabe K (2012). Role of lymphadenectomy in the management of urothelial carcinoma of the bladder and the upper urinary tract. *Int J Urol* 19(8):710–721.

95 Dominguez-Escrig JL, Peyronnet B, Seisen T, Bruins HM, Yuan CY, Babjuk M, Böhle A, Burger M, Compérat EM, Gontero P, Lam T, MacLennan S, Mostafid H, Palou J, van Rhijn BWG, Sylvester RJ, Zigeuner R, Shariat SF and Rouprêt M (2019). Potential Benefit of Lymph Node Dissection During Radical Nephroureterectomy for Upper Tract Urothelial Carcinoma: A Systematic Review by the European Association of Urology Guidelines Panel on Non-muscle-invasive Bladder Cancer. *Eur Urol Focus* 5(2):224–241.

96 Yanagisawa T, Kawada T, von Deimling M, Laukhtina E, Kimura T and Shariat SF (2023). Need for and extent of lymph node dissection for upper tract urothelial carcinoma: an updated review in 2023. *Curr Opin Urol* 33(4):258–268.

97 Bolenz C, Shariat SF, Fernandez MI, Margulis V, Lotan Y, Karakiewicz P, Remzi M, Kikuchi E, Zigeuner R, Weizer A, Montorsi F, Bensalah K, Wood CG, Roscigno M, Langner C, Koppie TM, Raman JD, Mikami S, Michel MS and Strobel P (2009). Risk stratification of patients with nodal involvement in upper tract urothelial carcinoma: value of lymph-node density. *BJU Int* 103(3):302–306.

98 Lucca I, Kassouf W, Kapoor A, Fairey A, Rendon RA, Izawa JI, Black PC, Fajkovic H, Seitz C, Remzi M, Nyirady P, Roupret M, Margulis V, Lotan Y, de Martino M, Hofbauer SL, Karakiewicz PI, Briganti A, Novara G, Shariat SF and Klatte T (2015). The role of adjuvant chemotherapy for lymph node-positive upper tract urothelial carcinoma following radical nephroureterectomy: a retrospective study. *BJU Int* 116(1):72–78.

99 Nazzani S, Mazzone E, Preisser F, Tian Z, Mistretta FA, Shariat SF, Montanari E, Acquati P, Briganti A, Saad F, Carmignani L and Karakiewicz PI (2019). Rates of lymph node invasion and their impact on cancer specific mortality in upper urinary tract urothelial carcinoma. *Eur J Surg Oncol* 45(7):1238–1245.

100 Mason RJ, Kassouf W, Bell DG, Lacombe L, Kapoor A, Jacobsen N, Fairey A, Izawa J, Black P, Tanguay S, Chin J, So A, Lattouf JB, Saad F, Matsumoto E, Drachenberg D, Cagiannos I, Fradet Y and Rendon RA (2012). The contemporary role of lymph node dissection during nephroureterectomy in the management of upper urinary tract urothelial carcinoma: the Canadian experience. *Urology* 79(4):840–845.

101 Fajkovic H, Cha EK, Jeldres C, Donner G, Chromecki TF, Margulis V, Novara G, Lotan Y, Raman JD, Kassouf W, Seitz C, Bensalah K, Weizer A, Kikuchi E, Roscigno M, Remzi M, Matsumoto K, Breinl E, Pycha A, Ficarra V, Montorsi F, Karakiewicz PI, Scherr DS and Shariat SF (2012). Prognostic value of extranodal extension and other lymph node parameters in patients with upper tract urothelial carcinoma. *J Urol* 187(3):845–851.

102 Xylinas E, Rink M, Margulis V, Faison T, Comploj E, Novara G, Raman JD, Lotan Y, Guillonneau B, Weizer A, Pycha A, Scherr DS, Seitz C, Sun M, Trinh QD, Karakiewicz PI, Montorsi F, Zerbib M, Gonen M and Shariat SF (2013). Prediction of true nodal status in patients with pathological lymph node negative upper tract urothelial carcinoma at radical nephroureterectomy. *J Urol* 189(2):468–473.

103 Roscigno M, Shariat SF, Freschi M, Margulis V, Karakiewizc P, Suardi N, Remzi M, Zigeuner R, Bolenz C, Kikuchi E, Weizer A, Bensalah K, Sagalowsky A, Koppie TM, Raman J, Fernandez M, Strobel P, Kabbani W, Langner C, Wheat J, Guo CC, Kassouf W, Haitel A, Wood CG and Montorsi F (2009). Assessment of the minimum number of lymph nodes needed to detect lymph node invasion at radical nephroureterectomy in patients with upper tract urothelial cancer. *Urology* 74(5):1070–1074.

104 Guo R, Zhu Y, Xiong G, Li X, Zhang K and Zhou L (2018). Role of lymph node dissection in the management of upper tract urothelial carcinomas: a meta-analysis. *BMC Urol* 18(1):24.

105 Inokuchi J, Kuroiwa K, Kakehi Y, Sugimoto M, Tanigawa T, Fujimoto H, Gotoh M, Masumori N, Ogawa O, Eto M, Ohyama C, Yamaguchi A, Matsuyama H, Ichikawa T, Asano T, Mizusawa J, Eba J and Naito S (2017). Role of lymph node dissection during radical nephroureterectomy for upper urinary tract urothelial cancer: multi-institutional large retrospective study JCOG1110A. *World J Urol* 35(11):1737–1744.

106 Wu DJ, Wong MN, Lee CT and Zynger DL (2023). The stratification of positive lymph nodes into pN1 and pN2 for upper urinary tract carcinoma is not prognostically significant. *Hum Pathol* 137:48–55.

107 Ouzzane A, Colin P, Ghoneim TP, Zerbib M, De La Taille A, Audenet F, Saint F, Hoarau N, Adam E, Azemar MD, Bensadoun H, Cormier L, Cussenot O, Houlgatte A, Karsenty G, Maurin C, Nouhaud FX, Phe V, Polguer T, Roumiguie M, Ruffion A and Roupret M (2013). The impact of lymph node status and features on oncological outcomes in urothelial carcinoma of the upper urinary tract (UTUC) treated by nephroureterectomy. *World J Urol* 31(1):189–197.

108 Abe T, Shinohara N, Muranaka M, Sazawa A, Maruyama S, Osawa T, Harabayashi T, Kubota K, Matsuno Y, Shibata T, Toyada Y, Shinno Y, Minami K, Sakashita S, Kumagai A, Takada N, Togashi M, Sano H, Mori T and Nonomura K (2010). Role of lymph node dissection in the treatment of urothelial carcinoma of the upper urinary tract: multi-institutional relapse analysis and immunohistochemical re-evaluation of negative lymph nodes. *Eur J Surg Oncol* 36(11):1085–1091.

109 Kodama Y, Kondo T, Matsumura N, Shimokawa T, Kohjimoto Y, Tanabe K and Hara I (2017). Molecular diagnosis of lymph node metastasis in patients with upper urinary tract cancer who underwent lymphadenectomy. *Int J Urol* 24(11):799–806.

110 Matsumoto R, Abe T, Takada N, Minami K, Harabayashi T, Nagamori S, Hatanaka KC, Yamashiro K, Kikuchi H, Osawa T, Maruyama S and Shinohara N (2020). Oncologic outcomes of laparoscopic radical nephroureterectomy in conjunction with template-based lymph node dissection: An extended follow-up study. *Urol Oncol* 38(12):933.e913–933.e918.

111 Zlotta AR, Ballas LK, Niemierko A, Lajkosz K, Kuk C, Miranda G, Drumm M, Mari A, Thio E, Fleshner NE, Kulkarni GS, Jewett MAS, Bristow RG, Catton C, Berlin A, Sridhar SS, Schuckman A, Feldman AS, Wszolek M, Dahl DM, Lee RJ, Saylor PJ, Michaelson MD, Miyamoto DT, Zietman A, Shipley W, Chung P, Daneshmand S and Efstathiou JA (2023). Radical cystectomy versus trimodality therapy for muscle-invasive bladder cancer: a multi-institutional propensity score matched and weighted analysis. *Lancet Oncol* 24(6):669–681.

112 Paik J, Ellis CL, Henriksen KJ and Chang A (2024). An International Survey of Genitourinary and Renal Pathologists Regarding Evaluation of the Non-Neoplastic Parenchyma in Kidney Cancer Specimens. *Int J Surg Pathol* 32(2):273–278.

113 Jia Y, Poor SMM, Dufault B, Lu V, Nayak JG, Pruthi DK and Gibson IW (2022). Chronic kidney damage pathology score for systematic assessment of the non-neoplastic kidney tissue and prediction of post-operative renal function outcomes. *Hum Pathol* 124:76–84.

114 Ellis RJ, Kalma B, Del Vecchio SJ, Aliano DN, Ng KL, Dimeski G, Ma L, Guard D, Bertram JF, Morais C, Oliver K, Wood ST, Gobe GC and Francis RS (2019). Chronic kidney cortical damage is associated with baseline kidney function and albuminuria in patients managed with radical nephrectomy for kidney tumours. *Pathology* 51(1):32–38.

115 Mork M, Hubosky SG, Roupret M, Margulis V, Raman J, Lotan Y, O'Brien T, You N, Shariat SF and Matin SF (2015). Lynch Syndrome: A Primer for Urologists and Panel Recommendations. *J Urol* 194(1):21–29.

116 Lonati C, Necchi A, Gómez Rivas J, Afferi L, Laukhtina E, Martini A, Ventimiglia E, Colombo R, Gandaglia G, Salonia A, Briganti A, Montorsi F, Mattei A, Simeone C, Carlo MI, Shariat SF, Spiess PE and Moschini M (2022). Upper Tract Urothelial Carcinoma in the Lynch Syndrome Tumour Spectrum: A Comprehensive Overview from the European Association of Urology - Young Academic Urologists and the Global Society of Rare Genitourinary Tumors. *Eur Urol Oncol* 5(1):30–41.

117 Hartmann A, Dietmaier W, Hofstadter F, Burgart LJ, Cheville JC and Blaszyk H (2003). Urothelial carcinoma of the upper urinary tract: inverted growth pattern is predictive of microsatellite instability. *Hum Pathol* 34(3):222–227.

118 Hollande C, Colin P, de La Motte Rouge T, Audenet F, Yates DR, Phe V, Ouzzane A, Droupy S, Ruffion A, de La Taille A, Guy L, Cussenot O, Rozet F, Xylinas E, Zerbib M, Spano JP, Khayat D, Bitker MO and Roupret M (2014). Hereditary-like urothelial carcinomas of the upper urinary tract benefit more from adjuvant cisplatin-based chemotherapy after radical nephroureterectomy than do sporadic tumours. *BJU Int* 113(4):574–580.

119 Rasmussen M, Madsen MG and Therkildsen C (2022). Immunohistochemical Screening of Upper Tract Urothelial Carcinomas for Lynch Syndrome Diagnostics: A Systematic Review. *Urology* 165:44–53.

120 Schneider B, Glass Ä, Jagdmann S, Hühns M, Claus J, Zettl H, Dräger DL, Maruschke M, Hakenberg OW, Erbersdobler A and Zimpfer A (2020). Loss of Mismatch-repair Protein Expression and Microsatellite Instability in Upper Tract Urothelial Carcinoma and Clinicopathologic Implications. *Clin Genitourin Cancer* 18(5):e563–e572.

121 Birtle A, Johnson M, Chester J, Jones R, Dolling D, Bryan RT, Harris C, Winterbottom A, Blacker A, Catto JWF, Chakraborti P, Donovan JL, Elliott PA, French A, Jagdev S, Jenkins B, Keeley FX, Jr., Kockelbergh R, Powles T, Wagstaff J, Wilson C, Todd R, Lewis R and Hall E (2020). Adjuvant chemotherapy in upper tract urothelial carcinoma (the POUT trial): a phase 3, open-label, randomised controlled trial. *Lancet* 395(10232):1268–1277.

122 Bajorin DF, Witjes JA, Gschwend JE, Schenker M, Valderrama BP, Tomita Y, Bamias A, Lebret T, Shariat SF, Park SH, Ye D, Agerbaek M, Enting D, McDermott R, Gajate P, Peer A, Milowsky MI, Nosov A, Neif Antonio J, Jr., Tupikowski K, Toms L, Fischer BS, Qureshi A, Collette S, Unsal-Kacmaz K, Broughton E, Zardavas D, Koon HB and Galsky MD (2021). Adjuvant Nivolumab versus Placebo in Muscle-Invasive Urothelial Carcinoma. *N Engl J Med* 384(22):2102–2114.

123 Reuter VE (2019). Urinary bladder, ureter and renal pelvis. In: Histology for Pathologists, 5th edition, SE Mills (ed), Wolters Kluwer, Philadelphia, PA.

124 Gupta R, Paner GP and Amin MB (2008). Neoplasms of the upper urinary tract: a review with focus on urothelial carcinoma of the pelvicalyceal system and aspects related to its diagnosis and reporting. *Adv Anat Pathol* 15(3):127–139.