COLLEGE of AMERICAN PATHOLOGISTS

Protocol for the Examination of Biopsy Specimens from Patients with Invasive Carcinoma of Renal Tubular Origin

Version: Kidney Biopsy 4.0.2.0 **Protocol Posting Date:** February 2020

The use of this protocol is recommended for clinical care purposes but is not required for accreditation purposes.

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

Procedure	Description
Biopsy	Includes specimens designated needle biopsy, incisional biopsy (wedge), and others
Tumor Type	**Description**
Renal cell carcinomas	Includes all renal cell carcinoma variants

This protocol is NOT required for accreditation purposes for the following:

Procedure
Resection (consider Kidney Resection protocol)
Tumor Type
Urothelial tumors (consider Ureter, Renal Pelvis protocol)
Wilm's tumors (Consider Wilm's Tumor protocol)
Lymphoma (consider the Hodgkin or non-Hodgkin Lymphoma protocols)
Sarcoma (consider the Soft Tissue protocol)

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Summary of Changes

Version 4.0.2.0
Resection and biopsy case summaries separated into discrete cancer protocols

Surgical Pathology Cancer Case Summary

Protocol posting date: February 2020

KIDNEY: Biopsy

Note: This case summary is recommended for reporting biopsy specimens but is NOT REQUIRED for accreditation purposes. Core data elements are bolded to help identify routinely reported elements.

Select a single response unless otherwise indicated.

Procedure
___ Needle biopsy
___ Incisional biopsy, wedge
___ Other (specify): _____
___ Not specified

Specimen Laterality
___ Right
___ Left
___ Not specified

Histologic Type (Note A)
___ Clear cell renal cell carcinoma
___ Multilocular cystic clear cell renal cell neoplasm of low malignant potential
___ Papillary renal cell carcinoma
___ Papillary renal cell carcinoma, Type 1
___ Papillary renal cell carcinoma, Type 2
___ Chromophobe renal cell carcinoma
___ Collecting duct carcinoma
___ Renal medullary carcinoma
___ MiT family translocation renal cell carcinoma
___ Xp11 translocation renal cell carcinoma
___ t(6;11) renal cell carcinoma
___ Mucinous tubular and spindle renal cell carcinoma
___ Tubulocystic renal cell carcinoma
___ Acquired cystic disease associated renal cell carcinoma
___ Clear cell papillary renal cell carcinoma
___ Hereditary leiomyomatosis and renal cell carcinoma-associated renal cell carcinoma
___ Succinate dehydrogenase (SDH) deficient renal cell carcinoma
___ Renal cell carcinoma, unclassified
___ Other histologic type not listed (specify): _____

Sarcomatoid Features (Note B)
___ Not identified
___ Present
Specify percentage of sarcomatoid element: _____%

Rhabdoid Features (Note B)
___ Not identified
___ Present

Histologic Grade (World Health Organization [WHO] / International Society of Urological Pathology [ISUP] Grade) (Note C)
___ G1: Nucleoli absent or inconspicuous and basophilic at 400x magnification

___ G2: Nucleoli conspicuous and eosinophilic at 400x magnification, visible but not prominent at 100x magnification
___ G3: Nucleoli conspicuous and eosinophilic at 100x magnification
___ G4: Extreme nuclear pleomorphism and/or multinuclear giant cells and/or rhabdoid and/or sarcomatoid differentiation
___ GX: Cannot be assessed
___ Not applicable

Necrosis (Note D)
___ Not identified
___ Present

Lymphovascular Invasion
___ Not identified
___ Present

Additional Pathologic Findings
___ None identified
___ Other pathology present (specify): _____

Comment(s)

Explanatory Notes

A. Histologic Type

The current World Health Organization (WHO) classification (2016) is based on the International Society of Urological Pathology (ISUP) Vancouver Classification of Renal Neoplasia 2012.[1,2]

Clear cell renal cell carcinoma
Multilocular clear cell renal cell neoplasm of low malignant potential
Papillary renal cell carcinoma
    Type 1
    Type 2
Chromophobe renal cell carcinoma
Collecting duct carcinoma
Renal medullary carcinoma
MiT family translocation renal cell carcinoma
Mucinous tubular and spindle cell carcinoma
Tubulocystic renal cell carcinoma
Acquired cystic disease associated renal cell carcinoma
Clear cell papillary/tubulopapillary renal cell carcinoma
Hereditary leiomyomatosis and renal cell carcinoma-associated renal cell carcinoma
Succinate dehydrogenase (SDH) deficient renal carcinoma
Renal cell carcinoma, unclassified
Papillary adenoma
Renal oncocytoma

Many subtypes of renal cell carcinoma, including many newly described variants, have differing clinical behaviors and prognosis.[1-4] Additionally the usage of adjuvant therapy is related to tumor subtype.[5] The concept of an emerging/provisional category of renal cell carcinoma was introduced in the 2012 ISUP Vancouver classification.[2] These tumors, while appearing distinctive, had not been fully characterized morphologically or by ancillary techniques. This category in the 2016 WHO classification includes the following entities: oncocytoid renal cell carcinoma (RCC) postneuroblastoma, thyroid-like follicular RCC, anaplastic lymphoma kinase (ALK) rearrangement-associated RCC, and RCC with (angio) leiomyomatous stroma.[1] For the purpose of the protocol, these emerging tumors should be classified under “other” and the name specified.

Occasionally more than 1 histologic type of carcinoma occurs within the same kidney specimen. Each tumor type should be separately recorded along with its associated prognostic factors.[6]

References

1. Humphrey PA, Moch H, Reuter VE, Ulbright TM, eds. *World Health Organization (WHO) Classification of Tumours. Pathology and Genetics of the Urinary System and Male Genital Organs*. Geneva, Switzerland: WHO Press; 2016.
2. Srigley JR, Delahunt B, Eble JN, et al. The International Society of Urological Pathology (ISUP) Vancouver classification of renal neoplasia. *Am J Surg Pathol*. 2013;37:1469-1489.
3. Murphy WM, Grignon DJ, Perlman EJ, eds. *Tumours of the Kidney, Bladder, and Related Urinary Structures.* AFIP Atlas of Tumour Pathology. Series 4. Washington, DC: American Registry of Pathology; 2004.
4. Srigley JR, Delahunt B. Uncommon and recently described renal carcinomas. *Mod Pathol*. 2009;22:S2-S23.
5. O'Brien MF, Russo P, Motzer RJ. Sunitinib therapy in renal cell carcinoma. *BJU Int*. 2008;101:1339-1342.
6. de Peralta-Venturina M, Moch H, Amin M, et al. Sarcomatoid differentiation in renal cell carcinoma: a study of 101 cases. *Am J Surg Pathol*. 2001;25:275-278.

B. Sarcomatoid and Rhabdoid Features

Sarcomatoid carcinoma is not a specific morphogenetic subtype of renal cell carcinoma but is considered as a pattern of dedifferentiation.[1,2-4] Sarcomatoid change in a renal cell carcinoma is associated with an adverse outcome.[1,4] Sarcomatoid morphology may be found in any histologic subtypes of renal cell carcinomas, including clear cell, papillary, chromophobe, collecting duct, and other rare and unclassified subtypes.[1,2-4] When the

background carcinoma subtype is recognized, it should be specified under histologic type (see Note A). Pure sarcomatoid carcinoma or sarcomatoid carcinoma associated with epithelial elements that do not conform to usual renal carcinoma cell types should be considered as unclassified renal cell carcinoma. Sarcomatoid morphology is also incorporated into the WHO/ISUP grading system as grade 4.

There is some indication that the percentage of sarcomatoid component in a renal cell carcinoma has prognostic importance.[2,4]

Rhabdoid features, like sarcomatoid, are a characteristic of high-grade disease. Rhabdoid cells have abundant eosinophilic cytoplasm with an eccentric nucleus often with a prominent nucleolus.[4-7] Rhabdoid changes are associated with an adverse outcome and in cases with rhabdoid morphology, about 25% of them also show sarcomatoid features).[1] Rhabdoid morphology is an important component of the new WHO/ISUP grading system (grade 4).[4] No solid evidence exists on the prognostic significance of the extent of rhabdoid morphology.[1]

References

1. Humphrey PA, Moch H, Reuter VE, Ulbright TM, eds. *World Health Organization (WHO) Classification of Tumours. Pathology and Genetics of the Urinary System and Male Genital Organs*. Geneva, Switzerland: WHO Press; 2016.
2. de Peralta-Venturina M, Moch H, Amin M, et al. Sarcomatoid differentiation in renal cell carcinoma: a study of 101 cases. *Am J Surg Pathol*. 2001;25:275-278.
3. Cheville JC, Lohse CM, Zincke H, et al. Sarcomatoid renal cell carcinoma: an examination of underlying histologic subtype and an analysis of associations with patient outcome. *Am J Surg Pathol.* 2004;28:435-441.
4. Delahunt B, Cheville JC, Martignoni G, et al. The International Society of Urological Pathology (ISUP) grading system for renal cell carcinoma and other prognostic parameters. *Am J Surg Pathol.* 2013;37:1490-1504.
5. Kuroiwa K, Kinoshita Y, Shiratsuchi H, et al. Renal cell carcinoma with rhabdoid features: an aggressive neoplasm. *Histopathology.* 2002;41:538-548.
6. Gokden N, Nappi O, Swanson PE, et al. Renal cell carcinoma with rhabdoid features. *Am J Surg Pathol.* 2000;24:1329-1338.
7. Leroy X, Zini L, Buob D, et al. Renal cell carcinoma with rhabdoid features. *Arch Pathol Lab Med.* 2007;131:102-106.

C. Histologic Grade

The WHO/ISUP grading system has supplanted the Fuhrman system as the grading standard.[1,2] This grading system has been validated for both clear cell and papillary renal cell carcinoma; however, it has not been validated for other RCC subtypes.[3,4] Nevertheless, the WHO/ISUP grade may be included for descriptive purposes. Currently it is recommended that chromophobe renal cell carcinoma not be graded with the WHO/ISUP system. Details are shown below:

Not applicable
Grade X- Cannot be assessed
Grade 1 - Nucleoli absent or inconspicuous and basophilic at 400x magnification
Grade 2 - Nucleoli conspicuous and eosinophilic at 400x magnification, visible but not prominent at 100x magnification
Grade 3 - Nucleoli conspicuous and eosinophilic at 100x magnification
Grade 4 - Extreme nuclear pleomorphism and/or multinuclear giant cells and/or rhabdoid and/or sarcomatoid differentiation

Although the grading system does reference the tinctorial characteristics of the nucleoli, the determining feature is the nucleolar prominence. Grade should be assigned based on the single high-power field showing the greatest degree of pleomorphism.

References

1. Humphrey PA, Moch H, Reuter VE, Ulbright TM, eds. *World Health Organization (WHO) Classification of Tumours. Pathology and Genetics of the Urinary System and Male Genital Organs*. Geneva, Switzerland: WHO Press; 2016.

2. Delahunt B, Cheville JC, Martignoni G, et al. The International Society of Urological Pathology (ISUP) grading system for renal cell carcinoma and other prognostic parameters. *Am J Surg Pathol.* 2013;37:1490-1504.
3. Sika-Paotonu D, Bethwaite PB, McCredie MRE, Jordan TW, Delahunt B. Nucleolar grade but not Fuhrman grade is applicable to papillary renal cell carcinoma. *Am J Surg Pathol.* 2006;30:1091-1096.
4. Delahunt B, Sika-Paotonu D, Bethwaite PB, et al. Grading of clear cell renal cell carcinoma should be based on nucleolar prominence. *Am J Surg Pathol.* 2011;135:1134-1139.

D. Necrosis

Tumor necrosis is an important prognostic factor in renal cell carcinoma.[1-3] It is recommended that both macroscopic and microscopic (coagulative) necrosis be recorded. The prognostic significance of necrosis independent of tumor stage has been identified in clear cell and chromophobe renal cell carcinoma.[2] The prognostic significance of necrosis in papillary renal cell carcinoma is controversial. Large papillary carcinomas not uncommonly display cystic necrosis and yet don't exhibit extra renal spread. Tumor necrosis as a prognostic factor cannot be assessed in a situation where patients have undergone presurgical arterial embolization.

At present, the prognostic significance of the extent of necrosis is unclear; however, it is recommended that this be recorded as a percentage.[3]

References

1. Delahunt B, Cheville JC, Martignoni G, et al. The International Society of Urological Pathology (ISUP) grading system for renal cell carcinoma and other prognostic parameters. *Am J Surg Pathol.* 2013;37:1490-1504.
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