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Platinum Priority – Guidelines

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The 2016 WHO Classification of Tumours of the Urinary System and Male Genital Organs—Part A: Renal, Penile, and Testicular Tumours

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Abstract

The fourth edition of the World Health Organization (WHO) classification of urogenital tumours (WHO "blue book"), published in 2016, contains significant revisions. These revisions were performed after consideration by a large international group of pathologists with special expertise in this area. A subgroup of these persons met at the WHO Consensus Conference in Zurich, Switzerland, in 2015 to finalize the revisions. This review summarizes the most significant differences between the newly published classification and the prior version for renal, penile, and testicular tumours. Newly recognized epithelial renal tumours are hereditary leiomyomatosis and renal cell carcinoma (RCC) syndrome–associated RCC, succinate dehydrogenase–deficient RCC, tubulocystic RCC, acquired cystic disease–associated RCC, and clear cell papillary RCC. The WHO/International Society of Urological Pathology renal tumour grading system was recommended, and the definition of renal papillary adenoma was modified. The new WHO classification of penile squamous cell carcinomas is based on the presence of human papillomavirus and defines histologic subtypes accordingly. *Germ cell neoplasia in situ* (GCNIS) *of the testis* is the WHO-recommended term for precursor lesions of invasive germ cell tumours, and testicular germ cell tumours are now separated into two fundamentally different groups: those derived from GCNIS and those unrelated to GCNIS. Spermatocytic seminoma has been designated as a spermatocytic tumour and placed within the group of non–GCNIS-related tumours in the 2016 WHO classification.
Patient summary: The 2016 World Health Organization (WHO) classification contains new renal tumour entities. The classification of penile squamous cell carcinomas is based on the presence of human papillomavirus. *Germ cell neoplasia in situ of the testis* is the WHO-recommended term for precursor lesions of invasive germ cell tumours.

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1. The new renal tumour classification

The Vancouver consensus conference of the International Society of Urological Pathology (ISUP) provided the foundation for much of the 2016 World Health Organization (WHO) renal tumour classification [1,2] (Fig. 1). The revision of the 2004 WHO renal tumour classification was performed after consideration of new knowledge about pathology, epidemiology, and genetics [3–5].

2. Important changes from existing renal tumour types

First, the new 2016 WHO classification refers to subtypes that have been named on the basis of predominant cytoplasmic features (eg, clear cell and chromophobe renal cell carcinomas [RCCs]), architectural features (eg, papillary RCC), anatomic location of tumours (eg, collecting duct and renal medullary carcinomas), and correlation with a specific renal disease background (eg, acquired cystic disease–associated RCCs) as well as molecular alterations pathognomonic for RCC subtypes (eg, MiT family translocation carcinomas and succinate dehydrogenase [SDH]–deficient renal carcinomas) or familial predisposition syndromes (eg, hereditary leiomyomatosis and RCC [HLRCC] syndrome–associated RCC). In contrast to the 2004 WHO classification, familial forms of RCC, which also occur in sporadic form (eg, clear cell RCC [ccRCC] in patients with von Hippel-Lindau [VHL] syndrome or chromophobe RCC in patients with Birt-Hogg-Dubé syndrome) are now discussed with the corresponding sporadic tumour types in joint chapters.

Second, multiple publications report no recurrence or metastasis in patients with multilocular cystic RCC [6]. Consequently, *multilocular cystic renal neoplasm of low*

WHO classification of tumours of the kidney

Renal cell tumours	
Clear cell renal cell carcinoma	8310/3
Multilocular cystic renal neoplasm of low malignant potential	8316/1*
Papillary renal cell carcinoma	8260/3
Hereditary leiomyomatosis and renal cell carcinoma–associated renal cell carcinoma	8311/3*
Chromophobe renal cell carcinoma	8317/3
Collecting duct carcinoma	8319/3
Renal medullary carcinoma	8510/3*
MiT family translocation renal cell carcinomas	8311/3*
Succinate dehydrogenase–deficient renal carcinoma	8311/3
Mucinous tubular and spindle cell carcinoma	8480/3*
Tubulocystic renal cell carcinoma	8316/3*
Acquired cystic disease–associated renal cell carcinoma	8316/3
Clear cell papillary renal cell carcinoma	8323/1
Renal cell carcinoma, unclassified	8312/3
Papillary adenoma	8260/0
Oncocytoma	8290/0
Metanephric tumours	
Metanephric adenoma	8325/0
Metanephric adenofibroma	9013/0
Metanephric stromal tumour	8935/1
Nephroblastic and cystic tumours occurring mainly in children	
Nephrogenic rests	
Nephroblastoma	8960/3
Cystic partially differentiated nephroblastoma	8959/1
Paediatric cystic nephroma	8959/0
Mesenchymal tumours	
Mesenchymal tumours occurring mainly in children	
Clear cell sarcoma	8964/3
Rhabdoid tumour	8963/3
Congenital mesoblastic nephroma	8960/1
Ossifying renal tumour of infancy	8967/0
Mesenchymal tumours occurring mainly in adults	
Leiomyosarcoma	8890/3
Angiosarcoma	9120/3
Rhabdomyosarcoma	8900/3
Osteosarcoma	9180/3
Synovial sarcoma	9040/3
Ewing sarcoma	9364/3
Angiomyolipoma	8860/0
Epithelioid angiomyolipoma	8860/1*
Leiomyoma	8890/0
Haemangioma	9120/0
Lymphangioma	9170/0
Haemangioblastoma	9161/1
Juxtaglomerular cell tumour	8361/0
Renomedullary interstitial cell tumour	8966/0
Schwannoma	9560/0
Solitary fibrous tumour	8815/1
Mixed epithelial and stromal tumour family	
Cystic nephroma	8959/0
Mixed epithelial and stromal tumour	8959/0
Neuroendocrine tumours	
Well-differentiated neuroendocrine tumour	8240/3
Large cell neuroendocrine carcinoma	8013/3
Small cell neuroendocrine carcinoma	8041/3
Phaeochromocytoma	8700/0
Miscellaneous tumours	
Renal haematopoietic neoplasms	
Germ cell tumours	
Metastatic tumours	

The morphology codes are from the International Classification of Diseases for Oncology (ICD-O) {917A}. 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. The classification is modified from the previous WHO classification {756A}, taking into account changes in our understanding of these lesions.
*New code approved by the IARC/WHO Committee for ICD-O.

Fig. 1 – World Health Organization (WHO) classification of tumours of the kidney. Reproduced with permission from the WHO International Agency for Research on Cancer [1].
WHO = World Health Organization.