

### EPIDEMIOLOGY:

Renal cell carcinoma (RCC) represents around 3% of all cancers and is the most common solid lesion within the kidney, accounting for approximately 90% of all kidney malignancies. Highest incidence in Western countries. 1.5:1 male predominance. Higher incidence in the older population.

**AETIOLOGY:** Risk factors: smoking, obesity, hypertension, diabetes, first-degree relative with kidney cancer.

| Recommendation   | Strength rating |
|--|-----------------|
| Increase physical activity, eliminate cigarette smoking and in obese patients reduce weight are the primary preventative measures to decrease risk of RCC. | Strong          |

### HISTOLOGICAL DIAGNOSIS:

**1. CLEAR-CELL RCC (ccRCC):** Well circumscribed and a capsule is usually absent. Often with haemorrhage and necrosis

Loss of chromosome 3p and mutation of the von Hippel Lindau (VHL) gene at chromosome 3p25 are frequently found

Worse prognosis compared to pRCC and chRCC, but this difference disappears after adjustment for stage and grade

**2. PAPILLARY RCC (pRCC):**

- **Type I:** associated with activating germline mutations of MET. Narrow papillae without any binding and a tough pseudocapsule. More frequent exophytic, with extrarenal growth and with low malignant potential. **Type I is more common and generally have a better prognosis than Type II**

- **Type II:** Heterogeneous group associated with activation of the NRF2-ARE pathway

**3. CHROMOPHOBE RCC (chRCC):** Loss of chromosomes Y, 1, 2, 6, 10, 13, 17 and 21 are typical genetic changes. **Prognosis relatively good.**

Relatively homogenous, well-demarcated mass without a capsule. It cannot be graded by the Fuhrman grading system because of its nuclear atypia.

### 4. OTHER RENAL TUMOURS

- **Renal medullary carcinoma:** very rare (< 0.5% of all RCCs). Young adults with sickle haemoglobinopathies. One of the most aggressive RCCs

- **Carcinoma associated with end-stage renal disease; acquired cystic disease-associated RCC:** 4% of these patients. Generally multicentric and found in younger patients (mostly male). Less aggressive. More frequent pRCC. Specific subtype occurring only in end-stage kidneys: Acquired Cystic Disease-associated RCC with indolent clinical behaviour

- **Papillary adenoma:** papillary or tubular architecture of low nuclear grade and may be up to 15 mm in diameter, or smaller

- **Hereditary kidney tumours:** 5-8% of RCCs. There are ten hereditary RCC syndromes associated with specific germline mutations, RCC histology, and comorbidities. Median age at diagnosis 37 years. Patients may require repeated surgical intervention (generally surveillance until the largest tumour reaches 3 cm and nephron-sparing approaches are recommended)

- **Angiomyolipoma:** benign mesenchymal tumour. It can occur sporadically or as part of tuberous sclerosis (TS) complex. The main complication is spontaneous bleeding. The major risk factors for bleeding are tumour size, grade of the angiogenic component, and the presence of TS.

- **Renal oncocytoma:** benign tumour representing 3–7% of all solid renal tumours. Histopathology remains the only reliable diagnostic modality.

| Recommendations   | Strength rating |
|---|-----------------|
| Manage Bosniak type III cysts the same as localised RCC, or offer active surveillance.  | Weak            |
| Manage Bosniak type IV cysts the same as localised RCC.   | Strong          |
| Treat angiomyolipoma (AML) with selective arterial embolisation or nephron-sparing surgery, in: <ul style="list-style-type: none"> <li>• large tumours (a recommended threshold of intervention does not exist);</li> <li>• females of childbearing age;</li> <li>• patients in whom follow-up or access to emergency care may be inadequate;</li> <li>• persistent pain or acute or repeated bleeding episodes.</li> </ul> | Weak            |
| Offer systemic therapy to patients in need of therapy with surgically unresectable AMLs not amenable to embolisation or surgery.  | Weak            |
| Offer active surveillance to patients with biopsy-proven oncocytomas, as an acceptable alternative to surgery or ablation.  | Weak            |
| Offer radical nephrectomy to patients with localised renal medullary carcinoma.   | Weak            |
| Base systemic therapy for renal medullary carcinoma on chemotherapy regimens containing cisplatin such as cisplatin plus gemcitabine.   | Weak            |

### STAGING (TNM, 2017) AND CLASSIFICATION SYSTEMS:

| T - Primary tumour       |   |       |    |
|--------------------------|---|-------|----|
| TX                       | Primary tumour cannot be assessed   |       |    |
| T0                       | No evidence of primary tumour   |       |    |
| T1                       | Tumour ≤ 7 cm or less in greatest dimension, limited to the kidney  |       |    |
| T1a                      | Tumour ≤ 4 cm or less   |       |    |
| T1b                      | Tumour > 4 cm but ≤ 7 cm  |       |    |
| T2                       | Tumour > 7 cm in greatest dimension, limited to the kidney  |       |    |
| T2a                      | Tumour > 7 cm but ≤ 10 cm   |       |    |
| T2b                      | Tumours > 10 cm, limited to the kidney  |       |    |
| T3                       | Tumour extends into major veins or perinephric tissues but not into the ipsilateral adrenal gland and not beyond Gerota fascia  |       |    |
| T3a                      | Tumour extends into the renal vein or its segmental branches, or invades the pelviccalyceal system or invades perirenal and/or renal sinus fat, but not beyond Gerota fascia* |       |    |
| T3b                      | Tumour grossly extends into the vena cava below diaphragm   |       |    |
| T3c                      | Tumour grossly extends into vena cava above the diaphragm or invades the wall of the vena cava  |       |    |
| T4                       | Tumour invades beyond Gerota fascia (including contiguous extension into the ipsilateral adrenal gland)   |       |    |
| N - Regional Lymph Nodes |   |       |    |
| NX                       | Regional lymph nodes cannot be assessed   |       |    |
| N0                       | No regional lymph node metastasis   |       |    |
| N1                       | Metastasis in regional lymph node(s)  |       |    |
| M - Distant Metastasis   |   |       |    |
| M0                       | No distant metastasis   |       |    |
| M1                       | Distant metastasis  |       |    |
| pTNM stage grouping      |   |       |    |
| Stage I                  | T1  | N0    | M0 |
| Stage II                 | T2  | N0    | M0 |
| Stage III                | T3  | N0    | M0 |
|                          | T1, T2, T3  | N1    | M0 |
| Stage IV                 | T4  | Any N | M0 |
|                          | Any T   | Any N | M1 |

A help desk for specific questions about TNM classification is available at <http://www.uicc.org/tnm>.  
\*Adapted based on the American Joint Committee on Cancer (AJCC), 8<sup>th</sup> Edn. 2017 [85].

### ANATOMICAL CLASSIFICATION SYSTEMS:

- **Preoperative Aspects and Dimensions Used for an Anatomical (PADUA) classification system** (Radius, Exophytic/Endophytic, Nearless to collecting system/sinus, Anterior/Posterior, location relative to polar lines)
- **R.E.N.A.L. nephrometry score** (radius, Exophytic/Endophytic, Longitudinal location in relation to sinus line, Relationship to renal rim, sinus and collecting system)
- **C-index** (numerical score based on the combination of tumor diameter and distance from tumor edge to the kidney center)
- **Arterial Based Complexity (ABC) Scoring System** (relationship of the tumor and arterial vasculature)
- **Zonal NePhRO scoring system** (Nearness to collecting system, Physical location of the tumor, Radius of the tumor and Organization of the tumor)

The use of such a system is helpful as it allows objective prediction of potential morbidity surgery and tumour ablation techniques and provides information for treatment planning and patient counselling.