Renal Tumors/Ca

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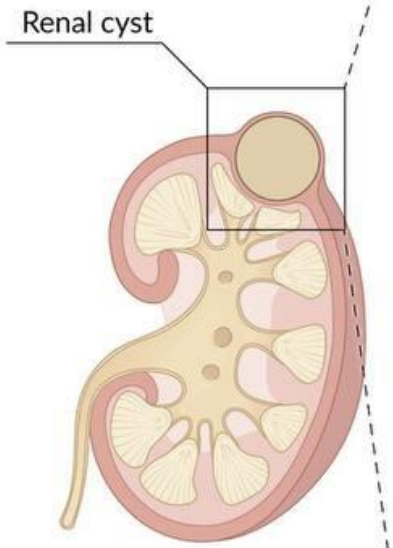
Definition

- Sacs of fluid that form in the Kidneys
- The Bosniak Classification, version 2019 defines a cystic renal mass as a mass based on subjective visual inspection; composed of less than approx. 25% enhancing components.



Bosniak class	Morphological features		Contrast enhancement	Management	Risk of malignancy
Type I	• Hairline-thin wall • No septa • No calcifications		No enhancement	No follow-up	Very low
Type II	• Thin wall • Few septa • Fine calcifications		No enhancement	No follow-up	Low
Type IIF	• Simple cyst < 3 cm	Homogeneous hyperattenuation on CT	No enhancement	No follow-up	Low
Type IIF	• Intrarenal cyst > 3 cm	Homogeneous hyperattenuation on CT	No enhancement	Follow-up	Very low to intermediate
Type IIF	• Minimally thickened wall • Many thin septa • Coarse calcifications		Enhancement not measurable	Follow-up	Very low to intermediate
Type III	• Irregular and thick wall and septa • Coarse calcifications		Enhancement	Surgery	High
Type IV	• Clearly defined soft lesions in wall and septa		Enhancement	Surgery	Very high

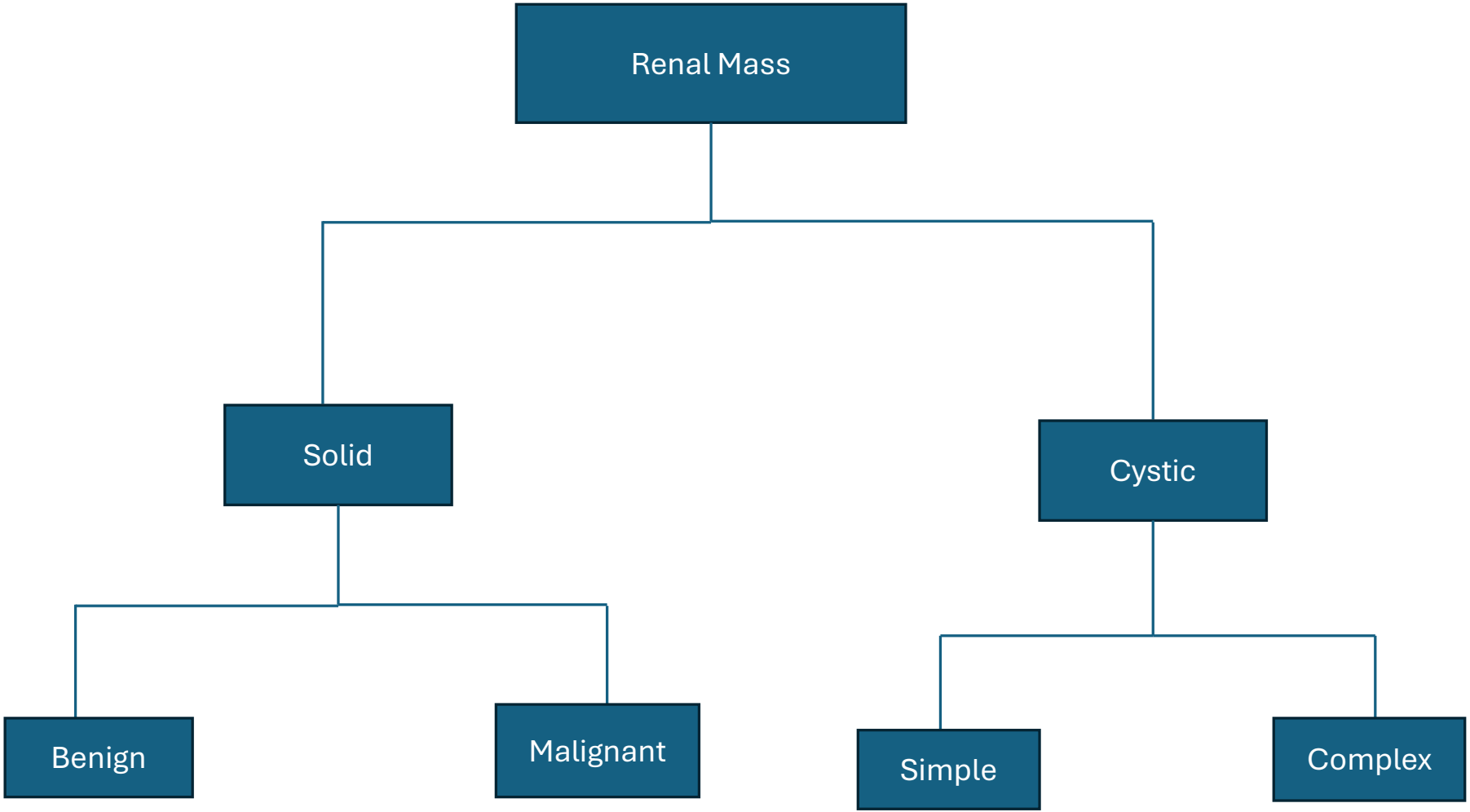
Treatment:

- Not indicated in most cases
- Indication for surgery: symptomatic cysts (e.g., pain) or risk of further complications (e.g., infection)
- Complex cysts require follow-up and must be removed if renal cell carcinoma is suspected (e.g., due to changes in echogenicity or shape).

Complications:

-Complications are rare.

- Cyst rupture
- Cyst infection
- Compression of adjacent tissue (e.g., of the ureter causing impaired urinary flow)

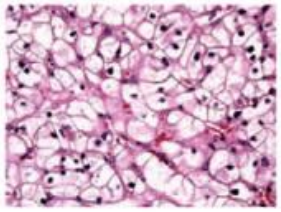
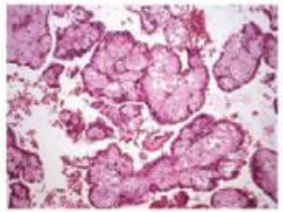
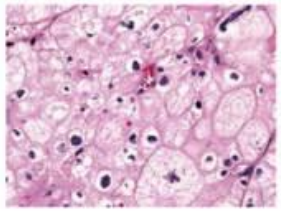

Renal Mass
Solid
Cystic
Benign
Malignant
Simple
Complex

Renal Cell Carcinoma

- Heterogeneous group of cancers derived from renal tubular epithelial cells.
- it accounts for >90% of cancers in the kidney,
- Men more affected than women (2:1).
- Peak incidence between 55 and 74 years.
- Median age at diagnosis is 64 yrs.
- When diagnosed at younger ages; a hereditary cancer kidney syndrome should be considered (3-5% of all RCCs).
- «Incidence rates have been increasing over time in most populatione
- but mortality rates have levelled off since
- 1990s (developed countries).

RCC

- The two forms are sporadic and hereditary.
- Approx. 4% of renal cell carcinomas are associated with hereditary factors.
- The structural alterations of both forms occur on the short arm of chromosome 3 (3p).
- The most common gene involved in the pathogenesis of RCC are the Von Hippel-Lindau (VHL)
- gene
- Both hereditary and sporadic cases of clear cell RCC, VHL abnormalities are a key in pathogenesis.

	Clear cell	Papillary	Chromophobe	
Histology				
Frequency	80%	10–15%	5%	1%

M/C type of RCC

Types	Freq	Cell of Origin	Etiology	Macroscopic	Microscopic	Prognosis
Clear Cell	70%	Proximal Convoluted Tubule	Sporadic or Inherited mutation of VHL gene on Chromosome 3p	- Yellow or Golden due to high intracellular lipid concentration.	- Clear cells - Polygonal cells arranged as cords or tubules (non-papillary growth) - Clear, glycogen, and/or lipid-filled cytoplasm - Unifocal, Unilateral growth	Depending on Stage
Papillary	10-15%	Proximal Convoluted Tubule	- Trisomy 17 - Trisomy 7 - Loss of Y chromosome	- Yellow or Golden due to high intracellular lipid concentration.	- Bilateral, multifocal growth possible. - Cuboidal, low columnar cells. - Cells grow in a papillary formations	Type 1 better than Type 2 (More aggressive, with poor prognosis)
Chromophobe	5%	Intercalated cells of the cortical collecting duct	Hypodiploidy	- Yellow or Golden due to high intracellular lipid concentration.	- Large Polygonal cells with a prominent cell membrane. - Eosinophilic cytoplasm - Perinuclear halo	Excellent prognosis
Oncocytic	1%	Intercalated cells of the cortical collecting duct	Unknown	- Yellow or Golden due to high intracellular lipid concentration.	- Orignate from oncocytomas - Similar to chromophobic RCC, but without perniculear halo. - Cells occur as tumor nests	Excellent prognosis
Collecting Duct	1%	Medullary Collecting Duct	Unknown	- Yellow or Golden due to high intracellular lipid concentration.	- Hobonail pattern: irregulary arranged malignant glandular cells within a fibrous stroma. - Medullary duct ca: A variant that is associated with sickle cell disease.	Aggressive tumor with poor prognosis

Risk Factors of RCC

- Smoking
- Obesity
- HTN
- Male, age >55
- Family Hx of RCC or hx of Herditary Syndromes
- Hx of Acquired Kidney disease

* Doctor also noted that there is an association with Dialysis

RCC clinical features

- Usually asymptomatic in the early stages
- Patients become symptomatic when the tumor has reached a large size (usually >10 cm) and/or if metastases are present
- The classical triad is (Hematuria, Flank pain, and a palpable mass).
- Only 10-15% of pts present with the triad
- Constitutional symptoms(Weight loss, fatigue, fever, night sweats, anemia)
- Symptoms of local and metastatic spread
- % present with one or more atypical symptoms of paraneoplastic syndromes and/or disseminated disease.

Hereditary Syndromes

Syndrome	Mutation	Clinical Features
Clear Cell Carcinoma		
Von Hippel Lindau	VHL	CNS hemangioblastomas, pheochromocytoma, pancreatic neuroendocrine tumor
PTEN Hamartoma Syndrome	PTEN	Lipomas, fibromas, acral keratosis, GI polyps; increased risk of cancers of the breast, thyroid, and endometrium; papillary renal carcinoma also seen
Familial Clear Cell with Chromosome 3 Translocation	Translocation chromosome 3	Clear cell kidney cancer
BAP1 Mutant Disease	BAP1	Melonoma, mesothelioma, epithelioid atypical Spitz tumors
Papillary Carcinoma		
Hereditary Leiomyomatosis	FH	Cutaneous and uterine leiomyomata; Papillary renal carcinoma type 2
Hereditary Papillary Renal Cancer	MET	Papillary renal carcinoma type 1
Other Histology		
Tuberous Sclerosis Complex	*TSC1, TSC2*	Facial angiofibromas, subependymal giant cell astrocytoma, subependymal nodules, CNS cortical tubules; renal angiomyolipoma
SDH-associated Renal Cancer	*SDHB, SDHC, SDHD*	Paraganglioma, pheochromocytoma; renal clear cell, chromophobe, or oncocytoma
Lynch Syndrome	*MLH1, MSH2*	Familial history of cancer, primarily colon endometrial, ovarian, small bowel, upper urinary tract urothelial carcinoma, pancreatic; clear cell and papillary renal carcinoma described (25)

Paraneoplastic Syndromes in RCC

Endocrine	Nonendocrine
Hypercalcemia	Amyloidosis
HTN	Anemia
Polycythemia	Neuromyopathies
Nonmetastatic Hepatic Dysfunction	Vasculopathy
Galactorrhea	Nephropathy
Cushing Syndrome	Coagulopathy
Alteration in glucose metabolism	Prostaglandin elevation

- Hypercalcemia is the most common of the paraneoplastic syndromes in patients with RCC those with hypercalcemia and RCC, approx. 75% have high stage lesions
- In up to one third of the cases, symptoms such as fever, weight loss, and fatigue are the first symptoms of RCC; Fever is found in 20%-30% of those with RCC and is the sole presenting complaint in approx. 2% of patients.

Complications caused by Local spread

- Varicocele

Rare, classically associated with left-sided RCC, Usually not seen with an RCC in the right kidney because the right gonadal vein empties directly into the inferior vena cava.

Malignant cells grow inside the left renal vein and occlude the ostium of the left gonadal vein.

- Budd-Chiari syndrome: caused by involvement of the IVC

Lower limb edema

Ascites

Hepatic dysfunction

Complications caused by Metastatic Disease

Overview

- Spread beyond the renal capsule affects the lymph nodes of the renal hilum and para-aortic nodes.
- Hematogenous spread occurs via renal vein and IVC.

- Pulmonary metastases:

Most common site of metastases

Hemoptysis

Dyspnea

- Bone metastases: second most common site of metastases

Bone pain

Pathological fractures

Investigations

- Imaging:

Abdominal/Pelvic US

CT Abdomen/ Pelvis

MRI Abdomen/ Pelvis

- Labs:

- Urinalysis
- CBC -> Anemia or Polycythemia (paraneoplastic)
- Creatinine -> Baseline function to guide management
- Estimated GFR -> Renal Function to guide management and for prognosis
- LDH-> Poor prognostic marker (> 1.5 upper limit)
- Corrected Calcium-> Poor prognostic marker (>2.5 upper limit)
- LFTs-> Paraneoplastic or metastasis
- Coagulation Profile

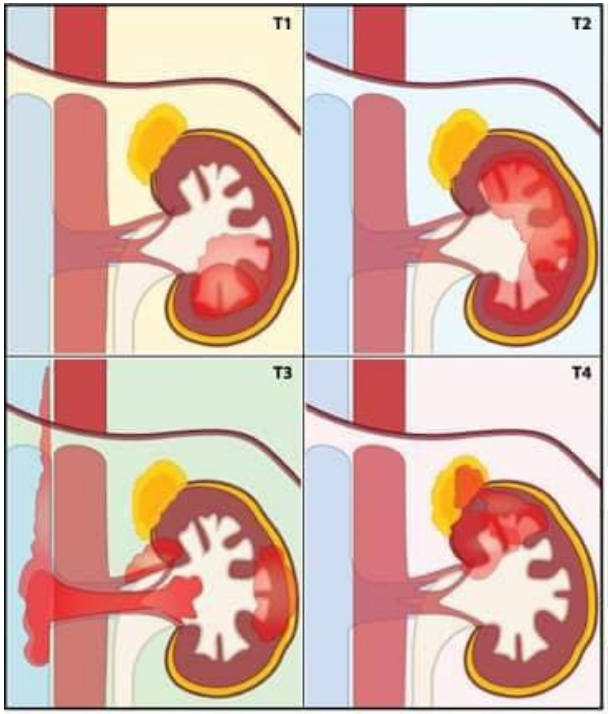
Metastatic Evaluation:

CT chest

MRI Brain/Spine

Bone Scan

PET SCAN



TNM	Involvement	Extent of Disease
T0	Primary not involved	
T1 T1a T1b	≤ 7 cm ≤ 4 cm ≥ 4 cm	limited to kidney
T2 T2a T2b	> 7 cm > 7 cm to ≤ 10 cm >10 cm	limited to kidney
T3 T3a T3b T3c	into major veins or perinephric tissues in renal vein or renal sinus fat into vena cava into vena cava	not beyond Gerota's fascia not beyond Gerota's fascia below diaphragm above diaphragm
T4	invasion beyond Gerota's fascia	including contiguous extensions & into ipsilateral adrenal gland

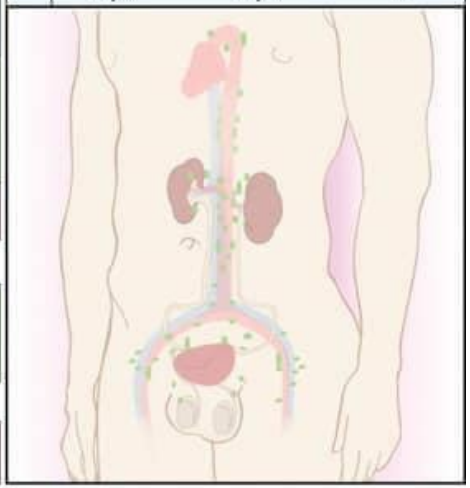
Regional

NX	Regional lymph nodes not assessed
N0	No lymph node involvment
N1	Regional lymph node involvment

Distant Metastases

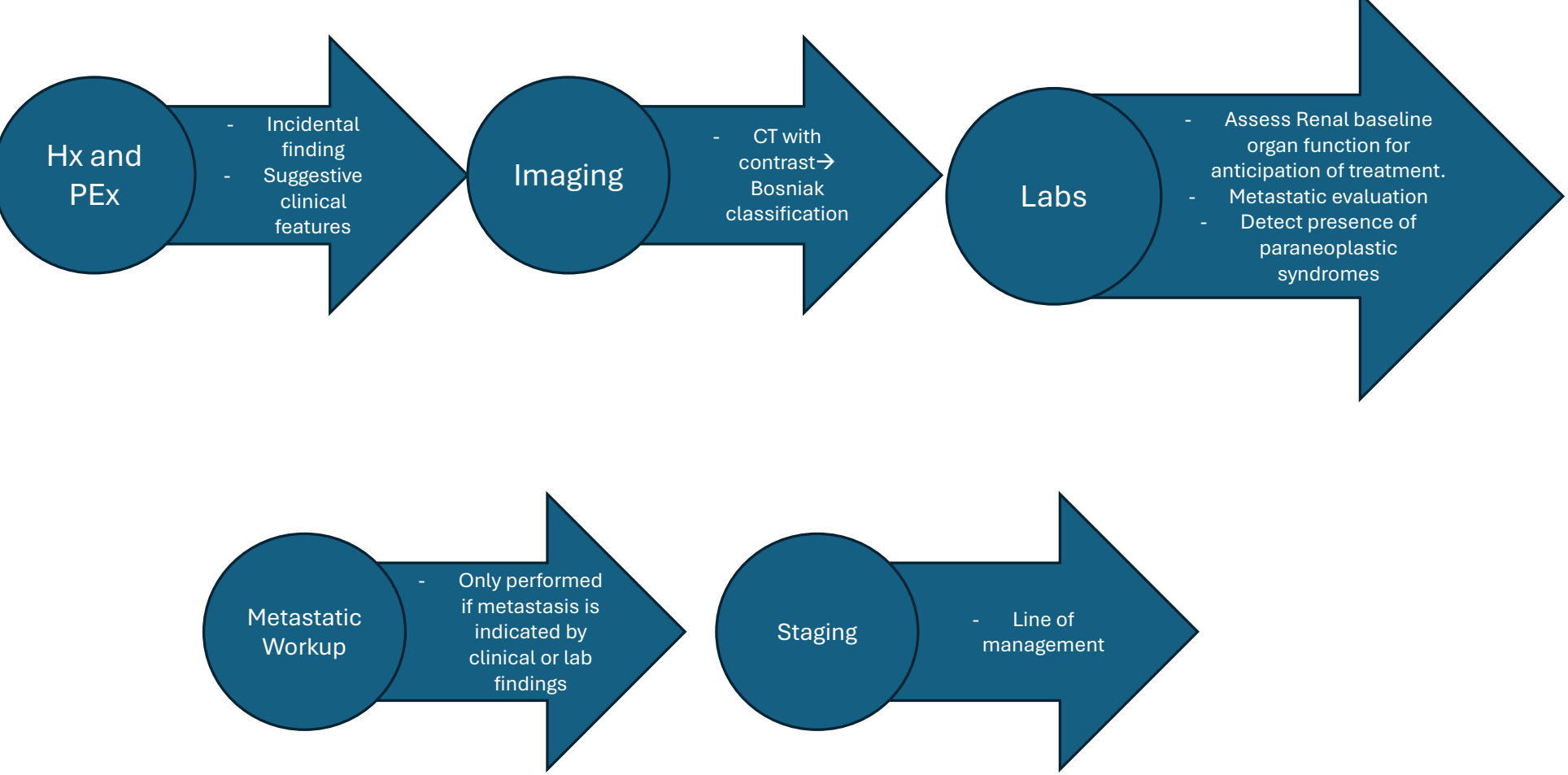
M0	No distant metastases
M1	Distant metastases

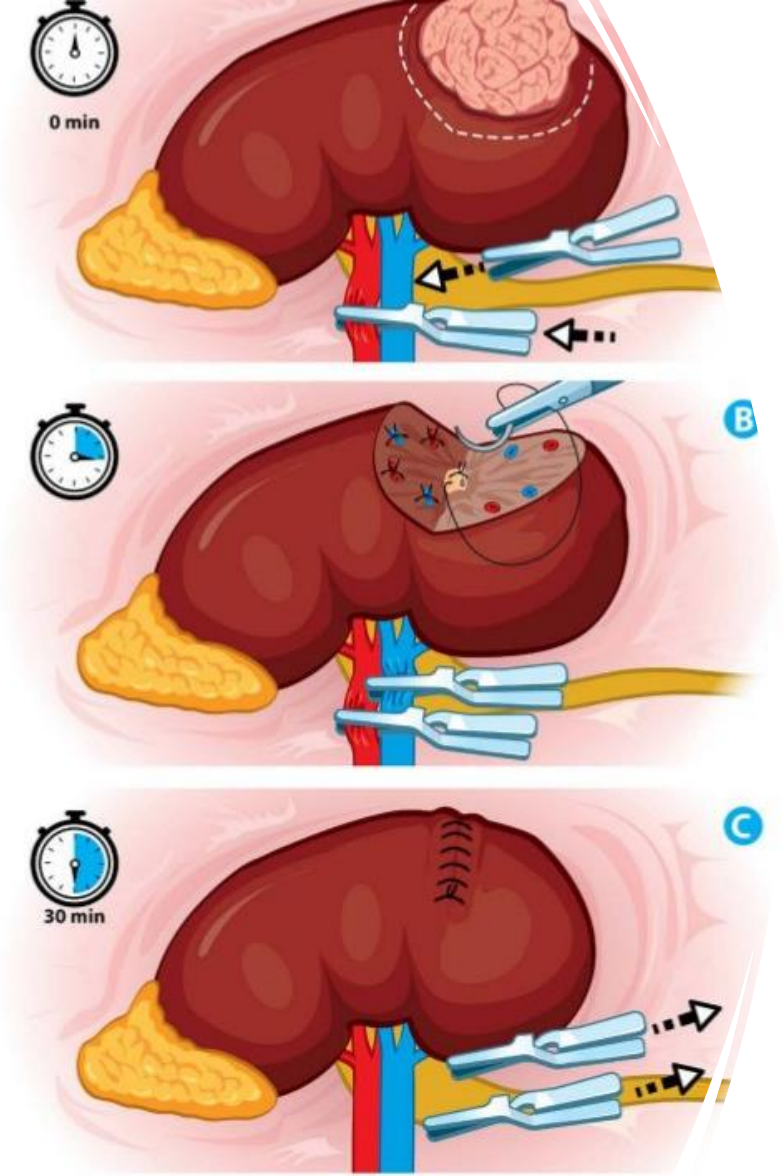
Anatomic Stage / Prognostic Groups			
I	T1	N0	M0
II	T2	N0	M0
III	T1 or T2, T3	N1 N0 or N1	M0 M0
IV	T4 Any T	Any N Any N	M0 M1



RCC: Tumor stages

- T1: tumor limited to the kidney: tumor size < 7 cm (T1a: < 4 cm; T1b: 4-7 cm)
- T2: tumor limited to the kidney; tumor size > 7 cm. (T2a: 7-10 cm; T2b: > 10 cm)
- T3: tumor extends into major veins or perinephric tissues but not Into the ipsilateral adrenal gland or beyond the Gerotas fascia
- T4: tumor invades beyond the Gerotas fascia to or the ipsilateral adrenal gland


Hx and PEx
- Incidental finding
- Suggestive clinical features
Imaging
- CT with contrast→ Bosniak classification
Labs
- Assess Renal baseline organ function for anticipation of treatment.
- Metastatic evaluation
- Detect presence of paraneoplastic syndromes
Metastatic Workup
- Only performed if metastasis is indicated by clinical or lab findings
Staging
- Line of management



Management

Partial Nephrectomy

Indications:

- Relative indications:

- Patients who are young and/or have a longer life expectancy

- Multifocal masses

- Comorbidities that impact renal function,

E.g., hypertension, diabetes mellitus, renal stones, BMI >40 kg/m2

- Absolute Indications :

- Patients with a T1a renal mass

- A solitary kidney

- Bilateral masses

- Familial RCC

- Preexisting Chronic kidney disease or proteinuria

Agents for the treatment of renal cell carcinoma		
Drug type		Examples
Targeted Therapy	VEGF receptor tyrosine kinase inhibitors	• Pazopanib • Sunitinib • Sorafenib • Cabozantinib • Tivozanib • Axitinib • Lenvatinib
	Anti-VEGF antibodies	Bevacizumab
	mTOR inhibitors	• Everolimus • Temsirolimus
Immunotherapy	Anti-PD-1 antibodies Anti-PD-1 antibodies are a type of immune checkpoint inhibitor	• Pembrolizumab • Nivolumab • Avelumab
	Anti-CTLA-4 antibodies Anti-CTLA-4 antibodies are a type of immune checkpoint inhibitor.	Ipilimumab
	Cytokines	• Interleukin-2 (aldesleukin) • Interferon alpha

Benign Renal Tumors

Renal papillary adenoma

- Very common
- Small (<3cm), round, yellow nodules in the renal cortex.
- Arise from tubular cells of proximal convoluted tubule.
- Asymptomatic, and often an incidental finding, that up to 25% of autopsies reveal renal papillary adenoma.
- Can be distinguished from RCC by biopsy.

Benign Renal Tumors

Oncocytoma

- Benign epithelial tumor that originates from the cells of collecting ducts
- M>F
- Gross appearance: Spherical, capsulated, and brown in color
- Diagnosis is pathologic, no reliable distinguishing clinical characteristics.
- No characteristics features on CT, Us, or MRI. Angiographic features include the spoke wheel appearance of tumor arterioles, and a “ lucent rim sign” of the capsule, but these findings are not invariable and similar findings have been reported in patients with RCC
- High grade oncocytomas may be intermixed with elements of RCC and can be found as coexisting lesions within the same or opposite kidney.
- The tumors are usually solitary and unilateral, although several bilateral cases and multiple oncocytomas occurring simultaneously haven been reported.
- Metastasis is extremely rare though the invasion of the lymphovascular spaces have been observed.

Benign Renal Tumors

Angiomyolipoma

- Usually a middle aged female.
- Sporadic
- Associated with the following syndromes:

Tuberous sclerosis (TSC) :

Sporadic lymphangioleiomyomatosis

- May present with flank pain, palpable mass or painless hematuria.
- Symptoms are related to the size of the tumor:

- Small (<4cm): usually asymptomatic .

- Large (>4cm):

1. mass effect on the healthy kidney tissue (CKD, and in severe cases may lead ESRD that needs dialysis).

2. Abnormal growth of blood vessels may rupture and cause massive and life-threatening retroperitoneal bleeding, and this can occur in 10% of cases (Wunderlich syndrome)

- Diagnosis:
- Hx & Pex
- Labs: CBC, KFT, urinalysis.
- Imaging:

U/S: Fat appears hyperechoic with no acoustic shadows.

CT: It is the only benign mass that can be distinguished on CT, where fat appears with negative density.

MRI: Fat appears bright on T1 and intermediate dark on T2

- Management:
- If <4cm and asymptomatic: observations with annual U/S,CT
- If >4cm or symptomatic:

Tumor excision due to risk of bleeding.