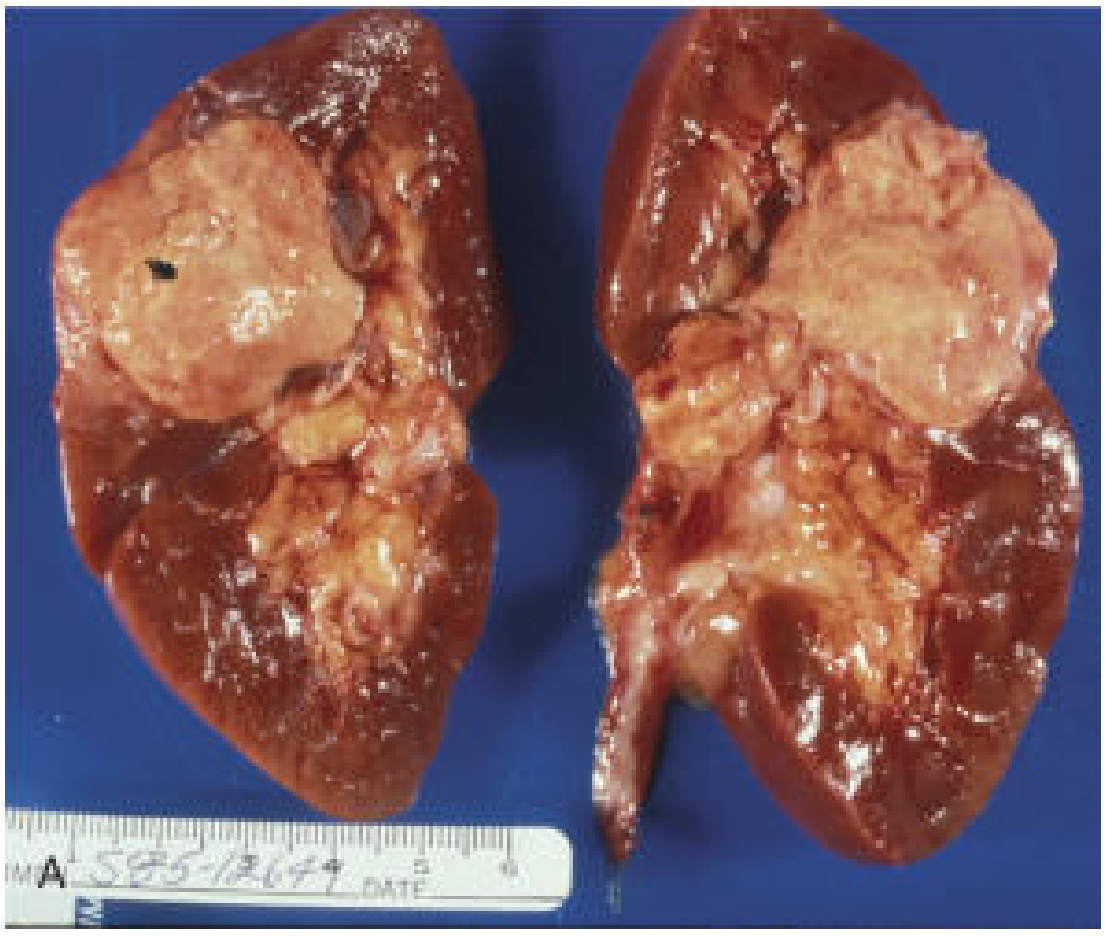
Renal Cell Carcinoma

Dept. of Surgery

Epidemiology

- Male predominance (M:F 1.5:1).
- Most common in sixth to eighth decades; peak incidence in sixth decade
- Metastatic disease in 30% at diagnosis, and eventually in 50% (lung, liver, bone, distant LN, adrenal, brain, opposite kidney, soft tissue)
- Most sporadic RCCs are unilateral and unifocal

- Stage at diagnosis is the most important prognostic factor
- Predominant histologic type: adenocarcinoma arising from tubular epithelium
- Adenocarcinoma subtypes:
  - clear cell (75–85%)
  - chromophilic/ papillary (10–15%)
  - chromophobe (5–10%)
  - oncocytic (rare)
  - Sarcomatoid (1–6%; poor prognosis)



Papillary (chromophilic) renal cell carcinoma extending into the collecting system

Risk factors

- Tobacco , urban environmental toxins (cadmium/ asbestos/ petrols), obesity, high dietary fat intake, acquired cystic renal disease from renal failure
- Association with von Hippel-Lindau disease:
  - autosomal dominant
  - loss of 3p
  - >70% chance developing RCC (almost all clear cell histology) risk of developing multiple other benign and malignant tumors (retinal angiomas, CNS hemangioblastomas, pheochromocytoma , pancreatic cancer)

Pathology

- Round to ovoid
- Circumscribed by a pseudo capsule of compressed parenchyma and fibrous tissue
- Nuclear features can be highly variable

Diagnosis

- Common signs and symptoms:
  - hematuria (80%)
  - flank pain (45%)
  - flank mass (15%)
  - classic triad of prior three only present in 10%
  - normocytic/normochromic anemia, fever, weight loss

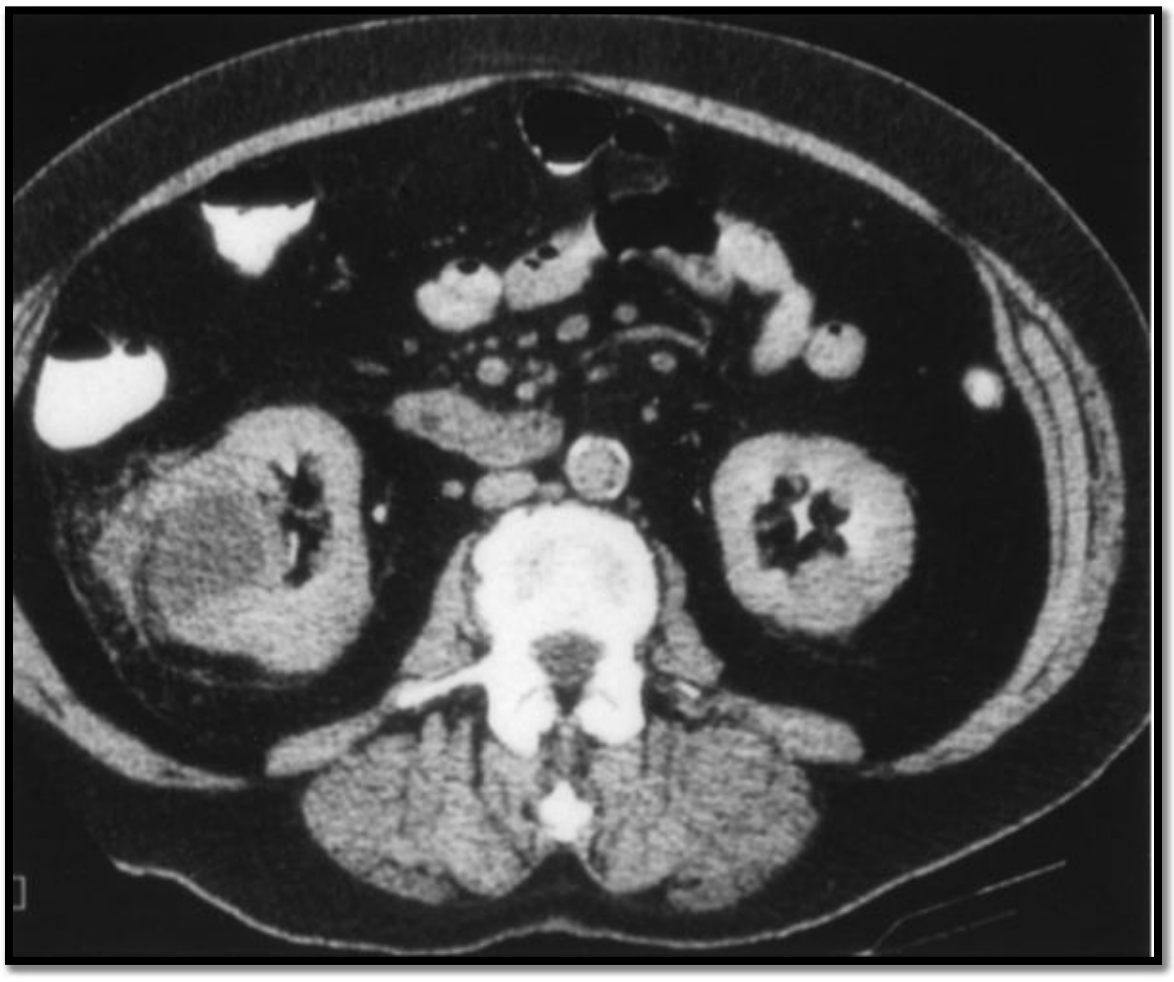
- Less common signs and symptoms:
  - hepatic dysfunction without mets
  - Polycythemia
  - hypercalcemia (occurs in 25% of patients with RCC mets)

Paraneoplastic syndromes in 20% of patients with RCC

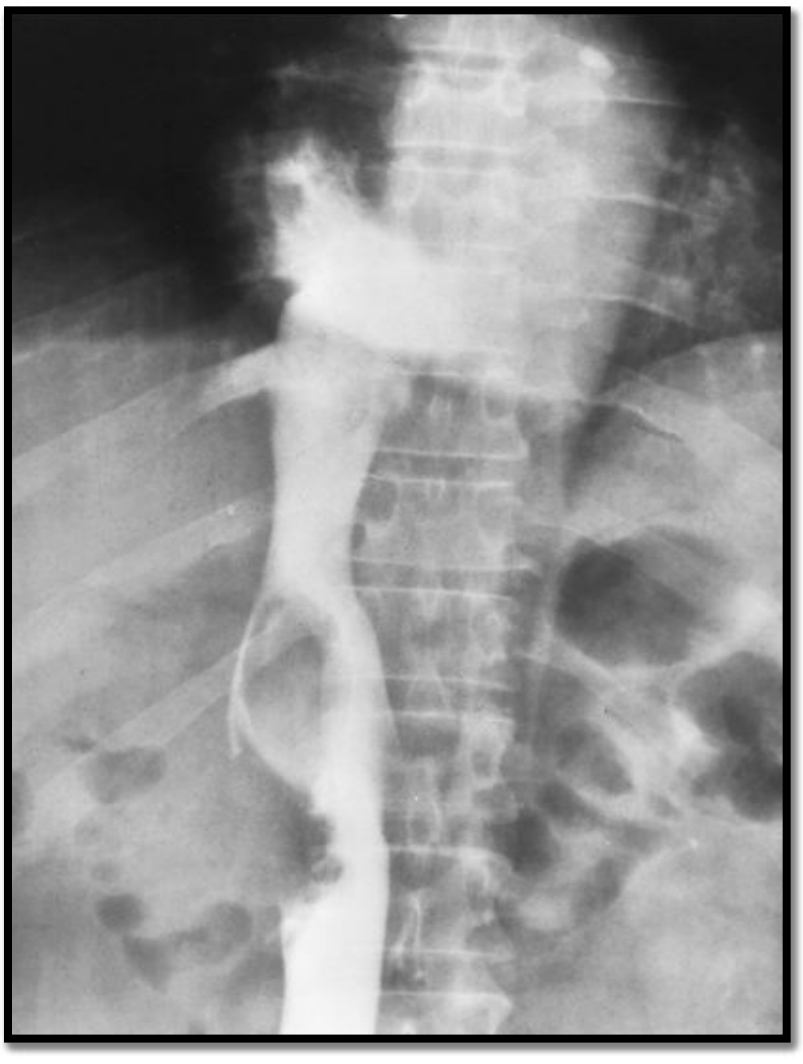
Syndrome	*Percentage*
Elevated erythrocyte sedimentation rate	55.6
Hypertension	37.5
Anemia	36.3
Cachexia, weight loss	34.5
Pyrexia	17.2
Abnormal liver function	14.4
Hypercalcemia	4.9
Polycythemia	3.5
Neuromyopathy	3.2
Amyloidosis	2.0

Diagnosis

- Labs: CBC, LFT, BUN/Cr, LDH, urinalysis
- Imaging:
  - CT abdomen
  - MRI abdomen if CT suggests IVC involvement
- Metastatic evaluation:
  - Chest X ray
  - Bone scan or MRI brain only if clinically indicated



CT scan shows right renal tumor with perinephric stranding suggesting invasion of the perinephric fat



Contrast inferior venacavogram in patient with a right renal tumor shows involvement of the subdiaphragmatic vena cava

- PET: equivocal findings on conventional imaging

- Percutaneous renal biopsy or aspiration: limited role

Staging AJCC 7th Edition

Primary tumor (T)

TX: Primary tumor cannot be assessed
T0: No evidence of primary tumor
T1: Tumor 7 cm or less in greatest dimension, limited to the kidney
- T1a: Tumor 4 cm or less in greatest dimension, limited to the kidney
- T1b: Tumor more than 4 cm, but not more than 7 cm in greatest dimension limited to the kidney

T2: Tumor more than 7 cm in greatest dimension, limited to the kidney
- T2a: Tumor more than 7 cm, but less than or equal to 10 cm in greatest dimension, limited to the kidney
- T2b: Tumor more than 10 cm, limited to the kidney

T3: Tumor extends into major veins or perinephric tissues, but not into the ipsilateral adrenal gland and not beyond Gerota's fascia
- T3a: Tumor grossly extends into the renal vein or its segmental (muscle-containing) branches, or tumor invades perirenal and/or renal sinus fat, but not beyond Gerota's fascia
- T3b: Tumor grossly extends into the vena cava below the diaphragm
- T3c: Tumor grossly extends into the vena cava above the diaphragm or invades the wall of the venacava

T4: Tumor invades beyond Gerota's fascia (including contiguous extension into the ipsilateral adrenal gland)

Regional lymph nodes (N)

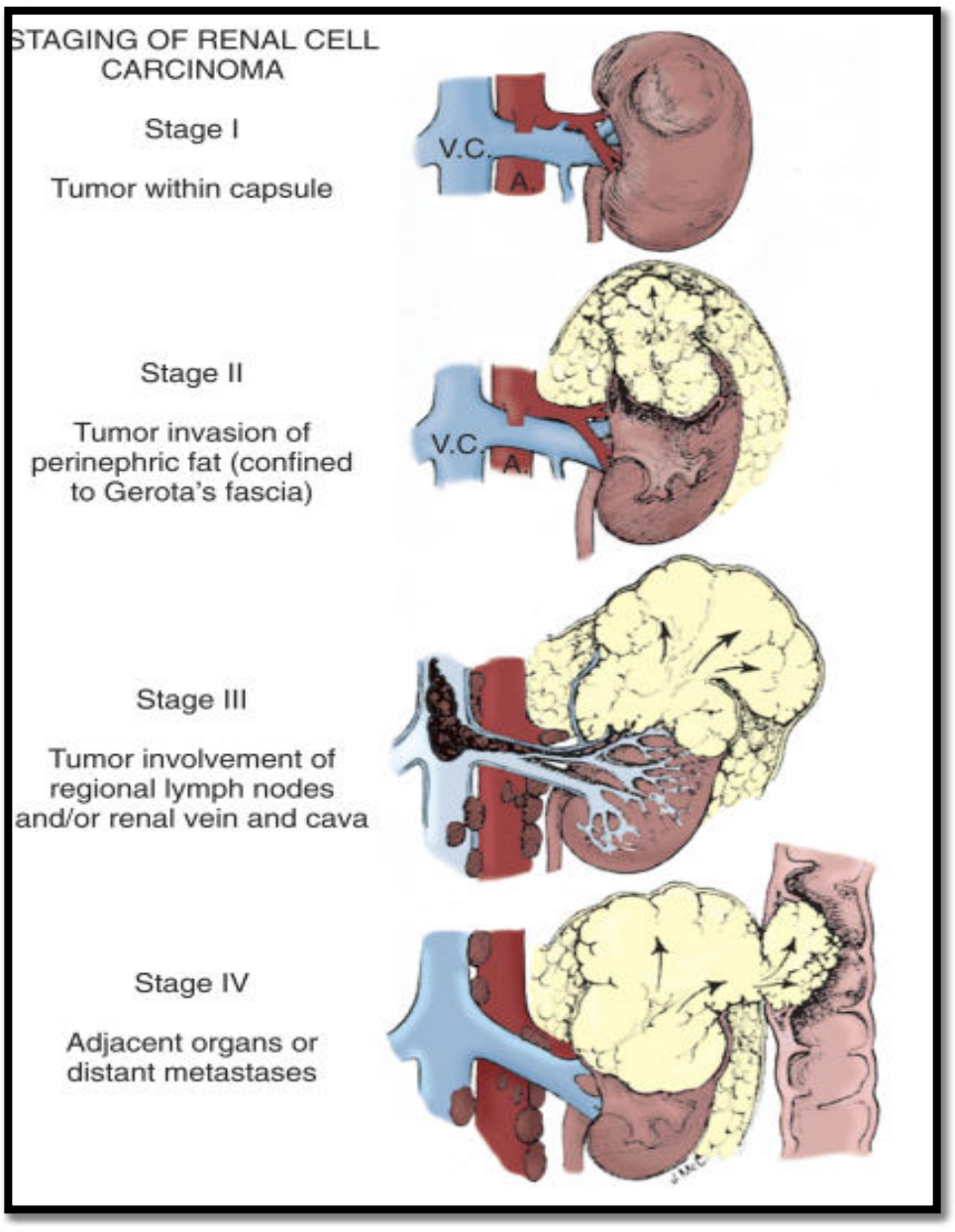
NX: Regional lymph nodes cannot be assessed
N0: No regional lymph node metastasis
N1: Metastasis in regional lymph node(s)

Distant metastasis (M)

M0: No distant metastasis
M1: Distant metastasis

Anatomic stage/prognostic groups

I: T1 N0 M0
II: T2 N0 M0
III: T1 or T2 N1 M0
T3 N0 or N1 M0
IV: T4 Any N M0
Any T Any N M1



Prognostic Factors For RCC

KEY POINTS: PROGNOSTIC FACTORS FOR RCC

Tumor Related	*Patient Related*	*Laboratory*
Stage	Performance status	Anemia
Grade	Symptomatic presentation	Thrombocytosis
Size	Constitutional symptoms	Hypercalcemia
Histologic subtype	Paraneoplastic syndromes	Elevated erythrocyte sedimentation rate
Sarcomatoid histology	Metastasis-free interval	Elevated alkaline phosphatase level
Tumor necrosis		CA-9 expression
Sites of metastasis		
Burden of metastasis		

Management

Stage I-III

Nephrectomy

- Open radical nephrectomy, but laparoscopic gaining popularity
- Nephron sparing surgery via partial nephrectomy, if possible (open or laparoscopic)
- Possible to spare adrenal gland in ~75% cases

No role for adjuvant chemo/immunotherapy

No widely accepted role for neoadjuvant or adjuvant radiotherapy.

Retrospective data suggest possible utility in select cases:

- Positive surgical margins
- Locally advanced disease with perinephric fat invasion and adrenal invasion (IVC/renal vein extension alone does not increase local recurrence significantly)
- LN+
- Unresectable (pre-op RT)

Stage IV

Cytoreductive nephrectomy: improved survival with nephrectomy followed by interferon alpha vs. interferon alpha alone

Systemic therapy

- Immunotherapy (IL-2, interferon alpha, or combination)
- High dose IL-2 only FDA approved treatment for
- Biologic agents show promise in recent trials
  - Bevacizumab
  - Sorafenib or sunitinib
  - Temsirolimus

Consider chemo (gemcitabine ± 5-FU or capecitabine)

Focal palliation of metastases

- RT alone
- Metastasectomy
- Combination of both