Renal and Ureteral Tumors

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Temple Health

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AUA Core Curriculum

https://university.auanet.org

1. Renal Neoplasms

- **a. Benign tumors**
- **b. Hereditary Syndromes**
- **c. Renal mass biopsy**
- **d. Localized RCC – etiology through treatment**
- **f. mRCC – risk models and new therapies**

2. Upper Tract Neoplasms

- **a. etiology, risks, diagnosis and Rx**

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Epidemiology

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US Mortality
% of all causes of death

Rank	Cause of Death	1975 (%)	2022 (%)
1.	Heart Diseases	37.8 →	26.2
2.	Cancer	19.2 →	22.7
3.	Accidents (unintentional injuries)	5.4	8.5
4.	COVID		6.9
5.	Cerebrovascular diseases	10.3	6.2
6.	Chronic lower respiratory diseases	2.3	5.5
7.	Alzheimer's disease	--	4.5
8.	Diabetes		3.8

https://www.cdc.gov/nchs/fastats/leading-causes-of-death.htm?utm_source=chatgpt.com

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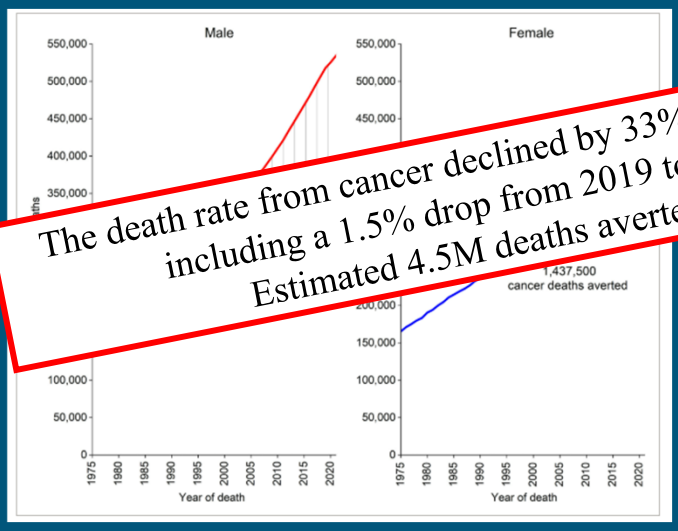
Investments in Cancer Care Generating Real World Results



The death rate from cancer declined by 33% (1991-2020)
including a 1.5% drop from 2019 to 2022
Estimated 4.5M deaths averted

CA: A Cancer Journal for Clinicians
The flagship journal of the American Cancer Society
ARTICLE | Open Access
Cancer statistics, 2025

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GU Cancers 2024

Site	Incidence/yr USA (2024)	Deaths 2024 (% of all GU cancers)	% of all cancer deaths
Prostate cancer	299,010	35,250 (52%)	~6%
Bladder cancer	81,180	17,100 (25%)	~3%
Kidney Cancer	81,000	14,000 (20%)	~2%
Testicular cancer	9,760	500 (0.7%)	<1%
Penile	2,100	500 (0.7%)	<1%
Adrenal	1,500	1000 (1.4%)	<1%
All Cancers	2,001,140 (24% are GU)	611,720	100%

US Death Causes Chart – chat gpt

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Risk Factors for RCC

- **Male gender**
- **Age (median age = 64 yo)**
- **Modifiable**
  - **Smoking (may abate >10y post cessation)**
  - **Obesity (stronger association in women)**
  - **HTN (epidemiologic and retrospective)**
  - **Exposures (low level evidence)**
    - **chronic diuretics, non-steroidal analgesics, and tricholorethylene (cleaning agent)**
    - **Insufficient evidence for Agent Orange ("limited or suggestive" evidence in prostate and bladder)**
- ***Getting a CT/MR/US***
  - **Targeted screening for those at genetic risk only**

Correa, Lane, Rini, Uzzo. Cancer of the Kidney. In Devita - Cancer: Principles and Practice of Oncology, 11th edition 2018

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Epidemiology:
Treatment Disconnect

Welch and Black: Overdiagnosis of Cancer rates JNCI 2010;102:605–613

https://seer.cancer.gov/statfacts/html/kidrp.html

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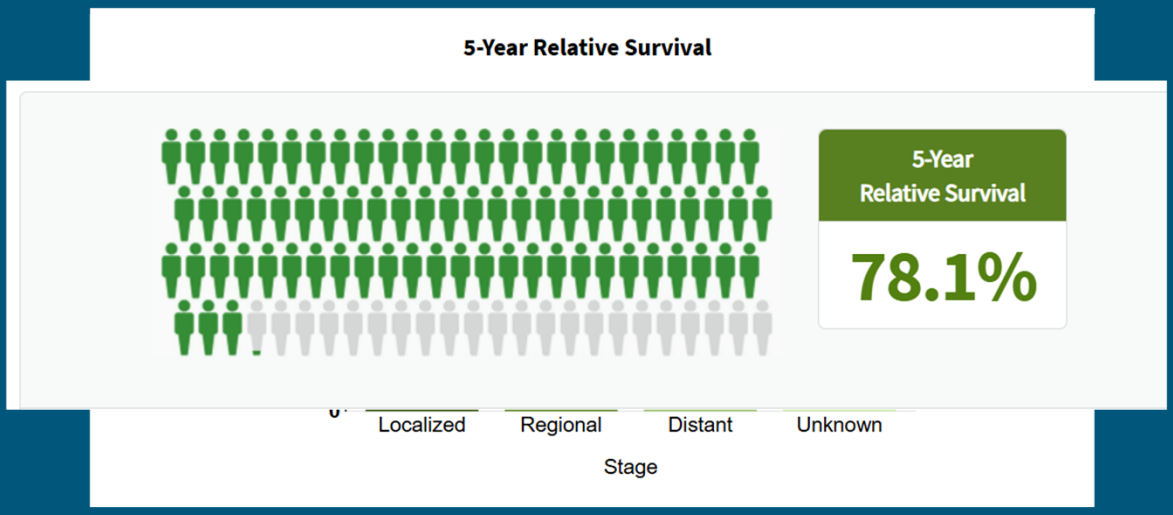
RCC 2024



https://seer.cancer.gov/statfacts/html/kidrp.html

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Take Home – RCC Epidemiology

- **Cancer is the second leading cause of death in US (1 in 4)**
- **RCC/renal pelvic cancer represent 20% of all GU and 2% of all cancers**
- **Incidence rising (incidental detection)**
- **Death rates slowly improving (improvements in systemic Rx)**
- **30-40% present with stage III-IV RCC**
- **25% of those with RCC die as a result of RCC within 5 years**

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Molecular Biology and RCC Syndromes

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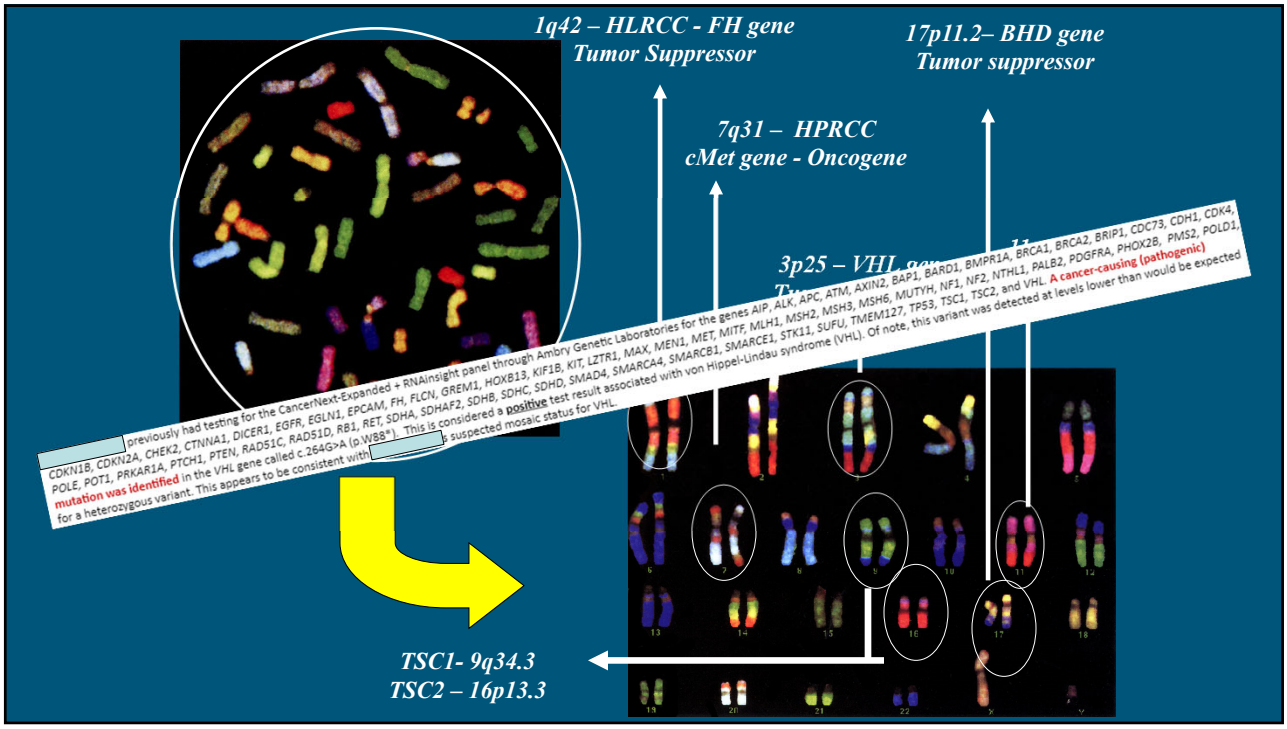

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RCC: Genetic Correlates

Tumor Type	*Cell of Origin*	*Genetic Alteration*
Clear cell	PCT	3p25 (VHL)
Papillary	Probable PCT	7q31 (c-met)
Chromophobe	Intercalated cells (DCT)	Multiple losses
Collecting duct	Collecting duct	Monosomy 1,6,14,15,22
Medullary SMARCB1 loss	Collecting ducts	(sickle cell trait)
Oncocytoma	Intercalated cells (DCT)	Loss of 1 and Y

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Hereditary RCC Syndromes

- von Hippel Lindau (VHL)
  - Hereditary clear cell RCC
- Hereditary Papillary RCC (HPRCC)
- Birt-Hogg Dubé (BHD)
  - Hereditary oncocytoma/Familial renal oncocytosis
- Hereditary Leiomyoma RCC (HLRCC)

Autosomal Dominant

•No definitive increase genetic risk of RCC with:
- •ADPCK
- •Acquired renal cystic disease associated with HD
- •Tuberous sclerosis (AML)

http://web.ncifcrf.gov/research/kidney/

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Hereditary Renal Cell Tumors

Syndrome	Gene (s)	Risk of RCC
von Hippel-Lindau (VHL) syndrome	VHL	30-40%
Hereditary papillary RCC	MET	100%
Birt-Hogg-Dubé (BHD) syndrome	FLCN	30%
Hereditary Leiomyomatosis and RCC (HLRCC) syndrome	FH	15-32%
Tuberous Sclerosis complex (TSC)	TSC1/2	<5%
Succinate Dehydrogenase B (SDHB) Syndrome (Hereditary Pheochromocytoma and Paraganglioma)	SDH B/C/D	<10%

EU Focus 5, 873-976, 2019; Genetic Testing in Kidney Cancer Patients: Who, When, and How? Sandy T. Lui, Brian Shuch

Advantage

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Features of Hereditary (germline) RCC mutations

- Believed to be present in 5% of all cases
- Higher clinical index of suspicion
  - Bilateral and multifocal
  - Younger patients (<46 years old)
  - Associations with other genetic/congenital/rare traits
  - Strong family history (need to ask provocative questions)
  - Non-ccRCC
  - Advanced stage RCC

JAMA Oncology | Original Investigation

Prevalence of Germline Mutations in Cancer Susceptibility Genes in Patients With Advanced Renal Cell Carcinoma

Maria I. Carlo, MD; Semanti Mukherjee, PhD; Diana Mandelker, MD, PhD; Joseph Vijai, PhD; Yelena Kemel, MS, ScM; Liying Zhang, MD, PhD; Andrea Knezevic, MS; Sujata Patil, PhD; Ozge Ceyhan-Birsoy, PhD; Kuo-Cheng Huang, MD; Almedina Redzematovic, MS; Devyn T. Coskey, BS; Carolyn Stewart, BA; Nisha Pradhan, BA; Angela G. Arnold, MS; A. Ari Hakimi, MD; Ying-Bei Chen, MD, PhD; Jonathan A. Coleman, MD; David M. Hyman, MD; Marc Ladanyi, MD; Karen A. Cadoo, MD; Michael F. Walsh, MD; Zsofia K. Stadler, MD; Chung-Han Lee, MD, PhD; Darren R. Feldman, MD; Martin H. Voss, MD; Mark Robson, MD; Robert J. Motzer, MD; Kenneth Offit, MD, MPH

JAMA Oncol 2018 Sep 1;4(9):1228-1235

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Birt-Hogg Dubet (BHD)

- **Syndrome includes:**
  - **Fibrofolliculoma**
    - **Located on skin of head and neck**
    - **Painless and develop after age 30**
  - **Multiple, bilateral RCC**
    - **Most commonly chromophobe/oncocytoma (oncocytosis)**
    - **Conventional (clear cell) and papillary can occur too**
  - **Other associations**
    - **Nevus, PTH adenomas, lipomas, oral mucosal papules**
    - **Pulmonary cysts and spontaneous pneumothorax (25%)**
    - **Colonic polyps and cancer**
  - ***17p11.2* – tumor suppressor –**
    - **encodes for folliculin protein (function unknown)**

http://web.ncifcrf.gov/research/kidney/

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Hereditary Leiomyoma RCC (HLRCC)

- **Syndrome includes:**
  - **Cutaneous leiomyomas – often painful**
  - **Uterine leiomyomas (fibroids)**
    - **Before age 30, multiple, painful**
  - ***"Type 2" papillary RCC* or collecting duct carcinoma**
    - **Tumors may be solitary or multiple and bilateral**
    - **Tumors capable of metastasis even when very small**
    - **Aggressive and may lead to death in patients in their 30s**
  - **Paragangliomas and Leydig cell tumors (testes)**
  - ***FH* gene mutation (1q42)**
    - **encodes for Krebs cycle enzyme fumarate hydratase [RCC is a metabolic Tumor]**
      - **Catalyzes malate to fumarate**
      - **Probable tumor suppressor**
  - **Can have FH deficient tumors without germline mutation**

http://web.ncifcrf.gov/research/kidney/

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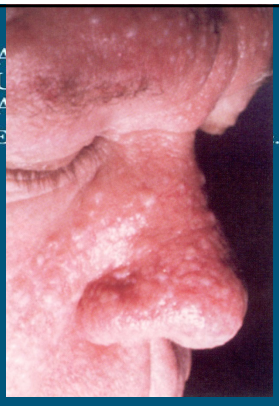
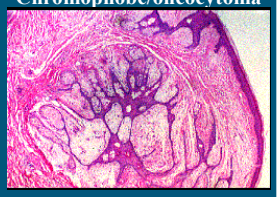
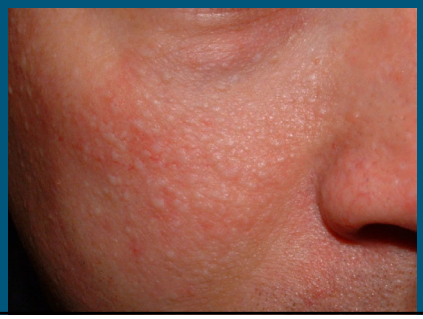
Cutaneous Lesions RCC



BHD

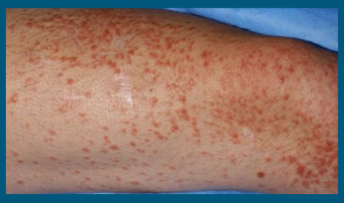
- -Head and scalp
- -Fibrofolliculomas
- -Painless
- - folliculin protein (*17p11)*
- -Chromophobe/oncocytoma





HLRCC

- - Anywhere
- - Uterine Leiomyomas
- - Painful
- - fumarate hydratase (1q42)
- -Aggressive papillary RCC



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Hereditary Papillary RCC (HPRCC)

- Rarest form of hereditary kidney cancer
- Manifestations confined to the kidney
  - *(no extra-renal findings)*
- Bilateral, multiple type 1 papillary RCC
- Histologic appearance identical in all tumors
- Mutation in the *cMet* oncogene (7q31)
  - MET protein is a cell surface receptor tyrosine kinase (HGF-receptor)

http://web.ncifcrf.gov/research/kidney/

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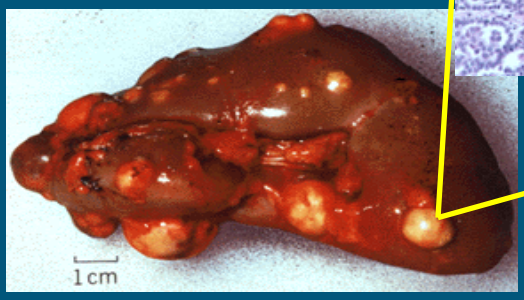
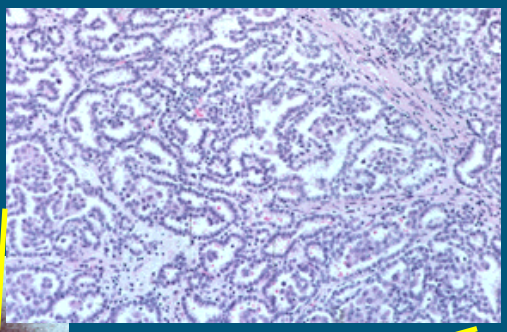
Hereditary Papillary RCC (HPRC)

7q31 – HPRC
cMet gene - Oncogene





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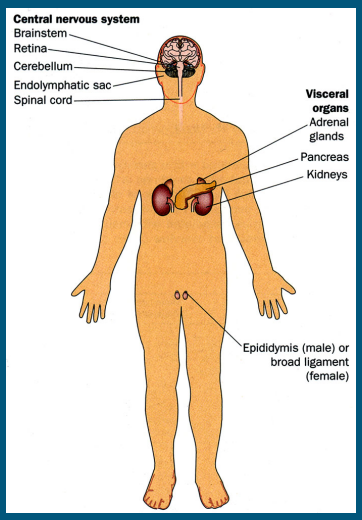
Von Hippel Lindau (VHL)

- **Syndrome includes:**
  - Retinal angioma – earliest
  - Endolymphatic sac (10%)
  - Hemangioblastomas (benign)
    - Mostly spine and cerebellum
  - Pancreatic cysts/islet tumors
  - Pheochromocytoma (type 2)
    - Missense mutations
      - Codes for an AA substitution
  - Epididymal cystadenoma
  - Kidney
    - RCC (clear cell)
    - Renal cysts (benign and malignant)



3p25 – tumor suppressor gene (pVHL)

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AUA Guidelines – Familial (germline) RCC Syndromes

Supplementary Table 1. Familial RCC Syndromes.[7,22]

Syndrome	Gene	Clinical Manifestations
Von Hippel-Lindau (VHL)	*VHL*	Clear cell RCC, Renal cysts, Hemangioblastomas of the central nervous system, Retinal angiomas, Pheochromocytoma
Hereditary Papillary Renal Carcinoma (HPRC)	*MET*	Type 1 papillary RCC
Birt-Hogg-Dube (BHD)	*FLCN*	Chromphobe RCC, Oncocytoma, Hybrid oncocytic/chromophobe tumors (HOCTs), Clear cell RCC (rare), Renal cysts, Cutaneous fibrofolliculomas, Lung cysts, Spontaneous pneumothorax
Hereditary Leiomyomatosis and RCC (HLRCC)*	*FH*	Type 2 papillary or collecting duct RCC, Cutaneous leioyomyomas, Uterine leiyomyomas
Succinate Dehydrogenase Kidney Cancer (SDH-RCC)*	*SDHB/C/D*	Clear cell RCC, Chromophobe RCC, Type 2 papillary RCC, Oncocytoma
Tuberous Sclerosis Complex (TSC)	*TSC1/2*	Angiomyolipomas, Clear cell RCC, Oncocytoma, Lymphangioleiyomyomastosis (LAM), Seizures, Mental retardation
Cowden/PTEN Syndrome Associated RCC (CS-RCC)	*PTEN*	Mucocutaneous lesions, Mucosal lesions, Facial trichilemmomas, Papillomatous papules, Clear cell RCC, Type 1 papillary RCC, Chromophobe RCC, and malignancies in other organ systems

*Renal cancers associated with these syndromes are typically more aggressive

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Fox Chase RCC Familial Risk Summary Recommendations

Hereditary RCC syndrome	Gene	RCC RISK	RCC SCREENING RECOMMENDATIONS
VHL	**VHL**	**40+ % BY AGE 60**	FROM AGE 16: ANNUAL ABD U/S; MRI ABD (KIDNEY/PANCR/ADRENAL) Q 2 YRS
BHD	**FLCN**	**20-35% mostly chRCC**	FROM AGE 20: ANNUAL MRI OF KIDNEYS (ABD/PELVIC CT WITH CONTRAST IS ALTERNATIVE). IF NO FAM HX AND 2-3 CLEAR SCANS, Q 2 YRS
HPRCC	**MET**	**UNCLEAR (HIGH) TYPE 1 PAPILLARY**	NO SPECIFIC GUIDELINES.
HLRCC	**FH**	**15-30%, TYPE 2 PAPILLARY**	FROM AGE 8: ANNUAL ABD MRI W/CONTRAST. ONCE A RENAL LESION IS IDENTIFIED, CT WITH/WITHOUT CONTRAST AND RENAL U/S.

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Take Home: Hereditary RCC Syndromes

- **4 Syndromes – VHL, BHD, HLRCC, HPRCC**
  - **All autosomal dominant**
    - **3 tumor suppressors (VHL, BHD, HLRCC)**
    - **1 oncogene (HPRCC)**
  - **Know the genes and histologies!**
    - **3p=VHL (clear cell), 17p=BHD (oncocytoma/chromophobe)**
      1q=HLRCC (type II pap = FH deficient RCC), 7q=HPRCC (type 1 pap)
  - **Misc**
    - **2 with skin manifestations (BHD, HLRCC)**
    - **1 with only renal manifestations (HPRCC)**
    - **pVHL complex regulates HIF1 and 2α (transcription factors)**
      - **Angiomas/hemangioblastomas, pancreatic cysts/tumors**
      - **pheochromocytomas, epididymal cystadenomas, ccRCC (#1 cause of death)**
    - **WilmsTumor = WT1/2 on 11p**

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Differential Dx and Pathology

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Differential Diagnosis of a Renal Mass

- **Benign**
  - **Infection**
    - Renal abscess, XGP, Malakoplakia
  - **Cysts**
    - Beware hyperdense cyst
    - ADPCK, MLCN
  - **AML** (fat poor)
  - **Oncocytoma**
  - **Vascular**
    - JGA, RA aneurysm, hemagioma, lymphangioma
  - **Perirenal**
    - Fibroma, adrenal adenoma/cyst
  - **Hydronephrosis**
    - May be segmental
    - Clots
  - **Pseudotumor** (column of Bertin)
    - DMSA Renal Scan
- **Malignant**
  - RCC variants
  - Collecting duct Ca
  - Urothelial
  - Lymphoma
  - Adult Wilms
  - Adrenal cortical Ca
  - Renal or RP sarcoma
  - Metastatic disease
    - Consider a biopsy
    - Should have other M+ sites

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Differential Dx - Clues

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- Fever, severe CVAT, + UA – pyelo, abscess
- "Problematic stones" – think XGP
- Spontaneous RP bleed – think RCC
- Look for fat – AML, liposarcoma
- Upper pole lesions – look at the adrenal
- Look at peri-renal soft tissues
- Ca^{++} round hilar lesion – think about a RA aneurysm
- Middle aged female – MLCN
- Solitary kidney central lesion – think pseudotumor
- Sickle cell trait – think medullary (SMARCB1 loss) carcinoma

- **DON'T DEPEND SOLELY ON THE RADIOLOGIST**
  - **Look at the films yourself!!**

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Components of RCC Pathology

- **Histology**
  - Cell type and origin
- **Nuclear grade**
  - Clear cell (Fuhrman classification (I – IV))
  - Papillary (type I and II)
- **Pathologic stage**
  - AJCC TNM classification (8th edition 2018)
- **Molecular pathology and cytogenetics**

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AUA Core Curriculum:

Benign Renal Mass

https:auau.auanet.org/core

Table 1. WHO Classification of Benign Renal Masses

Classification	Types
Epithelial Tumors	Onocytoma Papillary adenoma
Mesenchymal Tumors	Angiomyolipoma Leiomyoma Hemangioma Reninoma Schwannoma Lymphangioma
Mixed Epithelial and Mesenchymal Tumors	Mixed epithelial and stromal tumor Cystic nephroma
Metanephric Tumors	Metanephric adenoma Metanephric adenofibroma Metanephric stromal tumor

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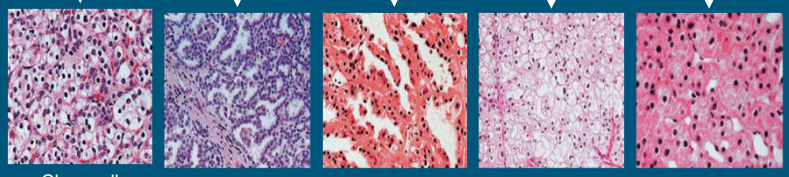
Histological Classification of Human Renal Epithelial Neoplasms

RCC



	Clear cell	Papillary type 1	Papillary type 2	Chromophobe	Oncocytoma
Type					
Incidence (%)	*75%*	*5%*	*10%*	*5%*	*5%*
Associated mutations	*VHL 3p*	*c-Met 7q*	*FH 1q*	*BHD 17p*	*BHD 17p*
Misc	***glycogen***				***central scar abundant mitochondria***

BHD=Birt-Hogg-Dubé, FH=fumarate hydratase, VHL=von Hippel-Lindau.

Modified from Linehan WM et al. *J Urol*. 2003;170:2163-2172.

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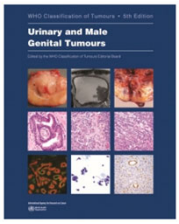

Evolving WHO Classification

2004 Edition

Renal cell tumors
Clear cell renal cell carcinoma
Multilocular clear cell renal cell carcinoma
Papillary renal cell carcinoma
Chromophobe renal cell carcinoma
Carcinoma of the collecting duct of Bellini
Renal medullary carcinoma
Xp11 translocation carcinoma
Carcinoma associated with neuroblastoma
Mucinous tubular and spindle cell carcinoma
Renal cell carcinoma, unclassified
Papillary adenoma
Oncocytoma

2016 Edition

Renal cell tumors
Clear cell renal cell carcinoma
Multilocular cystic renal neoplasm of low malignant potential
Papillary renal cell carcinoma
Chromophobe renal cell carcinoma
Collecting duct carcinoma
Renal medullary carcinoma
Mucinous tubular and spindle cell carcinoma
MiTF family translocation renal cell carcinomas
Hereditary leiomyomatosis and renal cell carcinoma-associated RCC
Tubulocystic renal cell carcinoma
Clear cell papillary renal cell carcinoma
Succinate dehydrogenase-deficient renal cell carcinoma
Acquired cystic disease-associated renal cell carcinoma
Renal cell carcinoma, unclassified
Papillary adenoma
Oncocytoma

2022 Edition

Renal cell tumors
Clear cell renal tumours
Clear cell renal cell carcinoma
Multilocular cystic renal neoplasm of low malignant potential
Papillary renal tumours
Papillary adenoma
Papillary renal cell carcinoma
Oncocytic and chromophobe renal tumours
Oncocytoma of the kidney
Chromophobe renal cell carcinoma
Other oncocytic tumours of the kidney
Collecting duct tumours
Collecting duct carcinoma
Other renal tumours
Clear cell papillary renal cell tumour
Mucinous tubular and spindle cell carcinoma
Tubulocystic renal cell carcinoma
Acquired cystic disease-associated renal cell carcinoma
Eosinophilic solid and cystic renal cell carcinoma
Renal cell carcinoma NOS
Molecularly defined renal carcinomas
TFE3-rearranged renal cell carcinomas
TFEB-altered renal cell carcinomas
ELOC (formerly *TCEB1*)-mutated renal cell carcinoma
Fumarate hydratase-deficient renal cell carcinoma
Succinate dehydrogenase-deficient renal cell carcinoma
ALK-rearranged renal cell carcinomas
SMARCB1-deficient renal medullary carcinoma

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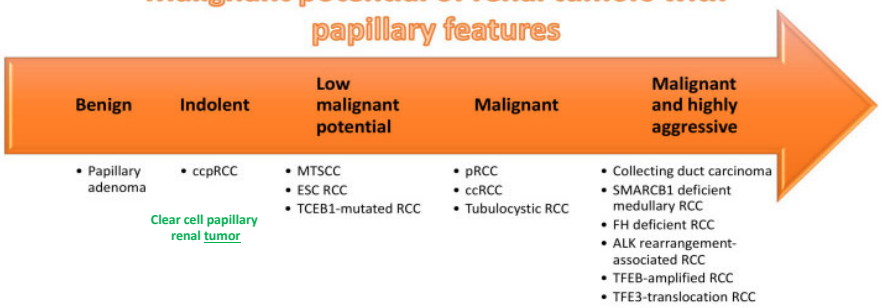
Malignant potential of renal tumors with papillary features



Lobo et al., *Biomedicines.* 2021

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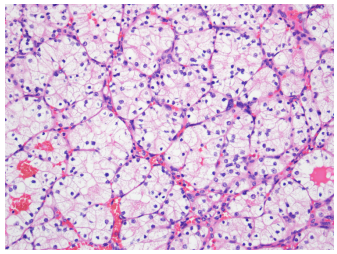
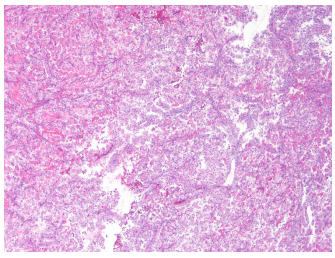
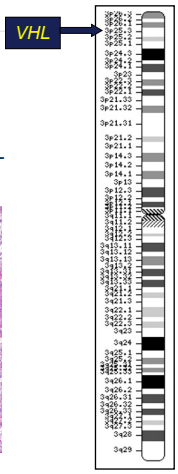
Clear Cell Renal Cell Carcinoma

- Most common form of renal cancer (60%-70%)
- Chromosome 3p alterations or mutation/hypermethylation of 3p25-26 (*VHL* gene) resulting in CAIX overexpression (of help diagnostically)







Alexander S. Taylor, Daniel E. Spratt, Saravana M. Dhanasekaran, Rohit Mehra; Contemporary Renal Tumor Categorization With Biomarker and Translational Updates: A Practical Review. *Arch Pathol Lab Med* 1 December 2019; 143 (12): 1477–1491. doi: https://doi.org/10.5858/arpa.2019-0442-RA; Image courtesy of Dr. Rohit Mehra

Advantage

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Grading and Staging

- WHO/ISUP grading has replaced Fuhrman grading and is applied to clear cell and papillary carcinomas only
- 8th edition AJCC staging is applied to all renal carcinomas and often correlates with outcomes

Advantage

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Papillary Renal Cell Carcinoma

- Approximately 15% of renal cancers (2nd most common type)
- Often multifocal, associated with adenomas (<1.5 cm)
- Trisomy of chromosomes 7 and 17, loss of chromosome Y

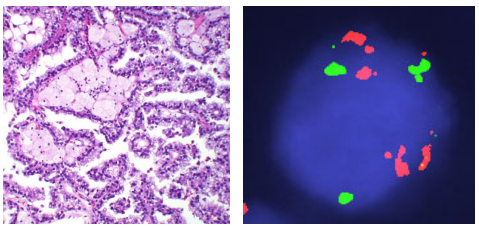


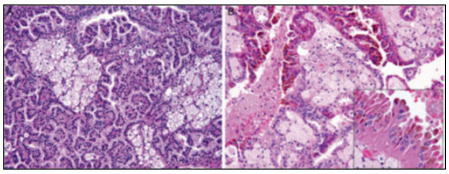
Image courtesy of Dr. Rohit Mehra

Advantage

36

Papillary RCC- Typing NOT Recommended

- PFS and CSS showed no significant association with the presence or amount of type 2 morphology
- 78% mutations shared between type 1 and type 2 areas
- chr 7/17 gains similar between type 1 and 2 areas
- PRCC with any classic type 1 regions best considered as type 1 PRCC



Murugan, P., Jia, L., Dinatale, R.G. *et al.* Papillary renal cell carcinoma: a single institutional study of 199 cases addressing classification, clinicopathologic and molecular features, and treatment outcome. *Mod Pathol* **35,** 825–835 (2022). https://doi.org/10.1038/s41379-021-00990-9

Advantage

37

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Nuclear Grading for RCC

- How much do cells look like "normal kidney cells"?
- Varies from I (low grade) to IV (high grade)
- Determinants of grade
  - Nuclear size
  - Irregularity of the nuclear membrane
  - Nucleolar (DNA) prominence
- Fuhrman grading/ISUP for conventional (clear cell)
- Type 1 (low) and Type 2 (high) for papillary

Fuhrman et al Am. J. Surg. Pathol., 6:655, 1982

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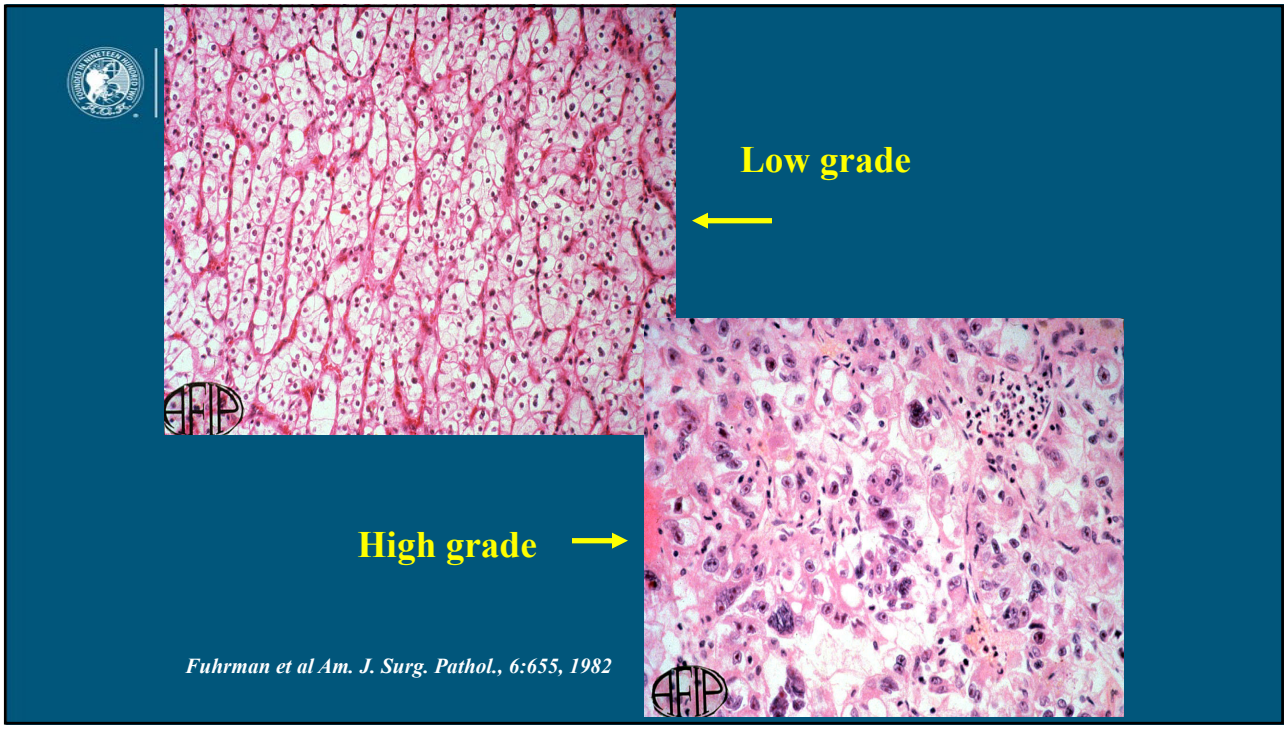

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Clinical Assays To Aid Diagnostic Work-Up

IHC and RNA-ISH as surrogate for genetic alterations/aberrations

- CA-IX IHC (VHL pathway)- Clear cell RCC.
- BRAF V600E IHC (mutation specific Ab) - Metanephric adenoma
- BAP1 IHC loss in RCC- mutation
- ALK IHC in RCC- translocation
- FH IHC - HLRCC associated RCC (genetic association)
- SDHB IHC - SDH deficient RCC (genetic association)
- VSTM2A RNA-ISH – MTSCC
- TRIM63 RNA-ISH- MiTF RCC

Advantage

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Clinical Assays To Aid Diagnostic Work-Up

Molecular assays

- FISH for TFE3/TFEB gene aberrations - MiTF RCC
- FISH for ALK-rearranged RCC
- FISH for trisomy 7/17- Papillary RCC
- FISH for 3p deletion- Clear cell RCC
- Clinical sequencing

(Targeted panel or Whole Exome DNA/RNA Sequencing)

Advantage

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Molecularly Defined Renal carcinomas

- TFE3-rearranged renal cell carcinomas
- TFEB-rearranged renal cell carcinomas
- ELOC (formerly TCEB1)-mutated renal cell carcinoma
- Fumarate hydratase-deficient renal cell carcinoma
- Succinate dehydrogenase-deficient renal cell carcinoma
- ALK-rearranged renal cell carcinomas
- SMARCB1-deficient renal medullary carcinoma

WHO Classification of Tumors
Urinary and Male Genital Tumors, 2022 Edition

Advantage

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Take Home - Differential Dx of Renal Masses

- Oncocytoma
- XGP
- MLCN
- Medullary carcinoma
- Pseudotumor
- RP bleed
- Collecting Duct Ca
- Clear cell RCC
- Sickle Cell trait/disease
- Glycogen
- Urothelium continuum
- Stone disease
- Mitochondria
- Undiagnosed Cancer
- Middle Aged Female
- Solitary kidney (DMSA)

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AUA Guidelines 2021

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AUA Guidelines 2021

(Published in 2 parts)

- Incorporates post treatment surveillance guidelines
- 45 guideline statements
- Evaluation and diagnosis (n=3)
- Counseling (n=6)
- Renal Mass Biopsy (n=4)
- Management
  - NSS (n=5)
  - RNx (n=1)
  - Surgical principles (n=5)
  - Thermal ablation (n=4)
  - Active Surveillance (n=4)
  - Followup after intervention (n=13)

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2021 RCC AUA Guidelines

- Continued emphasis on renal functional aspects/nephrology input
- Considerations for shared decision-making about AS explicitly defined
- Surgery:
  - Restricted role for RN, well defined selection criteria
  - Primary role for PN: T1a and otherwise
  - Selective utilization of TA: tumor <3 cm
- Adjuvant considerations
- Surveillance guidelines post treatment

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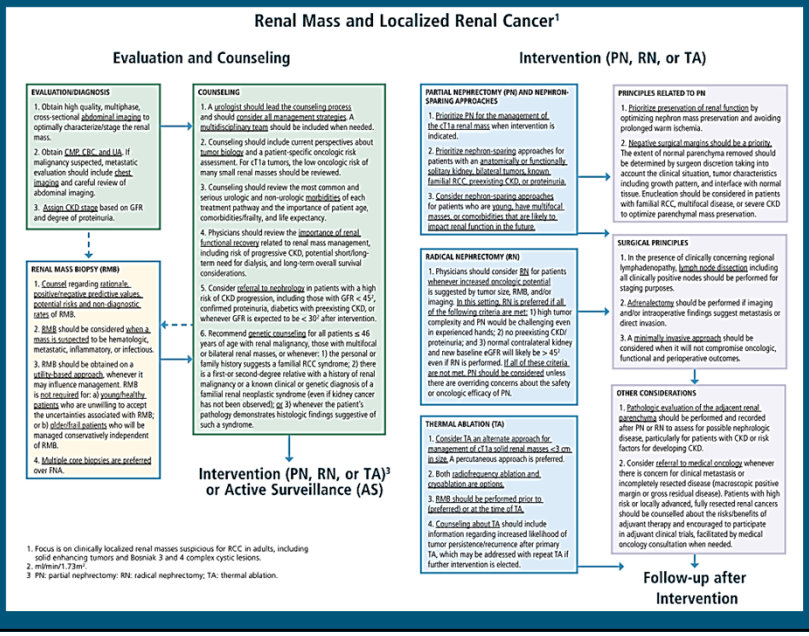
AUA Guidelines 2021



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Evaluation and Diagnosis: AUA 2021 guidelines

- **Detailed history/exam**
- **Laboratory evaluation**
  - **eGFR (creat), metabolic panel (Ca,$^{++}$ LFT), U/A (check for proteinuria)**
  - ***Assign CKD stage***
- **Radiographic evaluation:**
  - **AUA guidelines**
    - **CXR (Chest CT for symptoms or abnormal CXR)**
    - **Limited use of bone scan (pain, elevated alk phos or declining PS)**
    - **Limited use of head scan (neurologic symptoms)**
    - **Renal scan – not in the guidelines**
    - ***>90% M+ disease seen on CT A/P and CXR***
  - **Multiphase cross sectional imaging**
    - **Understand renal and intrarenal anatomy**
    - **Rarely need arteriography, Venography, MRA/MRV**
    - ***Assess tumor complexity/lesion for fat***
  - **NO DEFINED ROLE FOR PET SCANS (??G250 or sestamibi scan??)**

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KDIGO Classification of CKD Risk (2012)

Renal dysfunction that has persisted >3 months as defined / classified by:

1. Glomerular filtration rate (CKD-EPI GFR equation)
2. Proteinuria
3. Etiology of CKD

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. *Kidney Int Suppl 3:1, 2013*

Prognosis of CKD by GFR and albuminuria category

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
GFR categories (ml/min/ 1.73 m²) Description and range	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

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Renal Imaging

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Imaging of the Renal Mass

- **Mandatory**
  - CT scan
    - Three phases (pre/arterial/delayed)
    - Enhancement > 20HU
  - MRI
    - Pre/post gadolinium – r/o enhancement (> 20% increase ROI)
    - Often makes the lesion look worse than on CT
- **Optional**
  - Ultrasound – cyst vs solid (beware of hyperdense cyst – use doppler)
  - Vascular invasion –
    - Angiogram, venogram supplanted by MRI, TEE, 3D – CT
  - Renal function - MAG-3 renal scan used sparingly
  - Metastases - Bone scan, Head CT, Chest CT as clinically indicated
- **fdg-PET scan *rarely* useful**
  - Sensitivity low

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Cystic Renal Lesions

Bosniak Class	Cancer Risk	Rx	Comments
I (simple cyst)	0%	none	No enhancement Smooth, empty, HU<10
II May be hyperdense (protein/blood)	<10-20%	None or follow (IIF)	Few septa, HU <10 Thin linear Ca^{++}
III (Indeterminate)	50-60%	Remove	Thick irregular wall, HU > 15 Thick Ca^{++} Moderate septa May enhance
IV (Cystic RCC)	90+%	Remove	Enhancing nodules HU >15

Bosniak is CT based (not US)

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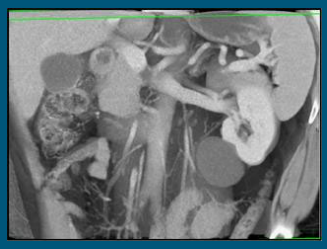
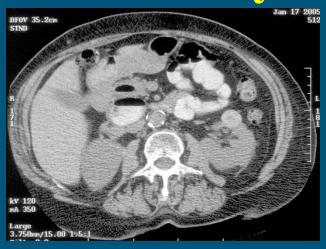
Bosniak Classification - Renal Cysts

I



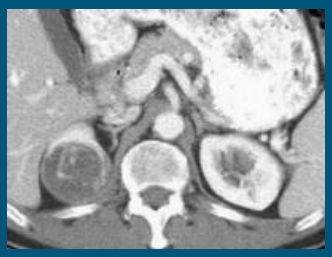
II



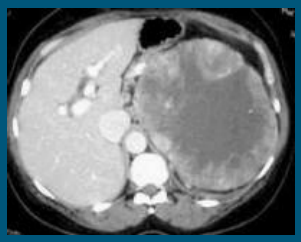
Cyst <20HU on precon studies

Hyperdense Cyst >70HU on precon studies

III



IV



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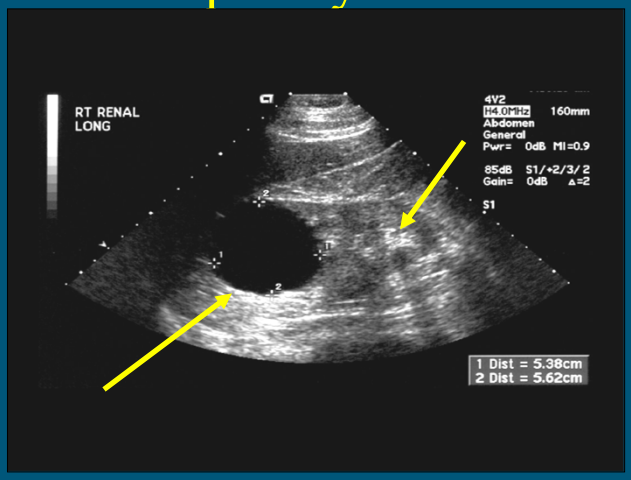
Simple Cyst on US



Full through transmission
No internal echoes
Posterior wall enhancement (bright)
- sharp acoustic interface

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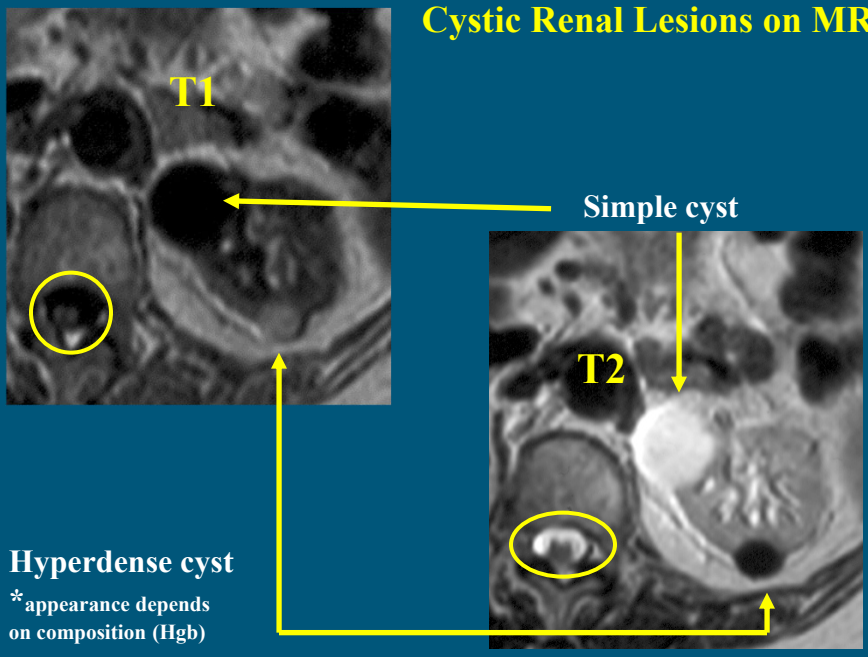
Cystic Renal Lesions on MRI



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Appearance of Fat

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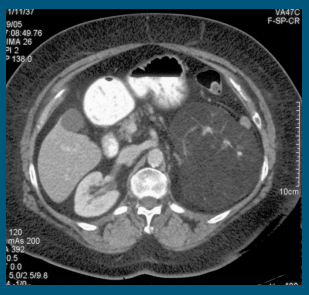
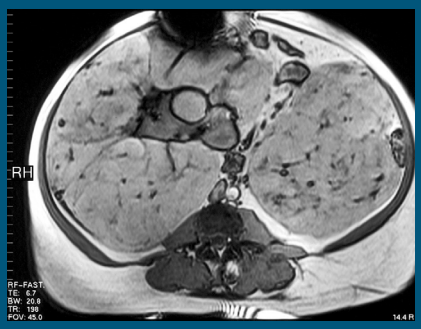
Look at surrounding tissues you know are made of fat
- Perirenal fat or renal sinus fat

US – Hyperechoic (white)
CT – low HU (black)
MRI – depends on technique used
- Generally bright





TSC1 = 9q34.3

TSC2 = 16p13.3

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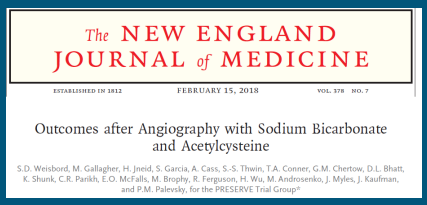
Risk of Contrast Agents

- IV contrast
  - Contrast allergy (provide steroid/anti-histamine preparation)
  - Nephrotoxicity
    - No absolute Creat/eGFR established (our lower cutoff b/w 30-40 cc/min)
    - Risk factors include Myeloma, diabetes, CRI, ***use of metformin (no longer)***
    - To decrease the risk – HYDRATE, use lower dose non-ionic or low osmolar contrast. [Acetylcystine 600 po BID of unproven benefit]


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 15, 2018 VOL. 378 NO. 7

Outcomes after Angiography with Sodium Bicarbonate and Acetylcysteine

S.D. Weisbord, M. Gallagher, H. Jneid, S. Garcia, A. Cass, S.-S. Thwin, T.A. Conner, G.M. Chertow, D.L. Bhatt, K. Shunk, C.R. Parikh, E.O. McFalls, M. Brophy, R. Ferguson, H. Wu, M. Androsenko, J. Myles, J. Kaufman, and P.M. Palevsky, for the PRESERVE Trial Group*

- N=5177 pts at high risk of renal complications (eGFR 15-45 or 45-60 with DM)
- Intra-arterial contrast!
- Randomized to iv bicarb vs iv NS + acetylcystine vs placebo
- Stopped early = no difference
- 4.5% rate of death/HD/ 50% increase Scr at 90d

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Risk of Contrast Agents

- Gadolinium (Many different agents in use)
  - Risk of Nephrogenic Systemic Fibrosis and fibrosing … associated with Gadolinium
  - Appears related primarily to ch…
    - Can occur …

Current ACR guidelines state that patients ***need not be screened for renal function*** prior to receiving group II gadolinium-based agents (eg Multihance)

…ntial some linear GBCA … risk and can be used safely in patients

…mates have highest risk of NSF

- Cumulative Effects on Cognitive Function unknown/unproven

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Slide 58

URG1 See new AUA guidelines where I wrote:
Uzzo, Robert G, 1/3/2021

URG2 The risks and benefits of the diagnostic study should be considered, including risks of radiation exposure (CT) and contrast administration to include contrast-induced nephropathy, or allergic reactions. Patients with eGFR <45 ml/min/1.73m2 undergoing CT with intravenous contrast should be considered for peri-procedural hydration. Administration of intravenous contrast should be avoided if possible in patients with severe CKD who are nearing dialysis. Administration of intravenous contrast can be used judiciously in patients on hemodialysis and timed just prior to receiving dialysis in coordination with nephrology. MRI is appropriate for patients with contraindications to iodinated contrast and may provide improved characterization of small renal tumors, particularly those less than 2 cm in diameter. The risks of gadolinium based contrast agents (GBCA) in patients with altered renal function have been of great interest since the description of Nephrogenic Systemic Fibrosis, a potentially lethal fibrosing dermopathy associated with soft tissue deposition and accumulation of gadolinium. (reference xcii from prior version). The risk appears related to the isoform of gadolinium used with group I GBCA agents ((Gadodiamide (Ominiscan®), Gadopentatate dimeguline (Magnevist®) and Gadoversetmide (OptiMark®)) having the highest risk while group II GBCA ((Gadobenate dimeglumine (MultiHance®) – Gadoteridol (ProHance®) – Gadoteric acid (Dotarem®) – Gadobutrol (Gadavist®)) associated with few if any unfounded cases of NSF. A recent systematic review of the risks of NSF in patients with CKD 4 and 5, noted the risks of NSF using group II GDCA was less than 0.07%. Current ACR guidelines on the use of contrast media state that patients need not be screened for renal function prior to receiving group II GBCA which are now considered safe at any level of eGFR.
Uzzo, Robert G, 1/3/2021

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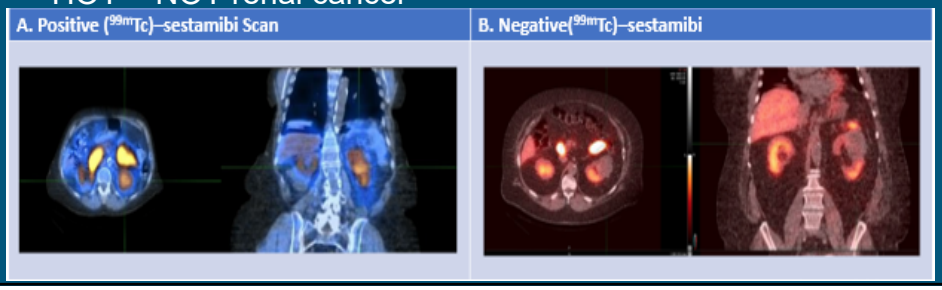
Sestamibi Scan

- Technetium-99m (^{99m}Tc)–sestamibi SPECT/CT
- May differentiate oncocytomas and hybrid oncocytic/chromophobe tumors (HOCTs) from renal cell carcinomas (RCC) on basis of mitochondrial concentration
- HOT = NOT renal cancer



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Paraneoplastic syndromes

Risk is about 20%

Cachexia/Fever (cytokines)	20-33%
Nephropathy (Ig formation)	27%
HTN (renin)	25%
Hypercalcemia -metastatic -non-metastatic (PTH like)	20%
Anemia (cytokine myelosuppression)	20-40%
Hyperglycemia	10-20%
Stauffer's* (? IL6)	3-20%
Erythrocytosis (epo)	1-8%
Amyloidosis	3-5%

*Non-metastatic hepatic dysfunction

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Rx of Malignant Hypercalcemia

- Mechanisms of malignant hypercalcemia
  - Tumor secretion of parathyroid related hormone
  - Osteolytic metastases with local release of cytokines
  - Tumor production of 1, 25 dihydroxy Vitamin D (calcitrol)
- Treatment:
  - Involve endocrinology

Treatment of hypercalcemia

Intervention	Mode of action	Onset of action	Duration of action
Isotonic saline hydration	Restoration of intravascular volume Increases urinary calcium excretion	Hours	During infusion
Calcitonin	Inhibits bone resorption via interference with osteoclast function Promotes urinary calcium excretion	4 to 6 hours	48 hours
Bisphosphonates	Inhibit bone resorption via interference with osteoclast recruitment and function	24 to 72 hours	2 to 4 weeks
Loop diuretics*	Increase urinary calcium excretion via inhibition of calcium reabsorption in the loop of Henle	Hours	During therapy
Glucocorticoids	Decrease intestinal calcium absorption Decrease 1,25-dihydroxyvitamin D production by activated mononuclear cells in patients with granulomatous diseases or lymphoma	2 to 5 days	Days to weeks
Denosumab	Inhibits bone resorption via inhibition of RANKL	4 to 10 days	4 to 15 weeks
Calcimimetics	Calcium-sensing receptor agonist, reduces PTH (parathyroid carcinoma, secondary hyperparathyroidism in CKD)	2 to 3 days	During therapy
Dialysis	Low or no calcium dialysate	Hours	During treatment

UpToDate 2018

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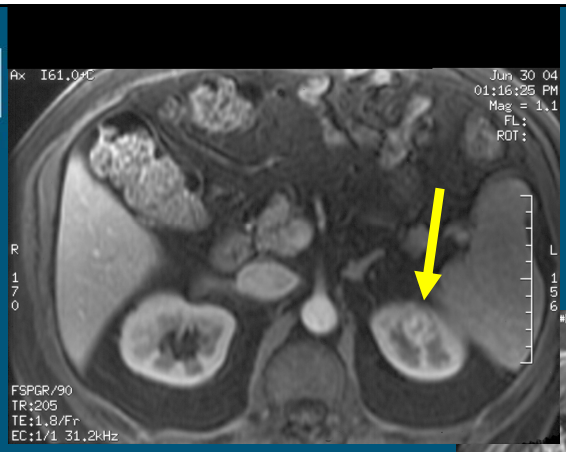
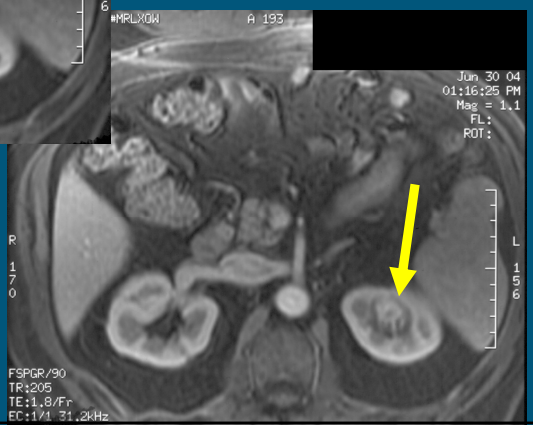
HTN and renal masses

63 yo poorly controlled HTN
- 5 meds
- Scr -1.6
- GFR – 47 cc/min
- MRA – no RAS





- Left NSS with IOUS
- Pathology c/w JG apparatus tumor
- Post op BP 130/70 on 2 meds

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Urological causes of HTN

- **RAS**
  - Atherosclerosis
  - FMD
- **Adrenal causes**
  - Pheochromocytoma
  - Hyperaldosteronism
  - Cushing's syndrome
- **Renal (JGA) tumors**

Renin levels

JGA cell tumors are rare – most commonly benign
- pts usually young (<30), hypokalemia, HTN, polydipsia, polyuria

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Counseling : AUA 2021 guidelines

- **Counseling should include:**
  - **Assessment of tumor biology**
    - The low oncologic risk of many SRMs (cT1a) should be reviewed
  - **Patient-specific risk assessment including:**
    - Gender, tumor size/complexity, histology (when obtained), imaging characteristics
  - **Most common and serious urologic and non-urologic morbidities of Rx**
    - importance of patient age, comorbidities/frailty, and life expectancy
  - **Risk of progressive CKD**
    - consider referral to nephrology if high risk of CKD progression
      - eGFR < 45, confirmed proteinuria, diabetics, whenever eGFR post Rx is expected to be < 30
  - **Genetic counseling for all RCCs <46 years old**

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Renal Mass Biopsy: AUA 2021 guidelines

- **Consider** if suspect hematologic, metastatic, inflammatory, or infectious
- **Not required** for:
  - Young or healthy patients who are not willing to accept the uncertainties associated with RMB
  - Older or frail patients who will be managed conservatively independent of RMB findings
- Multiple **core biopsies** are preferred over fine needle aspiration

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Renal Mass Biopsy: AUA 2021 guidelines

- **Needle biopsy is very safe**
  - Minor complication rates
    - 1% symptomatic complications with <2% requiring intervention
  - Very ***LOW RISK*** of seeding – no contemporary cases reported cases
- **Biopsy is accurate in determining presence of RCC**
  - Sensitivity = 97%; specificity 94%; PPV 99%; NPV = 81%
  - Non-diagnostic rate 14% (get a core not an FNA)
    - Repeat biopsy if non-diagnostic
  - Histology more difficult ("oncocytic tumor") but >80%
  - **Worse at predicting nuclear grade**
    - 30-60% accurate on nuclear grade
    - Underestimation more problematic (overestimated in <10%)
- ***Lowering biopsy threshold***
  - ***Especially in the elderly, infirmed and solitary/poorly functioning kidney***

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AUA Core Curriculum

https://auau.auanet.org/core

Table 3. Contemporary Outcomes from Renal Mass Biopsy Series Using an 18 Gauge Needle Technique

		Accuracy (%)				
Series	Number of Tumors	Diagnosis	Malignancy	RCC Subtype	Grade	Complications (%)
Lebret et al.[83]	119	79	86	86	74*	0
Maturen et al.[84]	152	96	Sensitivity 97.7 Specificity 100	N/A	N/A	1.3
Shannon et al.[85]	235	78	100	98	N/A	0.9
Volpe et al.[15,16]	100	84	100	100	75*	1.0
Wang et al.[17]	110	90.9	100	96.6	NR	1.8
Veltri et al.[86]	150	100	N/A	93.2	NR	0
Leveridge et al.[87]	345	80.6	99.7	88	63.5	0.3

Restricted to series with at least 100 biopsies performed for brevity

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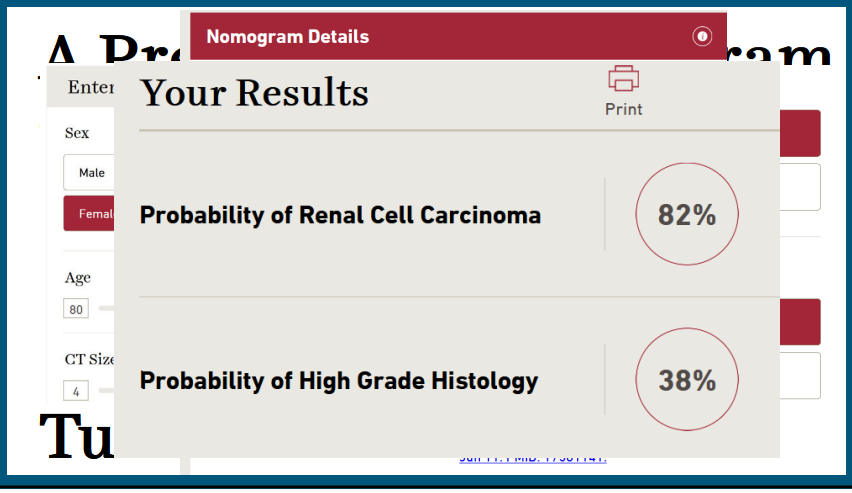
Am Urc Ass Edu

Assessing Risk in RCC: www.cancernomograms.com

Cancer Prediction Tools

Request a New Prediction Tool



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Complexity and Staging

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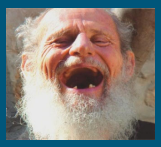
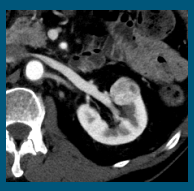
Tumor complexity - www.nephrometry.com

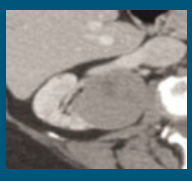
Not all patients pose the same surgical risk….

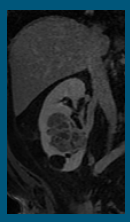
≠

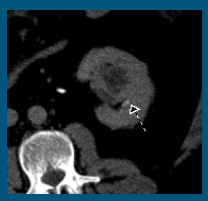


Not all tumors pose the same surgical risk….









AUA guideline statements # 1 and 5 - Evaluation and Counseling
Include discussion of tumor complexity

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TNM v8: T stage

T1a – Tumor ≤ 4 cm

T1b – Tumor 4 < x ≤ 7 cm

T2a: Tumor 7< x ≤ 10 cm, limited to kidney

T2b: Tumor > 10 cm, limited to kidney

T3a: Perirenal fat and/or renal sinus fat and/or invasion of renal vein or segmental branches (muscle containing) and/or pelvicalyceal system

T3b: Venous invasion of IVC below the diaphragm

T3c: IVC above diaphragm; invasion of IVC wall

T4: Tumor invades beyond Gerota's fascia or contiguous extension involving the ipsilateral adrenal

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AJCC - TNM Staging RCC

- **Regional Lymph Nodes (N)**
  - **Nx – regional nodes cannot be assessed**
  - **N0 – no regional nodal involvement**
  - **N1 – metastasis in a single regional LN**
- **Distant Metastases (M)**
  - **Mx – distant metastases cannot be assessed**
  - **M0 – no distant metastases**
  - **M1 – distant metastases**

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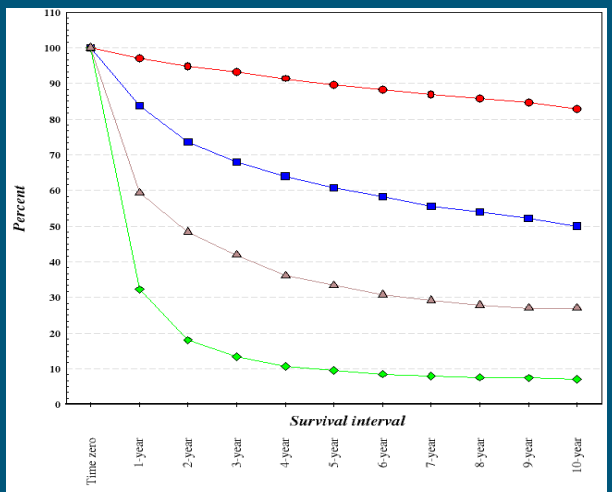
RCC Survival Rates by Stage at Diagnosis



Tumor sub-staging is an important prognostic variable

www.seer.cancer.gov

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Management for Localized RCC

(2021 AUA Guidelines + clinical pearls)

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www.auanet.org/guidelines

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Management of localized RCC

- **Excise**
  - Radical vs Partial
    - renal functional and metabolic implications
  - Open vs MIS
    - Complications and warm ischemic times
- **Ablate**
  - *Per AUA guidelines – need a pre-ablation biopsy*
  - Long term results unclear (median follow-up of all studies <24 mo.)
  - Parameters of success unknown
  - Ability to surgically salvage (difficult)
  - Does it change the natural history of the disease?????
- **Observe**
  - A short to intermediate term strategy
  - For elderly and vulnerable
  - Can you miss a window for cure?
    - Delayed intervention possible

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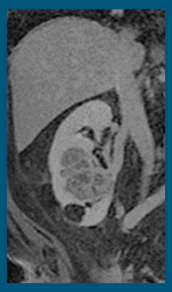
Radical/Partial vs Ablation vs Surveillance?

Patient Factors:
- Age
- Co-morbidities (PS)
- eGFR

Radiographic Factors:
- Size
- Location (hilar)
- Depth



Economic Factors:
- LOS
- Costs/work loss

Physician Factors:
- Training/Experience
- Biases

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NSS Management Principles : AUA 2021 guidelines

- **Prioritize Partial nephrectomy**
  - for the management of the cT1a renal mass
  - in anatomic or functionally solitary kidney, bilateral tumors, known familial RCC, preexisting CKD, or proteinuria
- **Consider Partial Nephrectomy**
  - in young pts
  - multifocal masses,
  - comorbidities likely to impact renal function in the future

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NSS Management Principles : AUA 2021 guidelines

- Prioritize preservation of renal function through **optimizing nephron mass preservation and avoidance of prolonged warm ischemia**
  - The exact threshold of warm ischemia at which irreversible damage begins to occur is not well defined, although most studies suggest approximately 25-30 minutes
- **Negative surgical margins** should be a priority
  - Precise extent of normal parenchyma removed should be determined by surgeon discretion
  - Consider tumor enucleation in patients with familial RCC, multifocal disease, or severe CKD

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RNx and Surgical Principles : AUA 2021 guidelines

- **Consider RN** if increased oncologic potential is suggested by:
  - tumor size, RMB, and/or imaging characteristics
  - In this setting, RN is preferred ***if all of the following criteria*** are met:
    - high tumor complexity and PN would be challenging even in experienced hands
    - no preexisting CKD or proteinuria
    - normal contralateral kidney and **new baseline eGFR will likely be >45**
- **Staging LN** dissection if clinically concerning lymphadenopathy
- **Adrenalectomy** if imaging and/or intraoperative findings suggest involvement
- **Consider MIS** if it doesn't compromise oncologic, functional and perioperative outcomes
- **Assess pathology** of adjacent renal parenchyma

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RNx and Renal Function: AUA 2021 Guidelines

- Mean change eGFR with RNx (25–40ml/min)
- Mean change eGFR with PNx (2-10ml/min)
- Depends on age and preexisting renal function
  - Mean risk of CKD3+ with RNx (30-60%)
  - Mean risk of CKD3+ with PNx (10-25%)

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Pearls for Resection

- Open approach increasingly uncommon
  - Very large (>20cm)
  - Extensive nodal or vein invasion
- Lymphatic drainage variable
  - Lymphadenectomy diagnostic not therapeutic
    - Remove any clinical/radiographically abnormal nodes (don't just pluck!!)
  - EORTC 30881 (4% of cN0 nodes are pN+)
- Adrenalectomy not routine - direct extension very unusual
    - Remove adrenal ONLY if radiographically abnormal or renal vein involvement
    - Unnecessary in large upper pole tumors if radiographically normal

(O'Malley et al J Urol 181; 2009)

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Open Approach

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- Arterial control
  - Ligate artery first (end artery)
  - Pre-op angioinfarction (uncommonly needed/helpful)
    - Difficult hilum (excessive nodal disease)
      - *Subramanian et al Urol May 2009 CCF n=225)*
- Venous Control
  - IVC thrombus (cast vs invasive clot)
  - Technique depends on level (note relation to hepatic veins)
    - Milk it back, mobilize liver (transplant), veno-veno, circulatory arrest
  - Pre-operative MRA/MRV
    - Intra-operative TEE helpful with clots above hepatic veins

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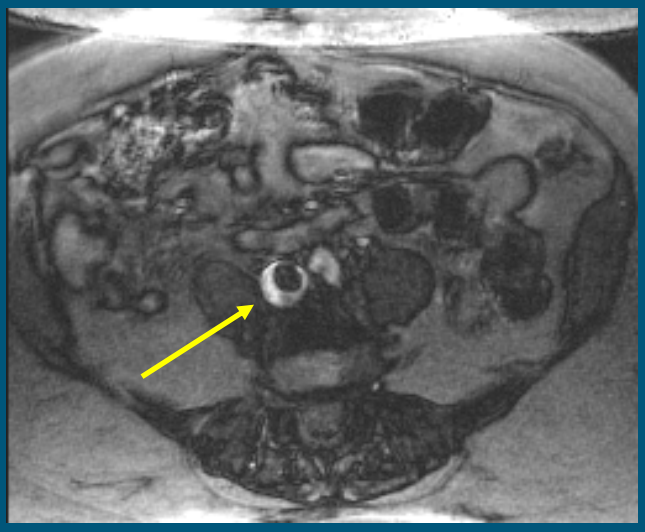

Clot usually low on T1 and T2
Bland thrombus does not enhance
Tumor thrombus may enhance

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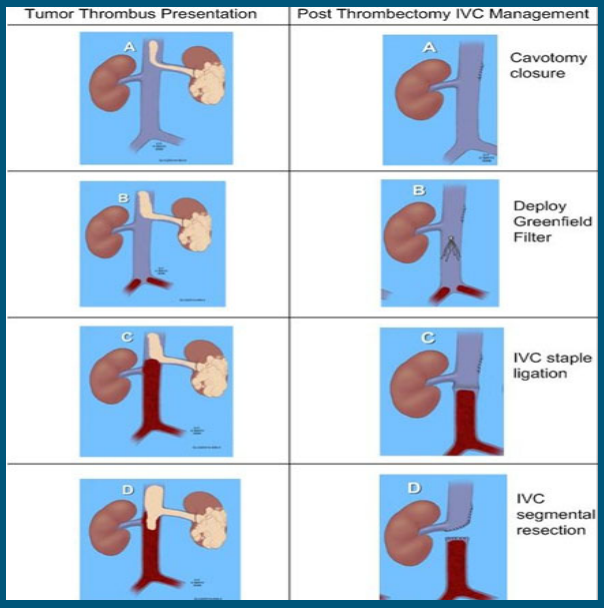
Handling Tumor Thrombus



- **Remove all tumor clot**
- **Leave bland clot**
- **Minimize risk of migration (filter or ligation)**

Blute et al J Urol 2007

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Anticoagulation and Renal Surgery

COLLECTIVE REVIEW

American College of Surgeons' Guidelines for the Perioperative Management of Antithrombotic Medication

Check for updates

Table 4. Summary of Recommended Perioperative Anticoagulation Management Strategies

Category	High bleeding risk procedure	Low bleeding risk procedure
High thromboembolic risk		
Warfarin	Give last dose 6 d before operation, bridge with LMWH or UFH, resume 24 h postoperatively.	Give last dose 6 d before operation, bridge with LMWH or UFH, resume 24 h postoperatively.
DOAC	Give last dose 3 d before operation,* resume 2 to 3 d postoperatively.	Give last dose 2 d before operation,* resume 24 h postoperatively.
Intermediate thromboembolic risk		
Warfarin	Give last dose 6 d before operation, determine need for bridging by clinician judgment and current evidence, resume 24 h postoperatively.	Give last dose 6 d before operation, determine need for bridging by clinician judgment and current evidence, resume 24 h postoperatively.
DOAC	Give last dose 3 days before operation,* resume 2 to 3 d postoperatively.	Give last dose 2 d before operation,* resume 24 h postoperatively.
Low thromboembolic risk		
Warfarin	Give last dose 6 d before operation, bridging not recommended, resume 24 h postoperatively.	Give last dose 6 d before operation, bridging not recommended, resume 24 h postoperatively.
DOAC	Give last dose 3 d before operation,* resume 2 to 3 d postoperatively.	Give last dose 2 d before operation,* resume 24 h postoperatively.

*In patients with CrCl < 50 mL/min on dabigatran, the last dose should be given 3 d before the procedure for low bleeding risk surgery, and 4 to 5 d before the procedure for high bleeding risk operation.
DOAC, direct oral anticoagulant; LMWH, low-molecular-weight heparin; UFH, unfractionated heparin.

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Take Home Message: Excision of Localized RCC

- **Excision most time tested primary Rx**
- **Open/MIS/Partial/Radical**
  - **Cancer metrics equal (local recurrence, CSS)**
  - **Perioperative complications differ**
  - **In most patients long term benefits favor nephron preservation**
- **Partial Nx feasible for most stage I/II RCC**
  - **Functionally superior (calculate eGFR/CKD stage preop)**
  - **Benefit of NSS on OS not fully understood**
- **Objectify difficulty/Risks – Nephrometry**
- **Judicious ischemia (<30 min warm ischemia)**
  - **Quality/quantity of parenchyma most important**

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Ablation for Stage I RCC: Concerns

- An alternate approach for the management of cT1a renal masses <3cm in size
- RFA and cryoablation are equivalent options
- Need a preoperative biopsy per AUA guidelines
- Collective long term data less than AS
  - mean follow-up <36-48 mo.
- No validated oncologic endpoints measured
  - Lack of enhancement ≠ DFS
  - Persistent/local recurrence 10-15%
  - Effect on natural history of SRM unknown
- Complication rates underreported and not inconsequential

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Active Surveillance and Expectant Management : AUA 2021 guidelines

- For pts with small solid or Bosniak 3/4 complex cystic renal masses, especially those <2cm, AS is an option for initial management
- Prioritize AS/expectant management when:
  - the anticipated risk of intervention or competing risks of death outweigh the potential oncologic benefits of active treatment

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Active Surveillance and Expectant Management : AUA 2021 guidelines

- If risk/benefit analysis for Rx is equivocal and prefer AS:
  - repeat imaging in 3-6 months to assess for interval growth
  - consider RMB for additional risk stratification
- If anticipated oncologic benefits of Rx outweigh the risks of Rx and competing risks of death, physicians should recommend active treatment.
  - Pursue AS only if the patient understands and is willing to accept the associated oncologic risk.

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Active Surveillance and Expectant Management : AUA 2021 guidelines

FACTORS FAVORING AS/EXPECTANT MANAGEMENT

Patient-related	Tumor-related
Elderly Life expectancy <5 years High comorbidities Excessive perioperative risk Frailty (poor functional status) Patient preference for AS Marginal renal function	Tumor size < 3cm Tumor growth < 5mm/year Non-infiltrative Low complexity Favorable histology Predominantly cystic

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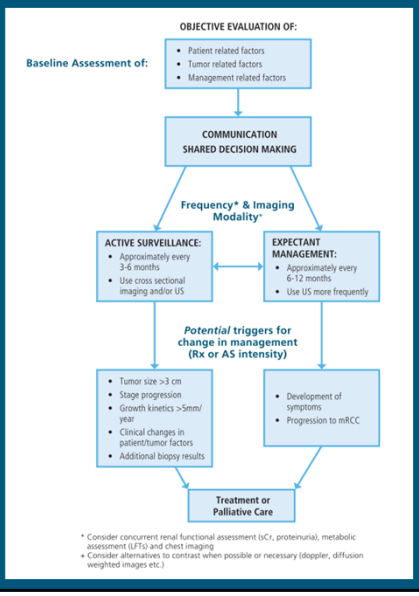
Active Surveillance and Expectant Management : AUA 2021 guidelines



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Growth and Progression of RCC under Active Surveillance

(18 non-redundant studies)

N	Median Growth Rate (cm/yr)	Range Median F/U Duration (mo.)	# progressed to mRCC
880	0.08 – 0.58	20-41	17 (1.9%)

Overall Mean follow-up = 34 months

Most useful in elderly and infirmed

Smaldone, Uzzo Cancer 118: 2012

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Post Operative Care
Complications
Surveillance

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Complications of Renal Surgery

- **Medical**
  - Perioperative
  - Include AUA guidelines for DVT prophylaxis
    - ASA may be used in pts with relative or absolute indications
- **Surgical**
  - Hemorrhage (adrenal) – beware of solitary adrenal!
  - Adjacent organ injury (pancreas on left esp. upper pole)
    - High intra/post-op index of suspicion (prolonged ileus/drain context)
    - Consult and drain
    - Slow with diet
  - Leak (5-25% depending on complexity and studies)
  - Delayed strictures

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Major Urologic Complications

MIS PN (9.0%)
OPN (6.3%)
RFA (6.0%)
Cryo (4.9%)
LRN (3.4%)
ORN (1.3%)

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Drains and Urinary Fistula

- Foley x 24h to prevent CAUTI
  - May continue in male pts with renal leak and BPH
- Drain management depends on:
  - Intraoperative course, outputs, ischemic time
    - Beware of delayed ATN and delayed leak
- JJ if outputs are >2-300/24hrs
  - Rule out obstruction
- Otherwise expectant management
  - Very rare not to close unless obstructed

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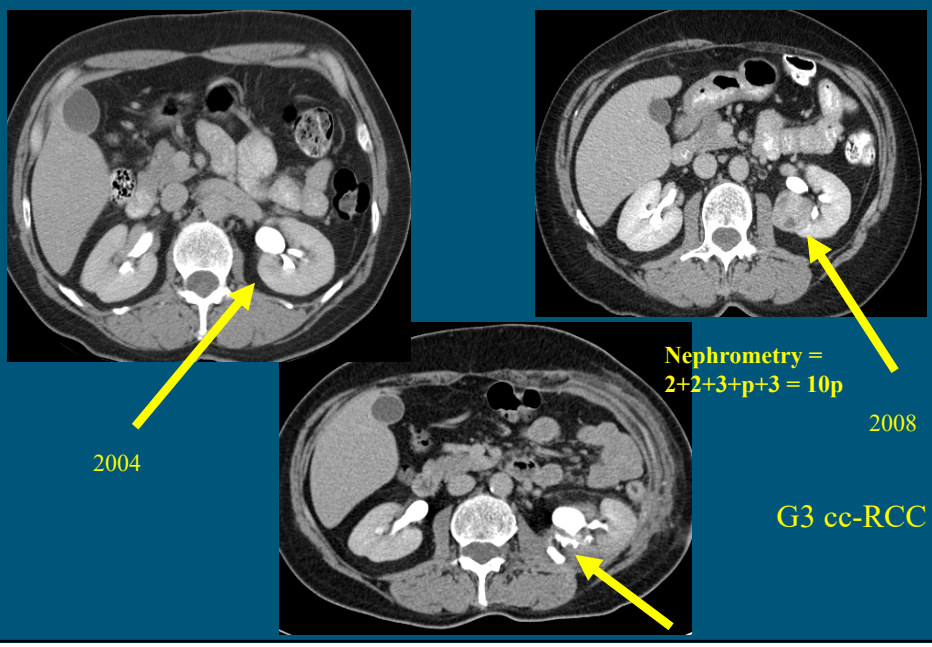
Drains and Urinary Fistula



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Recurrent RCC

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- ***Renal*** **recurrences:**
  - **0-7% ipsilateral renal risk following NSS**
  - **1-5% contralateral renal risk**
- ***Non-renal metastases*** **occur anywhere**
  - **Median time to recurrence 1-2 years (delayed >10+yrs possible)**
  - **50-80% of metastases are asymptomatic**
  - **> 70% identified on CXR and abdominal CT**
  - RCC pts from Nationwide Inpatient Sample, 1998 – 2007; 11,157pts
  - Most common sites
    - **Lung (45%)**
    - **Bone (30%)**
    - **LN (22%)**
    - **Liver (20%)**
    - Adrenal (9%)
    - Brain (8%)

Bianchi et al Ann Onc 2011

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Risk of recurrence following Surgery of localized RCC

	N	Primary outcome	Path Variables	Other Variables
UISS	477	OS	TNM Grade	PS
MSKCC	701	PFS	TNM Grade necrosis	Size Symptoms
D-SSIGN	1560	CSS	TNM Grade Necrosis	Size
Leibovich score	1671	PFS	TNM Grade Necrosis	Size
Karakiewicz	2474	CSS	TNM	Size Age Gender symptoms

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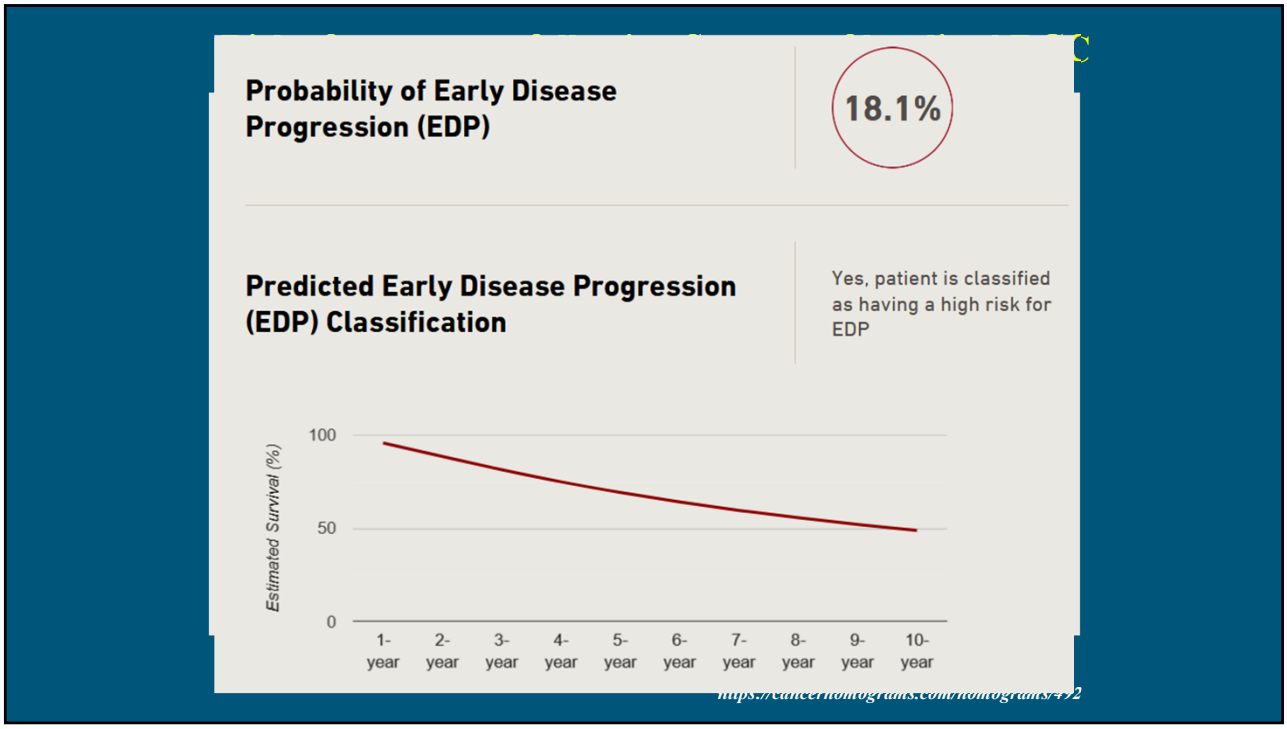

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AUA 2021 Guidelines Surveillance post Rx

Follow-up after Surgery or Thermal Ablation

FOLLOW-UP AFTER SURGERY

1. Patients who have been managed with surgery (PN or RN) for a malignant renal mass should be classified into one of the following risk groups for surveillance:

Low Risk (LR):	**pT1 and Grade 1/2**
Intermediate Risk (IR):	**pT1 and Grade 3/4 or pT2 any Grade**
High Risk (HR):	**pT3 any Grade**
Very High Risk (VHR):	**pT4 or pN1, or sarcomatoid/rhabdoid dedifferentiation, or macroscopic positive margin**

If final microscopic surgical margins are positive for cancer, the risk category should be considered at least one level higher, and increased clinical vigilance should be exercised.

2. Patients managed with surgery (PN or RN) for a renal malignancy should undergo abdominal imaging according to Table 1, with CT or MRI pre- and post-intravenous contrast generally preferred. After 2 years, abdominal ultrasound alternating with cross-sectional imaging may be considered in the LR and IR groups at physician discretion. After 5 years, informed/shared decision-making should dictate further abdominal imaging.

3. Patients managed with surgery (PN or RN) for a renal malignancy should undergo chest imaging (CXR for LR and IR, and CT chest generally preferred for HR and VHR) according to Table 1. After 5 years, informed/shared decision-making discussion should dictate further chest imaging and CXR may be utilized instead of chest CT for HR and VHR.

FOLLOW-UP AFTER THERMAL ABLATION

1. Patients undergoing ablative procedures with biopsy that confirmed malignancy or was non-diagnostic should undergo pre- and post-contrast cross-sectional abdominal imaging within 6 months (if not contraindicated). Subsequent follow-up should be according to the recommendations for the intermediate risk (IR) postoperative protocol (Table 1).

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AUA 2021 Guidelines Surveillance post Rx

TABLE 1: FOLLOW-UP PROTOCOLS BASED ON MONTHS AFTER SURGERY FOR RENAL CANCER *

RISK	3	6	9	12	18	24	30	36	48	60	72-84	96-120
LR				X		X			X	X	X	X
IR		X		X		X		X	X	X	X	X
HR		X		X	X	X	X	X	X	X	X	X
VHR	X	X	X	X	X	X	X	X	X	X	X	X

*Follow-up timeline is approximate and allows flexibility to accommodate reasonable patient, caregiver, and institutional needs. Each follow-up visit should include relevant history, physical examination, laboratory testing and abdominal and chest imaging. Overall, 30% of renal cancer recurrences after surgery are diagnosed beyond 60 months. Informed/shared decision-making should guide surveillance decisions beyond 60 months.

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Advanced Disease

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Adjuvant RCC Trials: The Middle Ages

"Incompletely effective surgery with more effective systemic therapy"

Trial	N	Clear Cell Only?	Duration of RX (years)	1° endpoint
ASSURE Sorafenib/Sunitinib	1943	No	1	DFS HR = 1.02 No change in DFS/OS
S-TRAC Sunitinib	615	Yes	1	DFS HR = 0.76 Improved DFS but not OS
SORCE Sorafenib	1656	No	1 vs. 3	DFS
PROTECT Pazopanib	1538	Yes	1	DFS HR 0.86 OS HR 0.79 P>0.05 for ITT 600mg
ATLAS Axitinib	700	Yes	3	DFS DMS stopped (futility)
ARISER G250	864	Yes	25 weeks	DFS and OS HR 0.97 and 0.99 No change in DFS/OS
EVEREST Everolimus	1537	No	1 (9 cycles)	RFS improved over placebo HR = 0.79 in very high risk pts

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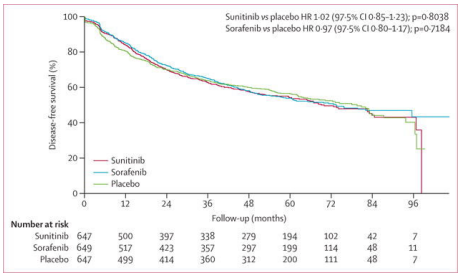
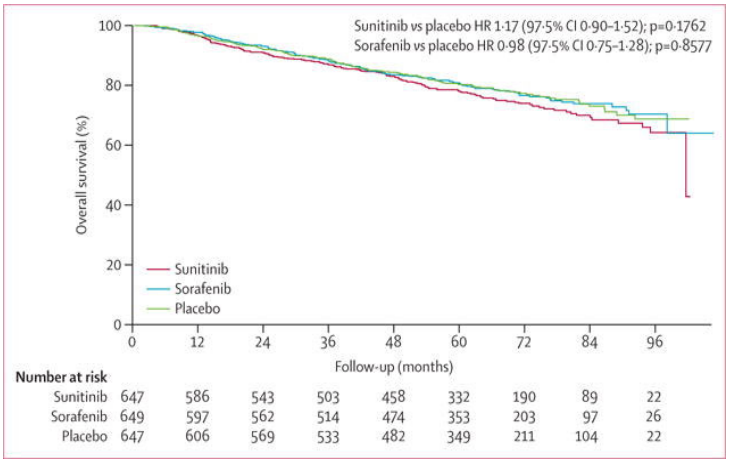
ASSURE Trial: Adjuvant Sunitinib vs. Sorafenib vs. Placebo





Reprinted from The Lancet, 387, Haas et al, Adjuvant sunitinib or sorafenib for high-risk, non-metastatic renal-cell carcinoma (ECOG-ACRIN E2805): a double-blind, placebo-controlled, randomised, phase 3 trial, 2008-16, Copyright 2016, with permission from Elsevier.

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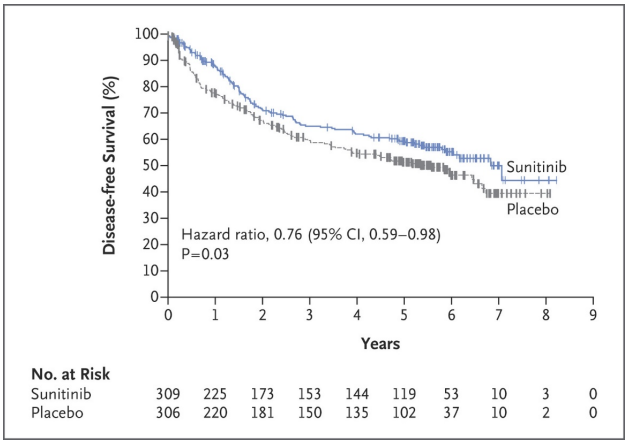
S-TRAC Trial: Sunitinib vs. Placebo in High-Risk RCC



From NEJM, Ravaud et al, Adjuvant Sunitinib in High-Risk Renal-Cell Carcinoma after Nephrectomy, 375(23), 2246-54.

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Perioperative Therapy in RCC

In the absence of guidelines, the most practical answer is to enroll onto a clinical trial

PROSPER	n=766	Nivolumab/Nephrectomy/Nivolumab vs. Nephrectomy alone	6 months
IMmotion 010	n=764	Atezolizumab vs. Placebo	12 months
KEYNOTE 564	n=950	Pembrolizumab vs. Placebo	12 months
CHECKMATE 914	n=800	Nivolumab + Ipilimumab vs. Placebo	24 weeks
RAMPART	n=1750	Durvalumab + Tremelimumab vs. Placebo	12 months

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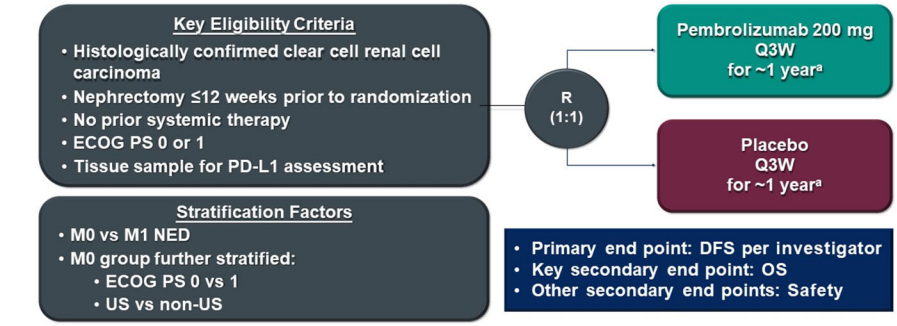
KEYNOTE-564 Study Design



DFS, disease-free survival; Q3W, every 3 weeks.
[a]≤17 cycles of treatment were equivalent to ~1 year.

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NEJM: 385 (8), 683-694, August 2021

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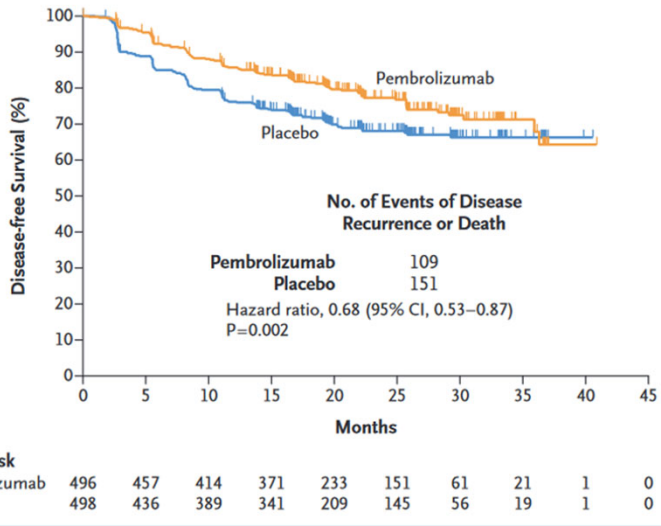
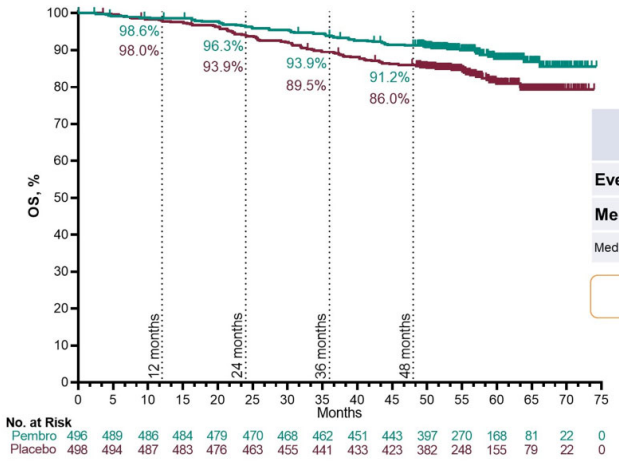
Prespecified Disease Risk Categories

Intermediate-High Risk		High Risk		M1 NED
pT2	pT3	pT4	Any pT	NED after resection of oligometastatic sites ≤1 year from nephrectomy
Grade 4 or sarcomatoid	Any grade	Any grade	Any grade	
N0	N0	N0	N+	
M0	M0	M0	M0	

NED, no evidence of disease.



Overall Survival, Intention-To-Treat Population



	Pembro (N = 496)	Placebo (N = 498)
Events, n	55	86
Median, mo (95% CI)	NR (NR–NR)	NR (NR–NR)

Median follow-up was 57.2 months (range, 47.9–74.5)

HR 0.62 (95% CI 0.44–0.87); *P* =.002*

* **denotes statistical significance**. P-value boundary for OS at IA3 was 0.0072 (1-sided) per Lan-DeMets O'Brien-Fleming spending approximation α-spending function. As this key secondary endpoint was formally met, any future OS analyses will be descriptive only.

Data cutoff date: September 15, 2023.

ASCO Advantage

Choueiri T, et al ASCO 2024

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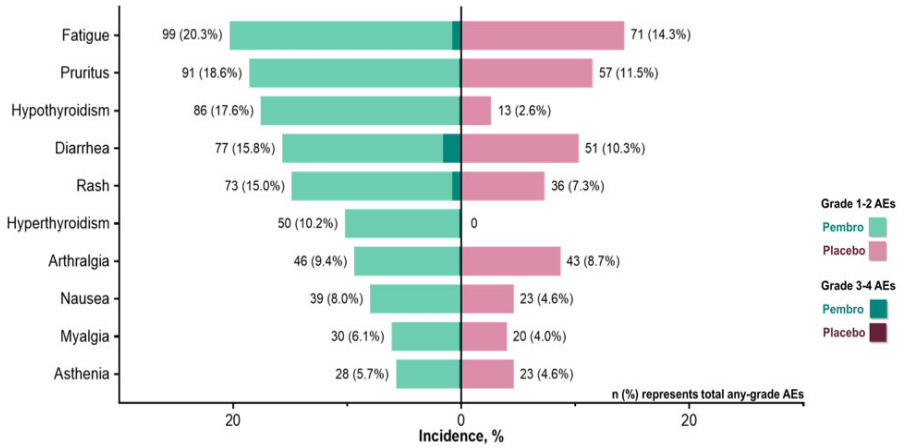
Adverse Events: 2 deaths, 32.4% Severe AEs



J Clin Oncol 39, 2021 (suppl 15; abstr LBA5)

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Keynote-564: Conclusions

- Adjuvant pembrolizumab significantly prolonged overall survival versus placebo in participants with clear cell RCC at increased risk of recurrence following surgery
  - 38% relative reduction in risk of death with adjuvant pembrolizumab versus placebo
  - Survival benefit was seen across key subgroups
- Continued disease-free survival benefit with pembrolizumab versus placebo was observed with further follow up
- All participants completed or discontinued study therapy by December 2020; safety findings did not change substantially since last analysis
- KEYNOTE-564 is the first study to show a statistically significant and clinically meaningful survival improvement with an adjuvant therapy in RCC
- These results further support adjuvant pembrolizumab as a standard of care after surgery in this disease setting

Choueiri T, et al ASCO 2024

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Adjuvant Therapy in RCC

Anti-VEGF therapy

- Role of in adjuvant setting is unclear
- Two positive trials with DFS benefit, no OS benefit

Immunotherapy

- Keynote 564 was the first trial to report positive DFS and OS results
- Prosper trial halted for futility – lower risk patients enrolled for neoadjuvant therapy may have contributed
- Toxicities of I-O can be substantial and long lasting
- Multiple other I-O trials ongoing

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Prognostic criteria for mRCC*

	MSKCC	Heng
Karnofsky PS	<80% = 1point	<80% = 1 point
Hgb	< lower limit = 1point	< lower limit = 1point
Corrected Ca^{++}	> 10mg/dl = 1 point	> Upper limit = 1 point
Time from dx to systemic Rx	< 1 year = 1 point	< 1 year = 1 point
LDH	>1.5 Upper limit	none
Neutrophils	None	> Upper limit = 1 point
Platelets	None	> Upper limit = 1 point
Favorable Risk **Intermediate Risk** **Poor risk**	0 points 1-2 points 3-5 points	0 points 1-2 points 3-6 points

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AUA Core Curriculum

https://auau.auanet.org/core

Table 8. MSKCC 2002 Risk Model Criteria

Risk Factors	Criteria
KPS, %	< 80
Time from diagnosis to treatment with systemic therapy, months	< 12
Hemoglobin	< Lower limit of reference range
Lactate dehydrogenase (LDH)	> 1.5 x upper limit of reference range
Corrected serum calcium, mg/dL	>10.0

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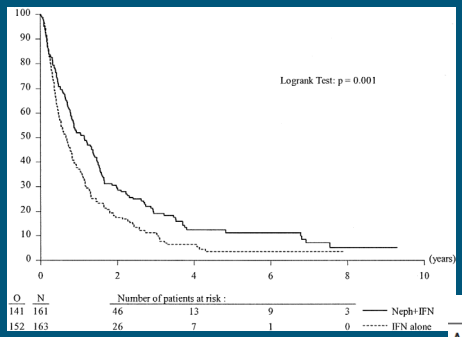
Is Cytoreductive Nephrectomy still SOC?

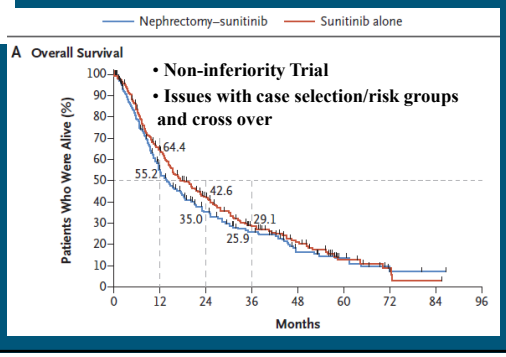


- Overall survival favored nephrectomy group (13.6 months vs. 7.8 months; p=0.001)
- N = 331 patients

SWOG Flanigan et al. NEJM 345; 2001

	Year 1	Year 2	Year 3
Sunitinib	64%	43%	29%
CRNx + Sunitinib	55%	35%	26%

CARMENA Mejean et al: NEJM 2018



- Non-inferiority Trial
- Issues with case selection/risk groups and cross over

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Cytoreductive Nephrectomy:

Clinical "rules"

- > 75% tumor debulking
- No CNS or liver metastases
- ECOG PS of
- favorable/intermediate risk
- Predominately clear cell histology
  - no sarcomatoid elements - ?bx

Will the patient receive effective systemic therapy post op?

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Role of Neoadjuvant TKIs:

- Institutionally based randomized level 1 data

- About 50% will a response
  - median 10-20% size reduction of primary tumor

- Most reduction in size occurs within 60 days

- ***Meaningful downstaging of primary RCC with TKIs uncommon***

- 2 cycles of TKIs then reassess

- If there is meaningful reduction – 2 more cycles then operate

Rini, Uzzo, Campbell et al 2015

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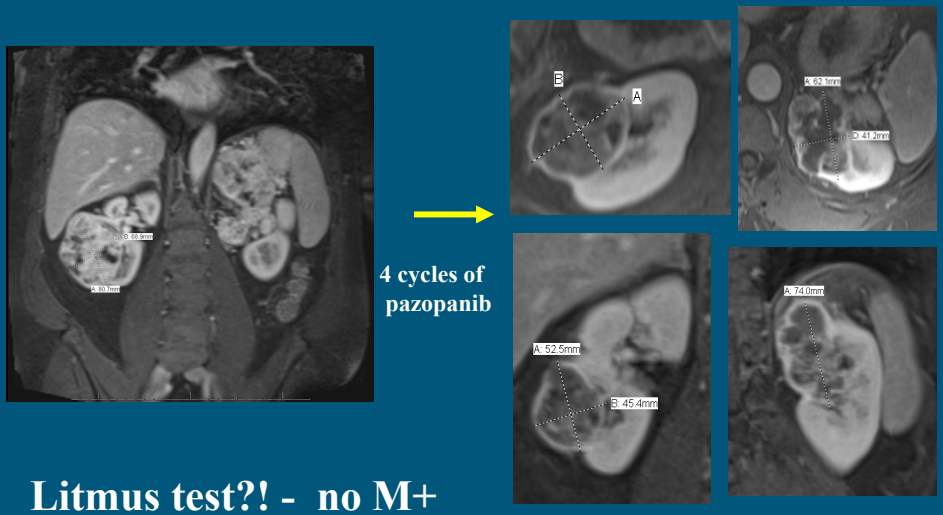
Neoadjuvant Pazopanib Trial



Litmus test?! - no M+

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When to Stop Targeted Rx Preop

	Half Life	5 half lives
Sunitinib	40-60 hours	8-12 days
Sorafenib	25-48 hours	5-10 days
Pazopanib	30 hours	7-8 days
Axitinib	3-6 hours	1-2 days
Temsirolimus	17 hours	4-5 days
Everolimus	28 hours	5-6 days
Bevacizumab	20 days	100 days

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Synchronous mRCC

- **Bilateral RCC (Synchronous *renal* RCC):**
  - **Estimated at 1-6% of non-hereditary RCC cases**
  - **Stage surgeries and perform NSS on *"easy side first"***
    - **Affords more options**
  - **96% cancer concordance – 46% benign concordance**
- **Synchronous non-renal metastases occur anywhere**
  - **Most are asymptomatic and identified in chest, abd/pelvis**
  - **Brain/Bone scan used if symptomatic, *PET scan not useful in RCC***

Site of pathologically confirmed mRCC
Lung (67%)
Bone (19%)
Liver (13%)
Distant Lymph Nodes 9%
CNS (4%)

Kunkle and Uzzo J. Urol. 177 (5): 1692, 2007

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Metastasectomy?

SBRT for oligomets new paradigm

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- **Best reserved for patients with**
  - **Long disease free intervals; low volume metastatic disease**
  - **Pulmonary most favorable**
    - **Liver/bone/brain – poor outcomes with resection**
- **80% of skeletal mets occur in axial skeleton, spine or pelvis**
  - **Proximal end of long bones more common**
  - **Surgical Rx if:**
    - **Weight bearing, lytic and >3cm**
- **EA8211-SOAR (NCT05863351)**
  - Currently enrolling patients to compare SABR followed by systemic therapy versus upfront systemic therapy in patients with oligometastatic advanced RCC. The primary endpoints include overall survival and treatment-related toxicity

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Systemic Therapies in RCC

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- **Chemotherapy = 4-6% ORR**
- **mAb against VEGF**
- **Tyrosine Kinase Inhibitors**
- **mTOR Inhibitors**
- **Checkpoint Inhibitors**
- **Other Immunologics**
- **Combinations and Sequences**

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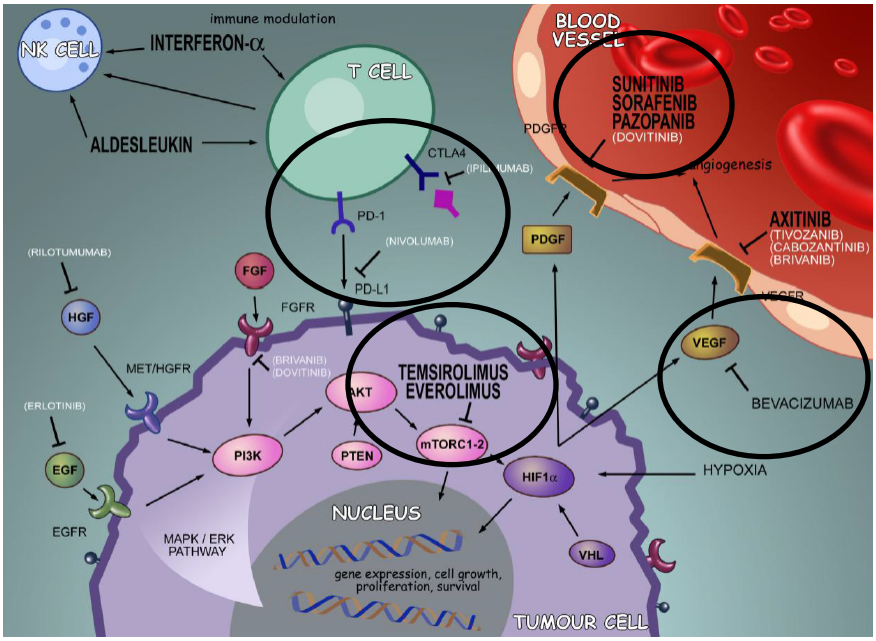

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Immunotherapy for mRCC

- **First generation**
  - **Marginal overall clinical benefit (10-15%)**
  - **IL-2 – for ccRCC only**
    - **CR 2-7% (durable)**
    - **Associated with capillary leak syndrome**
  - **IFN (rarely used except with bevacizumab)**

- **Second generation**
  - **PD1/PDL1 inhibition + CTLA4 Antibodies, others**
  - **Checkmate214 trial**
  - **Combination in intermediate/poor risk RCC = ORR 42% with CR=9%**
  - **Median PFS = 11.6mo, 93% had AE causing 22% discontinuation**

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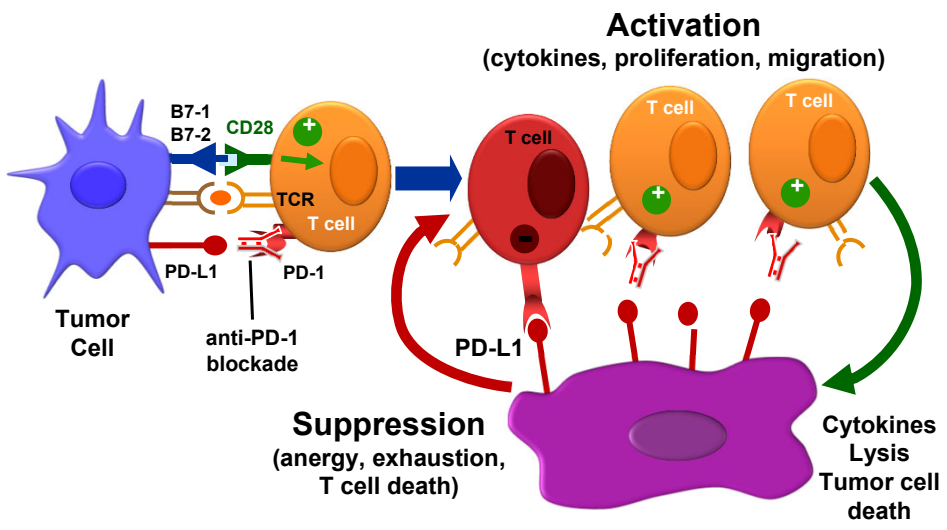
Anti-PD-1: Blocking T cell suppression



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2024 Update 1L mRCC (ITT populations)

All risk groups	CheckMate 214	Keynote-426	CheckMate-9ER	
Median followup (mo)	67.7 Ipi/Nivo v Sunt	42.8 Axi/pem v S		EV
Median OS and risk reduction death	55.7			NR 28%
ORR and CR%			55.7 12%	71 17%
		23.6	23.1	26
Median PFS and risk Reduction of primary reduction %	(39-NE) 12.3 14%	15.7 32%	16.6 42%	13.3 58%

ORR, PFS and OS differ based on risk groups
Favorable = 40-50%/19-28 mo/47-74 mo
Intermediate to poor = 42-57%/11-16mo/47-49mo

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Refractory mRCC - 2nd Line

Also in evolution and dependent on 1L Rx used

	AXIS	METEOR	TIVO-3	CHECKMATE-025	CANTATA
Treatment	Axi vs Sorafenib	Cabo vs Everolimus	Tivozanib vs Sorafenib	Nivo vs Eve	Cabo +Telaglenastat vs Cabo
mPFS (mo)	6.7	7.4	5.6	4.6	9.2
HR (95% CI)	0.66 (0.54-0.81)	0.51 (0.42-0.62)	0.73 (0.56-0.94)	0.88 (0.75-1.03)	0.94 (0.74-1.21)
ORR (%)	19%	17%	12.3%	25%	31%
mOS HR (95% CI)	0.97 (0.80-1.12)	0.66 (0.53-0.83)	0.91 (0.72-1.12)	0.72 (0.57-0.93)	--

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Toxicities of Systemic Therapies in RCC

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- **mAb against VEGF (iv)**
  - **Hypertension, proteinuria, poor wound healing**
  - **Longest half life**
- **Tyrosine Kinase Inhibitors (po)**
  - **HTN, fatigue, hand foot syndrome, nausea, diarrhea**
  - **LV dysfunction, hypothyroid, stomatitis, hematopoietic**
- **mTOR inhibitors (po/iv)**
  - **Stomatitis, pneumonitis**
  - **Hyperlipidemia**
- **Checkpoint inhibitors (iv/sc)**
  - **Autoimmune disorders**
- **HIF 2a inhibitors (po)**
  - **hypoxia**

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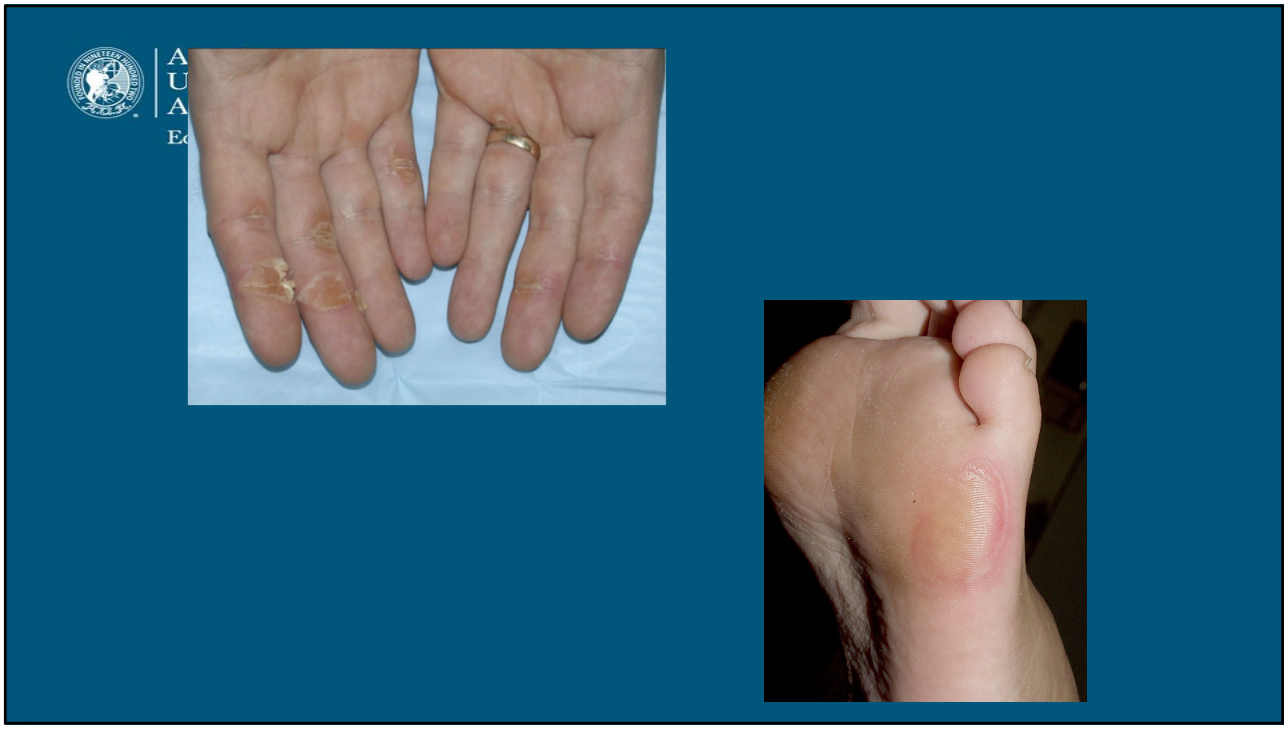

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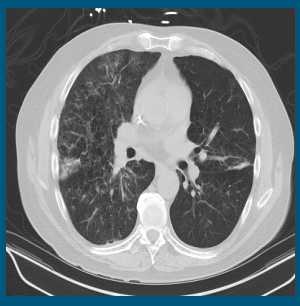
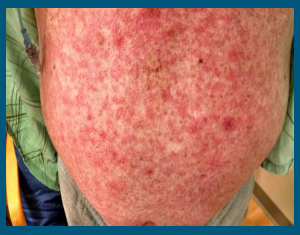
Autoimmune toxicities seen with checkpoint inhibitors

- Endocrinopathies
  - Hyper → Hypothyroid
  - Central adrenal insufficiency
- Pneumonitis
- Diarrhea / Colitis
- Rash
- Myositis
- Neurotoxicity
  - Guillain-Barré syndrome
  - Cranial Nerve Palsy





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Ureteral and Renal Pelvic Cancer

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AUA Core Curriculum

https://auau.auanet.org/core

Table 1. Etiology And Risk Factors For Upper Tract Urothelial Carcinoma
Smoking
Bladder cancer (CIS, multifocality, proximity to ureteral orifice)
Lynch syndrome
Aristolochic acid (Balkan nephropathy, Chinese and Taiwanese herbal nephropathy)
Arsenic
Analgesics
Occupational exposure (chemical, petroleum, plastic, coal, tar, dyes)
Chronic inflammation and infection
Cyclophosphamide

Table 2. Clinical Signs and Symptoms of Upper Tract Urothelial Carcinoma
Hematuria (75-82% of cases)
Flank pain
Dysuria
Symptoms of advanced disease
Common sites of metastases (liver, lungs, bones, and regional lymph nodes)

Table 4. Risk Factors for Advanced Upper Tract Urothelial Carcinoma
Positive cytology
Sessile tumor architecture
Multifocality
Hydronephrosis
Tumor size >3cm

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Differential Dx of Filling Defect

- Radiolucent stone
- Blood clot
- Renal papillae
- Fungus ball
- Extrinsic vascular compression
- Renal parenchymal tumor
- Urothelial Ca – 7% of all kidney tumors
- Ureteritis/Pyelitis cystica
- TB
- Endometriosis

Get a good history and look at the films yourself

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WHO Classification

- **Papillary urothelial lesion**
  - Papillary hyperplasia
  - Urothelial Papilloma
  - Papillary urothelial neoplasm of LMP (PUNLMP)
  - Low grade urothelial carcinoma
  - High grade urothelial carcinoma
- **Flat urothelial lesions**
  - Flat urothelial hyperplasia
  - Flat urothelial atypia
  - Urothelial atypia of unknown significance
  - Dysplasia
  - Carcinoma in situ

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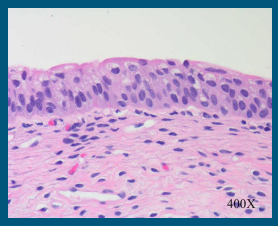
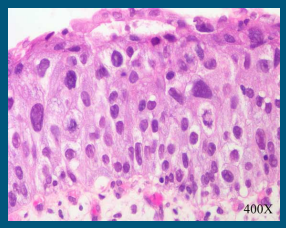


Normal urothelium
- < 7 layers thick
- umbrella cells
- Uniform nuclei



CIS
- large irregular nuclei
- Mitoses

JHH Epstein et al http://162.129.103.34/cgi-win/bladtutor.exe/definitions

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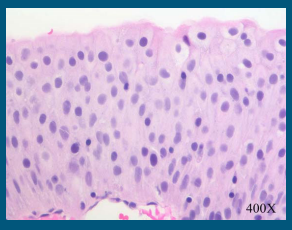
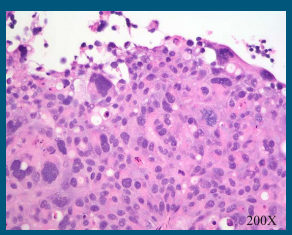


Low grade urothelial carcinoma
- Orderly
- variations in architecture
  - polarity
  - nuclear size and shape



High grade urothelial carcinoma
- Disorderly
- Irregular architecture
  - polarity
  - pleomorphism
  - clumped chromatin

JHH Epstein et al http://162.129.103.34/cgi-win/bladtutor.exe/definitions

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Evaluation/Diagnosis/Imaging

- Evaluation is similar to RCC
  - Hx and PE, LFT, Scr, check cytology, UA
  - FISH (UroVysion) ***not proven*** in upper tracts
  - Imaging of ureters/renal pelvic - CT urogram (preferred)
- Ureteroscopy
  - Selective cytology, brush, biopsy
- What is sufficient for a diagnosis?
  - Direct visualization with a positive bx/cytology is gold standard
  - Radiographic visualization with positive cytology
  - Beware of filling defect with "equivocal" or negative cytology
    - Consider clot or stone

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Lynch Syndrome

- Autosomal dominant inheritance
- Increasingly recognized/tested
- Colon cancer + UTUC
- Defect in DNA mismatch repair genes
  - MLH1, MSH2, MSH6, PMS2 or EPCAM gene
- Patients may respond better to I/O agents (more antigenic tumors?)

Risks associated with *MSH2* mutations (from NCCN Guidelines Version 1.2020: Lynch Syndrome)

Cancer Type	General Population Risk	Lynch Syndrome (*MSH2*) Risk	Mean Age of Onset
Colon	4.2%	33-52%	44 years
Endometrium	3.1%	21-57%	47-48 years
Stomach	<1%	0.2-9%	49-52 years
Ovary	1.3%	10-38%	43-44 years
Urinary tract	<1%	2-28%	52-61 years
Small bowel	<1%	1-10%	46-48 years
Pancreas	1.5%	0.5-1.6%	Not reported
Prostate	11.6%	4-16%	59 years
Breast	13%	13%	No data
Biliary tract	<1%	0.02 – 1.7%	57 years
Brain	0.6%	2.5-7.7%	No data

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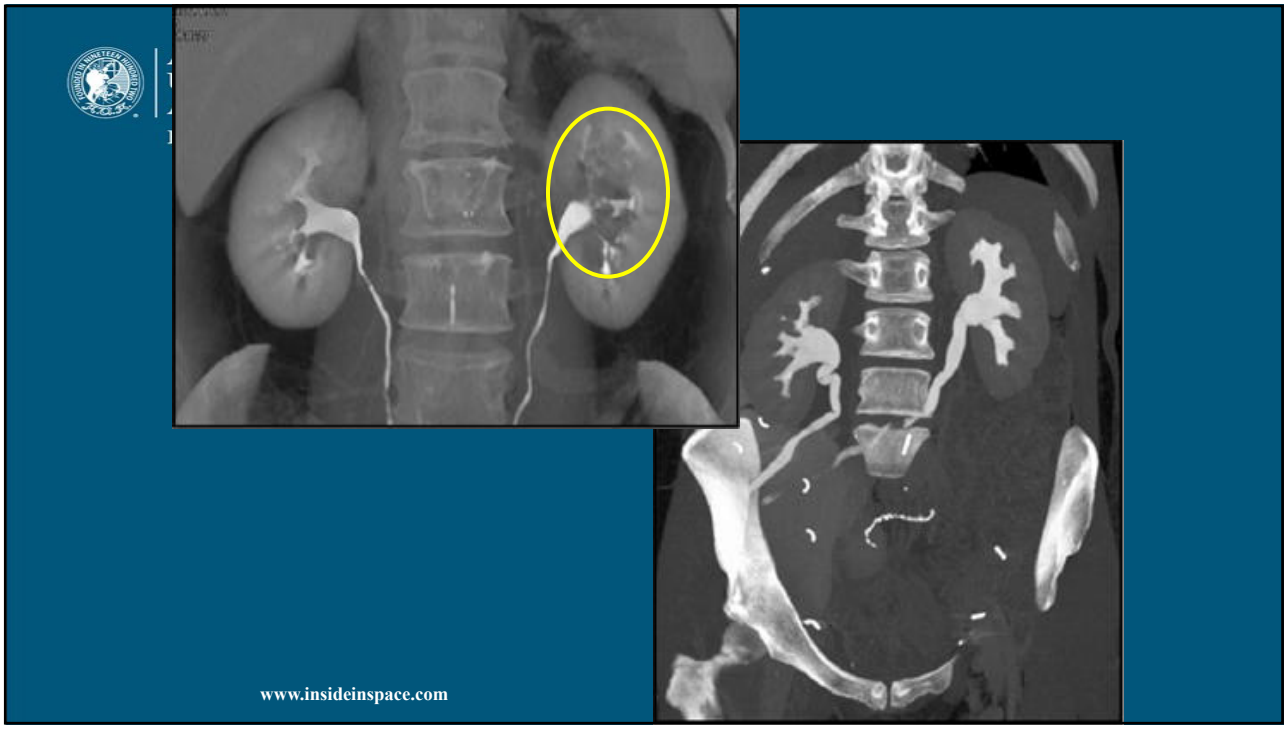

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AJCC Staging v8

- **Primary Tumor Stage (T)**
  - **Tx – primary tumor cannot be staged**
  - **T0 – no evidence of primary tumor**
  - **Ta - non-invasive**
  - **Tis – carcinoma-in-situ**
  - **T1 – invades lamina propria**
  - **T2 – invades muscularis**
  - **T3 – invades sinus/peri-ureteral fat or renal parenchyma**
  - **T4 – invades adjacent organs**
- **Nodal Staging**
  - **N1 – single node ≤ 2cm**
  - **N2 – node 2<x≤5cm**
  - **N3 – nodes > 5cm**

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Management

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- **Surgery**
  - Radical Nephroureterectomy
    - Laparoscopic preferred method
    - Distal ureter - en
    - ap
    - grade lesions that can't be handled ureteroscopically
    - High grade lesions for relative or imperative NSS indications
    - Clear bladder and remainder of upper tracts
  - Partial NTX for polar calyceal/infundibular lesions

Post op Intravesical chemo (gemcitabine) within 7 days depending on bladder closure (2gm in 100cc saline)

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Management

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- **Endoscopic management**
  - Ureteroscopic/nephroscopic
  - Low stage, low grade, unifocal lesions without CIS
  - Techniques similar to TURb and stone surgery
  - Re-evaluate results during 2nd look

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Management

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- **Local therapies**
  - **BCG of upper tracts difficult to administer**
    - **1/3 strength, drip at 20cm through 4fr stent; No dwell time**
    - **Higher risk of systemic absorption**
    - **Requires close surveillance since most patients have higher risk lesions**
    - **Most common complication is *urosepsis* (check culture and use a low pressure system)**
  - **Mitomycin gel (FDA approved for low grade low stage UTUC)**
    - **Induction + maintenance**
    - **60% CR at first endoscopy (Olympus trial Lancet Oncology June 2020)**

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Management

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- **Systemic therapy**
  - **Cisplatin based**
  - **If high stage/grade consider adjuvant chemoRx**
    - **POUT study**
      - **N=248 pts with T2-T4 N0-N3 UCC received gem/cis vs observation**
      - **Met early stopping rule**
      - **2y DFS was 70% for chemo and 51% for observation (HR=0.47 p=0.0009)**
  - **If large mass or bulky nodes, consider neo-adjuvant Rx based on eGFR**
  - **Immunotherapy (if cis-ineligible OR if tumor expresses PDL1)**
  - **Erdafitinib (po) = FGF-receptor inhibitor**

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Urothelial Cancer Agents

Name	MOA	T 1/2	Primary Toxicities	Primary Lab Effect
Vinblastine	Inhibits microtubules	24 hrs	Alopecia, paresthesia, HTN, Myelosuppression	Neutropenia
Methotrexate	Inhibits folic acid metabolism	10 hrs	Stomatitis, CNS toxicity	Neutropenia
Adriamycin	Intercalates DNA	3.5 hrs	Nausea, vomiting, arrhythmias	Neutropenia
Cisplatin	DNA Alkylating Agent	1 hr	Nephrotoxicity, neurotoxicity, nausea, vomiting, ototoxicity	eGFR, Low Mag, K^+, Ca^{++}
Carboplatin	DNA Alkylating Agent	6 hrs	Myelosuppression, nausea, vomiting, nephrotoxicity	Neutropenia, anemia, eGFR (at high doses)
Gemcitabine	DNA analogue replaces cytidine in DNA replication	10 hrs	Muscle pain, fever, headache, chills, fatigue, skin rash	LFT elevation, proteinuria
BCG	Unknown Attenuated mycobacteria	Unknown	Dysuria, urgency, fever	
Mitomycin C	Antitumor antibiotic activity Alkylation of DNA (cross linking and inhibition of DNA synthesis	1 hr	Bone marrow suppression long term, lung fibrosis, renal damage	Anemia
ImmunoRx (CPI)	Block PD1/LD-L1	1-3 weeks	Autoimmune effects	LFTs, thyroid, adrenal insufficiency

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Conclusions

- Very exciting time in GU oncology - RCC
- Be your own best and worst critic
- Become a "GU radiologist"
- Don't just treat the tumor – treat the patient
- Take something away from every case
  - Translational thinking
  - Learn by clinical extension
- Develop your own "bag of tricks"

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ARS Q1

The following correct statement is:

a) Brain aneurysms are a leading cause of death in patients with VHL
b) HPRCC is associated with uterine fibroids
c) The incidence of RCC in patients with Tuberous Sclerosis is in excess of 40%
d) Hereditary leiomyomatous RCC is associated with high grade papillary renal cancers

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ARS: Q2

- Which of the following histology of a small renal mass is considered benign:

a) clear cell papillary renal tumors
b) tubulocystic renal tumors
c) Mixed epithelial and stromal renal tumors
d) ALK associated renal tumors

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ARS: Q3

Which of the following is false regarding the mechanism of systemic therapies for renal and urothelial cancers:

a) PDL1 inhibitors block the programmed death receptor
b) b) TKIs prevent nuclear translocation of the HIF transcriptional factor
c) Cis-platin is a DNA alkylating agent
d) Mitomycin inhibits microtubules

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ARS: Q4

Which of the following pairs is incorrect:

a) Oncocytoma – increased # of Endoplasmic reticulum
b) Multilocular cystic nephroma – middle aged females
c) Medullary RCC- sickle cell trait
d) pseudotumor – diagnosed by a MAG-3 renal scan

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ARS: Q5

Management of hypercalcemia includes all of the following except:

a) Loop diuretics
b) Bisphosphonates
c) Glucocorticoids
d) Hydration with hypertonic saline

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GOOD LUCK!!

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