Contemporary Management of Renal Masses

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Outline

- Epidemiology
- Differential Diagnosis
- Evaluation
  - Imaging
  - Role for Biopsy
- Treatment
  - Surveillance
  - Surgery
  - Ablation
- Follow-up
- Cases

Renal Mass

- Increasing incidence with widespread use of cross-sectional imaging

- Renal lesions are seen in 15-25% of abdominal imaging studies
  - Most are benign cysts

- Majority are detected incidentally.
**Renal Mass- Differential Diagnosis**

<table>
<thead>
<tr>
<th>Malignant</th>
<th>Benign</th>
<th>Inflammatory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal Cell Carcinoma</td>
<td>Simple cyst</td>
<td>Abscess</td>
</tr>
<tr>
<td>- Clear Cell</td>
<td>Angiomyolipoma</td>
<td>Focal pyelonephritis</td>
</tr>
<tr>
<td>- Papillary</td>
<td>Oncocytoma</td>
<td>Xanthogranulomatous pyelonephritis</td>
</tr>
<tr>
<td>- Chromophobe</td>
<td>Metanephric adenoma</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>- Collecting duct</td>
<td>Cystic Nephroma</td>
<td></td>
</tr>
<tr>
<td>Urothelial Based</td>
<td>Mixed epithelial/stromal tumor</td>
<td></td>
</tr>
<tr>
<td>Urothelial carcinoma</td>
<td>Reninoma</td>
<td></td>
</tr>
<tr>
<td>Squamous cell</td>
<td>Leimyoma</td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>Pseudotumor</td>
<td></td>
</tr>
<tr>
<td>Wilms tumor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metastasis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Is it Benign or Malignant?**

- The question at hand.
- This can frequently determined by radiographic assessment.
- Size Matters
- Current trend is to biopsy more renal masses <4cm.

**Radiographic Assessment**

- Ultrasound
- CT
- MRI

**Key Point:**
- Need to determine enhancement
Ultrasound

- Reliable for differentiation of a solid lesion from fluid.
- Can establish the diagnosis of a simple cyst.

CT Scan

- Triple Phase (Renal Protocol)
  - Pre-contrast
  - Post-contrast (venous phase)
  - Delayed (10 min)

- Hounsfield Units (HU)
  - Represents the density of tissue

Enhancement

- Can only be determined if a contrast agent is used
  - CT – iodonated contrast
    - Enhancing Lesion = Pre-contrast to Post-contrast change in HU >15-20
  - MRI – Gadolinium
    - Slightly more subjective

Tissue HU

<table>
<thead>
<tr>
<th>Tissue</th>
<th>HU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone</td>
<td>+1000</td>
</tr>
<tr>
<td>Blood</td>
<td>40</td>
</tr>
<tr>
<td>Kidney</td>
<td>30</td>
</tr>
<tr>
<td>Water</td>
<td>0</td>
</tr>
<tr>
<td>Fat</td>
<td>-50</td>
</tr>
<tr>
<td>Air</td>
<td>-1000</td>
</tr>
</tbody>
</table>
MRI

- Pre and Post Gadolinium

Risk of Contrast Agents

- IV Contrast (CT)
  - Contrast Allergy
  - Nephrotoxicity
    - Avoid with severe renal impairment
    - Risk reduction: Hydration

- Gadolinium (MRI)
  - No nephrotoxicity
  - Risk of Nephrogenic Systemic Fibrosis in those with severe renal impairment (EGFR<30).

cG250 PET/CT: Radiolabeled Antibody

- 124I-cG250 (REDECTANE®)
  - Binds carbonic anhydrase IX
  - Clear cell RCC
  - Radiographic diagnosis

- No role for CT PET-FDG with renal tumors.

Fat

- Solid masses with areas of negative HU (<-20) indicate the presence of fat and are diagnostic of AMLs.
  - AML = Angiomyolipoma
  - AML is a benign tumor.
Renal Cysts

- The kidney is one of the most common locations in the body for cyst formation.
- Renal cysts are cavities derived from renal tubules.
- Composed of a layer of epithelial cells enclosing a cavity filled with urine-like liquid or semi-solid material.
- 20% by age 40
- 50% by age 60

Renal Cysts: Bosniak Classification

<table>
<thead>
<tr>
<th>Bosniak Class</th>
<th>Description</th>
<th>Cancer Risk</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>No enhancement Smooth Wall No Septa No Calcifications</td>
<td>0%</td>
<td>None</td>
</tr>
<tr>
<td>II</td>
<td>No enhancement Hairline Septa Fine Calcifications</td>
<td>Minimal</td>
<td>None</td>
</tr>
<tr>
<td>IIIF</td>
<td>No enhancement Hyperdense lesion Multiple Septa Thicker Calcifications</td>
<td>&lt;10%</td>
<td>Surveillance</td>
</tr>
<tr>
<td>III</td>
<td>Thickened Wall with Enhancement</td>
<td>50%</td>
<td>Surgery</td>
</tr>
<tr>
<td>IV</td>
<td>Enhancing Nodule</td>
<td>90%</td>
<td>Surgery</td>
</tr>
</tbody>
</table>

Adapted from Campbell-Walsh Urology 10th Ed.

Renal Cysts – Bosniak Classification

Case- Simple Renal Cyst
Imaging Interpretation

- Enhancing renal masses are most likely malignant.

- Simple Cysts (Bosniak Type I):
  - Can be diagnosed by U/S or CT.
  - Do not need follow-up.

- AMLs are benign and can be followed
  - >4cm = greater risk for spontaneous bleeding
    • Selective angioembolization vs. surgery

AML = Angiomyolipoma

Role for Biopsy

- Historically, renal masses have not been biopsied.
  - Most are malignant
  - Issues with accuracy/non-diagnostic rates
  - Fear of needle tract seeding
  - High reported complication rates

Role for Biopsy

- Current role for biopsy is expanding
  - Especially for masses <4cm

- Updated date on biopsy results are much improved.

Role for Biopsy

- Contemporary results of renal mass biopsy:
  - Diagnostic rate: 92%.
    • RCC Subtype Concordance: 80-100%
    • Fuhrman Grade Concordance: 50-70%
  - Complications: <5%
    • Hematoma most common

Marconi et al. Eur Urol 2015
Indications:
Renal Mass Biopsy

- R/o non-renal primary (mets or lymphoma)
- +/- R/o benign lesions
- Confirm diagnosis and histologic subtype in patients with metastases or unresectable lesions
- Confirm diagnosis:
  - Prior to ablative therapy
  - In patients considering observation when surgery is high risk

Biopsy only if it will change management

Tumor Size and Pathology

<table>
<thead>
<tr>
<th>Tumor Size</th>
<th>RCC</th>
<th>Benign*</th>
<th>High Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤2.0</td>
<td>75%</td>
<td>25%</td>
<td>4%</td>
</tr>
<tr>
<td>2.1-3.0</td>
<td>80%</td>
<td>20%</td>
<td>5%</td>
</tr>
<tr>
<td>3.1-4.0</td>
<td>84%</td>
<td>16%</td>
<td>25%</td>
</tr>
</tbody>
</table>

*Oncocytoma and AML – 75%

J Urol 2006; 176:896
**Renal Cancer 2015**

- **Incidence**
  - 61,560 new cases
  - 14,080 deaths

- **Peak incidence** 5th-7th decades

- **Men > Women**

- **Lifetime Probability of Developing Renal Cancer:**
  - 1 in 49 male (#7)
  - 1 in 84 female (#10)

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**Renal Cell Carcinoma – Risk Factors**

- **Tobacco Exposure**
  - May account for ~20% of cases

- **Obesity**
  - May account for ~40% of cases in US
  - Risk increases ~30% for every 5kg/m² increase in BMI

- **Hypertension**

- **Low socioeconomic status and urban background**

- **More than 100 chemicals have been investigated but none have been definitively established as causative in RCC**

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**Renal Cancer – Mortality**

<table>
<thead>
<tr>
<th>Site</th>
<th>Incidence/yr</th>
<th>Deaths 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate Cancer</td>
<td>220,800</td>
<td>27,540 (12%)</td>
</tr>
<tr>
<td>Bladder Cancer</td>
<td>74,000</td>
<td>16,000 (22%)</td>
</tr>
<tr>
<td>Kidney Cancer</td>
<td>61,560</td>
<td>14,080 (23%)</td>
</tr>
</tbody>
</table>

**Renal Cancer – Presentation and Survival**

<table>
<thead>
<tr>
<th>Stage at Diagnosis</th>
<th>Distribution</th>
<th>5-yr Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized</td>
<td>61%</td>
<td>91%</td>
</tr>
<tr>
<td>Regional (lymph nodes)</td>
<td>17%</td>
<td>63%</td>
</tr>
<tr>
<td>Distant (metastatic)</td>
<td>18%</td>
<td>11%</td>
</tr>
</tbody>
</table>

**Seer Database**

**Clinical Presentation**

- 80% incidental
- Flank pain
- Gross hematuria
- Palpable mass

"Classic Triad" <10%
- Microhematuria
- Paraneoplastic syndromes (10-20%)

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**Paraneoplastic syndromes**

- "Internist's Tumor"
  - Elevated ESR 55%
  - HTN 38%
  - Anemia 36%
  - Cachexia 35%
  - Pyrexia 17%
  - Elevated LFTs 14%
  - Hypercalcemia 5%
  - Polycythemia 4%
  - Neuromyopathy 3%

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**Clinical Presentation - RCC**

- Local Tumor Growth
  - Hematuria
  - Flank Pain
  - Abdominal Mass

- Metastasis
  - Persistent Cough
  - Bone Pain
  - Cervical Lymphadenopathy
  - Constitutional Symptoms

- Obstruction of IVC
  - Bilateral Lower Extremity Edema
  - Right-sided Varicocele (or nonreducing Varicocele)

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**Renal Cell Carcinoma: Histologic Subtypes**

<table>
<thead>
<tr>
<th>Type</th>
<th>Clear cell</th>
<th>Papillary</th>
<th>Chromophobe</th>
<th>Oncocytoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freq (%)</td>
<td>75</td>
<td>15</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>
### Hereditary RCC

<table>
<thead>
<tr>
<th>Disease</th>
<th>Gene (chromosome)</th>
<th>Histology</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>von Hippel-Lindau</td>
<td>VHL (3)</td>
<td>Clear Cell</td>
<td>75%</td>
</tr>
<tr>
<td>HLRCC*</td>
<td>FH (1)</td>
<td>Papillary Type 2</td>
<td>10%</td>
</tr>
<tr>
<td>Birt-Hogg-Dube</td>
<td>BHD (17)</td>
<td>Chromophobe/Oncocytoma</td>
<td>10%</td>
</tr>
<tr>
<td>Hereditary papillary RCC</td>
<td>Met (7)</td>
<td>Papillary Type 1</td>
<td>5%</td>
</tr>
</tbody>
</table>

*HLRCC = Hereditary Leiomyomatosis Renal Cell Carcinoma

### VHL: Renal Cell Carcinoma

- RCC occurs in 50% of VHL patients
  - Males=females in VHL
  - 4th to 5th decade (39)
  - Now most common cause of death

### Renal Cell Carcinoma: Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tumor</th>
<th>Lymph Nodes</th>
<th>Metastasis</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>T1 (&lt;7cm)</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>II</td>
<td>T2 (&gt;7cm)</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>III</td>
<td>T1 or T2</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3 (vein/fat)</td>
<td>N0 or N1</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>T4 (outside Gerota’s) Any T</td>
<td>Any N</td>
<td>Any M</td>
</tr>
</tbody>
</table>

### Treatment Options

- Surveillance

- Surgical Excision
  - Radical Nephrectomy
  - Partial Nephrectomy

- Needle Ablation
  - Cryoablation or Radiofrequency Ablation

- RCC does NOT respond to chemotherapy or radiation
Decision Making

- Tumor Characteristics:
  - Size
  - Location
  - Appearance

- Patient Characteristics
  - Comorbid disease
  - Life expectancy
  - Patient desire

Active Surveillance (AS)

- Incidentally detected tumors:
  - Small size (<4cm)
  - Elderly
  - Patients with significant comorbidity unfit for surgery

- Opportunity to observe the natural history of these small tumors.

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*Oncocytoma and AML – 75%

Active Surveillance

- Tumors <3cm
  - Risk of developing metastasis in 3 years is ~1%

- Average growth rate ~0.3cm/yr

- Most studies only have limited follow-up

- Follow-up protocol is not defined
  - Repeat imaging every 6-12 months
Active Surveillance

- AUA Guidelines:
  - “AS is a reasonable option for patients with a limited life expectancy or for those who are unfit for or do not desire intervention.”

Risk-adapted Management

- Biopsy can be helpful
- More favorable histology:
  - Papillary type 1
  - Chromophobe
  - Low grade:
    - Fuhrman grade 1 and 2.

Risk-adapted Management

- 5 yr Cancer specific survival:
  - Fuhrman Grade (clear cell RCC):
    - I: 94%
    - II: 88%
    - III: 63%
    - IV: 39%
  - Low (I&II): 90%
  - High (I&II): 61%

Surgery

- Approach?
  - Open vs. Laparoscopic vs. Robotic
- Radical vs. Partial Nephrectomy?
  - Nephron preservation
PARTIAL NEPHRECTOMY

- Partial nephrectomy oncologically equivalent to radical nephrectomy.
  Brou et al. J Urol 2010; 183:983

- L/S PN equivalent to Open PN with less morbidity.
  - Technical obstacles
  - MIS- more likely to have radical nephrectomy
  Gill et al. J Urol 2007; 178:41

- More attention has been given to the significant morbidity associated the chronic kidney disease (GFR<60).
  - Surgical vs. Medical
  - Nephron-preservation
  Leibovich et al. J Urol 2004; 171:1066
  Breau et al. J Urol 2010; 183:903

Chronic Kidney Disease (CKD)

- GFR <60 ml/min/1.73m² for at least 3 months

- Important consideration with significant associated morbidity and mortality

- RCC patients are NOT donor nephrectomy patients
  - Often have HTN and/or DM

- Median survival after starting dialysis is 2-2.5 years

Renal Cancer – Nephron Preservation

<table>
<thead>
<tr>
<th>CKD Stage (Estimated GFR (ml/min/1.73m²))</th>
<th>Death from Any Cause</th>
<th>Any Cardiovascular Event</th>
<th>Any Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD III (30-44)</td>
<td>1.8</td>
<td>2.0</td>
<td>1.5</td>
</tr>
<tr>
<td>CKD IV (15-29)</td>
<td>3.2</td>
<td>2.8</td>
<td>2.1</td>
</tr>
<tr>
<td>CKD V (&lt;15)</td>
<td>5.9</td>
<td>3.4</td>
<td>3.1</td>
</tr>
</tbody>
</table>

Indications for Nephron Sparing Surgery

- **Absolute/Imperative**: To prevent anephric state
  - Anatomic/Functional solitary kidney
  - Bilateral RCC
- **Relative**: Contralateral kidney is threatened by local, systemic, genetic conditions that may affect function
  - DM, HTN, stones, RAS, VHL
- **Elective**: NSS with a normal contralateral kidney

**Partial Nephrectomy**

- **GOALS**
  - Cancer Control
    - Margins
    - CSS
  - Preservation of renal function
    - Technical ability to perform NSS
    - ↓ Warm Ischemia time
    - Selective/no ischemia
  - ↓ Complications
  - ↓ Convalescence
- Robotics facilitates very difficult partial nephrectomies

**Partial Nephrectomy**

- Open
- Laparoscopic
- Robotic
- Approach is not as important as preserving nephrons → partial nephrectomy

**RAPN - Nationwide Inpatient Sample**

<table>
<thead>
<tr>
<th></th>
<th>RAPN</th>
<th>OPN</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (2008-2010)</td>
<td>9095</td>
<td>25461</td>
<td></td>
</tr>
<tr>
<td>Transfusion</td>
<td>5.8%</td>
<td>10.6%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Post-op Complications</td>
<td>22.1%</td>
<td>30.5%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LOS</td>
<td>3</td>
<td>4</td>
<td>ns</td>
</tr>
<tr>
<td>Prolonged LOS (&gt;75th %ile)</td>
<td>12.4%</td>
<td>34.8%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

RIGHT ROBOTIC PARTIAL NEPHRECTOMY

- Solitary Kidney
- BMI: 48
- Pre-op Cr: 2.03 (eGFR-37)
- Post op Cr: 2.10

Margin Assessment
ROBOTICS – Partial Nephrectomy

RAPN with unexpected venous thrombus video
Laparoscopic Radical Nephrectomy

Laparoscopic surgery is the preferred approach for most tumors.

Renal ablative techniques

- Potential for less morbidity/complications
- Allows treatment of older patients who are not good surgical candidates
- Potential for similar efficacy to partial nephrectomy for select masses

Indications for ablation of renal masses

- Solid renal lesion <3cm (T1a)
  - Not good candidates:
    - Tumor deep in the renal sinus
    - Adjacent to the renal hilum or ureter
    - Anterior tumors with adjacent bowel
- Best suited to treat renal lesions in patients with comorbidities that preclude a major surgical procedure
  - i.e. elderly, severe COPD, CV disease
- Renal insufficiency
- Solitary kidney
- Multifocal/Recurrent tumors secondary to VHL, BHD etc

Ablative Modalities

- Radiofrequency Ablation (RFA)
- Cryoablation
- Generally performed percutaneously with CT, MRI or U/S guidance.

Leveillee R, Wingo M. Ablation technologies for renal cell carcinoma. Oncology spectrum 1(2)
Percutaneous cryoablation

Laparoscopic cryoablation

Post-ablation imaging

2 weeks   6 weeks   3 months
### Treatment Options: LOCAL RECURRENCE FREE SURVIVAL

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Survival</th>
<th>Tumor Size (cm)</th>
<th>F/U (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RFA</td>
<td>87.0%</td>
<td>2.7</td>
<td>19</td>
</tr>
<tr>
<td>Cryo</td>
<td>90.6%</td>
<td>2.6</td>
<td>18</td>
</tr>
<tr>
<td>LPN</td>
<td>98.4%</td>
<td>2.6</td>
<td>15</td>
</tr>
<tr>
<td>OPN</td>
<td>98.0%</td>
<td>3.1</td>
<td>47</td>
</tr>
<tr>
<td>LRN</td>
<td>99.2%</td>
<td>4.6</td>
<td>18</td>
</tr>
<tr>
<td>ORN</td>
<td>98.1%</td>
<td>4.8</td>
<td>58</td>
</tr>
</tbody>
</table>

RFA=radiofrequency ablation; Cryo=cryoablation; LPN=laparoscopic partial nephrectomy; OPN=open partial nephrectomy; LRN=laparoscopic radical nephrectomy; ORN=open radical nephrectomy

Adapted from Campbell-Walsh Urology 10th Ed.

### Treatment Options - Summary

- **Surgery**
  - Gold Standard
  - Suitable for tumors of all sizes
  - Nephron-sparing when possible
  - Minimally invasive approaches available

- **Needle Ablation**
  - Tend to have higher local recurrence rates

- **Active Surveillance**
  - Long term outcomes unknown
  - Not best for younger/healthier patients

### Advanced Disease

- Surgery remains an integral part of the management of these patients.
  - Tumor thrombus in IVC
  - Regional Lymphadenopathy
  - Metastatic disease

- Surgery is the only treatment that offers the opportunity for cure

### Robotic Nephrectomy with IVC Thrombectomy

Robotic Nephrectomy with IVC Thrombectomy
Robotic Nephrectomy with IVC Thrombectomy

Robotic Nephrectomy with IVC Thrombectomy
Metastatic Renal Cell Carcinoma

- Cytoreductive nephrectomy

J Urol 2004; 171:1071

Case:
Simple Renal Cyst

Case:
2 cm Enhancing Renal Mass

Case:
Left 9 cm Renal Mass & 4 cm Adrenal Mass
### Conclusion

- Renal masses are typically found incidentally.
- A simple renal cyst can be diagnosed by U/S or CT and does not need follow-up.
- Most solid renal masses represent renal cell carcinoma.
- Nephron-sparing surgery should be performed when technically feasible.
- Most surgery can be performed in a minimally invasive fashion (laparoscopic/robotic).