Role of Biopsy to Characterize Small Renal Masses

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Small Renal Mass

Size < 4 cm  Incidental Discovery  Solitary
Disconnect: Diagnosis – Treatment – Outcome

- ↑ incidence small renal masses: ↑ 2-4% per year
- ↑ aggressive Rx → mostly radical nephrectomy
- Yet, overall mortality rates for RCC continue to increase
- Current practice is often discordant with what the literature supports

Chow et al. JAMA 1999
Small Renal Mass: c 1999

Solid Renal Mass

Malignant Potential Assumed
No Salvage Therapy Available
Limited Treatment Options

Open Radical Nephrectomy
Open Partial Nephrectomy
Renal Mass Biopsy: c. 1990’s

- Limited role (if any)
- Will not change management
- False negatives too prevalent $\rightarrow$ inaccurate
- Risk of complications
  - Hemorrhage
  - Pneumothorax
  - Tumor seeding (needle tract)
Laparoscopic Radical Nephrectomy: Great Seductress
Renal Function: Radical vs. Partial Nephrectomy

• 2000 pts undergoing kidney surgery @ MSK
• 662 pts: tumor size < 4 cm, normal renal fxn, normal contralateral kidney
• 26% had pre-existing CKD (eGFR < 60 cc/min)

<table>
<thead>
<tr>
<th>3-Year Probability</th>
<th>Partial Nx</th>
<th>Radical Nx</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GFR &lt; 60 cc/min</td>
<td>20%</td>
<td>65%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>GFR &lt; 45 cc/min</td>
<td>5%</td>
<td>36%</td>
<td>&lt; 0.001</td>
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</table>
Small Renal Mass: 2009

Benign
20%
Oncocytoma
Metanephric adenoma

Indolent Cancer
60%
Chromophobe
Papillary
Cystic RCC

Aggressive Cancer
(Potentially)
20%
Clear Cell

Renal Cortical Neoplasms → Heterogeneous Entity

Small Renal Mass: 2009

- **Benign**
  - 20%
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- **Indolent Cancer**
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  - Chromophobe
  - Papillary
  - Cystic RCC

- **Aggressive Cancer (Potentially)**
  - 20%
  - Clear Cell

- **Surgical Excision**
- **Thermal Ablation**
- **Active Surveillance**
Solid Renal Mass

- Benign:
  - 20% Oncocytoma
  - Metanephric adenoma

- Indolent Cancer:
  - 60% Chromophobe Papillary Cystic RCC

- Aggressive Cancer (Potentially):
  - 20% Clear Cell

Treatment Options:
- Surgical Excision
- Thermal Ablation
- Active Surveillance
Small Renal Mass

- Biopsy

**Benign**
- 20% Oncocytoma
- Metanephric adenoma

**Indolent Cancer**
- 60% Chromophobe
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**Aggressive Cancer** (Potentially)
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**Surgical Excision**
**Thermal Ablation**
**Active Surveillance**
Limitations of Renal Mass Biopsy

“Oncocytic neoplasm”

Oncocytoma  Chromophobe  Papillary
Molecular Markers for Small Renal Masses

• Clear Cell RCC: Carbonic anhydrase IX
• Atypical AML: HMB45
• Oncocytoma, Chromophobe: Cytokeratins

• Other Molecular Methods:
  – Electron microscopy: mitochondria vs. microvesicals
  – FISH
  – Genetic Profiling

• All could be incorporated to enhance diagnostic accuracy of renal mass biopsy
Renal Mass Biopsy: Paradigm Shift?

- What is the reality of renal mass biopsy in 2009?
- What is the data?
Renal Mass Biopsy: Prior to 2001

- 28 studies, 2474 patients
- Technical failure = 8.1%
- Indeterminate = 5.6%
- False negative: 4%: the REAL ISSUE
- Successful bx yielded accurate Dx in 81.9%
How Robust is this Data?

Compare with CT.....

- Enhancing, solid mass on CT: 80% RCC
- If treat all, sensitivity of CT is 100%, false negative rate is 0, but false positive rate is 20%
- Can we refine based on clinical parameters and tumor size?

Lane et al. J Urol 2008
Tumor Size and Risk of RCC

- 25% < 3.0 cm are benign
- 28% < 3.0 cm are indolent variant RCC (papillary or chromophobe)
- 47% < 3.0 cm are conventional clear-cell RCC
- 4% < 3.0 cm are high-grade conventional RCC
- Advanced pathological features uncommon < 3.0 cm:
  - Invasive of perinephric fat (1.7%)
  - Venous involvement (0.7%)
  - LN involvement (0.6%)
- Recurrence rates (2-3% at 5 yrs)

Frank et al. J Urol 2005
Risks of Renal Mass Biopsy

- Bleeding: 85-91% on CT if obtained routinely
- Hospitalized for observation or transfusion: 1-2%
- Loss of kidney: rare
Risks of Renal Mass Biopsy

- Pneumothorax: Passage between 11/12 ribs: traverses pleura 14-29% of time
- Above 11th rib: higher potential for pneumothorax
- Clinically significant pneumothorax: < 1%
Risks of Renal Mass Biopsy

- Tract seeding: rare, only 8 reported cases
- No reported cases since 1994
- Histology, some TCC or sarcomatoid RCC
- Infiltrative renal mass, do not bx if suspect TCC
Renal Mass Biopsy: 2001-present

- 2001-2007: 7 in vivo studies, 362 patients
- Major complications: 1 (0.3%)
- Technical failure: 19 (5.2%)
- Indeterminate: 14 (3.8%)
- False negative: 2 (0.6%), Main Concern
- False positive: 0 (0%)
Renal Mass Biopsy: 2001-present

• High degree of accuracy for benign vs. malignant

• Grade assessed correctly in 83% and 70% in 2 studies → never more than one grade off

• Histologic subtypes: 92% accurate

• Add FISH for 3, 7, 10, 13, 17, 21, and 3p25-26: ↑ accuracy from 87% (histopathology alone) to 94%

Lane et al. J Urol 2008
Indications for Renal Mass Biopsy in 2009

- Suspicion of lymphoma
- Febrile UTI and mass, suspect abscess
- Hx non-renal malignancy
  - If solitary, strongly enhancing, and no evidence of progression elsewhere, likely an RCC and Bx not indicated
- Bx at time of ablation
Patients that want or need to be considered for alternate Rx

- Advanced Age
  - Prohibitive Comorbidities
    - No Bx
    - Conservative Rx
      - Observation or Thermal Ablation

- Intermediate
  - Bx to Stratify Risk???
  - Several Options Considered

- Young Healthy
  - No Bx
  - Proactive Surgical Excision
Small Renal Mass

Biopsy: Histopathology, Molecular Markers

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Future: Renal Mass Bx
Future: Molecular Imaging

Small Renal Mass

Molecular Imaging: $^{125}$I-cG250 mAb CT-PET

Indolent RCC or Benign 80%

Clear-Cell RCC 20%

Surgical Excision

Thermal Ablation

Active Surveillance

Divgi et al. Lancet Oncol 2007
Index Patient 1:
Healthy; Clinical T1a

**STANDARD-PN:** Complete surgical excision by PN is a standard of care and should be strongly considered.

**STANDARD-RN:** Should be discussed as an alternate standard of care if PN is not technically feasible as determined by the urologic surgeon.

**OPTION-TA:** Cryoablation or RFA should be discussed as less-invasive treatment options, but local tumor recurrence is more likely, measures of success are not well defined, and surgical salvage may be difficult.

**OPTION-AS:** AS with delayed intervention should be discussed as an option for patients wishing to avoid treatment and willing to assume oncologic risk.

Campbell et al. *J Urol* 2009
Index Patient 2:
Major comorbidities: Increased surgical risk; Clinical T1a

**STANDARD-PN:** Complete surgical excision by PN is a standard of care and should be strongly considered.

**STANDARD-RN:** Should be discussed as an alternate standard of care with increased risk of CKD and surgical complications in this patient.

**RECOMMENDATION-TA:** Cryoablation or RFA should be discussed as less-invasive treatment options which may be advantageous in this high surgical risk patient, acknowledging the increased risk of local tumor recurrence compared to surgical excision.

**RECOMMENDATION-AS:** should be offered as an acceptable approach which can delay or avoid the need for intervention in this high-risk patient.

Campbell et al. *J Urol* 2009