What is the role of renal ablation in the context of active surveillance and partial nephrectomy

Surena F. Matin, MD, FACS
Maximal Preservation of Renal Function
We Lose Kidney Function As We Age
-HTN, DM Accelerate That Loss-

KEEP N = 45,311. NHANES N = 9,718.

CKD Definition
If eGFR by K/DOQI MDRD <60 ml/min/1.73 m² or;
If eGFR by K/DOQI MDRD ≥ 60 ml/min/1.73 m² abnormal albumin/creatinine ratio (ACR ≥30 mg/g)

KEEP Annual Data Report, 2006
Partial Nephrectomy: The Reference Standard

- >98% efficacy at >5 years
- Outcomes/feasibility likely linked to experience
- Hemorrhage (+/-urinary leak) most common complication
- Open partial remains excellent option, particularly for
  - Tumors requiring hypothermia or no ischemia (CKD)
  - Complex tumor resection/renal reconstruction
- Robotic partial nephrectomy offers minimally invasive option

AUA Guidelines for the small renal mass; Campbell SC J Urol 2009
Renal Ablation: Advantages

- Minimal anesthesia, recovery
- Well tolerated by “elderly”, high surgical or anesthetic risk, enlarging mass on active surveillance
- Less morbid for salvage after prior partial nx
- Minimal time off anticoagulants (drug-eluting stents)
Renal Ablation: Disadvantages

• RFA and Cryoablation associated with 88-90% efficacy in short term

• Patient must accept
  – Preablation biopsy
  – Routine follow up imaging at center
  – Postablation biopsies (possibly)

AUA Guidelines for the small renal mass; Campbell SC J Urol 2009
MD Anderson Experience 2002-2008

- 124 consecutive patients
- Biopsy for diagnosis
  - Used to do at same time as ablation
  - Now we do bx first and await cancer diagnosis
- RFA
  - Percutaneous: CT-guided (~80%)
  - Laparoscopic: US-guided (~20%)
Methods

• General anesthesia
• Multiple sequential overlapping ablations
• Complete tumor treatment in a single session
• Follow-up
  – CT or MRI within 6 weeks, and at 6, 12, 18, and 24 months
  – Semiannual or annual follow up afterwards
• Post-ablation biopsies starting in ~2006
  – Indications: any enhancement, growth, or failure to involute (even if no enhancement)

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Biopsy pre-RFA

- Renal cell carcinoma: 71%
- Oncocytic neoplasms: 16%
- Non-diagnostic: 5%
- No cancer: 3%
- Angiomyolipomas: 2%
- Malignant fibrous histiocytoma: 1%
- Leiomyosarcoma: 1%
- Smooth muscle neoplasm: 1%

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## Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N=124</strong></td>
<td></td>
</tr>
<tr>
<td>Median age, years (Range)</td>
<td>70 (24-85)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>83 (66.9)</td>
</tr>
<tr>
<td>Female</td>
<td>41 (33.1)</td>
</tr>
<tr>
<td>RFA Technique</td>
<td></td>
</tr>
<tr>
<td>Percutaneous</td>
<td>104 (83.9)</td>
</tr>
<tr>
<td>Laparoscopic</td>
<td>20 (16.1)</td>
</tr>
<tr>
<td>Tumor characteristic</td>
<td></td>
</tr>
<tr>
<td>&gt;50% Exophytic</td>
<td>56 (47.9)</td>
</tr>
<tr>
<td>&lt;50% Exophytic</td>
<td>37 (31.6)</td>
</tr>
<tr>
<td>Endophytic</td>
<td>24 (20.5)</td>
</tr>
<tr>
<td>Tumor diameter</td>
<td></td>
</tr>
<tr>
<td>Median (Range)</td>
<td>2.80 (1-7)</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>2.89 (1.24)</td>
</tr>
</tbody>
</table>

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## Complications

<table>
<thead>
<tr>
<th>Major Complications (15 patients)</th>
<th>N</th>
<th>Minor Complications (10 patients)</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross hematuria</td>
<td>6</td>
<td>Urinary retention</td>
<td>7</td>
</tr>
<tr>
<td>Acute hypertension</td>
<td>4</td>
<td>Pain</td>
<td>5</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>3</td>
<td>Transient acute renal failure</td>
<td>3</td>
</tr>
<tr>
<td>Perinephric hematoma</td>
<td>3</td>
<td>Paresthesia</td>
<td>2</td>
</tr>
<tr>
<td>Ureteral clot occlusion</td>
<td>3</td>
<td>Urinary tract infection</td>
<td>1</td>
</tr>
<tr>
<td>Splenic hematoma</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Port-site hernia</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Predictors of Major Complications

- Early in experience
- Larger tumor size
- Imperative indication
Renal Functional Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Median follow-up (months)</th>
<th>eGFR Pre-RFA</th>
<th>eGFR Post-RFA</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients (N=124)</td>
<td>24</td>
<td>64.3</td>
<td>57.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Two kidneys (N=103)</td>
<td>25</td>
<td>66.0</td>
<td>58.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Solitary kidney (N=21)</td>
<td>24</td>
<td>53.4</td>
<td>48.6</td>
<td>0.078</td>
</tr>
</tbody>
</table>

- Renal function preservation
  - Prevoo W Eur Urol 2010
  - Jacobsohn K Urol 2007
  - Weisbrod A AJR 2010

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Follow-up

- Radiographic: 25 months (range 1 to 76)
- Clinical: 36 months (1 to 88)
- Only 2 incomplete ablations (patient #1 and #5)
Incomplete Ablations

• Patient #1:
  – 42 year-old female, VHL
  – Percutaneous left RFA in 2002 → Repeat RFA
  – 6cm right renal tumor since presentation
  – Died of RCC in 2005

• Patient #5:
  – 66 year-old male
  – Percutaneous left RFA in 2002 → Repeat RFA
  – Died of pneumonia in 2005
Biopsy post-RFA

- 34 patients (27.4%)
- Indications for post-RFA biopsy
  - Failure to involute = 29 patients (85.3%)
  - Radiographic enlargement = 3 patients (8.8%)
  - Radiographic contrast enhancement = 2 patients (5.9%)
- Median time to biopsy
  - 23 months (range 8 to 68) after RFA
- 4 positive for RCC

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Biopsies

• Core biopsy + FNA (not just FNA)
  – Use of 18 ga coaxial needle
  – Nondiagnostic rate for *targetable* lesion is <15%

• Post-ablation:
  – Multi-site directed
  – If <2 cm, at least 2 cores are taken
  – If >2 cm, 4 quadrants + center (>4 cores)
Biopsy-Proven Zone of Ablation Recurrences

• Four biopsy-proven zone of ablation recurrences
  – 3 RCC
  – 1 oncocytic neoplasm
• One had radiographic enhancement with contrast
• Three (9.8%) with no significant involution and no radiographic enhancement
Zone of Ablation Recurrences

- All documented RCCs were treated
  - 1 with repeat RFA
  - 2 with salvage partial nephrectomy
  - All 3 are free of disease at 12, 26, and 32 months after re-treatment

- Patient with oncocytic neoplasm
  - Actively followed for 20 months with imaging
Treatment Improvements

• Perform multiple core biopsies before RFA
  – Wait for biopsy results before ablation
• Low threshold to biopsy post-ablation (after 6 months)
  – Multi site directed core biopsies (+/- FNA)
• Urology and Interventional Radiology both evaluate post-ablation images in addition to Radiologist
False Positive Imaging Findings
False Positive Imaging Findings

All necrosis and inflammation, NO cancer
False Negative Imaging Findings:
absence of contrast enhancement may not be the best determinant of success

- UT Southwestern (Cadeddu): 0% (n=19)

- Cleveland Clinic: ~17% (n=37; 6/13 positive bx had no enhancement)

- MD Anderson: ~10% (3/29 without involution)
  - Median time to biopsy 23 mos
  - Follow up 36 mos (1-88)
Immunostimulation by Ablative Therapy

Two clinical cases at our center have highlighted this phenomenon

– one patient having regression of all biopsy proven metastatic disease after RFA of the primary tumor

Sanchez-Ortiz R 2003
Another Patient with Tumor Regression After Ablation

Path: complete necrosis, extensive macrophage infiltration

8/08 Presentation

RFA of sacral met

10/08 Preop Films

Why does this not happen more frequently?

30 month follow up: NED
Inhibitory Pathways: Downregulation

- **Anti-CTLA-4 therapy (Ipilimumab)**
  - Improved survival (17% CR) in phase 3 study on melanoma patients (Oday et al 2010)

- **Anti-PD1 therapy (MDX-1106)**
  - Currently in phase 1/2 trials
Evaluation of Immunologic Responses After Renal Ablative Therapy
LAB09-0383

Patient with localized renal tumor

Biopsy and Ablative therapy of renal mass

Blood day 1

Blood week 4

6 months post ablation

Biopsy of ablated tissue 6-15 months post ablations

Blood

Cytokines
Antibody responses
T-cell functional assessment

Tissue
CD4+ subsets
CD8+
Macrophage
dendritic cell
Summary

- **Ablation has a narrow—but important—indication for treatment of a small renal mass**

- Because of
  - Favorable adverse event profile
  - Good renal function preservation
  - Less favorable oncologic control
Summary

- Patients must accept biopsy and need for follow up
  - Pre-ablation biopsy is mandatory for diagnosis
  - Consider post-ablation multi-site directed biopsies when no involution or if any concern

- Do not consider absence of enhancement as a certain sign of success