“Less is more: Merit of Non-Surgical Management of Kidney Cancer”

SATURDAY, AUGUST 20

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TAMPA, FL
Disclosures

- None related to this presentation
What’s the role of interventional oncology in non-surgical localized kidney cancer?

- Patient selection
- Procedural details
- Perioperative complications
- Short- and long-term oncologic and functional outcomes
Patient selection

Clinic visit → Laboratory → Diagnostic imaging → Tumor Board
Tumor Board
Multidisciplinary Approach

Medical Oncology
Radiology
Nuclear Medicine
Pathology

Radiation Oncology
Surgical Oncology
Interventional Oncology

Interventional Oncology

- Interventional Radiology Section
  - Physicians, PA’s, ARNPs, Nurses, technologists
- Roles in treatment of cancer patients
  - Diagnostic
  - Therapeutic or palliative
    - Cancer treatment, admission/management, clinic consultation, follow up
Ablative therapy

- Introduced more than two decades ago among the interventional options for the small renal masses (SRMs) (≤4 cm)

- Minimally invasive option

- Goal is oncologic outcomes similar to partial nephrectomy (PN) while preserving functional outcomes, minimizing perioperative complications, and decreasing long-term side effects

Local Kidney cancer directed therapy

- **Local**
  - Percutaneous Ablation
    - **Thermal**
      - Cryoablation
      - Radiofrequency ablation
      - Microwave ablation
    - **Non-thermal**
      - Irreversible electroporation (IRE)/Nanoknife
Local Kidney cancer directed therapy

Local

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Local Kidney cancer directed therapy

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Percutaneous Thermal Ablation

- **Extreme heat**
  - RFA, MWA

- **Extreme cold**
  - Cryoablation

Kidney

Kidney
• Thermal Ablation (TA) for small renal tumors
  – 4 cm or less in greatest dimension, limited to the kidney
  – Not surgical candidates
    – TA higher local recurrence than surgery
    – Long-term data have demonstrated durable outcomes for nephron sparing surgery, extended oncological efficacy is lacking for ablation and surveillance strategies

• No Randomized phase III trials comparing TA with surgical resection
American Urological Association recommendations

• For T1a (<4 cm tumor)
  • Patient with comorbidities, high surgical risk
    • TA vs. Active surveillance (AS)
  • Healthy patient
    • Less invasive treatment, potential higher local recurrence

• T1b (4-7 cm tumor)
  • High surgical risk
    • TA vs. AS
  • Healthy patients
    • TA and AS considered suboptimal

Level of evidence

- No RCT comparing ablation with any other alternative treatment or active surveillance

- Evidence from observational studies mostly retrospective or case–control and from several meta-analyses comparing CA with PN or RFA

- Difficulty of assessing survival outcomes due to relatively small sample size, short follow-up and the limited number of studies

- The extent to which ablation or AS alters the natural history of small renal masses is not yet established

Decision making

- Majority of small enhancing renal masses grow at a slow rate
- Metastatic and cancer specific death are low
- Serial radiographic data alone are insufficient to predict the true natural history of these lesions
- Calculated risk when following these tumors
- Basic biological data needed to assess the natural history of untreated renal masses
- Special conditions: recurrence in same kidney after surgery, or opposite kidney, solitary kidney, genetic predisposition for developing multiple tumors

To biopsy or not to biopsy

- Abdominal imaging: high diagnostic accuracy

- Needle biopsy not always necessary for diagnosis

- Considered for small lesions to guide active surveillance strategies, or treatment (caveat: Biopsy of small tumors associated with a relatively high rate of technical biopsy failure 22%)

- Suspicion of other types of cancer

Active Surveillance, Radiofrequency Ablation, or Cryoablation for the Nonsurgical Management of a Small Renal Mass: A Cost-Utility Analysis

Sasha N. Bhan, MD, MBA¹, Stephen E. Pautler, MD, FRCSC², Bobby Shayegan, MD, FRCSC³, Maurice D. Voss, MD, MBChB, FRACR, FRCPC⁴, Ron A. Goeree, MA⁵,⁶, and John J. You, MD, MSc, FRCPC⁷

¹Department of Radiology, McMaster University, Hamilton, ON, Canada; ²Divisions of Urology and Surgical Oncology, Departments of Surgery and Oncology, Western University, London, ON, Canada; ³McMaster Institute of Urology, St. Joseph’s Healthcare, Hamilton, ON, Canada; ⁴Department of Radiology, St. Joseph’s Healthcare, McMaster University, Hamilton, ON, Canada; ⁵Programs for Assessment of Technology in Health (PATH) Research Institute, St. Joseph’s Healthcare, Hamilton, ON, Canada; ⁶Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, ON, Canada; ⁷Departments of Medicine and Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, ON, Canada
Cost utility analysis: AS, RFA, CA

- Most effective and least costly strategy was AS with subsequent CA if needed
- On a quality-adjusted and discounted basis, immediate CA resulted in a similar life expectancy (3 days fewer) but costs $3,010 more
- RFA had decreased quality-adjusted life expectancies (82–87 days fewer than the dominant strategy) and higher costs ($3,231– $6,398 more)
- AS with delayed percutaneous CA, if needed, may be a safe and cost-effective alternative to immediate CA
- Still uncertainty in the relative long-term rate of progression to metastatic disease in patients managed with AS vs immediate CA
- RCT needed
Procedural details percutaneous TA

- **Image guidance:**
  - CT or Ultrasound guidance

- **Position:**
  - typically prone position. Less commonly, decubitus position

- **Anesthesia:**
  - general anesthesia, deep or conscious sedation

- **Hospital stay**
  - Observed overnight and discharged the following morning
Radiofrequency ablation (RFA)

**Mechanism**

- Rapidly alternating current
- Vibrating molecules
- Local energy deposition and heat formation near the probe
- Objective to heat tissues to 50°–100°C (122-212 F) for 4–6 minutes
- Slow “cooking” (time to cell death: <1 sec at 100°C, 15 min at 45°C

Distance from source

Temperature

Ablation margin 0.5-1 cm

Hong et al. J Vasc Interv Radiol 2010
RADIOFREQUENCY ABLATION

Impedance = \( \frac{V}{I} \)

Power = \( V \times I \)
RFA DEVICES

Courtesy ANGIODYNAMICS Starburst
Stages of RF Ablation

Frictional Heating

Conductive Heating Over Time
### Radiofrequency Ablation (RFA)

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>• Long track record</td>
<td>• Concerns for needle tract seeding</td>
</tr>
<tr>
<td>• Wide availability</td>
<td>• Skin pad burns</td>
</tr>
<tr>
<td>• Cost: relatively cheaper compared with “new”</td>
<td>• Limited ablation next to vessel</td>
</tr>
<tr>
<td>ablation modalities</td>
<td>• Size limitation: difficult (&gt;4 cm)</td>
</tr>
<tr>
<td>• Small probes</td>
<td>• Relatively slow</td>
</tr>
<tr>
<td>• Acceptable safety profile</td>
<td></td>
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<tr>
<td>• Helpful in periprocedural bleeding control</td>
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RFA outcomes

- Initial studies of renal RFA with early-generation generators with much less power
- At least 79% of tumors treatable with a single visit
- Local progression rates ranging from 0% to 9.7%. Need for long-term surveillance
- High degree of success if renal tumors less than 4 cm up to 100%
- Location and tumor size is a factor in local progression

Gervais DA, et al. AJR Am J Roentgenol 2005
Cryoablation (CA)

- Cryoprobe is a high-pressure, closedloop, gas expansion system
- Freezing-thawing cycles
- Tumors cells and feeding vessels are frozen, damaged leading to death
Cryoablation monitor
Iceball creation
Percutaneous Cryoablation Outcomes

- Fewer dedicated series than with RFA ablation
- Shorter follow up than RFA
- Initial success rates greater than 90%
- Important to track the durability of early outcomes in view of relatively late episodes of local progression with RFA or with surgical cryoablation
- Potential better outcomes: use as many as 8 probes and better patient selection in view of RFA experiences

Atwell TD et al. J Urol 2008
Complications

- Safety profile of CA is favorable with a reported major complication rate ranging from 3.2 to 8.6%.

- Similar to that of laparoscopic ablation and lower than for other surgical options (laparoscopic or open, partial or radical nephrectomy), which range between 11.5 and 13.8%.

## Percutaneous ablation complications

<table>
<thead>
<tr>
<th>Radiofrequency Ablation</th>
<th>Cryoablation</th>
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</thead>
<tbody>
<tr>
<td>• From 4% to 20.6%</td>
<td>• From 3% to 28%</td>
</tr>
<tr>
<td>• Most self-limited and minor</td>
<td>• Most self-limited and minor</td>
</tr>
<tr>
<td>• Hematuria</td>
<td>• Major complications most commonly related to hemorrhage</td>
</tr>
<tr>
<td>• Transient nerve injury</td>
<td>• Other complications similar to RFA: nerve injury or injury to the collecting system</td>
</tr>
<tr>
<td>• More serious complications can occur, including severe skin burns, ureteral injury, bowel (&lt;5%)</td>
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## RFA or Cryoablation?

<table>
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<tr>
<th></th>
<th>Radiofrequency Ablation</th>
<th>Cryoablation</th>
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<tbody>
<tr>
<td>Ease of use</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Speed</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Risk of bleeding</td>
<td>=</td>
<td>=</td>
</tr>
<tr>
<td>Damage to the collecting system</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Large tumors</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Central tumors</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Ability to monitor</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Radiation exposure</td>
<td>+</td>
<td>-</td>
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Hemorrhagic Complications of Percutaneous Cryoablation for Renal Tumors: Results from a 7-year Prospective Study

Bharat Kakarala¹ · Constantine E. Frangakis² · Ron Rodriguez³ · Christos S. Georgiades⁴
- 7-year prospective study: 261 renal CA, Pre- and postablation CT. Hemorrhagic complications were CTCAE tabulated.

- Percutaneous CA has a 3.5 % risk of significant hemorrhage, similar to that reported for other types of renal ablative modalities.

- 4 patients required transfusions, 2 emergent angiograms, one required both transfusion and angiogram, and 2 required bladder irrigation for outlet obstruction.

- MVA: patients [55 years with malignant tumors [2 cm requiring 2 or more probes yielded the highest PPV (7.5 %)]

- Low PPV does not support the routine use of embolization.
Cryoablation vs radiofrequency ablation for the treatment of renal cell carcinoma: a meta-analysis of case series studies

Regina El Dib*, Naji J. Touma† and Anil Kapoor*

*Botucatu School of Medicine, UNESP – Univ Estadual Paulista, Botucatu, Brazil, †Department of Urology, Queen’s University, Kingston, and *McMaster Institute of Urology, McMaster University, Hamilton, ON, Canada

Accepted for publication 30 September 2011
• 31 case series (20 CA, 11 RFA)
• Ablation therapies have similar efficacy and complication rates
• Need for RCT

El Dib et al. BJUI 2011
# Functional outcomes: Percutaneous vs laparoscopic ablation

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<tr>
<th>Percutaneous</th>
<th>Laparoscopic ablation</th>
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<tr>
<td>Significantly shorter anesthesia time</td>
<td>Similar post procedural pain and patient satisfaction</td>
</tr>
<tr>
<td>Shorter hospital stay (1.4 days vs 3.0 days; ( P &lt; 0.05 ))</td>
<td>Significantly higher efficacy rate in first-time surgical ablative procedures (94% vs 87%; ( P &lt; .05 ))</td>
</tr>
<tr>
<td>Earlier return to activity</td>
<td>Repeat ablation no difference (95% vs 92%)</td>
</tr>
<tr>
<td>Shorter time to recovery</td>
<td></td>
</tr>
<tr>
<td>Lower major complication rate: 3.1% versus 7.4% (( P &lt; 0.05 ))</td>
<td></td>
</tr>
<tr>
<td>Possible tract seeding but very rare</td>
<td></td>
</tr>
<tr>
<td>Easier to repeat</td>
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Microwave ablation (MWA)

- Newer heat-based ablation
- Creates a hyperthermic zone by agitating dipole water molecule in tissue, thereby increasing kinetic energy in the area
- Faster, and can provide higher temperatures than RFA with larger ablation volumes
- One or more antennas can be used
- Limited data
- Meta-analysis 2013 Martin et al: 51 studies. No difference in local or metastatic recurrence between CA and MWA in SRMs. MWA used more with open surgical access.
Irreversible electroporation (IRE)

- IRE: non-thermal ablation technique that induces cell death by electrocuting the tumor
- Preserves tissue architecture
- Not affected by near by blood vessels like thermal ablative therapies

Electroporation is a technique that increases cell membrane permeability by changing the transmembrane potential and subsequently disrupting the lipid bilayer integrity to allow transportation of molecules across the cell membrane via nano-size pores ("reversible electroporation").

Application of very high voltage electrical pulses induces irreversible disruption of cell membrane integrity resulting in cell death without the need for additional injury ("irreversible electroporation").
Non thermal Irreversible electroporation

- Selective damage only to the cell membrane
- Delivers quick bursts of energy through a set of electrodes inserted into and around the tumor
- Pulses create an electrical field of up to 3000 volts per cm
- A cell within range of the electric field will form pores in its fatty membrane, allowing ions to rush through
The efficacy and safety of irreversible electroporation for the ablation of renal masses: a prospective, human, in-vivo study protocol

Peter GK Wagstaff, Daniel M de Bruin, Patricia J Zondervan, C Dilara Savci Heijink, Marc RW Engelbrecht, Otto M van Delden, Ton G van Leeuwen, Hessel Wijkstra, Jean JMCH de la Rosette and M Pilar Laguna Pes

Follow-up After Ablative Techniques
- H P every 6 mo for 2 y, then annually up to 5 y after diagnosis
- Comprehensive metabolic panel and other tests as indicated every 6 mo for first 2 y, then annually up to 5 y after diagnosis
- Abdominal imaging:
  - Abdominal CT or MRI with and without contrast at 3–6 mo following ablative therapy unless otherwise contraindicated then CT, MRI, or US annually for 5 y
- Chest imaging:
  - Chest x-ray or CT annually for 5 y for patients who have biopsy-proven low-risk RCC, nondiagnostic biopsies, or no prior biopsy
- Repeat biopsy:
  - New enhancement, a progressive increase in size of an ablated neoplasm with or without contrast enhancement, new nodularity in or around the treated zone, failure of the treated lesion to regress over time, satellite or port site lesions
- Pelvic imaging, as clinically indicated
- CT or MRI of head or MRI of spine, as clinically indicated
- Bone scan, as clinically indicated

Continued on next page
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Adult Urology

Correlation of Radiographic Imaging and Histopathology Following Cryoablation and Radio Frequency Ablation for Renal Tumors

Christopher J. Weight, Jihad H. Kaouk, Nicholas J. Hegarty, Erick M. Remer, Charles M. O'Malley, Brian R. Lane, Inderbir S. Gill, Andrew C. Novick
Glickman Urologic Institute and Department of Radiology (EMR, CMOM), Cleveland Clinic, Cleveland, Ohio
Poor correlation between radiographic imaging and pathological analysis post RFA
Authors recommend post-RFA followup biopsy due to the significant risk of residual renal cell cancer without radiographic evidence
Clinical significance of these viable cells remains to be determined
In contrast, radiographic images of renal lesions treated with CA appeared to correlate adequately with corresponding histopathological findings
Other roles in the management of renal cancer

- Pre-operative embolization
- Combined embolization/ablation
- Palliation (pain control, metastectomy)
- Metastectomy
- Liver-directed therapies
Conclusions

- Interventional radiology offers multiple minimally invasive non-surgical treatments for localized kidney cancer
- Percutaneous cryoablation has initial outcomes and complications comparable to RFA
- Offers alternative to surgery
- Awaiting results on new thermal and non-thermal ablation techniques
Thank you