Management of High Risk Cystic Lesions of the Kidney

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Financial Disclosures

None
Background

- greater than 50% of adults greater than 50 years old have renal cysts, the vast majority being benign simple cysts.

- cystic renal lesions are increasingly being detected with utilization of cross-sectional imaging.

- the Bosniak Criteria for determining surgical cysts versus benign has been used for greater than 20 years in categorizing renal mass lesions.

- 4-7% of renal cell carcinoma have cystic component.
Background: **Renal cell carcinoma**

**Epidemiology**
- 3.8% of all new cancers
- Affects more males than females (3:2)

NCCN Guidelines (2019)
Multilocular Cystic Clear Cell Neoplasm of Low Malignant Potential

- A histologic variant of clear cell RCC (<5% of clear cell RCC)
- Formerly known as “multi-locular cystic RCC”
- Well-circumscribed, entirely cystic
- Cysts lined with single layer of clear cells (grade 1 nuclei)
- No recurrence or metastasis reported after resection
Cystic Renal Cell Cancer
30 yo male with gross hematuria cystic ccRCC. note para aortic lymphadenopathy
## Bosniak Classification of Renal Cysts

<table>
<thead>
<tr>
<th>BOSNIAK CLASSIFICATION</th>
<th>IMAGING CHARACTERISTICS</th>
<th>INCIDENCE OF MALIGNANCY</th>
<th>THERAPY</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Simple cyst with a hairline thin wall that does not contain septa, calcifications, or solid components. It measures water density in Hounsfield units and <strong>does not enhance</strong> with intravenous administration of a contrast agent.</td>
<td>1.7%</td>
<td><strong>No therapy or follow-up required</strong></td>
</tr>
<tr>
<td>II</td>
<td>Cyst may contain a few hairline thin septa and fine calcifications, or a short segment of slightly thickened calcification may be present in the wall or septa. Uniformly high-attenuation lesions &lt;3 cm (so-called high-density cysts) are well marginated and <strong>do not enhance</strong> with intravenous administration of a contrast agent.</td>
<td>18.5%</td>
<td><strong>No therapy or follow-up required</strong></td>
</tr>
<tr>
<td>IIF</td>
<td>Cysts may contain multiple hairline thin septa or minimal smooth thickening of their wall or septa. Their wall or septa may contain calcifications that may be thick and nodular, but <strong>no measurable contrast enhancement</strong> is present. These lesions are typically well marginated. Totally intrarenal nonenhancing high-attenuation renal lesions ≥3 cm are also included in this category.</td>
<td>18.5%</td>
<td><strong>Repeat imaging to assess stability of size and radiographic characteristics</strong></td>
</tr>
<tr>
<td>III</td>
<td>“Indeterminate” cystic masses have thickened irregular or smooth walls or septa in which <strong>measurable contrast enhancement</strong> is present.</td>
<td>33%</td>
<td><strong>Excision or ablation</strong></td>
</tr>
<tr>
<td>IV</td>
<td>Clearly malignant cystic masses can have all the criteria of category III but also contain <strong>enhancing</strong> soft-tissue components.</td>
<td>92.5%</td>
<td><strong>Excision or ablation</strong></td>
</tr>
</tbody>
</table>
Bosniak III & IV

- 67-100% are malignant

- the risk of malignancy is not clear-cut for Bosniak III and unnecessary surgery is a potential in up to 60% of lesions
Bosniak Category

III

IV

IV
Which one is malignant?
Malignancy Rate, Histologic Grade, and Progression of Bosniak Category III and IV Complex Renal Cystic Lesions

Mousessian; et al.. American Journal Of Roentgenology, 2017 Dec; Vol. 209 (6), pp. 1285-1290
100 Cystic Renal Lesions

A bar chart showing the percentage of malignant renal cysts for different Bosniak categories. The categories are:

- Bosniak IIF: 38% (3/8)
- Bosniak III: 40% (29/72)
- Bosniak IV: 90% (18/20)

The chart includes the following types of renal cell carcinoma (RCC):

- Clear cell RCC
- Papillary RCC
- Multilocular cystic RCC
- Unclassified RCC
- Chromophobe RCC

A star (*) indicates a statistically significant difference.
### TABLE 2: Association Between Nuclear Grade and Bosniak Category

<table>
<thead>
<tr>
<th>Fuhrman Nuclear Grade</th>
<th>Bosniak Category III</th>
<th>Bosniak Category IV</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>36 (10/28)</td>
<td>11 (2/18)</td>
<td>26 (12/46)</td>
</tr>
<tr>
<td>2</td>
<td>61 (17/28)</td>
<td>72 (13/18)</td>
<td>65 (30/46)</td>
</tr>
<tr>
<td>3</td>
<td>4 (1/28)</td>
<td>17 (3/18)</td>
<td>9 (4/46)</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Note—Data are percentage of lesions (no. of lesions/total lesions). Percentages do not total 100% because of rounding.

### TABLE 3: Association Between TNM Staging and Bosniak Category

<table>
<thead>
<tr>
<th>TNM Stage</th>
<th>Bosniak Category III</th>
<th>Bosniak Category IV</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>pT1a</td>
<td>86 (24/28)</td>
<td>78 (14/18)</td>
<td>83 (38/46)</td>
</tr>
<tr>
<td>pT1b</td>
<td>7 (2/28)</td>
<td>6 (1/18)</td>
<td>7 (3/46)</td>
</tr>
<tr>
<td>pT2</td>
<td>7 (2/28)</td>
<td>17 (3/18)</td>
<td>11 (5/46)</td>
</tr>
<tr>
<td>pT3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>pT4</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Note—Data are percentage of lesions (no. of lesions/total lesions). Percentages do not total 100% because of rounding.
Management of High Risk Cystic Lesions of the Kidney

Outline

- Renal Mass Biopsy

- Management Strategy
  - Active Surveillance
  - Thermal Ablation
  - Surgery
MGH Experience with Image Guided Biopsies of High Risk Cystic Renal Lesions

Harisinghani et al AJR 2003;180
MGH Experience

CT guided small renal mass biopsies (n=392)
18 men  10 women

Results:  17 (60.7%) positive for malignancy
          16 renal cell cancer, 1 lymphoma
          11 (39.3%) Benign (hemorrhagic cysts, adenoma, oncocytoma)
• 16 were surgically excised all correlated with the biopsy

• 1 lymphoma responded appropriately to chemotherapy

• none of the benign lesions progressed on follow up (negative predictive value was 100%)

• recommend elderly with comorbidity small renal mass biopsy is indicated for Bosniak III lesions

• up to 40% of patients can avoid surgery or treatment, negative biopsy of lesions under surveillance have not progressed (negative predictive value 100%)
Assumption 1:

- lesion growth or change in character (complexity) increases likelihood of malignancy

Assumption 2:

- Lesions are indolent and surveillance will not compromise outcome

Assumption 3:

- no change (stability) over 3-5 years then very low risk, (?) cease follow up
Progression = ↑ size and/or ↑ enhancement
Radiographic surveillance of minimally and moderately complex renal cysts

Gabr; et al.. BJU International, 2009 Apr; Vol. 103 (8), pp. 1116-9
• n=43  mean F/U 3 yrs

• 7 revealed progression, 39 no change

• lesion growth with no change in character 2
  1 malignancy
  1 benign

• lesion increase in character (hyperdense wall) enhancing nodule
  n=5  All were malignant

• 36 no change

• radiographic surveillance was effective, malignant lesions treated were still low grade
• active surveillance as per small renal mass protocol

• cross-sectional imaging CT/MRI every six months for three years, then yearly

• ensure stability reached; yearly for beyond midterm i.e. 5 years
59 year old male
Calcified cystic mass
Right kidney
Surveillance 5 yrs
Stable D/C from clinic
Managed by surveillance 11 years

Presents with thoracic inlet mass
Mediastinum mets
Isodense mass
Thermal Ablation in Cystic Renal Lesions III and IV (Consider Percutaneous Biopsy)
• RFA

• Cryo ablation

• Microwave
Thermal Ablation Left Upper Pole Renal Mass
Complete Response = No Enhancement
Imaging-guided radiofrequency ablation of cystic renal neoplasms

Allen; et al.. *American Journal of Roentgenology*, 2013 Jun; 200(6): 1365-1369. 5p
Image Guided RFA Cystic Renal Mass

- n=38  mean F/U 2.8 yrs  no progression

- non-surgical candidates (age, comorbidity)

- 61% malignancy by biopsy

- complications 5.3% one major CHF

- effective and safe treatment for cystic lesions
Surgical options for high risk cystic renal lesions
Principals of small renal mass management*

- Radical Nephrectomy
- Partial Nephrectomy (nephron sparing surgery)
- Open
- Laproscopic or Robotic

*caveat: consider nephrons sparing surgery for large (≥1b) cystic lesions as long-term response is excellent
52 YO Male with Left Flank Pain/ Hematuria

Calcified Mid Pole Lesion
Filling Defect Left Renal Pelvic Cystic Lesion
Lesion Exposed through Mini Flank Incision
Frozen Section Negative

Renal Hilum

Renal Pelvis
Stent and Renal Pelvis Reconstruction
Renal Pelvis Perinephric Fat Patch
Ectopic Solitary Pelvic Kidney with Solid/Cystic Mass
Intraoperative Ultrasound
Ectopic Pelvic Kidney
History of present illness

- Healthy 57 year old female
- Acute onset of right flank pain
- CT scan obtained
Small stone causing pyelocalycectasis and pain on the right

Incidentally discovered cystic lesion on the left
Cystic renal lesion
Cystic renal lesion
Cystic renal lesion
Cystic renal lesion
Mini Flank Incision
Cyst Enucleation is safe as it is surrounded by fibrous wall
Lack of Perinephric Fat Invasion (pt3a) ensures negative margins
Renorrhaphy
FG2 Cystic ccRCC
3 Month Follow Up - Normal eGFR
Surgical Resection Provides Excellent Outcomes for Patients With Cystic Clear Cell Renal Cell Carcinoma

Webster; et al.. Urology. 2007 70(5):900-904
## Comparison of clinical and pathologic features by cystic architecture for 2431 patients with clear cell RCC

<table>
<thead>
<tr>
<th>Feature</th>
<th>Yes n 85 n (%)</th>
<th>No (n 2346)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary tumor size</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5 cm</td>
<td>59 (69.4)</td>
<td>761 (32.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>5 to &lt;7 cm</td>
<td>17 (20.0)</td>
<td>465 (19.8)</td>
<td></td>
</tr>
<tr>
<td>7 to &lt;10 cm</td>
<td>7 (8.2)</td>
<td>575 (24.5)</td>
<td></td>
</tr>
<tr>
<td>≥10 cm</td>
<td>2 (2.4)</td>
<td>545 (23.2)</td>
<td></td>
</tr>
<tr>
<td><strong>2002 Primary tumor pathologic stage</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pT1a</td>
<td>54 (63.5)</td>
<td>579 (24.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>pT1b</td>
<td>22 (25.9)</td>
<td>566 (24.1)</td>
<td></td>
</tr>
<tr>
<td>pT2</td>
<td>8 (9.4)</td>
<td>459 (19.6)</td>
<td></td>
</tr>
<tr>
<td>pT3a</td>
<td>1 (1.2)</td>
<td>218 (9.3)</td>
<td></td>
</tr>
<tr>
<td>pT3b</td>
<td>0 (0.0)</td>
<td>475 (20.3)</td>
<td></td>
</tr>
<tr>
<td>pT3c</td>
<td>0 (0.0)</td>
<td>19 (0.8)</td>
<td></td>
</tr>
<tr>
<td>pT4</td>
<td>0 (0.0)</td>
<td>30 (1.3)</td>
<td></td>
</tr>
<tr>
<td><strong>Regional lymph node pathologic stage</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pNx and pN0</td>
<td>85 (100.0)</td>
<td>2219 (94.6)</td>
<td>0.021</td>
</tr>
<tr>
<td>pN1 and pN2</td>
<td>0 (0.0)</td>
<td>127 (5.4)</td>
<td></td>
</tr>
<tr>
<td><strong>Distant metastases (clinical stage)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cM0</td>
<td>85 (100.0)</td>
<td>1990 (84.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>cM1</td>
<td>0 (0.0)</td>
<td>356 (15.2)</td>
<td></td>
</tr>
</tbody>
</table>
## Comparison of clinical and pathologic features by cystic architecture for 2431 patients with clear cell RCC

### Cystic architecture

<table>
<thead>
<tr>
<th>Feature</th>
<th>Yes n 85 n (%)</th>
<th>No (n 2346)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002 TNM stage groupings</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>76 (89.4)</td>
<td>1078 (46.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>II</td>
<td>8 (9.4)</td>
<td>363 (15.5)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>1 (1.2)</td>
<td>510 (21.7)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>0 (0.0)</td>
<td>395 (16.8)</td>
<td></td>
</tr>
<tr>
<td>Nuclear grade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>35 (41.2)</td>
<td>227 (9.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2</td>
<td>49 (57.7)</td>
<td>1007 (42.9)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1 (1.2)</td>
<td>908 (38.7)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>0 (0.0)</td>
<td>204 (8.7)</td>
<td></td>
</tr>
<tr>
<td>Coagulative tumor necrosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>83 (97.7)</td>
<td>1650 (70.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Yes</td>
<td>2 (2.4)</td>
<td>696 (29.7)</td>
<td></td>
</tr>
<tr>
<td>Sarcomatoid differentiation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>85 (100.0)</td>
<td>2222 (94.7)</td>
<td>0.021</td>
</tr>
<tr>
<td>Yes</td>
<td>0 (0.0)</td>
<td>124 (5.3)</td>
<td></td>
</tr>
</tbody>
</table>

TNM = tumor node metastasis; COG = Eastern Cooperative Oncology Group; TNM = tumor node metastasis.
Cancer-Specific Survival

![Graph showing cancer-specific survival rates over years from surgery to last follow-up for cystic and non-cystic cases.](image-url)
Cancer-Specific Survival PT1

![Graph showing cancer-specific survival over years from surgery to last follow-up for Cystic and Non-Cystic cases. The survival rates decrease over time, with Cystic cases showing a slightly lower survival rate compared to Non-Cystic cases.](image-url)
Cystic renal cell carcinoma carries an excellent prognosis regardless of tumor size

Winters; et al. *Urol Oncol.*, 2015 Jun; 33 (12): 505

SEER Database

n=678 cystic clear cell cancer

n= 46,677 cc RCC (solid)
Hemorrhagic Cystic ccRCC
54-year-old male complains of right upper quadrant bulge.
54-year-old male complains of right upper quadrant bulge. Resected cystic ccRcc.
30 yo female felt bulge and left upper quad pain at volleyball
30 yo female with left upper quad pain
30 yo female with left upper quad pain
3 month Post-Op
Epithelioid AML
Conclusion

- incidence of complex (HR) cystic renal lesions increasing with increasing cross-sectional imaging

- RMB is accurate and prevents unnecessary surgery or changes management elderly/comorbidity

- the rate of malignancy for Bosniak III/IV is high but surgical outcomes are excellent. Bosniak classification does not predict aggressiveness (FG) and cures for Bosniak IV lesions are high as compared to solid clear cell renal cell cancer; favor NSS when possible

- obey oncologic surgical principles (laprascopic unroofing not acceptable)

- consider extending surveillance beyond midterm (5yrs) for high risk Bosniak lesions, especially young and healthy