The Incidental Renal Mass in the Primary Care Setting

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Abstract

• There are approximately 63,000 cases of renal cell carcinoma annually due to increased health awareness, cross sectional imaging, and the possible link of RCC to obesity.

• The potential of a cancer diagnosis is anxiety provoking in most patients as they receive their test findings by their primary care provider. Assurance should be a primary component of counseling at the onset along with a prompt referral to the urologic specialist, as the majority can be handled well.
Abstract

• Modern approaches to evaluation and treatment results in overwhelming good outcomes, with a cure rate in the 90-95 percent range. These small renal masses can often be managed in a noninvasive or minimally invasive manner.

• Renal cell carcinoma (RCC) accounts for an estimated 3-4% of the newly diagnosed adult malignancies and 2% of cancer mortality in the United States. The incidence of primary renal malignancy has been steadily increasing in the United States over the past two decades, and the average size of the renal masses discovered at presentation is getting smaller.
Abstract

- In the past, these lesions were identified with a classic triad of hematuria, flank pain, and abdominal mass, and only a small percentage, asymptomatic. The classic triad is now rarely seen, and approximately 61% of lesions are asymptomatic and smaller at the time of detection.

- Consideration of a natural growth history, patient age and co-morbidities, and tumor location will guide the clinical approach to these findings. Pathologic staging shows that approximately 10-20% of small renal masses are benign and a subgroup of malignant masses is indolent.
• Reasonable alternatives include active surveillance, thermal ablation, and surgical extirpation, which include both nephron sparing surgery, partial nephrectomy, or radical nephrectomy. Traditional open techniques, as well as minimally invasive techniques, including laparoscopy and robotic-assisted laparoscopy, are definitive options. Selective use of percutaneous biopsy also has a growing role in the current management of the incidental, asymptomatic small renal masses.
Abstract

• Objectives:
• Increase the Primary Care Provider’s Knowledge base and awareness of treatment options regarding this common Imaging finding and health risk.
• Discussion and analysis surrounding the treatment options for small renal masses.
• Provide supportive informed counseling to your primary care patient's as you give their test results prior to referral, and also as they return from the urologic specialist.
Incidental Renal Masses

• Primary Care Providers will often encounter the incidental renal mass during a preliminary work up for another presenting problem.

• ER evaluations for abdominal pain or trauma are frequently evaluated with cross sectional imaging prompting referral back to PCP/ Subsequent referral to the Urology Specialist - Urologic Oncologist
Classic Triad

- Classic Triad
  - 1. Hematuria
  - 2. Flank Pain
  - 3. Abdominal Mass

- Classic triad is rarely seen
- 61% of patients are asymptomatic and smaller at the time of detection.
Epidemiology- “Rise of the Machines”

- “Rise of the Machines”
- The increased rate of sophisticated abdominal and retroperitoneal imaging by various modalities
- US
- CT
- MRI

* Considerations - Renal function, Pacemaker
Imaging

- **Ultrasound** – non invasive, inexpensive, 98% accurate in distinguishing simple cysts from solid lesions

- **CT of Abdomen only** - method of choice for staging by visualizing the renal hilum, perinephric space, renal vein, vena cava, adrenals, lymphatics, adjacent organs
  - 1. CT with/without contrast for initial diagnosis
  - 2. CT with only for post surgical follow up
  - 3. Radiology guidelines to minimize exposure
Imaging

- **MRI of the abdomen only** - equivalent to CT for staging. The advantage is evaluation for patients with suspected vascular extension

- 1. MRI with and without contrast
Laboratory Studies

- Anemia occurs in 30% of patients
- Gross hematuria can be seen in 60% of cases
- Elevate sedimentation rate 75%

- All findings non specific
The Small Renal Mass

- **Definition**
  - Classic SRM, < 3cm Renal “Adenoma”
  - pT1a lesion
  - Renal Cell Carcinoma, < 7.5cm
  - Stage 1
Renal cell carcinoma

Left Kidney
Benign Tumors

- **Renal Oncocytoma**
- 3-5% of renal tumors
- **Angiomyolipoma**
- < 4cm annually > 4cm semiannually 25-30% of patients will be observed will require treatment in the form of embolization
- **Other rare tumors**
- Leiomyoma, hemangiomas, lipomas & juxtaglomerular cell tumors
Renal Cell Carcinoma

- Conventional Clear Cell  70-80%
- Papillary 10-15%
- Chromophobe  3-5%
- Collecting Duct <1%
- Renal medullary carcinoma
- Neuroendocrine
- Unclassified
Renal Cell Pathology

- Type: Clear Cell 75%, Papillary Type 1 5%, Papillary Type 2 10%
- Gene: VHL, Met, FH, BHD, Chromophobe 5%, Oncocytoma 5%
AJCC 7th Edition Staging System for RCC

T1: 
- Tumor ≤ 7 cm

T2: 
- Tumor > 7 cm

T3a: 
- Tumor侵犯Gerota's fascia
- Perinephric fat

T3b: 
- Tumor侵犯Gerota's fascia
- Perinephric fat
- Involved node

T3c: 
- Tumor侵犯Gerota's fascia
- Perinephric fat
- Involved nodes

T4: 
- Tumor侵犯Gerota's fascia
- Perinephric fat

N1: 
- Involved node

N2: 
- Involved nodes
Tumor Grading

- Fuhrman Grading (Fuhrman et al, 1982)
  - Fuhrman 1-IV
  - The system uses four grades based:
    - Nuclear size & irregularity
    - Nucleolar prominence
The Renal Mass

• Studies defined potential aggressiveness based on the presence of high risk pathologic features including Fuhrman nuclear grade III/IV, presence of type II papillary, sarcomatoid or collecting duct histology, presence of invasion into the renal sinus capsule or vasculature, or presence of metastasis at the time of diagnosis.
Prognosis

- Most clearly related to the stage of the disease at presentation
- Recent studies- 5 yr survival
- T1-T2  80-100% range
- T3  50-60% range
- Metastasis on Presentation 25-30%
Epidemiology

- Increased Total # of New Cases
- **Stage Shift in Diagnosis to lower-stage smaller tumors**

- Renal Cell # 2013 63,150 new cases and 16,680 deaths attributable to the disease

- RCC represents 5% of male cancers and 3% of female cancers

- RCC peak in sixth to seventh decade of life
Epidemiology

- True Emerging Risks

- Risks: Smoking [two fold increased risk]
  Obesity

- Ratio: Male/Female 2-3:1

- Genetic Factors Rare
Pathology

- Renal Mass-Bosniak Scoring System
- Simple Cyst ..... Solid Masses
- Others:
  - 1. Fibroma
  - 2. Oncocytoma
  - 3. Angiomyolypoma.[ AML]
  - 4. Sarcoma
  - 5. Lymphoma
Bosniak Classification of Cystic Masses

- **Bosniak I** Simple cyst  <2%
- **Bosniak II** Minimally complex cyst, thin wall  <5%
- **Bosniak IIF** Indeterminate, complex cyst with thicker septa  ~ 25%
- **Bosniak III** Suspicious indeterminate, thicker, regular, nodular walls w/ regular calcifications 7 septations  ~50%
- **Bosniak IV** Malignant, nodular or solid component  >90%
85% are accurately identified on Pre-Op Imaging

RCC are vascular tumors that tend to spread either by direct invasion through the renal capsule into the perinephric fat and adjacent visceral structures or by direct invasion into the renal vein.

Approximately 25-30% of patients have evidence of metastatic disease at presentation.
Hereditary Syndromes

- Von Hippel Lindau
- Hereditary papillay RCC
- Hereditary leimyomatosis & RCC
- Birt-Hogg-Dube syndrome
- Tuberous sclerosis
Multifocal Renal Carcinoma

Hereditary Papillary Renal Carcinoma (HPRC) Type 1
Burt Hogg Dube

Birt Hogg Dubé
Cutaneous Manifestations

VHL

VHL Gene Mutation

VHL Protein

HIF1-α, HIF2-α Accumulation

VEGF, Glut-1, TGF-α, EGFR

Angiogenesis, Glucose Transport, Autocrine Growth Stimulation
Small Renal Mass

- Small [<3 cm] renal lesions are now diagnosed frequently
- 85% will represent renal tumors
- Needle biopsy has 20-40% false negative rate.
- **Growth rate is 1-6 mm per year**
- **Metastatic potential is approximately 2%**
- Age and performance status of patient is a significant factor.
<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Percent Benign</th>
<th>Percent Indolent</th>
<th>Percent Aggressive</th>
<th>Percent Metastatic</th>
<th>Aggressiveness Criteria</th>
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<tbody>
<tr>
<td>Frank²⁴ (2003)</td>
<td>947</td>
<td>23%</td>
<td>54%</td>
<td>13%</td>
<td>NA</td>
<td>FG ≥3</td>
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<tr>
<td>Remzi²⁶ (2006)</td>
<td>287</td>
<td>20%</td>
<td>58%</td>
<td>22%</td>
<td>5%</td>
<td>Stage ≥T3a or metastatic</td>
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<tr>
<td>Schlomer²⁷ (2006)</td>
<td>206</td>
<td>23%</td>
<td>52%</td>
<td>25%</td>
<td>NA</td>
<td>FG ≥3</td>
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<tr>
<td>Pahernik²⁸ (2007)</td>
<td>653</td>
<td>17%</td>
<td>70%</td>
<td>13%</td>
<td>3%</td>
<td>FG ≥3, stage ≥T3a or metastatic</td>
</tr>
<tr>
<td>Lane²⁹ (2007)</td>
<td>852</td>
<td>20%</td>
<td>56%</td>
<td>24%</td>
<td>NA</td>
<td>FG ≥3 or stage ≥T3a</td>
</tr>
<tr>
<td>Mean Values</td>
<td></td>
<td>20%</td>
<td>60%</td>
<td>20%</td>
<td>4%</td>
<td></td>
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</tbody>
</table>

Abbreviations: FG, Fuhrman Grade; NA, Not Available.
## Natural History and Tumor Growth Rate

- **Table 2**

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>N</th>
<th>Mean cm Tumor Size</th>
<th>Mean cm/y Growth Rate</th>
<th>Mean Months Follow-up</th>
<th>Metastatic Progression (%)</th>
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</thead>
<tbody>
<tr>
<td>Basniak et al.,28 (1995)</td>
<td>40</td>
<td>1.73</td>
<td>0.36</td>
<td>39.0</td>
<td>0</td>
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<tr>
<td>Kato et al.,12 (2004)</td>
<td>18</td>
<td>2.0</td>
<td>0.42</td>
<td>26.9</td>
<td>0</td>
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<td>Lamb et al.,73 (2004)</td>
<td>36</td>
<td>7.2</td>
<td>0.39</td>
<td>27.7</td>
<td>1 (2.8%)</td>
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<tr>
<td>Volpe et al.,6 (2005)</td>
<td>32</td>
<td>2.48</td>
<td>0.10</td>
<td>38.9</td>
<td>0</td>
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<td>Wehle et al.,76 (2004)</td>
<td>29</td>
<td>1.83</td>
<td>0.12</td>
<td>32.0</td>
<td>0</td>
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<td>Abouassaly et al.,77 (2008)</td>
<td>110</td>
<td>2.5*</td>
<td>0.26</td>
<td>24.0*</td>
<td>0</td>
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<tr>
<td>Kouba et al.,78 (2007)</td>
<td>46</td>
<td>2.92</td>
<td>0.70</td>
<td>35.8</td>
<td>0</td>
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<td>Kunkle et al.,73 (2007)</td>
<td>106</td>
<td>2.0*</td>
<td>0.19*</td>
<td>29.0*</td>
<td>1 (1.1%)</td>
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<td>Youssif et al.,75 (2007)</td>
<td>41</td>
<td>2.2</td>
<td>0.21</td>
<td>47.6</td>
<td>2 (5.7%)</td>
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<tr>
<td>Crispen et al.,39 (2008)</td>
<td>173</td>
<td>2.45</td>
<td>0.285</td>
<td>31.0</td>
<td>2 (1.3%)</td>
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<td>Rosales et al.,6 (2010)</td>
<td>223</td>
<td>2.8*</td>
<td>0.34*</td>
<td>35.0*</td>
<td>4 (1.9%)</td>
</tr>
<tr>
<td>Mean values</td>
<td></td>
<td>2.7</td>
<td>0.31</td>
<td>33.0</td>
<td>1.2%</td>
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</table>

* Median values rather than mean values.
Management of Localized Kidney Cancer: Calculating cancer-specific Mortality & Competing Risks of Death for Surgery and Non Surgical Management

Sun, Becker, Tien et al 2013
Cancer-specific mortality and Other – Cause mortality

| Table 2 – Multivariable competing risks regression analyses estimating the effect of treatment type on the risks of cancer-specific mortality and other-cause mortality |
|-----------------------------------------------|------------------|------------------|------------------|------------------|
|                                               | PN vs NSM, HR (CI) | p value | RN vs NSM, HR (CI) | p value |
| Cancer-specific mortality                      |                  |        |                  |        |
| Primary analyses                               |                  |        |                  |        |
| Entire cohort, n = 10 595                      | 0.45 (0.24–0.83) | 0.01   | 0.58 (0.35–0.96) | 0.03   |
| T1a, n = 6443                                  | 0.41 (0.18–0.91) | 0.03   | 0.47 (0.23–0.98) | 0.04   |
| Subanalyses                                    |                  |        |                  |        |
| ≥75 yr, n = 4830                               | 0.48 (0.20–1.14) | 0.1    | 0.57 (0.32–1.03) | 0.1    |
| T1a and ≥75 yr, n = 2873                       | 0.39 (0.13–1.08) | 0.1    | 0.40 (0.16–1.01) | 0.1    |
| RCC only*, n = 7806                            | 0.26 (0.13–0.54) | <0.001 | 0.48 (0.27–0.85) | <0.01  |
| Year of diagnosis 2000–2005, n = 7077          | 0.40 (0.20–0.80) | <0.001 | 0.47 (0.26–0.84) | <0.01  |
| Other-cause mortality                          |                  |        |                  |        |
| Primary analyses                               |                  |        |                  |        |
| Entire cohort, n = 10 595                      | 0.51 (0.37–0.69) | <0.001 | 0.59 (0.45–0.79) | 0.03   |
| T1a, n = 6443                                  | 0.48 (0.32–0.70) | <0.001 | 0.61 (0.43–0.87) | 0.006  |
| Subanalyses                                    |                  |        |                  |        |
| ≥75 yr, n = 4830                               | 0.55 (0.36–0.83) | 0.004  | 0.61 (0.42–0.89) | 0.01   |
| T1a and ≥75 yr, n = 2873                       | 0.47 (0.28–0.77) | 0.003  | 0.56 (0.35–0.89) | 0.02   |
| RCC only*, n = 7806                            | 0.46 (0.31–0.67) | <0.001 | 0.53 (0.37–0.74) | <0.001 |
| Year of diagnosis 2000–2005, n = 7077          | 0.43 (0.29–0.62) | <0.001 | 0.52 (0.37–0.74) | <0.001 |

HR = hazard ratio; CI = confidence interval; PN = partial nephrectomy; NSM = nonsurgical management; RN = radical nephrectomy, RCC = renal cell carcinoma. All models were based on a two-stage residual inclusion model. Adjustment was made for patient age, sex, race, baseline comorbidities, socioeconomic status, marital status, tumor size, histological subtype, Fuhrman grade, and year of diagnosis.

* Secondary malignancies excluded.
Management

- **Active Surveillance**
  - 1. Cross Sectional Imaging  q 6 months then annually
  - 2. Assess stability/growth

- Population- **Opportunity for Advanced Practice Nurses in a specialty practice- Urologic Oncology**
Location

- **Location, Location, Location**

- Exophytic vs. Deep Central Location affects Management – upper pole close to pancreas, adrenal, liver, spleen, central lesions hard to ablate

- Lower pole exophytic lesions are ideal
Management

- Treatment with Cryoablation/ RFA
  - 1. Referral to Interventional Radiology
  - 2. Best for < 3 cm
RFA/Cryablation

- RFA uses alternating radiofrequency energy delivered by a probe, generating heat to achieve cell death & coagulation necrosis 70-105 C

- Cryoablation uses a probe- freezing tissue
Management

- Cryoablation/RFA
- Patients with
  - Marginal Function, Functional
  - Anatomic solitary kidney
  - Disinclined to undergo surgery
  - Synchrynous RCC
  - Wo NOT to ablate- healthy person under 65
Cryoablation of the Left Kidney

With Iceball
Renal Cell Carcinoma
Radiofrequency Ablation
Management

• Surgery

• Surgical Excision
  • 1. Minimally invasive  Laparoscopic or Robotic
  • 2. Open  Surgery  Partial or Radical
Nephron Sparing Surgery
Management

- Surgery
- Nephron Sparing argument – less chance for renal deterioration and possible renal failure
- Also preserves functions for other potential needs, e.g. chemotherapy for another cancer
- Argument against – individuals can still donate a kidney for transplant without significant risk to donor.
Nomogram for Competing Risks

- Kutikov, Egleston, Wong & Uzzo 2009

- Evaluation Overall and Competing Risks of Death in Patients with Localized Renal Cell Carcinoma Using a Comprehensive Nomogram
Nomogram for Competing Risks in Localized Renal Cell Carcinoma

Non-cancer death points:
- Race: Other, White, Black
- Sex: M, F
- Tumor size (cm): 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15
- Age: 30, 40, 50, 60, 70, 80, 90, 100

Kidney cancer death points:
- Race: Other, White, Black
- Sex: M, F
- Tumor size (cm): 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14
- Age: 30, 40, 50, 60, 70, 80, 90

Other cancer death points:
- Race: Other, White, Black
- Sex: M, F
- Tumor size (cm): 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14
- Age: 30, 40, 50, 60, 70, 80, 90

Total points: 0, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120

Probability of non-cancer death:
- 0.01, 0.01, 0.02, 0.02, 0.03, 0.03, 0.03, 0.03, 0.03, 0.03, 0.03, 0.03, 0.03

Probability of kidney cancer death:
- 0, 0.01, 0.01, 0.01, 0.02, 0.02, 0.03, 0.03, 0.03, 0.03, 0.03, 0.03, 0.03

Probability of other-cancer death:
- 0, 0, 0, 0, 0, 0.01, 0.01, 0.01, 0.02, 0.02, 0.03, 0.03, 0.03
Young patients with RCCA


- Results: Young patients more frequently underwent nephron sparing surgery and RLND compared to older patients. More Chromophobes.

- There was no significant increase in the predictive accuracy of the disease specific and all cause mortality
Young Patients with RCCA

Conclusions: Young patients with RCC (40yrs or younger) have significantly different frequencies of clinical and histopathological features, and a significantly lower all cause and disease specific mortality.
Open and Laparoscopic Surgery

Fig 2: muscle cutting incision (6 to 10 inch) used in traditional open donor nephrectomy surgery
Treatment for Smaller Lesions: Partial Nephrectomy or Tumor Ablation
Management

- Ipsilateral Adrenalectomy

- Finding within large cohorts, of tumors approx 7cm or above and tumors involving the upper pole, suggest that the synchronous adrenal involvement are 1-5%.

- Ipsilateral Adrenalectomy at the time of extirpative surgery for RCC is not advocated without radiologic or operative findings suggestive of adrenal involvement.
Follow Up

• Renal Cell Carcinoma
  1. Low Grade- Imaging @ 3 months, then annually x 3 years
  2. High Grade- Imaging @ 3 months, the every 6 months x 3 years
  3. Then at the discretion of the Urologic Oncologist
Follow Up

- Monitor Renal Function
- Refer to Nephrology
The contemporary role of renal mass biopsy in the management of small renal tumors. Lim, O’Neill Heilbrun et al.

Selective use of percutaneous biopsy

Tx, Non Surgical options, Advancements, predicting tumor behavior, cost effectiveness, Dx value, complications
Conclusions: The role of RMB in the setting of SRM has been expanding, knowing that 2-050% are removed by surgical excision have benign or indolent pathology, and low complication rates encourage wider adoption.
Supportive Informed Counseling

- Primary Care Providers

- Understand the natural history of small renal masses

- Recognize the small but real risk: Potential for metastasis 1-2%

- Appreciate comorbidities as part of the decision making process for management

- Knowledgeable about active surveillance, options w/renal ablation, surgical intervention
Supportive Informed Counseling

- Minimally invasive vs. open techniques
- Genetic Risk- Rare familiar renal cell carcinomas-
  & referred to geneticist.
- Routine Screening- Routine screening for family members not recommended
- Inquire during their annual general physical examination – compliance with Follow up w/ Urology or IR
Editorial

- Contemporary management of small renal masses: does practice environment matter?
Case Studies #1

• 50 year old male with a 5.2 x 3.5cm central renal mass?

• Recommendation
Case Studies #2

- 80 year old female with a 1.7 x 1.5 cm left posterior lower pole renal mass

- Recommendation
Case Studies #3

- 45 year old Nurse Practitioner Tx Right Open Radical
- Nephrectomy in 2007
- The final surgical pathology demonstrates a 14 cm Fuhrman grade, Papillary II renal cell carcinoma

What is her follow up?
Suggested Readings


Suggested Readings


Suggested Readings


Suggested Readings

Suggested Readings


Suggested Readings

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