Contemporary Surgical Management of Renal Cell Carcinoma

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• Most cases diagnoses incidentally
• Most cases diagnosed when tumor relatively small
• Most cases can be treated minimally invasively (laparoscopically)
• Most cases should consider partial nephrectomy
Estimated New U.S. Cases 2010

- 58,000* (4% of all U.S. malignancies)
  - 35,000 Male (7th in men)
  - 23,000 Female (8th in women)
- Deaths: 13,000
  - 8,000 Male (9th in men)
  - 5,000 Female

* 92% of cases are RCC, 7% TCC

*American Cancer Society Facts & Figures. 2010.*
## ACS 2010: Estimated Cases

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>192,280</td>
<td>Breast</td>
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<tr>
<td>Lung &amp; bronchus</td>
<td>116,090</td>
<td>Lung &amp; bronchus</td>
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<tr>
<td>Colon &amp; rectum</td>
<td>75,590</td>
<td>Colon &amp; rectum</td>
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<tr>
<td>Urinary bladder</td>
<td>52,810</td>
<td>Uterine corpus</td>
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<tr>
<td>Melanoma of the skin</td>
<td>39,080</td>
<td>Non-Hodgkin lymphoma</td>
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<tr>
<td>Non-Hodgkin lymphoma</td>
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<td>Melanoma of the skin</td>
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<tr>
<td>Kidney &amp; renal pelvis</td>
<td>35,430</td>
<td>Thyroid</td>
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<tr>
<td>Leukemia</td>
<td>25,630</td>
<td>Kidney &amp; renal pelvis</td>
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<tr>
<td>Oral cavity &amp; pharynx</td>
<td>25,240</td>
<td>Ovary</td>
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<tr>
<td>Pancreas</td>
<td>21,050</td>
<td>Pancreas</td>
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<tr>
<td><strong>All Sites</strong></td>
<td><strong>766,130</strong></td>
<td><strong>All Sites</strong></td>
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*Estimated New Cases*

ACS 2010: Estimated Deaths

<table>
<thead>
<tr>
<th>Estimated Deaths</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>88,900</td>
<td>70,490</td>
</tr>
<tr>
<td>Prostate</td>
<td>27,360</td>
<td>40,170</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>25,240</td>
<td>24,680</td>
</tr>
<tr>
<td>Pancreas</td>
<td>18,030</td>
<td>17,210</td>
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<tr>
<td>Leukemia</td>
<td>12,590</td>
<td>14,600</td>
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<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>12,090</td>
<td>Non-Hodgkin lymphoma 9,670</td>
</tr>
<tr>
<td>Esophagus</td>
<td>11,490</td>
<td>Leukemia 9,280</td>
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<tr>
<td>Urinary bladder</td>
<td>10,180</td>
<td>Uterine Corpus 7,780</td>
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<tr>
<td>Non-Hodgkin lymphoma</td>
<td>9,830</td>
<td>Liver &amp; intrahepatic bile duct 6,070</td>
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<tr>
<td>Kidney &amp; renal pelvis</td>
<td>8,160</td>
<td>Brain &amp; other nervous system 5,590</td>
</tr>
<tr>
<td>All Sites</td>
<td>292,540</td>
<td>All Sites 269,800</td>
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</table>
Renal Cell Ca

- M:F::2:1
- Bilateral 1-4%
- Peak age 50–70
RCC: Ethnic Disparities

- U.S. Cancer trends, in non-lung, smoking related malignancies

RCC: Ethnic Disparities

- Racial disparities in cancer mortality are decreasing between Blacks & Whites for tobacco-related cancers
- However, need to improve and equilibrate screening, prevention and treatment to all segments of population

RCC: Risk Factors

- Cigarette smoking
- Obesity
- Cadmium
- ADPCK / hemodialysis
- Von Hippel Lindau Syndrome
- Familial RCC
RCC & Tobacco

- Increased RR compared to non-smokers
  - RR: 1.5-2.0
- Dose-dependent:
  - Increased RR with # of cigs/day
- Cigar smokers with increased RR (for those who smoke > 14 cigars/week)

RCC & Tobacco

- RR of RCC greater for males smokers compared to female smokers
- RR is dose-dependent:
  - 1-9 cigs/day: 1.6
  - 10-20: 1.8
  - > 20: 2
- RR decreases after smoking cessation >10 yrs

RCC & Tobacco

- Increased RR for second-hand tobacco exposure
- RR 3.9 for men with >40 yrs of second-hand tobacco exposure
- Increased risk for those whose spouse smokes

Historical RCC

- “Internist’s Tumor”
- Virchow’s Triad:
  - Flank pain
  - Gross hematuria
  - Abdominal mass
Signs & Symptoms
Contemporary Signs & Symptoms

• Typically none

• Why?
  • Most renal masses are discovered incidentally during sono or CT

• > 60% of renal masses were incidental (1989-1993)

Signs & Symptoms
Poor prognostic signs and symptoms:

- Palpable, painful mass
- Constitutional signs: fever, night sweats, weight loss
- Elevated LFTs, ESR
Renal Cysts:

Bosniak Classification

- **Type 1**: Simple cyst
- **Type 2**: Thick walled / Border forming calcification
- **Type 3**: Septations/ non-border forming calcifications
- **Type 4**: Solid and cystic areas
Renal Cysts: Bosniak Classification

- Type I & II:
  - Non-malignant
  - Do not need any follow-up imaging
- Type III:
  - 50% risk of malignancy
  - Consider exploration
- Type IV:
  - 100% risk of malignancy
  - Cystic RCC
Renal Cysts: Bosniak Classification

- Type IIF:
  - “F”: needs follow-up
  - Yearly renal sonogram
  - Need to rule-out increased echogenicity, calcifications, thick-walled
Renal Mass Work-Up

- PA & Lat Chest X-ray
- Full labs
  - If LFTs abnormal: obtain bone scan
- Large tumor: consider Head CT
- Hematuria: need to perform cystoscopy and cytology (rule-out urothelial origin)
Biopsy?

- RCC is a radiographic diagnosis
- Tumor needs to be removed anyhow?
- Biopsy unreliable?
- **Caveat: who should have a biopsy**
  - H/o other malignancies
  - Non-typical radiographic appearance
  - Possibility of infection (abscess)
  - Consideration for observation
  - At time of cryo/RFA
Radiographic Diagnosis

- CT scan without and with IV contrast
  - RCC enhances with contrast
- Lymphadenopathy?
- Renal vein/IVC invasion?
- Pulmonary mets?
- Invasion into contiguous organs (liver)?
TNM Staging

T1: <7 cm limited to kidney
   T1a: <4 cm
   T1b: 4-7 cm
T2: >7 cm limited to kidney
T3: Beyond kidney, within Gerota’s
   T3a: Into renal vein
   T3b: Into IVC below diaphragm
   T3c: Into IVC above diaphragm
T4: Beyond Gerota’s & into adrenal
Open Radical Nx

**Incisions:**
- Flank
- Subcostal
- Chevron
- Thoraco-abdominal
- Midline
Lap Nephrectomy

- First performed in 1991 by Clayman
- Current gold-standard
- Either straight-lap or Hand-assisted lap
  - Single port?
- Kidney extracted through small incision in lower abdomen
  - Much less painful and morbid than flank incision
- LOS typically 1-2 days
Lap Nephrectomy

- Cancer control identical to open surgery
- Appropriate even for large tumors
- Lymphadenectomy can be performed laparoscopically
Lap Nx Instrumentation

- 12mm, 10mm and 5mm trocars
- Vascular control with endoscopic staplers and clips
  - Small vessels controlled with harmonic scalpel, ligasure
- Hand-Assist device: enables use of surgeon hand to dissect, retract, and remove specimen
Hand-Assist Device
• Retrospective review of 106 large tumors or tumors in obese patients
• March 1998-October 2000
• 3 institutions
HAL Nx for large tumors & obese pts

### TABLE II. Intraoperative parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Tumor Size (cm)</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;7 (n = 63)</td>
<td>≥7 (n = 32)</td>
</tr>
<tr>
<td>Left/right</td>
<td>26/37</td>
<td>14/18</td>
</tr>
<tr>
<td>OR time (min)</td>
<td>138 ± 76.5</td>
<td>198 ± 61.7</td>
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<tr>
<td>EBL (mL)</td>
<td>109 ± 130</td>
<td>167 ± 197</td>
</tr>
<tr>
<td>Conversions (n)</td>
<td>1 (1.5)</td>
<td>2 (6)</td>
</tr>
</tbody>
</table>

### TABLE III. Postoperative parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Tumor Size (cm)</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;7 (n = 63)</td>
<td>≥7 (n = 32)</td>
</tr>
<tr>
<td>LOS (days)</td>
<td>3.7 ± 1.3</td>
<td>3.7 ± 1.2</td>
</tr>
<tr>
<td>Parenteral narcotics (mg MSO₄₆)</td>
<td>36 ± 24</td>
<td>31 ± 22</td>
</tr>
<tr>
<td>Oral narcotics (tablets)</td>
<td>6 ± 5</td>
<td>5.5 ± 5</td>
</tr>
<tr>
<td>Hct change</td>
<td>4.7 ± 3.4</td>
<td>4.3 ± 2.1</td>
</tr>
<tr>
<td>Complications (%)</td>
<td>6 (9)</td>
<td>4 (12.5)</td>
</tr>
<tr>
<td>Convalescence (days)</td>
<td>18 ± 5</td>
<td>21 ± 6*</td>
</tr>
</tbody>
</table>

Lap Nx: efficacious in obese
Lap Nx: cosmetics

- Obviates risk of flank bulge & hernia
Partial Nephrectomy

- Typically performed via a flank incision
- Often now performed laparoscopically (especially if lesion exophytic)
- Slightly increased risk of complications compared to radical nephrectomy:
  - Bleeding
  - Urine leak
Indications for Partial Nx

Absolute:

- Solitary kidney
- Bilateral renal masses
- Severe renal insufficiency
Indications for Partial Nx

Relative:

- Contralateral kidney with pre-existing renal disease
  - e.g., stones, recurrent pyelo, UPJ obstruction
- Medical diseases predisposing to CRI
  - DM, HTN
- Known multi-focality
  - e.g., genetic syndromes
Indications for Partial Nx

Elective:
- Small lesions <4cm (<7cm?)
- Peripheral
- Young healthy patients

Partial Nx should be considered for most pts
Early Partial Nx

- Early procedures performed for solitary kidneys & bil renal mass
- Mayo clinic: 104 patients
  - 14 pts: extracorporeal RXN/autotransplant
  - 40 pts: Bil RCCs
  - 39 pts: solitary functioning kidney

Radical vs. Partial Nx: Cancer Control

- Multiple studies have demonstrated equivalent cancer-specific survival rates for patients with small renal masses (pT1a)
- Contemporary studies have demonstrated equivalent cancer control rates up to 7cm
### Radical vs. Partial Nx: Equivalent Cancer Control

<table>
<thead>
<tr>
<th>Study</th>
<th># patients</th>
<th>Median f/u (mo)</th>
<th>5-year cancer specific survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>McKiernan et al, 2002</td>
<td>173/117</td>
<td>26</td>
<td>99% 96%</td>
</tr>
<tr>
<td>Lee et al, 2000</td>
<td>183/79</td>
<td>40</td>
<td>95% 95%</td>
</tr>
<tr>
<td>Lau et al, 2000</td>
<td>164/164</td>
<td>47</td>
<td>97% 98%</td>
</tr>
<tr>
<td>Belldegrun et al, 1999</td>
<td>125/108</td>
<td>74</td>
<td>91% 98%</td>
</tr>
<tr>
<td>Butler et al, 1995</td>
<td>42/46</td>
<td>48</td>
<td>97% 100%</td>
</tr>
</tbody>
</table>

Risk factors for Recurrence

- Tumor size > 4 cm
- Fuhrman nuclear grade
- Multifocality
- Symptomatic presentation

RN vs. PN: Risk of CRI

- Multiple studies have demonstrated a lower risk of CRI in those undergoing partial Nx
- Studies compared those with nl contralateral kidneys and normal baseline Cr
- Increased risk of post-op CRI after partial Nx in those with increased age, higher baseline Cr
## Radical vs. Partial Nx: Risk of CRI

<table>
<thead>
<tr>
<th>Study</th>
<th># patients</th>
<th>F/u (mo)</th>
<th>RN</th>
<th>PN</th>
</tr>
</thead>
<tbody>
<tr>
<td>McKiernan 2002</td>
<td>173/117</td>
<td>26</td>
<td>1.0/1.5</td>
<td>1.0/1.0</td>
</tr>
<tr>
<td>Lau 2000</td>
<td>164/164</td>
<td>47</td>
<td>1.1/1.4</td>
<td>1.1/1.2</td>
</tr>
<tr>
<td>Indudhara 1997</td>
<td>71/35</td>
<td>41</td>
<td>1.0/1.9</td>
<td>0.9/0.8</td>
</tr>
<tr>
<td>Butler 1995</td>
<td>41/46</td>
<td>48</td>
<td>1.1/1.5</td>
<td>1.3/1.3</td>
</tr>
</tbody>
</table>

Can PN decrease mortality rate?

- Retrospective review of RN vs PN
  - 174 RN vs 116 PN
- No difference in cancer-specific mortality
- Yet, increased mortality risk for RN

**Conclusion:** PN obtains same cancer control with lower risk of CRI, which translates into overall mortality rate

Medina-Polo et al. Can PN preserve renal function and modify survival in comparison with RN. *Scan J Urol Nephrol*, 2011.
RN decreases survival in age <65

- Retrospective review of 648 patients
- RN (290) vs PN (358)

In patients < 65, RN had a RR of 2.1 compared to PN for death from any cause

PN: improved overall survival

- Retrospective review, single center, 500 patients with >4cm lesions, comparing PN vs RN
- Equivalent cancer specific survival
- PN associated with better overall survival
  - Secondary to decreased risk of CRI
  - Odds ratio 3.4 for RN vs PN

Weight et al. Elective Partial Nx for pT1b lesions. *Urology*, 2010
Partial Nx Complications

- Risk of ARF: 0-18%
  - However, based on older series with patients undergoing non-elective PN
  - Contemporary series report 0% risk in those with elective indications and pT1a lesions
  - Risk increased with tumor size >7cm, >50% parenchyma excised, ischemia time >60 min
Partial Nx Complications

- Risk of urinary leak: 2-21%
- Contemporary series report 0% risk
- Increased risk in lesions >4cm, central or hilar lesions, or those requiring extensive collecting system reconstruction
Matin et al. retrospectively compared 2 groups with < 4cm lesions, nl contralateral kidney, and nl baseline Cr

- 35 lap RN vs. 82 open PN
- Lap RN cohort had significantly decreased EBL, LOS, narcotic usage, operative time

Open Partial vs. Lap Radical

- The open PN cohort had significantly lower post-op Cr compared to Lap RN cohort

Obviously easier to perform lap RN: too many Lap RNs were being performed

Under Utilization of PN

- Review of SEER database (1988-2001)
- < 10% of patients with pT1 lesions had PN
- Trend: PN use increasing during series
  - However, even for lesions < 4cm, only 20% had PN in 2001

Conclusion: even for small masses, PN remains uncommon (though data 10 years old)

Partial Nx vs Radical Nx

Decision-making based on:

- Lesion size
- Lesion location
  - Peripheral vs. central location
- Patient age (and risk of future CRI)
- Co-morbidities
- Risk of recurrence (e.g., genetic syndromes)
- Risk of future CRI (e.g., DM, HTN)
Lap Partial Nx

- Advanced procedure
- Increased risk of bleeding if hilum not clamped
- No effective method of delivering cold ischemia
  - Need to work quickly with warm ischemia (limit to < 30 min)
  - Obviously easier for exophytic lesions
Lap Partial Nx

Improved outcomes now secondary to:

- Surgeon experience
- Fibrin sealants
- Argon-beam coagulator
- Laparoscopic bull-dog clamps
- Intra-op laparoscopic ultrasound
- Robot
Lap Partial Nx

- Equivalent cancer control as open PN
- Retrospective review of 875 LPN vs 1375 OPN
  - LPN cohort: smaller tumors, less symptomatic, shorter f/u
- Equivalent overall & cancer-specific survival at 7 years

**Conclusion**: either LPN or OPN should be performed (as opposed to RN)

Renal Cryotherapy

- Performed lap or via CT-guidance
- Freezes lesions up to 4 cm
- Can obtain biopsy prior to freezing cycles
- **Caveats:**
  - Patients need to be followed with serial CTs
  - May not be ideal for younger patients
  - Only medium-length f/u data
Renal RFA

- Radio Frequency Ablation
- Heats the lesions and induces coagulative necrosis
- Performed lap or via CT-guidance
- Same caveats as with cryo
Single sporadic small renal mass — not definitively benign according to imaging studies

Relatively young patients (<70 yr)
- No major coexisting condition
- Good life expectancy
- Good surgical risk

Discuss active surveillance and thermal ablation
Consider needle biopsy

Preferred option: surgery

Partial nephrectomy technically feasible
- Laparoscopic or open partial nephrectomy, depending on available surgical expertise

Partial nephrectomy technically difficult
- Image-guided ablation (percutaneous or laparoscopic)
  - Cryoablation
  - Radiofrequency ablation
  - Laparoscopic radical nephrectomy if thermal ablation not safe or not technically feasible

Elderly patients (≥70 yr)
- Coexisting condition
- Limited life expectancy
- Compromised renal function
- Poor surgical risk

Consider needle biopsy
Consider active surveillance
Consider thermal ablation

Preferred option if tumor increases in size, patient desires active treatment, or both:
- Percutaneous thermal ablation
- Cryoablation
- Radiofrequency ablation

Figure 4. Suggested Algorithm for Management of a Small Renal Mass.

Gill et al NEJM 2010
Conclusions

- RCC is a surgical diagnosis and treatment
- Most cases can be performed laparoscopically
- For smaller lesions and younger patients, partial Nx should always be considered