Genitourinary Oncology: Prostate and Renal Cancer

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Director, BCG Oncology,
(Bladder Cancer, Genitourinary Oncology)
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BCGOncology.com
Prostate Cancer

- Lifetime risk 17.6/20.6% W/AA; Death 2.8/4.7%.
- Incidence peaked 1992, 5yrs post PSA.
Prostate Cancer

- Prevention: What is practical? Finasteride?
- PSA: How good is it? Bad rap?
- Treatment: When and What?
- Cryotherapy?
- Robotic Assisted Lap Prostatectomy?
- Intermittent Hormone Therapy (IHT)?
Prostate Cancer Prevention

Potentially Effective Agents

• 5 alpha reductase inhibitors:
  – Finasteride (Proscar, Propecia)
  – Dutasteride (Avodart)
• Vitamins and minerals: Vitamins D, E, Selenium
• Cox-2 Inhibitors: Celebrex
• Synthetic hormones: SERMs/SARMs
• Dietary (tomatoes, cruciferous vegetables, green tea)
PCPT

- 18,882 men with PSA <3.0, age >55 years
- 7 year follow up
- Sextant biopsy rec. for PSA>4, abn. DRE
- PSA doubled during first 4 years, then multiplied by 2.3 to balance biopsies
- 8,997 (47.6%) reported
## CaP Detection in PCPT

<table>
<thead>
<tr>
<th></th>
<th>Finasteride</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>For Cause Biopsy:</td>
<td>1639 (37.5%)</td>
<td>1934 (41.7%)</td>
</tr>
<tr>
<td>% Pos. FC Biopsy:</td>
<td>435 (26.5%)</td>
<td>571 (29.5%)</td>
</tr>
<tr>
<td>% Clinical CaP:</td>
<td>435 (9.9%)</td>
<td>571 (12.3%)</td>
</tr>
<tr>
<td>CaP in any Biopsy:</td>
<td>803 (18.4%)</td>
<td>1147 (24.4%)</td>
</tr>
</tbody>
</table>
Cancer Characteristics in PCPT

- 98% clinically localized
- 22.2% in Placebo and 37% in the Finasteride group were Gleason 6 or greater
- 237 cases >6 in Placebo; 280 in Finasteride
- “Low-risk” men had 24.4% risk of cancer-four times that predicted at the beginning
Possible Reasons for Differences

- Highest PSA’s in finasteride arm recommended to equalize biopsies: non compliant men more likely to be biopsied
- Androgen deprivation can mimic histological changes of high grade CaP
- Finasteride may limit only low grade CaP
- Reduction in volume increases yield of biopsies, reducing sampling error
Finasteride Induction of High Grade Tumors

• If finasteride favors the growth of high grade tumors, the effect should increase with time.
• Increased high grade tumors were seen in the first year and did not increase with time.
PCPT
Radical Prostatectomy Findings

• 450 cases: similar % GG >8, positive margins, pathologic T stage, seminal vesicle invasion, and node positivity.

• More men in placebo group upgraded grade at RP, suggesting differences in grade could be a sampling artifact.
# CaP Detection During PLESS Study

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Finasteride</strong></td>
<td>1523</td>
<td></td>
</tr>
<tr>
<td>For cause or surgery</td>
<td>47/221</td>
<td>21.3%</td>
</tr>
<tr>
<td>End of study biopsy</td>
<td>25/169</td>
<td>14.8%</td>
</tr>
<tr>
<td>Total</td>
<td>72/390</td>
<td>18.5%</td>
</tr>
<tr>
<td><strong>Placebo</strong></td>
<td>1511</td>
<td></td>
</tr>
<tr>
<td>For cause or surgery</td>
<td>62/329</td>
<td>18.8%</td>
</tr>
<tr>
<td>End of study biopsy</td>
<td>15/127</td>
<td>11.8%</td>
</tr>
<tr>
<td>Total</td>
<td>77/456</td>
<td>16.9%</td>
</tr>
</tbody>
</table>

(66 more biopsies in Placebo)

McConnell, NEJM, 358:667
## MTOPS CaP in Biopsies

<table>
<thead>
<tr>
<th></th>
<th>Plac</th>
<th>Dox</th>
<th>Fin</th>
<th>Comb</th>
<th>All Fin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rx Bx</td>
<td>67</td>
<td>69</td>
<td>56</td>
<td>68</td>
<td>124</td>
</tr>
<tr>
<td></td>
<td>26(39%)</td>
<td>17(25%)</td>
<td>15(27%)</td>
<td>22(32%)</td>
<td>37(30%)</td>
</tr>
<tr>
<td>Study Bx</td>
<td>250</td>
<td>265</td>
<td>277</td>
<td>275</td>
<td>552</td>
</tr>
<tr>
<td></td>
<td>35(13%)</td>
<td>39(15%)</td>
<td>26(9%)</td>
<td>40(14%)</td>
<td>66(12%)</td>
</tr>
<tr>
<td>Total %</td>
<td><strong>8.3%</strong></td>
<td><strong>7.4%</strong></td>
<td><strong>5.3%</strong></td>
<td><strong>7.9%</strong></td>
<td><strong>6.6%</strong></td>
</tr>
</tbody>
</table>
PSA

- Correlates with risk of aggressive prostate cancer, but is a continuous, not a dichotomous variable.
- Positive predictive value is relatively low: 20-35%
- Negative predictive value of low PSA is imperfect: 85% in PCPT study.
- PSA density and kinetics improve accuracy
- PSA rise of only 2ng/ml/yr associated with increased risk of disease progression/death from prostate cancer.
PSA Failure Post RRP

- PSA over 0.2 post RRP is considered failure
- PSA recurrence: median time to metastasis is 8 yrs (Pound, JAMA, 251:1501); mets to death: 5 yrs.
- 10 yr overall survival not different: 88% with PSA failure, 89% without
- PSA doubling highly correlated with prognosis
Gemcitabine in TCC

• Phase II marker lesion study: 39 pts; 2gm/50ml resulted in 56% CR.

• Phase I/II marker lesion study: 27 pts;
  – 12% CR @ 500mg/50ml
  – 22% CR @ 1gm/50ml
  – 33% CR @ 2gm/50ml
Intravesical BCG: Antitumor Activity

- Induces inflammatory response
- Induces infiltration of lymphocytes and NK cells into the bladder wall
- Induces complex cellular immune response characterized by release of the following cytokines:
  - IL-1
  - IL-2
  - IL-6
  - IL-8
  - IL-10
  - IL-12
  - IFN-γ
  - TNF-α
  - GM-CSF
Rationale

- Prostate cancer occurs with advancing age and decreasing immune competence.
- Prostate cancer pts have reduced immunity
- Injection of BCG into human prostate cancer induces necrosis and granuloma
- 75% of men given intravesical BCG for bladder cancer have prostatic granuloma
Expanding the Roll of BCG Immunotherapy

Phase II-III Trial of Intravesical BCG in Prostate Cancer
Additional Animal Data

- In PA-III, Pollard found significant inhibition of prostate cancer with IV BCG.
- Morales found 50% remission of Dunning R3327H prostate cancer with mycobacterial cell walls.
- We found increase in survival from 44% to 73% with weekly BCG for 6 weeks (PA-III).
BCG in Prostate Cancer: Clinical Studies

- Guinan, ‘76: Improved immune responses and survival advantage in advanced cancer
- Guinan, ‘82: Controlled trial, BCG increased survival 5.6 to 8.1 months (P<0.05)
- Improved BCG immunotherapy and reduced tumor burden should greatly improve results
SWOG Study

• Three week maintenance BCG markedly improves CR and reduces recurrence and progression

• Prostate cancer was reduced from 14 in 179 men to 5/151 with maintenance BCG. Advanced disease was reduced from 6 (3C, 3D) to 1 (C), P=0.04

• All cancers reduced from 23% to 13%
BCG in Prostate Cancer

• BCG inhibits prostate cancer in animal models (rat and dog)
• BCG injected into prostate cancer produces granuloma and necrosis
• The 3 week maintenance schedule enhances response and significantly reduces prostate cancer incidence and appears to reduce stage progression
### Conservative Treatment of Localized Prostate Cancer in Men 55-74 yrs

<table>
<thead>
<tr>
<th>Gleason Grade</th>
<th>Prostate Cancer Mortality at 15 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-4</td>
<td>4-7%</td>
</tr>
<tr>
<td>5</td>
<td>6-11%</td>
</tr>
<tr>
<td>6</td>
<td>18-30%</td>
</tr>
<tr>
<td>7</td>
<td>42-70%</td>
</tr>
<tr>
<td>8-10</td>
<td>60-87%</td>
</tr>
</tbody>
</table>

Albertsen PC: JAMA. 1998; 280:975
Cryotherapy

- Unlike brachytherapy, high grade disease appears to not be resistant to cryotherapy
- Obstruction is not a contraindication
- Salvage therapy in radiation therapy failures
- Focal therapy? Male lumpectomy?
- Improved equipment, lower complications
- Results appear comparable to other Rx
High Standard Set by RRP

- OR Time 2.5 to 3 hours
- Hospitalization 2.2 days
- Catheter out 10-14 days
- Transfusion rate 5%
- Major complications low: Mortality 0.2%
- Biochemical DFS 59 to 83%
Early Lap RP Reports

• Guillonneau: 40 LAPRP cases
  – OR time 4.5 hours
  – Cath time 7.6 days
  – Transfusions 17.5%
  – Margins positive: 17.5%
  – Undetectable PSA: 90%

• Jacob: 20 LAPRP cases
  – OR time 6.4 hours
  – Cath time: 11 days
  – Transfusions 10%
  – Undetectable PSA: 100% at 6 mo.
Advantages of Lap Prostatectomy

- Literature and 2,000+ cases reviewed
- Significantly less postoperative pain
- Less blood loss
- Early return to full activity
- Shorter hospital stay
- Reduced number of complications
- Better cosmesis
- Lap, but not robotic prostatectomy is cost competitive

Learning Curve with Robotic RP

- Ahlering’s first 45 cases after one day training course
- 4 hour OR time after 12 cases
- Time, EBL, margin status stable after 12 cases

Ahlering TE: J Urol. 170:2003
Robotic v Lap Prostatectomy

- RLRP: Significantly shorter learning curve
- Major advantage for the non-laparoscopic surgeon
- Comparable outcomes
- Shorter operative time: 182 (141-250) versus 234 (151-453) min.
- Increased overall cost

Robotic (RLRP) versus Open RRP

- 279 pts, 176 RLRP; 103 RRP over 14 mo.
- Blood loss, transfusion, Hct compared
- RLRP: 191 mL versus 664 mL, P < 0.001
- Discharge Hct 36.8% v 32.8%, P< 0.001
- 1 pt versus 3 pts transfused
- Blood loss is significantly reduced with RALP; and it is nearly twice as popular!

Farnham SB: Urology. 2006; 67:360-3. (Vanderbuilt)
Intermittent Hormone Therapy (IHT): The New Standard?

- 68 randomized pts, 31 month follow up
- 3 yr progression: 7% IHT, 39% CHT (P=0.0052)
- 59% of time off treatment
- Reduced side effects and cost
- Multicenter trial: no advantage to continuous hormone therapy

Prostate Cancer Conclusions

- PSA is nonspecific with high incidence of false positives and false negatives
- Nonetheless, it is a remarkably useful screening and monitoring marker
- Finasteride lowers the risk of low grade prostate cancer, though marginally.
Prostate Cancer Conclusions

• Low grade prostate cancer has a relatively benign, long term course in most men.
  – Fewer than 30% with GG-6 Ca die at 15 yrs
  – Consider life expectancy, PSA, number of + biopsies to individualize treatment

• Cryotherapy is useful in marginal surgical candidates, and appears to be superior to brachytherapy in high grade Ca and men with outlet obstruction
Prostate Cancer Conclusions

- Radical prostatectomy is the gold standard Rx for organ confined prostate cancer
- PSA failure has surprisingly little effect on 10 yr survival: 88% vs 89%
- Robotic Radical Prostatectomy: the new RRP?
- IHT: the new standard for hormone therapy?
Renal Tumors

- 3% of all solid tumors
- 85% of renal malignancy is Renal Cell Ca (RCC)
Renal Cancer, 1975 to 1995

*JAMA. 1999;281:1628-1631*

- Annual increase: 2.3% white men, 3.1% white women, 3.9% black men, and 4.3% black women; greatest for localized tumors but also advanced tumors
- In contrast, renal pelvis cancer declined among white men and remained stable among white women and blacks
- Mortality increased in all groups
Renal Cancer Etiology

- Tobacco, cadmium, radiation, dialysis
- Risk factors: hypertension, increased body mass index, and red meat intake; inverse relation with intake of carotenes
- Four-fold increased risk with family history

Seminars in Oncol. 27:115-123, 2000
Curr Opin Oncol. 12:260-4, 2000
Renal Cancer Etiology

• Clear genetic factors: VHL gene on chromosome 3, mutation of VHL in clear, granular and sarcomatoid RCC but not papillary RCC
• Trisomy of 7 and 17 and loss of the sex chromosome: papillary tumors
• Chromophobe RCC: loss of chromosomes with a combination of monosomies
• Deletion (8p)/-8, +12, and +20: worse prognosis
Renal Cell Carcinoma


- Onset age 62, 82% with localized disease
- 41% T1 disease, 15% T2, 39% T3, 4% T4
- Fuhrman grade 1 or 2 in 51% of patients
- Stage and Grade associated with survival (P <0.0001 and P = 0.0028, respectively)
- In Stage M0, smokers had a significantly worse overall survival (P = 0.039)
<table>
<thead>
<tr>
<th>Year</th>
<th>&lt;2cm</th>
<th>&lt;2.5cm</th>
<th>&lt;3.0cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993</td>
<td>7.7%</td>
<td>14.4%</td>
<td>31.1%</td>
</tr>
<tr>
<td>1998</td>
<td>8.3%</td>
<td>16.5%</td>
<td>36.0%</td>
</tr>
<tr>
<td>2003</td>
<td>12.1%</td>
<td>22.4%</td>
<td>41.3%</td>
</tr>
</tbody>
</table>

UCSF, 2006
Changing Presentation of RCC

- Locally Advanced, Symptomatic:

- Is being replaced by Incidental:

- Often found by US:
US Trends in Partial Nephrectomy

% Surgically Treated Patients with Partial Nx

1988-90: 3.7%
1991-93: 4.7%
1994-96: 6.5%
1997-99: 7.9%
2000-02: 12.3%

Hollenbeck, 2005
Bosniak Cyst Classification

- I: Simple benign cyst
- II: Thin septa; calcification septum or wall; Hyperdense
- III: Thick, irregular calcification; irregular margin; thickened septa
- IV: Enhancing areas; irregular margin
Differential: Solid Renal Mass

- Renal Cell Ca
- Oncocytoma
- Adenoma
- Angiomyolipoma
- Transitional Cell Ca
- Metastatic Ca

- Renal pseudotumor
- Infarct
- Lobar Nephronia
- Abscess
- Vascular malformation
Renal Oncocytoma

- Benign, grade 1 tumor
- Distal tubule or collecting duct origin
- Round, uniform, “spoke wheel” pattern
- No chromosome 3p deletion as in RCC
- Diploid DNA
- Pre-op diagnosis difficult to establish
- Co-existent with RCC in 15-18%

Novick, A: AUA, 2006
Renal Cortical Adenoma

- Common, often microscopic, benign small solid tumor
- Asymptomatic, discovered incidentally
- Radiographically and histologically difficult to distinguish from low grade RCC
- Size and growth rate, but not biopsy, helpful in diagnosis
Risk of Metastasis Related to Tumor Size at Initial Diagnosis

Of 379 small (less than 3.0 cm) renal cell carcinomas, only 2.3% had metastatic disease

Bosniak, Radiology, 197:589, 1995
# Solid Renal Masses: Pathologic Features According to Size

<table>
<thead>
<tr>
<th>Size</th>
<th>% RCC</th>
<th>% High Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.0 cm</td>
<td>54%</td>
<td>2%</td>
</tr>
<tr>
<td>1-4 cm</td>
<td>79%</td>
<td>16%</td>
</tr>
<tr>
<td>4-7 cm</td>
<td>90%</td>
<td>30%</td>
</tr>
<tr>
<td>&gt;7 cm</td>
<td>94%</td>
<td>57%</td>
</tr>
</tbody>
</table>

MCR: J Urol. 170:2217, 2003
# Observation of Enhancing Renal Masses: Meta-analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>‘yr</th>
<th>N</th>
<th>T size</th>
<th>Follow</th>
<th>Growth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bosniak</td>
<td>’95</td>
<td>40</td>
<td>1.7 cm</td>
<td>39 mo</td>
<td>0.36cm/yr</td>
</tr>
<tr>
<td>Oda</td>
<td>’02</td>
<td>16</td>
<td>2.0 cm</td>
<td>25 mo</td>
<td>0.54cm/yr</td>
</tr>
<tr>
<td>Kassouf</td>
<td>’04</td>
<td>29</td>
<td>3.3 cm</td>
<td>32 mo</td>
<td>0.49cm/yr</td>
</tr>
<tr>
<td>Volpe</td>
<td>’04</td>
<td>32</td>
<td>2.5 cm</td>
<td>35 mo</td>
<td>0.10cm/yr</td>
</tr>
<tr>
<td>Wehle</td>
<td>’04</td>
<td>29</td>
<td>1.8 cm</td>
<td>32 mo</td>
<td>0.12cm/yr</td>
</tr>
<tr>
<td>Kato</td>
<td>’04</td>
<td>18</td>
<td>2.0 cm</td>
<td>27 mo</td>
<td>0.42cm/yr</td>
</tr>
<tr>
<td>Uzzo</td>
<td>04</td>
<td>34</td>
<td>3.0 cm</td>
<td>34 mo</td>
<td>0.21cm/yr</td>
</tr>
<tr>
<td><strong>Total:</strong></td>
<td></td>
<td>198</td>
<td><strong>2.4 cm</strong></td>
<td><strong>34 mo</strong></td>
<td><strong>0.28cm/yr</strong></td>
</tr>
</tbody>
</table>

Uzzo, 2005
# Size and Histopathology in Tumors

## Less than 4cm

<table>
<thead>
<tr>
<th>Tumor Size</th>
<th>pT3a</th>
<th>G3/G4</th>
<th>Mets</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3.0 cm</td>
<td>10.9%</td>
<td>4.7%</td>
<td>2.4%</td>
</tr>
<tr>
<td>3.1-4.0 cm</td>
<td>35.7%</td>
<td>25.5%</td>
<td>8.4%</td>
</tr>
</tbody>
</table>

*p<.001  p<.003  p<.05*

The aggressive potential of RCC increases beyond the tumor diameter of 3 cm

Marberger, 2006
Solitary, <4cm Renal Cell Carcinomas

- 90%: Low Stage (T1-2), Low Grade (I-II)
- 10%: Higher Stage (T3a-b), higher grade
- Metastasis is rare

Novick, AUA, 2006
Percutaneous Needle Biopsy of Solid Renal Mass

- High (35-40%) False Negative rate in establishing the diagnosis
- Recent studies, with improved imaging and the use of biological markers suggest improved diagnostic results in the future
- Low, but not a zero incidence of needle tract seeding, subsequent metastasis
Management of Small Renal Masses

• Selected cases: observation, but most (85%) enhancing masses are RCC. Most, but not all, grow slowly. No current reliable marker.
• Partial nephrectomy: spares nephrons. With normal contralateral kidney elective PN limited to tumors less than 4cm in size.
• Radical nephrectomy: greater margin of safety?
Partial Nephrectomy: Results in 485 Patients

<table>
<thead>
<tr>
<th>Tumor Size</th>
<th>Recurrence</th>
<th>5 yr Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2.5 cm (T1a)</td>
<td>2%</td>
<td>99%</td>
</tr>
<tr>
<td>2.5-4.0 cm (T1a)</td>
<td>7%</td>
<td>98%</td>
</tr>
<tr>
<td>4.0-7.0 cm (T1b)</td>
<td>14%</td>
<td>88%</td>
</tr>
<tr>
<td>&gt;7.0 cm (T2)</td>
<td>25%</td>
<td>82%</td>
</tr>
</tbody>
</table>

P=0.001 vs

Renal Function: Elective Partial versus Radical Nephrectomy

- Higher incidence of long term insufficiency (Cr >2mg/dl) after radical compared to partial nephrectomy (Lau, MCP 75:1236, 2000)

- Higher incidence of proteinuria with radical versus partial nephrectomy (Urol: 59, 816, 2002)
Partial vs. Radical Nephrectomy: 15 year Comparison in 328 Patients

- Patients matched for year of surgery, age, sex, renal function, and grade, stage, and size of tumor. 10 year recurrence-free survival rates were 95% and 99% for partial and radical nephrectomy patients, respectively. 15-year cause-specific survival rates were 91% for partial nephrectomy and 96% for radical nephrectomy.
- Hemodialysis was needed more often with radical nephrectomy and serum creatinine levels ($P = .003; 1.6 \text{ mg}\% \text{ vs } 1.3 \text{ mg}\%$) were higher.

Lau: unpublished, quoted by Ghavamian, eMedicine
## Follow Up for RCC

<table>
<thead>
<tr>
<th>Stage</th>
<th>H/P, Bloods</th>
<th>CXR</th>
<th>CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>pT1-2</td>
<td>Yearly</td>
<td>Yearly</td>
<td>q 2 yrs</td>
</tr>
<tr>
<td>pT3</td>
<td>Yearly</td>
<td>Yearly</td>
<td>q 6 mo x4 then yearly</td>
</tr>
</tbody>
</table>
Lap v Open Partial Nx: 100
Matched Cases, Cleveland Clinic

Laparoscopic (100)    Open (100)

• MS (mg):       20.2    252.5
• Hospital stay:  2 days  5
• Recovery:       4 weeks 6

• $P < 0.001$ for all

J Urol. 170:64, 2003
# Urologic Complications

<table>
<thead>
<tr>
<th></th>
<th>Lap</th>
<th>Open</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intraoperative</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal bleed:</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Ureteral injury:</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Postoperative</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine leak:</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>UPJ obstruction:</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Renal bleed:</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td><strong>total:</strong></td>
<td>11</td>
<td>2</td>
</tr>
</tbody>
</table>

P=0.01
## Complications Compared: Open and Lap Nephrectomy

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Bleeding</th>
<th>Urine Leak</th>
<th>Dialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Open:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Steinbach’95</td>
<td>140</td>
<td>1.4%</td>
<td>2.1%</td>
<td>0</td>
</tr>
<tr>
<td>• Beldegrun’99</td>
<td>146</td>
<td>2.1%</td>
<td>1.4%</td>
<td>0</td>
</tr>
<tr>
<td>• Novick’03</td>
<td>100</td>
<td>0</td>
<td>1.0%</td>
<td>0</td>
</tr>
<tr>
<td><strong>Lap:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Gill, 2005</td>
<td>200</td>
<td>9.5%</td>
<td>4.5%</td>
<td>2%</td>
</tr>
</tbody>
</table>

J Urol. 173:43, 2005
Lap Partial Nephrectomy: CCF

Biologic Hemostatic Agents

68, no Floseal 63, Floseal

• Hemorrhage: 12% 3%
• Urine Leak: 6% 1.5%
Lap Partial Nephrectomy 3yr Results

- 100 patients with median follow up of 3.5 yrs.
- No local or port site recurrence
- Overall survival: 86%
- Cancer-specific survival: 100%

Novick A: Cleveland Clinic 2006. AUA 2006
Minimally Invasive Ablative Procedures for Small, Solitary Renal Tumors

- Cyroablation
- Radiofrequency ablation
- Interstitial laser ablation
- Microwave ablation
- High intensity focused ultrasound
- Radiosurgery
Lap Partial Nephrectomy

Conclusions

• Contraindicated in large, multiple, or central/hilar tumors
• Less pain, shorter stay, more rapid recovery
• Currently bleeding, urine leak, and renal compromise are more common, but techniques/equipment are rapidly improving
Ablative Procedures: Issues and Concerns

- Control of extent of tissue destruction
- No accurate pathologic staging
- No pathologic confirmation of complete destruction, negative margins, histology
- Success measured by loss of enhancement on post operative imaging, progressive shrinkage, negative follow up biopsy, and long term cancer free survival
Cryotherapy of Renal Tumors: >5 yr Follow of 60 Patients

• Median tumor size 2.3 cm
• Median follow 6 years
• Local tumor recurrence: 6.7% (3 patients)
• Survival: Overall 82%  
  Cancer Specific 100%

Novick A: AUA, 2006
Percutaneous RFA

- Follow up CT shows a several patients with persistent post-treatment tumor enhancement
- Post op biopsy shows viable tumor in several patients, but retreatment is possible

Extracorporeal Renal Tumor Ablation

- High Intensity Focused Ultrasound (HIFU)
- Radiosurgery (cyberknife)
- Excision, laparoscopic or open, is the gold standard
- Ablation is promising, but long-term outcome data are pending
Angiogenesis Inhibition
In Metastatic Renal Cell Ca

- **FDA Approves Sutent for RCC based on two single arm studies!**
- **Study 1**
  106 patients who had failed cytokine therapy within 9 months.
- Daily doses of 50 mg Sutent on the 4-weeks-on/2-weeks-off schedule until evidence of disease progression.
- Partial response: **25.5%** (n=27), with a median duration of response to date of **27.1 weeks** (41.5% of subjects remained on protocol without evidence of progression to date).
FDA Approval of Sutent (sunitinib)

- **Study 2**: 63 RCC patients failing cytokine therapy received 50 mg, 4/2 regimen.
- Sutent produced partial tumor responses in **36.5%** (n=23), with a median response duration of **54 weeks**. At the time of approval, 11 patients remained on protocol, with ongoing disease responses.

FDA, 2006
Sutent (sunitinib) in RCC

- 750 patients with metastatic RCC randomized to alpha Ifn or alpha Ifn plus sunitinib.
- Progression free survival increased from 5 to 11 months*
- Responses increased from 6% to 31% *

*P<0.000001

Motzser, RJ: ASCO, 2006
Temsirirolimus in RCC

- Specific inhibitor of mTOR kinase
- **626** patients with poor risk factors and metastatic RCC randomized to Ifn, temsirolimus, or both
- **49% increase** in median **survival** in temsirolimus arm compared with Ifn; 15% increase in combined arm over Ifn
- 7.3 Ifn, 8.4 both, 10.9 month survival temsirolimus

Hudes GR: ASCO, 2006
Conclusions: Renal Cell Ca

- Partial nephrectomy is safe and effective for smaller (<4cm) peripherally located tumors
- Laparoscopic nephrectomy and partial nephrectomy are gradually gaining popularity
- For selected patients, ablation with cryotherapy, or less commonly radio frequency, is appropriate.
Conclusions Renal Cell Ca

- Adjuvant nephrectomy improves the survival of patients with metastatic RCC receiving Ifn, from 8 to 12 months.
- Oral tyrosine kinase inhibitors, sunitinib and temsirolimus, now markedly improve the treatment of metastatic disease.
6.5 Hour Robotic Bilateral Nephroureterectomy Cystoprostatectomy for Bladder, Renal & Prostate Cancer in a 73 y/o Dialysis Patient: Scar Smaller than Appendectomy