Indiana University Health

Kidney Cancer Association
13th Annual International International Symposium

Chicago, Illinois
October 24th, 2014
PARTIAL NEPHRECTOMY FOR T1B/2A TUMORS

Timothy A. Masterson, MD
Assistant Professor
Department of Urology
Indiana University Medical Center

Disclosures: none
AJCC Clinical Staging

- **TX**  Primary tumor cannot be assessed.
- **T0**  No evidence of primary tumor.
- **T1**  Tumor ≤7 cm in greatest dimension, limited to the kidney.
  - **T1a**  Tumor ≤4 cm in greatest dimension, limited to the kidney.
  - **T1b**  Tumor >4 cm but not >7 cm in greatest dimension, limited to the kidney.
- **T2**  Tumor >7 cm in greatest dimension, limited to the kidney.
  - **T2a**  Tumor >7 cm but ≤10 cm in greatest dimension, limited to the kidney.
  - **T2b**  Tumor >10 cm, limited to the kidney.
- **T3**  Tumor extends into major veins or perinephric tissues but not into the ipsilateral adrenal gland and not beyond Gerota fascia.
  - **T3a**  Tumor grossly extends into the renal vein or its segmental (muscle containing) branches, or tumor invades perirenal and/or renal sinus fat but not beyond Gerota fascia.
  - **T3b**  Tumor grossly extends into the vena cava below the diaphragm.
  - **T3c**  Tumor grossly extends into the vena cava above the diaphragm or invades the wall of the vena cava.
- **T4**  Tumor invades beyond Gerota fascia (including contiguous extension into the ipsilateral adrenal gland).

Guideline Recommendations

NCCN Guidelines Version 1.2015
Kidney Cancer

INITIAL WORKUP

- H&P
- CBC, comprehensive metabolic panel
- Urinalysis
- Abdominal/pelvic CT or abdominal MRI with or without contrast depending on renal insufficiency
- Chest imaging
- Bone scan, if clinically indicated
- Brain MRI, if clinically indicated
- If urothelial carcinoma suspected (e.g., central mass), consider urine cytology, ureteroscopy
- Consider needle biopsy if clinically indicated

STAGE

- Stage I (pT1a) Partial nephrectomy (preferred) or Radical nephrectomy (if partial not feasible or central location) or Active surveillance in selected patients or Ablative techniques for non-surgical candidates

PRIMARY TREATMENT

- Stage I (pT1b) Partial nephrectomy or Radical nephrectomy

- Stage II, III Radical nephrectomy

- Stage IV See KID-2

FOLLOW-UP

Follow-up (See KID-B) → Relapse See First-Line Therapy (KID-3)

Discussion
PNx for T1a tumors over time

**Figure 1.** Partial nephrectomy by year in patient subset with tumors 4 cm or less treated electively.

Thompson et al, 2009
PNx for T1b tumors over time

Figure 2. Partial nephrectomy by year in patient subset with tumors greater than 4 to 7 cm treated electively.

Thompson et al, 2009

Fig. 1 Utilization rate of partial nephrectomy in T1bN0M0 RCC patients, SEER 1988–2008.

Meskawi et al, IJU 2014
53.9% (2960/5483) of all tumors were > 4cm

TRENDS IN SEER/MEDICARE

Diffusion of Surgical Innovation Among Patients With Kidney Cancer

David C. Miller, MD, MPH\textsuperscript{1,2}
Christopher S. Saigal, MD, MPH\textsuperscript{1,2,3}
Mousumi Banerjee, PhD\textsuperscript{4,5}
Jan Hanley, MS\textsuperscript{3}
Mark S. Litwin, MD, MPH\textsuperscript{1,2,3,6}
and the Urologic Diseases in America Project

Impact of Laparoscopic RN on PN

Unintended Consequences of Laparoscopic Surgery on Partial Nephrectomy for Kidney Cancer

Robert Abouassaly, Shabbir M. H. Alibhai,* George Tomlinson, Narhari Timilshina and Antonio Finelli†

From the Division of Urologic Oncology, Princess Margaret Hospital and Department of Health Policy, Management and Evaluation (SMHA, GT, NT), University of Toronto, Toronto, Ontario, Canada

Figure 1. A, multinomial logistic regression model shows observed and predicted probability of ORN, LRN or PN with time. B, segmented regression reveals predicted (solid line) and projected (dashed line) proportion of patients treated with PN during observation, indicating statistically significant change in treatment trend as of 2003 (p = 0.001). Light dashed lines represent 95% CI.
Impact of CKD on survival

- Cohort of 1.12 million Kaiser Permanente patients
- CKD stage III or higher present in 18%
- CKD stage strongly/independently associated with:
  - hospitalizations
  - cardiovascular events
  - death


Table 2. Adjusted Hazard Ratio for Death from Any Cause, Cardiovascular Events, and Hospitalization among 1,120,295 Ambulatory Adults, According to the Estimated GFR.

<table>
<thead>
<tr>
<th>Estimated GFR</th>
<th>Death from Any Cause</th>
<th>Any Cardiovascular Event</th>
<th>Any Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥60 ml/min/1.73 m²†</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>45–59 ml/min/1.73 m²</td>
<td>1.2 (1.1–1.2)</td>
<td>1.4 (1.4–1.5)</td>
<td>1.1 (1.1–1.1)</td>
</tr>
<tr>
<td>30–44 ml/min/1.73 m²</td>
<td>1.8 (1.7–1.9)</td>
<td>2.0 (1.9–2.1)</td>
<td>1.5 (1.5–1.5)</td>
</tr>
<tr>
<td>15–29 ml/min/1.73 m²</td>
<td>3.2 (3.1–3.4)</td>
<td>2.8 (2.6–2.9)</td>
<td>2.1 (2.0–2.2)</td>
</tr>
<tr>
<td>&lt;15 ml/min/1.73 m²</td>
<td>5.9 (5.4–6.5)</td>
<td>3.4 (3.1–3.8)</td>
<td>3.1 (3.0–3.3)</td>
</tr>
</tbody>
</table>

CKD is Common Before and After Nephrectomy

- CKD is common prior to surgery
  - 22% - 26% have baseline CKD III or higher\textsuperscript{1-3}

- Among patients with Cr < 1.4 mg/dl, two kidneys, and small renal mass (< 4 cm):
  - Radical nephrectomy nearly always leads to CKD III or higher
  - Partial nephrectomy results in approximately 40% with new CKD III or higher within 6 years

References: \textsuperscript{1}Lane, J Urol, 2008; \textsuperscript{2}Clark, J Urol, 2010, \textsuperscript{3}Huang, Lancet Oncology, 2006
Nephrectomy Induced Chronic Renal Insufficiency is Associated With Increased Risk of Cardiovascular Death and Death From Any Cause in Patients With Localized cT1b Renal Masses

Christopher J. Weight,* Benjamin T. Larson,* Amr F. Fergany,*,† Tianming Gao,* Brian R. Lane,* Steven C. Campbell,‡ Jihad H. Kaouk,§ Eric A. Klein|| and Andrew C. Novick¶
Surgeon preference or tumor characteristics driving surgical approach?
- Technical difficulty
- Greater risk of complications
- Lack of training
- Under-appreciation of benefits
- Underutilization in...
  - Elderly, Females, Rural, increasing size
Issues at Hand: Radical vs Partial?

- Technical Feasibility?
- Cancer Control equivalence?
- Functional Outcomes?
- Complications?
- Selection?
  - Familial/Hereditary
  - Focality
  - Fuhrman grade/stage
  - Age/Medical Co-morbidity
Not Controversial…

• PN in...
  – Solitary kidney
  – Bilateral synchronous renal masses
  – Multifocal renal masses
  – Chronic Kidney Disease (i.e. eGFR <30-45)
  – Hereditary RCC
Not Controversial…

- RN in…
  - ESRD
  - Infiltrative tumors
  - Caval Thrombi
Controversial?

- PN with normal contralateral kidney and...
  - Solitary, sporadic, unilateral, solid renal masses >4cm?
  - Renal Sinus tumors?
  - Variant histologies?
Defining Cancer Outcomes

- Benign lesions in tumors >4cm
  - Incidence?
  - Role of renal mass biopsy?

- Short term
  - Pathologic surrogates
    - Surgical margins
    - Tumor violation

- Long term
  - Loco-regional recurrence
  - Cancer-specific survival
  - Overall survival
Benign lesions by size

Outcomes Following Partial Nephrectomy by Tumor Size

Paul L. Crispen, Stephen A. Boorjian, Christine M. Lohse, Thomas S. Sebo, John C. Cheville, Michael L. Blute and Bradley C. Leibovich*

*From the Departments of Urology (PLC, SAB, MLB, BCL), Health Sciences Research (CML) and Pathology (TSS, JCC), Mayo Clinic, Rochester, Minnesota

TABLE 2. Pathological features by tumor size

<table>
<thead>
<tr>
<th>No. Cn Tumor Size (%)</th>
<th>0–1 or Less</th>
<th>Greater Than 1–2 or Less</th>
<th>Greater Than 2–3 or Less</th>
<th>Greater Than 3–4 or Less</th>
<th>Greater Than 4–5 or Less</th>
<th>Greater Than 5–6 or Less</th>
<th>Greater Than 6–7 or Less</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>19 (100.0)</td>
<td>183 (99.5)</td>
<td>259 (99.2)</td>
<td>172 (98.8)</td>
<td>95 (96.6)</td>
<td>38 (94.7)</td>
<td>32 (100.0)</td>
</tr>
<tr>
<td>2002 Primary tumor classification:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pT1a</td>
<td>19 (100.0)</td>
<td>182 (99.5)</td>
<td>257 (99.2)</td>
<td>170 (98.8)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>pT1b</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>92 (96.6)</td>
<td>36 (94.7)</td>
<td>32 (100.0)</td>
</tr>
<tr>
<td>Histology:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignant</td>
<td>13 (65.4)</td>
<td>142 (77.6)</td>
<td>200 (77.2)</td>
<td>138 (80.2)</td>
<td>80 (84.2)</td>
<td>35 (92.1)</td>
<td>29 (90.6)</td>
</tr>
<tr>
<td>Benign</td>
<td>6 (31.6)</td>
<td>41 (22.4)</td>
<td>59 (22.8)</td>
<td>34 (19.8)</td>
<td>15 (15.8)</td>
<td>3 (7.9)</td>
<td>3 (9.4)</td>
</tr>
<tr>
<td>Malignant histology:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clear cell RCC</td>
<td>5 (32.1)</td>
<td>51 (32.5)</td>
<td>137 (32.5)</td>
<td>55 (31.7)</td>
<td>53 (31.7)</td>
<td>21 (5.5)</td>
<td>19 (35.8)</td>
</tr>
<tr>
<td>Papillary RCC</td>
<td>5 (26.3)</td>
<td>43 (23.5)</td>
<td>50 (19.3)</td>
<td>40 (23.3)</td>
<td>18 (19.0)</td>
<td>12 (34.3)</td>
<td>6 (18.5)</td>
</tr>
<tr>
<td>Chromophobe RCC</td>
<td>0 (0.0)</td>
<td>7 (3.8)</td>
<td>11 (4.3)</td>
<td>8 (4.7)</td>
<td>7 (7.4)</td>
<td>1 (2.6)</td>
<td>4 (12.5)</td>
</tr>
<tr>
<td>Collecting duct RCC</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (0.4)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>RCC not otherwise specified</td>
<td>0 (0.0)</td>
<td>1 (0.6)</td>
<td>1 (0.4)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Benign histology:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oncocytoma</td>
<td>2 (10.5)</td>
<td>28 (15.3)</td>
<td>46 (17.8)</td>
<td>31 (18.0)</td>
<td>8 (5.4)</td>
<td>3 (7.9)</td>
<td>1 (3.1)</td>
</tr>
<tr>
<td>Angiomyolipoma</td>
<td>2 (10.5)</td>
<td>12 (6.6)</td>
<td>12 (4.6)</td>
<td>3 (1.7)</td>
<td>6 (6.3)</td>
<td>0 (0.0)</td>
<td>2 (6.3)</td>
</tr>
<tr>
<td>Metanephric adenoma</td>
<td>0 (0.0)</td>
<td>1 (0.6)</td>
<td>1 (0.4)</td>
<td>0 (0.0)</td>
<td>1 (1.1)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Papillary adenoma</td>
<td>2 (10.5)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>RCC nuclear grade (607 pts):</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3 (23.1)</td>
<td>24 (16.9)</td>
<td>31 (15.5)</td>
<td>11 (8.0)</td>
<td>9 (11.8)</td>
<td>2 (5.7)</td>
<td>8 (27.6)</td>
</tr>
<tr>
<td>2</td>
<td>10 (76.9)</td>
<td>96 (67.6)</td>
<td>125 (62.8)</td>
<td>85 (61.6)</td>
<td>45 (56.3)</td>
<td>18 (51.4)</td>
<td>13 (44.8)</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>21 (14.8)</td>
<td>43 (21.5)</td>
<td>40 (29.0)</td>
<td>25 (31.3)</td>
<td>14 (40.0)</td>
<td>8 (27.6)</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>1 (0.7)</td>
<td>1 (0.5)</td>
<td>2 (1.5)</td>
<td>1 (1.3)</td>
<td>1 (2.9)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>
Role of Renal Mass Biopsy

• What we didn’t know then...
  - Grade
  - Stage
  - Histology

• Nondiagnostic Rate
  - 5-20%

• FNA + CB Accuracy
  - 96.5-100%

• Concordance with final histology and grade
  - 92%

Leveridge et al, Barwari et al, Hobbs et al, Londono et al, Halverson et al
RETROSPECTIVE COMPARATIVE OUTCOMES IN SURVIVAL WITH PN VERSUS RN FOR T1B RCC
T1b Comparative CSS: RN vs PN

Fig. 1. Cancer specific survival for 91 patients treated with NSS (98.3% ± 1.7% at 5 years) and 841 patients treated with RN (83.9% ± 1.3% at 5 years) for 4 to 7 cm RCC.

Fig. 2. Distant metastases-free survival for 91 patients treated with NSS (94.2% ± 3.3% at 5 years) and 841 patients treated with RN (83.2% ± 1.4% at 5 years) for 4 to 7 cm RCC.

Fig. 3. Recurrence-free survival for 91 patients treated with NSS (95.9% ± 3.4% at 5 years) and 841 patients treated with RN (97.5% ± 0.6% at 5 years) for 4 to 7 cm RCC.

**Table 2. Univariate and multivariate analyses**

<table>
<thead>
<tr>
<th></th>
<th>Univariate</th>
<th>Multivariate*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Risk Ratio (95% CI)</td>
<td>p Value</td>
</tr>
<tr>
<td>Ca specific survival:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSS</td>
<td>1.0 (reference)</td>
<td></td>
</tr>
<tr>
<td>RN</td>
<td>3.76 (1.20, 11.81)</td>
<td>0.023</td>
</tr>
<tr>
<td>Distant metastases-free survival:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSS</td>
<td>1.0 (reference)</td>
<td></td>
</tr>
<tr>
<td>RN</td>
<td>3.44 (1.27, 9.28)</td>
<td>0.015</td>
</tr>
<tr>
<td>Recurrence-free survival:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSS</td>
<td>1.0 (reference)</td>
<td></td>
</tr>
<tr>
<td>RN</td>
<td>0.32 (0.12, 0.85)</td>
<td>0.022</td>
</tr>
</tbody>
</table>

*Risk ratio adjusted for perinephric fat, renal vein and regional lymph node involvement, nuclear grade, histological tumor necrosis and histological subtype.
Survival Outcomes (Medicare): PN vs RN

Long-term Survival Following Partial vs Radical Nephrectomy Among Older Patients With Early-Stage Kidney Cancer

- From 1992-2007, 7138 Medicare beneficiaries with clinical stage T1 kidney cancer underwent partial (27%) or radical (73%) nephrectomy
- Used instrumental variable approach to control for measurable and unmeasurable differences
- Partial nephrectomy associated with 46% decreased risk of death
- No difference in cancer-specific survival
- For every 7 patients having partial rather than radical nephrectomy, prevent 1 death at 8 years

Figure 3. Predicted Survival Probabilities at 2, 5, and 8 Years After Treatment With Partial or Radical Nephrectomy.

Tan et al. JAMA, 2012
Comparative CSS Outcomes: tumors >4cm

- SEER 1988-2008
  - 16,333 T1b patients
  - 5- & 10-years CSS (propensity)
    - PN: 4.4 & 6.1% Mortality
    - RN: 6.0 & 10.4% Mortality
    - Propensity adjusted, p = 0.03
  - Competing risk analysis
    - Type of surgery non-predictor between RN & PN for cancer-specific mortality

Meskawi (WJU, 2014, 122)
RETROSPECTIVE COMPARATIVE OUTCOMES IN SURVIVAL WITH PN VERSUS RN FOR T2A RCC
T2 renal masses

Outcome of Stage T2 or Greater Renal Cell Cancer Treated With Partial Nephrectomy

Rodney H. Breau, Paul L. Crispens, Rafael E. Jimenez, Christine M. Lohse, Michael L. Blute and Bradley C. Leibovich*

- 69 pT2 - 3b partial nephrectomy patients
- Matched 3:1 radical nephrectomy
- Outcome analyses conducted
Survival Outcomes: T2 disease
Comparative Effectiveness for Survival and Renal Function of Partial and Radical Nephrectomy for Localized Renal Tumors: A Systematic Review and Meta-Analysis

Simon P. Kim, R. Houston Thompson, Stephen A. Boorjian, Christopher J. Weight, Leona C. Han, M. Hassan Murad, Nathan D. Shippee, Patricia J. Erwin, Brian A. Costello, George K. Chow and Bradley C. Leibovich*

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Hazard Ratio)</th>
<th>SE</th>
<th>Weight IV, Fixed, 95% CI</th>
<th>Hazard Ratio IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barbilas (34)</td>
<td>0.15700375</td>
<td>1.43689568</td>
<td>0.4%</td>
<td>1.17 [0.07, 19.56]</td>
</tr>
<tr>
<td>Becker (35)</td>
<td>-1.66073121</td>
<td>0.32748249</td>
<td>7.9%</td>
<td>0.19 [0.10, 0.36]</td>
</tr>
<tr>
<td>Bedke (36)</td>
<td>-0.69314718</td>
<td>0.72813397</td>
<td>1.6%</td>
<td>0.50 [0.12, 2.08]</td>
</tr>
<tr>
<td>Breau (18)</td>
<td>-0.04082199</td>
<td>0.33282509</td>
<td>7.6%</td>
<td>0.96 [0.50, 1.84]</td>
</tr>
<tr>
<td>Butler (19)</td>
<td>0.31481074</td>
<td>0.51427373</td>
<td>3.2%</td>
<td>1.37 [0.50, 3.75]</td>
</tr>
<tr>
<td>Crepel (37)</td>
<td>0.67294447</td>
<td>0.51095252</td>
<td>3.2%</td>
<td>1.96 [0.72, 5.34]</td>
</tr>
<tr>
<td>D'Armento (38)</td>
<td>0.10436002</td>
<td>1.48868589</td>
<td>0.4%</td>
<td>1.11 [0.06, 20.54]</td>
</tr>
<tr>
<td>Helledenthal (22)</td>
<td>-0.94160854</td>
<td>0.20687375</td>
<td>19.8%</td>
<td>0.39 [0.26, 0.58]</td>
</tr>
<tr>
<td>Jeldres (39)</td>
<td>0.77932488</td>
<td>0.42379257</td>
<td>4.7%</td>
<td>2.18 [0.95, 5.00]</td>
</tr>
<tr>
<td>Kim (24)</td>
<td>-0.04082199</td>
<td>1.20773832</td>
<td>0.6%</td>
<td>0.96 [0.09, 10.24]</td>
</tr>
<tr>
<td>Lau (25)</td>
<td>0.28517894</td>
<td>0.75978526</td>
<td>1.5%</td>
<td>1.33 [0.30, 5.90]</td>
</tr>
<tr>
<td>Lee (26)</td>
<td>0.25464222</td>
<td>0.41672252</td>
<td>4.9%</td>
<td>1.29 [0.57, 2.92]</td>
</tr>
<tr>
<td>Leibovich (40)</td>
<td>-0.47003363</td>
<td>0.60752523</td>
<td>2.3%</td>
<td>0.63 [0.19, 2.06]</td>
</tr>
<tr>
<td>Lerner (27)</td>
<td>0.27002714</td>
<td>0.25162232</td>
<td>13.4%</td>
<td>1.31 [0.80, 2.15]</td>
</tr>
<tr>
<td>Margulis (41)</td>
<td>-0.90386821</td>
<td>0.52056081</td>
<td>3.1%</td>
<td>0.41 [0.15, 1.12]</td>
</tr>
<tr>
<td>Patard (42)</td>
<td>-0.5798185</td>
<td>0.33574896</td>
<td>7.5%</td>
<td>0.56 [0.29, 1.08]</td>
</tr>
<tr>
<td>Simmons (29)</td>
<td>0.37156356</td>
<td>1.23052485</td>
<td>0.6%</td>
<td>1.45 [0.13, 16.17]</td>
</tr>
<tr>
<td>Thompson (12)</td>
<td>-0.67334455</td>
<td>0.38885411</td>
<td>5.6%</td>
<td>0.51 [0.24, 1.09]</td>
</tr>
<tr>
<td>Van Poppell (13)</td>
<td>0.72270598</td>
<td>0.62936443</td>
<td>2.1%</td>
<td>2.06 [0.60, 7.07]</td>
</tr>
<tr>
<td>Weight (30)</td>
<td>-0.26136476</td>
<td>0.32155354</td>
<td>8.2%</td>
<td>0.77 [0.41, 1.45]</td>
</tr>
<tr>
<td>Weight (31)</td>
<td>-0.91629073</td>
<td>0.76106239</td>
<td>1.5%</td>
<td>0.40 [0.09, 1.78]</td>
</tr>
</tbody>
</table>

**Figure 3.** Forest plot of pooled CSM HRs for PN vs RN in 21 studies

Heterogeneity: Chi$^2$ = 53.43, df = 20 ($P < 0.0001$); I$^2$ = 63%
Test for overall effect: Z = 3.77 (P = 0.0002)
Figure 2. Forest plot of pooled ACM HRs for PN vs RN in 21 studies

Figure 4. Forest plot of pooled severe CKD HRs for PN vs RN in 9 studies
PROSPECTIVE, RANDOMIZED COMPARATIVE OUTCOMES OF PN VS RN
EORTC Randomized Trial

A Prospective, Randomised EORTC Intergroup Phase 3 Study Comparing the Oncologic Outcome of Elective Nephron-Sparing Surgery and Radical Nephrectomy for Low-Stage Renal Cell Carcinoma

Hendrik Van Poppel\textsuperscript{a,*}, Luigi Da Pozzo\textsuperscript{b,1}, Walter Albrecht\textsuperscript{c}, Vsevolod Matveev\textsuperscript{d}, Aldo Bono\textsuperscript{e}, Andrzej Borkowski\textsuperscript{f}, Marc Colombel\textsuperscript{g}, Laurence Klotz\textsuperscript{h}, Eila Skinner\textsuperscript{i}, Thomas Keane\textsuperscript{j}, Sandrine Marreaud\textsuperscript{k}, Sandra Collette\textsuperscript{l}, Richard Sylvester\textsuperscript{k}

- Phase III, non-inferiority trial
- Accrual set at 1300 patients to assess a 3\% difference in 5-yr survival
- Between 1992 and 2003, 541 patients with a renal mass < 5 cm were randomized to partial or radical nephrectomy
- Trial closed in 2003 due to poor accrual
- Median follow-up 9 years
- Death in 117 (22\%), only 12 (2\%) from kidney cancer

Van Poppel et al, Eur Urol 2011
EORTC Randomized Trial

- Non-statistical difference in CSS
- OS:
  - Noninferiority- HR 1.5 (CI 1.03 - 2.16; p = 0.77)
  - Superiority
    - ITT:  p = 0.032
    - non-ITT HR:  p = 0.07
- Limitations
  - Only met 42% of accrual goal
  - 10% cross-over
  - Few deaths from RCC (2.2%)
  - Did not assess renal function pre- or post-op

Van Poppel et al, Eur Urol 2011
Renal Function in EORTC Randomized Trial

<table>
<thead>
<tr>
<th>eGFR</th>
<th>Outcome</th>
<th>No. (RN)</th>
<th>% (RN)</th>
<th>No. (NSS)</th>
<th>% (NSS)</th>
<th>Difference, %</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Last</td>
<td>eGFR &lt;60</td>
<td>152</td>
<td>58.7</td>
<td>98</td>
<td>38.4</td>
<td>20.3</td>
<td>(11.8–28.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>eGFR &lt;45</td>
<td>64</td>
<td>24.7</td>
<td>34</td>
<td>13.3</td>
<td>11.4</td>
<td>(4.7–18.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>eGFR &lt;30</td>
<td>17</td>
<td>6.6</td>
<td>9</td>
<td>3.5</td>
<td>3.1</td>
<td>(−0.7 to 6.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>eGFR &lt;15</td>
<td>3</td>
<td>1.2</td>
<td>2</td>
<td>0.8</td>
<td>0.4</td>
<td>(−1.3 to 2.1)</td>
<td></td>
</tr>
</tbody>
</table>

Scosyrev et al, Eur Urol, 2014
CKD-M(edical) vs CKD-S(urgical)

- 3,923 patients without CKD had radical or partial nephrectomy
- Median follow-up: 6.6 years (IQR: 4.8 – 8.7)
- 42% with new CKD stage 3 or higher
- CKD progression defined as GFR decline of >50% from post-op value
- Only 3% had CKD progression between post-op and latest follow-up

Lane et al. (2013)
COMPLICATIONS OF PN
EORTC Randomized Trial

A Prospective Randomized EORTC Intergroup Phase 3 Study
Comparing the Complications of Elective Nephron-Sparing Surgery and Radical Nephrectomy for Low-Stage Renal Cell Carcinoma

Hendrik Van Poppel a,b, Luigi Da Pozzo c, Walter Albrecht a, Veselod Matveev d, Aldo Bono e, Andrzej Borkowski f, Jean-Marie Marechal g, Laurence Klitz h, Ella Skinner i, Thomas Keane j, Ilse Claeissens k, Richard Sylvester k for the European Organization for Research and Treatment of Cancer (EORTC)
National Cancer Institute of Canada Clinical Trials Group (NCIC CTG)
Southwest Oncology Group (SWOG)
the Eastern Cooperative Oncology Group (ECOG)

- Severe Hemorrhage: 3.1% vs. 1.2%
- Urinary Fistulas: 4.4% vs. 0%
- Re-operation for complication: 4.4% vs. 2.4%
- Overall differences acceptable

Lap RN vs Lap PN

- Does EBL and operative time matter with regards to perioperative complications???
  - Deklaj et al (lapPN v lapRN)
    - LOS (2.1 vs 2.0)
    - EBL (233 v 112)
    - Transfusion (9 v 6)
    - OR time (228 v 175)
    - 3x’s greater intraop complication, 2x’s greater postop complication
## Complications: T2 masses & PN

<table>
<thead>
<tr>
<th>Characteristics in PN and RN cohorts</th>
<th>Baseline</th>
<th>PN 69</th>
<th>RN 207</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine leak</td>
<td>12</td>
<td>(17.5)</td>
<td>0</td>
</tr>
<tr>
<td>Retroperitoneal bleeding</td>
<td>2</td>
<td>(3)</td>
<td>2</td>
</tr>
<tr>
<td>Retroperitoneal abscess</td>
<td>3</td>
<td>(4.5)</td>
<td>2</td>
</tr>
<tr>
<td>Wound infection</td>
<td>1</td>
<td>(1.5)</td>
<td>6</td>
</tr>
<tr>
<td>Sepsis</td>
<td>1</td>
<td>(1.5)</td>
<td>2</td>
</tr>
<tr>
<td>Bowel ileus</td>
<td>8</td>
<td>(11.5)</td>
<td>19</td>
</tr>
<tr>
<td>Median days hospital stay (IQR)</td>
<td>6</td>
<td>(4–9)</td>
<td>5</td>
</tr>
</tbody>
</table>

Courtesy of RH Thompson
Conclusions

- Partial Nephrectomy is under-utilized as a treatment choice for larger renal masses.
- Partial Nephrectomy has comparable oncologic efficacy as Radical Nephrectomy in T1b and select T2a tumors.
- Partial Nephrectomy significantly reduces the incidence of S-CKD compared to Radical Nephrectomy.
- M-CKD is more common than we recognize, and severity correlates with long term survival.
- Complications are more common with Partial Nephrectomy compared to Radical Nephrectomy.
Take-Home

- Importance of emphasizing patient factors and not surgeon factors when making treatment decisions
- For healthy patients with minimal medical comorbidities, surgical approach likely has little impact on survival
- Benefits of nephron sparing surgery need to be weighed against higher risk of complications
- Randomized trials needed
THANK YOU