Partial Nephrectomy
Has the Pendulum Swung too far?
When is it Indicated in 2013?

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Objectives
- At the conclusion of this symposium the participants should be able to:
  - Employ surgical treatments for kidney tumors to optimize patient outcomes in terms of curing and preventing kidney disease in the future
- Potential COI
  - Investigator: GSK
  - Speaker, investigator: Pfizer

Disclaimer
- We still believe in PNx for:
  - Small renal tumors (T1a)
  - Whenever preservation of renal function is of premium importance
  - Beyond this we may be doing too many PNx
Guidelines 2009
Take Home Points

- **Save the kidney** whenever possible
  - Radical Nx → CKD → Morbid CVS events and increased Mortality
  - PNx is the reference standard for nephron-sparing: TA and AS have potential limitations and should not be used indiscriminately

Campbell SC, Novick AC, Belldegrun A, Blute ML, et al.,
Guideline for Management of the Clinical T1 Renal Mass
J Urol, 182:1271-5, 2009
**Index Patient 3:**
Healthy; Clinical T1b

- **STANDARD-PN**: Complete surgical excision by PN is an alternative standard of care, particularly when there is a need to preserve renal function.

- **STANDARD-RN**: Should be discussed as standard of care for patients with normal contralateral kidney.

- **OPTION-TA**: Cryoablation or RFA can/may be discussed as a treatment option which is less effective due to an increased risk of local recurrence. TA may represent suboptimal management for this healthy patient.

- **OPTION-AS**: AS with delayed intervention can/may be discussed as an option in patients who want to avoid surgery and are willing to accept an increased risk of tumor progression compared to RN or PN. AS may represent suboptimal management for this healthy patient.

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**Case Challenge**

- 52-yr-old female, presented to OSH 2011
- R renal mass: 6 cm, down to hilum
- SCr 0.79, eGFR 82
- RFS: L 58% R 42%
- eGFR: L 48 R 34
- Metastatic evaluation negative
- Otherwise extremely healthy
Management Options: Your choice?

- A. Renal Mass Biopsy
- B. Active Surveillance
- C. Thermal Ablation
- D. MIS PNx
- E. Open PNx
- F. MIS RNx
Management

- Robotic R PNx 9/11
- WIT 27 min, most of kidney saved per report
- Uneventful postoperative course
- Clear cell, G4, pT1b (6.0 cm), margins negative
- Final SCR 0.96, eGFR 67
- RFS: L 70% R 30%
- eGFR: L 47 R 20 (34 preop)
- Saved 59% of the function of the R kidney

What was Gained by PNx?

- Saved 59% of the function in the L kidney
  - eGFR 34 on L preop, 20 postop
- How important is this given eGFR in the contralateral kidney was 48, 47 on two different estimates (pre and postop)?
- What was lost?
- Is there a reasonable concern about oncologic outcomes?

10/12: 13 months later
Management Options: Your choice?

- 25% A. Active Surveillance
- 25% B. Thermal Ablation
- 25% C. Excision of nodules with possible PNx
- 25% D. Excision of nodules with Rad Nx and LND
Management: October 2012

- Open R Rad Nk, excision of all retroperitoneal fat including the nodules, as wide as possible
- Extensive LND
- Postoperative course uneventful
- Final SCr 1.18, eGFR = 54, all supplied by the contralateral kidney

Pathology/Prognosis

- Unfavorable
  - High grade clear cell and chromophobe → unclassified
  - Both nodules positive, but also microscopic infiltrative cancer throughout the perinephric fat → focal positive margin
  - Tumor in microvasculature
- Will be high risk to recur during the coming months/years

Visible Nodule
Outside of Visible Nodule

- Elective indication, normal contralateral kidney
- Some risk of morbidity (tumor down to hilum)
- Some oncologic risk → played out unfavorably
- Final analysis: in retrospect, would have been much better with RNx up front (most would agree)

PNx in this Case?

Lap Rad Nx: The Great Seductress

Is this really true?
How important is it to avoid Rad Nx?
Weighing the Value of PNx

Survival Advantage??
Renal Function
Oncologic Morbidity
PNx
Rad Nx

Meta-analysis of PNx vs. Rad Nx

- N = 36 studies, > 40,000 patients analyzed
- All but one retrospective, almost all subject to selection bias
- Advantages of PNx based on pooled estimates:
  - 61% risk reduction for severe CKD, p<0.0001
  - 19% risk reduction all cause mortality, p<0.0001
  - 29% risk reduction in cancer specific mortality, p=0.0002

Prospective Randomized Trial
Elective PNx vs. Rad Nx

- EORTC 30904: 268 PN vs. 273 Rad Nx
- Solitary tumor, ≤ 5.0 cm, normal contralateral kidney
- Advantage for RN related to lower morbidity
  - Severe postop bleed: 3.1% for PNx vs 1.2% for Rad Nx
  - Urinary Division: 4.4% for PNx vs 8.0% for Rad Nx
  - Reoperation: 4.4% for PNx vs 2.4% for Rad Nx
- Advantage for PNx with respect to better renal function
  - Mean SCr: 1.2 for PNx vs 1.4 for Rad Nx
- What about overall survival?
EORTC 30904

- 10 yr overall survival (median f/up 9.3 years)
  81% for Rad Nx vs 76% for PNx (p = 0.03)
- Tumor progression: 9 with Rad Nx and 12 with PNx (NS)
- Only 12 of 117 deaths due to RCC (4 Rad Nx, 8 PNx)
- Most common cause of death: Cardiovascular
  - 20 in Rad Nx group
  - 25 in PNx group

EORTC 30904

- No survival advantage for PNx!
  - Multicenter study, perhaps quality of PN was variable???
  - Study closed due to poor accrual
  - Renal function was not analyzed in comprehensive manner
  - Crossover: some patients switched groups after randomization (about 10%), but analysis was Intent-to-Treat
  - Only 9.3 years of follow-up

- Impact: despite limitations, this was a randomized study, and it presents very provocative data
- No matter how you want to interpret this, you have to concede: Suggests functional advantage related to PNx may not be as great as previously thought

Rad Nx: Normal Contralateral Kidney

There may be a difference between:
CDK from medical causes: the driver towards CKD is still operative
CDK due to surgery: the driver is no longer operative
What is the Impact of Surgically Induced CKD?

- CKD-M: medically induced CKD, driver is still present, associated with cardiovascular morbidity and increased mortality
- CKD-S: surgically induced CKD, driver is no longer present after surgery, what happens to these patients?

Lane BR, Campbell S, Demirjian S, Fergany A: Is the risk of progression and mortality in patients with surgically-induced chronic kidney disease lower than medical chronic kidney disease? AUA Abstract 1687, Atlanta, GA; May 22, 2012. Also, in press, J Urology

Study Design

- 4180 patients underwent RNx or PNx at our center
- CKD defined as eGFR < 60
- 1182 had preexisting CKD = CKD-M
- 927 developed CKD only after surgery = CKD-S
- Median follow-up 6.6 years
- Evaluated Annual Renal Function Decline after patient stabilized after surgery

Main Findings

- Annual Renal Functional Decline:
  - If > 4.0%, it was associated with 43% in mortality (p<0.0001)
  - Mean = 4.7% for patients with CKD-M
  - Mean = 0.7% for patients with CKD-S
Results and Conclusions

- CONCLUSION: CKD-M ≠ CKD-S
- CKD-M is more likely to progress than CDK-S, and has a greater impact on survival (at least with this extent of follow-up)
- Need further study, longer follow-up, all in progress

Survival Plot

EORTC 30904, Long-term Renal Function
Table 1: Demographics and Baseline Characteristics Grouped by Type of Kidney Disease

<table>
<thead>
<tr>
<th>Group</th>
<th>Medical (n=34,405)</th>
<th>Medical/Surgical (n=706)</th>
<th>Surgical (n=674)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>72 ± 12</td>
<td>69 ± 11</td>
<td>63 ± 11</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Male</td>
<td>15,078 (45)</td>
<td>403 (72)</td>
<td>413 (69)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>African-American</td>
<td>4,166 (12)</td>
<td>47 (8)</td>
<td>46 (8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>27,817 (82)</td>
<td>284 (50)</td>
<td>252 (42)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CHF</td>
<td>2708 (8)</td>
<td>27 (5)</td>
<td>10 (2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Baseline proteinuria</td>
<td>5535/21623 (26)</td>
<td>56/201 (28)</td>
<td>29/176 (16)</td>
<td>.016</td>
</tr>
<tr>
<td>New baseline eGFR</td>
<td>47 ± 10</td>
<td>38 ± 12</td>
<td>48 ± 8</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

1 Kidney disease is defined as eGFR < 60 ml/min/1.73 m²
2 eGFR is calculated by CKD-EPI formula.
3 Proteinuria is measured by dipstick (trace is considered negative).
4 New baseline is the highest GFR by 42 days following surgery.

Figure 1. Renal Function Before and After Surgery

Figure 2. Probability of 50% Drop in eGFR (or dialysis) in Three Years (Adjusted for Age, Gender, Race, Diabetes, Hypertension, and Heart Disease)
Weighing the Value of PNx

Survival Advantage???
Renal Function
Oncologic Morbidity
Rad Nx

2013 Where do we stand?
EORTC study blunts the impetus towards PNx

Normal Contralateral Kidney

T1a → T1b → T2a → T2b/T3

PNx → ??? → ??? → Rad Nx

Will need a randomized trial to resolve this issue for T1b-T2 renal masses

Figure 3. Probability of Mortality in Three Years (Adjusted for Age, Gender, Race, Diabetes, Hypertension, and Heart Disease)
Inclusion Criteria: Solitary, enhancing 4-10 cm renal mass (Clinical T1b2a) amenable to PN
Normal contralateral kidney
Negative Metastatic Workup; No previous history of RCC

Randomization

Group I PN
N = 256

Group II RN
N = 256

Primary Outcome: Overall Survival (at 5 and 10 years)
Secondary outcomes:
  - Disease specific survival, local and systemic recurrences
  - Renal function outcomes (Stage IV CKD, eGFR decline by >1/2)
  - Cardiac and metabolic sequelae