Conservative Surgical Treatment of Renal Tumours

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Surgical Controversies For RCC Treatment in 2014

• * Renal biopsy : actuarial role
• * Active Surveillance : is it safe?
• * Focal Therapy: which role ?
• * Nephron sparing surgery: why, when, how ?
• * Surgical Margins : impact on the patient outcome
RCC - STAGE MIGRATION

STAGE I
SIZE
4.1 cm
↓
3.6 cm

NATIONAL CANCER DATABASE (1993-2004)

Kane et al, Cancer 2008
Guideline for Management of the Clinical T1 Renal Mass

6.1.6 Recommendations

- Whenever technically feasible, nephron-sparing surgery is the standard procedure for solitary renal tumours up to a diameter of 7 cm.

- RN, particularly laparoscopic RN, is very appealing to patients and physicians but it is greatly overutilized. Nephron-sparing approaches should be considered in all patients with a clinical T1 renal mass as an overriding principle, presuming adequate oncologic control can be achieved, based on

Nephron-sparing surgery (partial nephrectomy) is appropriate in selected patients, for example:
- Small unilateral tumors (T1a and selected patients T1b)
- Uninephric state, renal insufficiency, bilateral renal masses, familial renal cell cancer
RCC - A Brief History of Time

Formal Radical Nx
Gregoire 1867

Radical Nx Series
Robson 1963

Lap Nx
Clayman 1969

Active Surveillance
Volpe, Jewett 2004

1st planned Nx
Simon 1869

Radical Nx
Robson 1903

Partial Nx
Novick / Van Poppel 1989

Lap Cryoablation
Gill 1998

1967

Robotic Partial Nx
Gettman 2004

Lap Partial Nx
Winfield/McDougal 1993

Ziya Kirkaly 2012
Surgical Approach To Renal Masses in 2014

- **Laparoscopy**: radical nephrectomy, partial nephrectomy, tumorectomy) LESS /NOTE
- **Robotics**: partial nephrectomy, radical nephrectomy
- **Open**: radical nephrectomy of large renal masses (>10 cm) or with renal vein /v.cava involvement. Partial nephrectomy of large tumors (> 5 cm) located in difficult sites (medium/central)
Nephron Sparing Surgery

• Why?

• When?

• How?
Cronic Kidney disease after Nephrectomy in patients with renal cortical tumors: retrospective cohort study

William CHuang, Andrew SLeeve, Angel M Sario, Mark Snyder, Andrew Mokars, Ganesh VRaj, Peter T Sardino, Paul Russo

Radical nephrectomy is a significant risk factor for the development of chronic kidney disease.

- 662 patients
- tumors < 4cm
- GFR <60 ml/Min in 3y
- GFR <45 ml/Min in 3y
- Nephrectomy 65%
- Partial nephrectomy 20%

Figure 3: Probability of freedom from new onset of GFR lower than 45 ml/Min per 1.72 m², by operation type
Chronic Kidney Disease and the Risks of Death, Cardiovascular Events, and Hospitalization

Alan S. Go, M.D., Glenn M. Chertow, M.D., M.P.H., Dongjie Fan, M.S.P.H., Charles E. McCulloch, Ph.D., and Chi-yuan Hsu, M.D.

CONCLUSIONS

An independent, graded association was observed between a reduced estimated GFR and the risk of death, cardiovascular events, and hospitalization in a large, community-based population. These findings highlight the clinical and public health importance of chronic renal insufficiency.
Comparison of Long-Term Results (Cancer Specific Survival) After Nephron-Sparing Surgery and Radical Nephrectomy in Treating 4 to 7 cm Renal Cell Carcinoma

Daimantas Milonas¹, Giedrius Skulčius¹, Ruslanas Baltrimavičius¹, Stasys Auškalnis¹, Marius Kinčius¹, Aivaras Matjošaitis¹, Inga Gudinavičienė², Giedré Smailytė³, Mindaugas Jievaltas¹

Medicina (Kaunas) 2013;49(5):223–8
pT1a RCC
SURGICAL OUTCOMES

Frank et al, J Urol 2005
Patard et al, J Urol 2004
CONCLUSIONS

Our results suggest that, compared with PN, RN may be associated with decreased overall survival in younger patients with small renal tumors. The basis for this association may result from a greater decrease in renal function after RN, although further investigation is needed. Nevertheless, these data provide further support for PN as the standard of care for managing most small renal masses.
Nephron Sparing Surgery : WHY?

- Because there is...
- no difference or better survival in favour of PN respect to radical nephrectomy (small renal masses)
- Local Recurrence after conservative surgery is very low
- And because .... radical nephrectomy determines an impairment in renal function (chronic kidney disease) that leads to a cancer specific survival reduction in time
Treatment Trends For Stage T1 Renal Cell Carcinoma

Matthew R. Cooperberg,* † Katherine Mallin, Christopher J. Kane‡ and Peter R. Carroll‡

Vol. 186, 394-399, August 2011
Partial Nephrectomy in cT2
Is it indicated?
Outcome of Stage T2 or Greater Renal Cell Cancer Treated With Partial Nephrectomy

Rodney H. Breau, Paul L. Crispin, Rafael E. Jimenez, Christine M. Lohse, Michael L. Blute and Bradley C. Leibovich*
From the Department of Urology, Mayo Clinic, Rochester, Minnesota

J Urol 2010;183:983

Figure 1. Patients treated with PN (red curve) vs RN (black curve). A, RCC specific survival (PN unadjusted HR 0.96, 95% CI 0.43–1.50, p = 0.489). B, overall survival (PN unadjusted HR 1.11, 95% CI 0.72–1.71, p = 0.642).
Outcome of Stage T2 or Greater Renal Cell Cancer Treated With Partial Nephrectomy

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Figure 2. Patients treated with PN (red curve) vs RN (black curve). A, metastasis-free probability (PN unadjusted HR 0.74, 95% CI 0.42–1.29, p = 0.29). B, isolated local recurrence-free probability (PN unadjusted HR 2.11, 95% CI 0.62–7.22, p = 0.234).
CONCLUSIONS

This study provides strong preliminary evidence of PN safety and efficacy for advanced RCC. Cancer specific outcomes in patients treated with PN were comparable to those in a well matched reference cohort treated with RN. The risk of postoperative complications was acceptable and renal function preservation was similar to that in patients with smaller tumors. Regardless of tumor stage nephron sparing surgery should be considered in all patients, including those with a normally functioning contralateral kidney.
Conservative Surgery For RCC: When?

- **Absolute indications**
  1. Solitary kidney
  2. Multifocal disease
  3. Chronic renal disease with an impairment of renal function
  
  **Objective:** to save patients from dialysis

- **Relative Indications**
  1. Normal contralateral kidney
  
  **Objective:** to preserve renal function and to save patients from chronic kidney diseases …… and prolong survival
Conservative Surgery for RCC: How?

- Type of surgery (enucleation vs partial vs emi)
- Technical problems during surgery (ischemia)
- Surgical approach (Open, Lap, Robotic)
Anatomic Classifications of SRMs

Preoperative Aspects and Dimensions Used for an Anatomical (PADUA) Classification of Renal Tumours in Patients who are Candidates for Nephron-Sparing Surgery

The R.E.N.A.L. Nephrometry Score: A Comprehensive Standardized System for Quantitating Renal Tumor Size, Location and Depth

<table>
<thead>
<tr>
<th>(R)adius (maximal diameter in cm)</th>
<th>1pt</th>
<th>2pts</th>
<th>3 pts</th>
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<tbody>
<tr>
<td>≤4</td>
<td>&gt;4 but &lt;7</td>
<td>≥7</td>
<td></td>
</tr>
<tr>
<td>≥50%</td>
<td>&lt;50%</td>
<td>Entirely endophytic</td>
<td></td>
</tr>
<tr>
<td>(E)xophytic/endophytic properties</td>
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<td></td>
<td></td>
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<tr>
<td>(N)earness of the tumor to the collecting system or sinus (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥7</td>
<td>&gt;4 but &lt;7</td>
<td>≤4</td>
<td></td>
</tr>
<tr>
<td>(A)nterior/Posterior</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(L)ocation relative to the polar lines*</td>
<td></td>
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</tr>
</tbody>
</table>

* suffix “h” assigned if the tumor touches the main renal artery or vein

- Entirely above the upper sinus line
- Entirely below the lower sinus line
- Crosses upper sinus line > 50%
- Crosses upper sinus line < 50%
- Entirely between the sinus lines

Kutikof et al., J Urol, 2009

Ficarra et al., Eur Urol, 2010
Type of Conservative Surgery for RCC

- **Tumor Enucleation**: removal of the tumor ONLY with its “capsule”. Results: decrease damage to normal renal tissue and same local recurrence rate (2%) (Carini et J Urol)

- **Partial Nephrectomy**: removal of the tumor with 1 cm or < of viable tissue around to obtain negative margins. Results: less residual parenchima and therefore less residual renal function

- **Emi-Nephrectomy**: Resection of half of the kidney. Results: concomitant reduction of at least 50% renal function

- **NB**: Haemostatic Sutures cause further renal damage
Pathophysiology of Ischemic Renal Damage:

Ischemia kills the kidney

Hypoxia
Aerobic Metabolism

Circulatory Arrest
Anaerobic Metabolism

“Reperfusion Injury”

CELL DEATH
Rat Model of Ischemic ARF
Postischemic Acute Renal Failure

Oberbauer et al. MEJM 2000

Time after Reperfusion
Tubule Epithelial Cells in ARF

Vital Cells

Sublethal Injury
- Cellular Dysfunction
- Polarity Loss
  - Loss of Paracellular Junctions
  - Loss of Cell – Matrix Adhesion
  - Loss of Paracellular Signaling
  - Exfoliation of Vital Cells from the Basal Membrane
- Altered Gene Expression
- Cellular Dedifferentiation
- Restitution, Proliferation

Lethal Injury
- Apoptosis
- Necrosis

adapted from Lieberthal W 1997, Kidney Int
bilateral RCC, CRI, e-GFR: 56 ml/min, BMI = 42, ASA III
• **Purpose:** safe duration of ischemia: solitary kidney

• **537 pts:** Cleveland and Mayo Clinic

• **no clamping:** 85 – warm: 174 – cold: 278

• **T size:** 2.5cm – 3.5cm – 4.0cm
Warm ischemia > 20 min, cold ischemia > 35 min
- higher incidence acute renal failure (p=0.002; p=0.003)
- increased risk chronic renal insufficiency (41% vs 19%)
- increased risk permanent dialysis (10% vs 4%)

Ischemia time up to 20 min safe
Pathophysiology of Ischaemic Renal Damage:

In addition, functional parenchyma is removed by the surgery and damaged by sutures.
2. Occlusion of artery and vein en bloc: Satinsky clamp

Most damage !!!!!!

RCC: Partial Nx – clamping
RCC: Partial Nx How to avoid parenchymal damage

- No ischemia
- Partial/regional ischemia
- Reduced ischemia time
- Cold ischemia
- Increasing the ischemic tolerance
RCC: Partial Nx – how to avoid parenchymal damage

- No ischemia
- Partial/regional ischemia
- Reduced ischemia time
- Cold ischemia
- Increasing the ischemic tolerance
1. Renal artery and vein are not dissected

2. Step by step excision of tumor – simultaneous hemostasis

3. Hemostasis:
   - Bipolar coagulation
   - Compression surgical sponge + hemostatic material
   - Argon beam coagulator

4. Sealing of cut surface:
   - Fibrin glue

7 patients: 1994 - 1996
Wedge Resection
Laparoscopic partial Nx for RCC

Limitations of Resection without Ischemia

1. Size: \( \approx 2\text{-}3\text{cm} \)

2. Location: superficial/exofitic Ts

\( \Rightarrow \) Wedge resection: tumor + 5 mm healthy tissue
Laparoscopic partial Nx for RCC

- Problem: Hemostasis

- better technology for optimal hemostasis required
“Zero Ischemia” Partial Nephrectomy: Novel Laparoscopic and Robotic Technique

Inderbir S. Gill *, Manuel S. Eisenberg, Monish Aron, Andre Berger, Osamu Ukimura, Mukul B. Patil, Vito Campese, Duraiyah Thangathurai, Mihir M. Desai

<table>
<thead>
<tr>
<th></th>
<th>Serum creatinine (mg/dl)</th>
<th>Estimated GFR ml/min per 1.73 m²</th>
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<tbody>
<tr>
<td>Preoperative (range)</td>
<td>0.9 (0.7–1.3)</td>
<td>75.3 (59.1–120)</td>
</tr>
<tr>
<td>Postoperative$ (range)</td>
<td>0.95 (0.7–1.7)</td>
<td>72.9 (44.5–120)</td>
</tr>
<tr>
<td>Absolute change (range)</td>
<td>0.0 (minus 0.1–0.5)</td>
<td>0.0 (minus 10.1–25.3)</td>
</tr>
<tr>
<td>Percent change (range)</td>
<td>0 (minus 11–42)</td>
<td>0 (minus 15–33)</td>
</tr>
</tbody>
</table>

GFR = glomerular filtration rate.

* Data presented for patients without complications to eliminate confounding factors.

$ At discharge (median: 3 d).
Zero ischemia $\rightarrow$ regional ischemia
central tumor - no ischemia
central tumor - no ischemia
peripheral tumor:
- ischemia
- laser
Laparoscopic partial Nx for RCC

Resection without Ischemia

*New Techniques*

- Microwave Tissue Coagulator
- Hydro-Jet
Zero ischemia - Laser

Partial Nx RCC Eraser 1318nm
RCC: Partial Nx. How to avoid parenchymal damage

- No ischemia
- Partial/regional ischemia
- Reduced ischemia time
- Cold ischemia
- Increasing the ischemic tolerance
Laparoscopic partial Nx: Resection clamp

Huyghes E – Storz: laparoscopic resection clamp

Storm FK, Urology 1975
Laparoscopic partial Nx for RCC

Cable-Tie Regional Hypoperfusion To Facilitate Laparoscopic Partial Nephrectomy

Corwin TS, Cadeddu A et al, J Endourol 2000, 14, Abstract BS 1-7
Laparoscopic partial Nx for RCC

Cable-Tie Regional Hypoperfusion To Facilitate Laparoscopic Partial Nephrectomy
Corwin TS, Cadeddu A et al, J Endourol 2000, 14, Abstract BS 1-7
Partial Nx – alternatives

Preo-Op Superselective Transarterial Embolization

Risk: Irreversible Parenchymal Damage

Simone G, J Endourol 2009
RCC: Partial Nx – how to avoid parenchymal damage

- No ischemia
- Partial/regional ischemia
- Reduced ischemia time
- Cold ischemia
- Increasing the ischemic tolerance
RCC: Partial Nx – alternatives

Increasing the ischemic tolerance of the kidney by hypothermia

- Cold perfusion
- Gelice
Hypothermia by arterial perfusion

Indication

- expected ischemia time
  > 20 - 30 min
  - central tumor
  - learning curve

Time factor is not relevant anymore
= NO STRESS
= function preserved

G Janetschek  J Urol  2004
RCC: Partial nephrectomy – Gelice

Gelice: Michel DGU 2009

Fresenius

Halle 2010
RCC: Partial nephrectomy – Gelice
RCC: Partial Nx – how to avoid parenchymal damage

- No ischemia
- Partial/regional ischemia
- Reduced ischemia time
- Cold ischemia
- Increasing the ischemic tolerance
CPZ conferred partial protection of renal function to kidney submitted to ischemia/reperfusion injury that seems to be not dependent on inhibition of lipid peroxidation
RCC: Partial Nx – alternatives

Increasing the ischemic tolerance of the kidney by protective drugs

N-acetylcysteine: antioxidant
Cortisone: antiinflammatory
Laparoscopic partial Nx for RCC

Pro:  - easy and fast approach
      - radical nephrectomy for stages cT1-2a standard of care

Con:  - difficult resection and reconstruction?
      - function?
      - oncologic outcome
## RCC partial Nx: Da Vinci

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>More degrees of freedom</td>
<td>No tactile feedback</td>
</tr>
<tr>
<td>3D</td>
<td>separation from patient</td>
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<tr>
<td>Ergonomics</td>
<td>Dependance from additional competent surgeon at table</td>
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<tr>
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<td>Limited availability of instruments: ultrasonic scalpel</td>
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<td>Additional time: Docking</td>
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<td>Dependance from Intuitive</td>
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<td>Costs</td>
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</table>
RCC partial Nx: Da Vinci

Advantages
- More degrees of freedom
- 3D
- Ergonomics

Disadvantages
- No tactile feedback
- Separation from patient
- Dependence on an additional competent surgeon at the table
- Limited availability of instruments: ultrasonic scalpel
- Additional time: Docking
- Dependence from Intuitive
- Costs
Positive Surgical Margins: Definition

• Presence of tumor cells outside the stained renal tissue evaluated by pathologist (after surgery)

• Tumor cells in renal fragment taken at the tumor base (during surgery – frozen)
# PSM: International Experience

<table>
<thead>
<tr>
<th>Author</th>
<th>N pts.</th>
<th>PSM</th>
<th>F-up (mos)</th>
<th>Rec. (%)</th>
<th>Mets (%)</th>
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<td>Sutherland</td>
<td>44</td>
<td>6.8</td>
<td>49</td>
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<td>J Urol ‘02</td>
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<td>Know</td>
<td>777</td>
<td>7</td>
<td>22</td>
<td>4 vs 0.5 NPSM</td>
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<td>J Urol ’13</td>
<td>943 RCC</td>
<td>2.2</td>
<td>NR</td>
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</table>

Prognostic Factors for PSM: * Solitary kidney, Grade (HG). Rec. in HG : 9.5%, Mets: 9.5% vs 0.7 and 0.2 in NSM
Conclusions

• "PSM does not appear to increase the long term risk of local recurrence or progression to metastatic disease and therefore the margin status should not be used as a measure of oncologic efficacy”
  (Yossepowich et al J Urol 2008)

• PS: non valid anymore

• **Final Message**
  PSM during surgery = extend dissection and fulgurate the tumor bed
  PSM after surgery  = NO further therapy. Follow the patient with US or CT
Nephron Sparing Surgery

• **Conclusions**
  
  • Radical nephrectomy is no longer the standard treatment for low-stage RCC (T1). These patients should undergo *nephron sparing surgery whenever possible.*
  
  • Limits: patients with large tumors (>7cm) have an increased risk of intrarenal recurrences
Thank You