Challenges in RCC surgery

JJ PATARD, MD, PhD
Paris XI University

Management options in VHL associated RCCs

- Observation,
- Radical nephrectomy,
- Renal parenchymal-sparing surgery,
  - Open, laparoscopic, robotic
- Renal transplantation
- Ablative procedures
  - radio-frequency ablation (RFA)
  - Cryoablation (CA)

Treatment Goals

- most VHL associated RCCs exhibit a consistent, predictable growth pattern and have a low propensity to metastasize at a size of less than 3 cm
- the treatment goal is to treat macroscopic renal tumors while preserving normal kidney function

Surgical challenges

- To treat multiple tumors
- To treat bilateral tumors
- To treat recurrent tumors
- to preserve long term renal function
  - Sparing renal parenchyma
  - Limiting renal ischemia damage
Oncological Issues

Renal Function Outcome, Overall Survival

Imperative Indications
Elective Indications ≤ 4 cm
Elective Indications > 4, ≤ 7 cm
Laparoscopic PN
Robotic PN
Ø > 7 cm
Down Staging with AAG


Better Understanding of Natural History of SRMs, Active Surveillance, Ablative Treatments
WIT, co-morbidities, non cancer related death

11/7/2014

The principles of PN

- Dissecting the kidney
- Controlling and Clamping renal vessels
- Removing the tumor with cold scissors
- Collecting system repair
- Haemostasis
- Parenchymal repair

Risks:
Severe Bleeding
Urinary Fistula
Renal function deterioration

Relation between tumor complexity and PN associated morbidity

- 390 patients operated by PN
- 44.6% open, 55.4% robotic
- Complexity scores:
  - Low: 28%
  - Moderate: 55.6%
  - High: 16.4%
- Median tumor size: 3.2 cm
- Overall Minor and major complication: 26.7% and 11.5%
- Minor complication rates: 26.6 vs 24.9 vs 32.8%; p = 0.45
- Major complication rates: 6.4 vs 11.1 vs 21.9%; p = 0.009

Simhan et al., Eur Urol 2011

3 approaches for doing a PN

- Open PN
- Laparoscopic PN
- Robotic PN
Results of OPN in sporadic RCCs

- Meta-analysis, 50 studies, 5037 tumors
- Mean age at diagnosis: 60.1 yrs
- Mean tumor size: 3.4 cms
- Mean follow-up: 54 months
- Local Recurrence rate: 2.6%
- Distant metastases: 5.6%
- Mean ischemic time 19 min
- Length of hospital stay 11.2j (5-7j)

---

Series of LPN (sporadic RCCs)

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of patients</th>
<th>Tumour size, cm</th>
<th>OPN, min</th>
<th>WLE, min</th>
<th>RRL, ml</th>
<th>LOS, days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jonas et al., 2012 [12]</td>
<td>71</td>
<td>2.5</td>
<td>205.5</td>
<td>71</td>
<td>395.1</td>
<td>6.7</td>
</tr>
<tr>
<td>O'Connor et al., 2011 [10]</td>
<td>49</td>
<td>2.7</td>
<td>179</td>
<td>52.8</td>
<td>185</td>
<td>3.6</td>
</tr>
<tr>
<td>Stief et al., 2010 [9]</td>
<td>49</td>
<td>3.2</td>
<td>207.7</td>
<td>25</td>
<td>193.1</td>
<td>6.8</td>
</tr>
<tr>
<td>Stief et al., 2009 [8]</td>
<td>49</td>
<td>3.2</td>
<td>207.7</td>
<td>25</td>
<td>193.1</td>
<td>6.8</td>
</tr>
<tr>
<td>Simon et al., 2007 [7]</td>
<td>280</td>
<td>3</td>
<td>258</td>
<td>174</td>
<td>141</td>
<td>3.4</td>
</tr>
<tr>
<td>Mantuano et al., 2007 [6]</td>
<td>21</td>
<td>2.6</td>
<td>201</td>
<td>189.4</td>
<td>173.6</td>
<td>4.2</td>
</tr>
<tr>
<td>Vincenzi et al., 2007 [5]</td>
<td>126</td>
<td>2.6</td>
<td>206</td>
<td>27</td>
<td>188</td>
<td>3</td>
</tr>
<tr>
<td>Nyc et al., 2006 [4]</td>
<td>60</td>
<td>2.4</td>
<td>174</td>
<td>20.4</td>
<td>22.7</td>
<td>3.7</td>
</tr>
<tr>
<td>Beaghley et al., 2005 [3]</td>
<td>67</td>
<td>2.3</td>
<td>203</td>
<td>189</td>
<td>188</td>
<td>2.4</td>
</tr>
<tr>
<td>Sleb et al., 2005 [2]</td>
<td>227</td>
<td>2.6</td>
<td>186</td>
<td>274</td>
<td>193</td>
<td>3.1</td>
</tr>
<tr>
<td>Mantuano et al., 2004 [1]</td>
<td>100</td>
<td>2.5</td>
<td>195</td>
<td>258</td>
<td>158</td>
<td>2.8</td>
</tr>
<tr>
<td>Orozco et al., 2003 [4]</td>
<td>41</td>
<td>2.2</td>
<td>225.5</td>
<td>267</td>
<td>190</td>
<td>2</td>
</tr>
<tr>
<td>Bokov et al., 2004 [5]</td>
<td>27</td>
<td>2.4</td>
<td>233</td>
<td>46</td>
<td>258</td>
<td>2.9</td>
</tr>
<tr>
<td>Cepel et al., 2007 [6]</td>
<td>77</td>
<td>2.7</td>
<td>212</td>
<td>307.2</td>
<td>308</td>
<td>3.1</td>
</tr>
<tr>
<td>Remenar et al., 2006 [7]</td>
<td>87</td>
<td>2.4</td>
<td>225</td>
<td>292</td>
<td>263.3</td>
<td>3.3</td>
</tr>
</tbody>
</table>

Kunkle et al. J Urol 2008
Crepel et al; Prog Urol 2007

Results of NSS in VHL associated RCC

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of patients</th>
<th>Tumour size, cm</th>
<th>Mean, min</th>
<th>RRL, ml</th>
<th>LOS, days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jilg et al., Fam Cancer, 2012</td>
<td>97 kidney treatments in 54 patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Series of RPN (sporadic RCCs)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Number of patients</th>
<th>Tumour size, cm</th>
<th>OPN, min</th>
<th>WLE, min</th>
<th>RRL, ml</th>
<th>LOS, days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Froghi et al., 2013</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Froghi et al., 2013

Jilg et al., Fam Cancer, 2012
Outcome following repeat PN

| Reference | Technique | Patients | No. of Tumors | No. of Clamps | No. of Renal Units | Mean Reduction in GFR (%)
|-----------|-----------|----------|---------------|----------------|-------------------|----------------
| Autorino et al., BJU2013 | | | | | | |

Results of NSS in very multiple tumors (> 20)

- 34 partial nephrectomies in 30 patients
- Removal of at least 20 tumors at NIH from 1993 to 2008.
- No deaths and only 1 renal unit was lost.
- Significant decrease in the estimated GFR at 3 months (67 vs 59 ml/min, p < 0.001).

Summary of the NIH experience

- 108 patients
- Percentage of patients requiring permanent Hemodialysis: 5%
- In patients who had undergone a median of 3 operations and all had bilateral renal surgery with a minimum FU of 10 years.
  - Nearly, 70% needed repeat renal surgery at a median of 6.2 years.
  - The median-estimated GFR for the entire group was 57 ml/min/1.73m²

Robotic PN in multiple tumors

- 19 tumours removed from 8 patients in 9 procedures.
- Median operative time: 200 min (150–300).
- Median tumour size: 1.9cm (0.4–4.8).
- Mean number of tumours removed per patient: 2.4
- Six off-clamp (31.5%) resected tumours
- Median warm ischaemia time: 21 min (10–35).
- Median estimated blood loss: 200 (100–500)
- No transfusion, no intraoperative complications or conversion to open surgery.
- Mean length of stay: 4.2 ± 0.97 days.
- Mean decrease in GFR: 4%
### Robotic PN in complex tumors

Borghesi et al., WJU 2013

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumors (n)</td>
<td>14</td>
<td>19</td>
<td>19</td>
<td>41</td>
</tr>
<tr>
<td>Median WIT (min) (IQR)</td>
<td>33 (28, 36)</td>
<td>50 (42-58)</td>
<td>52 (48-78)</td>
<td>24 (19-40)</td>
</tr>
<tr>
<td>PCS repair (%)</td>
<td>4 (27 %)</td>
<td>8 (50 %)</td>
<td>28 (57 %)</td>
<td>39 (25.2 %)</td>
</tr>
<tr>
<td>Median console time (min) (IQR)</td>
<td>279 (270-316)</td>
<td>700 (270-755)</td>
<td>115 (113-212)</td>
<td>314 (153-294)</td>
</tr>
<tr>
<td>Median blood loss (ml) (IQR)</td>
<td>164 (78-300)</td>
<td>260 (200-400)</td>
<td>130 (108-168)</td>
<td>130 (108-168)</td>
</tr>
<tr>
<td>Postoperative complication rate (%)</td>
<td>4 (28.6 %)</td>
<td>6 (31.6 %)</td>
<td>13 (26.3 %)</td>
<td>5 (12.2 %)</td>
</tr>
<tr>
<td>Grade Clavien ≥ 3 post complications (%)</td>
<td>3 (21.4 %)</td>
<td>1 (5.3 %)</td>
<td>1 (4.5 %)</td>
<td>5 (12.2 %)</td>
</tr>
</tbody>
</table>

### Off-clamp Robot-assisted Partial Nephrectomy

Off-clamp Robotic PN in complex tumors

Desai et al., Eur Urol 2014

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Superselective Clamping (n=36)</th>
<th>Main artery Clamping (n=18)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ischemia time, min, median (range)</td>
<td>11 (6-24)</td>
<td>11 (6-24)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Estimated blood loss, ml, median (range)</td>
<td>80 (25-1000)</td>
<td>350 (10-800)</td>
<td>0.25</td>
</tr>
<tr>
<td>Retransplantation, Inc. (%)</td>
<td>1 (2.7 %)</td>
<td>4 (22.2 %)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Hospital stay, d, median (range)</td>
<td>4 (3-10)</td>
<td>5 (3-10)</td>
<td>1.0</td>
</tr>
<tr>
<td>Postoperative complications, Inc. (%)</td>
<td>0 (0 %)</td>
<td>0 (0 %)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

### Lap/Rob NSS (± Cryo) in multiple tumors

Steinberg et al., 2004

27 renal tumors in 13 patients.
- Mean overall operative time = 4.3 hours
- Mean blood loss = 169 mL
- No intraoperative complications.
- 3 patients had postoperative complications, none requiring re-exploration.

<table>
<thead>
<tr>
<th>Group</th>
<th>Details</th>
<th>Mean OR Time (min)</th>
<th>Mean Blood Loss (ml)</th>
<th>Mean Ischemia/Cryosolation Time (min)</th>
<th>Complications (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Single LN encomposing both masses (n = 5)</td>
<td>230</td>
<td>117</td>
<td>40 (warm)</td>
<td>1 (postoperative pneumothorax)</td>
</tr>
<tr>
<td>2</td>
<td>Two separate LNs (n = 2)</td>
<td>305</td>
<td>325</td>
<td>40 (cold)</td>
<td>1 (DVVPE and postoperative bleeding)</td>
</tr>
<tr>
<td>3</td>
<td>LN plus cryotherapy (n = 2)</td>
<td>363</td>
<td>173</td>
<td>56 (warm) 16 (cryo)</td>
<td>1 (sepsis on day 15)</td>
</tr>
<tr>
<td>4</td>
<td>Two separate cryotherapy (n = 1)</td>
<td>250</td>
<td>141</td>
<td>15 (cryo)**</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>250</td>
<td>160</td>
<td></td>
<td>5/95 (23%)</td>
</tr>
</tbody>
</table>

*Note: DVT/PE = deep vein thrombosis and pulmonary embolism, DVVPE = deep vein and pulmonary embolism*
Surgery in VHL associated RCCs: changes in treatment paradigm

- 3 periods
  - 1988 to 1994—learning phase of nephron sparing surgery
  - 1995 to 2003—routine nephron sparing surgery
  - 2004 to 2009—the emergence of radio frequency ablation
- Mean tt age: 38 yrs
- 113p; 251 therapeutic procedures in 176 kidneys

Joly et al., J Urol 2011

Surgical Challenge in VHL/RCC

Conclusions

- NSS remains the standard of care for 1rst line treatment with excellent cancer control and long term renal preservation
  - Mini invasive approaches (robot) seem promising:
    - off clamp technique,
    - hybrid approaches (L/RPN+ ablation)
  - RFA or Cryo are emergent alternative 1rst line approaches
- Ablative techniques (RFA, CryoA) are becoming new standards in 2d et 3d line treatments