Surgical Management of VHL-related Renal Cancers

Presentation to the VHL Family Alliance Annual Meeting, Bethesda, MD

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October 18, 2014
Overview

• Background on VHL hereditary Renal Cancer Surgery
  – Define terms
  – Describe early history
  – Describe surgical principles for VHL renal surgery
• Technical Aspects of Partial Nephrectomy
  – Describe partial nephrectomy
  – Margins
  – Technical approaches
  – Renal functional outcomes
    • Impact of prolonged surgery on renal function
  – Rationale for Aggressive Renal Surgery
Glossary

- **VHL** - Von Hippel Lindau
- **ccRCC** – clear cell renal cell carcinoma
- **NSS** - nephron sparing surgery
- **PNx** – partial nephrectomy
- **RNx** – radical nephrectomy
- **BMF** – bilateral multifocal
- **SRM** – Small Renal mass
Definitions

• Vast majority of RCC patients are unilateral, unifocal
  – 4-25% who initially present unifocal, unilateral go onto develop multiple renal masses

• Multifocal = >1 tumor in a single kidney
  – 90% of multifocal are also bilateral
  – 3-11% clinically detected; up to 25% on path*8,11-15
  – Papillary RCC seems to have highest incidence6;7;16;17

• Bilateral = at least 1 tumor in both kidneys
  – >50% with bilateral tumors also multifocal2-4

Definitions

Enucleation of the tumor:
Cut out tumor leaving unaffected kidney tissue in place

Wide Margin of Resection of the tumor:
Remove a rim of unaffected kidney tissue surrounding the tumor
VHL Renal Surgical History

• Early papers report risk of ccRCC in VHL of >70%
• Onset of renal tumors occurs earlier than non-hereditary RCC (40 vs 64)
• Original treatment paradigm for bilateral renal tumors $\rightarrow$ bilateral RNx and transplant
• NSS surgery was pioneered as a reaction to this original treatment strategy
  – Began in late 1980s early 1990s
Hereditary Renal Cancer

• Despite controversy around partial nephrectomy, absolute indications exist
  – Hereditary renal cancer
  – Solitary kidney
  – Bilateral tumors

• Long-term studies show similar oncologic outcomes regardless of radical vs partial nephrectomy for small renal masses

• Hereditary renal cancers present unique challenges
Hereditary Renal Cancer Phenotypes

- **VHL** – mutation of VHL tumor suppressor gene on Chromosome 3, locus 3p25.1
  - Clear cell RCC (25-60% of affected patients)
  - Pheochromocytoma
  - Pancreatic cysts and neuroendocrine tumors
  - CNS hemangioblastomas
  - Cystadenomas (epididymis, mesosalpinx)
  - Autosomal dominant
VHL Surgical Principles

- Active surveillance
- 3cm rule
- enucleation
- “Reset the clock”
Surgical Considerations
VHL Preop
Not enough kidney left to function and avoid dialysis
Surgical Margins in PNx

• **DOGMA:** 2cm margin $\rightarrow$ 1cm margin $\rightarrow$

• **Novick et al** *(Urology 2002, 60:993-997)*

• Conclusion: width of resection margin after NSS does not correlate with long term disease progression.

• Fuhrman grade and TNM stage more important

• “a millimeter is a mile…”
Surgical Margins: do they matter?

- Literature review using nephron-sparing, partial nephrectomy, margin
- PSM = 0-7% in OPNx
- PSM = 0.7-4% in LPNx
- PSM = 3.9-5.7% in RPNx
- Complete tumor removal is the only factor
- PSM and high grade tumors increase risk of local recurrence
- Vast majority of patients will not recur despite PSM
- Frozen section offers little benefit over surgeons macroscopic assessment

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Marszalek, M et al  Eur Urol 2012 p757-763
Published Data

Feasibility and Outcomes of Repeat Partial Nephrectomy

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- Repeat PNx—N=51,
- 19.6% major complication or reoperation
- mean Cr increased 1.16 to 1.35,
- eGFR dropped from 95 to 85,
- 4% long term HD,
- median time to next surgery = 50mos,
  f/u=56mos
Salvage Partial Nephrectomy for
Hereditary Renal Cancer: Feasibility and Outcomes

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- Salvage PNx—N=13,
- 46% major complications,
- 23% loss of kidney,
- no HD in those whose kidneys were preserved
- Creatinine: 1.2 → 1.4
- eGFR: 95 → 79
Repeat Partial Nephrectomy on the Solitary Kidney: Surgical, Functional and Oncological Outcomes

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- Repeat PNx solitary—N-25
- # tumors =4 median
- EBL=2400,
- OR time =8.5hrs
- 52% complications
- no significant difference in eGFR at 1yr f/u
- 8 required repeat surgery median 36mos
- 95% metastasis free at 57mos
Post-RFA PNx—N=13
median time from RFA to surgery was 2.75 yrs,
#tumors=7 median
EBL=1500
OR time 7.8hrs
75% op notes reported “severe fibrosis,”
higher reoperation rate compared to repeat PNx series
Cr=1→1.1; eGFR= 91→81
low rate of visceral injury but 31% rate of pleural entry
Feasibility and Outcomes of Partial Nephrectomy for Resection of at Least 20 Tumors in a Single Renal Unit

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- N=30pts & 34 operations
- 1 lost kidney
- median 26.5 tumors removed
- eBL=3500mL
- OR time =9hrs
- >50% complication rate,
- eGFR=67→57
- subsequent intervention at median of 52 months
**Figure 4.** Representative MRI images pre and postoperatively.  

**A.** T1 weighted gadolinium-enhanced coronal MRI abdomen of right kidney pre-operatively on showing numerous multifocal renal tumors throughout the kidney.  

**B.** Right kidney post-operatively on T1 weighted gadolinium-enhanced MRI showing no renal tumors and post-operative changes.  

**Note:** RMxPNx performed on 8/22/2014: 31 tumors excised, 2500cc EBL, 0min ischemia
Rationale for Pushing the Envelope

Economic Burden of Repeat Renal Surgery on Solitary Kidney—Do the Ends Justify the Means? A Cost Analysis

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• Between 1989-2010
• Repeat renal surgery patients at NCI evaluated
• Costs calculated for RRS
• 33 patients underwent RRS on solitary kidney
• Hypothetical cohort of uncomplicated nephrectomy, fistula placement, dialysis
• Medicare reimbursement
Rationale for Pushing the Envelope

- 45% complication rate
- 87% maintained adequate renal function
- 96% metastasis-free
- Cost benefit realized at 0.68 years after surgery
- Benefit persists even calculating 50% underestimation of surgical costs
- HD cost estimated at $35,000/year (£18421/year)
Review

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Acknowledgements

• Dr. W. Marston Linehan
• Dr. Peter A. Pinto
• Dr. Piyush K. Agarwal
• Dr. Ram Srinivasan
• The UOB fellows
• The Georgetown residents
• The Walter Reed residents
• UOB staff
The End

Questions?